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GLAUCOMA

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ABSTRACT

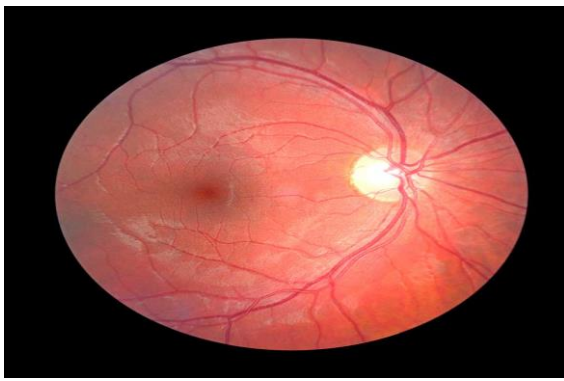
Glaucoma is the leading cause of irreversible blindness in the world. Due to its potential to cause permanent vision loss, it is important to understand how systemic conditions and their respective treatments can be associated with or increase the risk for developing glaucoma. In this review, we examined the literature for up-to-date discussions and provided commentary on glaucoma, its pathophysiology, and associated risk factors. We discuss systemic diseases and the impact, risk, and mechanism for developing glaucoma, including pharmacologically induced glaucoma; inflammatory and auto-immune conditions; infectious, dermatologic, cardiovascular, pulmonary, renal, urologic, neurologic, psychiatric and systemic malignancies: intraocular tumors; as well as pediatric, and genetic conditions. The goal of our discussion of systemic conditions including their commonality, mechanisms, treatments, and associations with developing glaucoma is to emphasize the importance of ocular examinations and follow-up with the multidisciplinary teams involved in the care of each patient to prevent unnecessary vision-loss.

KEY WORDS

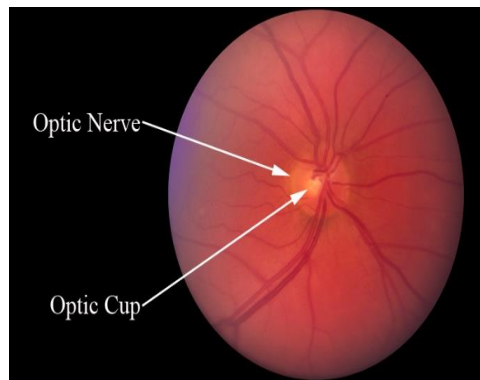
Ophthalmology, glaucoma, open-angle glaucoma, closed-angle glaucoma, diagnosis,treatment

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness in the world. In 2010, 60.5 million people were estimated to have glaucoma. In 2020, this number increased to 79.6 million. Glaucoma is more prevalent in persons of African and Hispanic descent [3,4], and patients with glaucoma can be asymptomatic for many years, making it likely that these measurements underestimate the true prevalence of the disease. Glaucoma is separated into two categories: open-angle and angle-closure. In the United States, more than 80% of patients have open-angle glaucoma, but closed-angle glaucoma contribute a significantly higher proportion of cases of severe vision loss. It is estimated that 68.56 million people worldwide have primary open-angle glaucoma and 17 million people worldwide have primary closed-angle glaucoma. Both categories of glaucoma can be acquired as primary or secondary diseases. Secondary causes of glaucoma be medications such as corticosteroids, systemic inflammation, intraocular and systemic tumours, or other predisposing conditions such as diabetes, hypertension, or genetic syndromes. Because of the permanent and lasting effects, it is important to understand how systemic conditions and their treatment can be associated with or lead to glaucoma. Before embarking on this discussion, it is useful to have a deeper understanding of glaucoma and its pathophysiology. Glaucoma is a degenerative optic neuropathy stemming from damage and progressive gradual loss of retinal ganglion cell (RGC) axons. The cell bodies of the RGCs are in the inner retina, and their axons comprise the optic nerve. They synapse in the lateral geniculate body. The gradual degeneration of RGCs and RGC axons of the optic nerve leads to the characteristic cupping of the optic nerve seen in ophthalmoscopy (see Figure 1B) and subsequent visual field defects⁽¹⁾.



