



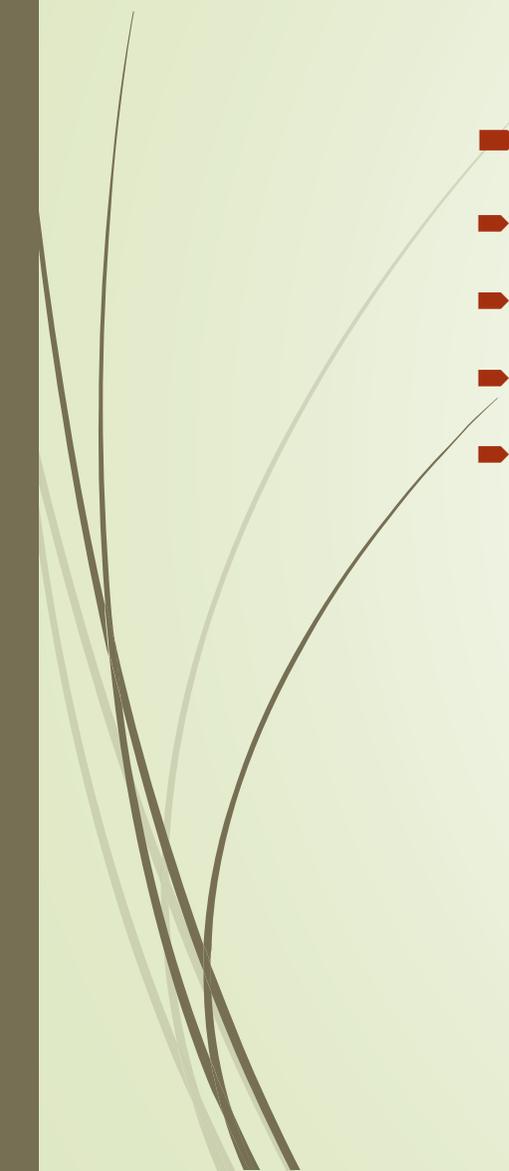


Glaucoma and diabetes

- The term glaucoma refers to a heterogeneous group of ocular disorders that share in common a characteristic optic neuropathy with corresponding visual field defects.

