

THE GLAUCOMAS
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Suggested Reading:

The Glaucomas in Slatter's Fundamentals of Veterinary Ophthalmology 4th edition by David J. Maggs, Paul E. Miller and Ron Ofri.

OBJECTIVES

1. Be able to describe how aqueous humor is formed, its pathway of flow, and the applied anatomy of the filtration angle.
 2. Be able to recognize the clinical signs of glaucoma
 3. Be able to appropriately apply in clinical cases the different medical and surgical treatment modalities available for primary and secondary glaucoma in both sighted and blind eyes
- I. INTRODUCTION** - Glaucoma is a group of diseases each with a specific etiology and unique therapy. The only unifying theme among these diseases is that intraocular pressure (IOP) is too high for the optic nerve and retina to function normally.
- A. Incidence** - Approximately 1 in every 119 dogs and 367 cats, making it one of the most frequent causes of irreversible blindness in dogs and cats.
- B. What is Normal IOP?** The normal range of IOP varies with examiner, tonometer, conversion table, breed, age and species.
1. IOP > 26 mm Hg (dogs) and > 32 mm Hg (cats) is abnormal with the Schiotz.
 2. Occasionally optic nerve damage occurs at lower IOPs.
 3. If IOP is very high (60-70 mm Hg) complete blindness may occur in 24-48 hours. Milder increases may result in vision loss over weeks to months.
- C. Successful Treatment Requires:**
1. A high index of suspicion on the part of the clinician allowing an early diagnosis or prophylactic therapy.
 2. Accurate IOP measurement with a tonometer.
 3. Aggressive treatment early in the course of the disease using both pharmacologic and surgical modalities.

II. AQUEOUS DYNAMICS AND GLAUCOMA

A. Function of Aqueous Humor

1. Holds ocular shape, makes eye more optically perfect.
2. Nourishes avascular tissues (lens, posterior cornea).
3. Carries away waste products of the lens and posterior cornea.

B. Principles of Glaucoma

1. **Total Flow In = Total Flow Out in normal eyes.**
2. **Non-pigmented ciliary body epithelium produces aqueous (flow in) by active and passive means. Active production predominates and is independent of IOP.**
 - a. **Passive diffusion** - Normally 1/3 of aqueous production. The blood-aqueous barrier prevents passage of relatively large molecules such as plasma proteins.
 - b. **Active Secretion** - Normally 2/3 of aqueous production. Partly controlled by carbonic anhydrase.
3. **Aqueous outflow occurs via the trabecular meshwork and uveoscleral routes. Trabecular outflow predominates.**
 - a. Aqueous flows from the posterior chamber over the anterior surface of the lens through the pupil into the anterior chamber.
 - b. Exits via 1 of 2 ways:
 - 1). **Iridocorneal Angle (drainage angle)** - Main route. Formed by the junction of the iris-ciliary body and the cornea-sclera. The angle consists of:
 - a). **Pectinate ligaments** - Thin strands spanning from the iris base to peripheral cornea at the limbus.
 - b). **Ciliary cleft** - Contains the **trabecular meshwork** - Main site of outflow from the anterior chamber to the vasculature.
 - c). **Collecting channels** lead to the **Scleral venous plexus**. Consists of 2-4 interwoven grossly visible large channels in the midsclera. This plexus communicates with the **episcleral veins** and the **general circulation**. In glaucoma, the episcleral veins become congested and the eye appears red.

2). **Uveoscleral route** - Aqueous flows through the iris or ciliary body interstitium to the choroidal circulation. 3-25% of total outflow.

4. **Glaucoma is almost always due to impaired outflow.** Glaucoma often results when egress of aqueous is impaired and production continues at a relatively excessive (although less than normal) rate. Continued aqueous humor production despite high IOP may initially appear maladaptive, but probably reflects the eye opting to maintain a major source of nutrition over IOP control. Common mechanisms of outflow impairment include:

a. Closure of the drainage angle secondary to:

1). Developmental abnormalities of the pectinate ligaments. These are almost always present in dogs with primary angle closure glaucoma (PACG) but since the vast majority of dogs with pectinate ligament dysplasia (goniodysgenesis) do not develop glaucoma, this disorder may be only the first “hit” of a two or more “hit” process.

2). Reverse pupillary block. This may be the second “hit” in PACG. The iris can move but the pupillary margin is tightly pressed against the anterior lens capsule. When the pupil is mid-range and pressure is somewhat greater in the anterior chamber than the posterior chamber, the iris is forced against the anterior lens capsule – preventing the anterior flow of aqueous humor.

3). An anteriorly positioned lens still attached to the zonules.

4). Increased axial length of the lens or vitreous.

c. Peripheral irido-corneal adhesions (peripheral anterior synechia).

d. Infiltration of the drainage apparatus with inflammatory or neoplastic cells/debris or new blood vessels.

e. Overt anterior lens luxations/subluxations.

f. Recession of the drainage apparatus secondary to trauma.

g. Accumulation of proteoglycans and other substances in the trabecular meshwork – common in primary open angle glaucoma.