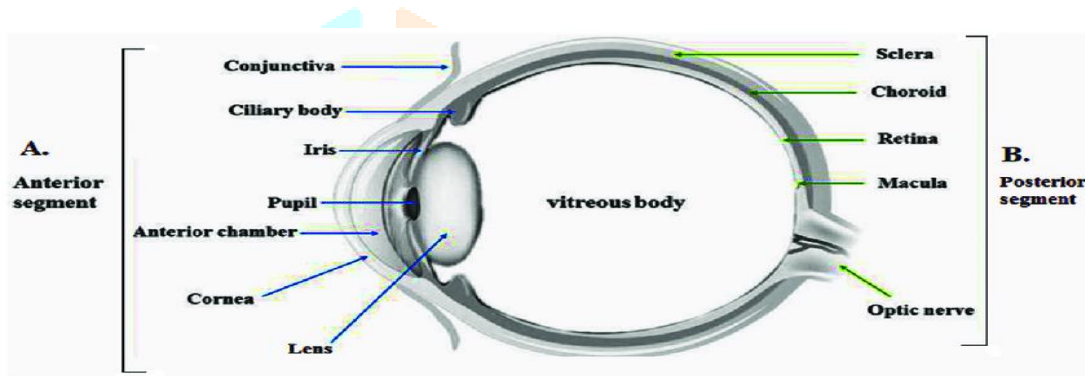
(A)Optical nerve (fig a)



(B) Glaucomatous optic nerve with cupping (fig b)

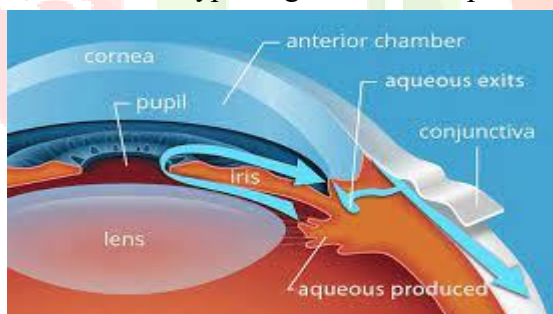
INTRAOCULAR PRESSURE

The IOP, in simplified terms, is the balance between the production and outflow of aqueous humor. Aqueous humor is the intraocular fluid that is produced to nourish ocular structures, and it is produced by the ciliary body, a tissue structure located posterior to the iris, which also suspends the intraocular lens. The secreted aqueous humor flows from behind the iris into the anterior chamber through the pupil and out of the eye via the drainage



Anterior view of the cornea, iris, pupil and sclera

The aqueous humor drains primarily through the trabecular meshwork, with a lesser, but unknown amount, exiting via the uveoscleral outflow pathway. Whether this trabecular meshwork is “open”, i.e., physically unobstructed, helps to define the type of glaucoma as open-angle or closed-angle⁽²⁾.



Aqueous humour

MAGNITUDE OF GLUCOMA

Worldwide Glaucoma is the leading cause of irreversible blindness worldwide, and the second most common cause of blindness after cataracts. It is responsible for 14% of blindness worldwide. It afflicts almost 70 million people, of whom 10% are believed to be bilaterally blind. Several population-based studies have contributed to our understanding of the incidence and prevalence of OAG within defined populations in the United States and other countries. In the Baltimore Eye Survey, the prevalence of OAG was significantly higher in blacks (4.7%) than in whites (1.3%). The Los Angeles Latino Eye Study found that Latinos in the United States have a prevalence of OAG of 4.7%. The prevalence of OAG in Asians varies widely, perhaps in part because the term Asian encompasses broad racial and ethnic categories. Rudnicka et al. documented OAG rates in Asia to range from 1 to 4%, whereas Ramakrishnan et al. found the prevalence of OAG in India to be 1.7%. In Asian populations, ACG is the main cause of morbidity from glaucoma. ACG blinds 10-times more people than OAG does, and the worldwide incidence of ACG is growing. While ACG represents only 10–15% of all glaucoma in the black and white populations, it accounts for a significant percentage of glaucoma that occur in Asian populations. The rate of ACG among

Chinese is three-times that of OAG. Approximately 91% of bilateral blindness in China is due to ACG. Vijaya et al. found that 2.75% of the population had angle closure and 0.88% had ACG. The Andhra Pradesh Eye Disease Survey in south India suggests that 0.7% of the population over 30 years of age has ACG⁽³⁾.

