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Glaucoma: Diagnosis and Therapy

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Glaucoma is a large, diverse group of vision impairing disorders that are united only by common theme of intraocular pressure (IOP) that is too high for the optic nerve and retina to function normally. This level is typically >25 mm Hg in dogs and >31 mm Hg in cats (Table-1).[1-4] The rate of vision loss is proportional to the degree of IOP elevation; with complete blindness resulting in days with marked increases in IOP, and over weeks to months for mild increases.[5] Some glaucomatous animals, however, may lose vision at an IOP usually regarded as normal.[6]

Elevated IOP in the absence of vision loss is termed ocular hypertension, which may or may not progress to overt glaucoma. Ocular hypertension occurs most notably as a sudden, transient increase in IOP a few hours after intraocular surgery;[7] but also may occur in stressed animals.[8] Both glaucoma and ocular hypertension must be differentiated from the more common false IOP increases resulting from tonometric technique or an uncooperative animal.

Incidence

According to the VMDB glaucoma affects approximately 1 in every 119 dogs and 367 cats.[5] Another survey found 0.9% of cats ≥ 7 years of age undergoing a routine preventative health screen found had abnormally elevated IOP and ocular disease.[8]

Anatomy And Physiology

Stable IOP depends upon balancing the production of aqueous humor (inflow) with its exit from the globe (outflow). Glaucoma usually is the result of impaired aqueous outflow and continued (although less than normal) aqueous humor production. Fluid is produced by *diffusion*, passive *ultrafiltration*, and *active secretion*.[9] The latter uses the enzyme carbonic anhydrase, requires energy, and accounts for approximately 70% of aqueous humor production.[9] Active secretion also continues at a relatively constant rate even if IOP becomes elevated,[10] presumably to continue to supply nutrients to the eye.

Aqueous humor exits the ciliary processes, enters the posterior chamber between the iris and the lens, flows through the pupil into the anterior chamber, and exits the eye mainly through the iridocorneal angle (ICA). The ratio of the height of

the pectinate ligaments in the ICA to the distance between the origin of the pectinate ligaments and the anterior corneal surface is used to classify the angle as open, narrowed, or closed.[11] From the ICA aqueous ultimately enters the vasculature. Aqueous drainage has also been demonstrated to occur via the interstitium of the ciliary body and iris (uveoscleral route).[12]

Vision loss, however, is the result of optic nerve damage and not impaired aqueous outflow. Axons of the retinal ganglion cells run parallel to the retinal surface and then turn 90 degrees to enter the multi-layered fenestrated meshwork of the lamina cribrosa before exiting the eye.[13] When IOP increases, the scleral lamina cribrosa bows posteriorly, thereby impairing axonal axoplasmic flow and also probably ocular blood flow.[13] Dying ganglion cells release glutamate and other compounds that can initiate a self-perpetuating cycle of apoptotic cell death in previously unaffected ganglion cells.[14] Eventually, loss of enough axonal tissue results in optic nerve head cupping - the hallmark of glaucoma.[13] Marked increases in IOP may also impair choroidal blood flow and cause ischemic damage in the photoreceptors and outer retina, which can also initiate an apoptotic cascade. [15]

Pathogenesis

Primary glaucomas have no obvious association with another ocular or systemic disorder, are typically bilateral, have a strong breed predisposition and are believed to have a genetic origin (Table-2). Primary glaucoma has 2 forms, primary open-angle glaucoma (POAG) in which the drainage angle appears gonioscopically normal (presumably because the impediment to aqueous outflow is deep to the pectinate ligaments) and primary angle-closure glaucoma (PACG) in which the drainage angle appears narrowed or closed. In dogs, PACG is at least 8 times more frequent than POAG.[5] Female dogs develop acute PACG 2.1 times more commonly than male dogs. [16]

Secondary glaucomas are twice as common as primary glaucomas in dogs (and even more common in cats) and are associated with another ocular or systemic disorder that results in altered aqueous humor dynamics.[5] Secondary glaucoma may be unilateral or bilateral, may or may not be inherited, and the gonioscopically visible drainage angle may be open or closed. Often the exact mechanism of the glaucoma is unclear.

There are a number of potential locations at which outflow may be impaired (Table-3), and therapy is directed at identifying the site of obstruction and treating that if possible. For example, PACG in dogs may be associated with shifts in the relative position or axial length of the lens, which leads to a functional block to aqueous outflow at the pupil, especially when it is mid-range in diameter.[17] Aqueous humor accumulates in the posterior chamber which shifts the peripheral iris anteriorly and closes the ICA. Initially the iris is simply apposed to the peripheral cornea, but soon peripheral anterior synechia form, and these prevent the angle from reopening.[18] Concurrent abnormalities of the ICA (goniodysgenesis) increase the risk of PACG but they alone are not sufficient to cause it.[5, 16] To circumvent this impediment to outflow, then, a miotic (demecarium bromide) would decrease the pupil blocking force of a mid-range pupil, and tighten the peripheral iris so it is less susceptible to "rolling" into the ICA.[16] This theory is supported by the ability of demecarium to delay the onset of PACG by almost 4-fold in the fellow normotensive eye in dogs with unilateral PACG.[16]

PACG in dogs may be classified as acute, subacute or chronic. Acute (a.k.a. congestive) PACG is the most common form in dogs.[5] It is characterized by a sudden onset of clinical signs and a marked rise in IOP, presumably the result of a sudden and unremitting obstruction at the pupil and the ICA. Subacute (or subclinical) PACG is characterized by repeated, self-limiting attacks with very mild or no clinical signs. Often these dogs ultimately either experience an overt acute attack or develop chronic PACG. Chronic PACG is an end-stage disease characterized by closure of the ICA by peripheral anterior synechia and chronically elevated IOP.[5, 11]

Other common mechanisms of glaucoma in dogs and cats include: peripheral irido-corneal adhesions, drainage apparatus neovascularization (pre-iridal fibrovascular membranes), overt anterior lens luxations/subluxations, intraocular neoplasia, and obstruction of the ICA by inflammatory debris or cellular material. The precise mechanism of primary open-angle glaucoma in dogs is unclear but it most likely is the result of subtle biochemical alterations in the trabecular meshwork that ultimately leads to increased resistance to aqueous outflow.[19] Glaucoma also can occur via a combination of mechanisms, and in some patients the mechanism is not known.