5. **Elevated IOP results in irreversible damage to the retina and optic nerve within 24-48 hrs. Acute glaucoma is a neurologic emergency.**

III. DIAGNOSIS OF GLAUCOMA - The clinician must maintain a high index of suspicion and concern over the possibility of glaucoma in order to make an early diagnosis when the prognosis

is the best. Glaucoma should be suspected in all red eyes in which the cause of the vascular injection is not obvious (e.g. simple corneal ulcer, foreign body etc.), and in eyes with unexplained corneal edema, pupillary abnormalities, chronic anterior uveitis, lens positional abnormalities or visual impairment - especially in breeds with a predisposition to glaucoma. Early signs may be subtle and consist of mild conjunctival vascular engorgement (often misdiagnosed as conjunctivitis), epiphora, pain, photophobia, and no overt visual impairment.

- A. Signalment and History** - Breed should make one very suspicious of glaucoma. Dog breeds most commonly affected with glaucoma (in descending order) as recorded by the Veterinary Medical Data Base for the years 1972 - 1992.

<u>Primary Open Angle</u>	<u>Closed Angle</u>	<u>Secondary</u>
Mixed Breeds	American Cocker Spaniel	Mixed Breeds
American Cocker Spaniel	Mixed Breeds	American Cocker Spaniel
Basset Hound	Basset Hound	Wire Fox Terrier
Boston Terrier	Samoyed	Toy Poodle
Miniature Schnauzer	Beagle	Boston Terrier
Beagle	Siberian Husky	Miniature Poodle
	Chow Chow	Labrador Retriever
	Wire Fox Terrier	Siberian Husky
	Toy Poodle	Basset Hound
	Standard Poodle	Beagle

B. Clinical Signs

1. Acute glaucoma

- a. Pain** - evidenced by blepharospasm, epiphora, third eyelid protrusion, and possibly reduced appetite and activity level, or increased time spent sleeping.
- b. Episcleral hyperemia** - Episcleral vessels indicate intra-ocular disease. These vessels are immobile, don't blanch with epinephrine and are deep blue-purple in color.
- c. Corneal edema** - Results from fluid being forced into the corneal stroma, and decompensation of the endothelium.
- d. Mydriasis** - The iris sphincter muscle is usually paralyzed at IOP's over 40 mm Hg.
- e. Cupping of the optic nerve head** - Pressure "blowing- out" the nerve through the weaker lamina cribrosa.

2. Chronic glaucoma

- a. Buphthalmia** - globe stretching. Almost always indicates a blind eye (except in

puppies with a thinner sclera and Shar Pei's with abnormally low scleral rigidity).

- b. Decreased pain** - Although these eyes are still painful, the animal may not demonstrate the same intense level of pain as seen in acute glaucoma.
 - c. Episcleral injection.**
 - d. Striate keratopathy (Haab's striae)** - Stretch marks or breaks in Descemet's membrane due to globe stretching.
 - e. Subluxated/luxated lens** - zonular breakdown due to globe stretching.
 - f. Iris degeneration** with persistently dilated pupil.
 - g. Cataracts** - due to impaired flow of aqueous humor.
 - h. Retinal lesions** - Cupped, grey optic disc; peripapillary or larger wedge-shaped alterations in tapetal reflectivity secondary to choroidal infarctions; retinal vascular attenuation.
 - i. Phthisis bulbi** - can be seen in very chronic cases when the ciliary body atrophies and the globe undergoes fibrosis.
- 3. Clinical signs in cats** are often more subtle than in dogs. Cats typically have relatively little ocular injection, and often have mydriasis and progressive buphthalmia as the only overt clinical signs.
- C. Tonometry** - Quantitative measurement of IOP has been the standard of care in human medicine for over 80 years. If you can't measure IOP you should refer all patients with an unexplained red eye to someone who can.
- 1. Digital** - Both index fingers are used alternately to indent the globe through the upper lid. Do not just retropulse the globe. Is notoriously inaccurate, and generally only useful in end-stage glaucoma when the IOP is very high and all hope of preserving vision is usually lost. Is not sensitive enough for early diagnosis or management of glaucoma.
 - 2. Indentation tonometry** - Schiottz - relatively inexpensive (\$100-150). It measures the amount of corneal indentation by one of a few known weights. Accurate results are obtainable and are dependent on practice, a clean instrument and good technique.
 - a. Technique** - Following topical anesthesia, IOP is measured in either the sitting or dorsal recumbency positions by vertically applying the instrument (with the 5.5 gm weight attached) to the center of the cornea and averaging 3 readings. Ideally, each reading should take 1-2 seconds to perform, and all 3 readings should be within 1-1.5

scale units of each other. If IOP is elevated, or one wishes to verify the accuracy of the 5.5 gm weight readings, the 7.5 or 10.0 gm weights are added individually to the 5.5 gm base weight (all 3 weights are never used simultaneously). In general, estimates of IOP with the 7.5 gm weight should be within 6 mm of Hg of those with the 5.5 gm weight.