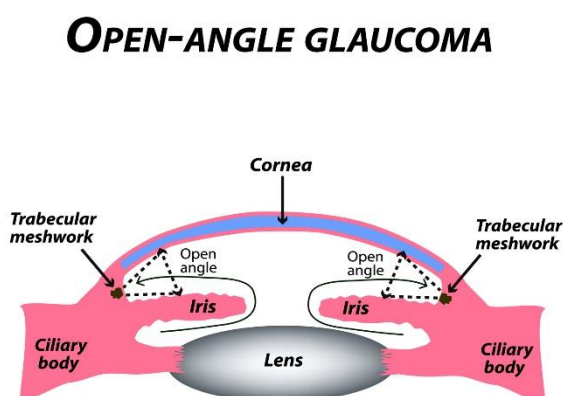
PATHOPHYSIOLOGY AND CLASSIFICATION

The pathophysiology of glaucoma is not completely understood, but is related to retinal ganglion cell death. A better understanding of the pathophysiological mechanisms involved in the onset and progression of glaucomatous optic neuropathy is crucial in the development of better therapeutic options.⁸ The normal physiological balance between the secretion of aqueous humour and the drainage thereof is affected by this condition. Aqueous humour is secreted by the ciliary body and drainage of the humour takes place via two independent pathways, namely the trabecular meshwork and the uveoscleral outflow pathway.^{9,10} The filtration is dependent on pressure gradients, blood pressure and increased IOP. Osmotic gradients produced by the active secretion of sodium and bicarbonate ions and other solutes, produce a pressure gradient that allows for the movement of the humour from the pool of ciliary stromal ultrafiltrate into the posterior chamber, thereby forming aqueous humour. Various receptors and transmitters are found in the ciliary epithelium and the smooth muscle structures of the eye. Carbonic anhydrase (primarily of the type II isozyme), α and β -adrenergic receptors, sodium and potassium-activated triphosphates, prostaglandins and muscarinic receptors all play a role in the normal functioning of the eye⁽⁴⁾.

CLASSIFICATION

OPEN ANGLE GLUCOMA

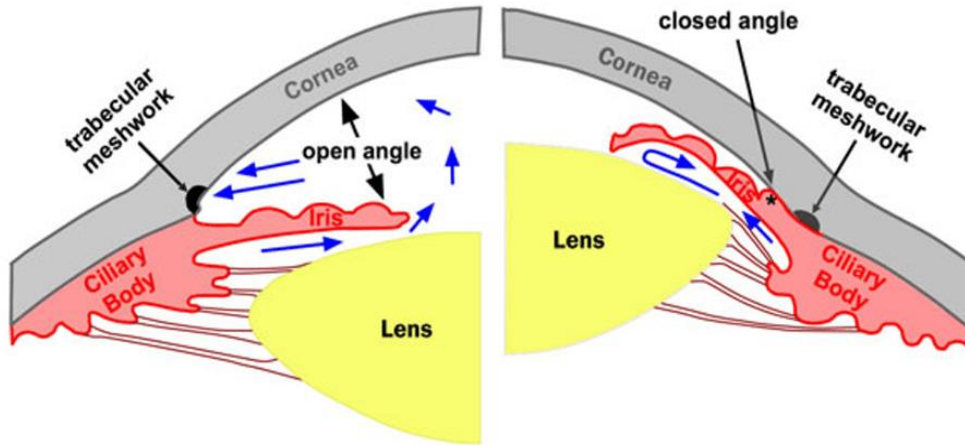
may result from optic nerve damage at any range of intra-ocular pressure. The rate of progression can be either fast or slow, with patients who may have had increased intra-ocular pressures and then only present with changes in the optic disk or visual fields at a much later stage. This increases the challenge to diagnose and treat open-angle glaucoma, because the early disease is often asymptomatic.



OPEN ANGLE GLUCOMA

CLOSED ANGLE GLUCOMA

may be due to a physical blockage of the trabecular meshwork. This can be more acute in onset. When the IOP is > 40 mmHg optic nerve damage and even permanent nerve damage (> 60 mmHg) can occur. However, since the trabecular meshwork is intrinsically normal, it is possible to restore the trabecular function by early removal of the synechiae before irreversible ultra-structural changes have occurred .

