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Chapter 12

THE GLAUCOMAS

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The glaucomas are a diverse group of diseases united only by the fact that intraocular pressure (IOP) is too high to permit the optic nerve and, in some species, the retina to function normally. Characteristic changes of glaucoma include disrupted axoplasmic flow in the optic nerve head, death of retinal ganglion cells and their axons, cupping of the optic disc, and visual impairment or blindness.

AQUEOUS PRODUCTION AND DRAINAGE

The production and drainage of aqueous humor are influenced not only by the anatomy of the anterior segment but also by a large number of endogenous compounds, including neurotransmitters, hormones, prostaglandins, proteins, lipids, and proteoglycans. Indeed, so many factors influence the production and drainage of aqueous humor that it is difficult to identify a single pathway or drug that is capable of dramatically lowering IOP in every patient.

Aqueous humor is produced in the ciliary body by both active (selective transport of larger or charged molecules against a concentration gradient) and passive processes (diffusion and ultrafiltration). In *diffusion,* lipid-soluble substances enter the aqueous humor by passing through the ciliary epithelial cell membrane in proportion to their concentration gradient across the membrane. *Ultrafiltration* is the passage of water and water-soluble substances (which are generally limited by their size or charge) through theoretical micropores in the cell membrane in response to an osmotic gradient or hydrostatic pressure.

Many substances in the blood pass by ultrafiltration from the ciliary capillaries into the stroma of the ciliary processes before accumulating behind the tight junctions of the nonpigmented ciliary epithelium (the site of the blood-aqueous barrier). Some substances, such as sodium and chloride ions, are then actively pumped across the membrane into the posterior chamber, thereby drawing water passively along this concentration gradient. This process may account for the majority of actively formed aqueous.

Aqueous humor is also produced via the enzyme *carbonic anhydrase,* which catalyzes the formation of carbonic acid from carbon dioxide and water as follows:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$$

Carbonic acid then dissociates, allowing negatively charged bicarbonate ions to pass to the aqueous. Although exactly how this leads to aqueous humor production is unclear, it appears that positively charged sodium ions, and eventually water, follow negatively charged bicarbonate ions into the posterior chamber. Drugs that inhibit carbonic anhydrase therefore decrease aqueous production and reduce IOP.

Aqueous exits the eye via several routes. In the *conventional* or *traditional outflow route* aqueous humor passes from the posterior chamber, through the pupil, and into the anterior chamber. Because of temperature differences between the iris and cornea, thermal convection currents occur in the anterior chamber, with aqueous near the iris rising and aqueous near the cornea falling. This is one reason cells and particulate matter in the anterior chamber may settle on the inferior corneal endothelial surface. Aqueous humor then leaves the anterior chamber by passing between the pectinate ligaments to enter the *ciliary cleft,* which contains the *trabecular meshwork* (Figure 12-1). After filtering between the beams of the sponge-like meshwork, aqueous crosses through the endothelial cell membranes of the meshwork to enter a series of radially oriented, blood-free collecting vessels collectively called the *angular aqueous plexus.* From there it enters an interconnected set of blood/aqueous-filled vessels (the *scleral venous plexus*) before draining either anteriorly via the episcleral and conjunctival veins or posteriorly into the vortex venous system and into the systemic venous circulation (Figure 12-2). Contraction of smooth muscle fibers of the ciliary muscle that insert into the trabecular meshwork are probably capable of increasing drainage of aqueous from the eye by enlarging the spaces in the trabecular meshwork. In most species the majority of aqueous humor (about 50% in horses, 85% in dogs, and 97% in cats) leaves the eye via the traditional outflow route.

The remainder of the aqueous humor leaves the eye via the *uveoscleral pathway* (see Figure 12-1). In this route aqueous humor passes through the root of the iris and interstitial spaces of the ciliary muscle to reach the *supraciliary space* (between the ciliary body and the sclera) or the *suprachoroidal space* (between the choroid and the sclera). From these locations aqueous humor may pass through the sclera into the orbit either via pores in the sclera where blood vessels and nerves enter the eye or between the scleral collagen fibers themselves. Outflow via this route may substantially increase in certain disease states and in response to certain antiglaucoma drugs, such as the prostaglandin derivatives.

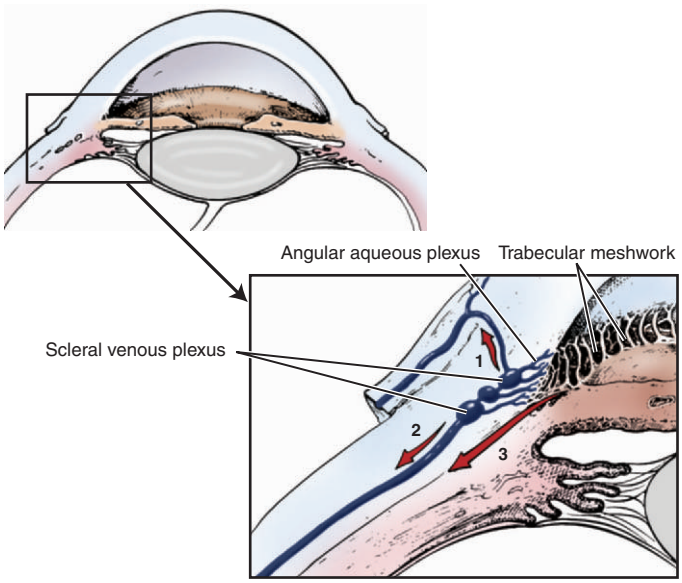


Figure 12-1. The routes of aqueous drainage from the canine iridocorneal angle. Aqueous humor passes between the beamlike pectinate ligament, then through the trabecular meshwork to enter the angular aqueous plexus and eventually the scleral venous plexus. From there, aqueous humor may drain *(1)* anteriorly to the episcleral and conjunctival veins, *(2)* posteriorly into the scleral venous plexus and vortex venous system, or *(3)* through the ciliary muscle interstitium to the suprachoroid and diffuse through the sclera (uveoscleral flow). (Modified from Martin CL [1993]: Glaucoma, in Slatter D [editor]: Textbook of Small Animal Surgery, 2nd ed. Saunders, Philadelphia.)

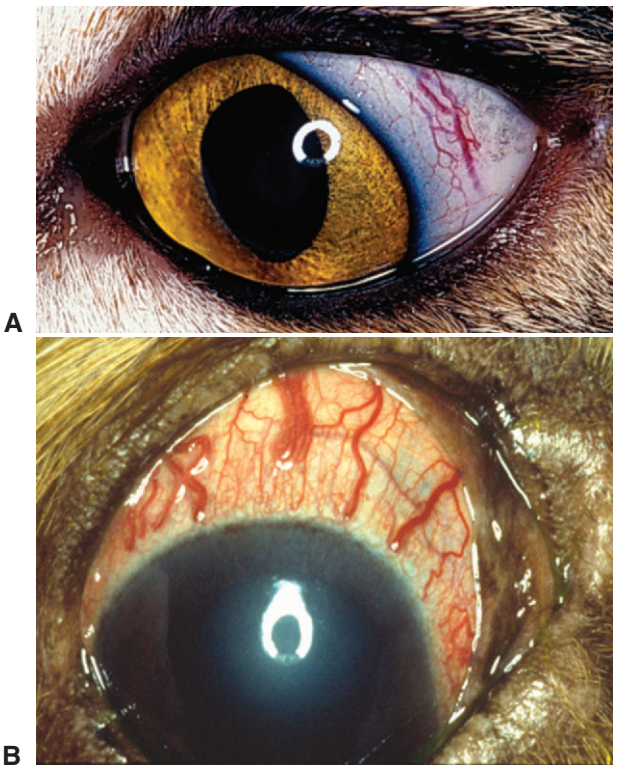


Figure 12-2. A, The scleral venous plexus is often visible in normal animals as a series of interwoven blood vessels several millimeters posterior to the limbus. **B,** Prominent episcleral and, to a lesser extent, conjunctival venous injection in a dog with glaucoma. Increased intraocular pressure compresses the intrascleral blood vessels, which drain posteriorly. This forces more blood through the episcleral and conjunctival veins—one reason the eye appears injected in glaucoma.

Balancing Aqueous Production and Outflow

IOP is the result of a delicate balance between production and outflow of aqueous humor (Figure 12-3). In glaucoma both production and outflow are altered. Usually a large percentage of the outflow pathway (perhaps as much as 80% to 90%) needs to be impaired before IOP starts to rise. If the outflow system is impaired to the point that IOP begins to increase, the eye usually attempts to compensate by reducing the passive production of aqueous humor. Active secretion, however, typically continues at a relatively normal rate, perhaps because if it did not, the avascular tissues of the eye that rely on aqueous humor for their nutrition would starve. Because the glaucomatous eye is functioning on a greatly diminished percentage of its normal levels of aqueous humor outflow and production, and because it has exhausted its usual compensatory pathways, pathologic processes or drugs that alter production or outflow only a small amount can have dramatic effects on IOP. This characteristic is one reason that glaucomatous eyes are typically more responsive to antiglaucoma drugs than normotensive eyes, but it also explains why IOP can rapidly rise to very high levels in a matter of 1 to 2 hours in some patients.

Often it is difficult to empirically predict the effect a given drug or its antagonist will have on IOP because many compounds affect both aqueous humor production and outflow—sometimes in complex and contradictory ways. For example, stimulation of β-adrenergic receptors in the ciliary processes increases intracellular cyclic adenosine monophosphate (cAMP), resulting in greater aqueous humor production. β-Adrenergic blocking drugs (e.g., timolol, betaxolol) decrease cAMP, thereby lowering aqueous humor production and ultimately reducing IOP. β-Blockers reduce IOP, however, only if the patient is awake and adrenergic tone is present. This means that although a drug such as timolol can reduce IOP in a cat when it is awake, the agent may not control IOP for the more than 20 hours a day the cat is sleeping.

As expected, β-adrenergic drugs such as epinephrine and its derivative dipivefrin may transiently increase IOP, presumably by increasing aqueous humor production via stimulation of cAMP. A few minutes after application of these drugs, however, IOP begins to decrease, and it stays reduced for several hours. This is because epinephrine also increases aqueous outflow via β_2 receptors in the trabecular meshwork, and does so to a greater degree than it increases aqueous humor production. Epinephrine may also lower IOP by (1) reducing blood flow to the ciliary body (thereby lowering aqueous production) and (2) increasing uveoscleral outflow by relaxing the ciliary muscle and recruiting prostaglandins. The latter means, which can be blocked by topical nonsteroidal antiinflammatory drugs, may result in further increases in uveoscleral outflow and additional decreases in aqueous humor production. Complex interactions such as this are but one reason why both β-adrenergic agonists and β-blockers lower IOP in many species. When one considers species and individual differences in the density, distribution, and type of receptors as well as differences in the cause of the glaucoma, it is easy to see why it can be difficult to precisely predict what effect a given drug will have on IOP in a particular patient.

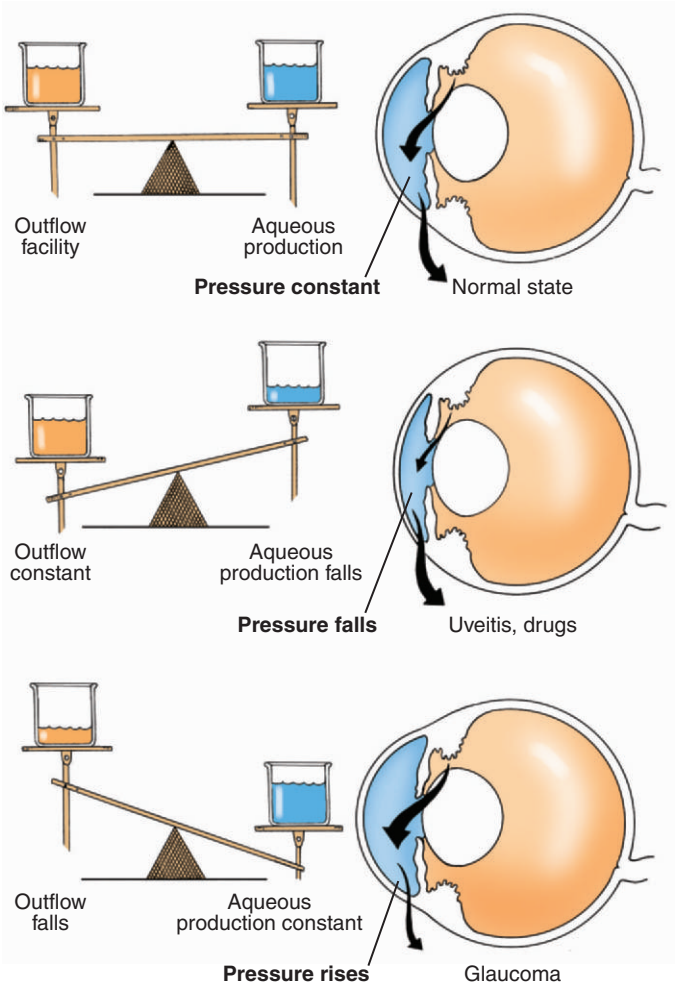


Figure 12-3. Common alterations in aqueous production and outflow facility and their effects on intraocular pressure.

Causes of Variations in Intraocular Pressure

Diurnal Variation

IOP varies slightly with time of day in many species, being the greatest in the morning and gradually declining over the course of the day in dogs and humans. The opposite phenomenon has been suggested to occur in cats, rabbits, and nonhuman primates.

Age

Both production and outflow of aqueous humor tend to decline with age, but production declines at a little faster rate than outflow in most individuals. In humans, aqueous production and IOP tend to decline after 60 years of age, although this tendency varies considerably with ethnic background and the presence of other diseases, such as systemic hypertension and obesity. Similarly, IOP in cats has been shown to decline approximately 1 mm Hg per year after 7 years of age. In a small percentage of humans, and perhaps animals, however, aqueous humor outflow is reduced to a greater degree than aqueous humor production, resulting in increased IOP with age.

Blood Flow

Disorders associated with substantially lower blood flow to the eye (e.g., dehydration, hypovolemic shock, cardiogenic shock) tend to result in lower IOP. A dog collar can significantly increase IOP if the dog is pulling against a leash or if the collar is too tight. Dogs with glaucoma probably should be exercised with a harness rather than a collar.

Drugs

In addition to the numerous antiglaucoma drugs that alter IOP, other drugs also may affect IOP. Most general anesthetics and tranquilizers cause IOP to fall. Ketamine may temporarily increase IOP, presumably owing to extraocular muscle spasm.

Ocular Inflammation

Both spontaneous and surgically induced inflammation lower aqueous production and IOP. A profound reduction in IOP is an important diagnostic clue to the presence of intraocular inflammation, especially uveitis.

DIAGNOSTIC METHODS

Tonometry

Measurement of and normal values for IOP are discussed in Chapter 5. It is suggested that the reader refer to that discussion before proceeding with this chapter. Despite its disadvantages, the most *economical* instrument in general veterinary practice is the Schiøtz tonometer with the *human* conversion tables. Surprisingly, dog-specific conversion tables for the Schiøtz tonometer do not agree as well with the more accurate applanation and rebound tonometers, and dog specific tables should *not* be used to convert Schiøtz scale readings to IOP estimates in dogs or cats. Two handheld tonometers that are more accurate and easier to use than the Schiøtz instrument are the Tono-Pen applanation tonometer and the TonoVet rebound tonometer. The ability to perform tonometry is essential to every veterinarian engaged in small animal practice. Tonometry minimizes the chances of making an important or even catastrophic error in diagnosis.

IOP should be determined in every red eye with an intact cornea and sclera.

Ophthalmoscopy

Direct and indirect ophthalmoscopy may be used to examine the optic nerve head for cupping of the optic disc, which is the hallmark of glaucoma. The red-free filter (green light) on many of these instruments facilitates examination of the optic nerve and retinal nerve fiber layer.

Gonioscopy

Gonioscopy is a very useful technique for examining the iridocorneal (filtration) angle and managing glaucoma. It is discussed in detail in Chapter 5. Gonioscopy allows the clinician to differentiate between *open-angle* and *closed-angle* glaucoma, to estimate the severity of the obstruction of the

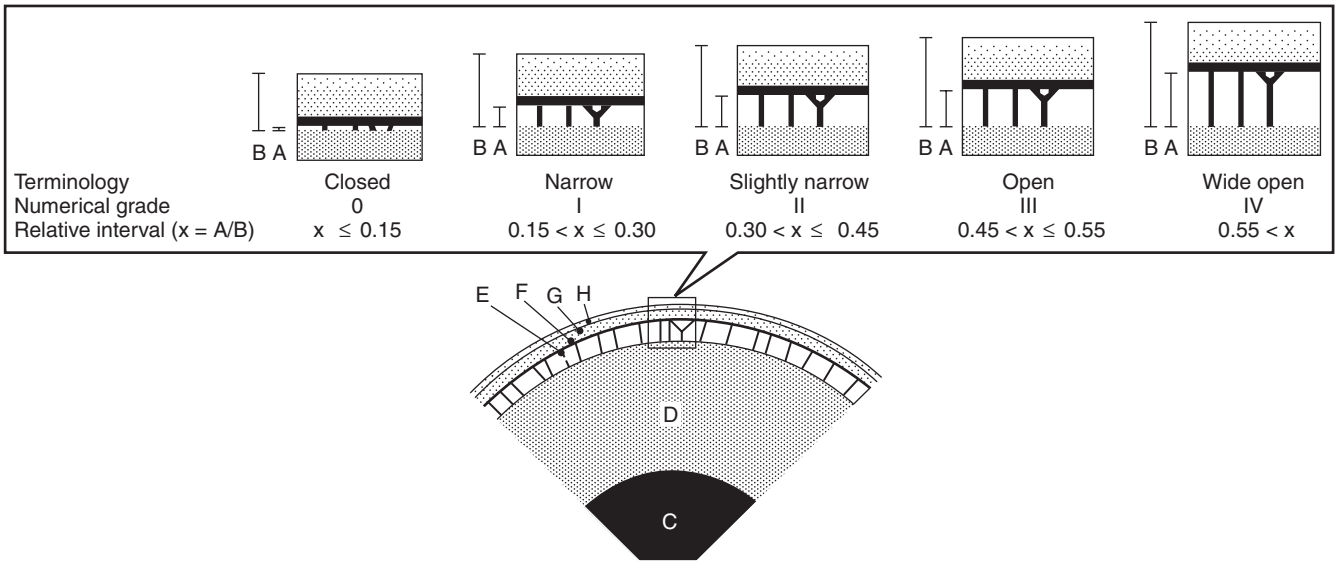


Figure 12-4. Schematic drawing of a grading system for the width of the iridocorneal angle. The ratio of the width of the anterior opening of the ciliary cleft *(A)* and the distance from the origin of the pectinate ligaments to the anterior surface of the cornea *(B)* is estimated. *C,* Pupil; *D,* iris; *E,* pectinate ligament; *F,* deep pigmented zone; *G,* superficial pigmented zone; *H,* cornea. (From Ekesten, B, Narfström K [1991]: Correlation of morphologic features of the iridocorneal angle to intraocular pressure in Samoyeds. Am J Vet Res 52:1875.)

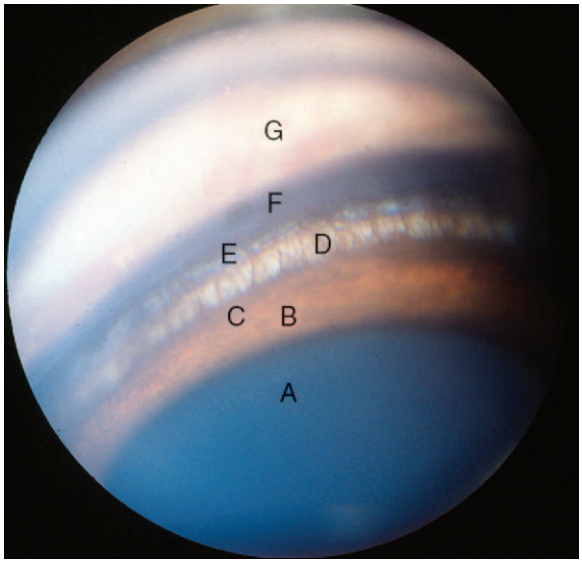


Figure 12-5. Goniophotograph of a normal dog. *A,* Pupil; *B,* iris; *C,* pectinate ligament strands *(thin brown lines); D,* bluish-white zone of the uveal trabeculae (trabecular meshwork); *E,* deep pigmented zone; *F,* superficial pigmented zone; *G,* cornea.