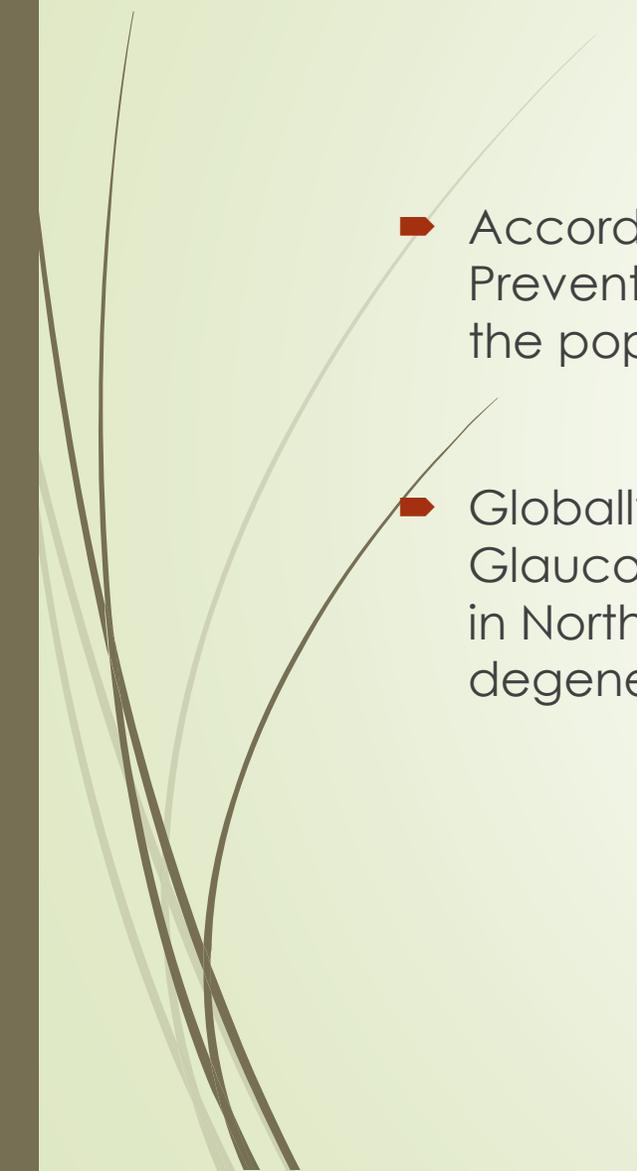


► **There are several subtypes of glaucoma including:**

- primary open-angle glaucoma (POAG)
 - secondary open-angle glaucoma (SOAG)
 - primary angle-closure glaucoma (PACG)
 - secondary angle-closure glaucoma, including neovascular glaucoma (NVG); congenital glaucoma; and juvenile open-angle glaucoma (JOAG).
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- ▶ These subtypes differ in terms of risk factors and pathophysiology, but untreated, the natural history of the disease may lead to irreversible blindness.
 - ▶ Reducing intraocular pressure (IOP) remains the only proven treatment to slow or prevent progression of visual loss.
 - ▶ This can be accomplished pharmacologically with topical and oral medications to decrease aqueous humor production or improve outflow, and when necessary, laser or surgical therapy.

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- ▶ Glaucoma and diabetes mellitus are two groups of diseases that result in significant public health burden and the management of glaucomatous disease in a patient with diabetes may be complex.
 - ▶ An understanding of potential interactions related to the coexistence of glaucoma and diabetes in the same patient by the ophthalmologist and primary care physician is very important to appropriately prevent serious ocular and systemic sequel.

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- ▶ According to figures from the Centers for Disease Control and Prevention (CDC), an estimated 29.1 million Americans (9.3% of the population) had diabetes in 2012 .
 - ▶ Globally, an estimated 347 million people suffer from diabetes. Glaucoma is the second leading cause of irreversible blindness in North America, trailing only age-related macular degeneration .

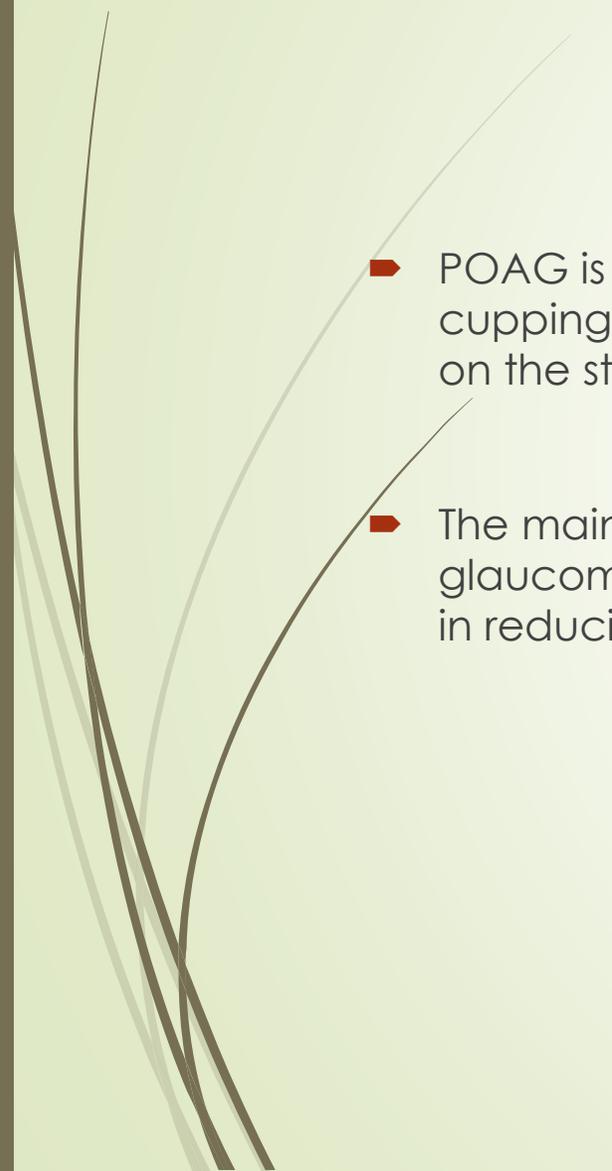
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- ▶ Worldwide, the estimated prevalence of glaucoma in 2010 was 60.5 million people and is expected to increase to nearly 80 million by 2020.
 - ▶ Diabetes mellitus has been implicated as a risk factor for the progression of POAG and the development of secondary angle-closure glaucoma caused by neovascularization of the iris and the anterior chamber angle and, thus, these two types of glaucoma will be the focus of this chapter.



Diabetes and primary open-angle glaucoma

- ▶ POAG is by far the most prevalent form of glaucoma globally and is frequently undetected and untreated, with estimates of up to 50% of patients with POAG unaware that they have the condition .
- ▶ This lack of disease recognition often results from the fact that POAG is, in the vast majority of cases, an asymptomatic disease until a late stage, when irreversible vision loss can occur over a short period of time.

