Due to budget cuts in the ophtho department, all our white coats will be marked with corporate logos.

Is that one mine?

No, sorry …

I'm afraid Nike, Reebok, and Adidas have already been claimed by the senior doctors.

What's left?

Would you prefer Viagra, Valtrex, or Monistat-7?

Crud!
Glaucoma is a disease where the optic nerve dies. We are not sure why or how this happens (there are many mechanical, vascular, and biochemical theories) but high intraocular pressure certainly seems to be associated, if not entirely the cause of optic nerve death. Glaucoma is one of the leading causes of preventable blindness in the U.S., and patients with acute glaucoma can develop irreversible vision loss within a few hours, so it is important that you understand how this disease works and recognize it in your patients.

The Aqueous Pathway
Before continuing we should review the pathway of aqueous humor flow. Aqueous is the fluid that fills the front part of the eye, and it is important for maintaining the shape of the eye and providing nourishment for the avascular lens and cornea. Aqueous humor is first produced by the ciliary body within the posterior chamber. After filling the posterior chamber, aqueous moves forward around the lens and flows through the pupil into the anterior chamber. As the anterior chamber fills, the aqueous spreads outwards into the angle formed by the iris and cornea. Within this irido-corneal angle the aqueous exits the eye by filtering through the trabecular meshwork into the Canal of Schlemm, where it returns back into the blood circulation. The pressure within the eye is maintained by this steady state of aqueous production and egress, and it is an imbalance in this equilibrium that causes the increased pressure associated with glaucoma.

Open vs. Closed-Angle Glaucoma
There are two categories of glaucoma and they have very different mechanisms. Open-angle glaucoma is the most common type in our country. It occurs from blocked aqueous drainage caused by an unidentified dysfunction or microscopic clogging of the trabecular meshwork. This leads to chronically elevated eye pressure, and over many years, gradual vision loss.

This differs from closed-angle glaucoma, also called “acute glaucoma,” which occurs when the angle between the cornea and iris closes abruptly. With this closure, aqueous fluid can’t access the drainage pathway entirely, causing
ocular pressure to increase rapidly. This is an ophthalmological emergency and patients can lose all vision in their eye within hours.

Let’s examine each of these types of glaucoma in more detail.

**Open-Angle Glaucoma**

The majority of glaucoma patients (about 80%) have chronic open angle glaucoma. Most patients are over the age of 40. This condition is more common in African Americans, but really anyone can get it. The major risk factors are family history, age, race, high eye pressure, and large vertical nerve cupping. More recently, thin-corneas have been found to be a major risk factor, though this mechanism is not well understood.

The underlying mechanism for open-angle glaucoma involves degeneration of the trabecular meshwork filter, usually by unknown causes, that leads to aqueous backup and chronically elevated eye pressure. With prolonged high pressure, the ganglion nerves in the retina (the same nerves that form the optic nerve) atrophy. The exact mechanism for this nerve damage is poorly understood and proposed mechanisms include stretching, vascular compromise, and glutamate transmitter pathways. As the ganglion nerves are progressively destroyed, vision is gradually lost.

Open-angle glaucoma has the reputation of being the "sneaky thief of sight" because the visual loss occurs so slowly that many patients don’t realize they have the disease until it is far advanced.

Because the disease is otherwise asymptomatic, detecting open-angle glaucoma requires early pressure screening.

**Presentation**

Open-angle glaucoma patients usually present with three exam findings: elevated eye pressure, optic disk changes, and repeatable visual field loss patterns.

1. **Pressure:** The gold standard for measuring eye pressure is with the Goldman applanation tonometer. This is a device mounted on the slit-lamp that measures the force required to flatten a fixed area of the cornea. Normal pressures range from 10 to 22 mm Hg. Keep
in mind that eye pressure can fluctuate throughout the day (typically highest in the morning) so the pressure should be checked with each visit and the time of measurement should be noted. Also, some glaucomatous eyes have a “normal” pressure. In other words, a “good pressure” doesn’t rule out glaucoma, nor does a high pressure necessarily indicate glaucoma.