Clinical Signs And Diagnosis

Clinical signs vary with the magnitude and duration of the IOP increase as well as with the inciting cause of glaucoma. Usually only when IOP exceeds 40 mm Hg, and the threat to vision is very great, do the classic signs of episcleral vascular injection, pupillary dilation and corneal edema appear. In secondary glaucoma the classic clinical signs of glaucoma are often masked by the primary disease. Additionally, cats, unlike dogs, typically exhibit relatively little ocular injection, and often mydriasis/anisocoria, and buphthalmia may be the only overt clinical signs.[8, 20] Therefore, IOP should be measured

in all red eyes in which the cause of the vascular injection is not obvious and in eyes with unexplained corneal edema, pupillary abnormalities, chronic anterior uveitis, lens positional abnormalities or visual impairment.

Increased Intraocular Pressure

Increased IOP is a major risk factor for vision loss from glaucoma, but IOP in-and-of-itself is NOT diagnostic for the presence or absence of glaucoma. The diagnosis can only be made in conjunction with a good ophthalmic history and examination. For example, the short-lived (hours) but marked (up to 60 mm Hg) IOP spikes that can occur after some ophthalmic surgeries do not result in overt vision loss, and therefore represent ocular hypertension and not glaucoma.[7] Alternatively, a single IOP measurement may be within the normal range and the animal can still be losing vision due to a glaucomatous apoptotic cascade as seen after an acute attack of PACG, between attacks of subacute PACG, and in chronically glaucomatous eyes where the ciliary body degenerates and IOP returns to normal. Finally, normal IOP in an eye with uveitis may be a harbinger of impending glaucoma, because such eyes usually have decreased aqueous humor production (or increased uveoscleral outflow) making some form of significant outflow obstruction necessary to keep IOP within the normal range.

The normal range of IOP varies with the species, age, breed, time of day, tonometrist, tonometer, and Schiotz conversion table.[1-5] In general, adult cats have a higher upper limit than dogs (Table-1), and older animals have lower IOP than younger animals. In cats over 7 years of age IOP may decline as much as 1.7 mm Hg/year.[8] It is not uncommon for IOP measurements to differ by 2-4 mm Hg between examiners and tonometers, and errors in technique can result in measurements that are inaccurate by as much as 10-20 mm Hg. One study that screened cats ≥ 7 yrs of age as part of a routine geriatric profile if IOP found that IOP values of ≥ 25 mm Hg, or >12 mm Hg difference between the eyes of the same cat, when combined with a cursory ophthalmic examination were useful thresholds for identifying at-risk animals.[8] A single, mildly elevated reading in the absence of clinical signs is insufficient to initiate anti-glaucoma therapy, but indicates that additional follow-up is warranted. Additional measurements, perhaps obtained over the course of a day (diurnal curves) may be useful in the early detection of glaucomatous animals. The sometimes episodic and unpredictable nature of IOP increases in acute PACG in dogs confounds the early diagnosis of PACG in some animals.

Schiotz Tonometry

If the instrument is clean, and good technique employed, this inexpensive device can be as accurate as an applanation tonometer.[3,4] Topical anesthesia is applied to the eye and the animal is made to sit, or lay on its back, so that the palpebral fissure is parallel to the ground. In order to avoid erroneously high readings, care must be taken to avoid excessive tension on the jugular veins by the animal's collar or assistant who is restraining the animal, and the eyelids must be retracted by opening them over the bony orbital rim rather than by applying traction to them at the eyelid margin and compressing the globe. The instrument, with the 5.5 gm weight attached, is then vertically applied to the center of the cornea and 3 scale readings are obtained. Each reading should be performed smoothly and take only a few seconds. All 3 readings should be within 1-1.5 scale units of each other. The 7.5 or 10.0 gm weights are used if IOP is elevated, or to verify the accuracy of the 5.5 gm weight readings. Estimates of IOP with the 7.5 gm weight are typically within 6 mm of Hg of those with the 5.5 gm weight.[3,4] Corneal scarring, edema, infiltrates, or thinning may result in inaccurate readings. The human conversion table provided with the tonometer correlates best with applanation tonometer readings in both dogs and cats.[3,4]

Applanation Tonometry

The Tono-Pen XL (Oculab) applanation tonometers small size, high accuracy, and ease of use makes it the instrument of choice for measuring IOP in domestic animals.[1,2] It flattens (rather than indents) a small region of the cornea, and allows IOP to be measured in almost any position. Each accepted reading is accompanied by an audible "click", and the device automatically takes 3 to 6 measurements and displays the mean IOP with the percent variance from high to low measurement. It is also applicable to large number of species, and readily mastered by technical staff. Tono-Pen measurements are less affected by corneal disease than Schiotz measurements. The Tono-Pen has also been advocated for routine screening of dogs of predisposed breeds and older cats for glaucoma - making it more cost-effective in a private practice setting.

Dilated Pupil

The pupil is typically mid-range to dilated when IOP exceeds 40-50 mm Hg. In many secondary glaucomas, however, the size and shape of the pupil is not a reliable indicator of the presence or abscence glaucoma.

Conjunctival and Episcleral Vascular Injection.

Varying degrees of vascular injection occur in most dogs, and to a lesser extent in cats. Eyes with mild IOP increases, however, may not be red at all, and in subacute PACG the eye appears normal between attacks.

Corneal Pathology

The degree of corneal edema varies considerably. Haab's striae, ("stretch marks" in Descemet's membrane) appear as broad, blue-white, curvilinear to branching lines on the inner aspect of the cornea in buphthalmic eyes. Exposure keratitis, axial corneal ulceration, and other degenerative corneal changes may also be seen.

Fundus Abnormalities

If IOP is mildly elevated the fundus often appears normal. Subtle retinal vascular attenuation, optic disc hemorrhages, and hyperemia or papilledema of the optic disc may be seen if the IOP increase is severe. Over time the optic nerve loses myelin , appears grayer, and becomes "cupped". With chronic IOP elevations the tapetum becomes diffusely altered in reflectivity, the retinal vasculature is attenuated and a peri-papillary ring of altered reflectivity appears around the degenerate optic nerve.

