GLAUCOMA IN ANIMALS: WHERE WE WERE, WHERE WE ARE, & WHERE WE'RE GOING

Seth Eaton, VMD, DACVO
Assistant Clinical Professor, School of Veterinary Medicine, University of Wisconsin – Madison
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Glaucoma is arguably one of the most frustrating ophthalmic diseases to manage and treat in veterinary medicine. Elevated intraocular pressure (IOP), whether acute or chronic, not only risks pain for affected animals but carries the inevitable consequence of blindness due to progressive optic nerve degeneration in untreated eyes. Many of the same challenges that we face when managing dogs and cats with this disease are shared by physicians treating human patients for various forms of glaucoma; and interestingly, the development of many of the drugs and devices currently used to treat human glaucoma were originally studied and shown to be efficacious in dogs.

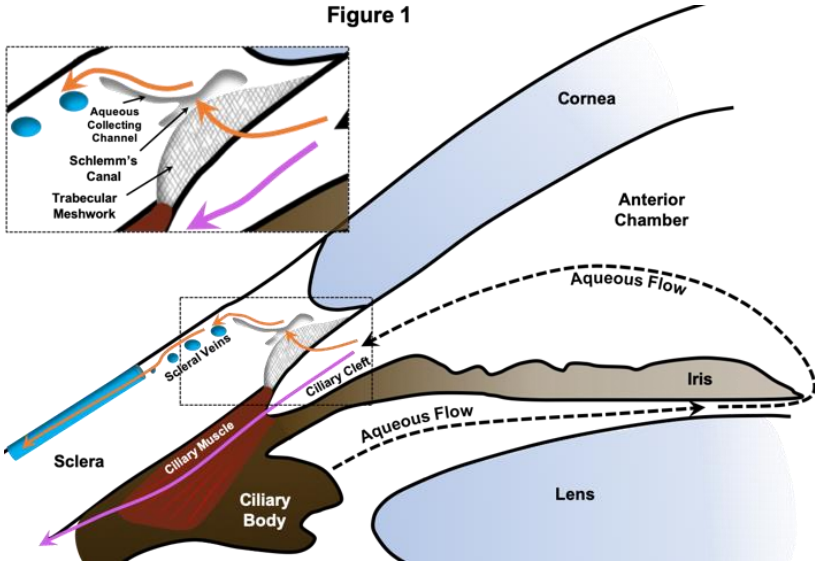
Despite the seemingly parallel paths by which glaucoma treatments have evolved over time in humans and animals, the long-term prognosis for comfort and maintenance of vision in affected animals remains much poorer than in human patients. There are a number of physiological and pharmacological factors that may explain this discrepancy, and may also inform the development of novel approaches to glaucoma therapy in all species moving forward. In both physician-based and veterinary ophthalmology, we are entering a new era of knowledge and innovation associated with novel drug development, advanced imaging technology, and acquisition of long-term follow-up data on human and animal patients. Collectively, these advances may refine and even change our paradigms for diagnosing and treating glaucoma in all patients.

THE FUNCTIONAL MORPHOLOGY OF NORMAL AND ABNORMAL AQUEOUS OUTFLOW

*How Aqueous Humor is **Normally** Supposed to Leave the Eye …*

The most common clinical forms of glaucoma in humans and animals are **hypertensive**, associated with elevated intraocular pressure (IOP) that develops secondary to impaired outflow of aqueous humor (AH). In humans, dogs, and cats, the functional morphology of the aqueous outflow pathways in the eye are comparatively similar. AH is normally produced in the ciliary body, flows through the pupil into the anterior chamber, and is delivered through the ciliary cleft to the aqueous drainage pathways adjacent to the base of the iris (see Figure 1). Aqueous humor then leaves the eye by one of two routes: the conventional pathway (orange arrows) or the unconventional pathway (pink arrow). Conventional outflow involves filtration of AH through the trabecular meshwork (TM), into Schlemm's canal (humans) or angular aqueous plexus (dogs and cats), and into scleral and

Figure 1



episcleral veins via systems of aqueous collecting channels. Alternatively, unconventional outflow bypasses the TM, directing AH to the supraciliary space via spaces between the ciliary muscle fibers. The normal contribution of the unconventional pathway to overall AH outflow, however, differs between species. The unconventional pathway is only responsible for <3% of aqueous outflow in normal cats, compared to up to 14 and 15% of outflow in humans and dogs, respectively.

