



Yesterday

- Glaucoma, a group of sight-threatening diseases that damage the eye's optic nerve, was known to be frequently associated with increased intraocular pressure (IOP), a build up of fluid pressure inside the eye.
- Available glaucoma therapies consisted of antiquated surgeries and pressure reducing drugs. Both treatment modalities had significant side effects and were of uncertain effectiveness.
- Early detection of glaucoma was not possible and treatments were administered late in the disease process.
- Lacking effective methods for early detection and treatment, patients with glaucoma often were not diagnosed until significant, irreversible vision loss had already occurred.
- Glaucoma was a major public health problem and the number one cause of blindness in African Americans

Today

- Approximately 2.2 million Americans have been diagnosed with glaucoma and the prevalence of the disease will rise to a projected 3 million by 2020.
- Thanks to several clinical trial studies sponsored by the National Institutes of Health (NIH), our understanding of glaucoma and its treatment has vastly improved.
- Glaucoma screening and diagnostic techniques have improved considerably, providing more precise visual assessment tests and biologic markers for the disease.
- NIH-sponsored research led to the development of prostaglandins, a new class of drugs that offers excellent IOP control with fewer side effects.
- The Early Manifest Glaucoma Trial (<http://www.nei.nih.gov/earlyglaucoma/>) found that early treatment of open angle glaucoma, the most common form of the disease, with pressure-reducing drugs delayed disease progression.

- The Ocular Hypertension Treatment Study (OHTS) (<http://www.nei.nih.gov/glaucomaeyedrops/>) found that treatment of intraocular pressure with pressure-reducing drugs delayed the onset of glaucoma. This clinical trial also found that certain characteristics such as age, African descent, high eye pressure, the anatomy of the optic nerve, and thinness of the cornea offer valuable prognostic indicators associated with developing glaucoma. These risk factors help clinicians determine which patients will likely go on to develop glaucoma and therefore benefit from pressure-reducing drugs. They also help identify those who do not require therapy, thus creating a substantial health savings.
- The prevalence of glaucoma is three times higher in African Americans than in non-Hispanic Whites. Additionally, the risk of visual impairment is higher and the age of onset is earlier than in Whites. About 70 percent of glaucoma cases are associated with a history of elevated intraocular pressure (IOP). The OHTS also found that early treatment of elevated IOP reduces the risk of developing glaucoma in African Americans.

Tomorrow

- A hallmark of glaucoma is the death of retinal ganglion cells (RGCs) in the optic nerve, which can lead to catastrophic vision loss. Current research is focused on developing neuroprotective therapies that protect RGCs in the optic nerve.
- Recent research suggests that increased intraocular pressure may prevent RGCs from receiving brain-derived neurotrophic factor (BDNF), a protein that is crucial to RGC survival, from neighboring cells in the optic nerve.
- NIH-supported researchers are using gene therapy to provide a lasting and direct supply of the BDNF protein in a rodent model of glaucoma.
- Another novel treatment approach involves implantable, biodegradable microspheres that contain glial-derived neurotrophic factor (GDNF), a protein known to promote neuronal cell survival. These

spheres delayed RGC loss in a rodent model of glaucoma.

- In still another novel neuroprotective approach, the drug phenytoin was able to prevent the cascade of biologic events that leads to RGC death in a rodent model.
- NIH recently launched the National Eye Institute Human Genetics Collaboration (NEIGHBOR) (http://www.nei.nih.gov/news/statements/glaucoma_initiatives.asp) and the Gene-Environment Interactions in Glaucoma (GLAUGEN) (http://www.nei.nih.gov/news/statements/glaucoma_initiatives.asp) initiatives to identify risk factors that influence the disease. NEIGHBOR is a consortium of 22 investigators at 12 institutions that will perform and analyze genome wide scans of 4000 people with and without glaucoma to identify genetic variants associated with the disease. The GLAUGEN consortium will collect data from 2400 individuals with and without glaucoma to examine the relationship between genes and environment. Identifying these risk factors will provide better clues into the underlying biological mechanisms that spur glaucoma.
- Recent research is providing a much better understanding of how increased IOP leads to optic nerve damage. A neurosignaling substance known as tumor necrosis factor-alpha was recently found to mediate pathology related to glaucoma. Blocking its presence reduced optic nerve damage in animal models of elevated IOP.
- Nerve cell regeneration is another approach to repairing neuronal tissue damaged by disease or injury. NIH-supported researchers recently provoked nerve cell regeneration in rodents by activating a nerve cell's natural growth capacity and using gene therapy to suppress the effects of growth-inhibiting factors.
- These and other promising therapeutic approaches may further improve the treatment of glaucoma and our ability to prevent vision loss.

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