Glaucoma

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KEYWORDS

• Glaucoma • Open-angle glaucoma • Angle-closure glaucoma
• Secondary glaucoma • Glaucoma treatment

KEY POINTS

- The term glaucoma refers to a group of conditions that have in common a progressive optic neuropathy characterized by optic disc excavation (cupping).
- Glaucoma is the leading cause of irreversible blindness worldwide.
- The most common type of glaucoma is primary open-angle glaucoma, a disease with a complex, multifactorial etiologic basis.
- Glaucoma is usually asymptomatic early in the disease.
- Intraocular pressure reduction is the only proven means of halting or slowing the progression of glaucoma. This pressure reduction can be accomplished with medical, laser, or surgical therapies.

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide.[1,2] The global prevalence of glaucoma in people aged 40 to 80 years is estimated to be 3.5%. With the growing number and proportion of older persons in the population, it is projected that 111.8 million people will have glaucoma in 2040.[3] Currently available treatments cannot reverse glaucomatous damage to the visual system; however, early diagnosis and treatment can prevent progression of the disease. In most cases, glaucoma is a chronic condition that requires lifelong management.

PATHOPHYSIOLOGY

Glaucoma is a term that refers to a group of progressive optic neuropathies characterized by excavation or cupping of the optic disc, apoptotic degeneration of retinal

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ganglion cells, and corresponding vision loss. Retinal ganglion cells transmit visual information to the brain through axons, which comprise the optic nerve. The optic disc is the site where retinal ganglion cell axons coalesce, make a 90° turn, and pass through the sclera and lamina cribrosa (a highly organized, multilayered, fenestrated connective tissue populated with astrocytes) to exit the globe as the optic nerve (**Fig. 1**). The cup is the depression in the center of the optic disc. In glaucoma, progressive enlargement of the cup occurs because of damage to the lamina cribrosa and loss of retinal ganglion cell axons (**Fig. 2**).

Glaucoma is a multifactorial disease process, and its pathogenesis is incompletely understood. Although much attention is focused on the role of intraocular pressure (IOP), other factors such as abnormal ocular blood flow, abnormal structural susceptibility of the lamina cribrosa, low intracranial pressure, autoimmunity, and mitochondrial dysfunction may also be involved.[4]

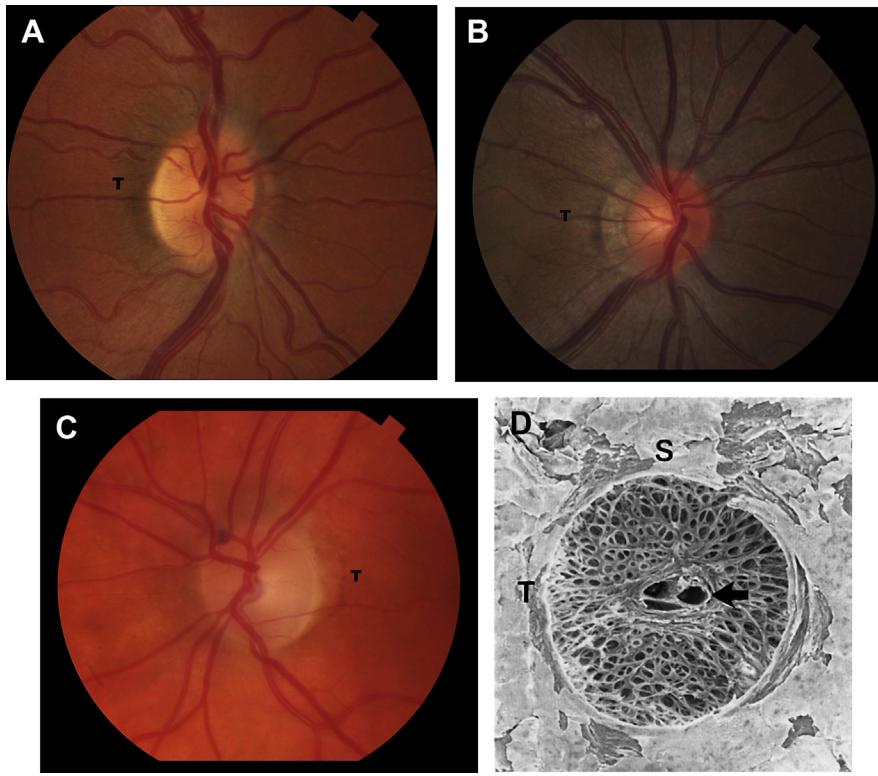

Fig. 1. (*A–C*) Healthy optic discs. (*A*) The central, yellow region is the cup and the surrounding pink tissue is the neural rim. The optic nerve is composed of the axons of retinal ganglion cells, most of which transmit visual information to the lateral geniculate nucleus. The striations visible in the retina are bundles of retinal ganglion cell axons in the retinal nerve fiber layer. The central retinal artery and vein enter the eye through the optic disc. (*B*) This normal optic disc has almost no discernible cup. (*C*) A normal left optic disc. (*D*) Scanning electron micrograph of the lamina cribrosa of the optic disc after trypsin digestion discloses a highly organized fenestrated network of connective tissue. The retinal ganglion cell axons traverse the lamina cribrosa where glial cells and capillaries support the neural tissue. The arrow marks the location of the central retina artery and vein. S, superior; T, temporal (lateral). ([*D*] *Courtesy of* Harry A. Quigley, M.D. Used with permission.)