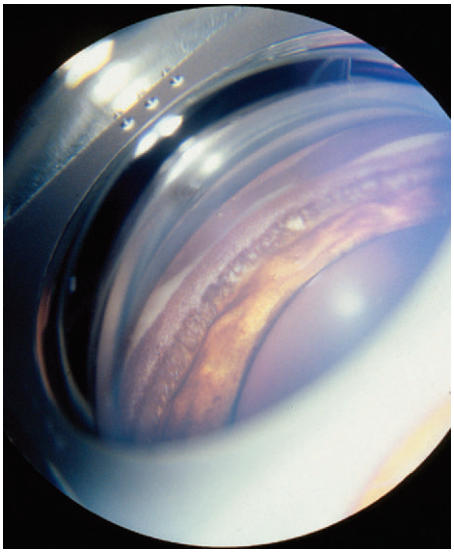


Figure 12-6. Normal canine iridocorneal angle as seen with a goniolens.

iridocorneal angle, and to evaluate the response to therapy (Figure 12-4). It does, however, require considerable practice to recognize the many normal variations and hence gonioscopy tends to be performed almost exclusively by veterinary ophthalmologists. Examples of gonioscopic findings are shown in Figures 12-5 to 12-11.

CLINICAL SIGNS

The effects of increased IOP on ocular tissues are similar regardless of the cause of the elevation. It is essential to consider whether the lesions and clinical signs observed *are associated with* or *result from* the cause of the increased pressure.

Glaucoma is one of the most commonly misdiagnosed eye conditions. Failure of owners to recognize the disease early in its course may prevent effective treatment of the first eye. Failure of clinicians to recognize onset in the second eye may prevent retention of sight.

The clinical signs of glaucoma in the dog are summarized in Figure 12-12. The signs present in a particular animal depend on the duration, intensity, and cause of the pressure elevation. In general the most obvious signs are associated with end-stage

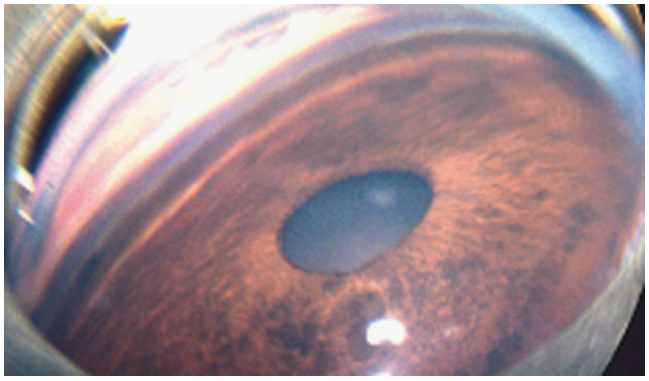


Figure 12-7. Gonioscopic view of the iridocorneal angle of a dog in which the angle is filled with liberated pigment. The physical width of the angle is normal, but the pigment occludes the trabecular meshwork and prevents readily identifying the pectinate ligament.

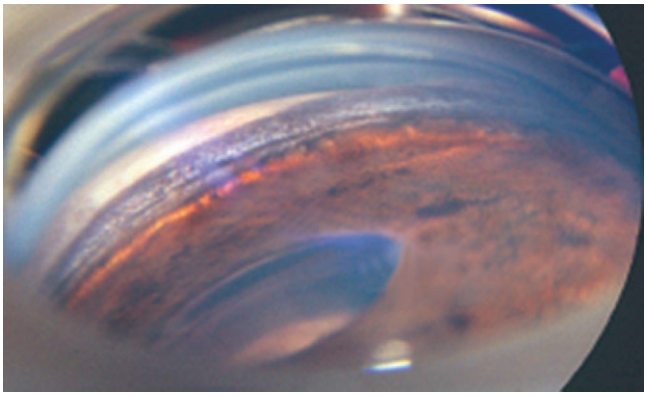


Figure 12-10. Marked pectinate ligament dysplasia characterized by large sheets of mesodermal tissue in a 7-year-old Bouvier dog. Although intraocular pressure is still within normal limits, aqueous humor can exit the eye only via a few small "flow holes" in the mesodermal sheets.

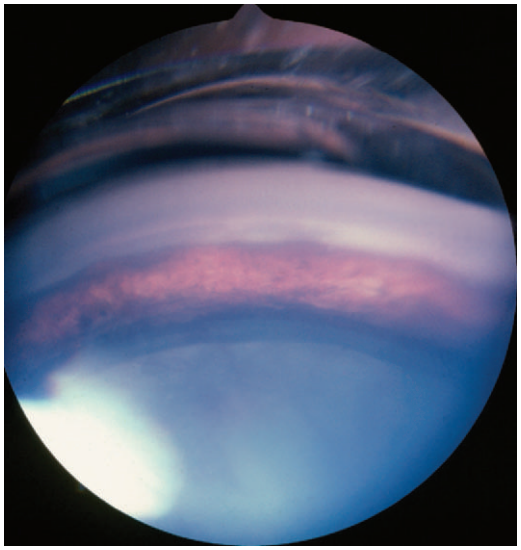


Figure 12-8. Gonioscopic view of a closed angle in a dog with secondary glaucoma. The retina was massively detached, resulting in forward shifting of the lens and, ultimately, of the iris into the iridocorneal angle. Note that the pectinate ligament cannot be seen.

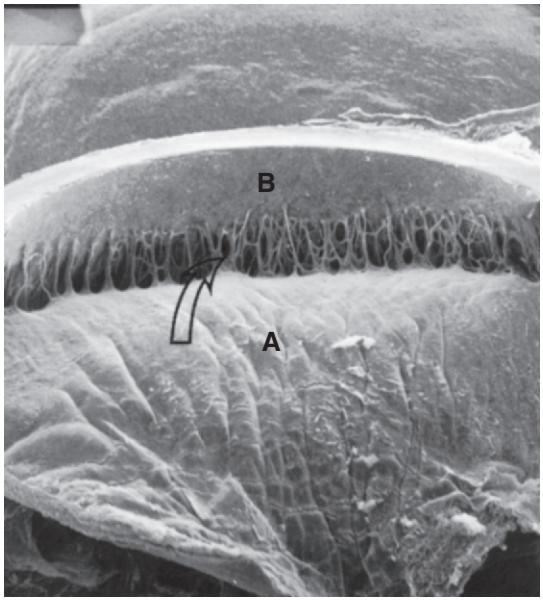


Figure 12-11. Scanning electron micrograph of a canine iridocorneal angle. *A*, Iris; *B,* cornea; *arrow,* pectinate ligament. (From Martin CL, Wyman M [1978]: Primary glaucoma in the dog. Vet Clin North Am 8:257.)

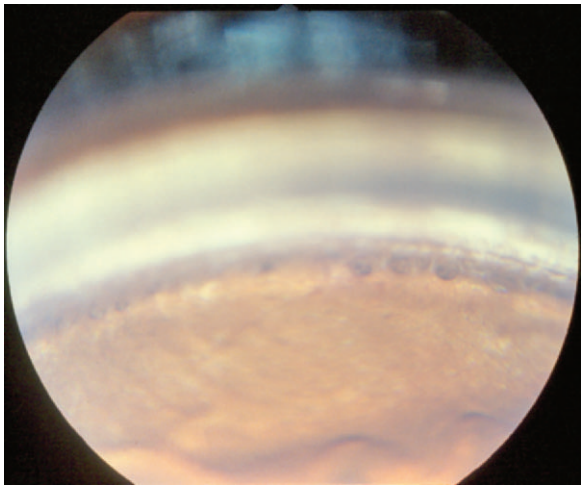


Figure 12-9. Mild pectinate ligament dysplasia characterized by broad-based pectinate ligament strands and a small region of "sheeting."

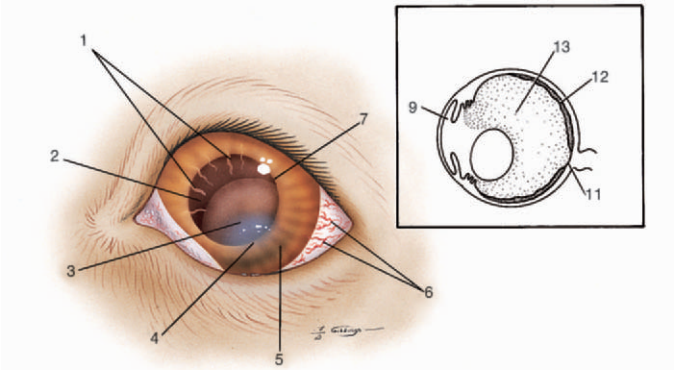


Figure 12-12. Clinical signs of canine glaucoma: *1,* Descemet's streaks (advanced cases); *2,* aphakic crescent; *3,* luxated lens (some cases); *4,* corneal edema; *5,* iris atrophy; *6*, enlarged episcleral vessels; *7,* fixed, dilated pupil; *9,* shallow anterior chamber; *11,* cupping of the optic disc; *12,* retinal atrophy and vascular attenuation; *13,* buphthalmos. Not shown: *8,* increased intraocular pressure; *10,* partial or complete loss of vision; *14,* ocular pain; *15,* loss of corneal sensitivity.

disease in which there is no hope of preserving vision. In the very early stages of glaucoma, in which there is a chance of preserving vision, the eye may appear normal and IOP may or may not be elevated. In some patients there is only a history of intermittent episcleral injection (especially in the evening) that spontaneously resolves, and IOP is normal on examination in the office. Glaucoma may be detected in these animals only by performing tonometry when the eye is red or, occasionally, by repeatedly measuring IOP over 24 hours. In other patients the eye may appear to be essentially normal and the only finding is increased IOP on tonometry. In these patients it is essential to differentiate glaucoma from increased IOP measurements associated with an uncooperative patient, technical problems with measuring IOP (excessive tension on the eyelids, a collar that is too tight, compression of the jugular veins during restraint, etc.), and malfunction of the instrument. Specialist assistance may be required to make the diagnosis of glaucoma in its early stages.

Increased Intraocular Pressure

IOP values exceeding 25 mm Hg in dogs and 27 mm Hg in cats in conjunction with compatible clinical signs are sufficient for a presumptive diagnosis of glaucoma. IOP values greater than 20 mm Hg are suspicious for glaucoma if other clinical signs, especially anterior uveitis, are present or if the patient is being treated for glaucoma. Often IOP exceeds 40 mm Hg by the time the owner notices changes in the eye. Frequent measurement of IOP is an integral part of diagnosis and treatment of the patient with glaucoma.

Pain, Blepharospasm, and Altered Behavior

An acute increase in IOP to 50 to 60 mm Hg or more is typically described by a human as "the worst headache of my life." It is likely that animals experience a comparable degree of pain with pressures in this range. If the IOP rise is acute, the dog may be blepharospastic, depressed, less active, timid, or, in rare cases, more aggressive. Some sleep more, eat less, vomit, and are less interested in play. On occasion they rub at the eye, but this behavior is an unreliable sign of glaucoma. Application of pressure to the affected eye through the upper lid or to the surrounding area may cause severe pain. If the condition is not treated, severe pain and blepharospasm are replaced by signs of chronic pain that many owners may not properly recognize as being attributable to glaucoma. Frequently the owner believes that the pet is simply "getting old" and this is why it is less active, sleeps more, and is less playful. A surgical procedure that alleviates the increased pressure (and accompanying pain) almost invariably results in a comment from the owner that the pet "acts like a new dog."

Elevated IOP should be considered to be painful even if the disease is chronic and the animal outwardly appears normal.

Engorged Episcleral Vessels

Engorgement of episcleral veins (see Figure 12-2, *B*) is one of the more common signs of increased IOP. Episcleral engorgement arises because the increased IOP reduces flow through the ciliary body to the vortex veins, and increased flow passes forward via anastomosing episcleral veins at the limbus (see Figure 12-1). Conjunctival capillaries may also be engorged, but usually to a lesser degree. Episcleral vascular engorgement is a sign of intraocular disease (anterior uveitis or glaucoma) and may be differentiated from superficial conjunctival vessel engorgement (which indicates ocular surface disease) by the following features:

- Episcleral vessels are larger, darker red, and more visible, and pass over a conjunctiva that is usually white or slightly pink. Superficial conjunctival vessels are brighter pink to red and cover a larger portion of the sclera.
- Episcleral vessels do not typically branch the closer they get to the limbus, whereas superficial conjunctival vessels do.
- Episcleral vessels blanch slowly or not at all after the application of topical 1% epinephrine, whereas superficial conjunctival vessels typically blanch within 1 to 2 minutes.

Corneal/Scleral Changes

Edema

Increased IOP impairs the function of the corneal endothelium, resulting in corneal edema. Typically the entire cornea is diffusely edematous in glaucoma, and the edema can be quite dramatic in acute glaucoma when IOP is very high (Figure 12-13). In advanced cases subepithelial bullae may form, which can lead to corneal ulceration if they rupture. In chronic glaucoma both superficial and deep vascularization, scarring, and pigmentation are common.

Buphthalmos and Descemet's Streaks

Chronic increases in IOP results in stretching of the cornea and sclera and enlargement of the globe (*buphthalmos;* Figure 12-14). Buphthalmos may be especially pronounced in young animals and in shar-peis, who have a more easily distended cornea and sclera than most adult dogs. Buphthalmic eyes are almost invariably blind, although limited vision may be retained for a while in some puppies and shar-peis. Buphthalmos is *irreversible* even if the pressure is later reduced, although a variety of surgical procedures are available to restore a cosmetically acceptable appearance.

By the time severe stretching has occurred, atrophy of the ciliary body may have reduced the IOP to normal and pain may be lessened. As the cornea stretches, linear ruptures in Descemet's

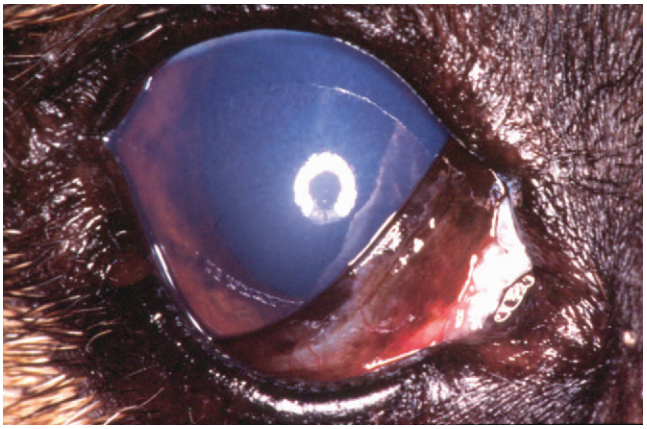


Figure 12-13. Diffuse corneal edema in a dog with glaucoma.

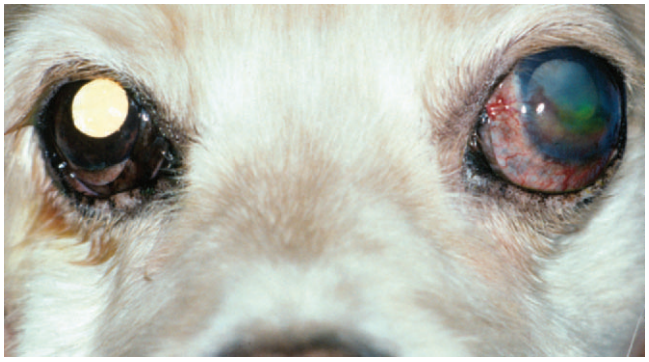


Figure 12-14. Buphthalmos in an American cocker spaniel with chronic primary angle-closure glaucoma. Exposure keratitis is also present.

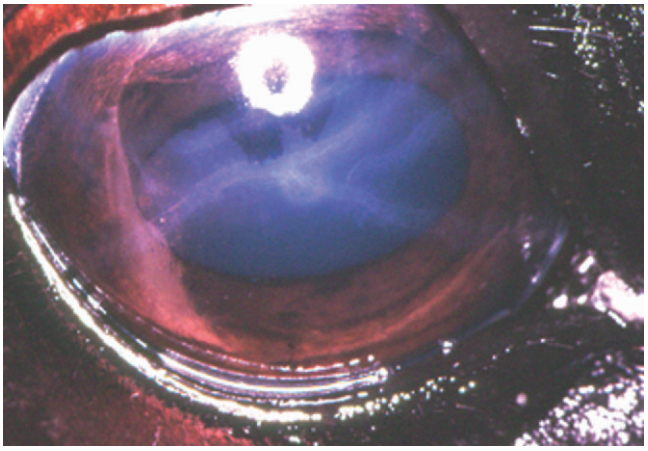


Figure 12-15. Curvilinear breaks in Descemet's membrane (Haab's striae) in the cornea of a horse with chronic glaucoma (intraocular pressure greater than 50 mm Hg).

membrane, called *Descemet's streaks (Haab's striae),* may occur (Figure 12-15).

Changes in Anterior Chamber Depth

Depth of the anterior chamber (distance between cornea and iris) is evaluated with an oblique focal source of light or, better yet, by biomicroscopy. Decreased depth of the anterior chamber is often associated with impediments to outflow through the pupil (because the lens and iris are in greater contact) and the iridocorneal angle (because the anterior chamber is more crowded). A shallow anterior chamber is an especially prominent sign in cats in which aqueous humor is misdirected into the vitreal cavity (resulting in a forward displacement of the lens and iris) and in any animal in which the lens is anteriorly luxated or subluxated. Therefore a shallow anterior chamber should alert the clinician to the possibility of glaucoma. Glaucoma may also be associated with an abnormally deep anterior chamber in animals with posterior lens luxation or in buphthalmic eyes.

Fixed Dilated Pupil

As IOP rises, the pupillary constrictor muscle becomes ischemic and the pupil dilates to midrange or larger (Figure 12-16). A dilated pupil, along with episcleral injection and pain, may be among the first signs noticed by the owner. Mydriasis is not an

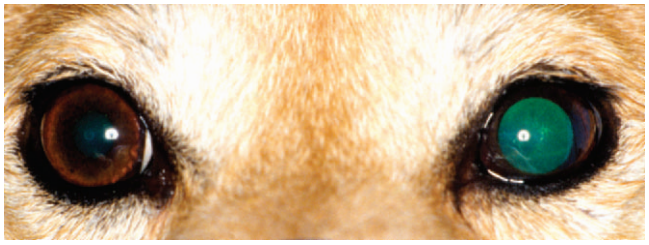


Figure 12-16. Mydriasis (and anisocoria) in a Shiba Inu dog with primary angle-closure glaucoma. A dilated pupil may be the result of ischemia of the iris sphincter muscle or interference with the function of the optic or ciliary nerves.

invariable sign of glaucoma— the pupil may be normal in mild IOP elevations, and miosis may be present in uveitis-induced glaucoma. In these latter cases, a careful examination is necessary to distinguish glaucoma from uveitis, and it is possible for both to be present in the same eye. In chronic glaucoma, or when IOP is acutely markedly elevated, the direct and consensual pupillary light reflexes are usually greatly impaired or absent. The longer glaucoma remains unresolved, the greater the chance that peripheral anterior synechiae will form and permanently block the drainage angle by fixing the peripheral iris in position.

Although a dilated, unresponsive pupil is consistent with glaucoma, it may be due to other diseases (e.g., progressive retinal degeneration, sudden acquired retinal degeneration syndrome, optic neuritis) and is not by itself diagnostic for glaucoma.