Ocular Pain

The degree of ocular pain varies and is related to the magnitude of the elevation in IOP, its duration, and the presence of other ocular abnormalities. Pain relief needs to be a primary goal of glaucoma therapy. Mild IOP elevations may be painless but acute, large elevations appear quite painful. Humans with acute PACG often complain of a severe, deep ache that may be accompanied by nausea, vomiting, bradycardia and profuse sweating. Frequently dogs with glaucoma have a decreased appetite, sleep more, are less active and or tolerant, but seldom do they rub or scratch at the eye. Although owners may not believe the pet with chronic glaucoma is painful, they will invariably comment that once IOP is reduced to normal levels, or the eye is removed, that the pet acts like "a new dog".

Decreased Vision

The rate of vision loss in glaucoma varies with the cause of the glaucoma and the magnitude/duration of the IOP increase. The imprecision with which vision can be measured in animals often prevents recognition of loss of the peripheral visual field in early glaucoma. In some animals with marked increases in IOP, vision may be lost, only to at least partially return days to weeks later if IOP is controlled. In some animals in which the apoptotic cascade has been initiated, however, vision loss may be slow but relentless over months to years, despite IOP remaining within normal limits.[6]

Buphthalmos

Globe stretching in response to increased IOP usually indicates end-stage disease and an irreversibly blind eye. Exceptions include young animals and Shar Pei's whose flexible sclera can stretch before vision is completely lost.

Luxated lens

A luxated lens may be the initiating cause of the glaucoma, or it may be a sequelae of globe stretching and lysis of the lens zonules.

Aqueous Flare

Aqueous flare may be present in uveitis-associated secondary glaucomas, but may also be seen to a mild degree in eyes with acute congestive PACG.

Glaucoma Therapy

Glaucoma therapy is driven by 4 questions. 1) Is IOP elevated? 2) Does the eye have the potential for vision? Aggressive medical and possibly surgical therapy is indicated if the eye still has vision, has only recently (in the last few days) become blind, or if there is uncertainty as to the visual potential of the eye. If the eye is irreversibly blind enucleation or one of the salvage procedures should be performed. The fellow eye should be carefully assessed. 3) What is the inciting cause of the glaucoma and can it be addressed directly? This usually requires a determination as to whether the glaucoma is primary or secondary and what is the mechanism of the glaucoma. And finally, 4) Can medical therapy permit the target IOP to be achieved and ocular pain controlled, or is surgery required? Some forms of glaucoma are best treated by medical therapy alone whereas in other forms, such as acute PACG, medical therapy serves only as a bridge to surgery. It is reasonable to expect only 10-15 mm Hg sustainable reduction in IOP by using currently available systemic and topical anti-glaucoma drugs.

The principal goal of therapy for all forms of glaucoma where there is a potential for vision is to reduce IOP to a "safe" level so that progressive visual impairment 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 for that species, and in some animals may be in the low teens or even single digits.[5, 6, 21] It is also likely this numerical value varies by animal, disease state, duration of the rise, tonometer etc. Although in humans sequential visual field testing aids in the detection of an IOP that is too high, a

clinically useful method of determining the safe upper limit of IOP in glaucomatous animals is not yet available. The author frequently uses an arbitrarily set target of ≤20 mm Hg as measured by Tono-Pen applanation tonometry although extrapolation of recent data from humans with advanced glaucoma to dogs suggests that this may need to be as low as 15-17 mm Hg to halt progressive optic nerve degeneration.[22]

Systemic Antiglaucoma Drugs

Hyperosmotic Diuretics

Hyperosmotic agents can markedly lower IOP, presumably by dehydrating the vitreous, but their systemic toxicity limits their use.[5, 23] Intravenous mannitol (1 gm/kg over 10-20 minutes) which has been heated or filtered (Argyle 5 micron filters, Sherwood Medical) so as to remove crystals prior to its administration more reliably reduces IOP than oral glycerol. IOP often drops from 60-80 mm Hg to normal within in a few hours, but this effect usually lasts only 12-48 hrs. If necessary mannitol can be repeated once at the 1 gm/kg dose. Side effects include headache; osmotic diuresis; and worsening of dehydration, renal failure, or pre-existing cardiovascular disease. Death may occur if crystals are administered IV, and fatalities have also been reported from pulmonary edema in animals also anesthetized with methoxyflurane. Glycerol (glycerin) at 1-2 gm/kg may be given orally in place of mannitol, but vomiting is common. Glycerol is not advised in diabetics.

Carbonic Anhydrase Inhibitors

These sulfonamide derivatives lower aqueous humor production by blocking carbonic anhydrase. Many systemic CAIs have been withdrawn from the market recently because their IOP lowering effects are comparable to that of the topical CAIs.[24]

The systemic CAIs dichlorphenamide and methazolamide are less toxic than acetazolamide. Adverse effects of systemic CAIs include: hypokalemia, metabolic acidosis, panting, anorexia, fatigue, depression, confusion, polyuria/polydypsia, vomiting and diarrhea, thrombocytopenia, blood dyscrasias, and nephrolithiasis. Oral potassium supplementation should considered in patients on the higher doses of systemic CAIs.

Topical Antiglaucoma Drugs

Most topical anti-glaucoma drugs are not labeled for use in animals and have been optimized for the human eye. Species and individual differences in the type and density of the various ocular receptors, however, make it possible that these drugs may have markedly different effects in animals than in humans.