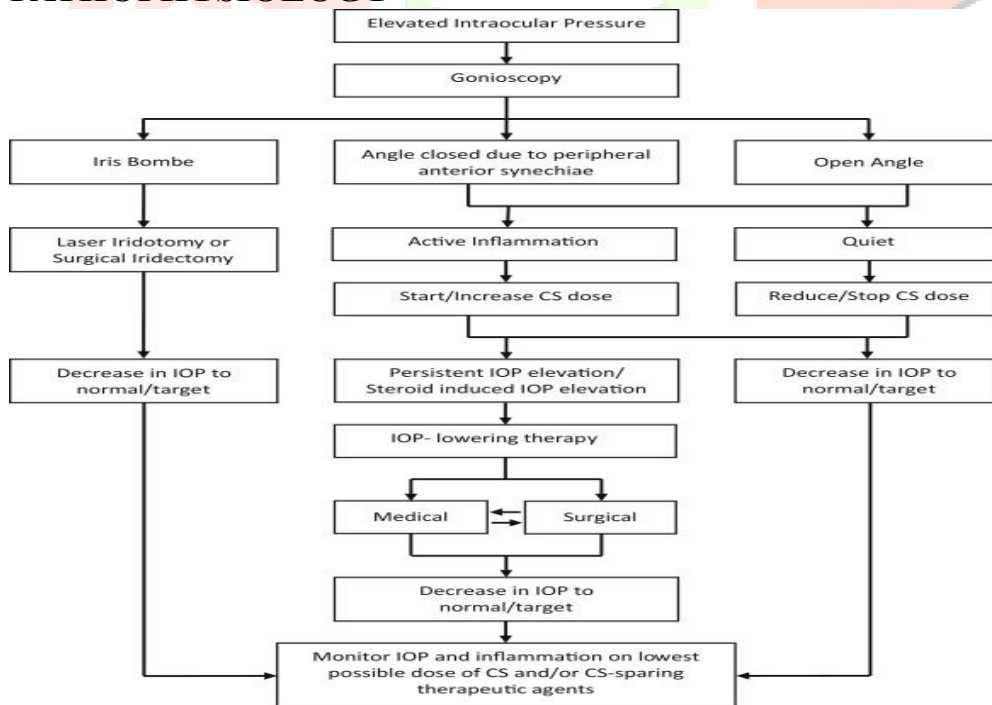


CLOSED ANGLE GLUCOMA

MEDICINE INDUCED GLUCOMA

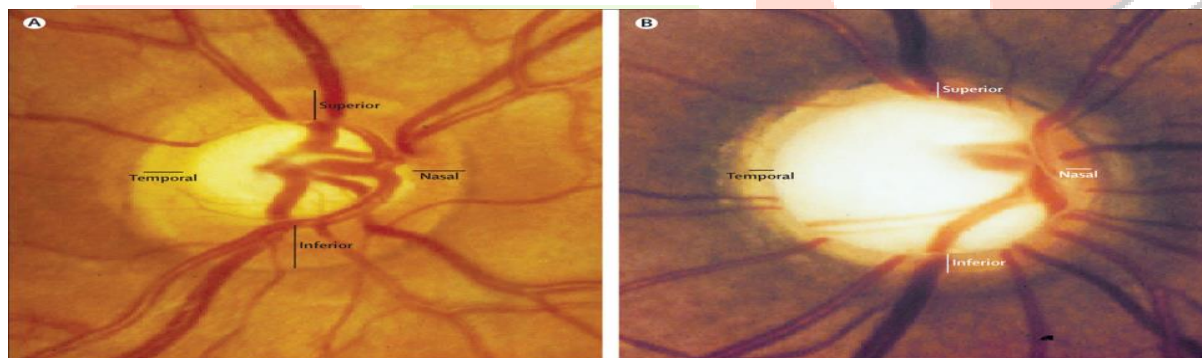
may be due to an increased intraocular pressure brought about by various medicines. Medicines may worsen pre-existing glaucoma or induce glaucoma based on their mechanisms of action, and patients' predisposition. Table III provides an overview of medicines that may induce or potentiate an increased intraocular pressure⁽⁵⁾.

PATHOPHYSIOLOGY



OCULAR PRESSURE

Intraocular pressure (normal range 10–21 mm Hg) is regulated by a balance between secretion of aqueous humour by the ciliary body in the posterior chamber and drainage of aqueous humour from the anterior chamber angle, either through the trabecular meshwork and Schlemm's canal or via the uveoscleral outflow pathway through the iris root into the uveoscleral interface (figure 3). Increased intraocular pressure is due to a decreased outflow facility of aqueous humour. In open-angle glaucoma, the aqueous humour has free access to the trabecular meshwork and Schlemm's canal in the anterior chamber angle. In secondary open-angle glaucoma, the outflow resistance through the trabecular meshwork and Schlemm's canal is increased due to a cause that is detectable by examination of the anterior ocular segment. These conditions include pigmentary glaucoma and exfoliative glaucoma.^{5,6} In primary open-angle glaucoma, the anterior chamber angle seems to be unremarkable. The level of intraocular pressure can vary strikingly and could be as low as 10 mm Hg. Optic-nerve damage in primary open-angle glaucoma can develop in the presence of normal levels of intraocular pressure, and this condition has been called normal-pressure glaucoma.^{7,8} In such situations, aqueous outflow resistance is normal or might only be slightly increased. In angle-closure glaucoma, the peripheral iris is in contact with the trabecular meshwork and the peripheral cornea. The peripheral iris blocks the anterior chamber angle so that aqueous humour no longer has access to the outflow system. In primary angle-closure glaucoma, the iridocorneal contact is due to forward bulging of the peripheral iris (so-called push mechanism), which is caused by a higher pressure in the posterior chamber behind the iris and a lower pressure in the anterior chamber. The pressure difference is due to increased flow resistance for the aqueous humour through the slit between the iris and lens in association with anatomical abnormalities, such as augmented forward bulging of the anterior lens pole (referred to as anterior lens vault), an enlarged contact area between the posterior iris and the lens surface, and an abnormal insertion of the iris root on the ciliary body.^{9–11} The condition is called primary angle-closure glaucoma when the raised intraocular pressure has caused damage to the optic nerve. In secondary angle-closure glaucoma, the iridocorneal contact is caused by the iris being pulled forward (so-called pull mechanism) into the angle because of, for example, neovascularisation in the iris and uveitis. Iris neovascularisation is usually provoked by ischaemic retinopathies such as diabetic retinopathy, with overproduction of vascular endothelial growth factor (referred to as neovascular glaucoma)⁽⁶⁾.