Lens Changes

Lens luxation in glaucoma may be either primary or secondary. A glaucomatous eye with a luxated, cataractous lens may have reached this state by one of several ways:

- Cataract (variety of etiologies) → lens-induced uveitis → glaucoma → buphthalmos → tearing of zonules → lens luxation
- Zonular malformation → lens luxation (or subluxation) → glaucoma → cataract
- Glaucoma (variety of etiologies) → buphthalmos → tearing of zonules → lens luxation → cataract

Lens luxation or subluxation may be recognized from the following signs:

- Presence of the lens *in front of* the iris (anterior luxation)
- Presence of an *aphakic crescent* in the pupil (most frequent in subluxation)
- Movement of the iris *(iridodonesis)* or lens *(phacodonesis)*
- Abnormally *shallow or deep anterior chamber*
- *Vitreous strands* in the pupil

If a luxated lens enters the anterior chamber and touches the corneal endothelium, a focal area of corneal edema may result. This opacity is frequently permanent, even if the lens is later removed. The continuous presence of a luxated lens in the anterior chamber damages the endothelium over a wider area and lowers the probability of successful surgical removal of the lens.

The recognition of how the final state was reached is important in determining which combination of therapeutic

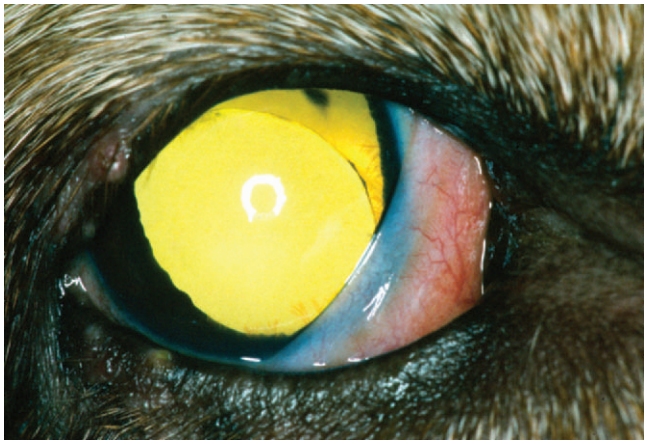


Figure 12-17. Chronic glaucoma in a basset hound resulting in buphthalmos and secondary tearing of lens zonules. The equator of the lens is visible superonasally that creates an aphakic crescent in this region.

methods is required. History and signalment are critical factors in differentiating between these various possibilities. In all three pathways the lens may be displaced anteriorly or posteriorly or may be in the plane of the iris (either superiorly or inferiorly). An *aphakic crescent* is formed when the lens zonules have broken for a portion of the circumference of the lens, and it is possible to visualize the tapetal reflex through a crescent-shaped space between the lens equator and the pupillary border (Figure 12-17). After luxation the lens frequently, but not invariably, becomes cataractous.

Primary lens luxation, as occurs in terriers and certain other breeds (Box 12-1), may result in pupillary block with acute elevations in IOP. The presence of *vitreous strands* in the anterior chamber in the absence of buphthalmos suggests primary lens luxation. In these animals the lens may be completely luxated or only partially luxated (subluxation), and usually the lens is not cataractous until it becomes luxated (Figures 12-18 and 12-19).

Primary glaucoma tends to occur in middle-aged to somewhat older dogs of certain breeds (Box 12-2), and the lens

Box 12-1 | **Inherited and breed predisposition to lens luxation in dogs**

Breeds in Which Lens Luxation Is Inherited

Border collie
Cairn terrier
Jack Russell terrier
Lakeland terrier
Manchester terrier
Miniature bull terrier
Norfolk terrier
Norwich terrier
Scottish terrier
Sealyham terrier
Skye terrier
Smooth haired fox terrier
West Highland white terrier
Tibetan terrier
Wirehaired fox terrier

Breeds with Predisposition to Lens Luxation

Australian shepherd
Basset hound
Beagle
Chihuahua
German shepherd
Greyhound
Miniature poodle
Miniature schnauzer
Norwegian elkhound
Pembroke Welsh corgi
Spaniel breeds
Welsh terrier
Toy poodle
Toy terrier

Modified from Gelatt KN, Brooks DE (1999): The canine glaucomas, in Gelatt KN (editor): Veterinary Ophthalmology, 3rd ed. Lippincott Williams & Wilkins, Philadelphia.

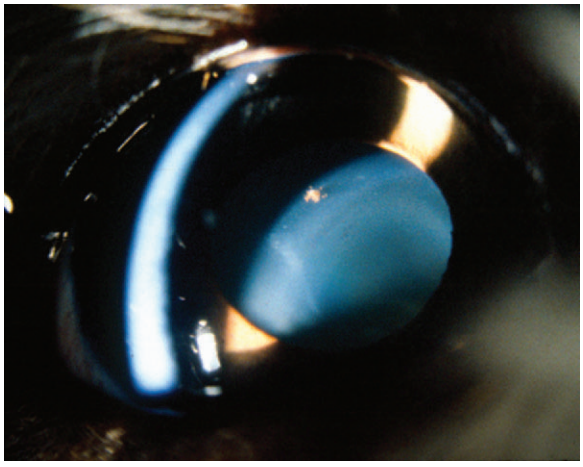


Figure 12-18. Lens subluxation in an 8-year-old wirehaired fox terrier. Notice that the anterior chamber is deeper superiorly than inferiorly, indicating that the lens has shifted position. The iris and lens also "trembled" when the eye moved (iridodonesis and phacodonesis).

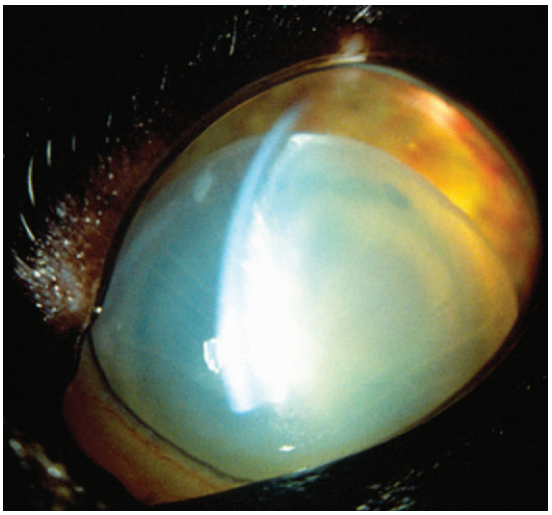


Figure 12-19. Complete anterior lens luxation associated with chronic uveitis in a cat. Secondary glaucoma was also present.

Box 12-2 | Breeds of dog most commonly affected with different types of glaucoma

Primary Open-Angle Glaucoma

Mixed breeds
American cocker spaniel
Basset hound
Boston terrier
Miniature schnauzer
Beagle
Chow chow
Siberian husky
Standard poodle

Closed-Angle Glaucoma

American cocker spaniel
Mixed breeds
Basset hound
Samoyed
Beagle
Siberian husky
Labrador retriever
Toy poodle

Secondary Glaucoma

Mixed breeds
American cocker spaniel
Wirehaired fox terrier
Toy poodle
Boston terrier
Miniature poodle
Labrador retriever
Siberian husky
Basset hound
Beagle

From Miller PE (1995): Glaucoma, in Bonagura JD (editor): Kirk's Current Veterinary Therapy XII: Small Animal Practice. Saunders, Philadelphia. Breeds are listed in descending order of frequency as recorded by the Veterinary Medical Data Base over a 20-year period.

subluxation or luxation does not occur until the globe has become buphthalmic and the lens zonules are stretched beyond the breaking point (secondary luxation). Similarly, primary cataract formation in a wide variety of breeds is frequently followed by lens luxation and glaucoma. Lens-induced uveitis from a secondarily luxated lens that has become cataractous from elevated IOP, and decreased IOP from the uveitis further complicate diagnosis and treatment. Thus the combination of glaucoma, cataract, and lens luxation in any particular eye may occur through several mechanisms and may be associated with a variety of IOP values at any given moment.

Lens luxation in a glaucomatous eye does not necessarily mean that luxation was the inciting cause of the glaucoma. The luxation may have *resulted from* the glaucoma.

Fundus Changes

Impaired Vision

Loss of some or all vision is a common sequela of glaucoma. In the early stages peripheral vision may be lost (Figure 12-20),

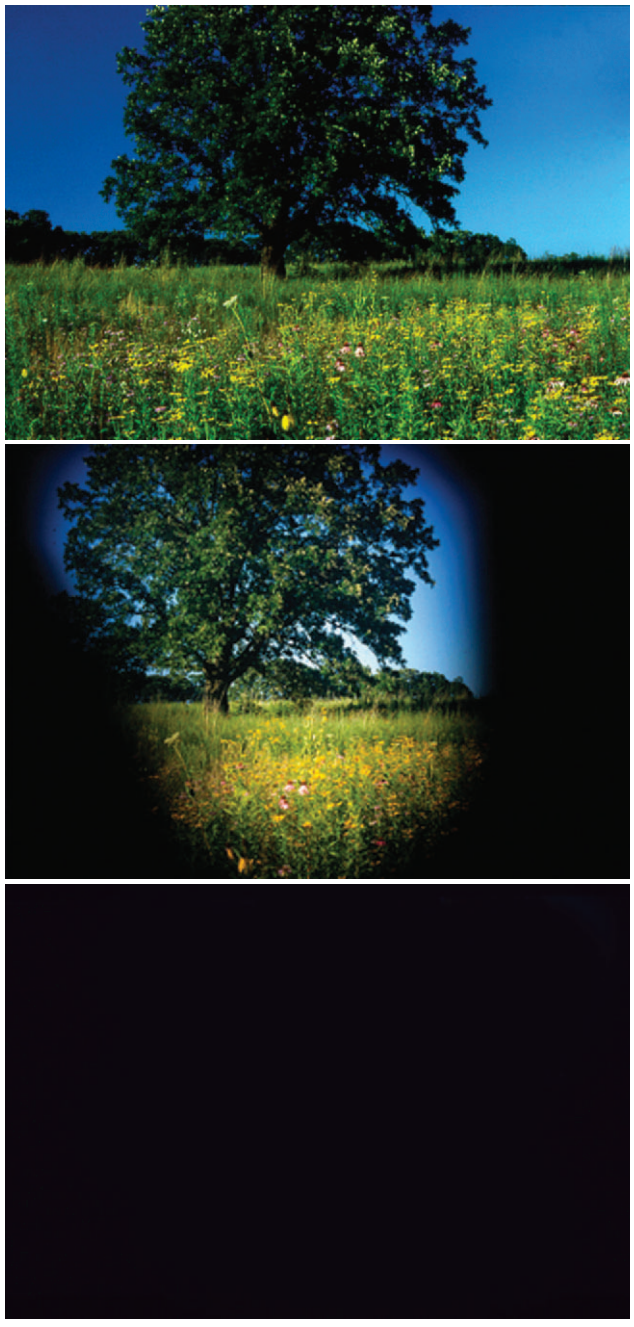


Figure 12-20. Simulated changes in vision due to glaucoma. **A,** Normal visual field. **B,** Moderate vision loss in glaucoma; the peripheral visual field is reduced but central vision may persist. **C,** End-stage glaucoma; vision is completely lost.

and it is difficult, if not impossible, to detect these changes in most animals. Complete vision loss can occur in a very short period (hours to a day) if the increase in IOP is very high, or over a period of weeks to months if the pressure increase is more insidious. Preservation of vision depends on control of IOP.

Optic Disc Cupping

Cupping, or posterior bowing of the optic disc through the lamina cribrosa, is the hallmark of glaucoma. Retinal nerve fibers run parallel to the surface of the retina and then turn

90 degrees to enter the multilayered, fenestrated meshwork of the lamina cribrosa before exiting the eye. Glial cells, blood vessels, and collagen beams form variably sized pores through which the optic nerve fibers pass. When IOP rises the scleral lamina cribrosa bows posteriorly, distorting the alignment of the pores and compressing the optic nerve fibers. Although this change may initially be so subtle as to not be detected ophthalmoscopically, it is sufficient to mechanically interfere with axonal axoplasmic flow and also probably with blood supply to the optic nerve head. Very large increases in IOP may also interfere with blood flow to the choroid and produce vision loss through ischemic damage to the photoreceptors and outer retinal layers. In acute glaucoma the optic disc may appear swollen in response to ischemia. Within a day or two the increased pressure may cause the disc to appear pale and compressed. As ganglion cell axons die, optic nerve head tissue is lost and pressure forces the lamina cribrosa outward (Figures 12-21 to 12-23). This change indicates irreversible damage to the optic nerve. Wallerian degeneration of the optic nerve follows (Figure 12-24).

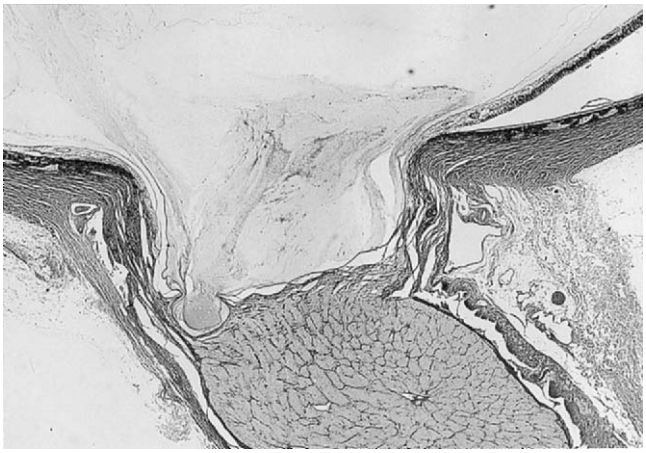


Figure 12-21. Cupping of the optic disc with loss of tissue anterior to the lamina cribrosa, which is bowing posteriorly. (From Slatter D [2003]: Textbook of Small Animal Surgery, 3rd ed. Saunders, Philadelphia.)

Retinal Degeneration

In advanced glaucoma, profound retinal atrophy with increased tapetal reflectivity occurs together with attenuation or complete loss of retinal vessels, atrophy of the pigment epithelium in the nontapetal fundus, and optic atrophy (grayish-white appearance; Figure 12-25). These findings are also present in advanced progressive retinal degeneration (progressive retinal atrophy). In progressive retinal degeneration the other signs of glaucoma are lacking, the disease is usually bilateral, the optic disc is not cupped, and differential diagnosis may be determined by the breed of dog and lack of other clinical signs of glaucoma. Ophthalmoscopically visible retinal and optic nerve lesions of glaucoma are irreversible.

Elevation of IOP decreases blood flow in the choroid, resulting in ischemia. This ischemia can be demonstrated func-

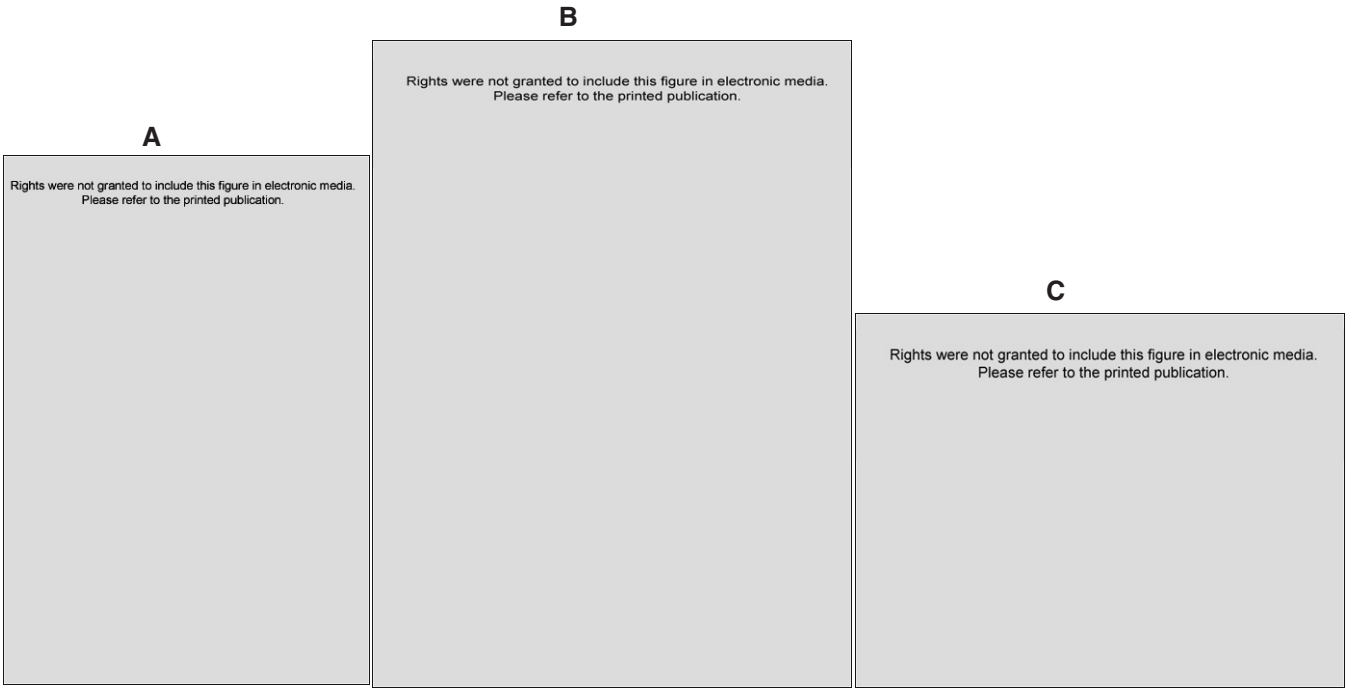


Figure 12-22. The scleral lamina cribrosa in normal and glaucomatous eyes. **A,** Normal (upper) and glaucomatous (lower) eye pore arrangement. From the normal pores in the normal eye, glaucoma causes pore misalignment and posterior movement or cupping of the lamina cribrosa. **B,** Trypsin digestion and scanning electron microscopy of a normal dog optic nerve head demonstrates the three-dimensional architecture of the scleral lamina cribrosa (original magnification, ×60). **C,** Trypsin digestion and scanning electron microscopy of a primary open-angle glaucomatous optic nerve head shows posterior displacement and loss of pore arrangement, which may impair axoplasmic and local capillary blood flow (original magnification, ×60). (From Brooks DE, et al. [1989]: Morphologic changes in the lamina cribrosa of beagles with primary open-angle glaucoma. Am J Vet Res 50:936.)

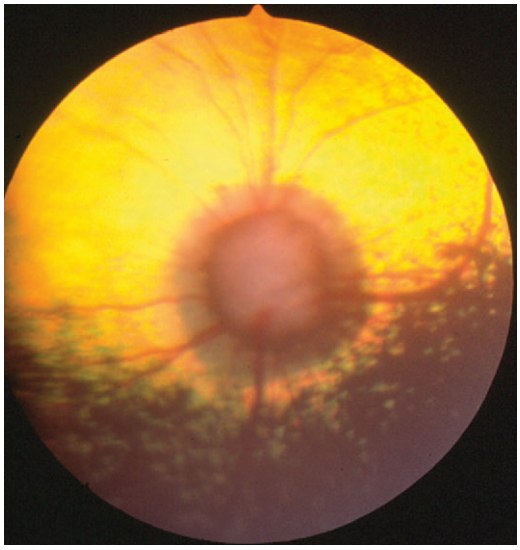


Figure 12-23. Optic disc cupping. Most retinal vessels disappear at the disc edge. The center of the disc is in focus below the level of the retinal surface and is grayish. There also is a peripapillary ring of altered retinal reflectivity. (Courtesy Dr. Christopher J. Murphy.)

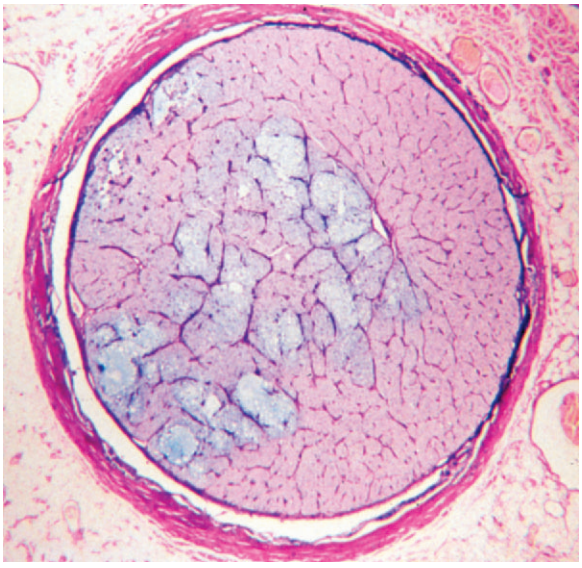


Figure 12-24. Cross-sectional view of the optic nerve of a dog with glaucoma. The paler blue areas represent degenerated nerve fiber axons. (Courtesy Dr. Richard R. Dubielzig.)