Topical Carbonic Anhydrase Inhibitors

Two topical CAIs are currently available, 2% dorzolamide and 1% brinzolamide (Azopt®, Alcon Laboratories). Dorzolamide is available alone as Trusopt® (Merck), and also in combination with 0.5% timolol as Cosopt® (Merck). The optimum dosing frequency has not been determined for animals, but one study of beagles with POAG found topical 2% dorzolamide q8hrs lowered IOP more than if it was given q12 hrs.[24] This study also suggested topical 2% dorzolamide q8hrs was comparable to oral methazolamide at 5mg/kg q12hrs combined with 2% dorzolamide q12hrs. Adding a systemic CAI to a topical CAI may provide some additional IOP reduction, but this also increases the possibility of systemic side effects.[24]

Miotics

Cholinergics: 2% pilocarpine (a direct-acting cholinergic) is a potent miotic and ocular hypotensive agent in dogs and cats. It lowers IOP by opening the ciliary cleft and facilitating the outflow. The higher concentrations of pilocarpine (3 or 4%) are more irritating, and seldom more effective enough to permit surgery to be avoided. Because pilocarpine can lead to a breakdown of the blood:aqueous barrier, some avoid using it if surgery is a possibility. Indirect-acting cholinergics (e.g. organophosphates such as echothiophate iodide and demecarium bromide) have a longer duration of action than pilocarpine, but their potential for toxicity limits their use to a q 12 to 24 hr schedule. The later drugs are also becoming more difficult to acquire commercially as newer drugs with equal or greater efficacy and fewer side effects are becoming available for use in humans.

Beta-blockers: The non-selective, beta1 and beta2-adrenergic antagonist, timolol, also produces miosis in cats, and in dogs.[25-27] The mechanism of the miosis is unclear, as this drug does not alter pupil size in humans.[25-26] Timolol is a potent ocular hypotensive in humans and is believed to act by suppressing the production of aqueous humor only while the patient is awake.[28] It appears to have, however, minimal efficacy in dogs and cats, with most studies showing either no or only a few mm Hg reduction in IOP in normal dogs and cats.[25-27] Timolol also may induce bradycardia in very small dogs

or cats. Nevertheless, it is used because it is additive to other anti-glaucoma drugs such as the cholinergics or CAIs, does not break down the blood-aqueous barrier like pilocarpine or latanoprost, and like many anti-glaucoma drugs may be more effective in glaucomatous eyes than those with normal IOP. A closely related compound, betaxolol, is a cardioselective beta1 antagonist that appears to be approximately as effective as timolol in lowering IOP in dogs and cats. Betaxolol (0.5% q12 hrs) has also been found to be effective as a glaucoma prophylactic agent in eyes at risk for developing acute PACG.[16]

Prostaglandin derivatives: In anterior uveitis natural prostaglandin (PG) compounds drop IOP to very low levels, in some cases lower than episcleral venous pressure (about 8 mm Hg), suggesting that they act by improving uveoscleral outflow.[29] The last few years have seen the development of PG-derivatives such as latanoprost that reasonably well separate the ocular hypotensive effect from the inflammatory effects of the PGs. Latanoprost lowers IOP by improving the uveoscleral outflow in humans and dogs, but is ineffective in cats because they lack the specific prostanoid receptor by which the drug acts.[30] Other prostanoids, however, effectively lower IOP in cats. The drug is a potent miotic in cats and dogs and much less so in human eyes. There are a number of anecdotal reports in which one or more topical doses of latanoprost rapidly dropped IOP from >50 mm Hg to normal levels in dogs with acute PACG, but in a radomized clinical trial it failed to prevent the marked acute IOP spikes that can follow cataract surgery.[31] At least 4 topical prostanoid compounds are, or will be, commercially available in the near future.

Mydriatics

Classically mydriatics have been avoided in treating PACG in veterinary medicine because of concerns that dilation of the pupil may increase the obstruction the drainage angle. The topical andrenergics, epinephrine and its close relative dipivalyl epinephrine, however, are moderately effective ocular hypotensive agents and most animals exhibit minimal mydriasis with these compounds.[32] The mechanism of action in dogs and cats has not been well described, but in humans they are believed to lower IOP by reducing aqueous production and increasing outflow. Another advantage of these compounds is that they do not break down the blood-aqueous barrier, making them useful in secondary glaucomas due to uveitis, and in primary glaucomas prior to, and after surgery.

Corticosteroids

Topical corticosteroids such as 1% prednisolone acetate or 0.1% dexamethasone (q6-12 hrs) may be used to limit breakdown in the blood-aqueous barrier caused by cholinergic antiglaucoma drugs, to treat low-grade uveitis associated with marked IOP elevations, and to control surgically induced uveitis. Corticosteroids may need to be used with caution in glaucomatous dogs and cats, however, as dogs receiving topical 0.1% dexamethasone for 6 months had a 5 mm Hg rise in IOP, and 1% prednisolone acetate BID produced a 3-6 mm Hg increase in IOP in cats after 22 days of therapy.[33, 34] In another study of glaucomatous beagles, topical 0.1% dexamethasone q 6 hrs increased IOP a mean of 5 mm Hg in the treated eyes within 2 weeks.[31] Systemic corticosteroids may stabilize ganglion cell membranes and possibly limit optic nerve damage due to the high IOP. They also may be useful in treating the reperfusion injury that can result when IOP is reduced to normal from high levels.

Emergency Medical Therapy For Acute Primary Angle-Closure Glaucoma

Eyes with acute PACG which still have the potential for vision are usually treated aggressively with a combination of anti-glaucoma drugs to quickly reduce IOP to as low a level as possible. Because it is uncommon for medical therapy alone to maintain a target IOP of $\leq$ 20 mm Hg surgery is usually then performed. It may be possible to medically control IOP in subacute PACG if the IOP is <40-45 mm Hg, the pupil is still reactive to light or a miotic, and gonioscopy fails to demonstrate significant degrees of peripheral anterior synechia. In these uncommon cases IOP might be controlled with a topical miotic (2% pilocarpine q6hrs) and an oral CAI (methazolamide 2.2-4.4 mg/kg PO q 8-12 hrs in dogs). If IOP is >45 mm Hg, the pupil is non-responsive to a miotic, or significant peripheral anterior synechia are seen on gonioscopy, surgery is required and a hyperosmotic such as mannitol (1gm/kg slow IV over 10-20 minutes) is added to a miotic and a CAI to get the IOP as low as possible prior to surgery. Anecdotal reports suggest that in some dogs with acute PACG IOP may be dramatically lowered by topical application of 0.005% latanoprost, even if IOP is > 45 mm Hg. Relatively favorable prognostic indicators include an IOP of < 50 mm Hg, ability to lower IOP to < 20 mm Hg with therapy, and clinical signs of less than 3 days duration at initial presentation.[21]

Follow-up

Whether surgery is performed or not, IOP is followed carefully postoperatively and topical/oral medications are slowly reduced over days to weeks so as to maintain IOP within the target range (typically <20 mm Hg). If surgery was not performed, and a miotic and systemic CAI come very close (2-3 mm Hg) to achieving the target IOP, a topical CAI

(dorzolamide or dorzolamide/timolol combination), an adrenergic mydriatic (1.0% epinephrine or dipivefrin), or a topical beta-blocker (timolol) can be added. These drugs may also be used in place of a miotic if the postoperative uveitis is significant. Topical latanoprost may also be a useful addition, but should be used with caution if significant surgically-induced uveitis is present. The clinician should realistically expect to achieve only a 2-8 mm Hg additional reduction in IOP with these medications.

