

Glaucoma

What is glaucoma?

Glaucoma is an eye disease in which the optic nerve becomes damaged, leading to a gradual loss of peripheral vision. If untreated, this can lead to tunnel vision and blindness. The cause is raised fluid pressure in the eyeball (called intraocular pressure).

The commonest form of glaucoma, primary or chronic open angle glaucoma (COAG), is especially dangerous, as there is usually no indication that anything is wrong until significant and irreversible loss of sight has occurred.

Fluid in the eye is constantly produced by a structure called the ciliary body. About 80 per cent escapes by flowing out through filter tubules called the trabecular meshwork into the canal of *Schlemm*, the remainder via the wall of the eye. Pressure rises if fluid outflow is restricted by pressure from the posterior chamber of the eye or by the filter tubules silting up.

Who does glaucoma affect?

Glaucoma affects about two per cent of the over 40s in the European Union, increasing with age to seven per cent by the age of 80. Surveys suggest that some 1.5 million people have the disorder, of whom only half have been detected. A genetic predisposition to develop the disease seems to play a role.

The worldwide prevalence of glaucoma is increasing, due in part to the rapidly aging population. It is estimated that, at the current time, there are more than 60 million people worldwide with glaucoma. About half of the individuals who have glaucoma are not aware of it.

Glaucoma is the second leading cause of blindness in the world, according to the World Health Organisation (WHO). By the year 2020, it is estimated that there will be 11 million individuals who are blind from glaucoma.

Primary angle-closure glaucoma is known to have varying prevalence among different ethnic groups. Certain ethnic populations are at higher risk, such as individuals of African ancestry and certain Asian populations. A particularly high incidence is also seen in Inuit in Canada. For Caucasians, there is a six times greater risk of developing the disorder if a near relative has it. It is responsible in whole or in part for 10 to 15 per cent of people being blind in the EU.

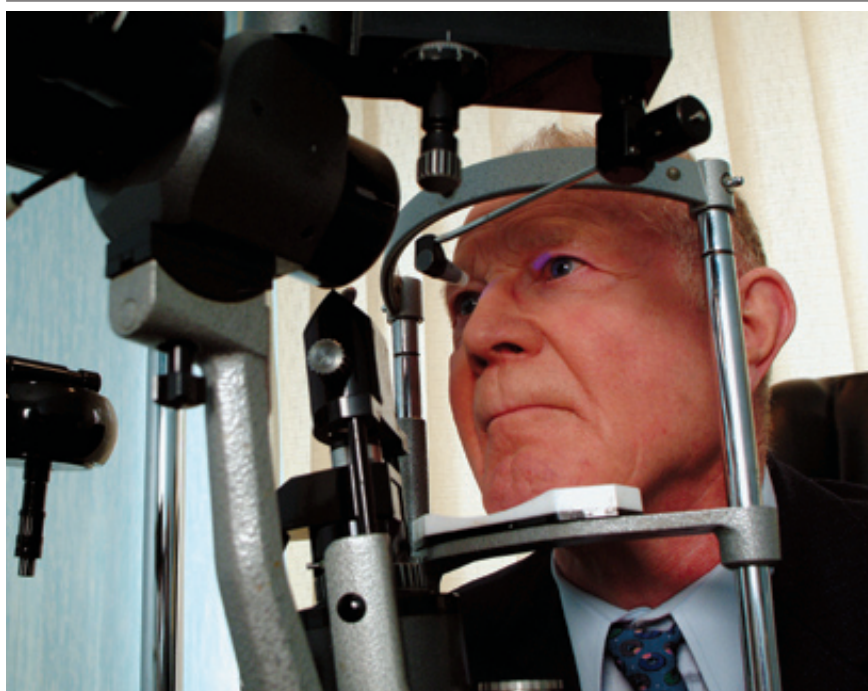
Present treatments

The key to preserving vision is timely diagnosis and treatment, through regular complete eye examinations. Most people with glaucoma require long-term treatment with medicines to reduce intraocular pressure (IOP), usually in the form of eye drops or gel.

Glaucoma is an eye disease in which fluid pressure in the eye damages the optic nerve.

It can lead to blindness.

Over the years, many medicines have been developed to reduce the fluid pressure and help take away the fear of blindness.



A laser operation to open the drainage channels, or surgery to create a new drainage channel through the top of the eyeball, may eventually be necessary, but are not suitable in all cases. The purpose of glaucoma treatment is to allow the patient to maintain his or her independence and quality of life.

Of the medicines developed to reduce intraocular pressure, the carbonic anhydrase inhibitors and the beta-blockers influence pressure by reducing the production of fluid in the eye. By contrast, the 'miotics' which stimulate muscarinic receptors in the ciliary muscle, causing the drainage network to relax and open, and prostaglandin analogues act to increase fluid outflow.

Another class of medicines, the *alpha-2* receptor agonists, acts on nerve endings and both reduces fluid production and increases outflow.