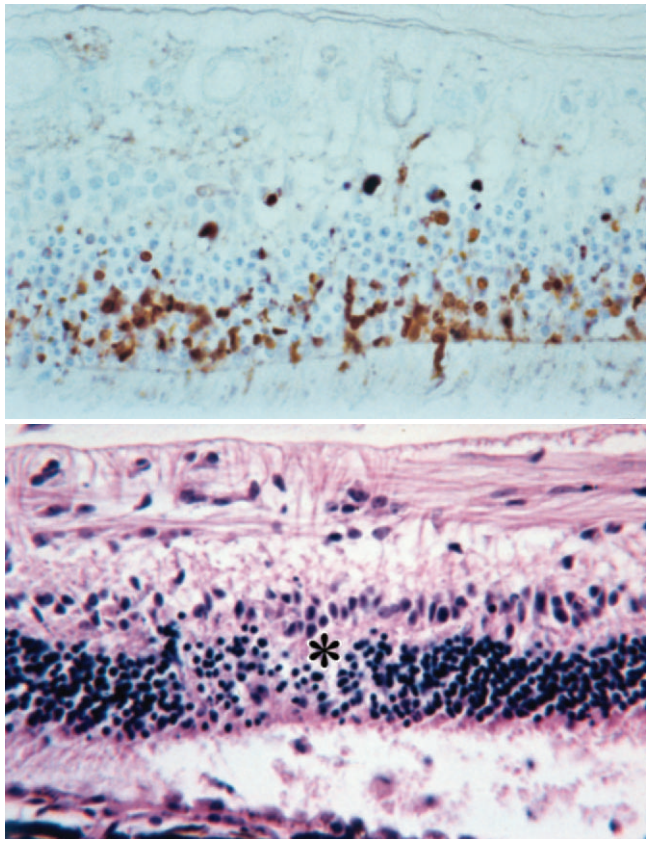


Figure 12-25. Retinal changes in acute primary angle-closure glaucoma. **A,** The retinal cells, which stain brown in this immunohistochemically stained section, are undergoing apoptosis. **B,** Histologic section of a retina showing segmental loss of nuclei in the photoreceptor layer *(*)*. (Courtesy Dr. Richard R. Dubielzig.)

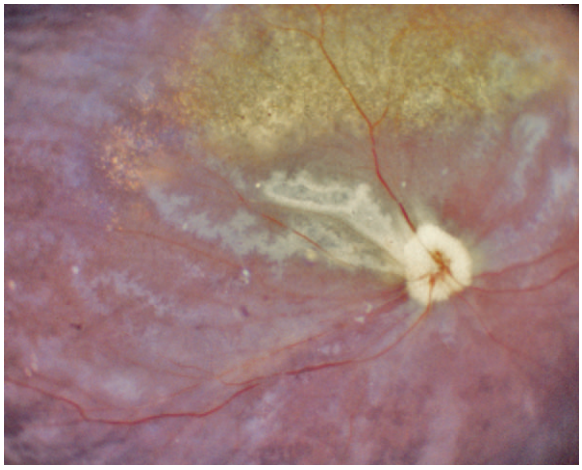


Figure 12-26. Postenucleation specimen from a dog with acute primary angle-closure glaucoma. Light-colored, roughly wedge-shaped regions of retinal necrosis, presumably secondary to impaired choroidal circulation, are apparent. (Courtesy Dr. Richard R. Dubielzig.)

tionally by depressed electroretinograms, and in some patients it is possible to visualize wedge-shaped defects in the retina that correspond to pressure-induced infarction of the choroidal blood supply (Figure 12-26). Early in glaucoma, if the pressure elevation is acute and very large, the photoreceptors in the retina undergo necrosis. In the next few days they begin to die by apoptosis as well. Ophthalmoscopically the cell death is seen as increased tapetal reflectivity. As in any other severe retinal atrophy, the condition is irreversible.

It has now been recognized that increased IOP may initiate a chain of events that can continue to impair vision despite return of IOP to within normal limits (Figure 12-27). In human primary open-angle glaucoma (POAG), in which the rise in IOP is more insidious and of usually smaller magnitude than in acute canine primary angle-closure glaucoma (PACG), vision loss is usually attributed mainly to retinal ganglion cell degeneration. Pressure-associated alterations in microcirculation and/or axoplasmic flow at the level of the lamina cribrosa may play a role in the death of ganglion cells in this form of glaucoma. Dying

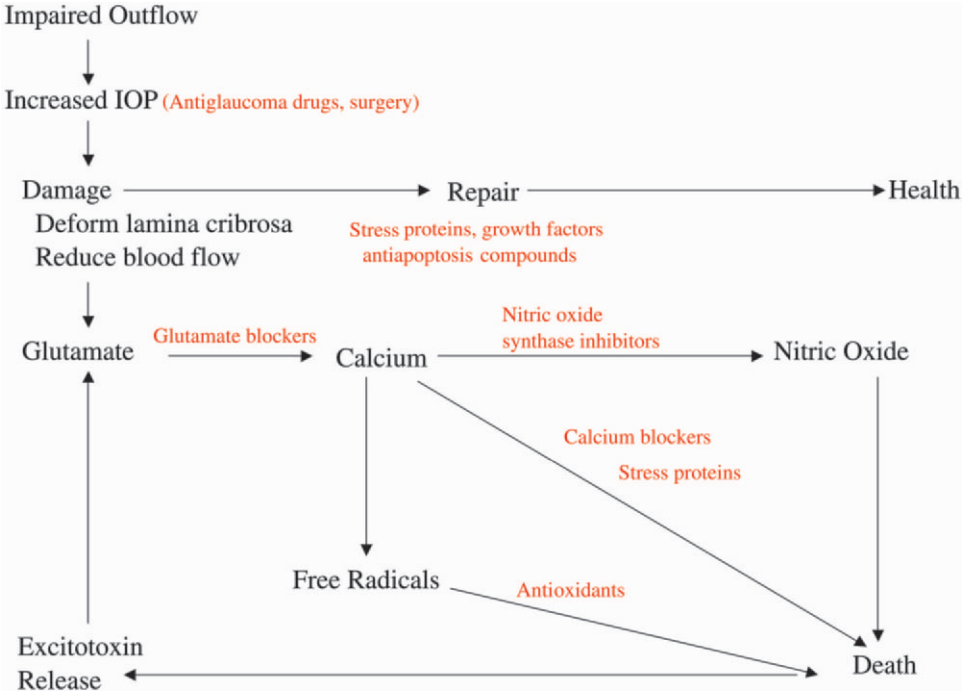


Figure 12-27. Cell death in glaucoma. Potential therapeutic interventions are in red. Once cell death begins, a self-perpetuating circle can occur that is not susceptible to intervention by current intraocular pressure–lowering medications or surgery.

ganglion cells may then release glutamate and other excitatory compounds that initiate a self-perpetuating circle of apoptotic cell death in previously unaffected neighboring ganglion cells. In dogs with acute PACG and more rapid/marked increases in IOP, one study found retinal damage to extend well beyond the ganglion cell layer. Within the first few days of an attack of acute PACG ganglion cell necrosis and segmental full-thickness areas of retinal attenuation consistent with infarction were apparent. As ganglion cell and retinal necrosis decreased over the ensuing days retinal cell death by apoptosis markedly increased. This finding suggests that in acute PACG, the marked increase in IOP not only interferes with axoplasmic flow through the lamina cribrosa but also causes ischemic necrosis of the retina. Again, as these cells die they initiate a vicious circle of progressive cell death due to apoptosis that continues despite normalization of IOP. This hypothesis would explain the clinical observation that even though IOP is controlled in some dogs with PACG, progressive vision loss still occurs.

Although this sequence of events is discouraging, it does offer the possibility for the development of additional therapeutic avenues for the treatment of glaucoma, including neuroprotective agents that prevent cell suicide via apoptosis, drugs that help maintain retinal/optic nerve blood flow and minimize ischemia, and modalities that interrupt reperfusion injuries when IOP is reduced from very high levels to normal. These differences in the histologic appearance among the various forms of glaucoma also reinforce the concept that glaucoma is not a single entity and that there are likely to be important differences in the cellular events leading to vision loss in patients with glaucoma.

CLASSIFICATION

Glaucoma almost invariably is the result of impaired aqueous humor outflow. In fact, in most patients with glaucoma aqueous humor production is less than normal (but still excessively high in view of the outflow capacity of the eye). The mechanism of this impairment may be etiologically classified as primary or secondary. *Primary glaucomas* have no consistent, obvious association with another ocular or systemic disorder, are typically bilateral, have a strong breed predisposition, and hence are believed to have a genetic basis (see Box 12-2). Primary glaucoma is subdivided into two main forms, *primary open-angle glaucoma,* 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,* in which the drainage angle appears gonioscopically narrowed or closed (Figures 12-28 through 12-33). In the dog, PACG is at least eight times more common than POAG. Acute PACG also is two times more common in female dogs than in male dogs. A similar sex predisposition has been found in humans with PACG and has been attributed to a generally shallower anterior chamber in women than in men.

Secondary glaucomas are at least twice as common as primary glaucomas in dogs (and even more common in cats) and are associated with other ocular or systemic disorders that alter aqueous humor dynamics. Secondary glaucoma may be unilateral or bilateral and may or may not be inherited; the physical width of the gonioscopically visible drainage angle may also be classified as open or closed. Often the exact mechanism by which outflow is impaired in secondary glaucoma is unclear.

Because glaucoma is almost always due to the impaired flow of aqueous humor, it can be very useful to classify glaucoma according to the location(s) of those impediments (Box 12-3). Impediments to the normal flow of aqueous humor commonly occur at the level of the ciliary body, pupil, trabecular meshwork, angular aqueous plexus, scleral venous system, or episcleral veins. Frequently the obstruction to outflow starts at one place

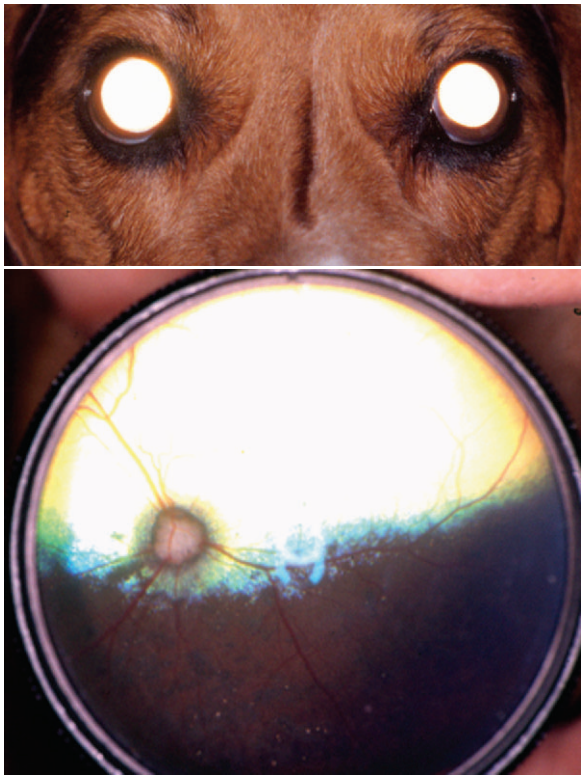


Figure 12-28. A beagle with chronic primary open-angle glaucoma. **A,** Both pupils are dilated and intraocular pressure is increased in both eyes (approximately 50 mm Hg). **B,** Fundus photograph of the same dog. The optic nerve is depressed from the surface of the fundus (cupped), has little myelin, and is darker than normal. The area surrounding the optic disc also has altered reflectivity.

(for example, the lens-pupil interface), but as the disease progresses, impediments to outflow also develop in more anterior structures (for example, at the iridocorneal angle; Figure 12-34), further worsening the problem. Therefore the longer the increased IOP persists, the more difficult it will be to successfully treat the patient.

The keys to successful therapy for glaucoma are early recognition of the problem, correct identification of the location of the impediment to outflow, and circumvention of that obstruction before additional impediments to outflow develop.

PATHOGENESIS

Primary Open-Angle Glaucoma

POAG is a bilateral disorder in which IOP tends to increase in a slow, insidious fashion simultaneously in both eyes in young to middle-aged dogs of certain breeds, most notably the beagle and the Norwegian elkhound (see Figures 12-28 and 12-29). Initially the gonioscopically visible angle is open. Over time the angle closes, the globe becomes buphthalmic, and the lens may subluxate. The precise mechanism of POAG in dogs is unclear, but it most likely results from subtle biochemical alterations in the trabecular meshwork that ultimately lead to greater resistance to aqueous outflow and increased IOP. In beagles, the defect appears to be inherited in an autosomal recessive fashion and may involve the glycosaminoglycan accumulation in the trabecular meshwork.

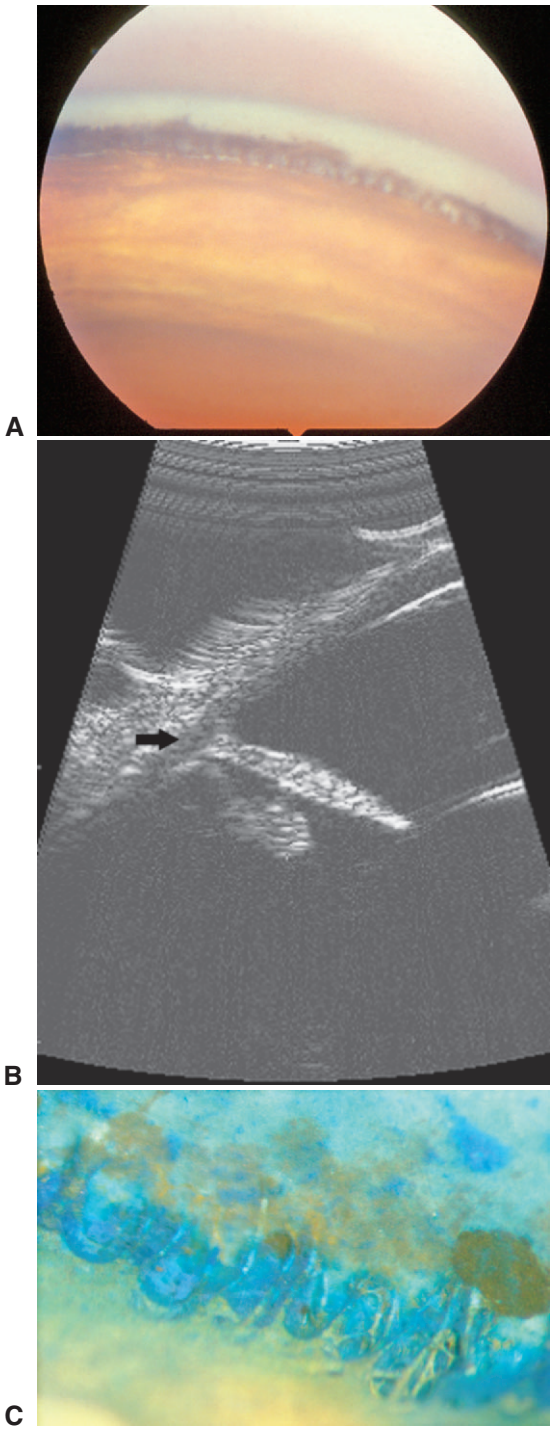


Figure 12-29. Primary open-angle glaucoma in a beagle (same dog as in Figure 12-28). **A,** The iridocorneal angle is gonioscopically relatively open. **B,** High-resolution ultrasound image of the anterior segment. Note that the iris does not have the same conformation as in dogs with primary angle-closure glaucoma (see Figure 12-31) and that the ciliary cleft is still open *(arrow)*. **C,** Dissecting microscope photo of a normal iridocorneal angle of a dog that has been stained to highlight the normal glycosaminoglycans (GAGs) in the trabecular meshwork (deep blue between the pigmented pectinate ligaments). Abnormal GAGs are believed to play a role in the genesis of primary open-angle glaucoma.

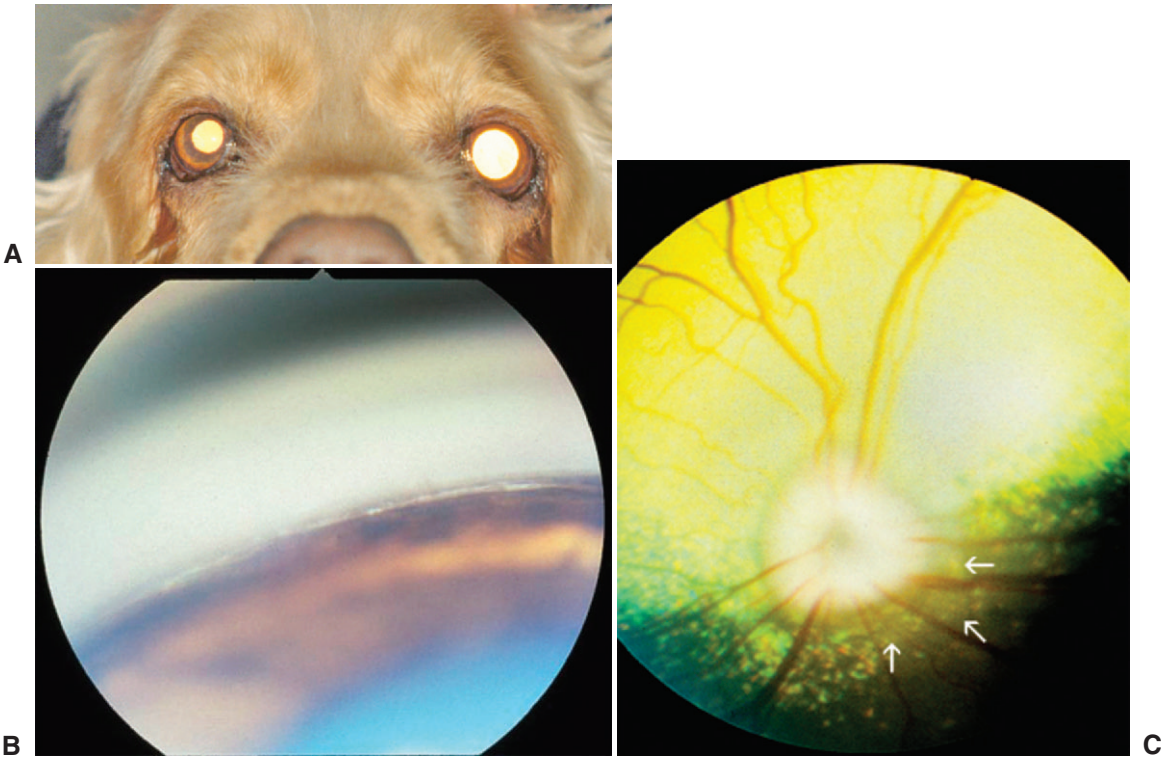


Figure 12-30. Acute angle-closure glaucoma in an American cocker spaniel. **A,** This disorder usually first manifests as a unilateral disease, but both eyes are ultimately affected. **B,** Gonioscopy shows that the iridocorneal angle is closed. **C,** In the acute stages the optic nerve is pale and there is subtle peripapillary swelling *(arrows)*.