You can also measure pressure with a device called a “Tono-Pen.” This expensive little gadget is handy for bed-bound patients and down in the emergency room, though it’s inaccurate in the wrong hands!

**Corneal Thickness can affect your pressure measurement:**

When we measure the pressure in the eye, we are actually measuring how much resistance we get when pressing on the cornea. This is analogous to kicking a car-tire with your foot or pressing your hand against a bicycle tire to estimate how much air pressure is inside. We do the same thing with the Goldman applanation tonometer mounted on the slit-lamp - we measure how much force it takes to flatten a 3mm diameter area of corneal surface.

The pressure measurements on the Goldman were calibrated using an average corneal thickness of approximately 540 microns. However, some patients have very thin or thick corneas. I like to describe these as “thin bicycle” or “thick truck-tire” corneas. When you press on a thick cornea (a truck-tire cornea) the pressure will seem higher than it really is! This makes sense … if you kick a flat truck-tire, it will still hurt your foot because that rubber is so darn thick. The opposite is true for thin corneas - they feel squishy no matter how much pressure is inside.

Knowing corneal thickness is important in a glaucoma clinic so we can calibrate the accuracy of our pressure readings. This is why we always check corneal thickness with an ultrasonic pachymeter on the first visit.
2. **Fundus Exam:** The optic disk looks striking in advanced glaucoma. In normal patients, the optic disk has a physiological indentation or “cup” that is less than one-third the disk diameter. With glaucoma, the ganglion nerve layer slowly dies away, and, as fewer ganglion nerves course through the optic disk, the amount of cupping increases. A cup to disk ratio greater than 0.5 or an asymmetry between the eyes suggests ganglion atrophy caused by glaucoma.

![Diagram of optic disk and neural rim]

**The I.S.N.T. Rule**

When you look at your patient’s optic nerve, you’ll notice that the cup doesn’t sit directly in the middle of the disk. The cup is slightly off-center – this makes sense as the optic nerve enters the back of the eyeball at an angle.

The space between the inner cup and surrounding disk is called the neural rim and is comprised of the actual retinal ganglion nerves. In a normal eye, this rim follows the ISNT rule of decreasing thickness … meaning that the Inferior rim is thickest while the Temporal rim is the skinniest.

![Diagram showing normal and abnormal neural rim]

With glaucoma, you often see vertical thinning and notching of the inferior and superior rims. This deviation from the ISNT rule is another clue that glaucoma might be killing off the nerve. You can also see undermining of the rim (as in the illustration on the right) where the blood vessels dive out of view under the rim edge.

3. **Visual Loss:** The vision loss from chronic glaucoma occurs in characteristic patterns that can be followed by automated perimetry (machines that map out the peripheral vision). The central vision is typically spared – in fact, late stage patients may have 20/20 central vision, but be otherwise legally blind because of peripheral blindness.
Treatment:
Since IOP (intraocular pressure) is the only risk factor we can treat, the primary treatment of glaucoma focuses on decreasing eye pressure to less than 20 mm Hg or even lower, depending upon the severity of disease. Treatment may be either medical or surgical.

Medical Treatment
Topical beta-blockers are the traditional therapy for these patients and have been around for decades. Beta-blockers work by decreasing aqueous humor production at the ciliary body. Unfortunately, systemic side effects can occur from nasal absorption, making it especially important to ask your patients about history of asthma, COPD, and cardiac problems.

These days, many physicians are using newer drugs like topical CAIs, alpha-agonists, and prostaglandin analogues for first-line therapy, as they have fewer systemic side effects.