b. Common Errors in Technique

- 1). Compressing the globe by retracting the lids at the lid margin rather than over the bony orbital rim (overestimates IOP).
- 2). Occluding the jugular veins during restraint (overestimates IOP).
- 3). Application of the tonometer off from vertical, to the sclera or third eyelid (IOP too high or too low).
- 4). Not resting the footplate completely on the cornea (IOP too low).
- 5). Prolonged application (subsequent IOPs will be lower and corneal ulceration is possible).
- 6). Corneal scarring, infiltrates, or thinning may also render the readings inaccurate as corneal resistance to indentation is altered.

c. Calibration tables - The human conversion table that comes with the tonometer is the preferred table for conversion of Schiottz scale readings to estimates of IOP in mm Hg in clinical practice in dogs and cats.

3. Applanation tonometry - The Mackay-Marg and Tono-Pen are generally regarded as the "gold-standards" in veterinary ophthalmology. These tonometers are fast, easy to use, less traumatic, unaffected by many corneal abnormalities and are the most accurate tonometers. Their expense (\$2,500+), however, can be an issue although many practitioners own a Tono-Pen and use it to screen dogs and cats for glaucoma.

4. Rebound tonometry – A small, lightweight plastic rod is projected towards the globe and the motion characteristics of how it reverberates off of the cornea is used to estimate IOP. Recently this device (the Tono-Vet) has been suggested to be more accurate than the Tono-Pen in dogs and horses and it is also applicable to measuring IOP in very small eyes (rats and ferrets).

D. Gonioscopy - A special lens is used to permit observation of the drainage angle. Critical in classifying the form of glaucoma and aids in patient management.

E. Ophthalmoscopy - Both direct and indirect ophthalmoscopy can be used not only diagnostically but also prognostically. If the optic nerve or retina are destroyed, therapy may be drastically altered. Menace reflexes and maze testing may help assess visual function.

IV. CLASSIFICATION OF GLAUCOMA

- A. Primary glaucoma** - Increased IOP without antecedent or concomitant ocular disease or injury. These are typically breed-related and probably are heritable. Primary glaucoma is sub-divided into open or closed angle by gonioscopy:
- 1. Primary Open Angle Glaucoma (POAG)** - Most common form in Caucasian humans but the least common, although most extensively investigated, form in dogs (laboratory Beagles). The onset is insidious and characterized by an initially mild to moderately elevated IOP (5-10 mm Hg increase) in both eyes. Vision loss is slow and often not detected until advanced. The cause lies in the metabolism of the trabecular meshwork.
 - 2. Primary Angle Closure Glaucoma (PACG)** - At least 8X more common than POAG in dogs. Often characterized by an initially unilateral, sometimes episodic, acute elevation in IOP that either spontaneously resolves or persists at very high levels (50-80 mm Hg). Approximately 50% of dogs will have an attack in the fellow eye in 5-10 months so it is a bilateral disease. The pathophysiology is complex and appears to involve pupil block and some form of abnormal development of the drainage apparatus. Often seen in Basset Hounds, arctic circle breeds, Cocker Spaniels and other breeds with pectinate ligament dysplasia. In this disorder the angle width itself may be normal but the pectinate ligaments form large solid sheets of tissue with or without “flow holes”. Angle structures deep to the flow holes may or may not be normal. IOP may stay normal for years, rising only in mid to older age. These dogs are also at risk for glaucoma secondary to uveitis because the holes are easily occluded by inflammatory debris. The majority of dogs with pectinate ligament dysplasia, however, remain normal for life. Acute attacks of PACG not only damage the optic nerve but may also cause retinal ischemia. This often leads to an apoptotic cascade of retinal and optic nerve cell death that can continue even if IOP is normalized.
- B. Secondary glaucoma** - Increased IOP as a complication of, or sequela to, other ocular diseases or injury. It is at least twice as common as primary glaucoma in dogs, and 7 times more common in cats. Causes include:
- 1. Lens Associated**
 - a. Luxated lenses** - terriers. Lens luxates before onset of glaucoma and the lens and/or vitreous blocks the pupil or drainage angle.
 - b. Intumescent lenses** - swollen lens causes narrowing of the angle by pushing the iris base anteriorly.
 - c. Phacolytic glaucoma** - lens protein induced uveitis with fibrosis of the drainage angle.
 - 2. Traumatic glaucoma**

- a. Hemorrhage (plugs filtration angle or form synechia).
- b. Puncture wounds or foreign bodies (uveitis).
- c. Drainage angle recession after trauma.

3. Inflammatory glaucoma - see uveitis lecture.

- a. Anterior peripheral synechia which closes the angle.
- b. Posterior synechiae - iris bombé.
- c. Angle obstruction with cells, debris and fibrin

4. Intraocular tumors

- a. **primary** - melanoma (iris or ciliary body), physical presence, showering emboli, or hemorrhage.
- b. **secondary** - anything (especially lymphosarcoma).