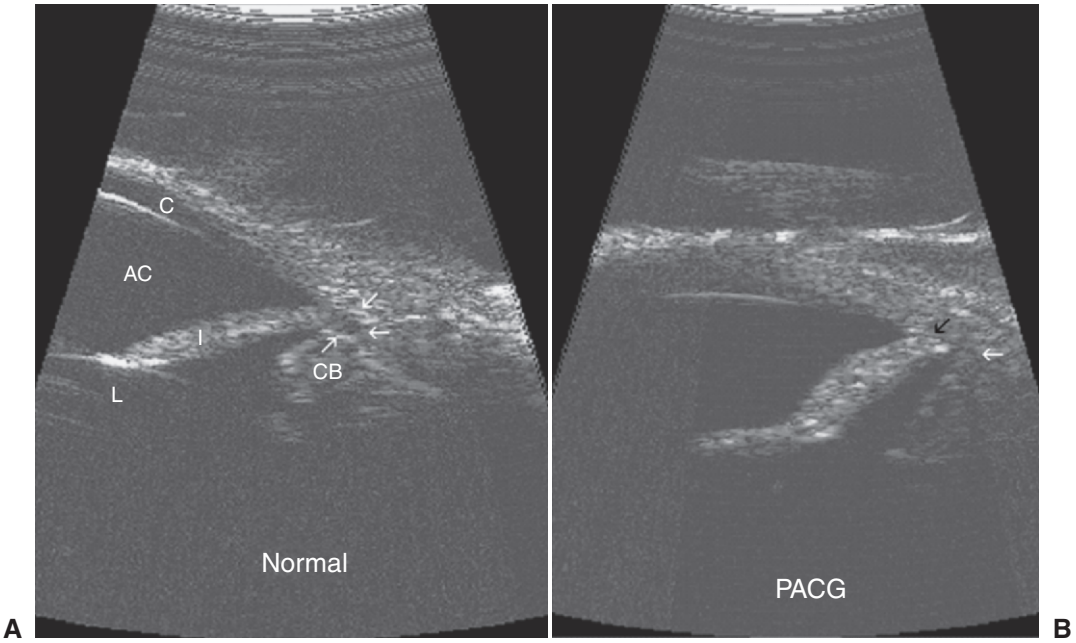


Figure 12-31. A, High-resolution ultrasound image of a normal eye. *AC,* anterior chamber; *C,* cornea; *CB,* ciliary body; *I,* iris; *L,* lens. White arrows outline the ciliary cleft. **B,** An eye with acute primary angle-closure glaucoma *(PACG)*. Note the sigmoidal shape of the iris, increased contact of the peripheral iris with the cornea *(black arrow),* and collapse of the ciliary cleft *(white arrow)*.

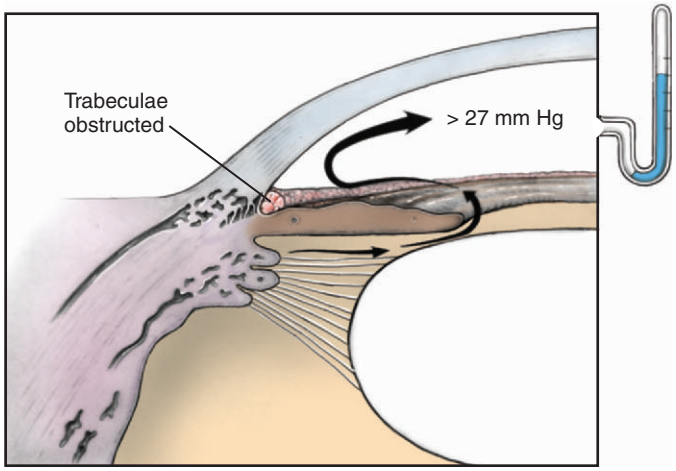


Figure 12-32. Open-angle glaucoma due to trabecular obstruction. The angle itself is normal gonioscopically.

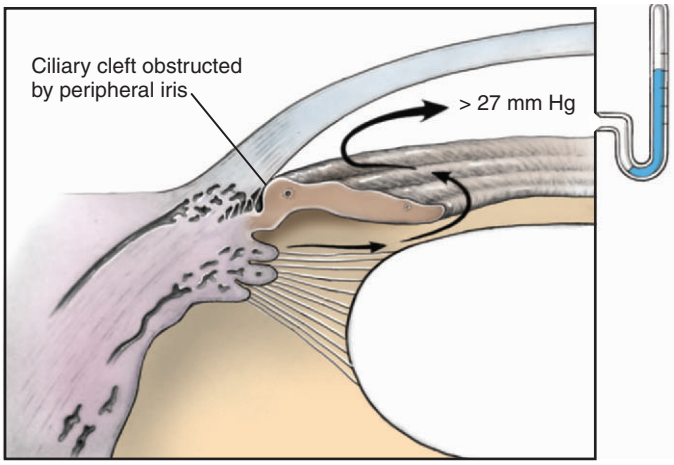


Figure 12-33. Closed-angle glaucoma. The peripheral iris prevents access by the aqueous to the ciliary cleft and drainage network. Obstruction at the pupil is also common in the closed-angle glaucomas.

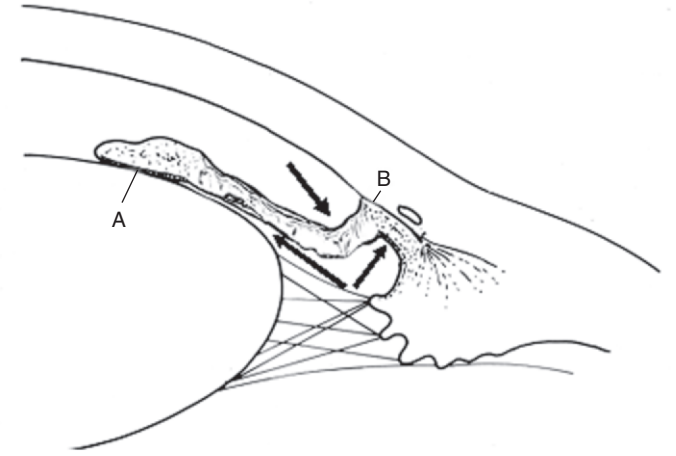


Figure 12-34. Proposed reverse pupillary block theory of the mechanism of primary angle-closure glaucoma in dogs. See text for complete description. Pectinate ligament dysplasia holds the peripheral iris in close contact with the inner surface of the cornea. Stress or excitement increases the choroidal pulse, forcing small aliquots of aqueous humor into the anterior chamber, which result in a slightly higher pressure in the anterior chamber than in the posterior chamber. This difference forces the iris against the lens near the pupil border, creating pupil block *(A)*. Prolonged increases in intraocular pressure lead to peripheral anterior synechia *(B)* and further impediment to aqueous humor outflow.

Box 12-3 | Glaucoma classification by location (posterior to anterior)

1. Ciliary body–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:
      (1) Luxated lens
      (2) Intumescent lens
   d. Posterior synechia/iris bombé
3. Trabecular meshwork:
   a. Primary open-angle glaucoma
   b. Secondary obstructions:
      (1) Preiridal fibrovascular membranes
      (2) Cellular/proteinaceous material:
         (a) Vitreous
         (b) Plasma proteins
         (c) Neoplastic cells
         (d) Red blood cells
         (e) Pigment
         (f) 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. Posttrabecular 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: more than one of the preceding mechanisms

Adapted from Slatter D (2003): Textbook of Small Animal Surgery, 3rd ed. Saunders, Philadelphia.

Primary Angle-Closure Glaucoma

PACG is also a bilateral disorder but it tends to manifest as an initially unilateral, rapid, marked increase in IOP in middle-aged to older dogs of certain breeds (see Figures 12-30 and 12-31, Box 12-2, and Table 12-1). An overt attack of glaucoma usually occurs in the initially normotensive fellow eye a median of 8 months after disease in the first eye becomes apparent. Again, the precise mechanism by which PACG occurs is uncertain, but there is a clear association with congenital pectinate ligament dysplasia (PLD or goniodysgenesis; see later). It is also associated with a female sex predisposition (approximately 2:1 female-to-male ratio), periods of stress or excitement, and dim light. Women also have a similarly higher risk of PACG than men, which has been attributed to a smaller, somewhat more "crowded" anterior chamber in women. Whether a similar phenomenon explains the female sex predisposition to PACG in dogs is unclear. Some dogs also experience transient, self-limiting episodes in which IOP spikes upwards but spontaneously returns to normal.

Table 12-1 | **Features of Canine Breed-Specific Glaucomas**

BREED	TYPE	USUAL PRESENTATION	ASSOCIATION WITH PECTINATE LIGAMENT DYSPLASIA	FEATURES
American cocker spaniel	Narrow to closed angle	Acute and chronic presentations	Infrequent	Most common primary glaucoma in United States. A series of self-limiting attacks may precede a final overt attack.
Chow chow	Narrow to closed angle	Acute and chronic presentations	Infrequent	Vision often retained with high pressures
Welsh springer spaniel	Narrow to closed angle	Acute and chronic presentations	No	Possible dominant inheritance
Bassett hound	Narrow to closed angle	Acute and chronic presentations	Common	Uveitis often also present but not clear if cause or effect
Flat-coated retriever	Narrow to closed angle	Acute and chronic presentations	Common	More common in England than in United States
Great Dane	Narrow to closed angle	Acute presentation	Common	More common in England than in United States
Samoyed	Narrow to closed angle	Acute and chronic presentations	Common	Lens is positioned anteriorly; pupil block may be involved
Bouvier des Flandres	Narrow to closed angle	Acute and chronic presentations	Common	May affect young dogs (1-3 yrs of age) as well as older (6-9 yrs of age)
Beagle	Open angle	Clinical cases rare; chronic syndrome	No	Autosomal recessive, angle closes late in disease. Clinical signs slow and insidious. Typically 2–5-yr-old dogs.
Norwegian elkhound	Open angle	Clinical cases rare; chronic syndrome	No	Vision often retained with high pressures Narrow to closed angle glaucoma with pectinate ligament dysplasia may also occur in breed

PLD is a condition in which the normally fine pectinate ligaments are replaced by tissues that range from a few broad-based, thick pectinate ligaments to large sheets of dysplastic tissue that cover varying amounts of the trabecular meshwork and deeper structures of the iridocorneal angle (see Figures 12-9, 12-10, 12-35, and 12-36). Large sheets of tissue may be punctuated by variably sized perforations ("flow holes") that permit aqueous humor to enter the trabecular meshwork. The deeper tissues of the iridocorneal angle may or may not be normal. Because the spaces within the trabecular meshwork tend to segmentally interconnect beneath the sheets of dysplastic pectinate ligaments, IOP tends to be normal even if only a few flow holes are present. Although virtually any breed of dog can be affected by PLD, the disorder is especially common in the basset hound, Bouvier des Flandres, American and English cocker spaniels, Norwegian elkhound, Siberian husky, dachshund, miniature poodle, Welsh terrier, wirehaired fox terrier, and Chihuahua.

PLD, however, is only one risk factor for PACG and in and of itself it is insufficient to cause glaucoma in all but the most extreme and rare case in which the dog is born with glaucoma (congenital glaucoma). Evidence for this view comes from the observation that even though PLD is present at birth, glaucoma

Figure 12-35. Sheets of mesodermal tissue obstructing access by aqueous to the ciliary cleft. Compare with the normal angle in Figure 12-11. Note the flow holes *(arrows)*. *C,* Cornea; *I,* iris; *S,* sclera. (From Martin CL, Wyman M [1978]: Primary glaucoma in the dog. Vet Clin North Am 8:257.)

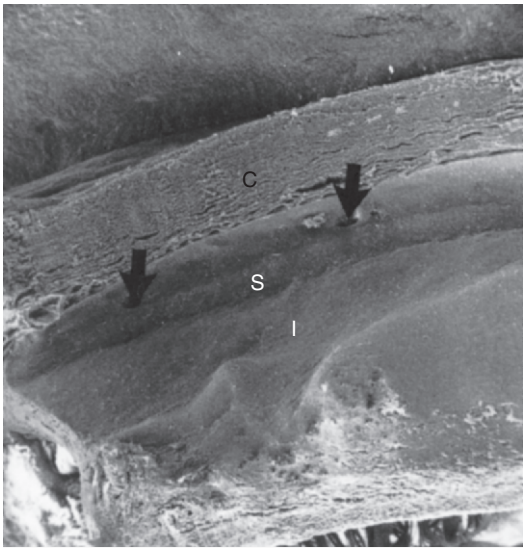


Figure 12-36. Lesion similar to the one shown in Figure 12-35, but with more extensive obstruction. *C,* Cut cornea; *I,* iris; *S,* sclera. Arrows delineate sheet with pores. (From Martin CL, Wyman M [1978]: Primary glaucoma in the dog. Vet Clin North Am 8:257.)

does not develop until the dog is typically middle-aged to old. Additionally, although virtually every dog in which PACG develops has PLD, only about 1% of dogs with PLD have glaucoma at some point in their lifetimes. This means that the vast majority of dogs with PLD never have glaucoma. Even if one limits the population to include only the dogs with the most extreme form of PLD (360-degree sheets with few flow holes), the risk of glaucoma increases to only about 15%. Finally, PLD alone does not explain the association of PACG with other risk factors, such as female sex predisposition, stress, and dim light. In the aggregate, these observations suggest that PLD is only the first step in a multistep process leading to PACG.

Recent imaging of the anterior segment in dogs experiencing an acute episode of PACG has led to a mechanistic theory, which holds that the event that initiates an attack may be impaired outflow at the level of the pupil (see Figures 12-30, 12-31, and 12-34). According to this theory, stress or excitement may raise heart rate and increase the difference between the systolic and diastolic blood pressures in the choroidal blood vessels. The increases in heart rate and pulse pressure result in a faster and larger forward "push" by the choroidal blood vessels on the posterior vitreous during systole. This force ultimately is transferred through the vitreous to the aqueous humor in the posterior chamber, causing an additional small bolus of aqueous humor to be forced through the pupil into the anterior chamber during systole. In the normal eye (or if the pulse pressure is normal) this fluid would simply flow back into the posterior chamber during diastole or, if trapped in the anterior chamber, it would force the iris more posteriorly, thereby opening the iridocorneal angle and allowing the additional fluid to exit via an expanded trabecular meshwork. In the eye at risk for PACG, however, exit of this small bolus of additional aqueous humor is impeded by abnormal pectinate ligaments, which may also prevent the angle from "popping open" in response to increased pressure in the anterior chamber. Alternatively, or perhaps in combination with PLD, age-associated declines in trabecular meshwork facility may also prevent the additional aqueous humor from escaping the anterior chamber. This results in a transient pressure differential in which pressure is slightly greater in the anterior chamber than in the posterior chamber. If the pupil is midrange in size the iris can be pressed more firmly against the lens, resulting in a "ball-valve" effect and a so-called reverse pupillary block (see Figure 12-34). A midrange to somewhat dilated pupil (as occurs in dimmer light or during excitement) is more floppy and readily pressed against the lens than a very large or very small pupil. Very large pupils tend to cause the iris to "slide" off the more highly curved equatorial region of the lens, and very small pupils tend to have an iris that is taut and more resistant to compression against the lens. The next systole results in the forcing of a little more aqueous humor from the posterior chamber into the anterior chamber, further increasing IOP. This process continues until IOP reaches a physiologic maximum (typically 60 to 80 mm Hg) that is related to systemic blood pressure and the resistance of the intraocular tissues. Intermittent, spontaneously resolving attacks may occur if reverse pupil block develops but the pupil dilates to the point at which it can "slide" off the more highly curved equatorial region of the lens and break the block at the pupil; this block would then allow the excess aqueous humor to flow back through the pupil into the posterior chamber. If the block is not broken at the pupil, the iridocorneal angle and ciliary cleft may further collapse, thereby worsening the attack and making effective therapy much more difficult even though the whole process is of relatively short duration.

PACG may also be classified as having the following potentially overlapping phases:

- *Latent:* The fellow, normotensive eye has all the risk factors that the overtly affected eye exhibits, except that IOP has not increased. This eye should receive prophylactic therapy, because in 50% cases the fellow eye will experience overt PACG in 8 months if untreated.
- *Intermittent:* Characterized by transient (minutes to hours) increases in IOP that spontaneously resolve.
- *Acute congestive:* Characterized by very rapid, marked (50 to 80 mm Hg) increases in IOP with overt clinical signs.
- *Postcongestive:* Refers to an eye that has been successfully treated for acute congestive glaucoma and now has a normal or subnormal IOP.
- *Chronic:* IOP is chronically elevated. This state may follow an acute congestive episode that does not respond to therapy. Less commonly, multiple episodes of intermittent angle closure may slowly close the angle and create a clinical course that is characterized by multiple transient spikes in IOP and a gradually rising IOP between the spikes.
- *Absolute:* End-stage disease. Vision is lost, the eye is usually buphthalmic, and many secondary changes are typically present (lens luxation, corneal ulceration, etc.).

Secondary Glaucomas

Obstruction of the Iridocorneal Angle

The iridocorneal angle may be of normal width and simply filled with cells or substances that impair outflow (so-called secondary open-angle glaucoma) or the angle may very gradually narrow until closed by peripheral anterior synechia, fibrovascular membranes, and so on (so-called secondary closed-angle glaucoma). In general, secondary open-angle glaucomas carry a somewhat

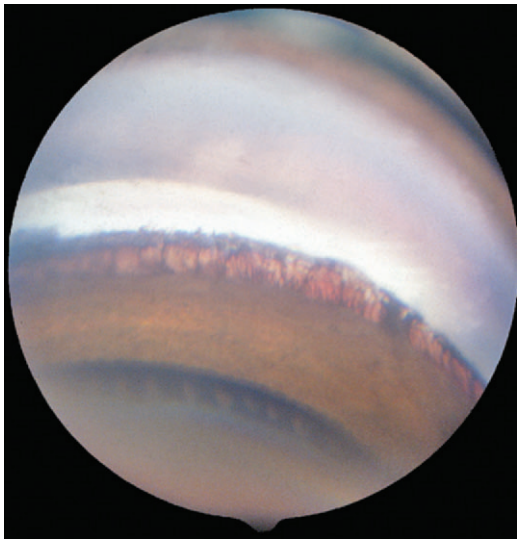


Figure 12-37. Goniophotograph showing blood in the trabecular meshwork. Intraocular pressure was elevated, but obvious hyphema was not clinically apparent.

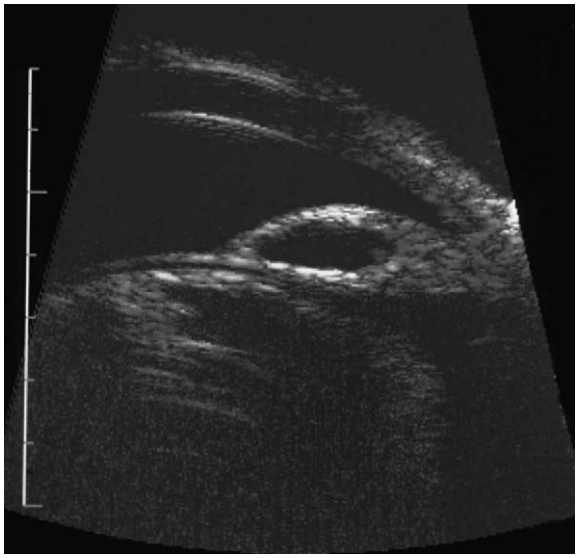


Figure 12-38. High-resolution ultrasound image in a dog with glaucoma secondary to iris bombé. The pupillary border is adherent to the anterior lens capsule and the remaining iris bows anteriorly. Additionally the ciliary cleft is collapsed, indicating that there are at least two obstructions to outflow in this patient. (Courtesy Dr. Ellison Bentley.)

better prognosis than secondary closed-angle glaucomas because the anatomy is less severely deranged. Examples of materials that may obstruct the trabecular meshwork are uveal cysts, neoplastic cells (especially melanocytes), inflammatory cells and debris, scar tissue (following chronic uveitis or intraocular surgery), red blood cells, macrophages filled with lens debris after capsule rupture (phacolytic glaucoma), vitreous, new blood vessels (preiridal fibrovascular membranes), air, viscoelastic materials used during intraocular surgeries, and epithelial cells originating from the cornea or conjunctiva. In many patients blocks may also exist at other locations in the eye (Figure 12-37).

Pupillary Block

In traditional pupillary block the flow of aqueous humor from the posterior chamber to the anterior chamber is impaired. This may result from direct physical adhesions between the iris and lens (*iris bombé*; Figure 12-38) due to chronic anterior uveitis or may simply reflect a condition in which the iris and lens are in tight apposition to each other but not physically fused (physiologic iris bombé). Pupillary block in the absence of physical adhesions commonly occurs in eyes in which the lens is very large (intumescent) or luxated into the pupillary aperture or when a portion of the lens zonules is disrupted and vitreous is able to move forward and occlude the pupil. In all forms of pupillary block glaucoma, however, aqueous accumulates in the posterior chamber, thereby increasing IOP. Very often, secondary angle-closure glaucoma complicates the latter stages of the process as the root of the iris is pushed forward into the angle. These apposed but not fused tissues (appositional closure) quickly lead to permanent adhesions and peripheral anterior synechia (synechial closure). Chronic low-grade uveitis due to lens movement also often leads to secondary angle closure.

