Glaucoma - Patho-physiology and rational treatment Chanchal Cabrera MSc, FNIMH, RH(AHG)

Glaucoma is a term describing a group of ocular disorders with multi-factorial etiology united by a clinically characteristic intraocular pressure-associated optic neuropathy.

This can permanently damage vision in the affected eye(s) and lead to blindness if left untreated. It is normally associated with increased fluid pressure in the eye (aqueous humour).

Worldwide, glaucoma is the second-leading cause of blindness after cataracts. It is the leading cause of blindness among African Americans. Glaucoma affects one in 200 people aged 50 and younger, and one in 10 over the age of eighty

Glaucoma affects 250,000 Canadians and is the second most common cause of vision loss in people over 65

There are several different types of glaucoma, all characterized by damage to the eye's optic nerve, which connects the retina to the brain.

If the optic nerve is damaged, it cannot send electrical impulses to the brain to produce a proper image. Most of the time in glaucoma, damage occurs when the optic nerve, or certain parts of the retina, get compressed as a result of high pressure inside the eye.

The nerve damage involves loss of retinal ganglion cells in a characteristic pattern. The many different subtypes of glaucoma can all be considered to be a type of optic neuropathy.

Raised intraocular pressure (above 21 mmHg or 2.8 kPa) is the most important and only modifiable risk factor for glaucoma.

However, some may have high eye pressure for years and never develop damage, while others can develop nerve damage at a relatively low pressure

Glaucoma can be roughly divided into two main categories, "open-angle" and "closed-angle" (or "angle closure") glaucoma. The angle refers to the area between the iris and cornea, through which fluid must flow to escape via the trabecular meshwork.

Open-angle glaucoma

• Accounts for 90% of glaucoma cases in the US.

- It occurs when fluid in the eye passes too slowly through a spongy meshwork connecting the cornea and the iris. This causes a buildup of pressure that damages the optic nerve.
- It is painless and does not have acute attacks. The only signs are gradually progressive visual field loss, and optic nerve changes.

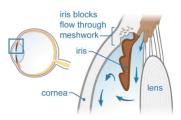


Closed-angle glaucoma

- Accounts for less than 10% of glaucoma cases in the United States, but as many as half of glaucoma cases in other nations (particularly Asian countries).
- About 10% of patients with closed angles present with acute angle closure crises characterized by sudden ocular pain, seeing halos around lights, red eye, very high intraocular pressure (>30 mmHg), nausea and vomiting, suddenly decreased vision, and a fixed, mid-dilated pupil. It is also associated with an oval pupil in some cases.

Acute angle closure is an emergency.

• In closed-angle glaucoma, the distance between the cornea and the iris closes completely, stopping fluid from draining from the eye.



Acute closed-angle glaucoma is a medical emergency and has a sudden onset of symptoms:

- Severe eye pain
- · Headaches (especially in dim light)
- Blurred vision
- Nausea
- Redness in the eye
- Haloes around lights

Causes of glaucoma

- Poor circulation eye tissues do not get enough circulation (mild ishcemia),low blood pressure
- Low blood sugar, in which case the body restricts blood supply in response to conserve energy.

Normal immune response to the mild ischemia is release of the inflammatory cytokines to restore the blood flow to the optic nerve. Over time the need to release inflammatory chemicals thickens the aqueous humor (PEX syndrome), increases in sticky proteins in the chambers and exhausts anti-oxidants used to neutralize the inflammation

Pseudoexfoliative amyloid like material moves into the aqueous humor and then gets deposited on the trabecular meshwork, causing oxidative damage and obstruction. Obstruction of the trabecular meshwork then causes elevation of the intraocular pressure (IOP) and resultant glaucoma.

In this sense glaucoma is a condition of congestion and poor drainage of the eye.

