Glaucoma is the most commonly acquired optic neuropathy. It represents a public health challenge because it causes an irreversible blindness. Pathogenesis of glaucoma depends on several interacting pathogenetic mechanisms, which include mechanical effects by an increased intraocular pressure, decreased neurotrophine-supply, hypoxia, excitotoxicity, oxidative stress, and the involvement of autoimmune processes. Data from population-based surveys indicate that one in 40 adults, older than 40 years, has glaucoma with loss of visual function, which equates to 60 million people worldwide being affected and 8.4 million being bilaterally blind. Even in developed countries, half of glaucoma cases are undiagnosed. The two most common types of glaucoma—primary open-angle glaucoma and primary angle-closure glaucoma—have different risk factors. Until recently, there were no randomized clinical trials that showed the effectiveness of lowering eye pressures with medications or surgery in patients with glaucoma. However, in 1998 a randomized clinical trial showed the benefit of lowering eye pressure in patients with glaucoma who had eye pressures of 24 mm Hg or less. Because glaucoma is treatable, and because the visual impairment from glaucoma is irreversible, early detection of the disease is critically important.
INTRODUCTION:
Glaucoma is the second leading cause of blindness worldwide.\(^1\,^2\) As per World Health Organization estimates, globally 4.5 million people are blind due to glaucoma\(^1\) (http://www.who.int/blindness/causes/priority/en/index6.html) and by 2020 the number of blinds due to glaucoma will increase to 11.2 million.\(^2\) It was also estimated that Bilateral blindness will be present in 5.9 million people with OAG and 5.3 million people with ACG in 2020\(^2\) i.e., vision less than 20/400 or 3/60 in the better eye.\(^2\) The blindness caused by glaucoma is irreversible. Although several eye conditions are variants of glaucoma, the most common types of glaucoma are primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG). Asia accounts for a disproportionate number of PACG cases, whereas the prevalence of POAG is more evenly distributed throughout the world.\(^2\) Although PACG and POAG are characterized by damage to the optic nerve and visual field loss, they differ in terms of whether the trabecular meshwork is obstructed by the periphery of the iris. This difference affects the medical and surgical management of the two diseases. In PACG the iris obstructs the trabecular meshwork in the angle of the eye, whereas in POAG the trabecular meshwork seems to be open and unobstructed by the iris (figure 1). A procedure known as Gonioscopy is used to differentiate between the two types of glaucoma. Gonioscopy involves examination of the anterior chamber with a lens that enables the observer to visualize the angle between the cornea-sclera and iris. Gonioscopy requires skill and training and is difficult to use in screening situations. The loss of peripheral vision, depth perception, and contrast sensitivity associated with glaucoma can have a major effect on an individual’s life. Injuries caused by car crashes and falls are associated with the types of visual impairments that arise in glaucoma; such injuries can occur even if a person has excellent central acuity.\(^3\),\(^4\)

**Primary open-angle glaucoma**

**Definition and diagnosis**
POAG has an adult onset, is usually bilateral, and has no noticeable symptoms in most patients until the later stages of the disease when patients lose their central vision.\(^5\),\(^6\) In the USA, POAG has an age-adjusted prevalence of 1·55%.\(^7\) Although POAG has conventionally been characterized as a disease of raised eye pressures, it is currently defined as a group of ocular diseases that may cause characteristic, progressive changes in the optic nerve head, visual field loss, or both.\(^5\)

![Figure 1. Glaucomatous eye depicting flow of fluid (source: national eye institute)](image-url)
The characteristic changes in the optic nerve head are increased cupping or excavation, notching, or thinning of the neuroretinal rim, disc hemorrhages, asymmetry of the amount of optic-nerve cupping between the two eyes of the patient, and loss of the retinal nerve fiber layer.\(^5,6\) Eyes with cup-to-disc ratios equal to or greater than 0·55 are at increased risk of developing glaucomatous visual field loss compared with eyes with cup-to-disc ratios of less than 0·55.\(^8\) Disc hemorrhages and notches can be identified easily with careful direct ophthalmoscopy. Thus, a clinician with a direct ophthalmoscope can at least screen for features of a glaucomatous optic nerve, although the sensitivity and specificity of classification based on these assessments are 59% and 73%, respectively.\(^8\) The most common way to measure how well the optic nerve functions is the assessment of the eye’s ability to detect the brightness of small points of light both centrally and peripherally. This type of examination is called visual field testing and can be done with careful manual techniques (static and kinetic) or automatic static threshold techniques.\(^5\) A diagnosis of glaucoma can be made even if neither optic-nerve damage nor visual-field loss is present, because a clinician may infer that optic-nerve damage and visual-field loss will occur because of the level of the eye pressure. Epidemiological studies show that as eye pressure increases, there is a corresponding increase in the risk of glaucomatous optic-nerve damage and visual field loss.\(^3\)

