Recent advances in the diagnosis and management of glaucoma

Parham Azarbod BSc, MRCS, FRCOphth, Laura Crawley BSc, MRCP, FRCOphth, Faisal Ahmed FRCOphth, M Francesca Cordeiro PhD, MRCP, FRCOphth, Philip Bloom FRCS, FRCOphth

Reducing intraocular pressure remains the only treatment option in glaucoma, however, prompt evaluation and management can prevent blindness and a lifetime of disability. Our Drug Review outlines the key points and recent advances in diagnosis and management.

A leading cause of bilateral blindness, glaucoma is thought to affect around 70 million people worldwide, 10 per cent of whom are estimated to be bilaterally blind. Given that glaucoma is associated with ageing, it is estimated that by 2020 around 80 million people will have glaucoma. While the exact pathophysiology of the condition remains unclear, the end result of glaucoma is progressive loss of neurons in the retinal nerve fibre layer leading to visual loss and eventual blindness in untreated cases.

There are two main types, primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG), which differ in terms of the underlying mechanism as well as presentation. POAG (see Figure 1) is the most common type in the UK and is often picked up on routine screening as it is asymptomatic in the earliest stage. The disease affects outflow primarily, with resistance at the level of the trabecular meshwork causing raised intraocular pressure (IOP). This is thought to cause damage of the optic nerve at the level of the lamina cribrosa, where mechanical factors as well as local microvascular changes and pressure gradient across the lamina cribrosa result in damage to the axons and then retinal ganglion cell death.

By contrast, acute PACG characteristically presents acutely with symptoms of redness, haloes around lights, severe pain, blurred vision and vomiting. The underlying mechanism is obstruction of the drainage through the anterior chamber angle by mechanical blockage of the angle by the iris. This causes a large acute rise in IOP, and without timely intervention can result in a devastating and irreversible loss of vision. Indeed acute PACG is the commonest cause of bilateral irreversible blindness in the world. Apart from pupil block, other mechanisms of angle closure include plateau iris configuration (abnormality at the level of the iris/ciliary body), lens-induced glaucoma and aqueous misdirection syndrome. With increasing awareness of PACG by community screeners and advancing imaging techniques such as optical coherence tomography (OCT), early treatment by...
laser iridotomy or lens extraction could reduce the incidence of the potentially devastating outcome of an acute attack.

The modern glaucoma specialist, as well as drawing on his/her own clinical experience, is also guided by the ever emerging literature and, in the UK particularly, on evidence-based guidelines produced by Royal College of Ophthalmologists, the European Glaucoma Society (EGS; updated June 2014), and NICE (Pathways for management update April 2014) framework. While a detailed account of the management of all glaucoma types is beyond the scope of this review, here we aim to highlight the most recent EGS and NICE guidelines, as well the recent developments in the management of POAG.

**Key points and advances in diagnosis**

As highlighted in NICE clinical guidance 85, the diagnosis of glaucoma is reached through the analysis of several components (see Table 1), taking account of their risk factors (see Table 2).

Goldmann applanation tonometry (GAT) remains the gold standard for measurements of IOP, which currently is the only modifiable risk factor in glaucoma. The Imbert-Fick law is the principle behind this instrument, which is essentially calibrated to provide a pressure reading based on the degree of indentation of the central cornea produced by the instrument. The degree of indentation is known to be influenced by the central corneal thickness (CCT), which is taken into account when interpreting the measurements.

While GAT tends to be the method used by the ophthalmologist, the non-contact method of pneumotonometry (‘air puff’) is more commonly used by the optometrist when screening for glaucoma. Although less operator dependent, the latter method can overestimate the IOP. Apart from potential corneal influences, a disadvantage of GAT measurements in clinics is that this method only represents a ‘snapshot’ measure of the IOP, which has in fact been shown to undergo diurnal changes, with more fluctuations in glaucoma patients. There has been recent interest in 24-hour IOP measurements and the development of a device known as Triggerfish in which the sensor is embedded in a contact lens worn by the patient. This device is not currently in clinical use, but it does highlight the importance of considering diurnal IOP variations when assessing patients, although it does not provide a direct measure of IOP. A compromise, which is current practice in assessing IOP fluctuations, is ‘phasing’ of the pressure over a 10 hour period of office hours. Another device that is gaining increasing popularity is the rebound tonometer (Icare), which, following an appropriate but short training period, has been shown to produce reasonably accurate results used by allied healthcare professionals. This device is particularly

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**Table 1.** All suspected glaucoma and ocular hypertension patients should have the following tests at diagnosis as per NICE guideline CG85

<table>
<thead>
<tr>
<th>Test Description</th>
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<tr>
<td>IOP measurement using Goldmann applanation tonometry.</td>
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<tr>
<td>Central corneal thickness measurement.</td>
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<tr>
<td>Peripheral anterior chamber configuration and depth assessments using gonioscopy.</td>
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<tr>
<td>Visual field assessment using automated perimetry.</td>
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<td>Optic nerve assessment, dilated stereoscopic slit lamp biomicroscopy.</td>
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**Table 2.** Risk factors identified through cross-sectional population-based studies

<table>
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<tr>
<th>Risk Factor</th>
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<tr>
<td>Age (prevalence increases with age).</td>
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<tr>
<td>IOP (risk of POAG increases by 11–12% in Caucasians, 10% in Afro-Caribbeans, 18% in Latinos for each 1mmHg increase in IOP).</td>
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<tr>
<td>Race/ethnicity (higher prevalence in those of African descent) Family history (close to 10-fold increased risk).</td>
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<tr>
<td>CCT (up to 40% increased risk of developing POAG per 40µm thinner CCT).</td>
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<tr>
<td>Myopia (&gt;–3 diopters).</td>
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<tr>
<td>Ocular perfusion pressure (nocturnal dips in blood pressure in those being treated for systemic hypertension).</td>
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<td>Others include diabetes, migraine, Raynaud’s syndrome and obstructive sleep apnoea.</td>
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Figure 1. Optic disc appearance: normal (left image); patient with POAG (right image); POAG is often picked up on routine screening.
useful in children as no anaesthesia is required and it is better tolerated than GAT.