Surgical Therapy In Eyes With The Potential For Vision

Preoperative Considerations

The key determinants in selecting the appropriate procedure are the etiology of the glaucoma and the extent and quality of vision. Ideally the primary cause of the glaucoma is treated directly, but in some outflow obstructions this may not be possible, and the surgeon is forced to indirectly treat the problem by reducing aqueous humor production. Particular attention should also be paid to the patient's general physical health as altered hydration, electrolyte, and acid-base status are common. Blood gas and acid-base status along with serum potassium levels may also need to be assessed prior to inducing anesthesia especially if a systemic CAI has been recently administered. Rehydration may be necessary in animals that have received mannitol or who have not been eating or drinking well due to ocular pain. Preoperative parenteral anticholinergics (atropine or glycopyrrolate) do not appear to precipitate glaucoma in normal dogs or exacerbate it in those with glaucoma.[36]

Surgery to Increase Aqueous Humor Outflow

Glaucoma surgeries in eyes with the potential for vision consist of those that increase aqueous humor outflow (e.g. gonioimplantation, filtering procedures) and those that decrease aqueous humor production (cyclophotocoagulation, cyclocryosurgery). A combination of an outflow-enhancing and an inflow-reducing procedure may be more effective than either one alone at controlling IOP and preserving vision.[6] In current clinical practice gonioimplantation, cyclophotocoagulation, or cyclocryosurgery are the dominant surgical procedures used to treat potentially visual eyes. If the eye is irreversibly blind, enucleation, evisceration and intrascleral prosthesis, or a cyclodestructive procedure, are more appropriate.

Regardless of the location or method of their creation, however, fibrosis over the filtering site typically results in failure of these procedures to control IOP within a few weeks to months after surgery. A number of artificial aqueous humor shunts (gonioimplants) have also been used to try to create a pocket through which aqueous can filter into the subconjunctival space and thereby circumvent the flow-limiting effect of fibrosis. I currently prefer a valved gonioimplant (Ahmed) that remains closed at low IOP, but opens to allow aqueous to exit when IOP usually exceeds 8-12 mm Hg. Antimetabolites such as Mitomycin C or 5 fluoruracil also are useful in limiting the fibrosis over the body of the implant, and improving the long term filtering capacity of the device. Adjunctive medical ant-glaucoma therapy, or a limited cyclodestructive procedure may also be used to fine-tune IOP once gross control is achieved with the implant.[6]

Procedures that Reduce Aqueous Humor Production

Cyclodestruction is indicated in medically uncontrollable primary glaucoma where the eye still has the potential for vision, and as a globe salvage procedure for the relief of chronic ocular pain in irreversibly blind eyes. The success rate is much lower in eyes with glaucoma secondary to chronic anterior uveitis, pre-iridal fibrovascular membranes or retinal detachments. Relative contraindications include intraocular neoplasia, hyphema, and anterior lens luxation.

Cyclocryosurgery

Both liquid nitrogen or nitrous oxide are acceptable cryogens, but some surgeons feel liquid nitrogen may be more reliable because it achieves a colder temperature. After freezing, anti-glaucoma drugs are continued as prior to surgery. If the eye has the potential for vision the IOP is carefully followed for several days, and then at 1 and 2 weeks. If the eye is irreversibly blind, anti-glaucoma drugs are continued for 10-14 days and the patient is reevaluated at that time. Marked postoperative IOP spikes can persist for days after surgery, and repeated aqueocentesis may be necessary to control IOP. Tapping the anterior chamber, however, can be detrimental as it exacerbates the uveitis, risks introducing bacteria or damaging the lens, and probably increases the reperfusion injury to the retina and optic nerve. If IOP is well controlled 2 weeks postoperatively, the anti-glaucoma medications may be gradually tapered. The timing of further follow-up examinations varies by response to therapy.

Complications include an acute IOP spike, uveitis, exposure keratoconjunctivitis, neurotrophic keratitis, hyphema, retinal detachment, recurrence of glaucoma, and phthisis bulbi with a cosmetically unacceptable globe. The relatively high frequency of these complications makes cyclocryosurgery unacceptable as a prophylactic measure in the normotensive fellow eye of an animal with glaucoma in the other eye.[37]

Success rates vary with duration of follow-up, whether IOP control or preservation of vision was the goal, and whether the owner permits more than one freezing episode. If IOP control, but not vision, is the goal and multiple procedures are allowed, cyclocryosurgery can have a success rate as high as 90%.[38] If the eye has the potential for vision at the outset, the success rates at preserving vision may be as high as 60% at 6 months postoperatively.[38] Unfortunately, as for all glaucoma surgeries, the success rate declines the longer the follow-up. If IOP begins to rise again additional medical and or surgical therapy is required. In general, cats seem to have a lower success rate than dogs.

