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REPORTER'S FILE

A New Understanding of Glaucoma

By PETER JARET

For years, [glaucoma](#) was defined as elevated pressure within the eye that leads to vision loss. And for years experts knew there were glaring gaps in that definition. Many people with abnormally high intraocular pressure never develop glaucoma. As many as one in three people who do get the disease have normal or even low pressure.

As researchers have tried to resolve those contradictions, a new paradigm for understanding glaucoma has emerged. Glaucoma isn't simply an eye disease, experts now say, but rather a degenerative nerve disorder, not unlike [Alzheimer's](#) or [Parkinson's disease](#).

"All three of these diseases affect aging populations and involve selective loss of certain populations of neurons," said Dr. Neeru Gupta, a professor of ophthalmology and director of the glaucoma unit at the University of Toronto. "Parkinson's affects motor control. Alzheimer's affects cognition. Glaucoma disrupts vision. But the closer we look, the more they seem to have in common."

Even the official definition of glaucoma, a disease that accounts for more than eight million cases of [blindness](#) worldwide, has changed. Today, diagnosis is based on just two features: visible damage to the optic nerve, which leads from the retina at the back of the eye to the brain, and loss of peripheral vision, which can be measured by a simple test in an eye doctor's office.

"Intraocular pressure is nowhere to be found in the definition, which shows you how the field has changed," said Dr. Stuart McKinnon, an associate professor of ophthalmology and neurobiology at [Duke University](#) School of Medicine.

Researchers still recognize high pressure within the eye as a leading risk factor for glaucoma. And ophthalmologists still use the familiar screening test that shoots a puff of air at the front of the eye to measure pressure and screen for the disease. But since about 30 percent of people with the disease have normal or low pressure, there's obviously something else at work.

What's clear is that glaucoma begins with injury to the optic nerve as it exits the back of the eye. The damage then spreads, moving from one nerve cell to adjoining nerve cells. "In glaucoma, we've shown that when your retinal ganglion cells are sick, the long axons that project from the eye into the brain are also affected, resulting in changes that we can detect in the vision center of the brain," Dr. Gupta said. The phenomenon, called transsynaptic damage, occurs in Alzheimer's and

Parkinson's disease as well.

Experts are still deciphering what causes initial injury to the optic nerve. Although elevated intraocular pressure clearly increases the danger, some researchers suspect that steep fluctuations in pressure may be even more damaging.

“A structure in the optic nerve called the lamina cribosa is designed to act like a trampoline, going up and down in response to normal changing pressure,” said Dr. Rohit Varma, director of the glaucoma service at Keck School of Medicine at the [University of Southern California](#). “But if those fluctuations become extreme enough, they may end up injuring the optic nerve.”

Another culprit may be perfusion pressure, or the difference between pressure within the eye and overall [blood pressure](#). Low perfusion pressure occurs when pressure within the eye is high and systemic blood pressure is low. “When perfusion pressure drops, there's not enough blood flow getting to the optic nerve and the retina,” Dr. Varma said. Lack of adequate blood flow may damage not only the optic nerve but also supporting tissues around it.

Then again, some people may have optic nerves that are simply more or less vulnerable to a variety of stresses, experts say.

That possibility has led to a search for drugs to protect susceptible nerves from injury. Several promising candidates are under investigation, including a drug called memantine (Namenda), which is now approved to treat Alzheimer's, and riluzole (Rilutek), used to treat [Lou Gehrig's disease](#).

There is growing optimism that what works for one neurodegenerative disease, as these examples suggest, may be helpful for others. For researchers trying to understand the details of what goes wrong in such disorders, glaucoma may offer an easier model to study than a brain disease like Alzheimer's. The optic nerve is the only nerve that can be examined visually, by peering through the pupil. And the visual system is a relatively compact structure that researchers already understand in great detail.

For now, the only treatments available for glaucoma work by lowering pressure in the eye, either by decreasing the production of fluid or increasing its outflow. Even in patients with normal intraocular pressure and early signs of the disease, lowering pressure has been shown to significantly slow the progression of nerve damage. Most antiglaucoma drugs are delivered as eye drops, which may need to be used once or several times a day. When drops aren't enough, laser treatments and surgery can be used to allow excess fluid to flow out of the eyes.

Despite effective treatments, many people suffer some preventable loss of peripheral vision. One problem is that the disease too often goes undetected. About half of the estimated 2.2 million Americans with glaucoma are not aware that their vision is at risk because they have not been tested, surveys suggest. The longer the disease goes untreated, the greater the loss of vision. Worldwide, an estimated 60 million people have glaucoma, and that number is expected to reach 80 million by 2020.

Another hurdle is getting patients who know they have glaucoma to take their medicine. “Glaucoma is typically diagnosed before patients notice any [vision problems](#),” said Dr. Robert C. Cykiert, clinical assistant professor of ophthalmology at the Langone Medical Center at [New York University](#). “So telling them they

could go blind if they don't use their eye drops is like telling someone with high [cholesterol](#) that they could have a [heart attack](#) if they don't take a statin. A lot of people don't take the threat seriously enough."

A 2003 study found that half of patients in a health maintenance organization never filled their initial prescription for eye drops. One in four patients failed to refill their [prescriptions](#) a second time, another survey found, even though eye drops need to be used every day to be effective.

While scientists search for better treatments for glaucoma, the second-leading cause of blindness, people can take action to give themselves the best chance: get a regular glaucoma screening exam, and if glaucoma is diagnosed, take the treatment regimen seriously. Your sight depends on it.

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