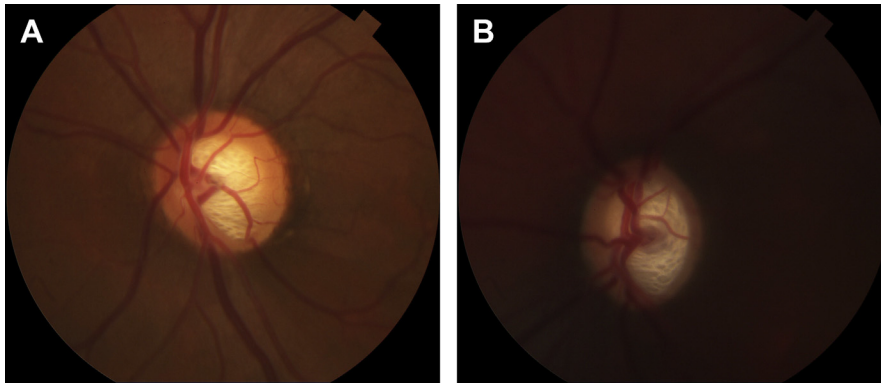

Fig. 2. (*A,B*) Examples of glaucomatous optic disc cupping. The optic disc cups are enlarged as a result of loss of neural rim tissue and lamina cribrosa damage. The pores of the lamina cribrosa are visible at the base of the cups.

Increased IOP is thought to damage the lamina cribrosa, resulting in loss of the normal structural and metabolic support of the retinal ganglion cell axons and impaired axoplasmic transport.[5,6] Decreased neurotrophic signaling to the retinal ganglion cells likely results in the initiation of apoptosis. IOP reduction is the only proven means to halt or slow the progression of glaucoma.

IOP is determined by the balance of aqueous humor production, aqueous humor outflow, and episcleral venous pressure. Aqueous humor is produced by the ciliary body and supports the metabolic processes of the avascular tissues in the anterior segment of the eye. Aqueous humor outflow takes place through 2 pathways originating in the anterior chamber angle: through the trabecular meshwork and Schlemm canal (conventional outflow), and through uveal tissues (unconventional outflow) (**Fig. 3**).

Tonometers used in clinical practice provide an estimate of IOP. Depending on the instrument used, IOP is determined by measuring the force required to flatten an area of the cornea, the amount of indentation of the cornea, or the deceleration of a probe rapidly projected onto the cornea. Many tonometers are available, including the Goldmann applanation tonometer, noncontact tonometers that use a column of air to flatten the cornea, rebound tonometers (ICare), and hand-held tonometers (TonoPen). Goldmann applanation tonometry is commonly used in clinical practice and in clinical trials (**Fig. 4**).

Although higher IOP plays a major role in glaucoma, it is not a defining criterion. Although the upper limit of normal IOP is often defined as 21 mm Hg, a large proportion of patients with glaucoma have an IOP lower than this, and not all patients with higher IOP (known as ocular hypertension) develop glaucoma.[7,8] As such, it is important to consider IOP as a continuous risk factor across the entire physiologic range.

Poor perfusion of the optic nerve may also contribute to disease development and progression.[9] Ocular perfusion pressure (OPP) is estimated in various ways. In general terms, it is the difference between systemic blood pressure and IOP. In population-based surveys, lower OPP has been identified as a risk factor for glaucoma and for the incident development of glaucoma.[10] Other studies have shown that lower OPP is an independent risk factor for worsening of the disease. Accordingly, for patients with severe glaucoma, overly aggressive treatment of systemic hypertension should be avoided.

