Glaucoma, in ancient Greek, meant “clouded” or “a blue-green hue” — possibly a description of the corneal oedema that occurs in acute angle closure glaucoma. Since the time that this language was in common use, the concept of glaucoma has evolved with more understanding of the disease and risk factors.

Glaucoma is now defined as a “progressive optic neuropathy with characteristic structural changes in the optic nerve head and functional changes in the visual field, in the absence of other ocular disease or congenital anomalies”. If left untreated, the condition can lead to irreversible blindness.

High intraocular pressure (IOP) was used previously as a diagnostic criterion for glaucoma. More recently, however, it has been recognised as the most important risk factor for the disease. This is because glaucoma can occur even with normal IOP (ie, normal pressure glaucoma or low pressure primary open angle glaucoma). Normal IOP is 10–21mmHg. IOP is known to increase by 1mmHg every decade after the age of 40 years in the western population. There is a circadian cycle of IOP, with maximum levels between 8am and 11am and minimum levels between midnight and 2am. The normal diurnal variation is 3–5mmHg, but this is wider in untreated glaucoma.

Patients in whom the optic nerve and visual field show no signs of glaucomatous damage but the IOP is above the normal range (ie, >21mmHg) are diagnosed with ocular hypertension. About 10 per cent of such patients may convert to primary open angle glaucoma (POAG) (see below).

Structural changes

As mentioned above, characteristic structural changes occur in the optic nerve head of patients with glaucoma. The optic disc (the point at which the nerve fibres from the retina merge to form the optic nerve) becomes excavated (ie, cavities form), with loss of retinal nerve fibre layer (RNFL). This occurs progressively, from the temporal part of the disc (which is thinnest) through to the neuroretinal rim (which is thickest). The loss of RNFL is either localised or diffuse.

The optic disc cupping (ie, excavation) occurs more in the vertical direction initially — known as vertical ovalisation of the cup. Other signs of damage to the optic disc in patients with glaucoma include splinter haemorrhages, asymmetric cupping (a difference in the cup to disc ratio between the two eyes), notching of the optic nerve rim and pallor of all or part of the disc. Disc cupping is the major difference between glaucomatous optic neuropathy and other optic neuropathies. The anatomy of the eye is presented in Figure 1 (p252).

Functional changes

The functional changes from glaucoma include the progressive deterioration of the visual field due to the death of the retinal ganglion cells. This usually begins in the midperiphery, often in the superior field, and may progress in a centripetal (ie, towards the centre) fashion to leave behind a central or a temporal island of vision. Sometimes...
there can be a reduced perception to light. The localised visual field defects correspond to the RNFL loss.

Other functional changes include loss of colour sensitivity, especially for short-wavelength (ie, blue) light. Testing with blue light short-wavelength perimetry has been demonstrated to be more sensitive for diagnosing and monitoring glaucomatous visual field loss than the standard achromatic (ie, having little or no hue) perimetry. Other changes include loss of spatial resolution, loss of motion detection and loss of temporal contrast sensitivity. These changes occur much before the visual field defects can be seen on standard perimetry. At least 40 per cent of the retinal nerve fibres are damaged before visual field defects are picked up on standard perimetry.

Causes

The exact mechanisms that lie behind these distinct structural and functional changes are not known. Many theories exist as to how a raised IOP can be one of the factors that initiates glaucomatous damage. These include, for example, that it produces vascular dysfunction by causing ischaemia to the optic nerve and that it causes mechanical dysfunction by compressing the axons at the lamina cribrosa (a sieve-like structure in the optic nerve head). Other possible mechanisms of glaucomatous damage unrelated to IOP include damage from deprivation of neuronal growth factors, excessive retinal glutamate, free nitrate radicals, immune-mediated nerve damage and oxidative stress. Changes at the level of the lamina cribrosa are thought to play an important part in the development of glaucoma. There is compression and displacement of the lamina cribrosa and a selective loss of retinal ganglion cells. There is also a blockage of both orthograde and retrograde transport in retinal ganglion cells. This causes intraxonal collections of vesicles and mitochondria, and disorganisation of microtubules at the level of lamina cribrosa, resulting in selective degeneration of the optic nerve fibres. In some cases, impaired microcirculation, either by itself or in combination with a raised IOP or other pathological mechanism, is thought to cause the optic nerve damage. This leads to the appearance of glaucomatous cupping of the optic disc. The cascade of events leading to the typical appearance of the optic disc is unique to glaucomatous optic neuropathy.

Importantly, there is a great variation in the susceptibility of the optic disc to glaucomatous damage. In some cases, even high pressures do not cause any damage, while in other patients normal IOP can result in severe damage. Mechanisms that raise IOP are covered in the second article in this special feature (pp255-62).