*Despite the above similarities between humans, dogs, and cats described above, the underlying structural or functional **cause** for the dysfunction of the aqueous outflow pathway will differ between species.*

*Why Canine Glaucoma is Both Similar **AND** Dissimilar to Human Glaucoma …*

In research, the dog is commonly used as a model for hypertensive glaucoma in humans, particularly in the development of novel drugs for the reduction of IOP. There are, however, considerable anatomical and physiological differences between dogs and humans that complicate the use of the dog as a model. The most common form of hypertensive glaucoma in humans is **primary open angle glaucoma (POAG)**, in which the iridocorneal angle is conformationally open and appears clinically normal despite a functional reduction in normal aqueous outflow. In humans, this disease is heritable with other risk factors including age, ethnicity, and concurrent disease such as diabetes mellitus. A similar, heritable form of POAG has been well-characterized in a colony of Beagles and is occasionally recognized in client-owned Beagles, affecting young dogs (< 2 years of age). However, the most common form presenting in client-owned dogs is **primary angle *closure* glaucoma**, a presumed heritable form associated with a conformationally *narrow* or *closed* angle. In these eyes, narrowing and/or dysgenesis of the iridocorneal angle and ciliary cleft, the space between the base of the iris and the peripheral cornea, limit the amount of aqueous that can filter into the trabecular meshwork. Additionally, PACG in dogs more frequently presents as an *acute* crisis, whereas human and canine POAG are more slowly progressive and insidious diseases characterized by more gradual vision loss. Other comparative anatomical differences exist such as the lack of a true Schlemm's canal and structural and ultrastructural differences in the optic nerve and retina; however, the ultimate significance of these differences is not completely understood.

In addition to primary glaucoma, both humans and dogs can develop **secondary glaucoma** in which pre-existing or concurrent intraocular disease such as uveitis, intraocular neoplasia, or lens instability cause structural obstruction of the aqueous humor outflow pathways.

*Why Feline Glaucoma is Both Similar **AND** Dissimilar to Human Glaucoma*

In cats, glaucoma most commonly forms **secondary** to intraocular disease, typically due to obstruction of the trabecular meshwork by neoplastic or inflammatory cells, inflammatory debris, or scarring However, multiple forms of **primary congenital** and **primary breed-associated glaucoma**, more similar to those of humans, have been characterized in domestic cats; and recent investigations have demonstrated abnormalities not just in the trabecular meshwork but in the more distal aspects of the conventional outflow pathways in cats, namely the aqueous collecting channels and scleral vasculature. These fundamental comparative differences in pathophysiology offer compelling insight to explain why some species respond favorably to standard glaucoma drugs while others, like cats, do not.

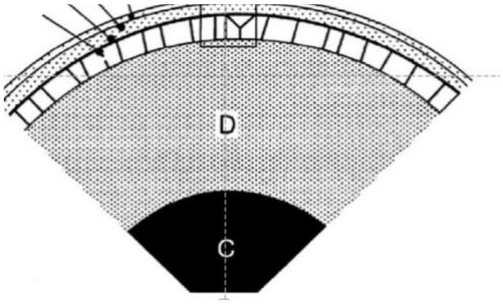
DIAGNOSIS AND MEDICAL TREATMENT OF CANINE GLAUCOMA

Canine Primary Glaucoma

What are our diagnostic tools for assessing glaucoma risk and *preventing* glaucoma?