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- ▶ As many as 50% of retinal ganglion cells may be lost prior to the development of visual field defects and, due to physiologic overlap of visual fields from both eyes, these early defects are rarely noticed by patients.
 - ▶ Thus, screening of at-risk populations is critically important in preventing vision loss.
 - ▶ Numerous epidemiologic studies have shown several consistent risk factors, including old age, family history, African heritage, high intraocular pressure, and low corneal thickness.

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- ▶ POAG is diagnosed by the presence of characteristic optic nerve cupping, often with corresponding visual field defects depending on the stage at diagnosis.
 - ▶ The mainstay of treatment for POAG as with other forms of glaucoma is IOP lowering, which has been shown to be effective in reducing the rate of glaucoma progression.



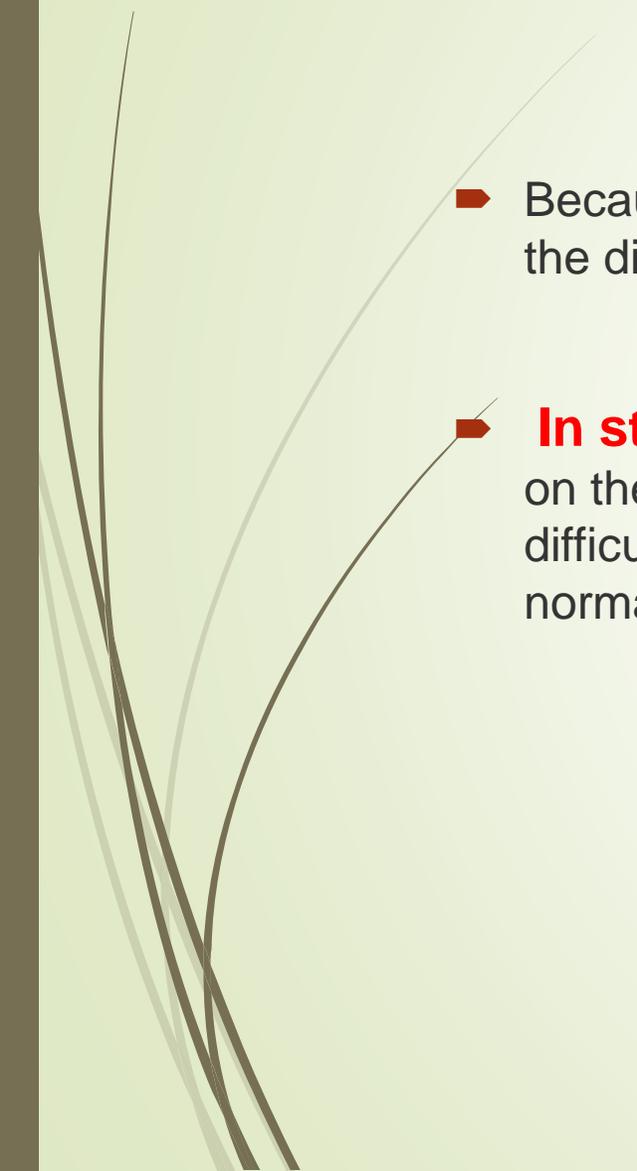
neovascular glaucoma

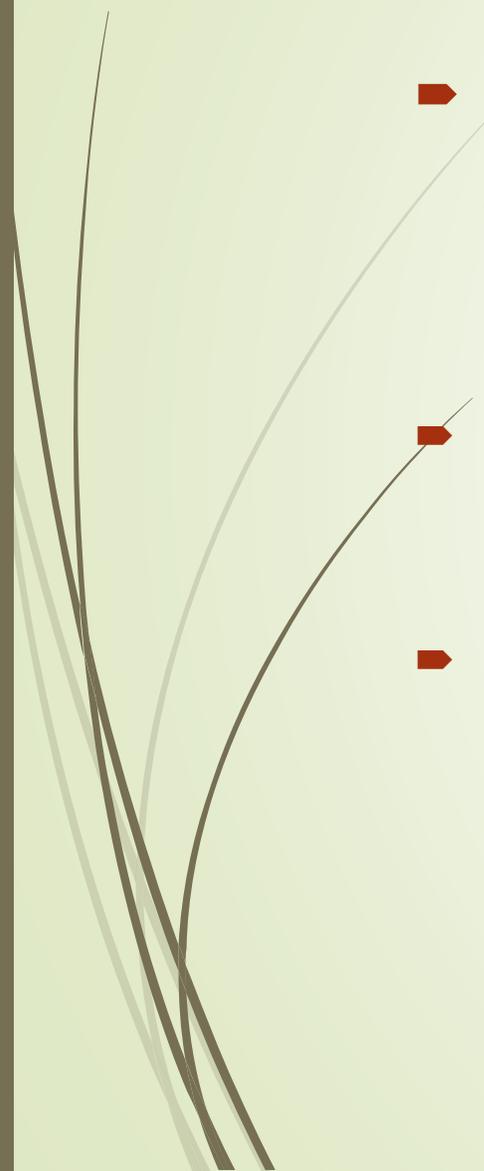
- ▶ **neovascular glaucoma** is a secondary glaucoma usually associated with severe retinal hypoxia.
- ▶ Most eyes suffering from this condition have ischemic changes, although about 3 percent of cases are associated with inflammation without ischemia.¹
- ▶ How we treat these patients depends on the cause of the ischemia, the stage of the disease and the individual's visual potential.