Cyclophotocoagulation (CPC)

An alternative procedure is to transclerally treat the ciliary body with a diode or neodymium-yttrium aluminum garnet (Nd:YAG) laser. A number of treatment protocols have been suggested, all with varying spot size, duration of application, and number of applications. A major factor with both lasers is the relatively reduced absorption of laser energy by lightly pigmented eyes. This variable substantially lowers the predictability of the outcome of the procedure, and may explain why CPC is less effective in cats, which are normally more lightly pigmented. As with cyclocryosurgery, treatment success (defined as control of IOP but not necessarily preservation of vision) is approximately 80% at 2-6 months, about 65% at 6 months, and 50% at 1 year or more.[39]

Combined Procedures

The combination of a cyclodestructive procedure and a gonioimplant offers some theoretical advantages in treating glaucomatous eyes with the potential for vision.[6] First, the implant may serve to blunt the often substantial postoperative IOP rise that can last for days to weeks. This IOP spike often snuffs out what remaining vision was present, and simply turns the procedure into only a globe salvage operation. Secondly, outflow facility is often so poor that in order to adequately control IOP, aqueous production must be reduced to such low levels that the lens becomes cataractous. These eyes do very poorly with lens extraction surgery and the cataract is as blinding as glaucoma. If limited cyclodestruction is performed and a gonio-implant is placed, aqueous humor production may be allowed to continue at a diminished, but relatively higher rate and this may better preserve the health of the eye. If the eye is irreversibly blind there is little to recommend a combined procedure over other globe salvage procedures or enucleation.

Surgery for Secondary Glaucoma in Eyes with the Potential for Vision

Cilio-vitreo-lenticular block (Aqueous Misdirection)

A common mechanism of glaucoma in older cats appears to be misdirection of aqueous humor into the vitreal space, with subsequent anterior shifting of the lens and iris.[20] This condition affected as many as 1 in 125 cats over 7 years of age in one large feline exclusive private practice.[8] The characteristic features are a marked, uniform shallowing of the anterior chamber in the absence of iridonesis and other signs of anterior lens luxation. The condition is a form of malignant glaucoma in which the site of obstruction to aqueous flow is at the level of the ciliary body, equator of the lens, and the anterior vitreous. These cats can be managed by traditional anti-glaucoma drugs, although miotics should be avoided because of the strong possibility of creating a pupil block glaucoma as the iris constricts over the protruding lens. If medical therapy fails to control IOP, a pars plana vitrectomy to alleviate the cilio-vitreo-lenticular block may be successful. Simple lensectomy is typically insufficient because the intact posterior lens capsule assumes an obstructing role. Therefore, if the lens is removed an anterior vitrectomy should also be performed.

Glaucoma secondary to an Anteriorly Luxated Lens

Luxated Lens Removal

In some animals lens subluxation or luxation is the result of the glaucoma and globe stretching with zonulolysis. In other animals the lens luxation may precede the glaucoma, and the increased IOP is secondary to pupillary block by the lens or vitreous, or infiltration of the drainage apparatus by liberated vitreal elements. In yet other animals lens luxation may be the result of chronic uveitis and the IOP rise may actually be from pre-iridal fibrovascular membranes and impaired outflow via the drainage apparatus rather than a mechanical impediment to outflow by the lens itself. Finally, there appears to be an association between primary open angle glaucoma and lens luxation. In the later case this may be the result of a malformation in elements that are shared both by the drainage apparatus and the lens. Therefore, extraction of a luxated or subluxated lens may completely resolve the glaucoma, or may be simply a futile endeavor that exacerbates IOP control because of the inflammation it creates.

Nevertheless, it is prudent to remove an anteriorly luxated lens in an eye with the potential for vision because of the very high risk of pupil block glaucoma, damage to the corneal endothelium, and because many eyes will do well once the lens is removed. A lens in the posterior chamber without a rise in IOP is usually not removed because of the high risk of complications such as retinal detachment, vitreal hemorrhage etc. If the eye is irreversibly blind, but painful, there seems

to be little point in removing the lens when one the salvage procedures will more effectively and inexpensively address the problem.

Glaucoma associated with Hyphema

Intact red blood cells, with or without proteinaceous blood constituents or remnants of the red blood cell membrane may result in secondary glaucoma. If trauma is not the obvious cause of the hyphema a thorough ocular and systemic work-up is necessary.

Uncomplicated hyphema is best managed conservatively by limiting exercise and pulling against leashes/collars. An Elizabethan collar should be considered. If IOP is increased a topical beta-blocker, epinephrine, or topical/systemic carbonic anhydrase inhibitor may be used. If the IOP increase is unresponsive to these drugs, systemic hyperosmotics may be used, but there is a small risk of a paradoxical increase in IOP if they escape the vasculature and pull water into the eye. Surgical removal of the clot is only a last resort if medical therapy cannot control IOP.

Uveitis Induced Glaucoma

Therapy for uveitis-induced glaucoma directed at identifying the cause of the uveitis and addressing that as specifically as possible. The elevated IOP, however, also needs to be treated. When appropriate, topical and systemic corticosteroids can be quite useful, as can a single injection of flunixin megulmine (0.1 to 0.25mg/kg IV). Often IOP will substantially decrease within hours after a systemic corticosteroid or NSAID is given.

Certain traditional anti-glaucoma therapies are best avoided in many cases of uveitis-induced glaucoma. Mannitol may pass through a disrupted blood aqueous barrier and draw water into the eye, thereby raising IOP. This theoretical concern, however, does not appear to occur frequently in a clinical setting. Pilocarpine and latanoprost may exacerbate uveitis as do cyclodestructive procedures.

Uveitis-induced glaucoma with iris bombé may be treated by laser iridotomy or synechiolysis. In practical terms, however, attempts at restoring a natural outflow system are often futile and the new opening or gonioimplant quickly scars over in an inflammed eye. Therefore, uveitis induced glaucoma is frequently unresponsive to surgical therapy and one of the globe salvage procedures or enucleation frequently is the final result.

Neoplastic Glaucoma

In the vast majority of eyes with neoplastic associated glaucoma, enucleation is indicated - if not for diagnostic purposes then to relieve ocular pain. In select circumstances palliation with systemic chemotherapy may be an alternative to enucleation.