**Screening**

Since the prevalence of POAG in the USA population is reported to be 1·55%, the positive predictive value of an instrument such as the scanning laser polarimeter, which images the nerve fibre layer of the retina, would only be 17·8%, even though the procedure has a sensitivity of 96% and a specificity of 93%.\(^9\) In the Prevent Blindness America Visual Field Screening Study\(^10\) the Henson visual-field analyser had 100% specificity in 82 healthy individuals and 97% sensitivity in 39 patients with moderate-to-severe visual-field loss.\(^10\) In line with these findings, the Glaucoma Advisory Committee of Prevent Blindness America recommends that screening for POAG should include both eye pressure measurements and an approved method to test visual fields. A complete eye examination includes 5 common tests to detect glaucoma: tonometry, ophthalmoscopy, perimetry, gonioscopy, and pachymetry. Ophthalmoscopy (Figure 2)\(^11\) is fundamental to all types of glaucoma. It examines the shape and color of the optic nerve. Normal-tension glaucoma is diagnosed by observing the optic nerve for signs of damage. A nerve that is cupped or is not a healthy pink color is a cause for concern. With a vertical cup-to-disk (C: D) ratio of 0·6 or greater, glaucoma should be suspected. Often, glaucoma affects the eyes asymmetrically; one cup appears larger than the other. Thus >0·2 asymmetry between the C: D ratios of both eyes should also suggest glaucoma.
**Etiology and risk factors**

The debate continues about whether damage to the optic nerve is caused by eye pressures that are too high, decreased blood flow to the optic nerve head, or both factors. Irrespective of what causes the damage, the end result is that ganglion-cell death in glaucoma is by apoptosis (programmed cell death), because of the lack of trophic factors. In addition, autoimmune reactions, increased concentrations of nitric oxide, and raised concentrations of glutamate may contribute to ganglion cell death in POAG.

Demographic risk factors for POAG are African descent and older age (>70 years). In the population-based Baltimore Eye Survey in the USA, African-Americans were four times more likely to have glaucoma than white people. White people and African-Americans aged 70 years or older were 3·5 and 7·4 times more likely to have glaucoma than white people and African-Americans aged 40–50 years, respectively.

In the Baltimore Eye Survey, first-degree relatives of patients with POAG had 2·9 times greater odds of having glaucoma than non-relatives. In a population-based familial aggregation study in Rotterdam, the lifetime risk of glaucoma was 9·2 times higher in siblings and offspring of glaucoma patients than in siblings and offspring of controls. There have been suggestions that diabetes mellitus, systemic hypertension, migraine headaches, and myopia may be risk factors for POAG, but so far, the evidence is inconclusive.

**Genetics**

In 1996 and 1997, the first major gene loci for POAG, GLC1A and GLC1B, were described. The GLC1A gene encodes myocilin, the trabecular meshwork-induced glucocorticoid response protein. GLC1A is located on chromosome 1; the mechanisms by which mutations in this gene cause raised eye pressures and damage to the optic nerve are unknown. The GLC1B gene, located on chromosome 2, is associated with normal-to-moderately raised eye pressures and optic-nerve damage. Several other genes that increase the risk of POAG have since been identified. The GLC1C gene, mapped to chromosome 3, is associated with increased eye pressures and cup-to-disc ratios greater than or equal to 0·7 or an abnormal result on a visual-field test.

**Management**

The goal in the treatment of POAG is to prevent further loss of functional vision during the remainder of a patient’s life and to avoid an adverse impact on the patient’s quality of life. The prevention of loss of vision is mainly achieved by lowering the eye pressure to a threshold that is deemed to be safe for the ganglion cells given the current amount of damage in the optic nerve head (target intraocular pressure). Topically applied ocular or oral medications are usually the first step in the management of POAG. Currently there are five classes of medications that are used to lower eye pressure: topical cholinergic agonists or parasympathomimetics, topical β-adrenergic antagonists, topical adrenergic agonists, topical prostaglandin analogues, and topical and oral inhibitors of carbonic anhydrase (Table 1). When topical medications are prescribed, it is helpful to inform the patient to close his or her eyes after the administration of the eye drop for at least 1 min. While the eyes are closed, the patient can place a finger near the nose and press against the nasolacrimal duct to help further reduce systemic absorption of the eye drop (figure 3). The European Glaucoma Society recommends the following steps in their flow chart on the management of POAG: medications first, then argon laser trabeculoplasty if treatment does not lower eye pressure sufficiently, and finally
If medications, argon laser trabeculoplasty, and trabeculectomies are ineffective in lowering a patient’s eye pressure, then the placement of drainage devices or cilio destructive procedures are recommended. In certain cases, drainage devices or cilio destructive procedures may be done instead of an initial trabeculectomy; because of the high likelihood of a trabeculectomy failing.  