Screening for glaucoma is usually performed as part of a standard eye examination. Testing for glaucoma should include measurements of the intraocular pressure via tonometry, changes in size or shape of the eye, anterior chamber angle examination or gonioscopy and examination of the optic nerve to look for any visible damage to it, or change in the cup-todisc ratio and also rim appearance and vascular change. A formal visual field test should be performed

Examining / Measuring	Name of Test
The inner eye pressure	Tonometry
The shape and color of the optic nerve	Ophthalmoscopy
The complete field of vision	Perimetry
The angle where the iris meets the corr	nea Gonioscopy
Thickness of the cornea	Pachymetry

Non-modifiable risk factors - things you can't change:

- Increased age
- Female gender
- Naturally high levels of pressure in the eye
- Family history of glaucoma
- Nearsightedness

• Ethnicity: People of African or Hispanic descent have a greater risk of open- angle glaucoma. Those of Asian or Inuit descent have an increased risk for other types of glaucoma.

Modifiable risk factors - things you can change

- Manage diabetes and high blood pressure.
- Protect your eyes from injuries and infections.
- If you have other risk factors, talk to your eye doctor before using antihistamines, antidepressants, dilating eye drops or steroids, or beginning a weight training program

Physical exercise provides a long-term benefit of reducing the incidence of low ocular perfusion pressure (OPP). The results showed that study <u>participants who</u> engaged in moderate physical exercise approximately 15 years prior to the study had a 25 percent reduced risk of low OPP that could lead to glaucoma.

"It appears that OPP is largely determined by cardiovascular fitness," said study author Paul J. Foster, MD, PhD, of the University College London Institute of Ophthalmology. "We cannot comment on the cause, but there is certainly an association between a sedentary lifestyle and factors which increase glaucoma risk."

Managing glaucoma

Conventional treatment options include steroid eye drops, laser therapy (especially for the narrow angle variety) and surgery.

Eye pressures are lowered with eyedrops (that reduce fluid secretion) or surgery (which opens holes in the trabecular meshwork), but the underlying disease process still exists.

Common classes of drugs used

- Alpha Agonist
- Beta Blockers
- Carbonic Anhydrase Inhibitors
- Cholinergic (Miotic)
- Combined Medications
- Prostaglandin Analogs http://www.glaucoma.org/treatment/medicationguide.php

Allan Tillotson

"The ideal medicine for glaucoma should improve microcirculation to the back of the eye, nourish and moisturize the intra-eye membranes, restore antioxidant status, reduce IOP (intra-ocular pressure), calm stress, and improve fluid drainage"

Diet for glaucoma

Tyrosine kinase inhibitors (TKI) and protein kinase C inhibitors (PKCI) relax the trabecular meshwork without tightening the ciliary muscle (Wiederholt et al., 2000). Found in high amounts in beans, including yellow split pea, black turtle beans, baby lima beans, large lima beans, anasazi beans, red kidney beans, red lentils, soybeans, black eyed peas, pinto beans, mung beans, azuki beans.

Quercetin is also a TKI, so also eat lots of yellow skinned onions, drink some green tea, and eat garlic and broccoli.

Natural compounds that inhibit PTK

- Caffeic Acid Phenethyl Ester (CAPE) (from Propolis)
- Curcumin
- Emodin
- Flavonoids including apigenin, luteolin, quercetin, genistein
- Hypericin (light activated)
- Parthenolide
- Catechins from green tea especially EGCG
- Forskolin from Coleus forskolii
- Ursolic acid (Rosmarinus off and Ocimum sanctum)

Natural compounds that inhibit PKC

- CAPE (from Propolis)
- Curcumin
- Emodin
- Flavonoids including apigenin, luteolin, quercetin, EGCG
- Hypericin (light activated)
- Omega 3 fatty acids (EPA / DHA)
- Selenium
- Vitamin E
 - IP6 (inositol hexaphosphate)

Antioxidants

Some research suggests that **antioxidants** may be helpful in managing glaucoma, but it is not known whether they can help prevent vision loss. Alpha-lipoic acid, Vitamin C, beta-Carotene, Vitamin E, lutein, zinc, selenium, melatonin, glutathione, green tea, grape seed extract, resveratrol, fish oil, and omega-3.