(fig a)

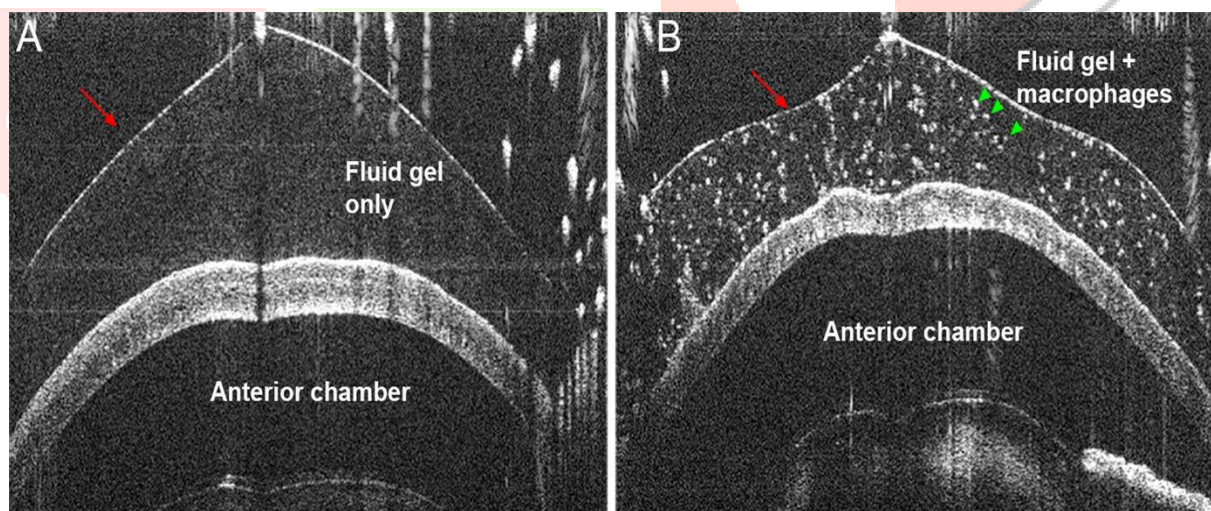
(fig b)

GLUCOMA

Risk factors

The main risk factors for both development and progression of glaucoma are older age,^{3,43–46} an intraocular pressure too high in relation to the pressure sensitivity of the optic nerve head,^{7,47–51} ethnic background,^{44,52} a positive family history for glaucoma, stage of disease, and high myopia.^{53–55} Findings of a randomised placebo-controlled trial showed that medical lowering of intraocular pressure resulted in preservation of visual field in patients with open-angle glaucoma.⁵¹ In a meta-analysis of population-based studies, the odds ratio for primary open-angle glaucoma was 1.73 (95% CI 1.63–1.82) for each decade increase in age beyond 40 years.³ Similarly, the prevalence of primary angle-closure glaucoma increased with older age. The Asian population had the highest prevalence of primary angle-closure glaucoma (1.20%, 0.46–2.55).³ Sex has been associated inconsistently with the prevalence of open-angle glaucoma, yet in two meta-analyses of population-based glaucoma studies, a higher prevalence of primary open-angle glaucoma was reported in men than in women.^{3,47} High myopia with a myopic refractive error of roughly more than –8 diopters was another strong risk factor for glaucoma.^{53–56} Correspondingly, findings of the Singapore Malay Eye Study showed an association between moderate or high myopia (worse than –4 diopters) and a higher prevalence of primary open-angle glaucoma.⁵⁵ Diagnosis of glaucomatous optic neuropathy can be missed in myopic eyes because intraocular pressure is