Salvage Surgical Procedures for Glaucoma

Globe salvage procedures or enucleation are indicated if the eye is irreversibly blind and IOP cannot be maintained within the normal range without specific therapy. No single procedure is appropriate for every patient. One consideration is the postoperative cosmetic appearance and the resistance of the owner to enucleation, especially when glaucoma is bilateral. This resistance must not be underestimated and some owners view globe salvage as the only alternative to euthanasia. Although evisceration and intrascleral prosthesis is generally the most reliable procedure for producing a cosmetic end-result, it is contraindicated in the presence of an intraocular tumor, if there is intraocular infection, or if the cornea is substantially compromised. Additionally, performing an evisceration and intrascleral prosthesis in which the cornea is grossly abnormal, or where KCS demands frequent topical therapy, may be less acceptable to the owner than enucleation. Cyclodestructive procedures (cyclocryosurgery or CPC) may also salvage irreversibly blind globes. Repeat cyclodestruction may be necessary, and in some animals the procedure is ineffective at controlling IOP. Nevertheless cyclodestructive procedures are relatively inexpensive and are very useful if the owner does not wish to "give-up" just yet despite a grave prognosis for vision.

Evisceration and Intrascleral Prosthesis

A black silicone sphere 1-2 mm larger than the desired horizontal corneal diameter is chosen prior to surgery. Usually this is done by measuring the corneal diameter of the normal fellow eye so that the 2 eyes will be approximately equal. Most implants range from 17-22 mm in diameter. The greatest cosmetic appearance is achieved in animals with dark irides and where the pupil is normally minimally distinguishable from a distance.

Enucleation

Enucleation is the most effective procedure for treating a blind, painful glaucomatous eye and has the lowest overall complication rate. It is also, however, the least satisfactory in terms of postoperative cosmetic appearance. It is the procedure of choice if an intraocular tumor or infection is present, or if the owner requires a high degree of certainty that

only one surgery will ever be required. An orbital prosthesis can improve the postoperative cosmetic appearance especially in dogs with short periocular hair, but these may not be required in animals in which the hair can be groomed so as to "fill-in" the resulting orbital defect.

References

1. Miller PE, et al: Clinical comparison of the Mackay-Marg and Tono-Pen applanation tonometers in the dog. *Prog Vet Comp Ophthalmol 1*:171, 1991.

2. Miller PE, et al: Evaluation of two applanation tonometers in cats. *Am J Vet Res 52*:1917, 1991.

3. Miller PE, Pickett JP: Comparison of the human and canine Schiotz tonometry conversion tables in clinically normal cats. *J Am Vet Med Assoc. 201*:1017, 1992.

4. Miller PE, Pickett JP: Comparison of the human and canine Schiotz tonometry conversion tables in clinically normal dogs. *J Am Vet Med Assoc. 201*:1021, 1992.

5. Miller PE: Glaucoma. *In* Bonagura JD (ed): *Kirk's Current Veterinary Therapy XII Small Animal Practice*. W.B. Saunders Co, Philadelphia, 1995, pp1265-1272.

6. Bentley E, et al: Combined cycloablation and gonioimplantation for treatment of glaucoma in dogs: 18 cases (1992-1998). *J Am Vet Med Assoc 215*:1469, 1999.

7. Miller PE, et al: Mechanisms of acute intraocular pressure increases after phacoemulsification lens extraction in dogs. *Am J Vet Res 58*:1159, 1997.

8. Kroll MM, et al: Intraocular pressure screening as part of a routine health profile in older cats. *Trans Am Coll Vet Ophthalmol 31*:7, 2000.

9. Caprioli J: The ciliary epithelia and aqueous humor. *In* Hart WM (ed): *Adler's Physiology of the Eye*, Ninth edition. Mosby-Year Book, St Louis, 1992 pp 228-247.

10. Bill A: Effects on longstanding stepwise increments in eye pressure on the rate of aqueous humor formation in a primate (Cercopithecus ethiops). *Exp Eye Res 12*:184, 1971.

11. Ekesten B, Narfström K: Correlation of morphologic features of the iridocorneal angle to intraocular pressure in Samoyeds. *Am J Vet Res 52*:1875, 1991.

12. Gelatt KN, et al: Uveoscleral outflow of aqueous humor in the normal dog. *Am J Vet Res 40*:845, 1979.

13. Brooks DE, et al: Histomorphometry of the optic nerves of normal dogs and dogs with hereditary glaucoma. *Exp Eye Res 60*:71, 1995.

14. Brooks DE, et al: Vitreous body glutamate concentration in dogs with glaucoma. *Am J Vet Res 58*:864, 1997.

15. Whiteman AL, et al: Morphologic and immunohistochemical features of canine acute primary angle closure glaucoma. *Invest Ophthalmol Vis Sci 41*:S516, 2000.

16. Miller PE, et al: The efficacy of topical prophylactic antiglaucoma therapy in primary closed angle glaucoma in dogs: A multicenter clinical trial. *J Am Anim Hosp Assoc 36*:431, 2000.

17. Ekesten B: Correlation of intraocular distances to the iridocorneal angle in Samoyeds with special reference to angle-closure glaucoma. *Prog Vet Comp Ophthalmol 3*:67, 1993.

18. Mapstone R: The mechanism and clinical significance of angle closure. *Glaucoma 2*:249, 1980.

19. Gum GG, et al: Histochemical localization of glycosaminoglycans in the aqueous outflow pathways of normal beagles and beagles with inherited glaucomas. *Prog Vet Comp Ophthalmol 3*:52, 1993.

20. Miller PE, et al: Aqueous misdirection and ciliovitreolenticular block as a cause of glaucoma in cats. *Trans Am Coll Vet Ophthalmol, 30*:40, 1999.

21. Clines J, et al: A retrospective study evaluating the prognosis for intraocular pressure reduction and restoration or maintenance of vision following treatment for the acute onset of primary glaucoma in canine patients. *Trans Am Coll Vet Ophthalmol 30*:58, 1999.

22. The AGIS Investigators: The advanced glaucoma intervention study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. *Am J Ophthalmol 130*:429, 2000.

23. Lorimer DW, et al: The effect of intravenous mannitol or oral glycerol on intraocular pressure in dogs. *Cornell Vet 79*:249, 1989.

24. Gelatt KN, Mackay EO: Changes in intraocular pressure associated with topical dorzolamide and oral methazolamide in glaucomatous dogs. *Vet Ophthalmol.4*:61-67, 2001.

25. Wilkie DA, Latimer CA: Effects of topical administration of timolol maleate on intraocular pressure and pupil size in dogs. *Am J Vet Res 52*:432, 1991.

