Glaucoma and Ocular Hypertension

Description

Glaucoma refers to a group of eye conditions that lead to damage to the optic nerve head with progressive loss of retinal ganglion cells and their axons. This leads to a progressive loss of visual field. There are typical optic nerve changes on slit-lamp examination. Glaucoma is usually associated with an intraocular pressure (IOP) above the normal range. However:

- 20-52% (this varies between populations) of patients with glaucoma have IOP within the normal range. Patients with normal IOP who develop the characteristic changes associated with open-angle glaucoma are said to have low tension or normal pressure glaucoma.
- Many patients have raised IOP for years without developing the changes of glaucoma. This condition is referred to as ocular hypertension.

Prior to 1978, glaucoma was defined as IOP above 21 mm Hg in an eye (the normal range is considered to be 10-21 mm Hg with 14 being the average). More recently glaucoma has been understood as an abnormal physiology in the optic nerve head that interacts with the IOP, with the degree and rate of damage relating to both factors.

Editor's Note

Nov 2017 - Dr Hayley Willacy recommends the recently released NICE Guideline on diagnosis and management of glaucoma. Amongst other recommendations they suggest that before referral for further investigation, people should be offered all of the following tests: central visual field assessment using standard automated perimetry (full threshold or supra-threshold); optic nerve assessment and fundus examination using stereoscopic slit lamp biomicroscopy (with pupil dilatation if necessary), and optical coherence tomography (OCT) or optic nerve head image if available; intraocular pressure (IOP) measurement using Goldmann-type applanation tonometry and peripheral anterior chamber configuration and depth assessments using gonioscopy or, if not available or the patient prefers, the van Herick test or OCT.

Types of glaucoma

There are several glaucoma subtypes, although all are considered optic neuropathies. Glaucoma may be primary or secondary to other conditions.

Primary glaucoma

This may be:

- Congenital or acquired.
- Open-angle or closed-angle, depending on how the aqueous outflow is impaired.
- Closed-angle glaucoma may be:
  - Acute.
  - Chronic.
  - Intermittent.
  - Superimposed on chronic open-angle glaucoma.

- Variants of primary glaucoma include:
  - Pseudoxfoliative glaucoma.
  - Pigmentary glaucoma.
  - Primary juvenile glaucoma.

Secondary glaucomas

These include:

- Inflammatory glaucoma - eg, with uveitis.
- Phacogenic glaucoma (caused by the lens - eg, capsular rupture).
- Secondary to any intraocular haemorrhage.
- Traumatic.
- Neovascular (eg, rubeosis iridis).
- Steroid-induced.
- Associated with ocular tumours.

Absolute glaucoma

The end stage of glaucoma is referred to as absolute glaucoma. There is no functioning vision, the pupillary reflex is lost and the eye has a stony appearance. The condition is very painful and is treated by destructive processes.
Pathophysiology of glaucoma[3, 4]

The primary problem in glaucoma is disease of the optic nerve. The pathophysiology is not fully understood, but there is a progressive loss of retinal ganglion cells and their axons. In its early stages it affects peripheral visual field only but as it advances it affects central vision and results in loss of visual acuity, which can lead to severe sight impairment and complete loss of vision.

For most types of glaucoma, optic neuropathy is associated with a raised IOP. This has given rise to the hypothesis of retinal ganglion apoptosis, whose rate is influenced by the hydrostatic pressure on the optic nerve head and by compromise of the local microvasculature. The resulting optic neuropathy gives rise to the characteristic optic disc changes and visual field loss.

However, in normal tension glaucoma (NTG), IOP is in the normal range and this has led to other theories including vascular perfusion problems or an autoimmune component. Others have postulated that the optic nerve head is particularly sensitive in these patients, with damage occurring at much lower IOPs than in normal individuals. This could explain why these patients benefit from IOP-lowering medication[4].

In open-angle glaucoma, flow is reduced through the trabecular meshwork (whose role is absorbing aqueous humour). This is a chronic degenerative obstruction which occurs painlessly. By contrast, in acute closed-angle glaucoma the iridocorneal angle is closed by forward displacement of root of the iris against the cornea, so that aqueous humour cannot flow from the posterior to the anterior chamber and the pressure build-up is rapid and painful.