Unfortunately, dogs with primary angle-closure glaucoma (PACG) are often presented when signs of acutely elevated IOP are recognized by owners with significant and possibly blinding damage to the optic nerve and retina having already been sustained. With one visual eye remaining, assessment of a dog's risk and proactive treatment and monitoring could theoretically delay or even prevent onset of glaucoma. Historically, techniques such as gonioscopy and ultrasound biomicroscopy have been used in dogs to try to assess risk for PACG or POAG, but have often been considered of questionable sensitivity, specificity, and predictability. However, with newer technology, the emergency of genetic testing, and acquisition of longer-term and more robust follow-up data, we're discovering that these diagnostic tests may have more meaningful predictive value than previously appreciated.

The grading scheme originally proposed by Ekesten and Narfström evaluates both the width of the iridocorneal angle and the presence or absence of sheeting of the pectinate fibers, and is probably the most widely used system by veterinary ophthalmologists. Using this system, the examiner uses anatomical landmarks to assign a score for **angle narrowing** (ranging from 0 for a closed angle to 4 for an angle that's wide open); and this is done for each quadrant. Then, the amount of sheeting or pectinate fiber dysgenesis is quantified based on a similar scale, with one indicating high severity sheeting and 4 indicating no sheeting. Some glaucoma investigators will calculate a value called the **angle index** from these findings, which factors in the width of the ICA and the overall % of the angle affected by sheeting around the entire 360 degrees of angle circumference. These 2 values are then calculated into 1 number that is used to estimate the % overall capacity for outflow through the iridocorneal angle compared to an angle that is wide open with no sheeting.



In the Bouvier des Flandres, the value of the angle index was validated by an almost 9-year longitudinal study of approximately 100 dogs. This study found that there was a strong association between development of glaucoma and the angle index ($p<0.001$), with the odds of glaucoma doubling for each 0.20 unit decrease in the angle index value. Dogs with an angle index of less than or equal to 1 had a 21% risk of developing PACG compared with a risk of 1.9% for other dogs.

In addition to gonioscopy, some veterinary ophthalmologists also use high-frequency ultrasound to assess what gonioscopy can't show, namely the status of the ciliary cleft, the space behind the pectinate ligament that provides an avenue for aqueous humor to filter into the trabecular meshwork. In some eyes, it's possible for the angle to appear narrowed on gonioscopy, but for the ciliary cleft behind it to be open. It's hard to quantify yet what this means but this may be very important for long-term monitoring of affected dogs.

Fortunately, PACG in dogs most commonly presents asymmetrically with one eye affected before the fellow eye. In dogs diagnosed with PACG in one eye, the literature reports an approximately 50% risk of elevated IOP in the fellow eye within 6-8 months. One prospective study, however, has reported a favorable effect of prophylactic topical treatment with a beta blocker or demecarium bromide/prednisolone acetate in "at-risk" eyes, extending the mean interval from 6-8 months to nearly 3 years. Therefore, many veterinary ophthalmologists may recommend prophylactic treatment with one of these drugs.

What are my therapeutic options for treating eyes with *active* primary glaucoma?

The cornerstone of therapy for canine PACG is sustained, long-term reduction of IOP. This requires medication administration for the life of the affected dog since primary glaucoma can be managed but not cured. The medical approach to management of canine PACG is also most frequently **multimodal**, employing drugs with differing mechanisms of action in order to most efficiently and effectively control IOP. Most drugs administered to reduce intraocular pressure act by one of two primary mechanisms: **reduction of aqueous humor production** at the ciliary body, or **increase in drainage of aqueous humor**. Intensive treatment is indicated during the acute crisis, with gradual reduction in the number and frequency of medications as IOP is controlled and determination of the prognosis for return to vision becomes clearer.