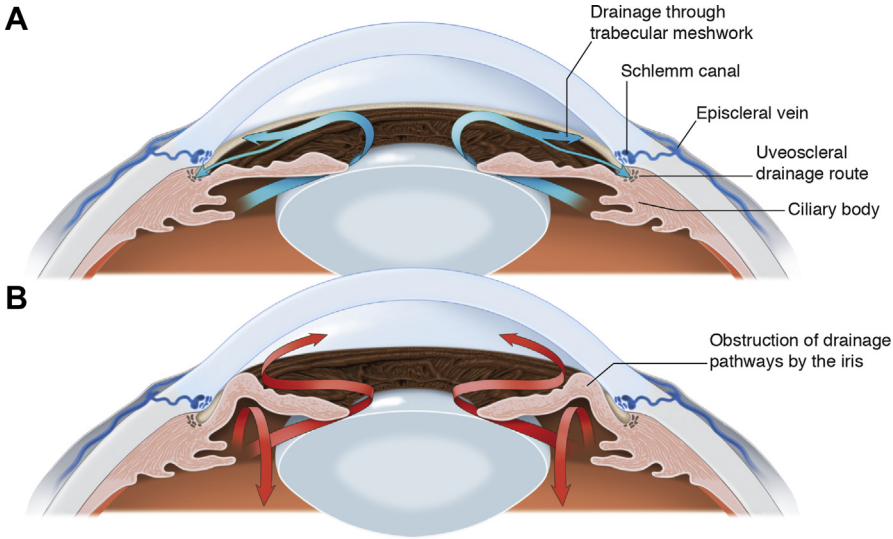

Fig. 3. Aqueous humor is produced by the ciliary body in the posterior chamber. This fluid then flows through the pupil into the anterior chamber. (*A*) Fluid can only exit the eye through structures in the anterior chamber (iridocorneal) angle. These structures are the trabecular meshwork (conventional outflow) and the ciliary body face (unconventional outflow). In most cases of open-angle glaucoma, increased resistance through the trabecular meshwork causes increase in IOP; however, no obstruction is clinically visible. (*B*) In primary angle closure, anatomic crowding of the iris and natural crystalline lens causes abnormal resistance of aqueous humor flow through the pupil. This pupillary block impairs the flow of aqueous humor through the pupil. Higher pressure posterior to the iris causes it to bow anteriorly into the iridocorneal angle and block the trabecular meshwork. (© 2021 American Academy of Ophthalmology; Used with permission.)

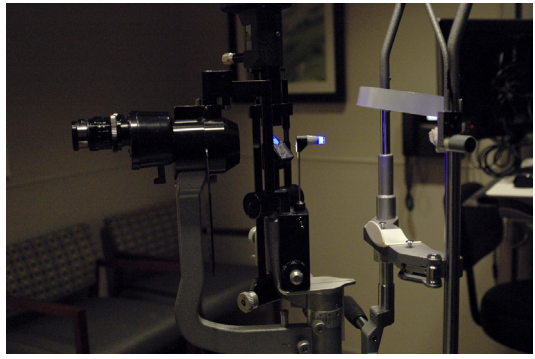

Fig. 4. The Goldmann applanation tonometer is widely regarded as the reference standard for clinical use. It measures the force (dynes) required to flatten a small area of the cornea, which is approximately equal to IOP/10 mm Hg. A topical anesthetic and fluorescent dye are required. While viewing the fluorescein-containing corneal tear film with the slit lamp microscope through a split-image prism, the examiner detects a visible end point that signifies corneal flattening.

CLASSIFICATION

The glaucomas can be classified into open-angle glaucomas (OAGs) and angle-closure glaucomas (ACGs) to describe the anatomic status of the anterior chamber angle (Table 1). Each of these is further divided into primary or secondary, indicating the absence or presence, respectively, of other clinically identifiable ocular or systemic disorders to account for the glaucoma. The childhood glaucomas, such as primary congenital glaucoma and others associated with disorders of ocular development, are rare and are not discussed here.

The anterior chamber angle, or the iridocorneal angle, is the location of the trabecular meshwork and is a critically important region for aqueous humor outflow (see Fig. 3). The anatomic status of the angle (open or closed) is determined by ophthalmic examination.

Most eyes with glaucoma have increased resistance of outflow through the trabecular meshwork, which is usually associated with increased IOP. In eyes with open-angle glaucoma, this increase in resistance occurs in the absence of a clinically visible obstruction in the angle (see Fig. 3A). In contrast, angle closure refers to the anatomic configuration in which the peripheral iris is in contact with the trabecular meshwork, thereby obstructing outflow of aqueous humor. The most common mechanism by which angle closure occurs is pupillary block, a condition in which abnormally tight contact between the iris and lens can cause increased resistance of aqueous flow through the pupil. This condition results in a pressure gradient that causes the iris to bow forward and obstruct the trabecular meshwork (see Fig. 3B). Pupillary block is most common in hyperopic (far-sighted) eyes that have more crowded anterior segments.

Table 1
Glaucoma classification and selected examples

Open-Angle Glaucoma	Angle-Closure Glaucomas	Childhood Glaucomas
Primary open-angle glaucoma	Primary angle-closure glaucoma	Primary congenital glaucoma
Secondary OAGs	• Pupillary block	Juvenile open-angle glaucoma
• Pigmentary glaucoma	• Plateau iris	Glaucoma following (congenital) cataract surgery
• Pseudoexfoliation glaucoma	Secondary angle-closure glaucoma	Glaucoma associated with nonacquired systemic anomalies
• Uveitic glaucoma (can also have a combined, angle-closure mechanism)	• Medication induced	• Axenfeld-Rieger syndrome
• Steroid-induced glaucoma	• Lens induced	• Peters anomaly
• Traumatic glaucoma	• Neovascular	• Aniridia
• Glaucoma associated with increased episcleral venous pressure (eg, carotid-cavernous fistula, cavernous sinus thrombosis, thyroid eye disease)	• Iridocorneal endothelial syndrome	Glaucoma associated with nonacquired systemic disease
	• Ciliary body or iris cyst or tumor	• Chromosomal disorders
		• Connective tissue disorders
		• Metabolic disorders
		• Neurofibromatosis
		• Sturge-Weber syndrome
		• Congenital rubella

Primary OAG (POAG) and primary ACG (PACG) are the two most common forms of glaucoma. It is estimated that the number of people blind from glaucoma in 2020 globally is 11.1 million.[11] Disease burdens of POAG and PACG differ based on geographic regions and ethnic groups. POAG prevalence is highest among blacks and Hispanic people, and PACG is most prevalent among Asian and Inuit people.[3]

Excluding the childhood glaucomas, more than 60 forms of secondary glaucoma have been described. These forms can occur because of numerous underlying mechanisms, including trauma, intraocular bleeding, neoplasia, inflammation, neovascularization retinal ischemia, and exposure to a variety of medications (see **Table 1**).