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- ▶ Potential causes of neovascular glaucoma include diabetic retinopathy; central retinal vein occlusion; branch retinal vein occlusion; ocular ischemic syndrome; tumors; chronic inflammation; chronic retinal detachment; and radiation retinopathy.
 - ▶ **(The most common causes are diabetes, CRVO and BRVO.)**

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- ▶ Retinal ischemia triggers the release of vasoproliferative factors, including vascular endothelial growth factor, fibroblast growth factor and interleukin-6.
 - ▶ VEGF promotes the formation of fenestrations in new, immature vessels, allowing vascular hyperpermeability and increasing the level of inflammatory mediators in the eye; this may cause pain, independent of intraocular pressure

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- ▶ As vasoproliferative factors diffuse anteriorly from the retina to the anterior segment, fibrovascular proliferation in the angle causes obstruction of the trabecular meshwork and progressive synechial closure of the angle.
 - ▶ The inevitable rise in IOP leads to **neovascular glaucoma**

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- ▶ Because the impact of the disease evolves over time, it's important to stage the disease when you encounter it.
 - ▶ **In stage 1**, neovascularization occurs on the iris. You'll see tufts of vessels on the anterior iris, usually at the pupillary margin. (Note: These may be difficult to see in dark irides.) Because the angle is unaffected, the IOP is normal at this stage of the disease.

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- **In stage 2**, secondary glaucoma develops. Abnormal blood vessels now extend to the angle, causing fibro-blastic membranes to form there, blocking the trabecular meshwork—but without synechial closure.
 - At this stage the angle still appears to be open, but intraocular pressure begins to rise.
 - (Unfortunately, it tends to remain elevated, even if you achieve regression of the neovascularization.)

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- **Stage 3** is marked by secondary angle-closure glaucoma.
 - The myofibroblasts formed by the abnormal blood vessels contract, leading to synechial closure of the angle and elevated IOP.

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- When managing a patient with neovascular glaucoma you need to address at least four things that will affect whether the patient retains or loses vision:
 - presence of abnormal blood vessels;
 - excessive VEGF factor inside the eye;
 - inflammation;
 - (depending on the stage of the disease) elevated intraocular pressure.



Regression of abnormal blood vessels

- ▶ To address this part of the disease we inject intravitreal anti-VEGF therapy, usually bevacizumab (Avastin) or ranibizumab (Lucentis).
- ▶ The neovascular growth will not disappear, but it will collapse within a few days to a week after injection as a result of diminished vascular permeability.
- ▶ The anti-VEGF agents also help by decreasing the pain associated with the inflammation that accompanies the disease, independent of making the blood vessels go away. (Unfortunately, these drugs only have a transient impact, so repeat injections may be necessary).



Addressing the ischemic drive to neovascularization and reducing inflammation

- The former is best addressed via retinal ablation, whether it's panretinal photocoagulation or cyclocryoablation.
- This will produce a sustained reduction of the ischemic drive that produces the vasoproliferative factors, along with a reduction in the amount of VEGF-producing tissue.
- Topical corticosteroids can be used to reduce inflammation.



Lowering the elevated pressure

- ▶ When treating neovascular glaucoma you also have to treat the elevated IOP. You can do this using medical therapy, including beta blockers, topical or oral carbonic anhydrase inhibitors, alpha-adrenergics or prostaglandin analogues.
- ▶ The prostaglandin analogues are equivocal because they can be pro-inflammatory, but they're often used anyway, trying to prevent a bad situation from becoming worse.
- ▶ Atropine increases uveoscleral outflow and diminishes congestion, helping make the patient more comfortable. You should avoid anticholinergics such as pilocarpine because they can potentiate inflammation.

