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Canine, Feline and Equine Glaucoma

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Definition of Glaucoma

Glaucoma is an elevation in intraocular pressure (IOP) with resultant retinal ganglion cell and optic disk damage leading to blindness if uncorrected. Normal intraocular pressure can be anywhere from 10-35 mmHg depending upon the examiner, tonometer, conversion table, breed, age and species. Glaucoma occurs where there is obstruction to the flow of aqueous humor anywhere along the pathway of its normal flow. Aqueous humor is secreted by the epithelium of the ciliary processes into the posterior chamber and reaches the anterior chamber by crossing the pupil. It exits the eye through the pectinate ligament via two different routes. In the conventional route, the aqueous humor passes the ciliary cleft, which contains the trabecular meshwork, and enters the scleral venous plexus draining either anteriorly via the episcleral and conjunctival veins or posteriorly into the vortex venous system and into the systemic venous circulation (corneoscleral outflow pathway). In the non-conventional route, the aqueous humor drains into the ciliary muscle interstitium to the suprachoroid and diffuses through the sclera (uveoscleral outflow pathway). The balance between these routes is established by the ciliary muscle tone, with more fluid leaving the eye via the uveoscleral pathway when the ciliary muscle is relaxed than when it is contracted. In most species, the majority of the aqueous humor (about 50% in horses, 85% in dogs and 97% in cats) leaves the eye via the conventional outflow route (Slatter). The intraocular pressure rises when the production of aqueous humor exceeds its outflow. Because of the great reserve capacity of the aqueous drainage mechanism, extensive impairment to outflow (up to 80-90%) must occur in order for glaucoma to develop. Visual impairment as a result of collapsed lamina cribrosa pores, reduced optic nerve axoplasmic flow, and retinal ganglion cell death can develop within 24 to 48 hours if the IOP is extremely elevated, or can develop slowly over weeks or months if IOP is only mildly elevated.

Classification of Glaucoma

Primary (Inherited) Glaucoma

This type of glaucoma is characterized by increased IOP without preceding or concurring ocular disease. It is typically breed-related and variably heritable. Affected dogs and their close relatives should therefore not be bred, but unfortunately glaucoma does often not become apparent until after breeding age has been reached.

1. Primary Open Angle Glaucoma (POAG) – A bilateral disorder in young to middle-aged animals in which IOP tends to increase in a slow, insidious fashion simultaneously in both eyes, characterized by an initially mildly to moderately IOP (5-10 mmHg). The angle initially appears open, but eventual iridocorneal angle and sclerociliary cleft closure occurs in animals 4-6 years of age. This form is rare in animals, although it is the most extensively investigated form in dogs (laboratory Beagles). The mechanism is thought to be related to the presence of the glycoprotein myocilin within the extracellular matrix of the trabecular meshwork and nearby sclera, possibly creating resistance to the aqueous humor outflow in dogs with...
spontaneous glaucoma. As for myocilin, the transmembrane cell-surface protein CD-44 was shown to be increased in the aqueous humor and non-pigmented ciliary epithelium in the eyes of glaucomatous Beagles. It is therefore possible that myocilin and CD-44, and perhaps their aggregates and other proteins with affinity to the trabecular meshwork glycosaminoglycans, may play a role in the onset of canine glaucoma, even if mutations in their corresponding genes have yet to be detected in affected dogs.

2. Primary Angle Closure Glaucoma (PACG) – Most primary glaucomas in dogs are of this type, being at least eight times more common than open angle glaucoma. The glaucoma occurs because of some form of abnormal development of the drainage angle (goniodysgenesis). It is often seen in Basset Hounds, Arctic Circle breeds, Cocker Spaniels and other canine breeds with pectinate ligament dysplasia or imperforate pectinate ligament. In this disorder, the trabecular meshwork may appear normal, but the pectinate ligaments form large solid sheets of tissue that lack the appropriate perforation to allow the drainage of aqueous humor. The alterations are generally bilateral, but not necessarily of equal extent, so the glaucoma is often present initially only in one eye. The age of onset of glaucoma varies and it is not unusual to see cases of delayed clinical glaucoma in dogs with 8-10 years of age. The second most prevalent type of goniodysgenesis is characterized by profound arrest in the maturation of the trabecular meshwork such that the ciliary cleft is filled with tissue resembling anterior uveal mesenchyme (trabecular hypoplasia). Such animals generally have true congenital glaucoma. It is important to remember that the remodeling of the trabecular meshwork in dogs and cats continues for several weeks after birth, so that one should avoid over-interpreting apparent angle solidification of the trabecular meshwork in very young carnivores.