SYMPTOMS

Glaucoma usually progresses slowly, and thus patients often remain asymptomatic until the disease is severe. Population-based surveys suggest around 50% of people with glaucoma are unaware of their diagnosis, even in developed nations.[12–14] Severe, acute IOP increase usually results in pain and decreased vision. Moderately increased IOP, which is much more common in glaucoma, is usually imperceptible to the patient.

When patients are symptomatic, the description of glaucomatous vision loss as tunnel vision is a commonly held misconception.[15] Except in very advanced disease, areas of glaucomatous visual field loss are commonly described by patients as blurred areas, not absolute scotomas. As the damage becomes severe, patients describe their vision as diffusely foggy or dark. In late stages, glaucoma may progress to total loss of light perception.[16]

DIAGNOSTIC EVALUATION

Because glaucomatous vision loss is irreversible, early diagnosis and treatment is essential to prevent morbidity. Screening and identification of high-risk patients by ophthalmologists allows the early detection of glaucoma. All adults more than the age of 40 years should have examinations to screen for various disease processes, including glaucoma.[17]

Examination

The complete and accurate diagnosis of glaucoma requires a thorough ophthalmic examination. Glaucomatous optic disc damage, excavation or cupping, can be visualized with ophthalmoscopy (see **Fig. 2**).[18,19] Because glaucomatous damage typically occurs in the inferotemporal and superotemporal regions of the optic nerve, a larger vertical compared with horizontal cup-to-disc ratio may be observed, with the cup often extending abnormally close to the inferior or superior border of the optic disc.[20]

Early diagnosis of glaucoma may be challenging because there is wide variation in the appearance of the healthy optic nerve and overlap in the clinical appearance of the optic nerve among some normal eyes and some eyes with glaucoma. Diagnosis often requires longitudinal evaluation and documentation of structural change in the optic nerve of persons suspected of having early glaucoma.

Physicians other than ophthalmologists may be able to detect glaucomatous optic disc damage with direct ophthalmoscopy; however, the view through an undilated pupil is often poor and the absence of a stereoscopic view severely limits the clinician's ability to accurately detect optic disc excavation.

Imaging

Photographs can be useful for monitoring the appearance of the optic disc and detecting pathologic change over time. The advent of optical coherence tomography (OCT)

has revolutionized the ability to monitor the anatomic structures affected by glaucoma. OCT is a noninvasive imaging technique that relies on the use of Michelson interferometry to decode the interference patterns of light reflected from intraocular tissues. It allows quantitative measurement of the optic nerve, the retinal ganglion cell axon layer (known as the retinal nerve fiber layer), and the layer of the retinal ganglion cell bodies (**Fig. 5**). Structural changes such as retinal nerve fiber layer thinning typically occur before the development of functional losses detectable by conventional visual field testing.[21]

Perimetry

Formal testing to evaluate the central and midperipheral portions of the visual field is important for the diagnosis and management of glaucoma. The goal of testing is to determine the minimum intensity of light stimuli detectable at locations in the central 30° of the visual field at 6° intervals.

Characteristic patterns of glaucomatous visual field damage correspond with the location of injury to retinal ganglion cell axon bundles at the level of the lamina cribrosa. The location of injury coupled with the anatomic organization of the axon bundles results in visual field defects that typically respect the horizontal midline early in the disease (**Fig. 6**). In contrast, defects respecting the vertical midline indicate central neurologic lesions.[22]

GENETICS

Although certain types of developmental glaucomas are mendelian disorders, most cases of POAG and PACG result from a complex interaction of genetic and