*OSMOTICS***:** Agents like mannitol and glycerin act by reversing the osmotic gradient that normally exists between the uveal vasculature and intraocular humors; they reduce aqueous humor production and dehydrate the vitreous body by decreasing plasma ultrafiltration and drawing fluid from the eye into the intravascular space. This effectively "de-congests" the eye and reduces IOP. However, this is likely only effective if the blood-ocular-barriers that normally establish the physiologic osmotic gradient are intact. In eyes with secondary glaucoma due to uveitis, for example, "leaky" blood-ocular-barriers will permit some degree of passage of an osmotic agent into the intraocular space, reducing the effect of the drugs. Furthermore, the effect of osmotic agents is only temporary; therefore, these medications are only indicated in the treatment of acute glaucoma. **Mannitol** (20%) is administered intravenously at a dose of 1-2 g/kg over 20-30 minutes, typically exerting an effect within 30-60 minutes after administration, and lasting for 6-8 hours. **Glycerin** is administered orally during an acute glaucoma crisis. It is available in 50% or 75% solutions, dosed at 1-1.5 g/kg, typically mixed with food. Like mannitol, its effect is typically observed within 60 minutes of administration and lasts for up to 10 hours, though the absorption and effect can vary between individual dogs, and it can induce nausea and vomiting. Osmotic agents should be used with caution in any patient with clinical dehydration, renal insufficient, or structural cardiac disease. Glycerin, unlike mannitol, is metabolized to glucose after administration and should not be used in diabetic patients.

BETA BLOCKERS: Topical beta blockers like 0.25% or 0.5% **timolol maleate** decrease IOP by reducing aqueous humor production at the level of the ciliary body. In general, ophthalmic beta blockers have a weak effect on reducing IOP, but their effects may be enhanced in patients with active glaucoma. Typically given BID-TID, their activity may also be more potent when administered in tandem with carbonic anhydrase inhibitors. Caution should be used in small dogs in which systemic absorption may result in bradycardia/bradyarrhythmias or may exacerbate active inflammatory lower airway disease.

CARBONIC ANHYDRASE INHIBITORS (CAIs): CAIs are arguably the most universally indicated drugs in the treatment of all forms of glaucoma, primary and secondary. CAIs reduce IOP by inhibiting carbonic anhydrase at the level of the ciliary body, reducing production of aqueous humor. Topical CAIs like **dorzolamide** and **brinzolamide** are typically administered BID-TID and exert their hypotensive effect 4-6 hours following initiation of administration. The most common adverse effects of topical CAIs are contact hypersensitivity and idiosyncratic dry eye. Oral CAIs like **methazolamide** are also prescribed in some cases for canine glaucoma at a dose of 2-5 mg/kg BID-TID. At higher ends of the dose range, however, systemic side effects consistent with metabolic acidosis (panting, lethargy) and hypokalemia due to kaliuresis may be observed and limit therapeutic benefit.

PROSTAGLANDIN ANALOGS: The development of prostaglandin analogs (PGAs) in the late 1990s made a significant impact on the treatment and long-term management of glaucoma in both humans and dogs. Ophthalmic PGAs like **latanoprost**, **travoprost**, and **bimatoprost** are potent ocular hypotensive agents, reducing IOP by encouraging aqueous outflow via alternative (unconventional) pathways within the base of the iris and ciliary body. PGAs are typically administered once daily to BID when used as maintenance therapy, but can be very powerful adjuncts to or even replacements for osmotic agents in the treatment of acute glaucoma, exerting an effect in many eyes within 30-60 minutes following a single topical dose. However, due to their prostanoid effects which can be pro-inflammatory, PGAs should be used with caution in eyes with secondary glaucoma due to uveitis. Furthermore, they are contraindicated in any eye with glaucoma secondary to anterior lens luxation, as they produce a potent miosis which can result in pupillary block, driving IOP up rather than down.

NEW DRUGS:* Recently, two new drugs have been FDA-approved for treatment of glaucoma in the United States, though large studies in client-owned dogs are not yet published. **Netarsudil (Rhopressa™) is a topical ophthalmic rho kinase inhibitor that reduces IOP by reversibly relaxing the trabecular meshwork tissue and increases aqueous outflow, while also reducing intravascular pressure in the episcleral veins contributing to IOP reduction. In rabbit studies, this drug reduced IOP significantly within 30 minutes, with maximal effect at 1-3 hours, representing a faster time to efficacy than many other drugs. However, abstracts presented in November 2019 demonstrated no clinically significant IOP reducing effect of this drug in normal dogs (dogs without glaucoma) or in dogs with primary open angle glaucoma (POAG).