Ciliary Body–Vitreous–Lens Block

Sometimes called "aqueous humor misdirection" or "malignant glaucoma," ciliary body–vitreous–lens block glaucoma develops when aqueous humor flows posteriorly into the vitreal cavity or

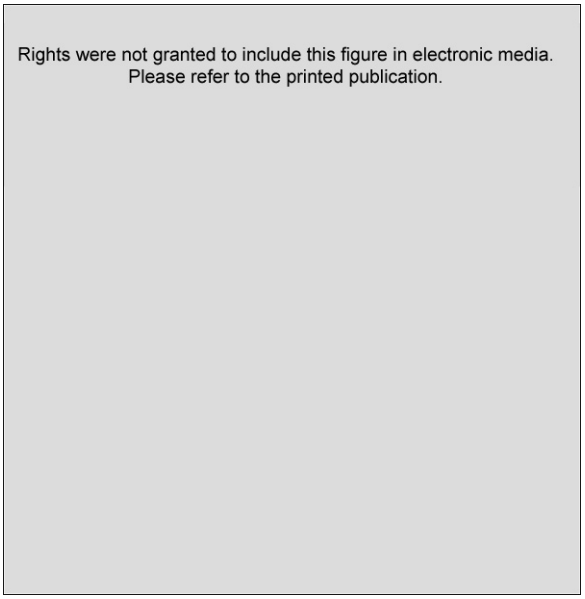
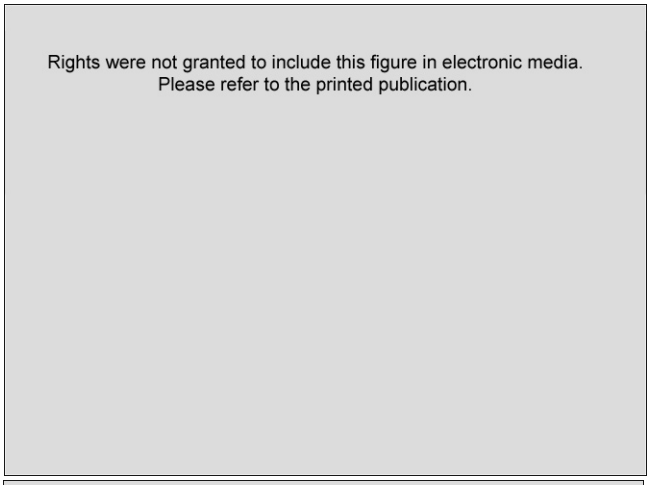


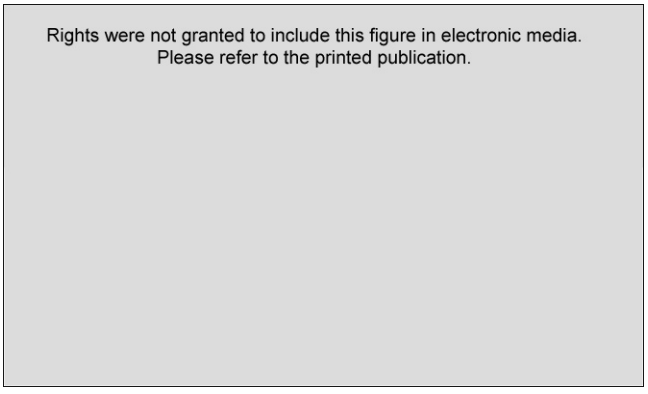
Figure 12-39. Proposed concept of ciliovitreolenticular block demonstrating the potential locations misdirected aqueous humor may collect in the vitreal cavity, including in the anterior peripheral vitreous *(A),* as lacunae in the central vitreous *(B),* diffusely throughout the vitreous *(C),* and between the posterior vitreous and retina *(D)*. Increased fluid in the vitreal cavity displaces and condenses the anterior vitreal face, leading to anterior shifting of the lens-iris diaphragm. Eventually glaucoma occurs as more and more fluid is trapped within the vitreal cavity by a barrier created by the anterior ciliary body, displaced vitreous, and lens. Additionally, glaucoma may result from a cascade of obstruction to flow through the pupil and then at the iridocorneal angle/ciliary cleft. (From Czederpiltz JMC, et al. [2005]: Putative aqueous humor misdirection syndrome as a cause of glaucoma in cats: 32 cases. J Am Vet Med Assoc 227:1476.)

between the vitreous and the retina (Figures 12-39 and 12-40). The remaining vitreous is forced anteriorly, compressing its proteins and forcing them between the ciliary body and the lens. This tends to impair the forward flow of aqueous humor

A



B



C

Figure 12-40. Feline aqueous humor misdirection syndrome. **A,** Frontal view; mild anisocoria is present. **B,** Affected cat eye viewed from the side. The anterior chamber is uniformly very shallow. **C,** Normal cat eye for comparison purposes. (From Czederpiltz JMC, et al. [2005]: Putative aqueous humor misdirection syndrome as a cause of glaucoma in cats: 32 cases. J Am Vet Med Assoc 227:1476.)

at the level of the ciliary body and to displace the entire lens–iris diaphragm anteriorly, shallowing the anterior chamber. Pupillary block is common, and in the later stages of the process secondary angle closure develops as well. A syndrome of aqueous humor misdirection, shallow anterior chamber, pupil dilation, and glaucoma is common in older cats. It can be differentiated from a luxated/subluxated lens by the absence of iridodonesis and phacodonesis.

Combined-Mechanism Glaucoma

Glaucoma also can occur via a combination of mechanisms, and in some patients it is not yet possible to definitively ascertain the mechanism by which IOP increases.

TREATMENT

The higher the IOP and the longer it remains increased, the less the chance that vision can be restored; 24 to 72 hours of very high IOP usually results in irreversible vision loss.

The specific actions of the antiglaucoma drugs are discussed in Chapter 3. Ideally the primary cause of the glaucoma should be treated directly. In some outflow obstructions, however, direct treatment may not be possible, and the surgeon is forced to treat the problem indirectly by reducing the production of aqueous humor. Regardless of cause, urgent therapy is required if vision is to be preserved. Often a combination of medical and surgical therapy is required, and the specific drugs and procedures chosen depend on the cause and stage of glaucoma and, to a significant extent, on the clinician's personal experiences.

Effective client education is essential in the therapy of glaucoma. Many owners' sole experience with glaucoma has been with POAG in older humans. In this disorder there is no pain, the rise in IOP is very slow and generally mild, and vision can often be maintained for the remainder of the person's life with medical therapy alone. The clinician should be careful to explain to the owner of an animal with glaucoma that there are many types of glaucoma and that treatment strategies used for POAG in older people are not appropriate for the vast majority of cases of glaucoma in animals (or other forms of glaucoma in humans, for that matter). Because many forms of glaucoma initially manifest with only one eye affected but are bilateral disorders, it is also imperative to inform the client about the clinical signs that should prompt him or her to seek medical attention in the event of an attack in the animal's fellow eye.

Primary glaucoma is a bilateral disease in dogs. Once a diagnosis of glaucoma has been made in one eye, the remaining eye should receive prophylactic medication and regular pressure checks.

The first step in the treatment of the animal with newly diagnosed glaucoma is to determine whether (1) the disorder is acute and the eye still has the potential for vision or (2) the problem is chronic and the eye is irreversibly blind (Figure 12-41). Regardless of the cause of the glaucoma, aggressive, potentially toxic, and expensive medical therapy is generally of limited to no value in patients with end-stage disease and an irrevocably blind eye. The clinician can more effectively treat such patients by identifying the cause of the glaucoma (neoplasia, lens luxation, primary angle closure, hyphema, etc.) and then performing the appropriate surgical procedure (cyclodestruction, enucleation, evisceration with intrascleral prosthesis, etc.) in conjunction with evaluating the risk of glaucoma in the remaining eye. If the affected eye has the potential for sight, however, aggressive attempts to lower IOP should be instituted. In these cases the next step is to determine the inciting cause of the glaucoma and directly address that cause, if possible.

Emergency Treatment of Acute Glaucoma

Glaucoma is usually treated by a veterinary ophthalmologist after the family veterinarian has made the initial diagnosis and provided emergency therapy.

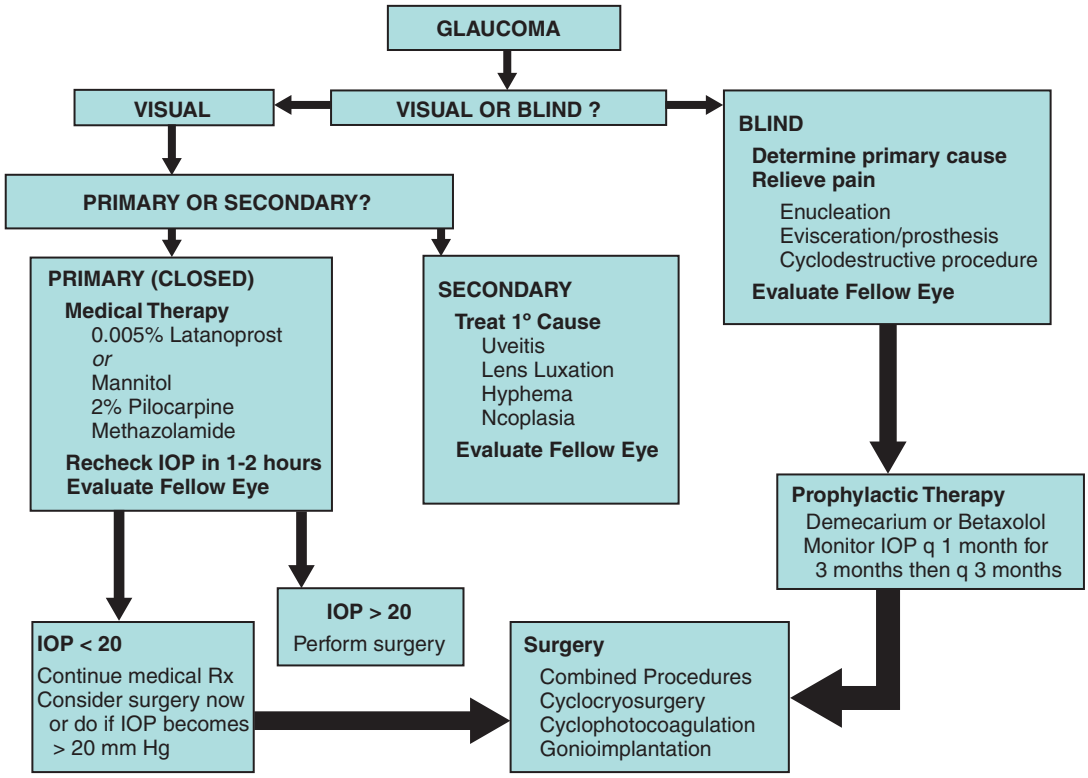


Figure 12-41. Flow chart for the treatment of glaucoma.

Box 12-4 | **Emergency therapy for primary angle-closure glaucoma in an eye with the potential for vision**

1. Latanoprost 0.005%: 1 to 2 drops topically and recheck intraocular pressure in 1 to 2 hours

If latanoprost is unavailable or ineffective:

1. Mannitol (1.0 to 1.5 g/kg IV): 5.0 to 7.5 mL/kg of 20% solution over 15 to 20 minutes
2. Methazolamide or dichlorphenamide: 2.2 to 4.4 mg/kg orally every 8 to 12 hours for dogs
3. Pilocarpine (2.0% drops): 1 drop every 10 minutes for 30 minutes, then every 6 hours

Water should be withheld for several hours after administration of mannitol.

Systemic dexamethasone (0.1 mg/kg IV) or topical 0.1% dexamethasone (every 6 to 8 hours) may be useful as well if pressure-induced ischemia has resulted in significant intraocular inflammation.

If the other eye is still normotensive, prophylactic therapy consisting of demecarium bromide (0.25% every 24 hours at bedtime with a topical corticosteroid) or betaxolol 0.5% every 12 hours should be instituted.

Early identification of the cause of the glaucoma and rapid reduction of IOP are essential to prevent permanent damage; Box 12-4 summarizes emergency treatment for PACG in an eye that still has the potential for vision. Although the initial response to medical therapy may be dramatic, *definitive treatment, usually surgical, must follow* medical therapy in order to control IOP in the long term in most patients. Except in very specific circumstances, medical therapy alone is generally not effective in the long-term control of most forms of glaucoma in animals and humans.

Reduction in pressure with this regimen is usually rapid (1 to 2 hours) but temporary (12 to 36 hours). If the eye responds to latanoprost, this medication should be continued every 12 hours until the patient can be evaluated by a specialist. Mannitol is very potent but it also can be quite toxic, so its use is limited to eyes with the potential for vision. If IOP remains elevated after a single injection of mannitol the 1.0 g/kg dose may be repeated in 4 hours if necessary, but long-term use should be avoided. Because mannitol solution is at or near the saturation point it may need to be heated or put through a 5-µm filter to avoid intravenous injection of crystals and potentially fatal consequences. Mannitol lowers IOP by dehydrating the vitreous along with the rest of the animal. Side effects include headache, osmotic diuresis, and worsening of dehydration, renal failure, or cardiovascular disease. Deaths due to pulmonary edema also have been reported if mannitol is given to animals anesthetized with methoxyflurane. A hyperosmotic agent should be used with caution if the blood-ocular barrier is not intact (uveitis, hyphema), because a leaky barrier may allow mannitol to enter the vitreous, thereby pulling water into the vitreal cavity and increasing IOP.

Oral glycerin at 1 to 2 mL/kg orally is an alternative to mannitol, although it is a less reliable ocular hypotensive drug and frequently induces vomiting. The probability of vomiting may be reduced by dividing the dose into thirds and giving it chilled or mixed with food. Glycerin is contraindicated in diabetic patients. On rare occasions glycerin may be used every 8 hours for up to 5 days if toxicity is not significant. Glycerin is occasionally dispensed for the owner to administer to treat a sudden

attack of glaucoma immediately before seeking professional assistance.

Boxes 12-5 through 12-7 summarize emergency treatment for glaucoma associated with, or due to, specific circumstances or diseases.

Long-Term Management of Glaucoma

In most cases, definitive therapy for glaucoma is surgery (cyclocryotherapy, laser cyclophotocoagulation, gonioimplantation, evisceration with intraocular prosthesis insertion, or enucleation). If required, antiglaucoma drugs may supplement surgery and fine-tune IOP control. Certain types of glaucoma (e.g., uveitis-induced or hyphema-associated) may be treated medically first; if medical therapies fail, surgical methods may then be used. Glaucoma following primary lens luxation may be controlled medically if the lens remains posterior to the iris.

Surgical Therapy for Glaucoma

Particular attention should also be paid to the patient's general physical health before surgery, because alterations in hydration, electrolyte, and acid-base status are common in animals that have malaise, inappetence, and so on from the pain associated with high IOP or that have received antiglaucoma drugs. Blood gas and acid-base status along with serum potassium levels may also need to be assessed before induction of anesthesia, especially if a systemic carbonic anhydrase inhibitor (CAI) has been administered recently. Preoperative rehydration may be necessary in animals that have received mannitol.

Glaucoma procedures used to treat eyes with the potential for vision are classified according to whether they increase aqueous humor outflow (e.g., gonioimplantation, filtering procedures) or decrease aqueous humor production (cyclophotocoagulation, cyclocryosurgery). A combination of outflow-enhancing and inflow-reducing procedures may be more effective than either one alone at controlling IOP and preserving vision. In current clinical practice gonioimplantation, cyclophotocoagulation, and cyclocryosurgery are by far the dominant surgical procedures used to treat an eye with the potential for retaining vision. If the eye is irreversibly blind, enucleation, evisceration with intrascleral prosthesis, and perhaps a cyclodestructive procedure are more appropriate.

Surgery to Increase Aqueous Humor Outflow

Historically a number of procedures to increase outflow (iridencleisis, corneoscleral trephination, cyclodialysis, and sclerectomy) have been used alone or in combination in an effort to address glaucoma due to impaired outflow of aqueous humor. These procedures would theoretically address the root cause of the glaucoma and allow for more normal nutritional support for the cornea and lens, because they would enable aqueous humor production to continue at more normal levels. Full- or partial-thickness holes in the sclera, however, have been plagued by fibrosis over the filtering site and long-term failure to control IOP in most patients. Artificial aqueous humor shunts (gonioimplants) with or without pressure-sensitive valves (to prevent IOP from getting too low) have also been used to try to create a pathway for aqueous to drain from the eye, but these also have the problem of development of a scar tissue–lined,

Box 12-5 | Emergency therapy for uveitis-induced glaucoma

1. Identify underlying cause and directly address it if possible.
2. Systemic dexamethasone (0.1mg/kg IV) or flunixin meglumine (0.1 mg/kg IV)
3. Topical dexamethasone (0.1% every 2 to 4 hours) or prednisolone acetate (1.0% every 2 to 4 hours)
4. Carbonic anhydrase inhibitors either topically (dorzolamide 2% alone or in combination with timolol, or brinzolamide 1%, both every 8 hours) or systemically (methazolamide or dichlorphenamide: 2.2 to 4.4 mg/kg orally every 8 to 12 hours for dogs and 1 to 2 mg/kg every 8 to 12 hours for cats)
5. If additional intraocular pressure lowering required, consider adding in topical timolol 0.5% every 8 to 12 hours, epinephrine 1% every 6 to 8 hours, or dipivefrin 0.1% every 6 to 8 hours.
6. Usually, pilocarpine, latanoprost, and systemic hyperosmotics should be avoided.

Box 12-6 | Emergency therapy for hyphema-associated glaucoma

1. Identify underlying cause and directly address it if possible.
2. Topical dexamethasone (0.1% every 2 to 4 hours) or prednisolone acetate (1.0% every 2 to 4 hours)
3. Carbonic anhydrase inhibitors either topically (dorzolamide 2% alone or in combination with timolol or brinzolamide 1%, both every 8 hours) or systemically (methazolamide or dichlorphenamide: 2.2 to 4.4 mg/kg orally every 8 to 12 hours for dogs and 1 to 2 mg/kg every 8 to 12 hours for cats) or together
4. If additional intraocular pressure lowering is required, consider adding in topical timolol 0.5% every 8 to 12 hours, epinephrine 1% every 6 to 8 hours, or dipivefrin 0.1% every 6 to 8 hours.
5. Usually, systemic hyperosmotics should be avoided.
6. The use of topical pilocarpine or atropine is controversial.

Box 12-7 | Emergency therapy for lens luxation–associated glaucoma

1. If lens in anterior chamber, dilate pupil with atropine 1% or tropicamide 1.0%.
2. Topical dexamethasone (0.1% every 2 to 4 hours) or prednisolone acetate (1.0% every 6 to 8 hours)

If ineffective:

1. Mannitol (1.0 to 1.5 g/kg IV): 5.0 to 7.5 mL/kg of 20% solution over 15 to 20 minutes
2. Carbonic anhydrase inhibitors either topically (dorzolamide 2% or brinzolamide 1%, both every 8 hours) or systemically (methazolamide or dichlorphenamide: 2.2 to 4.4 mg/kg orally every 8 to 12 hours for dogs and 1 to 2 mg/kg every 8 to 12 hours for cats)
3. If additional intraocular pressure lowering required, consider adding topical epinephrine 1% every 6 to 8 hours or dipivefrin 0.1% every 6 to 8 hours.
4. If the lens is in the anterior chamber, pilocarpine, timolol, and latanoprost should be avoided.

Referral to a specialist for further evaluation is advisable.