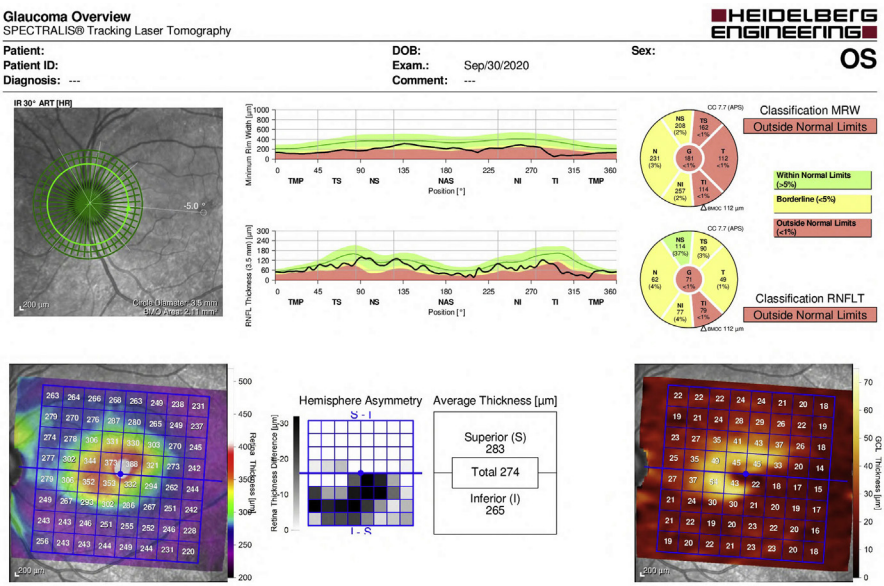

Fig. 5. OCT analysis of the posterior segment of an eye with glaucoma. The neural rim thickness, retinal nerve fiber layer thickness, and macular thickness are all decreased because of glaucoma damage. Serial testing can be performed to monitor neural tissue thickness for change over time.

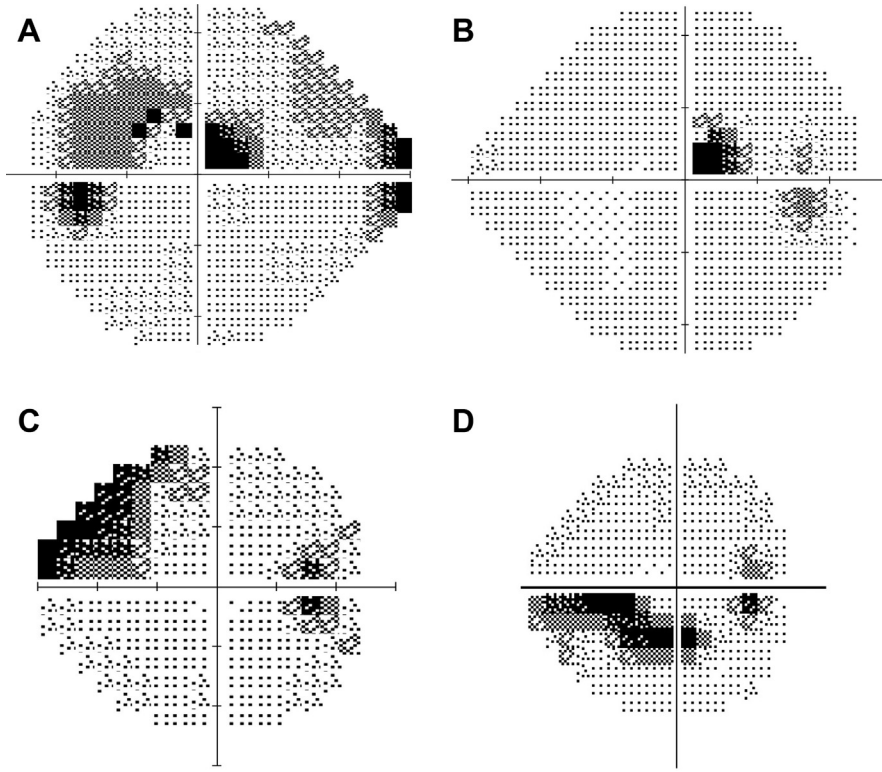

Fig. 6. (*A,B,C, D*) Four examples of typical glaucomatous visual field defects. Note that the defects generally respect the horizontal meridian. During testing, patients press a button to indicate a stimulus has been observed. Darker areas in these gray-scale maps of the central 30° of the visual field represent locations in which brighter-intensity stimuli are required for the patient to detect the stimulus.

environmental factors.[23–25] More than 100 genetic susceptibility loci associated with POAG have been identified, allowing the development of a polygenic risk score that has been shown to predict an increased risk for advanced disease and earlier disease onset.[26] Further research is needed to refine genetic screening and identify novel pathways for therapeutic intervention.[23,27] Family members of patients with glaucoma should be advised to undergo screening.

PRIMARY OPEN-ANGLE GLAUCOMA

Clinical Diagnosis

POAG, the most common form of glaucoma, is typically bilateral but often asymmetric in severity.[3] Because patients are usually asymptomatic early in the disease, early detection requires screening and monitoring of certain high-risk patients (**Table 2**). High-risk patients classified as glaucoma suspects are in 2 major categories: those with ocular hypertension (IOP>21 mm Hg in absence of evidence of optic disc or visual field damage) and those with an optic nerve appearance suspicious for glaucomatous damage.[30] Such patients should be examined by an ophthalmologist at least annually to monitor for evidence of conversion to definite POAG from progressive structural (optic disc or retinal nerve fiber layer) or functional (visual field) damage.[30] Some

Table 2
Selected risk factors for glaucoma

Primary Open-Angle Glaucoma[28]	Primary Angle-Closure Glaucoma[29]
• Older age	• Older age
• Increased IOP	• Family history of angle closure
• Family history of glaucoma	• Asian or Inuit descent
• African race or Latino/Hispanic ethnicity	• Hyperopia (far-sightedness)
• Myopia (near-sightedness)	• Female sex

patients with ocular hypertension with high-risk characteristics may be treated with medication or laser to decrease the IOP in order to reduce the risk of the development of POAG.