Secondary Glaucoma

This type of glaucoma develops secondarily to a number of ocular disorders including lens luxation, uveitis, and intraocular tumors. It is at least twice as common as primary glaucoma in dogs, and seven times more common in cats. It is most commonly associated with posterior synechiae as a sequel to anterior uveitis. As a result of the posterior synechiae, pupillary block, and eventual peripheral anterior synechiae, iris bombé may develop. Other frequent causes of secondary glaucoma include occlusion of the trabecular meshwork or pupil by pre-iridal fibrovascular membrane, neoplasia, and primary anterior lens luxation in terrier dogs with zonular dysplasia.

Stages of Disease

1. Early Non-Congestive Glaucoma – IOP elevation causes only mild pathologic changes.
2. Acute Congestive Glaucoma – There is little to no aqueous outflow and extreme elevation in IOP (>50 mmHg). Compression of the ciliary cleft and vessels leads, respectively, to increased drainage via episcleral and conjunctival veins (congestion) and iris sphincter ischemia, resulting in mydriasis.
3. End Stage Glaucoma – The eye is enlarged and permanently blind. IOP may vary considerably.
Clinical Signs of Glaucoma

1. **Early Non-Congestive Glaucoma** – Epiphora, blepharospasm, conjunctival injection (hyperemia).
2. **Acute Congestive Glaucoma** – Scleral injection (compression of the ciliary cleft increases drainage via episcleral and conjunctival veins), corneal edema (increased hydrostatic pressure forces the aqueous humor into the cornea), Haab’s striae (white, linear streaks in the cornea representing breaks in the Descemet’s membrane), severe pain (evidenced by blepharospasm, epiphora, third eyelid protrusion and possibly reduced appetite and activity level), mydriasis (due to iris sphincter ischemia resultant of compression of the ciliary vessels), and loss of vision (due to retinal and optic nerve damage).
3. **End Stage Glaucoma** – Globe enlargement (buphthalmos; an enlarged eye generally indicates a blind eye, except in puppies with a thinner sclera and Shar Pei’s with abnormally low scleral rigidity), retinal degeneration (tapetal hyper-reflectivity and vascular attenuation), corneal ulcers and bullous keratopathy (presumably as a result of endothelial dysfunction and corneal edema from elevated IOP), decreased pain (although the affected eye is still painful, the animal may not demonstrate the same intense level of pain as in the acute stage), optic nerve cupping, and ciliary body atrophy leading to subluxated/luxated lens due to zonular breakdown (this may require months). Phthisis bulbi can be seen in very chronic cases when the globe undergoes fibrosis.

Lesions Causing Glaucoma

**Primary Glaucoma** – In globes with this type of glaucoma there is almost always a readily detected maldevelopment of the iridocorneal angle. This may be due to a dysplastic pectinate ligament characterized by a broad band of mature iris stroma that inserts into the termination of the Descemet’s membrane in place of the normal perforated pectinate ligament, occasionally accompanied by deposits of periodic acid-Schiff (PAS)-positive material representing a thickened basal membrane, or due to persistent mesodermal tissue within the ciliary cleft (trabecular hypoplasia). No primary histologic lesions are apparent in cases of open-angle glaucoma.

**Secondary Glaucoma** – Ocular alterations in globes with this type of glaucoma will be variable and generally indicative of the primary ocular disease or injury that leads to either papillary blocks and/or trabecular occlusion. Such primary alterations include luxated and cataractous lenses, puncture wound, hyphema and drainage angle recession following trauma, angle obstruction by inflammatory exudate and fibrovascular membrane, melanocytic cell proliferation, iridociliary cysts and pigment cell exfoliation, intraocular primary or metastatic tumors, retinal detachment, and vitreal prolapse into the anterior chamber.