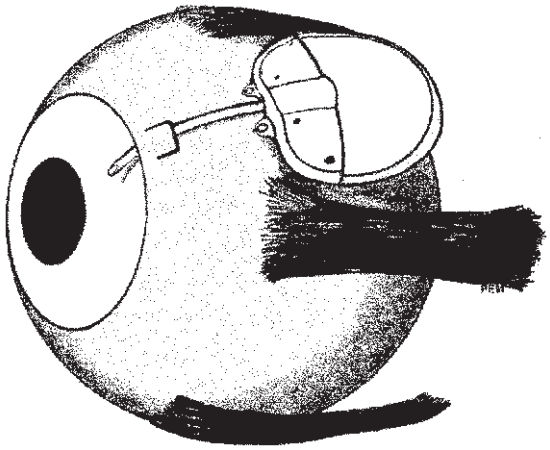


Figure 12-42. Positioning of an Ahmed gonioimplant. The conjunctiva has been removed for clarity. The implant is sutured to the sclera between the extraocular muscles so that the leading edge is 8 to 10 mm posterior to the limbus. A small tunnel incision is made in the sclera for the tubing to enter the anterior chamber. The implant has a one-way valve that opens when pressure exceeds approximately 8 mm Hg. (From Slatter D [2003]: Textbook of Small Animal Surgery 3rd ed. Saunders, Philadelphia.)

cystlike space that again becomes relatively resistant to the flow of aqueous humor (Figure 12-42). In an effort to avoid fibrosis around the drainage device, some surgeons have placed the distal end of the tubing into the frontal sinus, parotid salivary duct, nasolacrimal duct, or the orbit. None of these approaches, however, has been demonstrated to be more effective than subconjunctival drainage, and endophthalmitis is always a risk if the tube is placed in structures that communicate with the outside environment. Use of an antimetabolite such as mitomycin C or 5-fluorouracil may limit fibrosis over the body of the implant and improve its long-term filtering capacity. Adjunctive medical antiglaucoma therapy, or a limited cyclodestructive procedure, may also be used to fine-tune IOP control once control is achieved grossly with the implant.

Surgery to Reduce Aqueous Humor Production

Although these procedures do not address the underlying reason for the glaucoma (impaired outflow), they can be quite effective at lowering IOP. Techniques for destroying the portion of the ciliary body that make aqueous humor include cyclocryotherapy with either liquid nitrogen or nitrous oxide, cyclophotocoagulation (cyclophotoablation) with either a diode or neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, cyclodiathermy, focused ultrasound, and chemical ablation. In practical terms, however, only cyclocryosurgery and cyclophotocoagulation are reliable and used with any regularity today. These are relatively crude procedures because they require the surgeon to estimate both the degree of outflow impairment and the amount of cyclodestruction necessary to match that impairment. Often the outflow facility is so severely compromised that the eye is highly sensitive to even minor alterations in aqueous production, resulting in a relatively narrow margin for error in these estimates. Too little destruction can result in persistence of the glaucoma, and too much can lead to phthisis bulbi. It is also not uncommon for outflow to be so severely impaired that aqueous humor production must be reduced to levels that cannot maintain normal ocular health, resulting in cataract formation or corneal endothelial decompensation and vision loss even though IOP is controlled. Failure to control IOP in the long term with these procedures is the result of inadequate destruction of the ciliary body, regeneration of the ciliary epithelium, and progressive angle closure with loss of additional outflow capacity. Despite these limitations, however, a cyclodestructive procedure is more appealing as a single procedure than a gonioimplant or filtering procedure because it is faster, technically easier, less expensive to perform, and repeatable.

Cyclodestruction is indicated in cases of medically uncontrollable primary glaucoma in an eye that still has the potential for vision and for the relief of chronic ocular pain in an irreversibly blind eye in an animal whose owner wishes to preserve the globe. The success rate is much lower in eyes with glaucoma secondary to chronic anterior uveitis, preiridal fibrovascular membrane formation, or retinal detachments. Relative contraindications include intraocular neoplasia, hyphema, and anterior lens luxations.

Cyclocryotherapy

Controlled application of intense cold to the sclera overlying the ciliary body causes necrosis of the ciliary body and reduced aqueous production. Both liquid nitrogen and nitrous oxide are acceptable cryogens, but some surgeons believe liquid nitrogen to be a more reliable agent, perhaps because it achieves a colder temperature than nitrous oxide.

Preoperatively dexamethasone (0.1 mg/kg IV) and flunixin meglumine (0.1 mg/kg IV) are administered in anticipation of the severe uveitis than may follow cyclocryosurgery. Precise application of the cryoprobe over the ciliary processes and avoiding the 3 and 9 o'clock positions is essential. If the globe is approximately normal size, a 3-mm (diameter) nitrous oxide glaucoma cryoprobe is centered 5 mm posterior to the limbus (Figure 12-43). If the globe is enlarged, the cryoprobe is centered 5.5 to 6.0 mm posterior to the limbus. Gentle pressure on the globe, slightly indenting it, enlarges the extent of the ciliary destruction by shortening the distance between the cryoprobe and target tissue and by reducing blood flow to the area. Usually six to eight spots are frozen for 2 minutes when nitrous oxide instrumentation is used. Timing begins when the probe achieves a temperature of –70° to –80° C, a range that correlates with a temperature in the ciliary body of at least –10° C, which is

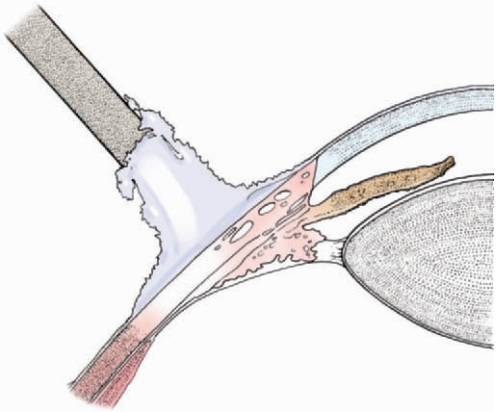


Figure 12-43. Cryoprobe cooled by liquid nitrogen, positioned 5 mm posterior to the limbus and adjacent to the ciliary body. (Modified from Roberts SM, et al. [1984]: Cyclocryotherapy. Part I: evaluation of a liquid nitrogen system. J Am Anim Hosp Assoc 20:823.)

necessary to cause cyclodestruction. If liquid nitrogen is used, the probe is placed in the same location, but the cryogen is circulated through the probe until the ice ball extends 1 mm past the limbus into clear cornea, after which the freeze is terminated. The larger size of the tip (2.5 × 6.5 mm) and the more profound freeze usually allows fewer sites to be frozen (perhaps as few as two to four).

At the conclusion of the procedure a subconjunctival injection of 0.5 to 1.0 mg of dexamethasone or other suitable corticosteroid may be given. Systemic analgesics may be necessary in some animals because freezing can induce significant ocular pain. The marked chemosis that follows freezing can result in exposure conjunctivitis and/or keratitis, so a partial temporary tarsorrhaphy may also be performed at the conclusion of the procedure.

Marked conjunctivitis, chemosis, and uveitis should be expected. Topical 0.1% dexamethasone/triple antibiotic ophthalmic ointment is administered every 4 to 6 hours, depending on the degree of inflammation. Antiglaucoma drugs are continued as before surgery, and 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, antiglaucoma drugs are continued for 10 to 14 days, after which the patient is reevaluated. Marked postoperative IOP spikes can persist for days after surgery, and occasionally aqueocentesis may be necessary to control IOP in the immediate postoperative period. Tapping the anterior chamber, however, can be detrimental because doing so exacerbates the uveitis, risks introducing bacteria or damaging the lens, and probably increases the chance of reperfusion injury to the retina and optic nerve. If IOP is well controlled 2 weeks postoperatively, the antiglaucoma medication dosage may be gradually tapered. The timing of further follow-up examinations varies according to response to therapy and whether the eye has the potential for vision.

Complications include the aforementioned IOP spike, uveitis, exposure keratoconjunctivitis, neurotrophic keratitis if the long posterior ciliary nerves are damaged, hyphema, retinal detachment, recurrence of glaucoma, and phthisis bulbi with a cosmetically unacceptable globe. The relatively high frequency of these complications indicates that cyclocryosurgery should not be performed as a prophylactic measure in the normotensive fellow eye of an animal with glaucoma.

Success rates vary with the 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, not vision, is the goal and the owner will allow multiple procedures to be performed, cyclocryosurgery can have a success rate as high as 90%. If the eye has the potential for vision at the outset, the rates of vision preservation may be as high as 60% at 6 months postoperatively. Unfortunately, as for all glaucoma procedures, the success rate declines with the length of 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. Certain breeds (cocker spaniel, Siberian husky, Norwegian elkhound, chow chow, and shar-pei) may require more aggressive ciliary body destruction to ensure long-term IOP control.

Laser Cyclophotocoagulation

An alternative method of destroying the ciliary body processes is transscleral irradiation of the ciliary body with a diode or Nd:YAG laser. Laser therapy has the advantages of being more controllable and potentially causing less reaction than cyclocryotherapy. It can also be repeated with less risk of hypotony. It suffers from the disadvantage of frequently requiring more than one treatment and of having a higher failure rate than cyclocryotherapy. Laser cyclophotocoagulation is exclusively performed by ophthalmic surgeons trained and experienced in its use.

Combined Procedures

The combination of a limited cyclodestructive procedure and a gonioimplant (with or without adjunctive medical therapy) offers some attractive theoretical advantages in treating glaucomatous eyes with the potential for vision. They include (1) blunting of the postoperative IOP spike that often accompanies a cyclodestructive procedure and can destroy the last vestiges of vision the patient has, (2) allowing for a greater level of aqueous humor production postoperatively so as to improve intraocular nutrition and reduce the chance a blinding cataract will occur, and (3) allowing for a finer control of IOP in the postoperative period. In one retrospective study a combination of the two procedures appeared to be more effective than a single procedure and allowed more than 50% of patients to retain vision for at least 1 year after an overt attack of angle-closure glaucoma. Combining procedures also allowed for a greater percentage of patients to maintain IOP within the normal range, even though vision was ultimately lost either because of progressive retinal and optic nerve degeneration secondary to an apoptotic cascade or because of cataract. The frequent follow-up visits, additional expense, and potentially greater complications of a combined procedure, however, do not allow for it to be advocated for the treatment of irrevocably blind eyes, for which the goal of therapy is simply pain relief.

Lens Luxation

The clinician should be aware that primary lens luxation is bilateral and usually hereditary, although very commonly the patient initially presents with an overt luxation in only one eye. An acute episode of glaucoma associated with lens luxation is managed as previously described in this chapter. If the eye is irreversibly blind the clinician should consider enucleation, evisceration with intrascleral prosthesis, or perhaps a cyclodestructive procedure. Lens extraction is seldom indicated in blind eyes because it is more costly than other procedures and because other impediments to outflow (e.g., at the angle) are usually present and cause glaucoma to persist postoperatively.

Longer-term therapy for an eye with the potential for vision and glaucoma attributable to a subluxated or luxated lens depends on the position of the lens and whether or not other impediments to outflow are present. If lens luxation is acute and the lens has luxated posteriorly, the eye may be treated with miotics to ensure that the lens does not enter the anterior chamber. Many animals tolerate a lens in the vitreous for long periods without recurrences of glaucoma, provided that medications are continued. If the lens is opaque and interferes with vision in the vitreous or has very recently become luxated, or if the pupil will not effectively constrict, intracapsular lens extraction may be performed, although the prognosis is guarded even when the procedure is performed by experienced surgeons.

If the lens has luxated into the plane of the pupil or anterior chamber, most surgeons prefer to remove it by either intracapsular lens extraction or phacoemulsification. Alternatively, the pupil may be dilated and an attempt made to get the lens to fall back into the vitreous. If the lens does fall into the vitreous, miotics may then be used in an effort to ensure that it remains there. If it does not, it should be surgically removed. The long-term success of any of these treatment strategies hinges on whether the patient has either POAG or peripheral anterior synechia and secondary angle-closure glaucoma in addition to the lens luxation. Unfortunately, both of these conditions commonly occur in patients with primary lens luxations thereby greatly reducing the probability of maintaining a comfortable and sighted eye over the long term.

Glaucoma Secondary to Uveitis

Gonioscopy is performed once emergency therapy has been implemented and the inflammation has been reduced. If the angle is open, medical therapy may be slowly reduced in accordance with control of the uveitis. The ability of topical dexamethasone 0.1% to increase IOP in normal dogs and dogs with POAG is of uncertain importance in the treatment of dogs with uveitis-induced glaucoma. In a clinical setting the relatively small rise in IOP attributable to topical corticosteroids is masked by the much more dramatic changes in IOP induced by inflammation of the ciliary body and the compromise of the drainage angle (both of which may be returned to more normal values by the use of topical corticosteroids). Therefore it seems reasonable to use topical corticosteroids for the treatment of uveitis-induced glaucoma, although these agents should not be employed indiscriminately.

If peripheral anterior and posterior synechiae are present, and pressure does not fall with emergency therapy, the prognosis for retaining vision is very poor. If the eye still has vision and an open iridocorneal angle, laser iridotomy may be attempted to create a new hole in the iris to allow aqueous to bypass the occluded pupil; however, the iris holes usually seal closed with time. Laser iridotomy is much less effective in eyes that also have peripheral anterior synechia and angle closure because it does not resolve this additional impediment to outflow at the level of the angle. Gonioimplantation may also be attempted, but frequently this procedure fails because the tube rapidly occludes with inflammatory debris and the subconjunctival filtering bleb rapidly scars. A cyclodestructive procedure may also be attempted although it frequently exacerbates the uveitis, possibly leading to even more synechia and outflow impairment. If the eye is irreversibly blind the clinician should consider enucleation (with histopathology to determine the cause of the uveitis), evisceration with an intrascleral prosthesis (again with histopathology; it should not be performed if neoplastic or infectious causes of the uveitis are suspected), or, in carefully selected cases, a cyclodestructive procedure.

Glaucoma Secondary to Intraocular Neoplasia

Melanoma of the iris or ciliary body is a relatively common cause of secondary glaucoma in dogs and a less common one in other species. In most cases, enucleation, with or without an orbital prosthesis, is the treatment of choice. In very select cases iridocyclectomy (removal of a portion of the iris and ciliary body), cyclocryotherapy, or laser photocoagulation is successful in treating circumscribed tumors. By the time glaucoma is present the tumor is usually too advanced for this type of therapy. Glaucoma secondary to lymphosarcoma may respond to medical antiglaucoma therapy and definitive systemic chemotherapy. In general evisceration with placement of an intrascleral prosthesis is to be avoided in patients with presumed intraocular neoplasia.

Absolute Glaucoma

Absolute glaucoma is the end stage of chronic, increased IOP with buphthalmos, severe degenerative changes in most ocular tissue, blindness, and, almost invariably, *pain*. Although the patient with absolute glaucoma frequently shows no pain on palpation of the eye, and the owner may not believe the animal has pain, enucleation of the affected eye almost invariably results in increased playfulness and improvements in the patient's demeanor. This observation leaves little doubt that chronic glaucoma is a painful condition in the vast majority of animals.

The goal of therapy for absolute glaucoma is to provide pain relief and address any cosmetic concerns the owner may have. Eyes with end-stage glaucoma are best treated by enucleation (with or without an intraorbital prosthesis), evisceration with intrascleral prosthesis, or a cyclodestructive procedure.

Evisceration with Intrascleral Prosthesis

Evisceration with intrascleral prosthesis is indicated if the owner desires to maintain a more cosmetically pleasing eye. After a careful assessment of the eye (Box 12-8), the globe is eviscerated via removal of the internal contents through a limbal incision, leaving a scleral and corneal shell. After hemorrhage is controlled a silicone prosthesis is inserted (Figure 12-44). The enlarged globe shrinks to the size of the prosthesis over the next 3 to 4 weeks. During this time the cornea may vascularize and appear red. This appearance eventually resolves, and the cornea assumes its final gray or black color. The extent of pigmentation is impossible to predict, and owners are so advised before surgery. Prostheses may also be used after severe injury, when phthisis bulbi is beginning, to preserve a

Box 12-8 | Indications and contraindications for intraocular prosthesis insertion

Indications

Chronic glaucoma ± buphthalmos
Prevention of phthisis bulbi
Blinding ocular trauma (may be used even after penetrating corneal wounds)
Chronic, noninfectious uveitis

Contraindications

Intraocular neoplasia
Panophthalmitis
Ulcerative keratitis
Senile degenerative keratopathy
Degenerative corneal disorders
Foci of bacterial infection (e.g., severe untreated dental disorders, discospondylitis, otitis externa)

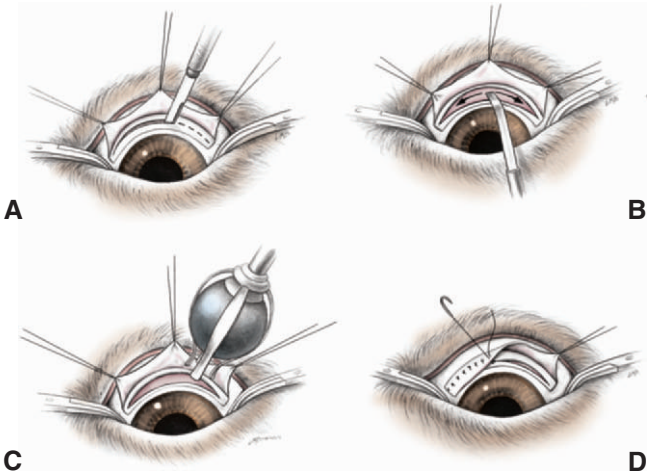


Figure 12-44. A, A fornix-based conjunctival flap is prepared, and the sclera is incised parallel to the limbus. **B,** Ocular contents are removed by dissection between the choroid and the inner scleral layers, leaving only the corneoscleral shell. **C,** A silicone prosthesis 1 mm larger than the limbal diameter of the other, normal eye is inserted with a prosthesis inserter. **D,** The sclera and conjunctiva are closed with interrupted or simple continuous absorbable sutures.

cosmetically acceptable eye. Prostheses have been successfully inserted into equine eyes with glaucoma previously unresponsive to medications and cyclocryotherapy. Although this procedure is generally quite successful, complications include ocular pain in the immediate postoperative period, ulcerative keratitis (potentially with exposure or extrusion of the prosthesis), keratoconjunctivitis sicca, infection, and recurrence of an unsuspected tumor. Because of the last possibility, all excised tissue should be histologically examined.

Enucleation

Once an eye has been thoroughly evaluated and a diagnosis of absolute glaucoma with pain has been made, the owner may decide to have the eye removed. An intraorbital prosthesis may or may not be placed, depending on the owner's wishes. See Chapter 17 for the technique.

All enucleated eyes should be examined by an experienced veterinary ophthalmic pathologist.

FELINE GLAUCOMA

The general principles of glaucoma therapy also apply to feline glaucoma. In general, normal feline IOP tends to be greater than that of the dog and to decline with age. One study found normal IOP for young cats with the Tono-Pen to be 20.2 ± 5.5 mm Hg with a range of 9 to 31 mm Hg, whereas the Tono-Pen yielded readings of 12.3 ± 4.0 mm Hg (range 4 to 21 mm Hg) in cats 7 years or older. The exact incidence of glaucoma in cats is unclear, although data from the Veterinary Medical Data Base suggested that 1 in 367 cats presenting to a University Teaching Hospital had glaucoma. In contrast, a prospective evaluation in a feline exclusive private practice found that 0.9% of cats 7 years or older had abnormally high IOP on tonometric screening.

Secondary glaucoma, most frequently due to chronic uveitis or intraocular neoplasia, is approximately 19 times more common than primary glaucoma in cats. Inherited congenital POAG has been described in Siamese cats, but acute PACG as seen in dogs is rare to nonexistent in cats. The rise in IOP in the vast majority of cats tends to be slow and insidious, and the condition is usually unilateral. Many cats with glaucoma initially present for another ocular disorder (chronic uveitis, iris color change, intraocular mass). Another common presentation, especially for those with aqueous humor misdirection syndrome (see earlier description in this chapter), is anisocoria with slowly progressing buphthalmos. The buphthalmos can be quite extreme in some animals. Ocular pain also tends to not be as obvious as in dogs, perhaps because the rise in IOP is typically not as abrupt or as high as in dogs, but there is no reason to believe that the condition is not painful in cats like it is in other species. Often the inciting cause is difficult to identify by the time the patient is first seen.