Assessment of anterior chamber angle through gonioscopy is essential in the diagnosis and assessment of glaucoma patients. Anterior chamber imaging techniques are increasingly used to complement the gonioscopy findings and in particular to provide an objective method to assess treatment. The techniques include ultrasound biomicroscopy, anterior segment OCT, Scheimpflug photography, and the scanning peripheral anterior chamber depth analyser (SPAC). Of these, anterior segment OCT is the most routinely used in current clinical practice. However, these imaging techniques cannot replace slit lamp gonioscopy, as they cannot assess the angle for areas of permanent closure (peripheral anterior synechiae).

While stereoscopic slit lamp examination of the disc is a crucial part of the diagnosis, evidence suggests that even among experts there is lack of agreement in disc assessment. It is therefore very useful to obtain baseline disc photographs at the time of diagnosis and use serial disc photography (eg Kowa 3D fundus camera) for objective disc assessment during the follow-up period. With continued improvement in imaging software, the use of technology in serial disc assessments has now become an integral part of glaucoma management and is particularly useful in cases where automated perimetry has low reliability. Imaging devices include scanning laser polarimetry (GDx-ECC), Heidelberg retinal tomography (HRT) and OCT.

Automated perimetry remains the gold standard method of assessing functional nerve damage in glaucoma. There are several summary indices used to assess progression which include the mean deviation (MD) and the visual field index (VFI). There has been renewed interest in pointwise assessment of the visual field, ie analysing individual points within the visual field.
The current NICE guideline on POAG divides patients into those with ocular hypertension (OHT), glaucoma suspect and POAG with subgrouping depending on IOP. A detailed discussion of these guidelines is beyond the scope of this review, however the treatment principles will be discussed below.

The main treatment strategies for POAG can be divided into conservative (not discussed further here), laser, medical and surgical treatment.

**Medical treatment**
There is little change to the class of drugs used in the treatment of glaucoma (see Table 3), however, there has been an increase in the number of preservative-free as well as fixed-combination drugs (combined with a beta-blocker) including bimatoprost/timolol (Ganfort), brinzolamide/timolol (Azarga), brimonidine/timolol (Combigan) and latanoprost/timolol (details for these can be found in the BNF). The IOP-lowering effects of the fixed combinations may be slightly different compared to that of unfixed preparations, although they are generally thought to be clinically equivalent. By having a reduced number of medications and less potential side-effects from preservative, the adherence with treatment is thought to increase.

Of considerable interest has been the development of neuroprotective treatment, which is still being investigated as a future treatment option.

**Laser treatment**
Ytrrium-aluminium-garnet (YAG) laser peripheral iridotomy, which is used in cases of PACG has been the main type of laser used in the past. For POAG, the previously used argon laser trabeculoplasty has now largely been replaced by Q-switched, frequency-doubled 532nm Nd:YAG pulsed laser, known as selective laser trabeculoplasty (SLT). This technique has been shown to reduce the IOP by up to 6mmHg over long periods (five years). It can, therefore, be used as first-line treatment in selective cases, or as second-line or complementary treatment in other patients. An advantage of this laser is its repeatability. Another type of laser that is now being increasingly offered by many centres in the UK is endoscopic cyclo-photocoagulation (ECP) used to treat mild to moderate cases, often in combination with cataract surgery (see Table 4).

**Surgical treatment**
A recent trend has been the move towards early cataract surgery (clear lens extraction) in patients with narrow-angle glaucoma not responding to YAG laser iridotomy or iridoplasty.

Beyond trabeculectomy and the insertion of glaucoma drainage devices where there has been little change in the principles of the technique, there have been recent advances in procedures collectively known as minimally invasive glaucoma surgery (MIGS). These can be divided into two groups based on the surgical approach: ab interno and ab externo. Ab interno procedures include: trabeculotomy (Trabectome, excimer laser), trabecular micro-bypass (iStent), suprachoroidal stent (Cypass) intracanalicular scaffold (Hydrus) and subconjunctival implant (Aquesys). Ab externo procedures include: canalooplasty,
Stegmann Canal Expander and Suprachoroidal Gold Micro Shunt. Of these, the two most commonly used procedures currently in the UK are trabeculotomy and the insertion of iStent, both of which have been shown to be effective in reducing IOP.

Conclusion
Glaucoma remains largely a silent disease, where awareness and hence prompt evaluation and treatment of individuals can prevent blindness and a lifetime of disability. While it is useful to consider a therapeutic ladder when treating patients with glaucoma (see Figure 2), treatment options should be considered individually based on patient stage of glaucoma, risk factors, rate of progression of disease, local expertise and local policy. New diagnostic technologies and tools as well as innovation and modifications in laser/surgical techniques continue to emerge and provide improvement in glaucoma care.

Further reading

Glaucoma: diagnosis and management of chronic open angle glaucoma and ocular hypertension. NICE CG85. April 2009.


Declarations of interest
None to declare.

Mr Azarbod is a fellow in glaucoma, Ms Crawley is a consultant ophthalmologist, Mr Ahmed is a consultant ophthalmologist, Francesca Cordeiro is a UCL professor of retinal neurodegeneration and glaucoma studies and honorary consultant ophthalmologist and Professor Bloom is a consultant ophthalmologist at Western Eye Hospital, Imperial College Healthcare NHS Trust, London.