typically within the normal range and the myopic appearance of the optic nerve head makes detection of glaucomatous changes difficult. Study findings have suggested that the main factor for the myopia-associated increase in glaucoma susceptibility is the myopia associated enlargement of the optic disc.⁵⁶ Secondary stretching and thinning of the lamina cribrosa in association with an elongation and thinning of the parapapillary tissues could lead to pronounced changes in the biomechanics of the optic nerve head and an increase in glaucoma susceptibility. Another factor could be the biomechanics of the optic nerve dura mater, which pulls on the peripapillary sclera in eye movements and increases the stress and strain of the lamina cribrosa.⁵⁷ Socioeconomic status affects early detection of glaucoma and initiation of and adherence to treatment;^{58,59} therefore, this factor is associated with prognosis of the disease. Whether nutritional status and diet have an effect on the prevalence and incidence of any form of glaucoma is unclear. The relation between primary open-angle glaucoma and diabetes mellitus,^{60,61} arterial hypertension,^{62,63} body-mass index,⁶⁴ obstructive sleep apnoea,⁶⁵ and oral contraceptive use⁶⁶ is uncertain. Although controversial, low CSF pressure and low ocular perfusion pressure, including a low systemic blood pressure, might potentially have a role in glaucoma.^{22,28–31,67–69} A thin central cornea has been deemed a risk factor for glaucoma because a thin cornea leads to falsely low measurements of intraocular pressure.^{43,70} Furthermore, a thin cornea could be a structural risk factor because of a hypothetical association with a thin lamina cribrosa.^{71–73} An association between corneal thickness and thickness of the lamina cribrosa has, however, not been shown yet.⁷¹ Correspondingly, in an east Asian population,^{72,73} corneal biomechanical variables—eg, corneal hysteresis and corneal resistance factor—were not correlated with the severity of primary angle-closure glaucoma, nor was central corneal thickness associated with glaucoma. The main systemic risk factors for development of primary closure of the anterior chamber angle are older age, east Asian ethnic origin, and female sex, in addition to the main ocular risk factor of axial hyperopia. The hyperopic eye has a small anterior chamber, a thick and more anteriorly positioned lens, a thick iris, and greater forward bulging of the anterior lens pole (or anterior lens vault).^{9,10,74,75} The reduced space in the anterior chamber leads to a higher risk of a blockage of the anterior chamber angle by peripheral iris tissue in mid-mydriasis. The angle obstruction can occur acutely, leading to acute and painful angle-closure glaucoma, or it might develop chronically, associated with painless chronic angle-closure glaucoma⁽⁷⁾.



(fig a)

(fig b)

ANTERIOR PORTION OF EYE

SYMPTOMS

Differences in the time of onset between open-angle and closed-angle glaucoma are related to the pathophysiology of the condition. General differences in the clinical presentation of glaucoma are depicted

DIAGNOSIS

Because chronic forms of glaucoma are painless, measurable visual-field defects do not develop at an early stage of glaucoma, and defects generally do not occur at homonymous locations in both visual fields, self-detection of glaucoma by affected individuals usually occurs at a late stage of the disease. The mainstay of detection of glaucoma is examination of the optic nerve head and retinal nerve fibre layer.^{102–106} Glaucomatous changes of the optic nerve head include loss of neuro-retinal rim, leading to enlargement of the optic cup, deepening of the optic cup (partly reversible if the intraocular pressure is reduced to normal or subnormal levels), development and enlargement of the parapapillary beta zone, thinning of the retinal

nerve fibre layer, and optic disc haemorrhages, which are signs of progression of the disease.^{107–109} These changes can be assessed by simple ophthalmoscopy or by imaging techniques such as spectral-domain optical coherence tomography, which is useful in particular for follow-up examinations.^{106,110} Tonometry is an essential part of the diagnosis and follow-up of glaucoma, although intraocular pressure cannot be taken as the main criterion for diagnosis of the disease because many patients with glaucoma can present with normal intraocular pressure. In the Japanese population-based Tajimi study,¹¹¹ intraocular pressure was 21 mm Hg or less in 92% of patients with primary open-angle glaucoma. Intraocular pressure is the primary modifiable risk factor and its modulation is central to the management of glaucoma, but it is a fairly weak diagnostic criterion. The dependence of tonometric measurements on the central corneal thickness and curvature has to be taken into account.¹¹² In eyes with abnormally thick corneas, tonometry gives falsely high readings, potentially leading to overdiagnosis, and in eyes with abnormally thin corneas, tonometric measurements are falsely low, with the risk of underdiagnosis of glaucoma. Central corneal thickness and corneal curvature should, therefore, be measured once so that tonometric readings can be corrected accordingly. Perimetric visual-field examination is the second technique in the diagnosis and follow-up of glaucomatous optic-nerve damage.^{7,47,48} Many optic nerve fibres can be lost before perimetric defects are detected; therefore, the diagnostic precision of this technique increases with the stage of glaucoma.¹¹³ Perimetry describes the subjective psychophysical defect as experienced by the patient, but it has fairly high intervisit variability, so at least three perimetric examinations could be necessary to detect visual-field deterioration reliably. Other psychophysical tests—including assessment of glaucoma-related colour vision deficiency, impaired dark adaptation, increased photophobia, and decreased contrast sensitivity—are important for the quality of vision of the patient. These modalities, however, are not measured routinely because of high interindividual and intraindividual variability. A potential future development is application of optical coherence tomography angiography to visualise the superficial and deep retinal vascular network and, in particular, the peripapillary radial vascular network.¹¹⁴ Assessment of the peripapillary radial vascular network could help in the diagnosis and follow-up of glaucomatous optic neuropathy in highly myopic eyes, in which most other diagnostic methods fail⁽⁸⁾.