Latanoprostene bunod (Vyzulta™) is a pharmacologically-altered PGA with dual action. In addition to its ability to increase unconventional aqueous outflow, it liberates nitric oxide which increases conventional outflow through the trabecular meshwork, at least partially due to relaxation of the collecting vessels of the sclera. In Beagles with POAG, Vyzulta was ~2X more effective than Xalatan for reducing IOP. There are no published studies evaluating this drug in dogs with PACG to date.

Surgical Treatment of Canine Glaucoma

When medical therapy fails to control IOP, the best option for eyes with the potential for maintaining vision is surgical intervention. However, an optimized, standard-of-care surgical approach for primary glaucoma has not been determined; instead, there are multiple tactical

approaches that can be used to control IOP. Aqueous humor shunts like the Ahmed valve have been used for decades to provide an alternative aqueous outflow pathway. The Ahmed valve and similar devices are surgically implanted, with a tube extending into the anterior chamber to receive aqueous humor and conduct it into the base or "footplate", which is surgically placed in the subconjunctival space. Short- and long-term failures of these shunts, however, are associated with obstruction of the valve by fibrin or fibrosis of the subconjunctival tissue over the footplate, respectively. Therefore, many surgeons advocate use of cyclodestructive procedures to reduce aqueous humor production either instead of or in conjunction with placement of a valve. **Transscleral cyclophotocoagulation (TSCPC)** involves ablation of the ciliary body through the sclera using a diode laser. This procedure is inherently "blind" as the ciliary processes cannot be directly visualized during the procedure and the surgeon must rely on measurements and approximated landmarks. Furthermore, use of laser energy in this manner can induce considerable postoperative uveitis. Numerous studies have been performed to determine success rates, most often measuring the percentage of patients retaining vision at one year (1Y) using these procedures, but have yielded variable results. For primary glaucoma, studies evaluating TSCPC alone typically carry 1Y success rates hovering around 50%. Studies investigating combined approaches with both TSCP and an Ahmed valve vary between 41-89%.

Use of **endolaser cyclophotocoagulation (ECP)**, in which a diode laser and fiberoptic camera are introduced into the eye via an intraocular surgical approach, permits direct visualization of the ciliary processes during laser treatment. Due to this visualization and the need for lower laser energy levels compared to TSCPC, proponents of this approach cite lower complication rates. There are no peer-reviewed publications describing long-term results using of ECP in dogs to date. However, in one abstract describing results following ECP in the largest cohort of dogs with both primary and secondary glaucoma, a 1Y rate of IOP control was achieved in 83%, with vision retention in 73%; in that same study, success rates from dogs with follow-up data at 4 years postoperatively were 65% for IOP control and 44% for vision retention.

Most recently, **micropulse transscleral laser**, which produces lower levels of heat in laser-treated tissue with putatively decreased risk for complications, has been investigated in dogs. Two peer-reviewed publications have been published in small cohorts of dogs with primary or secondary glaucoma with IOP control rates at approximately 1 year between ~40-65%.

Canine Secondary Glaucoma

Secondary glaucoma in dogs develops due to acute or chronic uveitis associated with swelling and congestion of the iris, development of structural adhesions and narrowing of the iridocorneal angle, and/or or obstruction of the aqueous outflow pathways due to accumulation of cells and inflammatory debris within the trabecular meshwork. While some drugs like CAIs and beta blockers may be effective in reducing IOP in affected eyes, a successful therapeutic approach must include administration of systemic and/or anti-inflammatory medications, and ultimately determination and treatment of the underlying cause. Due to associated structural changes and inflammation as well as the often persistent or recurrent nature of the underlying disease, most cases of canine secondary glaucoma are not ideal candidates for surgical treatment.

DIAGNOSIS AND TREATMENT OF FELINE GLAUCOMA

Though is considered a less common clinical diagnosis in the cat, the clinical features of feline glaucoma are much more subtle and insidious than in dogs. Therefore, it may be more commonly undiagnosed. Cats are only rarely painful with increased IOP and the feline eye does not present with the same degree of episcleral redness or corneal edema as other species like the dog. In cats, perhaps the most reliable indicator of glaucoma is a **dilated pupil**. Furthermore, cats often maintain vision for much longer, even in the face of chronically elevated IOP and globe enlargement. Furthermore, glaucoma was a causative or associated factor in nearly 29% of feline globes submitted to the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW).