Prostaglandin analogues like latanoprost (Xalatan™) are the newest of these glaucoma drugs, and they are very popular as a first-line agent. They work by increasing aqueous humor outflow. They do have some side effects, though. They can make eyelashes grow longer (many patients actually like this), and in a few patients may darken the iris color, turning green and blue eyes brown.
Surgical Treatment for Chronic Glaucoma

If eyedrops aren’t working, there are several surgical techniques available to relieve eye pressure. One common surgery is the trabeculectomy, where an alternate drainage pathway is surgically created. A small hole is cut through the superior limbus, so that aqueous can drain under the conjunctiva. This can be very effective in decreasing pressure. However, if the patient is a rapid healer the conjunctiva can scar down, so anti-metabolites like mitomycin-C are often applied to the site. If this surgery doesn’t work, a plastic tube-shunt can be inserted into the anterior chamber that drains to a plate fixed under the conjunctiva further back behind the eye.

Several laser procedures can also help to release pressure. Argon laser trabeculoplasty (ALT) can be used to burn portions of the trabecular meshwork itself. The resulting scarring opens up the meshwork and increases outflow. A laser can also be used to burn the ciliary body to decrease aqueous production at its source, but this is usually a last resort.

Acute Glaucoma

Acute glaucoma is a medical emergency. The most common mechanism is pupillary block. This occurs when the lens plasters up against the back of the iris, blocking aqueous flow through the pupil. This resistance produces a pressure gradient (this is a good buzz word to memorize) across the iris that forces the iris and lens to move anteriorly. When the iris moves forward, the irido-corneal angle closes, blocking the trabecular meshwork. Without an exit pathway, aqueous fluid builds up, eye pressure increases rapidly, and the optic nerve is damaged from stretching and decreased blood supply.

This sequence of events can occur for many reasons, and people with naturally shallow anterior chambers such as hyperopes (far-sighted people with small eyes) and Asians are predisposed to developing angle closure. One inciting condition that is typical in acute glaucoma is pupil dilation -- many patients describe onset of their symptoms occurring while in the dark or during stressful situations. When the iris dilates, the iris muscle gets thicker and the irido-corneal angle becomes smaller, making it more likely to spontaneously close. Along those lines, medications that dilate the eye, such as over-the-counter antihistamines and cold medications, also predispose angle closure.
Presentation
A patient in the middle of an acute glaucoma attack will present with an extremely red and painful eye, often complaining of nausea and vomiting. On exam, you’ll find their pupil sluggish and mid-dilated. Pressures in the affected eye can be very high, often 60 mm Hg or higher. The eye will feel rock hard, and you can actually palpate the difference between the eyes with your fingers. One classic sign that patients often describe is seeing halos around lights. This occurs because the cornea swells as water is pushed under high pressure through the endothelium into the corneal stroma. This corneal swelling also makes it hard for you to see into the eye, further complicating diagnosis and treatment.

Acute Glaucoma Exam Techniques:
Ophthalmologic examination for acute glaucoma involves measuring the eye pressure, accessing the anterior chamber angle, and a fundus exam.

One trick to determine whether an angle is shallow is to shine a simple penlight across the eyes. If the iris is pushed forward, it will cast a shadow. Additionally, an ophthalmologist can visualize the angle directly through gonioscopy. Here’s how it works:

Gonioscopy:
Normally, the inner “iris-cornea angle” cannot be seen with a microscope because the cornea-air interface creates “total internal reflection.” However, we can use a goniolens, which is a special glass lens with mirrors on its sides, to look directly at the angle. When the glass lens is placed directly onto the cornea, the cornea-air interface reflection is broken and light from the angle can escape and be seen through the mirrors.
Acute Glaucoma Treatment

In cases of acute glaucoma, you want to decrease the pressure in the eye as quickly as possible. A "kitchen sink" approach is often used, throwing many treatments on at once. You can decrease aqueous production using a topical beta-blocker like Timolol and a carbonic anhydrase inhibitor like Diamox. Also, osmotic agents such as oral glycerin or IV mannitol (even ethanol, in a bind) can be given systemically to draw fluid out of the eye and back into the bloodstream. Finally, a miotic such as pilocarpine may be helpful in certain cases to constrict the pupil and thus open up the outflow angle. You can also use topical glycerin to transiently dehydrate/clear the cornea to aid with examination.