Epidemiology

- Glaucoma is one of the most common eye conditions encountered in primary and secondary care.
- The World Health Organisation estimated that in 2010 glaucoma accounted for 8% of severe sight loss globally, and is the leading irreversible (the most common overall cause remains cataract)[6].
- Disability adjusted life years attributable to glaucoma more than doubled between 1990 and 2010 due to the worldwide increase in the number of older people.
- In the UK glaucoma is the second most common cause for registration of visual impairment, accounting for 9-12% of registrations in people over the age of 65 years.
- The social burden and economic burden of glaucoma are likely to increase in the future because of longer life expectancy and an ageing population.
- Primary open-angle glaucoma (POAG) is the most common type of glaucoma, accounting for over 70% of cases.
- Ocular hypertension affects 3-5% of the population over 40 years of age but only a small proportion of these people develop glaucoma.
- If glaucoma is completely untreated, progression to severe sight impairment typically takes 25-70 years from onset. Patients of African ethnicity are significantly more likely to become blind[3, 4].

Risk factors[3, 4]

- Raised IOP particularly >26 mm Hg.
- Myopia.
- Diabetes.
- Positive family history: incidence increases x 2-4 for those with an affected sibling.
- Ethnicity: some ethnic groups have increased incidence of glaucoma. People of East Asian and Inuit ethnicity have an increased incidence of closed-angle glaucoma (20-40 times in the Inuit), but a low incidence of open angle glaucoma[7]. People of African descent are three times more likely to develop open-angle glaucoma[8].
- Gender: women are three times more likely than men to develop angle-closure glaucoma due to their shallow anterior chambers.
- Prolonged use of steroids.
- Conditions which severely restrict blood flow to the eye - eg, diabetic retinopathy, central retinal vein occlusion.
- Eye trauma.
- Uveitis.
- Systemic hypertension.

Assessing glaucoma[9]

The onset of open-angle glaucoma is insidious and patients are often unaware that they have it. They may have severe disease despite good visual acuity. Those with more advanced disease may be aware of a shadow in their vision or a reduction in visual acuity. However, a normal visual field in one eye may mask the presence of a defect in the affected eye until the disease is fairly advanced.

Diagnosis of this silent disease is critical. If it is missed, the window of opportunity to stop progression may be lost. If it is wrongly diagnosed, inappropriate medication may be lifelong. In some cases, diagnosis is evident, particularly with the secondary glaucomas.

Patients with suspected glaucoma need a thorough ocular examination to rule out co-pathology or other possible diagnoses. Assessments are the same for glaucoma patients and those with - or suspected to have - ocular hypertension (see 'Ocular hypertension', below).

Initial assessment
See also the separate Examination of the Eye article.
From the front of the eye to the back, the examinations particularly relevant in the assessment of glaucoma are listed here. They are all painless and can be carried out in a clinic setting:

- **Gonioscopy** - this is a technique used to measure the angle between the cornea and the iris to assess whether the glaucoma is open-angle or closed-angle. A mirror is placed on the surface of the numbed eye to allow the operator to measure the angle directly.

- **Corneal thickness** - this influences the IOP reading. If it is thicker than usual, it will take greater force to indent the cornea and an erroneously high reading will be obtained. (The opposite is true for a thin cornea.) Corneal thickness is measured by pachymetry.

- **Tonometry** - this is the objective measurement of IOP, usually based on the assessment of resistance of the cornea to indent. The normal range is considered to be 10 mm Hg-21 mm Hg. There are various tonometers available but the most frequently used in a hospital setting is Goldmann's applanation tonometer.

- **Optic disc examination** - this is key, as it is a direct marker of disease progression. Optic disc damage is assessed by looking at the ratio of the diameters of the pale centre (cup) to the overall size of the disc. The normal cup:disc ratio is 0.3, although it can be up to 0.7 in some normal people:
  - Glaucoma is suggested by an increase in cupping with time, rather than by cupping alone. Marked but stable cupping may be hereditary.
  - The intra-observer variability in optic disc evaluation has been markedly reduced by the more routine use of ocular coherence tomography (OCT), which not only produces excellent visual records but is able to provide quantification of several data including exact cup:disc ratio and areas of neuro-retinal thinning.

- **Visual fields** - these can be assessed using perimetry machines which objectively document what the patient perceives in the periphery of their vision. These assessments require the co-operation of the patient and can also be affected by fatigue, spectacle frames, miosis and media opacities. Where this is not possible, the assessor will have to rely on IOPs and cup:disc ratios alone. See also the separate Visual Field Defects article.

Glucoma may affect a person’s ability to drive and may mean their licence to do so is withdrawn. See the link in 'Further reading & references' below, regarding the DVLA rules relating to ability to drive.

**Monitoring**

Once diagnosis is confirmed, IOPs, optic disc assessment and visual fields are regularly monitored. If the central corneal thickness has been altered - eg, by laser refractive surgery or onset of corneal pathology - this will also require reassessment.

**Ocular hypertension**

- **Definition** - this term is used where the IOP is found to be >21 mm Hg on two consecutive occasions in the absence of any detectable glaucomatous damage. It is a major risk factor for the development of glaucoma. Lowering IOP has been shown to decrease this risk.