The vast majority of cases of feline glaucoma are **secondary**, developing due to preceding ocular disease. Approximately half of these cases are secondary to neoplasia (i.e. LSA, feline iris melanoma), and about 25% due to immunopathologic uveitis, often of unknown etiology. As with dogs, treatment with topical medications may be effective in reduction of IOP and management of inflammation in affected eyes, identification and treatment of the underlying disease is critical to success. Similarly, most cases of feline secondary glaucoma are not considered candidates for surgical treatment.

Topical carbonic anhydrase inhibitors (CAIs), such as 2% dorzolamide TID, are integral therapeutic agents in the treatment of feline glaucoma. While oral CAIs (i.e. methazolamide) can be effective at reducing IOP, cats are exceptionally sensitive to the gastrointestinal and metabolic side effects of these medications so they should be avoided. Caution should be used in prescribing topical beta blockers in cats with cardiac disease or lower airway disease (i.e. feline asthma). Unfortunately, prostaglandin analogs effective in treatment of human and canine glaucoma (i.e. latanoprost, travoprost, bimatoprost) do not effectively reduce IOP in the feline eye, as cats do not have the appropriate prostaglandin receptors. Furthermore, outflow via the unconventional pathway is lower in cats compared to other species; thus, pharmacologic modulation of this route by PGAs may produce a less robust effect.

While drugs like CAIs and beta blockers may be effective in reducing IOP in affected eyes, a successful therapeutic approach must also include administration of systemic and/or anti-inflammatory medications, and ultimately determination and treatment of the underlying cause. Due to associated structural changes and inflammation as well as the often persistent or recurrent nature of the underlying disease, most cases of canine secondary glaucoma are not ideal candidates for surgical treatment.

Feline primary glaucoma is comparatively rare, though certain breeds may be predisposed including the Siamese, Burmese, and Persian. Primary disease in cats may take the form of both open-angle and congenital glaucomas. In feline primary glaucoma, clinical signs are typically subtle as progressive increase in IOP is more insidious. Histologic evaluation has shown that, unlike forms of primary glaucoma in humans and dogs, the pathology underlying poor aqueous outflow in cats may lie well beyond the iridocorneal angle and instead within the scleral aqueous collecting vessels or even the veins that eventually receive aqueous humor from the eye.

Aqueous misdirection glaucoma is an uncommon but well-characterized form of slowly-progressive feline glaucoma, typically affecting older cats. This form of glaucoma is often bilateral, but typically begins unilaterally, causing pupil dilation and anisocoria. The characteristic

clinical finding in affected eyes is a dramatically but uniformly shallow anterior chamber. The exact cause in unknown but based on ultrasonographic and histopathologic studies, the putative mechanism is misdirection of aqueous humor into the vitreous instead of the anterior chamber, leading to accumulation of "pools" of aqueous fluid within the vitreous body. The vitreous expands, leading to forward displacement of the lens and iris, eventually narrowing and even collapsing the iridocorneal angle, leading to impaired aqueous outflow and increased IOP. Unfortunately, while surgical intervention (phacoemulsification and anterior vitrectomy) may be curative in some patients (especially those treated early in the course of disease), it may be ineffective in those patients with chronic disease. Since this disease commonly affects older cats, topical medical therapy is often elected. Topical CAIs can be very effective in reducing IOP in affected eyes and may be sufficient for long-term management of IOP in cats with AMG.