Ultimately, these patients need surgical treatment to avoid recurrence of their angle closure. A high intensity laser can burn a hole through the iris and create a communication between the posterior and anterior chambers. This relieves the pressure gradient (there’s that buzzword again!) across the iris, and allows it to move back into a normal position. The trabecular meshwork then opens and allows aqueous fluid to flow freely out of the eye. This laser procedure is typically performed on both eyes because these patients are predisposed to having attacks in the other eye as well.

Other types of glaucoma

1. Neovascular Glaucoma:
This can occur in diabetic patients or those with a retinal vein occlusion. VEGF production from areas of ischemic retina can float forward through the...
pupil and promote neovascularization of the iris. In the early stages, a fibrous membrane forms on the iris-cornea angle that blocks outflow and forms an open-angle glaucoma. At later stages of neovascularization, the new vessels actually pull the iris forward and cause a closed angle glaucoma that is essentially irreversible. You treat this by lasering the peripheral retina to decrease the angiogenic VEGF production and decrease the rate of neovascularization. Neovascular glaucoma is very hard to treat and most of these patients end up needing a surgical intervention like a tube-shunt.

2. Pigment Dispersion Syndrome (PDS):
This occurs when the pigmented back surface of the iris rubs against the radial zonules supporting the lens. Little flecks of pigment are shed into the aqueous and end up clogging the trabecular meshwork drain. This process usually occurs in young white males with myopic eyes. They suffer from attacks of high pressure after exercise when pigment gets rubbed off and temporarily blocks the trabecular drain. You can see this pigment in the trabecular meshwork on gonioscopy, and even find trans-illumination defects of the iris at the slit-lamp.

Some of the pigment will stick to the inner-corneal surface, and because of convection currents in the aqueous, form a vertical line of pigment on the inner corneal surface called a Krukenberg spindle.

3. Pseudoexfoliation Syndrome (PXF)
In this systemic condition, basement membrane-like material is deposited throughout the body. This material adheres to the anterior lens capsule, creating a rough surface. As the overlying iris dilates and contracts with daily activity, pigment is rubbed off and clogs the trabecular drain. These patients also suffer from zonular instability, making cataract operations difficult.

Summary
That is glaucoma in a nutshell. Chronic, open-angle glaucoma is very common (in this country) and leads to gradual vision loss, while acute closed-angle glaucoma is infrequent but an emergency that needs urgent treatment to avoid blindness.

It’s just as we feared, Superman. You’ve got optic nerves of steel!
1. What is glaucoma? What actually causes damage to the neurons and optic nerve with glaucoma?
Nobody is sure exactly “what glaucoma is” but at its most basic, glaucoma is gradual death of the optic nerve. If anyone asks you for the definitive definition (or if a glaucoma specialist corners you), just say “nobody knows” or “death of the optic nerve.” If you say “high pressure” you’ll be laughed at (glaucoma specialists are odd ducks). The optic nerve damage arises from pressure, stretching, sheer forces, vascular compromise, or some kind of hormone regulator - we’re not sure of the exact mechanism.

2. What is the flow-pathway for aqueous fluid? Where is it made, and where does it leave the eye?
Aqueous is first produced by the ciliary body. It then flows forward through the pupil into the anterior chamber. Finally, aqueous drains through the trabecular meshwork and back into the venous system via the Canal of Schlemm.

3. What’s the difference between open-angle and closed-angle glaucoma? How about chronic versus acute glaucoma?
Open angle is a common, chronic condition where aqueous drainage is impaired. Closed-angle glaucoma is caused by acute closure of the irido-corneal angle leading to blockage of ALL aqueous drainage – an ophthalmologic emergency that can quickly lead to blindness.