5. Vitreal prolapse into the anterior chamber occluding the pupil - Also known as aphakic glaucoma since tends to occur following lens luxation or cataract removal.

V. THERAPY FOR GLAUCOMA - See Flow Chart. The goal of therapy is to save or return vision through control of IOP either by medical and/or surgical means. Aggressive treatment must be instituted promptly as increased IOP can result in irreversible damage to the retina and optic nerve in as little as 24-48 hrs. If the owner is interested in maintaining vision, most patients should be referred to a specialist. It is unsatisfactory to try a course of drops for a week and then refer when the medication didn't work and the eye is now irreversibly blind. It is also inappropriate to mistake the ocular disease for less vision threatening entities such as conjunctivitis or anterior uveitis, or to not identify glaucoma as the cause of vision loss in the first eye because prophylactic therapy for the remaining visual fellow eye may be of benefit.

A. Therapy is determined by asking four questions:

- 1. Is IOP elevated?** - Tonometry confirms the diagnosis and allows the response to treatment to be accurately assessed.
- 2. Is the eye potentially sighted or irreversibly blind?** Aggressive medical therapy is usually indicated only if vision is still present or has just recently been lost, or if there is uncertainty as to the eye's visual status. Seldom are potentially toxic and expensive antiglaucoma drugs worthwhile in irreversibly blind eyes.

3. **Is the glaucoma primary or secondary?** Primary glaucoma is generally treated differently than secondary glaucoma. The small IOP elevations in POAG suggest that it may, at least initially, be controllable by drugs.
4. **Can medical therapy control IOP and ocular pain, or is surgery needed?** Most forms of glaucoma in veterinary medicine are surgical diseases and antiglaucoma drugs generally are only used as a bridge to surgery or as an adjunct when additional minor IOP reductions are needed postoperatively. Existing antiglaucoma drugs alone, or even in combination, are rarely capable of maintaining more than a 10-15 mm Hg reduction in IOP, and seldom prevent progressive visual loss. The efficacy of some of these drugs may also diminish over a few weeks to months, either as a result of tachyphylaxis or progressive angle closure. Finally, because virtually every evaluation of antiglaucoma drug efficacy in dogs has been performed in either normal dogs or dogs with POAG, the effectiveness of these drugs in dogs with the more common PACG is unclear.

VI. VISUAL OR POTENTIALLY SIGHTED EYES - See Flow Chart. Because of the heterogeneous etiologies of the IOP rise, no single therapeutic regime can be advocated for all cases of glaucoma. The principal goal of therapy for either primary or secondary glaucoma is the reduction of IOP to a "safe" level, i.e. a pressure at which progressive visual impairment and optic nerve damage no longer occurs. It is probable that for the vast majority of dogs and cats this target IOP is substantially lower than the high normal limit of 25-30 mm Hg, and may be in the low teens or even single digits in some animals. Unfortunately, this numerical level varies by animal, disease state, tonometer, and tonometerist; and a method for clinically determining the safe upper limit of IOP for dogs and cats with glaucoma is not yet available. When treating glaucomatous patients I try to maintain IOP below an arbitrarily set target of ≤ 20 mm Hg (measured by applanation tonometry or Schiotz using the human conversion table).

A. Visual Eyes with Acute Primary Glaucoma - Emergency Medical Therapy. In acute PACG with very high IOP anti-glaucoma drugs are used aggressively and often in combination so as to reduce IOP to as low a level as quickly as possible. Slowly lowering IOP by sequentially adding drugs over a period of days only results in blindness. Once IOP is reduced medically, surgery is often performed because drugs alone often cannot maintain IOP in the target range of ≤ 20 mm Hg. If initial IOP is $<40-45$ mm Hg and the pupil still reacts to light, I will try a topical 0.005% latanoprost alone. If IOP does not normalize in 1-2 hours (or if IOP is initially >45 mm Hg) I add in an oral/topical carbonic anhydrase inhibitor and consider mannitol. Antiglaucoma drugs, **in order of decreasing ocular hypotensive effect** include:

1. **Hyperosmotic diuretic agents** - Often reduces IOP from very high levels (60-80 mm Hg) to normal for a short time by dehydrating the vitreous which is 98% water. IOP begins to decrease in 10-15 minutes and lasts for 12-24 hrs. Side effects include headache; osmotic diuresis; and worsening of dehydration, renal failure, or pre-existing cardiovascular disease. Fatalities have been reported following IV administration of crystals and from pulmonary edema in animals anesthetized with methoxyflurane.