PRIMARY ANGLE CLOSURE

Clinical Diagnosis

Some patients with narrow anterior chamber angles develop primary angle closure, the term used to describe the presence of adhesions of the iris to the trabecular meshwork and/or ocular hypertension without glaucomatous optic nerve damage. Over time, some patients with primary angle closure go on to develop primary angle-closure glaucoma, the distinguishing characteristic being the presence of optic nerve damage.

Usually, primary angle closure is a chronic, asymptomatic process. Uncommonly, patients with narrow angles can present with acute primary angle-closure crisis. In this condition, deep eye pain, headache, blurred vision, halos or rainbows around lights, eye redness, and nausea occur as a result of sudden and severe IOP increase triggered by pupillary block.

Risk factors for primary angle closure include ocular features that are associated with crowding of the anterior segment, such as hyperopia (far-sightedness), as well as older age and a family history of the disease.[31] The condition is more prevalent in women and patients of Asian or Inuit descent.[32] Laser iridotomy may be performed prophylactically in some patients with narrow angles in the absence of other disease-associated features.

SECONDARY GLAUCOMAS

Secondary glaucomas encompass a broad spectrum of diseases. By definition, they have a clinically identifiable cause for IOP increase. Some examples of secondary glaucomas are discussed here.

Pseudoexfoliation Glaucoma

Pseudoexfoliation glaucoma is the most common secondary glaucoma.[33] Abnormal extracellular matrix material in the outflow pathway leads to IOP increase.[34] Pseudoexfoliation syndrome is a systemic disorder of the extracellular matrix that has several ocular consequences and has also been shown to be associated with an increased risk of pelvic organ prolapse and inguinal hernia. It is clinically characterized by the presence of abnormal fibrillar deposits on the surface of the lens and iris that can be detected by examination with slit lamp biomicroscopy (**Fig. 7**). The condition is rare in patients less than 65 years of age. The prevalence is 5% among persons 75 to 85 years of age in the United States and as high as 25% in Scandinavia. A genome-wide association study led to the discovery of a strong association with

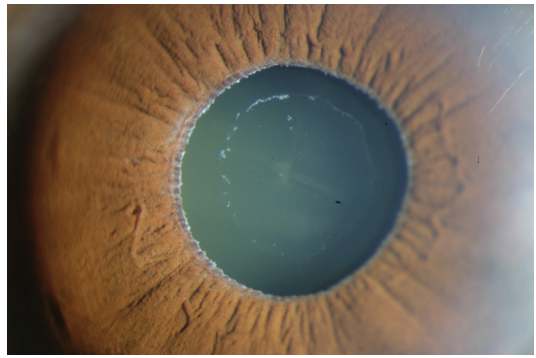

Fig. 7. Pseudoexfoliation syndrome. Abnormal fibrillar deposits of elastin and collagen on the surface of the lens and pupil border. The condition is commonly associated with the development of increased IOP and secondary open-angle glaucoma.

variants of *LOXL1* (lysyl oxidase–1); these were present in greater than 99% of affected individuals and ~80% of controls.[35] The abnormal fibrillar material is thought to arise as a result of abnormal maintenance of elastin and collagen. Other genetic and environmental factors, such as ocular ultraviolet light exposure, likely play a strong role in the development of this disorder.[36,37]

Neovascular Glaucoma

Conditions such as diabetic retinopathy, retinal vascular occlusions, and carotid artery obstructive disease can lead to retinal ischemia with a resultant release of proangiogenic factors such as vascular endothelial growth factor (VEGF). Neovascularization can then develop in the anterior segment of the eye and over the iridocorneal angle, obstructing aqueous humor outflow.

Patients usually present with symptomatic, acute IOP increase. A 2-pronged treatment strategy is used. Retinal laser photocoagulation and intraocular injections of anti-VEGF agents are used to induce regression of the neovascular tissue, and medical and surgical therapy are used to decrease the IOP. Although many patients do well with modern therapy, some patients experience severe vision loss, often because of the underlying cause for the retinal ischemia. Patients with neovascular glaucoma require optimization of their underlying vasculopathic risk factors to mitigate the risk of additional vascular events.

Steroid-Responsive Ocular Hypertension

Chronic corticosteroid therapy may, in some individuals, result in increased resistance to outflow through the trabecular meshwork and thereby cause IOP increase. Although this is most common with ophthalmic or oral steroid therapy, it can occur with steroid administration through any route (eg, nasal, inhaled, dermatologic, and intra-articular).[38] IOP can increase after 2 weeks of treatment and is typically reversible after cessation of steroid exposure.[39]

Medication-Induced Angle Closure

Medications may induce unilateral or bilateral acute angle closure by 2 different mechanisms (**Table 3**).[41] The first, pupillary block, is most likely to occur when the pupil is in a mid-dilated state. In susceptible patients with narrow angles, agents that can cause subtle pupil dilatation, such as adrenergic agonists and anticholinergic drugs, may trigger an acute angle-closure crisis. The second is an idiosyncratic reaction in which

Table 3
Medications that may cause acute angle closure

Drug Class	Drug
Adrenergic drugs	Phenylephrine (ophthalmic) Naphazoline (intranasal) Salbutamol (inhaled)
Anticholinergic drugs	Atropine (ophthalmic) Oxybutynin Scopolamine Botulinum toxin (intramuscular)
Antidepressant drugs	Venlafaxine Escitalopram Bupropion
Sulfonamide drugs	Topiramate Acetazolamide[a] Methazolamide[a]

[a] Carbonic anhydrase inhibitors such as acetazolamide and methazolamide are still indicated for use as IOP-lowering agents and angle closure caused by exposure to these medications is rare.[40]

sulfonamide agents, most commonly topiramate and carbonic anhydrase inhibitors, cause edema of the ciliary body leading to forward displacement of the lens and iris and bilateral angle closure. Rapid identification and removal of the offending agent, medical therapy to decrease the IOP, and systemic corticosteroids can help decrease the risk of vision loss.