4. What are the risk factors for developing primary open-angle glaucoma?
This is an important list and since I glossed over them in the chapter, here they are again:
- High intraocular pressure (obviously)
- Age
- Family history
- Race (African American and Hispanics)
- Suspicious optic nerve appearance (large vertical cupping)
- Thin central corneal thickness (** remember this one!)
There are other possible risk factors, but I’d focus on those listed above. These risk factors explain why we always ask our patients about familial history and why we check pachymetry (corneal thickness by ultrasound) on the first glaucoma visit.

5. What do we measure to monitor and follow progression in glaucoma patients?
We generally check three things: pressure, disk changes by photograph, and visual fields. Good stereo slides are difficult to obtain, so many doctors use other imaging modalities like HRT or OCT.

6. What does corneal thickness have to do with glaucoma (as far as risk for developing glaucoma)?
The OHTS clinical trial showed that people with thin corneas are at higher risk for developing glaucoma, independent of other risk factors. We’re not sure why, but it’s believed that people with thin corneas are anatomically predisposed to optic nerve damage. We measure corneal thickness using a small ultrasound probe (this is called pachymetry) with all new glaucoma patients.

7. What’s a normal eye pressure? Does a patient with pressure of 14 have glaucoma?
About 10 to 22. While glaucoma is classically associated with high pressure, there is a significant minority of patients with glaucoma who actually have “normal” pressure. Also, pressure fluctuates throughout the day so we typically write down the time in our notes. Some studies have noted higher rates of glaucoma in people with large diurnal shifts in eye-pressure.

8. A glaucoma suspect is found on first visit to have a pressure of 19. Her corneal thickness, however, measures only 450 microns. Do you think her actual eye pressure is HIGHER or LOWER than 19?
Definitely higher. This patient has thin “bicycle-tires corneas” that “feel soft” when measured by the Goldman applanation. This woman’s corrected pressure is probably well over 22, increasing her risk for glaucomatous progression.

9. What kind of vision loss occurs with glaucoma?
Typically loss of eyesight occurs in the periphery where it is less noticeable. Scotomas (areas of visual field loss) in glaucoma tend to follow certain patterns that start in the mid-periphery. Many patients don’t notice visual symptoms until the disease is far progressed. Generally, the central vision is spared until very late stages of glaucoma.
10. Why can’t you see the trabecular meshwork with the slit-lamp microscope?
This area is hard to see because the trabecular drain is tucked in the “angle” formed by the iris and inner cornea. We can’t see this area directly because of “total internal reflection” at the cornea-air interface. Gonioscopy allows direct visualization of the trabecular meshwork by interrupting the cornea-air interface with a glass lens.

11. What mechanisms do the glaucoma drops use to decrease pressure?
Drops either decrease the amount of aqueous produced at the ciliary body or increase the aqueous outflow from the eye (generally via the uveal-scleral pathway or by direct improvement of trabecular meshwork outflow).

12. What retinal findings do you see with glaucoma?
You see increased cupping of the optic disk, usually in a vertical pattern that goes against the ISNT rule. You can sometimes see hemorrhages at the disk and “undermining” of the blood vessels as they exit the disk.

13. How can diabetes cause acute glaucoma?
Retinal ischemia can produce VEGF. As this molecule floats forward it can cause neovascularization of the iris, forming vascular membranes that cover the trabecular meshwork and clog the drainage angle. This leads to a severe neovascular glaucoma that is hard to manage.

14. You have a patient who appears to have a shallow anterior chambers and occludable angles. Would you use pilocarpine?
In most cases, yes. Pilocarpine will constrict the pupils -- by flattening the iris you potentially open up the drainage angle next to the trabecular meshwork. Pilocarpine will also decrease pressure in the eye by affecting aqueous production and egress. You probably wouldn’t use it long term in patients with occludable angles though, as pilo has a lot of side effects such as headache and blurry vision. Ultimately, anyone with occludable angles needs a laser peripheral iridotomy to equalize the pressure between anterior and posterior chambers.
“The earrings were daring, but that nose-ring is too much!”