26. Wilkie DA, Latimer CA: Effects of topical administration of timolol maleate on intraocular pressure and pupil size in cats. *Am J Vet Res 52*:436, 1991.

27. Gum GG, et al: The effect of topical timolol maleate on intraocular pressure in normal beagles and beagles with inherited glaucoma. *Prog Vet Compar Ophthalmol 1*:141, 1991.

28. Topper JE, Brubaker RF: Effects of timolol, epinephrine, and acetazolamide on aqueous flow during sleep. *Invest Ophthalmol Vis Sci 26*:1315, 1985.

29 Stjernschantz JW. From $PGF_{2\alpha}$-isopropyl ester to latanoprost: A review of the development of xalatan. *Invest Ophthalmol Vis Sci 42*:1134-1145, 2001.

30. Studer ME, et al: Effects of 0.005% latanoprost solution on intraocular pressure in healthy dogs and cats. Am J Vet Res 61:1220, 2000

31. Stuhr CM, et al: Intracameral carbachol is superior to topical latanoprost in preventing post-operative intraocular pressure rises after cataract extraction. *Trans Am Coll Vet Ophthalmol 31*:33, 2000.

32. Gwin RM, et al: Effects of topical L-epinephrine and dipivalyl epinephrine on intraocular pressure and pupil size in the normotensive and glaucomatous beagle. *Am J Vet Res 39*:83, 1978.

33. Keates EU, et al: Loteprednol etabonate: a new steroid without ocular hypertensive effect. *Invest Ophthalmol Vis Sci 32*:947, 1991.

34. Zhan GL, et al: Steroid glaucoma: corticosteroid-induced ocular hypertension in cats. *Exp Eye Res 54*:211, 1992.

35. Gelatt KN, Mackay EO: The ocular hypertensive effects of topical 0.1% dexamethasone in beagles with inherited glaucoma. *J Ocul Pharmacol Ther 14*:XXX, 1998.

36. Frischmeyer KJ, et al: Parenteral anticholinergics in dogs with normal and elevated intraocular pressure. *Vet Surg 22*:230, 1993.

37. Vestre WA, Brightman AH: II: Effects of cyclocryosurgery on the clinically normal canine eye. *Am J Vet Res 44*:187, 1983.

38. Schmidt GM, et al: Retrospective survey of cyclocryotherapy for the control of canine glaucoma. *Trans Am Coll Vet Ophthalmol 14*:55, 1983.

39. Cook C, et al: Diode laser transcleral cyclophotocoagulation for the treatment of glaucoma in dogs: results of six and twelve month follow-up. *Vet Compar Ophthalmol 7*:148, 1997.

Table-1. Normal IOP for dogs and cats as determined with 2 applanation tonometers and the Schiotz tonometer (using the 5.5 gm weight) and 3 conversion tables. Ranges reflect 95% confidence intervals. Miller PE: Glaucoma. *In* Bonagura JD (ed): *Kirk's Current Veterinary Therapy XII Small Animal Practice*. W.B. Saunders Co, Philadelphia, 1995, pp1265-1272.

	Applanation Tonometry		**Schiotz Tonometry**			
	Tono-Pen	MacKay-Marg	Scale	1955 Human Table[1]	1977 Dog Table[2]	1988 Dog Table[3]
Dog ±s.d.	16.8 ± 4.0	17.1 ± 3.9	4.9 ± 1.5	18.0 ± 4.1	30.9 ±4.7	19.7 ± 3.7
Range	9-24	9-25	2-8	10-26	21-40	12-27
Cat ±s.d.	20.2 ± 5.5	22.2 ± 5.2	3.9 ± 1.4	21.6 ± 5.0	35.0 ± 5.8	27.1 ± 5.9
Range	9-31	12-32	1-7	12-32	23-49	15-39

[1] The 1955 human calibration table is supplied with the tonometer.

[2] From: Peiffer RL, Gelatt KN, Jessen CR, et al: Calibration of the Schiotz tonometer for the normal canine eye. Am J Vet Res 38:1881, 1977.

[3] From: Martin CL: Glaucoma. *In* Slatter DH (ed): *Textbook of Small Animal Surgery, 2nd edition*. W.B. Saunders Co, Philadelphia, 1993 pp 1263-1276.

Table -2. Breeds of dog most commonly affected with glaucoma (in descending order) as recorded by the Veterinary Medical Data Base over a 20 year period. Used with permission from Miller PE: Glaucoma. *In* Bonagura JD (ed): *Kirk's Current Veterinary Therapy XII Small Animal Practice*. W.B. Saunders Co, Philadelphia, 1995, pp1265-1272.

Primary Open Angle	Narrow/Closed Angle	Secondary
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

Table -3. Glaucoma Classification by Location (Posterior to Anterior)

1. Ciliary-Vitreous-Lens (Malignant Glaucoma)
    a. Block at ciliary body, vitreous and lens with posterior pushing of lens-iris diaphragm
2. Pupil
    a. Relative block due to iris to lens apposition
    b. Vitreous within pupil aperture
    c. Lens within pupil aperture

- Luxated lens
- Intumescent lens

d. Posterior Synechia/Iris bombé

3. Trabecular meshwork
   a. Primary Open Angle Glaucoma
   b. Secondary Obstructions
      1) Pre-iridal fibrovascular membranes
      2) Cellular/Proteinaceous Material
         - Vitreous
         - Plasma proteins
         - Neoplastic cells
         - Red blood cells
         - Pigment
         - Epithelial downgrowth through corneal perforation
   c. Primary Angle Closure Glaucoma
      1) Appositional closure
      2) Synechial closure
   d. Secondary Angle Closure Glaucoma
      1) Peripheral Anterior Synechia
      2) Ciliary body swelling/inflammation/cysts
      3) Neoplasia
      4) Anterior shifts of lens-iris diaphragm
4. Post-trabecular Forms
   a. Angular aqueous plexus
   b. Scleral outlet channels
   c. Episcleral vein obstructions
5. Developmental anomalies of the outflow system
6. Idiopathic mechanisms
7. Combined mechanism glaucoma

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