- **Epidemiology** - ocular hypertension is estimated to affect 3-5% of individuals aged over 40; about one million people in England.

- **Management** - the IOP, the central corneal thickness and the age of the patient will determine whether treatment is instigated or not:
  - For those who are not treated, ongoing monitoring is essential, as there is a risk of converting to POAG.
  - For those who do require treatment, this involves IOP-lowering drugs (discussed in the separate Primary Open-angle Glaucoma article).
  - There is considerable variation in practice with regards to who is treated and who is not but the National Institute for Health and Care Excellence (NICE) guidelines should reduce this variation.
  - Patients will be monitored six-monthly to yearly.

- **Outcome** - the Ocular Hypertension Treatment Study found that the 'conversion rate' to glaucoma is 9% over five years in untreated patients, compared to 4.4% in treated individuals. There is no absolute way of predicting which of these patients will go on to ‘convert’ but risk factors include:
  - Older age.
  - Higher IOP.
  - Larger cup-to-disc ratio.
  - Thinner central corneal thickness.

**Treatment of glaucoma**

Specific treatments for glaucoma are discussed in the relevant clinical articles. However treatments include:

- Medication, usually eye drops, to lower IOP. Poor compliance with medication is common. Medications include:
  - Prostaglandin analogues - eg, latanoprost.
  - Topical beta-adrenergic antagonists - eg, timolol.
  - Alpha-2 adrenergic agonists - eg, brimonidine.
  - Miotics - eg, pilocarpine, echothiophate.
  - Carbonic anhydrase inhibitors - eg, dorzolamide.
- Trabeculectomy - removal of part of the trabecular meshwork. This is the most common surgery performed for glaucoma.
- Canaloplasty - uses a microcatheter to increase the drainage of Schlemm’s canal.
- Laser surgery - a temporary measure to increase the outflow of aqueous humour.
- Drainage implants - a flow tube is implanted into the anterior chamber and drains fluid out to an area under the conjunctiva, called a bleb.
- Sclerectomy - a procedure similar to trabeculectomy but with additional excision of part of the sclera.

### Primary open-angle glaucoma
See the separate Primary Open-angle Glaucoma article for more details.

### Angle-closure glaucoma
See the separate Angle-closure Glaucoma article for more details.

### Normal tension glaucoma (low tension glaucoma)\[^{5, 12}\]
NTG is a subtype of the open-angle glaucomas. Patients have statistically normal IOPs but modification of the IOP remains the best established treatment approach. There is increasing evidence that IOP independent factors such as vascular dysregulation contribute to the pathology.

- **Nature** - glaucomatous optic neuropathy with an open iridocorneal angle, in the absence of a raised mean IOP on diurnal testing.
- **Risk factors** - include old age, female gender. May be associated with the Raynaud’s phenomenon, migraines, paraproteinaemia.
- **Management** - as for POAG with the aim to reduce IOP by 30%. It is also recommended that systemic blood pressure be monitored over 24 hours, as NTG may be associated with nocturnal systemic hypotension and a significant nocturnal drop warrants a review of antihypertensive medication (calcium-channel blockers are preferable). When medication does not stabilise nerve damage, glaucoma filtering surgery is the best treatment. Further research is ongoing.
- **Outcome** - there is often a delay in diagnosis, resulting in more advanced visual field defects. Patients with unilateral defects have a $40\%$ chance of developing defects in the fellow eye over five years.

### Secondary glaucomas
Several eye disorders lead to an increase in IOP sufficient to present a risk to optic nerve structure and function. These secondary glaucomas cause a reduction in outflow of aqueous humour, caused by inflammatory debris, intraocular haemorrhage and growth of new blood vessels in the angle (neovascular glaucoma) resulting from ocular vascular diseases of the eye\[^{13}\].

- **Neovascular glaucoma:**
  - This is a serious condition which arises as a result of iris neovascularisation (rubeiosis iridis).
  - It occurs following episodes of hypoxia as may occur in ischaemic retinal vein occlusion, advanced diabetic eye disease, central retinal artery occlusion, intraocular tumours, long-standing retinal detachment and where there has been chronic intraocular inflammation.

- **Pseudoexfoliative (PXF) glaucoma, also called exfoliative glaucoma:**
  - This arises secondary to pseudoexfoliation syndrome, whereby a dusty grey deposit of extracellular amyloid-like material is deposited on the anterior lens capsule, the zonules, the ciliary body and in the trabecular network, so clogging the latter up.
  - It is more likely to occur in older ($\geq$40-year-old) females.

- **Pigmentary glaucoma:**
  - Pigment deposits from the posterior surface of the iris block the drainage system as with PXF.
  - It is more likely to occur in young (20- to 40-year-old), male, Caucasian myopes.