Types of glaucoma

There are various types of glaucoma. Broadly the disease can be classified into four groups:

- **Primary open angle glaucoma** This is the most common type of glaucoma in people over the age of 50. The anterior chamber is deep and there is reduced aqueous outflow through the trabecular meshwork, which in turn causes the IOP to increase.
- **Normal-tension glaucoma** In this type of glaucoma, the IOP is within the statistical normal. However, there may be poor blood flow to the optical disc or increased susceptibility to disc damage at lower IOP.
- **Primary angle closure glaucoma** The IOP increase is caused by closure of the anterior chamber angle. This may be of acute or chronic type.
- **Secondary open angle or angle closure glaucoma** These types of glaucoma result from other ocular conditions or treatments.

Risk factors

A number of factors have been identified as having an association with glaucoma. Those with a strong association include:

- **IOP** High IOP is the most important risk factor for developing glaucoma. The
risk of glaucomatous damage increases with increasing IOP (especially above 22mmHg). 9 10 11

Age Incidence of POAG is higher in elderly than younger patients. The prevalence is 0.7 per cent between 50 and 59 years, 1.8 per cent between 60 and 69 years and 3.2 per cent between 70 and 79 years. 12

Corneal thickness Patients with corneal thickness greater than 588µm are less likely to progress to POAG. Patients with normal tension glaucoma have a higher incidence of thinner corneas. 13

Race The risk of developing glaucoma is 4.3 times higher in Afro-Caribbeans than white Americans. 14 The rate of disease progression is also more rapid in Afro-Caribbeans. 15 The incidence of acute angle closure glaucoma (in which the IOP rises very quickly) is more common in South East Asians, Chinese and Eskimos than in black people. 16

Family history The mode of inheritance for POAG is polygenic. A positive family history increases the relative risk of POAG. If a parent has the disease the age-adjusted odds ratio is two, 17 and if the sibling has the disease it is increased to 3.69. 18

Factors with moderate association with glaucoma include:

Sex Females are at greater risk of normal tension glaucoma (2:1) and also chronic angle closure glaucoma (4:1). 19

Myopia Population-based studies have shown that there is an increased incidence of glaucoma in myopic patients (ie, short-sighted). 20

Factors with weak association with glaucoma include:

Diabetes Micro-angiopathy may be a causative factor for the pathogenesis of glaucoma. The relation between diabetes and glaucoma is not strong. Some studies have shown increased incidence while some other have not. 21 22

Migraine and vasospasms Patients with vasospastic disorders such as migraine have been shown to have a higher risk of developing normal tension glaucoma than POAG. 23

Systemic hypertension Some studies have shown a positive association between a raised IOP and a raised blood pressure, while others have not shown the association.

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Diagnosis and monitoring

The diagnosis of the glaucomatous condition and the type of glaucoma, as well as the monitoring of disease progression, are performed by a number of different tests on the eye. The main tests are set out below.

IOP assessment The clinical measurement of IOP can be carried out with a range of different instruments, some more reliable than others. Indentation tonometry, for example, is based on the principle that the force required to deform the eye ball is directly proportional to the pressure within the eye. This technique, which uses a Schiotz tonometer, needs the patient to be supine and is hardly used these days.

Applanation tonometry is based on the principle of Imbert-Fick, which equates the IOP to a ratio of variable force required to flatten a fixed area of the cornea with the area of flattening. Goldmann applanation tonometry consists of applanating a fixed area of the corneal surface with a prism-head of 3.06mm diameter. Goldmann tonometry is the gold standard against which other tonometers are measured. There are, however, sources of error with Goldmann tonometry, which include:

- Inter-patient variation in central corneal thickness — thick corneas cause overestimation of IOP and thin corneas cause underestimation of IOP
- Calibration error — about 5 per cent of tonometers have an error of >2mmHg
- Insufficient quantity of fluorescein (to outline and make clearly visible to the observer the area of cornea applanated) may result in an underestimation of IOP by 5mmHg
- Excessive tears in fluorescein may lead to an overestimation of IOP by 2—4.6mmHg
- Poor illumination can cause underestimation of IOP
- Astigmatism can cause an underestimation or overestimation of IOP, depending on the type
- Corneal oedema can cause an underestimation of IOP
- Eccentric gaze may increase the IOP
- Blepharospasm and restrictive neck clothing can increase the IOP
- Breath-holding can reduce IOP

- Intraobserver variability can account for errors of 2—3 mmHg

Other types of tonometer are set out in Panel 1.