- a. **Mannitol** - Most effective hyperosmotic and my choice in acute primary glaucoma in eyes with the potential for vision. Use mannitol 20% for injection at 1gm/kg slow IV over 20 minutes. Repeat in 4 hours if needed. Should be heated/filtered (Arygle 5 micron filters, Sherwood Medical) to avoid injecting crystals IV.
 - b. **Glycerin** – Not as reliable as mannitol. Give 1-2 ml/kg PO, repeat in 8 hours if needed. May cause vomiting. In rare cases can use q8 hrs for up to 5 days as long as toxic effects are not clinically significant. Contraindicated in diabetics.
2. **Prostaglandin derivatives: Latanoprost 0.005%** (Xalatan - Pharmacia) – PGs were initially discovered to be responsible for the very low IOP in patients with uveitis and subsequently were developed to treat glaucoma. Latanoprost is a topical PG (PGF₂α derivative) pro-drug that is cleaved by corneal esterases to the active drug. In primates it works by increasing uveoscleral outflow, although it also induces a marked miosis in dogs and cats (unlike in primates where it does not change pupil size) and so may also have other mechanisms of action in those species. It does *not* lower IOP in cats, perhaps because they lack the FP receptor. Dose is BID to occasionally TID. Side effects include topical irritation, exacerbation of uveitis, and in primates it can change iris color and cause eyelash growth. It has become a first-choice drug for alleviating the pupil block in acute PACG and is useful in certain other forms of glaucoma. There are a number of other commercially available topical prostanoids including: travoprost 0.004%, unoprostone 0.12%, and bimatoprost 0.03% but they seem to offer little over latanoprost. All PGs can have very different effects depending on dose, frequency, and species.
3. **Carbonic Anhydrase Inhibitors** - IOP may be reduced 20-30% with topical and systemic CAIs. These drugs may be given concurrently with a hyperosmotic in acute PACG. Act by reducing active aqueous secretion presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and water transport across the ciliary processes. Adverse effects of systemic CAIs include: hypokalemia, metabolic acidosis, panting, anorexia, fatigue, depression, confusion, polyuria/polydypsia, vomiting and diarrhea, thrombocytopenia, blood dyscrasias, and nephrolithiasis. Occasionally need to supplement with potassium (potassium chloride, 600 mg/22.7 kg PO q 24 hr). In contrast to many topical agents, the CAIs generally maintain their IOP lowering effects over time.
- a. Topical CAIs - **dorzolamide 2%** (Trusopt^R Merck & Co) and **brinzolamide 1%** (Azopt^R Alcon). Dose q8 hr. Dorzolamide is also available in combination with the beta-blocker timolol as Cosopt^R (Merck & Co). Topical CAI's do not alter the electrolyte and acid-base status like systemic CAIs. They lower IOP an amount comparable to, or slightly less than the systemic CAIs. May be irritating but in humans brinzolamide is suggested to be slightly less irritating.
 - b. **Methazolamide (Neptazane^R)** or **Dichlorphenamide (Daranide^R)**. Systemic CAIS that are becoming more difficult to obtain. Dose is 2.2 - 4.4 mg/kg PO q8-12 hrs (dogs) and 1-2 mg/kg q8-12 hrs for cats.

- c. Other systemic CAIS: Acetazolamide is cheap but very toxic.
- 4. Parasympathomimetic Miotics** - Increase aqueous outflow by contracting the longitudinal ciliary muscle and less so by inducing miosis. Are not effective due to muscular paralysis if IOP is greater than 40-50 mm hg. Often used in combination with hyperosmotics and CAI's in managing acute severe PACG. Side effects include ocular irritation associated with ciliary spasm and a breakdown of the blood-aqueous barrier, thereby worsening uveitis. Systemically may cause salivation, vomiting, diarrhea, sweating and exacerbate the toxicity of organophosphate flea products. Some prefer a mydriatic adrenergic (epinephrine derivative) or a beta-blocker to pilocarpine if surgery is contemplated because of a reduced potential for blood-aqueous barrier breakdown.
- a. **Pilocarpine 2%** - (bid-qid). Best choice in acute primary glaucoma. A direct acting parasympathomimetic that mimics acetylcholine. Concentrations > 2% are more irritating, marginally more effective, and rarely permit surgery to be avoided.
 - b. Indirect parasympathomimetics (anticholinesterases). Although they have a longer duration of action than pilocarpine I usually don't use them in acute primary glaucoma because their onset of action is longer than pilocarpine and their potential toxicity limits their use at a q12 - 24 hr schedule. They are probably most appropriate as a prophylactic agent for the fellow eye.
 - 1). **demecarium bromide** (Humorsol^R) 0.125-0.25% SID-BID – a good drug but has become very hard to get.
 - 2). echothiophate iodide (Phospholine iodine^R) 0.03-0.25% SID-BID. Less preferable.
- 5. Adrenergics** - Indicated as an adjunct to miotics and oral CAIs or in cases of uveitis-induced glaucoma where pilocarpine or latanoprost may worsen the uveitis. IOP is lowered by vasoconstricting the ciliary body thereby reducing aqueous production and also by improving outflow. Adverse effects include irritation, tearing, hyperemia, and chemosis. Occasionally they dilate the pupil and may worsen PACG.
- 1). **epinephrine bitartrate** - 1 to 2% BID to QID topically.
 - 2). **dipivalyl epinephrine** (Propine^R) 0.1% BID. Less irritating than epinephrine but more expensive.
- 6. Beta Blockers** – This group is one of the most potent topical antiglaucoma drugs in humans but are much less effective in animals. Their mechanism of action is believed to be by decreasing aqueous production although, unlike in humans, they also induce miosis in dogs and cats and therefore may also change outflow. They also do not work well if the animal is sleeping. Timolol may cause bradycardia.