- **Exposure to corticosteroids can lead to secondary glaucoma.**

Initial treatment for secondary glaucoma is to stabilise or inhibit the underlying disorder. For neovascular glaucoma, this therapy can be laser treatment for the retina and injection of inhibitors of vascular endothelial growth factor. Glaucoma related to PXF and pigment dispersion syndrome is managed with drugs and possibly laser treatment or surgery. Neovascular glaucoma involves panretinal photocoagulation and possibly retinal surgery.

The outcome is is usually good although patients with rubeiotic glaucomas tend to fare badly, as they by definition have advanced ocular comorbidity to have developed rubeiosis iridis.

### Primary congenital glaucoma
See the separate Congenital Primary Glaucoma article for more detail.
Other types of glaucoma[14, 15]

- **Inflammatory glaucoma** - this difficult condition presents with fluctuating IOPs and a ciliary body shutdown. It is the most common cause of severe sight impairment in children and young adults with chronic anterior uveitis. Steroid responders (a rise in IOP in response to steroid treatment for the inflammation itself) present the most tricky management issues. Treatment is broadly drug-based but severe cases may require surgery too.

- **Lens-related glaucoma** - the lens may either cause a phacolytic glaucoma (a hypermature cataract sheds proteins which clog up the drainage system) or phacomorphic glaucoma (where the lens swells and bulges forward, compressing the trabecular meshwork). Both need prompt cataract surgery, although this is associated with a greater risk of complications than routine cataract surgery.

- **Traumatic glaucoma** - red blood cells can block the trabecular meshwork (this is particularly the case in patients with sickle-cell haemoglobinopathies); angle recession (where blunt trauma ruptures the face of the ciliary body and damages the trabecular meshwork) also results in glaucoma in 6-9% of patients over a ten-year period.

- **Iridocorneal endothelial (ICE) syndrome** - this frequently unilateral condition (typically affecting young- to middle-aged women) is characterised by iris abnormalities which are associated with glaucoma in 50% of cases. Treatment is medical and surgical.

- **Glaucoma in phacomatoses** - Sturge-Weber syndrome is associated with early presentation of patients with glaucoma (60% within the first two years of life) and neurofibromatosis-1 patients may also (uncommonly) present with unilateral, congenital glaucoma.

- **Iridocorneal dysgenesis** - this can arise in a number of conditions (Axenfeld-Rieger syndrome, Peters’ anomaly, aniridia) and is variously associated with glaucoma, the management of which lies within the remit of specialised units.

- **Ghost cell glaucoma** - degenerate erythrocytes left behind after a vitreous haemorrhage (± cataract surgery) and hyphaema may block up the trabecular meshwork so giving rise to glaucoma. These patients benefit from medical treatment but may require iridectomy of the anterior chamber.

- **Glaucoma in cavernous sinus fistula** - secondary glaucoma may come about as a result of raised episcleral venous pressure (resulting from a generalised increase in orbital venous pressure) impairing the aqueous outflow. If there is anterior segment ischaemia, neovascularisation may also complicate things. Medical treatment is required until the shunt resolves or is treated.

- **Glaucoma in intraocular tumours** - development of glaucoma depends on the site of the tumour but it occurs in about 5% of affected eyes.

- **Glaucoma in ciliochoroidal detachment** - in the event of a detachment of the ciliary body or choroid, there is an anterior displacement of the lens-iris complex resulting in shallow iridocorneal angles which may close off. Treatment is medical and surgical.

- **Glaucoma in epithelial ingrowth** - occasionally, after anterior segment trauma (including surgery), conjunctival and corneal epithelial cells migrate from the external surface of the eye, through the wound and grow across the structures within. This may block off the aqueous outflow. Treatment involves surgery and cryotherapy.

- **Glaucoma in iridoschisis** - this is a rare condition in which the iris atrophies. It is associated with glaucoma in 90% of cases. Laser treatment is necessary, followed by drug treatment.

**Further reading & references**

- Glaucoma Focus; Royal National Institute of Blind People (RNIB) and International Glaucoma Association (IGA)
- Assessing fitness to drive: guide for medical professionals; Driver and Vehicle Licensing Agency
- Glaucoma referral and safe discharge - Anatomical clinical guideline; Scottish Intercollegiate Guidelines Network - SIGN (March 2015)
- Glaucoma: diagnosis and management; NICE Guidelines (November 2017)


6. Causes of blindness and visual impairment World Health Organization


9. Glaucoma referral and safe discharge - Anatomical clinical guideline; Scottish Intercollegiate Guidelines Network - SIGN (March 2015)

10. Glaucoma; NICE Clinical Guideline (April 2009)


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