Lesions Resulting from Glaucoma

Lesions associated with glaucoma are correlated with the duration and severity of the process, as well as with the distensibility of the globe. Enlargement of the globe (*buphthalmos* or *megaloblobus*) occurs most prominently in young puppies with acute glaucoma secondary to...
anterior uveitis and in species with thin scleras such as cats. In the cornea, diffuse edema is seen as a result of IOP injury of the corneal endothelium, eventually progressing to corneal fibrosis and vascularization. Corneal stretching can lead to horizontal breaks in the Descemet’s membrane (Haab’s striae). Ocular enlargement can also cause failure of complete closure of the eyelids, resulting in corneal desiccation and eventual ulceration or possibly adaptive keratinization if the ocular enlargement develops slowly. Cataract is common, probably as a result of lens malnutrition associated with stagnation of the aqueous humor. The lens may be subluxated or luxated. Atrophy of the anterior uvea is most obvious as thinning and flattening of the ciliary processes. The ciliary cleft and trabecular meshwork are frequently collapsed, making evaluation for goniodysgenesis difficult. Lastly, retinal lesions are typical, characterized by variable atrophy of the inner layers. In dogs specifically, retinal atrophy may sometimes be full-thickness and accompanied by gliosis. Additionally in this species, the dorsal half of the retina is generally less severely affected by the atrophy than the ventral retina. Cupping of the optic disk accompanied by malacia and gliosis of the optic nerve is pathognomonic for glaucoma, but it does not rule out this diagnosis if not present.

It can be difficult to differentiate primary and secondary changes in a glaucomatous globe. For instance, cataract and lens subluxation may lead to, or result from, glaucoma. Breed predisposition may be helpful in determining whether a lesion is the cause or consequence of glaucoma.

Species Differences

There are several species differences in the structure of the filtration angle and in the degree of alternative routes of aqueous outflow. The horse has a very thick pectinate ligament and an inconspicuous corneoscleral trabecular meshwork and scleral venous plexus. As a result, the alternative (non-conventional) outflow pathway is much more important in this species than in dogs and cats. Cats have, in contrast, very delicate pectinate fibers, a very large open ciliary cleft and a conspicuous scleral venous plexus, with minimal (about 3% of aqueous outflow) use of the uveoscleral outflow pathway. In dogs, this alternative outflow accounts for 15-25% of the outflow of aqueous humor.

In dogs, glaucoma affects approximately 1.7% of the population in North America (approximately 1 in every 120 dogs), with approximately 0.9% being due to primary glaucoma (goniodysgenesis). The other leading causes of glaucoma in dogs are posterior synechiae with iris bombé, pre-iridal fibrovascular membrane, anterior uveal melanoma, and anterior lens luxation.

In cats, glaucoma is less common than in dogs, affecting approximately 1 in every 370 cats. In this species, it is predominantly secondary to lymphonodular anterior uveitis and diffuse iris melanoma; however, primary open-angle glaucoma can also occur in this species, primarily in Burmese and Siamese cats. A relatively recent study showed that about 1 in 150 cats older than 7 years of age had elevated IOP, most frequently due to aqueous humor misdirection, pushing the lens forward, blocking the pupil, and compressing the filtration angle. Posterior synechiae is strangely rare in cats. Clinical signs in cats are often much more subtle than in other species, with mydriasis and progressive buphthalmos frequently the only overt clinical signs. Histologically, retinal ganglion cells often persist in cats under circumstances that in dogs would have caused overt retinal atrophy. In contrast, optic disk cupping is more frequent in cats due to their thin sclera and lamina cribrosa.
Horses are a distant third to the dog in the development of glaucoma. However, glaucoma may have been underdiagnosed in this species until recently because instrumentation to measure the IOP in horses was unavailable and pain is not manifest as acutely as in dogs. Glaucoma in this species appears to affect most frequently older animals, Appaloosas, and animals with a previous history of anterior uveitis. Pre-iridal fibrovascular membrane formation across the pectinate ligament is the most frequent cause, but there is generally very little evidence of inflammation histologically. In horses with glaucoma with no obvious anterior peripheral synechiae, elevation of intraocular pressure may be due to obstruction of alternative uveal routes of aqueous outflow. Rarely, primary glaucoma may occur as congenital buphthalmos in newborn foals, associated with developmental abnormalities of the iridocorneal angle or more severe anterior segment dysgenesis. However, while there are rare reports of primary glaucoma in horses, a diagnosis of true primary glaucoma in this species remains controversial.

Glaucoma in other species is rare.

References