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- You can also do surgery to treat the high pressure. One option is trabeculectomy, although it's important to note that your results will be much better if you use antimetabolites.
 - At 12 months, in various studies, 66 percent of neovascular glaucoma patients were controlled after trabeculectomy with antimetabolites while only 20 percent were controlled without antimetabolites.

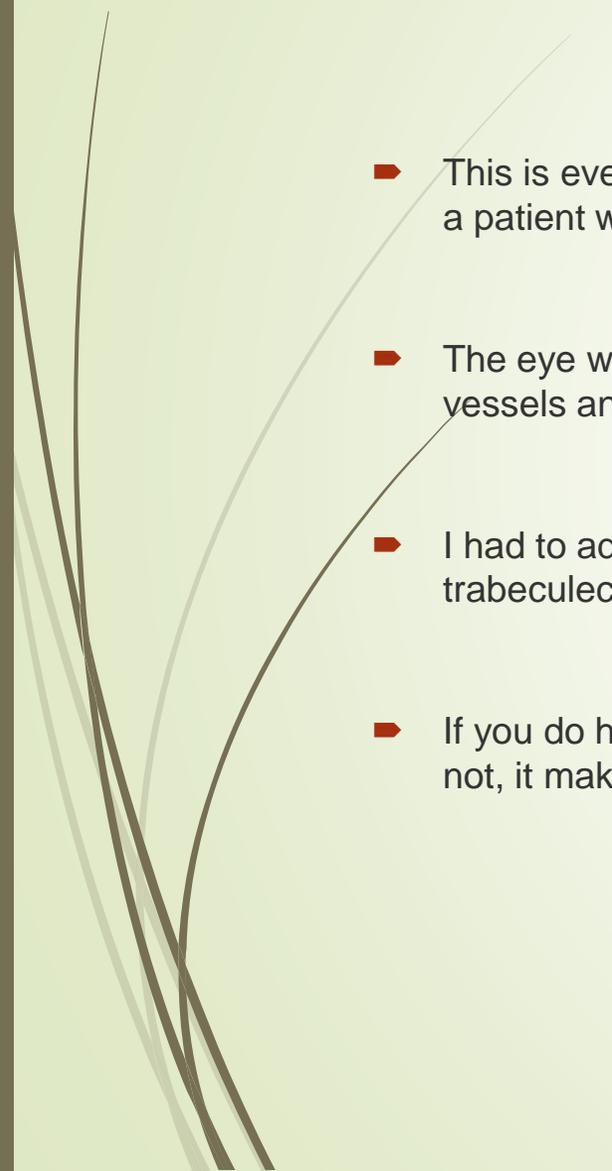
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- Overall, the success rate tends to be poor with trabeculectomy because of the risk of inflammation and the presence of abnormal blood vessels.
 - (Other factors that increase the risk of failure in this situation include being younger than 50 years old, having had a previous vitrectomy, cataract surgery or retinal detachment, and having a lot of blood inside the eye.)
 - There's no question that a neovascular glaucoma patient undergoing trabeculectomy will do better if the eye has controlled inflammation and neovascularization

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- ▶ Another surgical option is to implant a tube shunt.
 - ▶ Many surgeons choose this over trabeculectomy because it's less affected by inflammation, which can cause closure of the trabeculectomy.
 - ▶ shunt control IOP in 60 to 89 percent of these patients for the first year; however, the success rate diminishes to 10 to 46 percent at five years. (The type of tube used—e.g., Molteno, Baerveldt or Ahmed—doesn't seem to affect the success rate.²)



- ▶ The question then becomes, which surgery is best for treating neovascular glaucoma?

- ▶ The Tube vs. Trab study excluded patients with neovascular glaucoma; however the literature in general suggests that trabeculectomy is less likely to be successful, simply because inflammation is such a big factor in this disease

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- This is even more important if the need to reduce pressure is urgent. I recently treated a patient who came in with neovascular glaucoma and a pressure of 70 mmHg.
 - The eye was painful. In that situation, I couldn't afford to wait until the abnormal blood vessels and inflammation had subsided.
 - I had to address all concerns at the same time, so I chose a tube shunt rather than trabeculectomy.
 - If you do have time to address the inflammation, then either surgery may be effective; if not, it makes the most sense to implant a tube shunt.