- 1). Timolol maleate 0.5% q12hr, monitor heart rate in small dogs/cats.
 - 2). Betaxolol HCL 0.5% q12 hr, a cardioselective (β -1) blocker
 - 3). Metipranolol HCL 0.3% q12 hr a less expensive beta blocker than timolol
- 7. Anti-inflammatories** - Often added to reduce uveitis secondary to the IOP rise, the miotic drugs, or surgery. I often use **1% prednisolone acetate** topically at the same frequency as pilocarpine. Corticosteroids may need to be used with caution in patients with glaucoma, however, as dogs receiving topical 0.1% dexamethasone for 6 months demonstrated a 5 mm Hg IOP rise. A similar study in a select population of cats demonstrated a 3-6 mm Hg increase with 1% prednisolone acetate BID after 22 days. Clinical cases of steroid-induced glaucoma, however, have not been reported in dogs or cats.
- 8. Follow-Up** - IOP is closely monitored and medications are slowly adjusted over several days to weeks as long as IOP is maintained at ≤ 20 mm Hg. Surgery, however, is usually required to maintain target pressures as IOP tends to increase over time. Osmotic diuretics are discontinued first, followed by the CAIS if possible. Many animals are maintained on:
- a. Topical pilocarpine 2% BID-QID or 0.005% latanoprost BID-TID.
 - b. Topical 1% prednisolone acetate BID-QID (same frequency as pilocarpine or latanoprost) to control any miotic-induced uveitis.
 - c. A topical or systemic CAI
 - d. Occasionally an epinephrine compound or beta blocker is added if IOP is slightly higher (2-3 mm Hg) than desired.

B. Visual Eyes with Primary Glaucoma - Surgical Therapy - See Flow Chart. Surgery is indicated if medical therapy cannot lower IOP sufficiently over the entire 24 hour period, if the owners are unwilling to dedicate themselves to daily therapy, or if wide variations in IOP occur from day to day. Surgery should be performed quickly before irreversible retinal or optic nerve damage occurs. Many veterinary ophthalmologists prefer to medically lower IOP and then perform surgery without waiting to see if IOP will go back up or if it will be unstable.

- 1. Surgery to increase aqueous outflow** - In theory, these procedures are less likely than cyclodestructive procedures to result in post-op vision loss from corneal changes or cataracts because they allow a higher level of aqueous production and hence a more normal level of intraocular nutrition and waste removal. Scarring with occlusion of the outflow site and a subsequent rise in IOP, however, remains a significant problem and may force the clinician to resort to cyclodestructive procedures.

- a. **Gonioimplants** - Silicone, silastic, or nylon tubes with or without valves are placed in the anterior chamber and allow aqueous to drain into the subconjunctival space around the implant bodies. Complications include somewhat difficult surgical technique, closure of the tube orifice or lumen by scar tissue, and tube migration with exposure of the tube. Additionally, the devices can cost several hundred \$. Anti-proliferative agents such as mitomycin-C may reduce fibrosis of the filtering bleb and improve the implants ability to achieve target pressures. Tissue plasminogen activator is also a potent addition to the glaucoma surgeons armamentarium as it lyses intraocular fibrin clots and reduces the matrix for future fibrosis and occlusion of the tube. I prefer a gonioimplant with a pressure-sensitive valve (Ahmed glaucoma valve, models S-1 or S-2, New World Medical Inc.) in combination with limited cyclocryosurgery. Medical therapy may used post-operatively to fine-tune IOP control.
- b. **Filtering procedures** - Create new outflow routes by making holes in the iris, sclera, or disinserting part of the ciliary body. Only a 30-50% short term success rate. Often scar over in 1-6 mo. Recent advances in microsurgical technique, and anti-proliferative agents such as 5-FU or Mitomycin C, however, may rekindle interest in filters.

2. Surgery to decrease aqueous production

- a. **Cyclocryosurgery** - The ciliary body is frozen through the sclera with nitrous oxide or liquid nitrogen in 3-7 spots. If the ciliary body regenerates enough, or freezing is insufficient, IOP may rise again. Up to 40% need repeat cryosurgery.
- b. **Cyclophotocoagulation** - A diode or Nd:YAG laser is used to destroy the ciliary body transclerally as the pigment in the ciliary body preferentially absorbs the laser wavelength. Its advantage over cyclocryosurgery is that it generates less inflammation, making it the preferred technique for reducing aqueous production if it is available.