TREATMENT

IOP reduction is the only proven means of halting or slowing the progression of glaucoma.[8,28,42–44] Even patients with POAG in whom baseline IOP is less than or equal to 21 mm Hg benefit from treatment to further decrease the IOP.[45] First-line treatment is typically either a topical IOP-lowering medication or laser trabeculoplasty (discussed later).[46]

In primary angle-closure disease, pupillary block must also be addressed. In addition to IOP-lowering medications, iridotomy or lens extraction is required.[47]

Treatment of severe, acute IOP increase of any cause can usually be accomplished with topical and oral medications, sometimes in combination with systemic hyperosmotic agents such as mannitol or glycerin. When the underlying cause is pupillary block, iridotomy or lens extraction should then be performed as soon as possible. Although acute angle-closure crisis is typically unilateral, about half of fellow eyes can develop an acute crisis within 5 years, necessitating prophylactic iridotomy or lens extraction.[29,48] Unlike most cataract surgery, which is performed with the aim of improving vision, the primary goal of lens extraction for angle closure is to open the iridocorneal angle by replacing the large natural lens with a thin artificial lens.

Medical Therapy

Topical glaucoma medications decrease IOP by reducing aqueous humor production or improving outflow (**Table 4**). The most frequently used medication class is the prostaglandin $F_{2\alpha}$ analogues. These agents activate matrix metalloproteases, which degrade collagen in the ciliary body, allowing increased outflow of aqueous humor directly through this tissue (unconventional outflow). Approximately half of patients require 2 or more medications to adequately decrease their IOP.[50]

Table 4
Topical glaucoma medications

Class	Mechanism	Side Effects	Contraindications/ Considerations
Prostaglandin $F_{2\alpha}$ Analogue (teal cap) • Latanoprost • Travoprost • Bimatoprost • Tafluprost	↑ AH outflow	Iris and periocular skin color change (irreversible), eyelash growth, conjunctival hyperemia	Active uveitis
Rho kinase inhibitor (white cap) • Netarsudil	↑ AH outflow ↓ EVP	Conjunctival hyperemia and hemorrhages, pain, blurred vision	—
β-Blocker (yellow cap) • Timolol • Levobunolol • Caretolol • Betaxolol (β_1 selective)	↓ AH production	Bradycardia, bronchospasm, hypotension, reduced exercise tolerance Betaxolol with lower risk of pulmonary side effects	Asthma/COPD, severe CHF, second-degree or third-degree AV block, bradycardia Less effective in those already on high-dose systemic β-blocker
$Alpha_2$ agonist (purple cap) • Brimonidine • Apraclonidine	↓AH production ↑AH outflow	Conjunctivitis, dry mouth, fatigue, systemic hypotension	Infants and children
Carbonic anhydrase inhibitor (orange cap) • Dorzolamide • Brinzolamide	↓AH production	Ocular irritation, allergic dermatitis, metallic taste, corneal edema	Sickle cell disease Caution in patients with sulfa allergy, although may be considered[49]
Cholinergic agonist (green cap) • Pilocarpine	↑AH outflow	Blurred vision, difficulty with night vision, headache, paradoxic angle closure, retinal tear	Ocular inflammation

Abbreviations: AH, aqueous humor; AV, arteriovenous; CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease; EVP, episcleral venous pressure.

Systemic absorption of topically administered ophthalmic medications occurs through the nasolacrimal drainage system. Because of the absence of first-pass hepatic metabolism, serum levels can reach those achieved with oral administration of, for example, timolol. This condition can lead to serious adverse events, particularly associated with the use of topical β-blockers and $alpha_2$-adrenergic agonists. Eyelid closure and nasolacrimal occlusion (application of digital pressure to the region over the nasolacrimal sac) can enhance intraocular penetration of medications and reduce systemic absorption.[51]

Laser Surgery

Laser trabeculoplasty

Laser trabeculoplasty is a procedure in which laser energy is applied to the trabecular meshwork with a resultant reduction in the resistance to aqueous outflow. Although the mechanism is incompletely understood, it likely involves the recruitment of monocytes and replication of pigmented endothelial cells in the trabecular meshwork.[52]

Laser peripheral iridotomy

Laser peripheral iridotomy (LPI) can be performed for angle closure with pupillary block. Laser energy is used to create a small hole in the peripheral iris, allowing aqueous humor to bypass the pupil. After an LPI, many patients have persistently increased IOP and require additional treatment.[53]

Incisional glaucoma surgery

In patients with inadequately controlled IOP despite medical and laser therapy, a variety of incisional surgery approaches may be used. In addition, initial surgical therapy may be considered for patients who present with advanced disease.