Moderate exercise lowers eye pressure and perhaps improves blood supply to the optic nerve. A number of studies have shown that exercise has pressurelowering effects. One study reported that moderate exercise was associated with a 14% decrease in intraocular pressure (IOP), another found that persons engaged in aerobic exercise for 10 minutes experienced a decrease in IOP, and two trials reported that persons who exercised for 3 months had a moderate IOP decrease lasting for 3 weeks after the exercise program ended.

CASE REPORT AND COMMENTARY

Woman aged early 50s

Sudden onset in early 2012 of acute (narrow) angle glaucoma. Asymptomatic and diagnosed on routine annual eye exam.

Grandmother had glaucoma (type unknown) Treated immediately with laser surgery. First surgery was unsuccessful and she changed doctors and repeated the procedure.

1 week of prednisone drops after second surgery. No drugs or drops being used at time of consultation. Possible scarring from the botched first surgery made it hard to assess the extent of glaucoma symptoms. Generally low energy and run down

Known heart valve defect (location unknown) causing occasional palpitations from anxiety or stress. Blood pressure low at 100 / 78 mmHg and generally low standard body temperature.

Neck and shoulder pain, mostly from poor ergonomics at desk

Chronic (almost constant), sub-acute migraine. Left sided pain, photophobia, no nausea. Occasional flare ups of acute pain when she prefers a warm body and a cold face.

Usually a result of exposure to perfumes or chemicals. Managed without pain killers most of the time but almost always has a headache in the left side. Drinking 3 – 4 beers helps (3 – 4 times week). 4 cups of coffee daily seems to help temporarily.

On presentation symptoms were tired, sore eyes; maximum computer use of 15 minutes before aggravation of symptoms; bolts of sharp pain in the eyes many times in a day with no apparent trigger or cause; some blurring of vision. The eyes were dry prior to surgery but are not afterwards.

Tincture formula

- Euphrasia sp. (eyebright) 20 mL •
- Withania somniferum (Ashwagandha) 15 •
- Taraxacum off. (dandelion leaf) 10 •
- Ginkgo biloba (Ginkgo) 10 ٠
- Centella asiatica (gotu kola) 10 ٠ 10
- Panax ginseng (Ginseng) ٠
- Coleus forskolii (coleus) 10 ٠
- Salvia miltiorrhiza (dan shen) 10 •

100 mL / week

dosed at 7.5 mL (1 1/2 tsp.) twice daily in hot water before meals

Plus home made marijuana tincture, 1:4, 90% ethanol. Dosed at $\frac{1}{2}$ tsp. evening and bed time

Tea blend

Hawthorn flower and leaf	200 g
Linden	100 g
Oat tops	75 g
Rosemary	25 g

Put 3 Tbsp. in a pot and cover with 4 cups boiling water. Steep overnight; strain off and drink the next day. Can be sweetened to taste with honey while still warm

Headache blend

Salix alba (willow)	20
Petasites sp. (butterbur)	15
Viburnum opulus (cramp bark)	15
Scutellaria lateriflora (skullcap)	15
Tanacetum parthenium (feverfew)	15

Chelidonium majus (celandine)	10
Anemone pulsatilla (pasque flower)	5
Stachys betonica (betony)	5

Dosed at 2.5 mL (1/2 tsp.) in hot water every 15 minutes as needed for acute pain

Supplements

All from Natura Health Products Dosage total per day

Beyond Essential Fats 2 tsp. daily with meal Inflammaway 2 caps twice daily CVResQ (resveratrol, quercitin & CoQ10) 2 caps twice daily Amino Max 4 caps at bed time Night Gain 2 caps at bed time, 3 weeks on and 1 week off, at bedtime

Supplement Dosage total per day

Alpha lipoic acid R(+)-lipoic acid		50mg
Biotin		100mcg
Advanced B complex		3 capsules
Green Tea (Camellia sinesis) Extract		3 x 700mg (3
caps)		
Bilberry & grape seed extract	3 capsules daily	
Turmeric root	3 capsules daily	

Case outcome

One week after commencing treatment patient was almost symptom free. Pre-surgical evaluation revealed normal intra-ocular pressures in both eyes. Surgery was cancelled. Patient continues to use protocol at half doses and remains symptom free now over 1 year later