C. Prophylactic Medical Therapy for the Fellow Eye in Primary Glaucoma - Although PACG typically presents as a unilateral disease, the initially normotensive fellow eye usually becomes overtly glaucomatous in a median of 8 months. Preventative medication may delay or prevent the onset of glaucoma in the fellow eye (median > 32 months) or may make it more amenable to therapy should it become overtly glaucomatous. 89% of veterinary ophthalmologists employ some form of prophylactic therapy in the fellow eye of dogs with unilateral glaucoma. Only a small percentage, however, would use preventative therapy in dogs which have abnormal drainage angles but never have had an attack of glaucoma in either eye.

1. Demecarium Bromide (Humorsol^R) 0.125% SID at bedtime. A very effective drug but recently has become very difficult to obtain. An alternative may be 0.005% latanoprost.
2. Betaxolol 0.5% BID. Also demonstrated to be effective as a prophylactic but it too has recently become hard to obtain.

3. 1% prednisolone acetate suspension SID to BID - To control any low grade uveitis.
4. Follow-up - Measure IOP monthly for the first 3 months then at 3 month intervals. Progressively rising IOP, IOP exceeding 20 mm Hg, changes in the appearance of the retina or optic nerve head, or an episode of acute glaucoma warrants an increase in the frequency of the topical drugs, adding a CAI, or surgery.

D. Visual Eyes with Secondary Glaucoma - Medical Therapy - See Flow Chart. Although therapy is directed at the primary disease in these cases, the IOP elevation cannot be ignored if pressure-induced destruction of the optic nerve head is to be avoided.

1. **Uveitis-associated glaucoma** - Watch out for glaucoma in patients with uveitis and normal IOP because aqueous production is reduced in uveitis. A normal IOP in the face of uveitis implies that the drainage angle is compromised and suggests IOP may increase once the inflammation is controlled. A thorough uveitis diagnostic work-up is indicated unless trauma or lens-induced uveitis are the known causes. Treat the uveitis aggressively with systemic (IV and oral corticosteroids or one dose of flunixin meglumine IV) and/or topical corticosteroids once systemic infectious diseases are ruled out. Topical miotics (pilocarpine and latanoprost) risk iris bombe and may exacerbate anterior uveitis by further breaking down the blood-aqueous barrier. Topical epinephrine or dipivefrin q6-12 hrs, or beta-blocker (timolol) are better choices in mild (5-10 mm Hg) increases and inflammation. Topical and/or systemic CAIs are added in greater IOP elevations. Mannitol may cross an incompetent blood-aqueous barrier and further raise IOP. Atropine usually is avoided because of the potential for angle narrowing. Lens removal in animals with lens-induced uveitis and secondary glaucoma typically has a high complication rate due to the uveitis and often fails to preserve vision in the long term.
2. **Luxated-lens-associated glaucoma** - Common in terriers. Attempts to trap a posteriorly luxated lens behind the pupil with miotics is often unsuccessful, and can result in acute glaucoma if the drug is administered when the lens is in the pupillary plane or anterior chamber. Markedly intumescent (swollen) lenses, especially in diabetics, can also lead to glaucoma by moving the iris base anteriorly and occluding the drainage angle. The latter is also a surgical emergency. If the lens is in the anterior chamber and IOP is high I dilate the pupil with tropicamide in an effort to break the pupillary block.
3. **Hyphema-associated glaucoma** - IOP needs to be carefully monitored in patients with a significant anterior chamber hemorrhage as glaucoma is often a sequela of RBCs occluding the drainage apparatus. Determine etiology with a work-up with special care to rule out neoplasia. I tend to use topical epinephrine or dipivefrin which may vasoconstrict bleeding vessels and cause a mild pupil dilation (reducing the chance of synechia and iris bombe). If the blood is clotted, tissue plasminogen activator into the anterior chamber may lower IOP. Oral CAIs can also help. Mannitol may increase IOP.
4. **Neoplasia-associated glaucoma** - Primary intraocular tumors such as melanoma or ciliary

body adenoma/adenocarcinoma frequently result in glaucoma. Lymphosarcoma or metastasis to the eye by numerous other malignant tumors also have been reported to cause glaucoma. Although systemic chemotherapy may resolve the IOP rise in some intraocular neoplastic processes (e.g. lymphosarcoma), enucleation is often best.

E. Visual Eyes with Secondary Glaucoma - Surgical Therapy -See Flow Chart - Treat the primary etiology if possible. These are usually referrals.

1. Iris bombe' with glaucoma - iridectomies to bypass the pupil often seal over post-operatively but may be the only treatment modality available.
2. Luxated lens - Remove the lens.
3. Vitreal prolapse - vitrectomy.
4. Hyphema - Surgical draining of the hyphema may help some patients and worsen others. Injection of tissue plasminogen activator into the anterior chamber may be a better solution - especially if the blood is clotted.