TREATMENT

OPEN ANGLE GLUCOMA

The only proven and generally accepted treatment to reduce the risk of further progression of glaucomatous optic neuropathy is to lower intraocular pressure.^{49,51,115} Reduction of intraocular pressure is achieved by drug treatment, laser therapy, or surgery. The goal is to lower the intraocular pressure towards an individual target level at which further progression of glaucomatous optic nerve damage is unlikely. The target intraocular pressure for a particular eye is estimated based on the pretreatment intraocular pressure, the severity of damage, presence of risk factors for progression, life expectancy, and potential for adverse effects from treatment. The aim is usually for a reduction in intraocular pressure of 20–50%. The greater the pre-existing optic-nerve damage and the more risk factors present, the lower the target pressure is set. The target intraocular pressure should be reanalysed periodically by assessing whether the optic-nerve damage is stable or has progressed. Several categories of topical drugs for lowering intraocular pressure are available. The choice of drug is affected by cost, adverse effects, and dosing schedules. In general, prostaglandin analogues (eg, latanoprost, tafluprost) are the first-line medical treatment; when delivered once in the evening, these drugs lower intraocular pressure by improving uveoscleral outflow. Local side-effects include elongation and darkening of eyelashes, loss of orbital fat (prostaglandin-associated periorbitopathy) with resulting enophthalmos, iris darkening in eyes with greenish-brown iris colour, and periocular skin pigmentation. surgery. Miotics do not have major systemic side-effects. Prostaglandin analogues, carbonic anhydrase inhibitors, and miotics reduce intraocular pressure during both day and night, whereas β adrenergic blockers and α adrenergic agonists are effective mostly during daytime. Most drug groups can be combined with each other. A new class of topically applied drugs is the ρ kinase inhibitors (eg, ripasudil), which have finished phase 3 trials and are expected to be approved in 2017.^{116–118} These drugs reduce intraocular pressure by increasing the transtrabecular outflow and, potentially, by decreasing the production of aqueous humour. After topical application of an eye drop, gentle occlusion of the lower lacrimal duct—or just to close the eyes for a few minutes—is recommended. These measures greatly reduce the amount of drug passing through the lacrimal drainage system on to the mucosa of the oropharynx where the drugs are easily absorbed and, by avoiding breakdown by the hepatic system, can lead to systemic side-effects. In eyes with an open anterior chamber angle, drug treatment could be augmented by, or in some cases replaced by, laser therapy (laser trabeculoplasty) to the trabecular meshwork, in particular if the target intraocular pressure is not achieved

by use of drugs (particularly in poorly compliant patients). Independent of concurrent drug treatment, laser intervention can reduce the intraocular pressure by a few additional mm Hg. The good safety profile of laser trabeculoplasty is combined with fairly low efficacy. If the intraocular pressure-lowering effect is not sufficient, incisional glaucoma surgery has to be done, usually under local anaesthetic but occasionally under topical anaesthesia. In patients with poor compliance or those intolerant to drug treatment, incisional surgery can also be done as the first step in the treatment of glaucoma. A panoply of surgical antiglaucomatous procedures has been developed in the past decade. Creating an additional outflow pathway from the eye for the aqueous humour, all surgical techniques (eg, trabeculectomy) risk reduced longterm success secondary to fibrosis around the subconjunctival exit point of the fistula. During and after surgery, antimetabolites are applied to the surgical site to decrease the fibrotic response and to keep the fistula site open. Glaucoma implant drainage devices are another surgical option and act by channelling the aqueous humour through a tube out of the eye into the subconjunctival space. These devices are similarly effective in lowering intraocular pressure to trabeculectomy⁽⁹⁾.