There has been much public attention on marijuana as a possible treatment of glaucoma. Inhalation of marijuana does lower eye pressures. As it is thought that sustained lowering of eye pressure is likely to confer greater benefit, the amount of marijuana smoke needed to produce clinical benefits may be associated with substantial side-effects, and thus, marijuana is not recommended as a treatment for glaucoma.

<table>
<thead>
<tr>
<th>Class of drug</th>
<th>Generic names</th>
<th>Mechanism and duration of action</th>
<th>Selected side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical cholinergic agonists</td>
<td>Pilocarpine drops and gel, carbachol, echothiophate iodide, demacarium bromide</td>
<td>Increase aqueous outflow; duration of action from 6 to 1 week</td>
<td>Increased bronchial secretion, nausea, vomiting, diarrhea, increased myopia, eye or brow pain, decreased vision, apnea</td>
</tr>
<tr>
<td>Topical β-adrenergic antagonists</td>
<td>Timolol, levobunolol, cateolol, metipranolol, betaxolol</td>
<td>Decreased aqueous production; duration of action 12-36h</td>
<td>Congestive heart failure, bronchospasm, bradycardia, depression, confusion, impotence, worsening of myasthenia gravis, raised cholesterol</td>
</tr>
<tr>
<td>Topical adrenergic agonists</td>
<td>Epinephrine, dipivefrin, apraclonidine, brimonidine</td>
<td>Decreased resistance to aqueous outflow and decreased aqueous production; duration of action 8-12h</td>
<td>Increased blood pressure, tachyarrhythmias, tremor, headache, anxiety, conjunctival injection, pupillary dilation, allergic reactions</td>
</tr>
<tr>
<td>Topical or oral inhibitors of carbonic anhydrase</td>
<td>Topical dorzolamide, brinzolamide, oral acetazolamide, methazolamide, dichlorphenamide</td>
<td>Decreased aqueous production; duration of action 6-12h</td>
<td>Malaise, anorexia, depression, paresthesias, serum electrolyte abnormalities, renal calculi, blood dyscrasias, allergic reactions, bitter or sour taste</td>
</tr>
<tr>
<td>Prostaglandin analogues</td>
<td>Latanoprost</td>
<td>Increased aqueous outflow; duration of action 24-40h</td>
<td>Increased iris pigmentation, hypertrichosis, increased pigmentation of lashes</td>
</tr>
</tbody>
</table>

*with echothiophate iodide or demacarium bromide after administration of succinylcholine*
Primary angle-closure glaucoma  
Diagnosis and epidemiology

The main feature distinguishing primary closed-angle glaucoma from primary open-angle glaucoma is that the angle, the site of aqueous outflow in the eye, is obstructed by apposition of the iris, resulting in an anatomically closed angle (defined if at least 270° of the angle is occluded). Like open-angle glaucoma, closed-angle glaucoma is predominantly an asymptomatic disease with individuals often unaware they have the disorder until advanced visual loss has occurred. In less than one third of cases, patients may present with acute primary angle closure, a clinical condition characterized by marked conjunctival hyperemia, corneal edema, amid dilated unreactive pupil, a shallow anterior chamber, and very high intraocular pressure, usually greater than 30mm Hg. Such patients often complain of ocular pain, nausea, vomiting, and intermittent blurring of vision with haloes noticed around lights.

Patients with PACG may present with acute raised eye pressures, a mid-dilated pupil, a red eye, or nausea and vomiting, whereas in other cases they may have no complaints or may complain of a non-specific headache, eye pain, or halos around lights.

The diagnosis of PACG requires an assessment of the anterior chamber angle to find out if the trabecular meshwork is blocked by the peripheral iris. If a skilled observer, slit-lamp, and gonioscopy lens are not available, a presumptive diagnosis of PACG may be made with the oblique flashlight test. In this test, a penlight or flashlight is held off to the side and parallel to the iris of the eye with the beam shining across the anterior chamber. If the whole iris is illuminated, the angle is judged to be open. If a shadow is cast on the iris near the nose, then the angle is deemed to be narrow or closed.