THE FUTURE OF GLAUCOMA THERAPY IN VETERINARY MEDICINE

Due at least partially to differences in underlying etiologies and pathologies, the drugs that are being developed for treatment of glaucoma in human patients may not adequately treat glaucoma in canine or feline patients. Thus, there is a greater sense of urgency underscoring the need for expansion of the body of research and development within the veterinary field. Despite decades of research and experience with canine and feline primary glaucoma, we still know very little about inheritance patterns, precise disease pathophysiology within the anterior segment, and the microscopic mechanisms underlying retinal and optic nerve degeneration. Furthermore, there is still poor consensus among veterinary ophthalmologists regarding the classification and nomenclature used to describe iridocorneal angle abnormalities and other features of glaucoma in the eyes of affected animals. Therefore, efforts will need to be focused on standardizing the methods used to grade the iridocorneal angle, particularly on advanced ophthalmic imaging (see below), as well as refining classification and staging of glaucoma in animals. It is also very important to gain a better consensus among veterinary ophthalmologists regarding when and how we clinically monitor animals at risk for glaucoma (i.e. intervals for recheck, methods for periodic structural and functional testing, etc.).

A large component of this effort must involve a dedicated focus on understanding disease mechanisms and being able to identify and quantity a dog's risk for primary glaucoma. This at least partially depends on continued acquisition of follow-up data on all canine and feline patients diagnosed with primary glaucoma. Advanced *in vivo* ophthalmic imaging will also be a critical part of these efforts, as modalities such as optical coherence tomography (OCT), anterior segment angiography, and adaptive optics become more accessible in veterinary ophthalmology departments and clinics. Additionally, monitoring technology such as telemetry will enable more continuous tracking of IOP in affected patients, allowing a better understanding of how IOP behaves when an animal is not in the hospital while also affording owners and clinicians an earlier chance to intervene should IOP increase.

When it comes to therapeutics, veterinary investigators must be innovative when approaching the development of drugs for reduction of IOP in affected canine and feline eyes, while also ensuring that owners can remain compliant long-term. Given the slow process associated with developing a drug and bringing it to market, one strategy that will likely be at the forefront is the use of intraocular sustained-release implants that can provide a better and more efficient way to administer the drugs we have now. The other aspect of canine primary glaucoma treatment that

must be a component of these efforts involves refinement of our current surgical options as well as development of novel surgical approaches. In human ophthalmology, the area of minimally-invasive glaucoma surgery (MIGS), characterized typically by micro-implants that enhance aqueous outflow, has rapidly expanded over the past 5-10 years and could play an important role in our approach to canine and even feline glaucoma, particularly primary forms.

Secondary glaucoma must also continue to be a part of this discussion for both dogs and cats. Typically, surgical implants and other medical approaches carry lower or at least more variable success rates than in primary disease due to the associated inflammation and structural abnormalities. With innovative strategies using novel or even already-marketed drugs like ranibizumab (Lucentis™) which inhibit vascular endothelial growth factor (VEGF) in human patients with age-related macular degeneration (AMD), we may find better success in managing secondary glaucoma patients for longer periods of time after the initial insult.

As with other areas of medicine and veterinary medicine, much of our future success in treating disease likely involves identification of predisposing or contributing genetic factors and targeting those factors with gene-based therapies. One such example is gene therapy, in which an investigational viral vector-based therapeutic approach has shown remarkable early success in managing primary open angle glaucoma (POAG) in Beagle dogs with a mutation of the ADAMTS10 gene. ADAMTS genes are responsible for microfibril formation, stability, and integrity within the eye's trabecular meshwork (TM). In Beagles, a missense mutation in ADAMTS10, a gene responsible for secretion of proteinases integral in extracellular matrix formation in the TM, results in abnormal plaque formation around the trabecular fibrils. These plaques lead to functional reduction in aqueous outflow and increased IOP. One group of investigators recently recognized this mutation as a candidate for gene therapy. Using an AAV vector that specifically targets the TM, they demonstrated some outstanding and compelling results in a small cohort of three young Beagle dogs with POAG (~1.5 to 2.0 years of age). A small volume of a formulation containing this vector was injected once into the anterior chamber of one eye in each dog. Each dog was monitored for two years. Compared to the untreated eye, there was a dramatic and well-maintained reduction in IOP in 2/3 dogs, beginning approximately 1-2 months after the injection, maintained for 105 weeks. Furthermore, untreated eyes showed morphologic evidence of glaucomatous damage to the optic nerve, whereas damage was not evident in treated eyes.

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