VII. IRREVERSIBLY BLIND EYES

A. Blind Eyes with Primary or Secondary Glaucoma - Medical Therapy - Usually treatment in these cases is limited to pain relief until a definitive surgical procedure can be performed. Although potentially useful in the short term for pain relief seldom are toxic and/or expensive drugs (a systemic CAI or hyperosmotic) indicated on a chronic basis in blind eyes. In my experience, owners frequently grossly underestimate the degree of discomfort associated with a blind glaucomatous globe and they usually report the animal is a "new pet" after a definitive surgery to lower IOP. Short term management may include:

1. Tramadol, carprofen or other systemic analgesic.
2. Topical dorzolamide q 8hours or latanoprost q12hrs. Occasionally topical or systemic CAI's, or even hyperosmotics are used on a short term basis.
3. If the globe is buphthalmic artificial tear ointments 2-5 times a day to keep the cornea moist and prevent exposure keratitis and associated ocular pain until definitive surgery.

B. Blind Eyes with Primary Glaucoma - Surgical Therapy - See Flow Chart. Humans with IOP elevations of 50-60 mm Hg often complain of pain similar to a migraine headache, and most owners will comment that the pet is "more like its old self" once IOP is effectively reduced surgically. It is critical, however, that the risk to the remaining visual eye be carefully determined, and preventative therapy begun if indicated.

1. **Enucleation +/- an orbital prosthesis** - My general preference for irretrievably blind eyes

where the owner is not concerned about cosmetic appearance because it has the fewest complications and permits histopathologic assessment of the affected eye that may allow the clinician to develop the most effective preventative measure for the fellow eye.

2. **Evisceration and intraocular prosthesis** - Most cosmetic. Probably should be avoided in eyes with glaucoma secondary to infectious or neoplastic causes. Has a slightly higher complication rate than enucleation because the patient maintains its own fibrous tunic and may either traumatize the ocular surface or experience corneal degeneration.
3. **Cyclodestructive Procedures** - Either cryosurgery or laser cyclophotocoagulation may allow maintenance of the globe but are less predictable at controlling IOP than the above 2 therapies and may need to be repeated. In my experience some animals develop a cataract and lens-induced uveitis with subsequent re-development of ocular pain, glaucoma or phthisis bulbi.
4. **Intravitreal Gentamicin injection** - Blind eyes only! In my experience this is the poorest choice because it has the highest complication rate, lowest predictability, and frequently yields less than satisfactory long-term results. Its only advantage is that gentamicin chemically destroys the ciliary body relatively inexpensively and quickly. Therefore it may be best used in elderly patients with a high anesthetic risk and where the goal is to try to eliminate pain as cheaply as possible. Often a secondary lens-induced uveitis results and there are anecdotal reports of intraocular tumors developing after an intravitreal gentamicin injection.
 - a. Some outflow must be present. Don't perform on animals with uveitis or neoplasia-induced glaucomas.
 - b. Use a 20 gauge needle and enter the eye 8 mm caudal to the limbus angling for the optic nerve. Withdraw 0.5-1.0 ml of vitreous and inject 10-20 mg of gentamicin. (If vitreous is not liquefied remove some aqueous humor instead). A topical antibiotic/corticosteroid ointment is applied 3-4/day until the eye is quiet.
 - c. Has a high (50%) failure rate to control IOP and has other complications such as hyphema, chronic uveitis, cataract formation and phthisis bulbi.

C. Blind Eyes with Secondary Glaucoma - Surgical Therapy

1. Enucleation - probably the best choice in most cases.
2. Evisceration and intraocular prosthesis in non-infectious, non-neoplastic cases (lens luxation etc.)
3. Cyclocryosurgery or laser cyclophotoablation may be used in carefully selected cases as long as outflow exists.

VIII. GLAUCOMA IN SPECIES OTHER THAN THE DOG - The cat is second and the horse a

distant third to the dog in the development of glaucoma. Almost invariably glaucoma in species other than the dog are secondary. The same general principles for the dog apply to other species although drug doses are not well worked out.

- A. Feline Glaucoma** - The majority of cases are secondary to chronic low grade uveitis, intraocular neoplasia (melanomas), trauma, or aqueous humor misdirection syndrome. Symptoms are much more subtle in the cat and often consist of only a relatively quiet eye with slow progressive buphthalmia and pupillary dilation. Normal feline IOP is higher than the dogs and goes up to 32 mm of Hg with the Schiotz tonometer. Recently one study showed that about 1 in 150 cats >7 years of age have elevated IOP – most frequently due to aqueous humor shunting into the vitreous (instead of flowing anteriorly). This aqueous humor misdirection pushes the lens forward and blocks aqueous humor leaving through the pupil and also facilitates closure of the drainage angle.
 - B. Equine Glaucoma** - The vast majority of cases are secondary to chronic uveitis and carry a very poor prognosis. Occasionally seen as a congenital buphthalmia in newborn foals. The horse has a very large uveo-scleral outflow which may make it very resistant to developing glaucoma. Normal equine IOP is higher than that of the cat or dog.
- IX. NEURO-PROTECTANTS** - Although not yet commercially available there is an intense search for drugs which protect the optic nerve and retina from the effects of elevated IOP. A number of avenues are currently being explored including drugs which protect the neuro-retina or optic nerve from reperfusion injury once IOP is lowered, or prevent these cells from undergoing apoptosis in response to glutamate liberation from damaged neural elements.