About 50 per cent of glaucoma patients use two or more medicines to control their intraocular pressure (IOP). Prostaglandin analogues are the most prescribed glaucoma products, accounting for more than a third of prescriptions, with beta-blockers following with some 25 per cent of prescriptions.

In clinical studies it has been shown that formulations which combine a prostaglandin analogue with a beta-blocker give the same reduction in IOP as the two used concomitantly, without a significant increase in side-effects. Other combination glaucoma products contain a beta-blocker plus a carbonic anhydrase inhibitor. Combination products reduce dosing frequency and improve compliance in patients who need dual therapy.

What's in the development pipeline?

Further fixed-dose combination products with superior efficacy in reducing IOP are in clinical trials.

Surgical treatment of glaucoma to create a new drainage channel (*trabulectomy*) has the potential to lower intraocular pressure on a long-term basis. However, it is often only temporarily successful, due to the blockage of the ducts by fibrosis through the actions of a natural substance known as transforming growth factor *beta* (TGF β). There is a monoclonal anti-TGF *beta*₂ antibody in Phase 3 trial to reduce the failure rate of glaucoma drainage surgery.

The longer-term future

A much wider range of medicines and surgical options is now available for the treatment of glaucoma and the greatest need in healthcare terms is for increased awareness of the need for screening. Checking for ocular hypertension or open-angle glaucoma is a simple and painless procedure that can easily be done during a routine eye test and is vital for anyone over the age of 40 or with a close relative with this condition.

Results of a population-based study show that long-term use of cholesterol-lowering treatments, including statins, may be associated with a reduced risk of glaucoma among patients with cardiovascular disease.

The use of lipid-lowering compounds known as statins for 24 months or more significantly reduced the risk of developing glaucoma, as did the use of non-statin cholesterol-lowering medicines. However, more investigations are warranted to find out whether these treatments may provide additional therapy for glaucoma.

In July 2003, researchers reported that they had discovered genes related to a predisposition to primary angle glaucoma. The finding – though still preliminary – may help to pave the way for early genetic testing and diagnosis.

Other studies have identified a gene, transforming growth factor- β (TGF- β), as an important factor involved in the pathogenesis of the disease. Elevated amounts of TGF β are found in the aqueous humour of patients with primary open angle glaucoma.

TGF- β has also been shown to elevate intraocular pressure. Preclinical research is being carried out to determine whether blocking TGF- β activity would halt or minimise its adverse consequences. This strategy has already been used to successfully suppress ocular inflammation and fibrosis in an animal model.

Glaucoma results in the programmed cell death of retinal ganglion cells. A number of naturally occurring proteins known as neurotrophic factors have been shown to promote retinal ganglion cell survival and regeneration. The therapeutic use of these molecules is limited due to the loss of effectiveness when they are delivered for prolonged periods.

Researchers try to identify the pathways that are activated by neurotrophic factors. This may lead to new avenues for using neurotrophic factors as effective therapies for glaucoma.

In general, there are several areas of particular focus in glaucoma research: (i) new approaches designed to protect the optic nerve against damage caused by glaucoma, to restore vision lost to glaucoma and eventually reverse blindness by restoring or regenerating the function of the optic nerve cells, and to explore the feasibility of achieving transplantation of optic nerve cells; (ii) research into the genetic causes of the various forms of glaucoma, particularly the identification of the genes responsible, with the long-term goal of finding ways to reverse these genetic defects; and (iii) the use of nanotechnology for monitoring intraocular pressure, diagnosing and monitoring damage to the optic nerve and delivering medicines and other therapies.

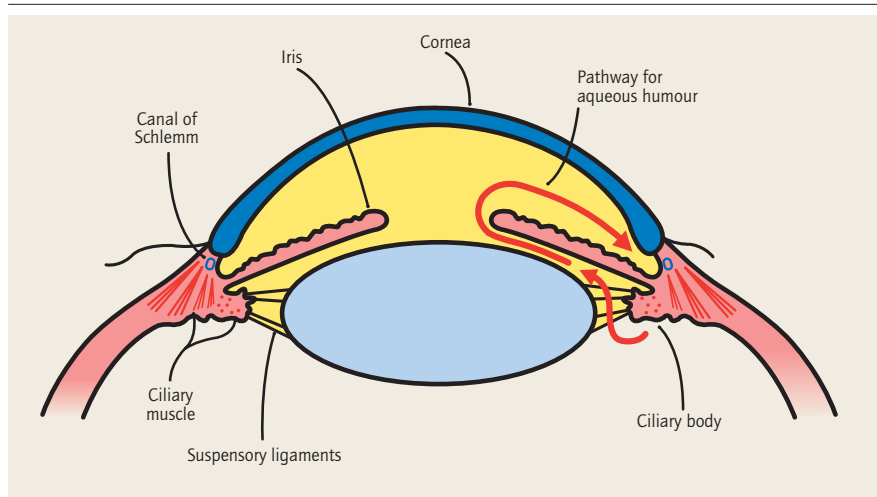


FIGURE 1: The human eye showing the route of fluid flow in relation to the structure

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