Glaucoma surgeries include procedures designed to either reduce resistance to aqueous humor outflow in the conventional pathway or create a new pathway for aqueous humor outflow. The former category is known as minimally invasive glaucoma surgery (MIGS) and typically involves implantation of a microstent allowing bypass of the trabecular meshwork or scaffolding of the Schlemm canal. Alternatively, the trabecular meshwork can be incised or disrupted. These procedures are often performed in conjunction with cataract surgery and usually have a safety profile similar to that of cataract surgery alone.[54] The magnitude of IOP reduction is often modest; therefore, these procedures are typically indicated for patients with mild to moderate glaucoma damage.[55]

Glaucoma tube shunt surgery and trabeculectomy are fistulizing procedures that involve the creation a new outflow track for aqueous humor to the subconjunctival space, and typically result in larger magnitudes of IOP reduction compared with MIGS.

Glaucoma tube shunt surgery involves implanting a tube in the eye that shunts aqueous to a silicone plate located at the equator of the globe, around which aqueous can diffuse into surrounding extraocular tissues (**Fig. 8**). In trabeculectomy surgery, a scleral flap is created, underneath which an ostium into the anterior chamber is created (**Fig. 9**). Aqueous humor flows through the ostium and scleral flap, into the subconjunctival space, forming a bleb, which is an aqueous humor–filled elevation of the conjunctiva under the upper eyelid. Despite the use of local antifibrotic therapy

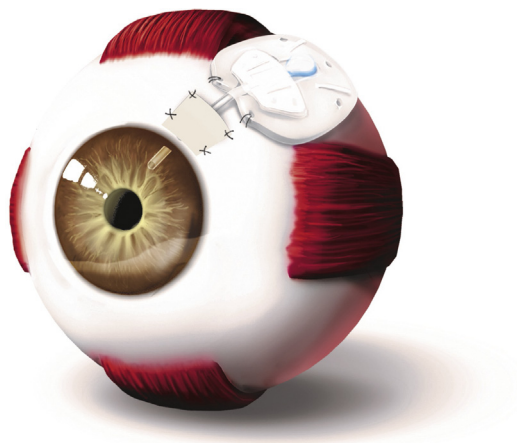

Fig. 8. Glaucoma tube shunt surgery. Drainage devices can be used to provide an alternative path for aqueous outflow and IOP reduction. A tube is inserted into the anterior chamber of the eye and is connected to a plate that is placed underneath the conjunctiva and serves as a spacer around which aqueous humor can diffuse into extraocular tissues. The entire device is made of silicone. (Figure courtesy of the New World Medical. Used with permission.)

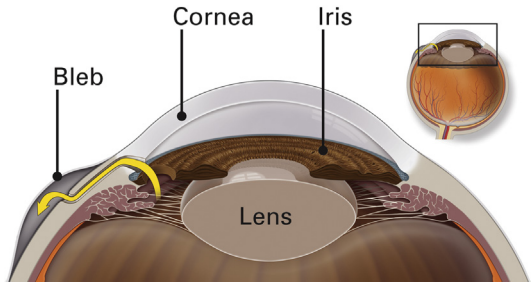

Fig. 9. In trabeculectomy, an ostium into the anterior chamber is fashioned under a scleral flap located under the upper eyelid. This ostium allows aqueous humor to exit the eye in a controlled fashion. Aqueous humor accumulates under the conjunctiva, forming an area of elevation called a bleb. (Courtesy of the American Academy of Ophthalmology. Used with permission.)

at the time of surgery, the formation of subconjunctival fibrotic tissue can result in subsequent failure.

The risk of adverse events associated with these procedures is substantial; therefore, these procedures are typically only performed in patients at high risk of symptomatic progression of their disease. Because a direct pathway between the subconjunctival space and intraocular structures is created, there is an ongoing risk of intraocular infection ranging from 0.5% over 5 years for tube shunt surgery to 1.5% to 2% for trabeculectomy. Symptoms or signs of infection, including redness, photophobia, pain, and vision loss, should be urgently evaluated by an ophthalmologist.[56,57]

DISCUSSION AND SUMMARY

Although irreversible, glaucomatous damage can be halted or slowed with early detection and appropriate treatment. At present, the only proven means of treatment is IOP reduction with medications, laser treatment, and incisional surgery. Physicians can play a significant role in the early detection of glaucoma by identifying risk factors and optic disc cupping on examination, referring appropriate patients for ophthalmic consultation, and by educating patients that glaucoma requires medication adherence and regular follow-up.

CLINICS CARE POINTS

- Glaucoma is the leading cause of irreversible blindness worldwide.[3]
- Because of the slowly progressive nature of the disease process, almost all patients are asymptomatic until late stages of the disease.
- Acute angle-closure crisis, although rare, results in decreased vision, eye and periorbital pain, eye redness, and nausea.[32]
- Risk factors for both POAG and PACG include older age and family history.[28,29] Patients with glaucoma should be reminded to advise family members to be evaluated by an ophthalmologist.

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