PRIMARY ANGLE CLOSURE GLUCOMA

The treatment of acute angle closure differs profoundly from the therapeutic regimen for open-angle glaucoma. In acute angle closure, acutely raised intraocular pressure is lowered first by drugs, including miotics as first-line treatment (eg, pilocarpine), repeatedly instilled in short intervals, and other drugs used in chronic open-angle glaucoma (eg, timolol, latanoprost, brimonidine). The aim is to open up the angle by inducing a miosis and pulling the peripheral iris tissue out of the angle. An alternative could be immediate laser iridoplasty.¹²² As definitive treatment, peripheral laser iridotomy, which forms a pathway for aqueous humour flow between the posterior chamber and anterior chamber by creating a small hole in the peripheral iris, is mandatory for all patients with primary angle-closure. This technique reduces the pressure differences between both chambers so that the peripheral iris can flatten and be retracted out of the anterior chamber angle. If done at an early stage, one procedure can result in lifelong cure. If the procedure is delayed, peripheral anterior synechiae can form, and if not released by surgical intervention within a few days to weeks, further circumferential adhesions can occur, resulting in an irreversible closure of the whole anterior chamber angle and blockage of the outflow system. Non-pupillary block mechanisms (eg, plateau iris) can cause a considerable proportion of angle closure in people from east Asia, an ethnic group that has a higher propensity for angle-closure glaucoma. Post-iridotomy procedures to further lower intraocular pressure, if needed, are similar to those undertaken for the treatment of open-angle glaucoma. They include topical application of anti-glaucomatous drugs and incisional antiglaucoma surgery, including trabeculectomy or lens extraction with implantation of glaucoma drainage implants. Since the risk of acute angle closure is usually similar between both eyes, laser peripheral iridotomy should be done prophylactically in the contralateral eye of a patient presenting with unilateral primary angle closure. Evidence from a clinical trial shows that clear-lens extraction has greater efficacy and is more cost-effective than laser peripheral iridotomy for treatment of primary angle-closure glaucoma,¹²³ and this technique could be considered as an option for first-line treatment in which cataract surgery combined with goniosynechiolysis successfully normalised the intraocular pressure in patients with persisting peripheral anterior synechiae between iris and cornea and raised intraocular pressure after periphery iridotomy⁽¹⁰⁾.

CONGENITAL GLUCOMA

Treatment of congenital glaucoma is mainly surgical. Procedures used include goniotomy or trabeculotomy, in which the inner wall of Schlemm's canal is opened into the anterior chamber.

FUTURE DEVELOPMENT

The noted growth in prevalence of cataract surgery and the increase in prevalence of axial myopia, in particular in Asia, might decrease the occurrence of angle-closure glaucoma in the future.¹²⁵ Ongoing studies that investigate the benefits of iridotomy in patients with angle closure from east Asia will provide guidance on the efficacy of this treatment in these populations, in which angle-closure is fairly prevalent among adults.¹²⁶ Topically applied ρ kinase inhibitors might become an additional pillar in the medical treatment of glaucoma.^{116–119} Novel sustained-release delivery systems— eg, intracameral injection of slow-release intraocular pressure-lowering drug pellets or topically applied cyclodextrins—are being tested in trials.^{127,128} Such systems might reduce the problems associated with poor adherence and ocular surface damage that can occur with long-term use of topically applied eye drops. Better understanding of patient-reported outcomes and experience might further improve the practical success of glaucoma treatment.³⁷ Third, research is needed to examine the role of retinal vein pulsations and retinal venous blood pressure in the pathogenesis and diagnosis of glaucomatous optic neuropathy.¹³¹ Fourth, an assessment should be done of the cause of parapapillary beta zone.¹³² Fifth, investigations are needed into

the reasons for increased glaucoma susceptibility in patients with high myopia.^{53–56} Finally, research is awaited into the biomechanics of the optic nerve dura mater and its effect on the optic nerve head.⁵⁷ Another area for future development is to further investigate exfoliation syndrome, with respect to its genetics, proteomics, molecular biology, cellular processes, and systemic manifestations.^{133,134} Several potential novel treatments for glaucoma are under investigation or could be explored. First, studies are underway to investigate induction of a re-sprouting of retinal ganglion cell dendrites to increase the receptive field of the still-existing ganglion cells.¹³⁵ Second, studies are in progress to refine the existing surgical techniques to reduce the risk of a postoperative scarring of the filtering bleb, leading to treatment failure. Finally, work to further assess the application of stem cells⁽¹¹⁾.

CONCLUSION

Glaucoma, as one of the leading causes of blindness globally, may have devastating consequences if left undetected and untreated for too long. The mainstay of pharmacological intervention in glaucoma is to reduce the IOP. This may be achieved via one of two main mechanisms, namely to reduce the formation of aqueous humour, or to promote its drainage. In future, adding the new Rho-kinase inhibitor, ripasudil, to existing treatment regimens may increase the achievable level of reduction in the IOP. Patients with glaucoma should be carefully assessed and monitored, whilst following a step-wise approach to their treatment. It is vital that the target IOP is reached to prevent any further deterioration in a patient's visual field loss.

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