Gonioscopy Gonioscopy is a technique for assessing the angle of the anterior chamber of the eye to determine whether it is open or closed. This assessment is essential in diagnosing the type of glaucoma and the most appropriate treatment, and needs to carried out periodically to detect the emergence of any additional condition. Different types of gonioscopy are:

- Direct gonioscopy This allows for direct visualisation of the angle and is used principally to view the angle in children with congenital glaucoma. The two types of direct lens are Koepppe and Swan-Jacob goniolenses.
- Indirect gonioscopy This approach uses a mirror mounted on a contact lens which helps to visualise the angle. It can be used with slit-lamp (a high-intensity light source that can be focused to shine as a slit) and the angle can be seen with high magnification and illumination. The types of indirect lens include Goldmann and Zeiss goniolens.

Optic disc assessment Optic disc assessment is an important part of the examination. Significant loss of retinal ganglion cells and optic nerve fibres occur before functional visual loss is apparent by conventional visual field testing methods. The following assessment of the optic disc is carried out at the time of diagnosis and subsequently at every follow-up visit:

- Optic disc The size and shape of the optic disc are determined.
- Neuroretinal rim The more of the rim that is lost the more likely glaucoma is present. Other signs of possible glaucoma include pallor and focal notching of the rim.
- Optic cup Normally the optic cup is horizontal and oval. The size of the cup

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Panel 1: Types of tonometer for measuring intraocular pressure (other than the Goldmann tonometer)

- Perkins hand-held tonometer This type of tonometer is useful for bed-bound or anaesthetised patients.
- Air-puff tonometer This type of tonometer does not require topical anaesthesia and is often the instrument of choice for screening by optometrists.
- Pulsair tonometer These measurements with this type of tonometer are comparable to those obtained using a Goldmann tonometer.
- Tono-pen Results obtained from using this type of tonometer correlate well with those obtained using the Goldmann tonometer. It is useful in eyes with distorted or oedematous cornea. There is a slight overestimation at low IOP and underestimation at high IOP.
increases with retinal ganglion cell death. Asymmetry between the two eyes of >20 per cent is pathological.

- **Splinter haemorrhages** These are not seen in normal eyes. They are seen in 4–7 per cent of eyes with glaucoma and are most frequently seen in normal pressure type glaucoma.23

- **Peripapillary atrophy** Large areas of atrophy in the beta zone (adjacent to the optic disc) are seen in POAG.

Documentation of optic disc changes is important in the monitoring of the patient with glaucoma. The cup:disc ratio is the most common parameter recorded. This can be done by drawing in the patient’s notes or using optic disc stereo-photography or Heidelberg retinal tomography.

**RNFL assessment** RNFL is performed usually on a slit-lamp using green light or wide-angled red-free photography. There is a generalised atrophy of the RNFL with ageing. However, in early stages of glaucoma, the RNFL atrophy is seen as a wedge-defect radiating from the disc.

Documentation of the RNFL can be performed qualitatively by drawing in the patient’s notes or by quantitative methods. Quantitative methods of RNFL analysis are still in research but look set to be important tools in the future for assessing patients who have ocular hypertension or in whom glaucoma is suspected. This is because RNFL can detect the changes that occur well before they can be detected using visual field assessment. Some of the methods of quantitative assessment include:

- RNFL photographs using wide-angle red-free light on a fundus camera
- Scanning laser ophthalmoscope

**Visual field assessment** The visual field is the area perceived when both eyes are open. It is sometimes described by patients with glaucoma as an island in the sea of darkness. The visual acuity reduces towards the periphery. Visual fields are tested for each eye independently. Two of the different types of perimetry used to test visual acuity are set out in Panel 2.

### Conclusion

Glaucoma is a progressive optic neuropathy that is associated with characteristic structural changes in the optic nerve head and functional changes in the visual field. Although a raised IOP is not the only cause of glaucoma, it is the only parameter that can currently be changed by pharmacological intervention. Information about the physiological causes of raised IOP and the drugs used in the treatment of glaucoma are set out in second article of this special feature.*

#### Panel 2: Types of perimetry used to assess visual acuity

- **Kinetic perimetry** In this type of perimetry, a stimulus is moved from a non-seeing to a seeing area along set meridians. Kinetic perimetry provides a two-dimensional measurement of the field of vision. The equipment most commonly used in this type of perimetry is the Goldmann perimeter.

- **Static perimetry** This type of perimetry provides three-dimensional boundaries of the visual field. Here, the size and location of the target remains the same but the brightness is varied to measure the retinal sensitivity or threshold. The equipment commonly used are the Hensen, Humphrey and Octopus peripherals.

### References


*Hospital Pharmacist online

Hospital Pharmacist is available online at www.pjonline.com/hp/index.html. The website contains the current issue and an archive of back issues from January 2000 onwards. There are also links to the regular features in Hospital Pharmacist (eg, Life-long Learning, meeting reports, comments, careers, focus on technicians, etc). The site also contains advice to contributors to Hospital Pharmacist, information about the annual Hospital Pharmacist conference, a link to The Pharmaceutical Journal careers page and information on subscribing to the journal.