Common causes of glaucoma in cats include feline aqueous humor misdirection syndrome, chronic low-level lymphocytic plasmacytic uveitis with the formation of preiridal fibrovascular membranes, and neoplasia such as diffuse iris melanoma and uveal lymphoma. In one study *Toxoplasma* was implicated in 79%, feline corona virus in 27%, feline immunodeficiency virus in 23%, and feline leukemia virus in 6%. The most common clinical signs are dilated pupil, lens luxation, buphthalmos, exposure keratitis, and retinal degeneration. Cats with uveitis and prominent lymphoid nodules in the iris and iris erythema are considered to be at high risk for eventual development of glaucoma. Cats with positive *Toxoplasma* titers are more effectively treated with a combination of clindamycin and topical corticosteroid than with either drug alone.

Medical therapy for glaucoma in cats is similar to that in the dog, although cats tolerate some glaucoma medications poorly and may respond differently to antiglaucoma drugs. For example, latanoprost and the other commercially available prostaglandins do not lower IOP in cats, although they can induce profound miosis. The topical CAI brinzolamide did not lower IOP in normal cats when administered every 12 hours but may do so when given every 8 hours to cats with glaucoma. A related topical CAI, dorzolamide given every 8 hours, is effective in lowering IOP in glaucomatous cats. As in dogs, topical application of dexamethasone or 1% prednisolone acetate has increased IOP in cats, but the clinical significance of this finding is unclear. Additionally, unilateral topical administration of 0.5% tropicamide can raise IOP an average of approximately 3.5 mm Hg in both the treated and untreated eyes, and in some cats this increase may be as much as 17 to 18 mm Hg in the treated and untreated eyes. These observations reinforce the concept that cats are anatomically and physiologically distinct from dogs and that some therapies appropriate for the dog may not be transferable to the cat.

Although surgical therapy for feline glaucoma is similar to that for dogs, cyclocryotherapy must be quite aggressive if used, and liquid nitrogen is recommended as the cryogen to limit treatment failures. Cyclodestructive procedures are often unsuccessful in the long term in cats, perhaps because of the nature of their glaucoma. Evisceration with insertion of an intrascleral prosthesis may be performed, although the cosmetic results with a black silicone ball are less satisfactory than that achieved with dogs because of the normally brightly colored feline iris and vertically oriented slit pupil. Varying the color of

the sphere and tattooing a slit pupil onto the cornea can improve the postoperative appearance of the globe. Enucleation, with or without the placement of an intraorbital prosthesis, is a reasonable procedure in cats. There are some suggestions, however, that cats may reject an intraorbital sphere more frequently than dogs.

EQUINE GLAUCOMA

Normal equine IOP is higher than a cat's or dog's, averaging approximately 23 mm Hg and ranging up to the low to mid 30s. Glaucoma is less commonly recognized in horses than in dogs or cats, perhaps because the uveoscleral pathway constitutes a greater percentage of the equine outflow pathway. Although primary glaucoma appears to occur in horses, the most common form is glaucoma secondary to chronic anterior uveitis or intraocular neoplasia. Appaloosas, horses with concurrent equine recurrent uveitis, and horses older than 15 years are at greater risk of glaucoma. Clinical signs of equine glaucoma include corneal striae (caused by rupture of Descemet's membrane), buphthalmos, decreased vision, lens luxation, loss of the pupillary light reflex, mild anterior uveitis, optic nerve atrophy, optic disc cupping, and elevated IOP. Because many horses with glaucoma also have anterior uveitis, the pupil is often miotic or normal in size and is not dilated as is common in other species. A feature that complicates both the diagnosis and therapy of equine glaucoma is that the IOP fluctuates markedly, and frequent measurements may be necessary to demonstrate the presence of glaucoma and the effects of treatment. The reason for this fluctuation is unclear but it may involve compression of the globe by the orbicularis oculi or extraocular muscles. Auriculopalpebral nerve block may be required to obtain accurate applanation tonometry in fractious horses, and sedatives may significantly decrease IOP.

The principles of medical and surgical therapy for glaucoma in other species apply to horses with glaucoma, although the response to antiglaucoma medications in horses may be different from that in dogs and cats. Studies of antiglaucoma drugs in horses often yield conflicting results, suggesting that there may be considerable interindividual variations in the responsiveness of this species to many antiglaucoma drugs. For example, topical pilocarpine given alone can increase IOP in many, but not all, horses. The mechanism for this finding is unclear but may involve exacerbation of preexisting uveitis, pupillary block, or a reduction in the uveoscleral outflow pathway. Atropine, which stabilizes the blood aqueous barrier and may increase uveoscleral outflow, can reduce IOP in many normal horses and in horses with glaucoma secondary to chronic uveitis. Atropine can, however, also raise IOP in some horses. The prostaglandin derivative latanoprost does not lower IOP in normal horses (or does so only by 1 to 2 mm Hg) and can be quite irritating. Other studies have indicated that topical prostaglandins exacerbate elevated IOP in horses with glaucoma. Only timolol or the topical CAIs seem to consistently lower IOP in horses. Systemic CAIs may be prohibitively expensive in horses, and their efficacy and safety has not been determined. Antiglaucoma therapy in the horse often involves a combination of antiglaucoma and antiinflammatory drugs. Unfortunately, the therapy of primary equine glaucoma is largely empirical owing to our lack of understanding of the pathogenesis of the condition.

A cyclodestructive procedure (cyclocryotherapy, laser cyclophotocoagulation) may be used in equine eyes that have the potential for vision and in an attempt to maintain a comfortable, but blind eye. One study suggested that an effective Nd:YAG laser protocol in horses with glaucoma is a power setting of 11 W, duration of 0.4 second, applied 5 mm posterior to the limbus at 60 sites, resulting in a total energy dose of 264 J. Additionally, equine glaucoma has been effectively treated with an intrascleral prosthesis and enucleation (with or without an intraorbital prosthesis). Despite the best efforts of the clinician, however, the long-term prognosis for retaining vision in a glaucomatous equine eye is poor.

BIBLIOGRAPHY

Abrams KL (2001): Medical and surgical management of the glaucoma patient. Clin Tech Small Anim Pract 16:71.

Bentley E, et al. (2003): Use of high-resolution ultrasound as a diagnostic tool in veterinary ophthalmology. J Am Vet Med Assoc 223:1617.

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

Bentley E, et al. (1996): Implantation of filtering devices in dogs with glaucoma: preliminary results in 13 eyes. Vet Comp Ophthalmol 6:243.

Biros DJ, et al. (2000): Development of glaucoma after cataract surgery in dogs: 220 cases (1987-1998). J Am Vet Med Assoc 216:1780.

Bjerkas E, et al. (2002): Pectinate ligament dysplasia and narrowing of the iridocorneal angle associated with glaucoma in the English springer spaniel. Vet Ophthalmol 5:49.

Blocker T, van der Woerdt A (2001): The feline glaucomas: 82 cases (1995-1999). Vet Ophthalmol 4:81.

Brinkmann MC, et al. (1992): Neodymium:YAG laser treatment of iris bombé and pupillary block glaucoma. Proc Vet Comp Ophthalmol 2:13.

Brooks DE (1999): Equine ophthalmology, in Gelatt KN (editor): Veterinary Ophthalmology, 3rd ed. Lippincott Williams & Wilkins, Philadelphia.

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

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

Chavkin MJ, et al. (1992): Seroepidemiologic and clinical observations of 93 cases of uveitis in cats. Prog Vet Comp Ophthalmol 2:29.

Cook C, et al. (1997): Diode laser transscleral cyclophotocoagulation for the treatment of glaucoma in dogs: results of six and twelve months' follow-ups. Vet Comp Ophthalmol 7:148.

Cullen CL (2004): Cullen frontal sinus valved glaucoma shunt: preliminary findings in dogs with primary glaucoma. Vet Ophthalmol 7:311.

Cullen CL, Grahn BH (2000): Equine glaucoma: a retrospective study of 13 cases presented at the Western College of Veterinary Medicine from 1992-1999. Can Vet J 41:470.

Czederpiltz JM, et al. (2005): Putative aqueous humor misdirection syndrome as a cause of glaucoma in cats: 32 cases (1997-2003). J Am Vet Assoc 227:1434.

Davidson HJ, et al. (2002): Effect of topical ophthalmic latanoprost on intraocular pressure in normal horses. Vet Ther 3:72.

Davidson MG, et al. (1991): Phacoemulsification and intraocular lens implantation: a study of surgical results in 182 dogs. Vet Comp Ophthalmol 1:233.

Deehr AJ, Dubielzig RR (1998): A histopathological study of iridociliary cysts and glaucoma in golden retrievers. Vet Ophthalmol 1:153.

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

Ekesten B, Torrang I (1995): Age-related changes in ocular distances in normal eyes of Samoyeds. Am J Vet Res 56:127.

Ekesten B, Torrang I (1995): Heritability of the depth of the opening of the ciliary cleft in Samoyeds. Am J Vet Res 56:1138.

Gelatt KN, Brooks DE (1999): The canine glaucomas, in Gelatt KN (editor): Veterinary Ophthalmology, 3rd ed. Lippincott Williams & Wilkins, Philadelphia.

Gelatt KN, Mackay EO (2004): Prevalence of the breed-related glaucomas in pure-bred dogs in North America. Vet Ophthalmol 7:97.

Gelatt KN, Mackay EO (2004): Secondary glaucomas in the dog in North America. Vet Ophthalmol 7:245.

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

Gelatt KN, Mackay EO (2001): Effects of different dose schedules of latanoprost on intraocular pressure and pupil size in glaucomatous beagles. Vet Ophthalmol 4:283.
Gelatt KN, Mackay EO (1998): The ocular hypertensive effects of topical 0.1% dexamethasone in beagles with inherited glaucoma. J Ocul Pharmacol Ther 14:57.
Gelatt-Nicholson KJ, et al. (1999): Comparative Doppler imaging of the ophthalmic vasculature in normal beagles and beagles with inherited glaucoma. Vet Ophthalmol 2:97.
Glover TL, et al. (1995): The intracapsular extraction of displaced lenses in dogs: a retrospective study of 57 cases (1984-1990). J Am Anim Hosp Assoc 31:77.
Gorig C, et al. (2006): Comparison of the use of new handheld tonometers and established applanation tonometers in dogs. Am J Vet Res 67:134.
Gum GG, et al. (1993): Effect of topically applied demecarium bromide and echothiophate iodide on intraocular pressure and pupil size in beagles with normotensive eyes and beagles with glaucoma. Am J Vet Res 54:287.
Gum GG, et al. (1992): Effect of hyaluronidase on aqueous outflow resistance in normotensive and glaucomatous eyes of dogs. Am J Vet Res 53:767.
Gwin RM, et al. (1978): 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.
Gwin RM, et al. (1977): The effect of topical pilocarpine on intraocular pressure on pupil size in normotensive and glaucomatous beagles. Invest Ophthalmol Vis Sci 16:1143.
Hamor RE, et al. (1994): Intraocular silicone prostheses in dogs: a review of the literature and 50 new cases. J Am Anim Hosp Assoc 30:66.
Hampson EC, et al. (2002): Primary glaucoma in Burmese cats. Aust Vet J 80:672.
Herring IP, et al. (2000): Effect of topical 1% atropine sulfate on intraocular pressure in normal horses. Vet Ophthalmol 3:139.
Kato K, et al. (2006): Possible association of glaucoma with pectinate ligament dysplasia and narrowing of the iridocorneal angle in Shiba Inu dogs in Japan. Vet Ophthalmol 9:71.
Knollinger AM, et al. (2005): An evaluation of a rebound tonometer for measuring intraocular pressure in dogs and horses. J Am Vet Med Assoc 227:244.
Kroll MM, et al. (2001): Intraocular pressure measurements obtained as part of a comprehensive geriatric health examination from cats seven years of age or older. J Am Vet Med Assoc 219:1406.
Lannek EB, Miller PE (2001): Development of glaucoma after phacoemulsification for removal of cataracts in dogs: 22 cases (1987-1997). J Am Vet Med Assoc 218:70.
Martin CL (1975): Scanning electron microscopic examination of selected canine iridocorneal angle anomalies. J Am Anim Hosp Assoc 11:300.
Martin CL (1969): Gonioscopy and anatomical correlations of the drainage angle of the dog. J Small Anim Pract 10:171.
Martin CL, Wyman M (1978): Primary glaucoma in the dog. Vet Clin North Am 8:257.
Martin CL, Wyman M (1968): Glaucoma in the basset hound. Am J Vet Res 29:379.
McIlnay TR, et al. (2004): Evaluation of glutamate loss from damaged retinal cells in dogs with primary glaucoma. Am J Vet Res 65:776.
McLaughlin SA, et al. (1995): Intraocular silicone prosthesis implantation in eyes of dogs and a cat with intraocular neoplasia: 9 cases. J Vet Med Assoc 207:1441.
Meek LA (1988): Intraocular silicone prosthesis in a horse. J Am Vet Med Assoc 193:343.
Miller PE, et al. (2000): The efficacy of topical prophylactic antiglaucoma therapy in primary closed angle glaucoma in dogs: a multicenter clinical trial. J Am Anim Hosp 36:431.
Miller PE, et al. (1997): Mechanisms of acute intraocular pressure increases phacoemulsification lens extraction in dogs. Am J Vet Res 58:1159.
Miller PE, et al. (1990): Evaluation of two applanation tonometers in horses. Am J Vet Res 51:935.
Miller PE, Picket JP (1992): Comparison of the human and canine Schiøtz tonometry conversion tables in clinically normal cats. J Am Vet Med Assoc 201:1017.
Miller PE, Pickett JP (1992): Comparison of the human and canine Schiøtz tonometry conversion tables in clinically normal dogs. J Am Vet Med Assoc 201:1021.
Miller TL, et al. (2001): Description of ciliary body anatomy and identification of sites for transscleral cyclophotocoagulation in the equine eye. Vet Ophthalmol 4:183.
Miller TR, et al. (1995): Equine glaucoma: clinical findings and response to treatment in 14 horses. Vet Comp Ophthalmol 5:170.
Morris RA, Dubielzig RR (2005): Light-microscopy evaluation of zonular fiber morphology in dogs with glaucoma secondary to lens displacement. Vet Ophthalmol 8:81.
Mughannam AJ, et al. (1999): Effect of topical atropine on intraocular pressure and pupil diameter in the normal horse eye. Vet Ophthalmol 2:213.
Nasisse MP, et al. (1990): Treatment of glaucoma by use of transscleral neodymium:yttrium aluminum garnet laser cyclocoagulation in dogs. J Am Vet Med Assoc 197:350.
Nasisse MP, Glover TL (1997): Surgery for lens instability. Vet Clin North Am Small Anim Pract 27:1175.
O'Reilly A, et al. (2003): The use of transscleral cyclophotocoagulation with a diode laser for the treatment of glaucoma occurring post intracapsular extraction of displaced lenses: a retrospective study of 15 dogs (1995-2000). Vet Ophthalmol 6:113.
Pauli AM, et al. (2006): Effects of the application of neck pressure by a collar or harness on intraocular pressure in dogs. J Am Anim Hosp 42:207.
Pickett JP, et al. (1993): Equine glaucoma: a retrospective study of 11 cases. Vet Med 88:756.
Plummer CE, et al. (2006): Comparison of the effects of topical administration of a fixed combination of dorzolamide-timolol to monotherapy with timolol or dorzolamide on IOP, pupil size, and heart rate in glaucomatous dogs. Vet Ophthalmol 9:245.
Read RA, et al. (1998): Pectinate ligament dysplasia (PLD) and glaucoma in flat coated retrievers. I: objectives, technique and results of a PLD survey. Vet Ophthalmol 1:85.
Reilly CM, et al. (2005): Canine goniodysgenesis-related glaucoma: a morphologic review of 100 cases looking at inflammation and pigment dispersion. Vet Ophthalmol 8:253.
Ridgway MD, Brightman AH (1989): Feline glaucoma: a retrospective study of 29 clinical cases. J Am Anim Hosp Assoc 25:485.
Riggs C, Whitely RD (1990): Two cases of intraocular silicone prostheses in eyes with traumatic corneal lacerations. J Vet Med Assoc 196:617.
Roberts SM, et al. (1984): Cyclocryotherapy. Part I: evaluation of a liquid nitrogen system. J Am Anim Hosp Assoc 20:823.
Roberts SM, et al. (1984): Cyclocryotherapy. Part II: clinical comparison of liquid nitrogen and nitrous oxide cryotherapy on glaucomatous eyes. J Am Anim Hosp Assoc 20:828.
Rosenberg LF, et al. (1996): Cyclocryotherapy and noncontact Nd:YAG laser cyclophotocoagulation in cats. Invest Ophthalmol Vis Sci 37:2029.
Samuelson D, et al. (1989): Morphologic features of the aqueous humor drainage pathways in horses. Am J Vet Res 50:720.
Samuelson DA, et al. (1983): Orthograde rapid axoplasmic transport and ultrastructural changes of the optic nerve part II: beagles with primary open angle glaucoma. Glaucoma 5:174.
Sapienza JS, et al. (2000): Golden retriever uveitis: 75 cases (1994-1999). Vet Ophthalmol 3:241.
Sapienza JS, van der Woerdt A (2005): Combined transscleral diode laser cyclophotocoagulation and Ahmed gonioimplantation in dogs with primary glaucoma: 51 cases (1996-2004). Vet Ophthalmol 8:121.
Slater MR, Erb HN (1986): Effects of risk factors and prophylactic treatment on primary glaucoma in the dog. J Am Vet Med Assoc 188:1028.
Smith PJ, et al. (1996): Ocular hypertension following cataract surgery in dogs: 139 cases (1992-1993). J Am Vet Med Assoc 209:105.
Smith PJ, et al. (1986): Unconventional aqueous humor outflow of microspheres perfused into the equine eye. Am J Vet Res 47:2445.
Studer ME, et al. (2000): Effects of 0.005% latanoprost solution on intraocular pressure in healthy dogs and cats. Am J Vet Res 61:1220.
Stuhr CM, et al. (1998): The effects of intracameral carbachol on postoperative intraocular pressure rises after cataract surgery in dogs. J Am Vet Med Assoc 212:1885.
Takiyama N, et al. (2006): The effects of a timolol maleate gel-forming solution on normotensive beagle dogs. J Vet Med Sci 68:631.
Tinsley DM, Betts DM (1992): Clinical experience with a glaucoma drainage device in dogs. Vet Comp Ophthalmol 4:77.
van de Sandt RR, et al. (2003): Abnormal ocular pigment deposition and glaucoma in the dog. Vet Ophthalmol 6:273.
van der Linde-Sipman JS (1987): Dysplasia of the pectinate ligament and primary glaucoma in the Bouvier des Flandres dog. Vet Pathol 24:201.
van der Woerdt A, et al. (1998): Normal variation in, and effect of 2% pilocarpine on, intraocular pressure and pupil size in female horses. Am J Vet Res 59:1459.
Whigham HM, et al. (1999): Treatment of equine glaucoma by transscleral neodymium:yttrium aluminum garnet laser cyclophotocoagulation: a retrospective study of 23 eyes of 16 horses. Vet Ophthalmol 2:243.
Whitely D, et al. (1985): Implantation of intraocular prostheses in dogs. Comp Cont Ed Pract Vet 7:802.

Whiteman AL, et al. (2002): Morphologic features of degeneration and cell death in the neurosensory retina in dogs with primary angle-closure glaucoma. Am J Vet Res 63:257.
Wilcock BP, et al. (1991): Glaucoma in horses. Vet Pathol 28:74.
Wilkie DA, Gilger BC (2004): Equine glaucoma. Vet Clin North Am Equine Pract 20:381.
Willis AM, et al. (2002): Advances in topical glaucoma therapy. Vet Ophthalmol 5:9.
Willis AM, et al. (2001): Effects of topical administration of 0.005% latanoprost solution on eyes of clinically normal horses. Am J Vet Res 62:1945.
Wood JL, et al. (1998): Pectinate ligament dysplasia and glaucoma in flat coated retrievers. II: assessment of prevalence and heritability. Vet Ophthalmol 1:91.