In PACG one of the mechanisms for the obstruction of the trabecular meshwork by the iris is pupillary block or the inability of the aqueous humor to leave the posterior chamber behind the iris, because of the apposition of the iris to the lens of the eye. This inability of aqueous humor to flow around the lens of the eye results in a pressure gradient between the posterior and anterior chambers of the eye. This pressure gradient causes a forward bowing of the peripheral iris that then obstructs the trabecular meshwork (figure 1). Another mechanism is called creeping angle closure and involves the development of peripheral anterior synechiae, even when there is a patent peripheral iridotomy.

People of Eskimo, Chinese, or Asian Indian descent are at increased risk of PACG. In Wales in the UK the prevalence of PACG in people older than 40 years was 0.09% and the prevalence of POAG was 0.5%, whereas the prevalence of PACG in Alaskan Eskimos was 2.6% in people older than 40 years. In a Chinese population, the prevalence was 1.37% for PACG, compared with 0.11% for POAG, and in an Asian Indian population, the prevalence of PACG in individuals age 30–60 years was 4.33% versus 0.41% for POAG. Patients with PACG, especially Chinese and Asian Indians, may not have acutely increased eye pressures and symptoms because of chronic, creeping angle closure.

Additional risk factors for PACG include a family history of the disease, age of 30 years or more, female sex, and hypermetropic eyes. First-degree relatives of Eskimos with PACG have a 3.5-time greater risk of developing PACG than the Eskimo population in general. In white people, the prevalence of PACG in first-degree relatives ranges from 1 to 12%. Although there have been formal recommendations to start screening for PACG at age 40, studies from India and China indicate that screening at age 30 years or older would be more appropriate. The prevalence of PACG peaks in individuals aged 50–69 years. Women are reported to be at increased risk of PACG if they are white, Eskimo, or Chinese. In the Asian Indian population, there was not a significant difference in the
prevalence of PACG between men and women.\textsuperscript{48} White people who have hypermetropic eyes are at increased risk of PACG.\textsuperscript{55} This increased risk is consistent with the finding that patients with PACG have shallower anterior chambers and smaller-sized globes than individuals who do not have PACG. Lowe\textsuperscript{56} has postulated that these smaller, more-crowded eyes are predisposed to the blockage of the trabecular meshwork by the peripheral iris.

\textbf{Management}

Medications for PACG are similar to those used in POAG (panel 1). In the management of an acute attack of PACG, treatment with miotics, \(\alpha\)-adrenergic agonists, \(\beta\)-adrenergic blockers, inhibitors of carbonic anhydrase, and systemic hyperosmotic agents may be used to help lower the eye pressure and arrest the attack. Yet, the primary management of PACG is the placement of a laser iridotomy or opening in the peripheral iris. This hole effectively eliminates the forward bowing of the iris and obstruction of the trabecular meshwork by the iris.\textsuperscript{48} The presence of a patent iridotomy does not mean that the patient does not need further follow-up or medications. Additional concerns include permanent synechiae of the iris to the trabecular meshwork before the iridotomy, undetected trabecular damage from temporary apposition of the iris to the trabecular meshwork, and the possibility of creeping angle closure. Some patients need chronic medications to lower the eye pressure despite the presence of a patent iridotomy. The medications used are similar to those used in the treatment of POAG. In patients with chronic PACG who do not respond to medications, the next step is trabeculectomy with or without antimetabolites or drainage devices. Argon laser trabeculoplasty is contraindicated in these eyes if there is more than 90 degrees of angle closure.\textsuperscript{42}

\textbf{CONCLUSION}

If current trends prevail, the worldwide prevalence of POAG and PACG will continue to increase. Attempts to reduce substantially the visual impairment and blindness associated with glaucoma will need more aggressive detection, so that more people with glaucoma are aware that they have this disease. Also needed is more careful management of POAG and PACG that incorporates lessons learned from current research. Because of the health, social, and economic consequences of blindness, the burden of POAG and PACG falls not only on patients and their physicians, but also on society. Thus, disease-control strategies need to go beyond the simple suggestion that primary care physicians screen routinely for the disease. Broader public information campaigns might highlight the need for periodic eye examinations, especially among individuals with a family history of the disease or other risk factors for glaucoma.

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