

This series of informative articles is for those interested in learning more about the health of the PBGV breed.

Understanding Glaucoma

Glaucoma is a frustrating disease. For a long time, we've thought of glaucoma as a plumbing problem in the eye. Fluid can't get out of the eye, intraocular pressure goes up and you (or your dog) have glaucoma. Sooner or later, vision is lost and, in dogs, if the pressure can't be controlled the eye usually has to be removed. This is disturbing to dogs and their owners, of course, but also to those of us in the veterinary community who prefer to make eyes better rather than taking them out.

I ended up removing her eye. Gonioscopy revealed a severely narrowed-to-closed ICA in her bad eye, but also in her good eye, and she is now on glaucoma medication to try to slow development of disease in that eye.

I'd also like to tell you about another one of my patients. He is a 12-year-old American Cocker Spaniel. His eye has been a little red lately, and his owner wasn't sure his vision was entirely normal. Sometimes the eye looks cloudy, but that seems to go away on its own. Pressure in the eye was

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To assess the eye's "plumbing" we have traditionally relied on two tests: intraocular pressure measurement and gonioscopy. Intraocular pressure measurement rarely tells us anything useful before it's too late. Gonioscopy, on the other hand, is meant to provide us with information before a problem occurs. This test involves using a special lens, which is placed directly upon the eye, to view the iridocorneal angle, or the space at the outer edge of the iris where fluid exits the eye. The iridocorneal angle, or ICA, is the first part of the main pathway for fluid drainage from the eye. It is spanned by a structure called the pectinate ligament. The pectinate ligament should look like thin strands of tissue, through which fluid can flow freely. When an ophthalmologist performs gonioscopy, he or she is evaluating the width of the ICA and the appearance of the pectinate ligaments. In dogs, unlike in humans, most glaucoma is of the closed-angle and goniodysgenesis-related types. This means that the angle is too narrow (closed-angle), or the pectinate ligament, instead of being composed of small strands, is made up of broad sheets of tissue (goniodysgenesis). Both of these problems are present from birth. It would seem to make sense that either one of these problems would inhibit the flow of fluid from the eye and would cause glaucoma, and one would think that this would occur at an early age.

One of my recent patients seems to illustrate this idea nicely. She is a Siberian Husky, just a little over a year old, who came to see me with a painful, red eye. On presentation, pressure in her eye was 52 mm Hg (normal is 12 to 25 mm Hg) and she was irreversibly blind in the eye.

barely elevated, at 27 mm Hg, and he responded normally to hand motion and light. Gonioscopy in both eyes revealed a severely narrowed ICA. I sent him home with glaucoma medication and he is doing well so far.

The problem? Both of these patients have glaucoma, and their ICAs appear almost identical on gonioscopy. Why, then, does the Husky have severe disease as a very young dog while the Cocker has reached his later years with only mild symptoms? And what about another recent patient of mine, a seven-year-old Anatolian Shepherd, who also has end-stage glaucoma in one eye but who has no abnormalities on gonioscopy? These three dogs, taken together, illustrate some of the limitations of gonioscopy and also remind us that glaucoma must involve more than just obstruction of fluid outflow from the eye.

Gonioscopy is still a useful test, but it is only one piece of data. Dogs with narrow or abnormal angles are at increased risk for glaucoma, and their owners should be educated regarding signs of disease. These dogs are not guaranteed to develop glaucoma, however, and we cannot predict timing of glaucoma should it occur. Most dogs with glaucoma develop the disease in mid-life, with some variation noted between breeds. The fact that most do not develop disease as puppies or young adults suggests that some other set of factors must be involved – something must progress over time. It is also important to understand that gonioscopy allows evaluation of only the outermost portion of the drainage pathways, and that a dog considered normal on gonioscopy may have abnormalities of the deeper portions of the pathways (the trabecular

continued on page 40

Glaucoma *continued from page 38* meshwork and ciliary cleft). These deeper portions of the drainage pathways can sometimes be evaluated using high-resolution ocular ultrasound. An abnormal ICA on gonioscopy should be considered a risk factor, not a diagnosis. On the other hand, normal gonioscopic evaluation should not be taken to mean that an individual (and his or her offspring) will never develop glaucoma.

Glaucoma in humans is defined as a disease of progressive loss of retinal cells and optic nerve fibers, which may or may not involve increased intraocular pressure. Up to 25 percent of humans with glaucoma have never had a documented increase in intraocular pressure, and 10 percent of humans over the age of 40 have elevated intraocular pressure without evidence of glaucoma. These facts, along with our findings in dogs, suggest that we need to look at risk factors other than just abnormalities of the eye's drainage pathways. These may include changes in the tissues of the optic nerve, inflammation within the eye, autoimmune activity and other causes of stress to the cells of the retina and optic nerve.

The optic nerve, where it leaves the eye, passes through a meshwork of connective tissue. In some individuals, it is thought that this meshwork is less resistant to stress and therefore more vulnerable to small increases in intraocular pressure than average, causing it to collapse easily. In other individuals, similar processes may affect the meshwork within the drainage pathways and around the optic nerve, leading to deposits of material and closure of both meshworks. If the meshwork of the drainage pathways is affected, pressure goes up in the eye. If the meshwork around the optic nerve is affected, however, growth factors and other important molecules cannot flow through the optic nerve fibers to the cells of the retina, and those cells die. This can cause glaucoma without an increase in intraocular pressure.

Lack of antioxidants and damage to the mitochondria (the part of a cell that produces energy to keep the cell alive) may also play a role in development of glaucoma. The body's own immune system may act inappropriately and damage retinal and optic nerve cells too. It can be overwhelming to try to keep up with all these new theories about glaucoma, but it is also very exciting as it means that we will have new therapies available in the near future that may help dogs and humans with glaucoma retain vision. As with many diseases, though, these treatments are likely to be most effective if they can be instituted before glaucoma develops, or at least before the disease progresses significantly.

This brings us back to the idea of screening. As mentioned above, gonioscopy and thorough ocular examination are still important. However, as we begin to understand more about the causes of glaucoma, we have the chance to develop new screening tools as well. In the future, we may be able to test an individual's blood or aqueous

humor (the fluid inside the eye) for markers of oxidative stress, inflammation, or tissue deposition.

Genetic testing may also be possible, and has received a good deal of attention and funding lately. However, glaucoma is almost always a disease that develops because an individual has multiple risk factors, not just one risk factor. This means that it is also, in most cases, not a disease controlled by a single gene. Genetic testing, like gonioscopy or any other single test we might perform, is not likely to be conclusive, but it is still worthwhile. It offers another piece of useful information that must then be considered in the context of a dog's family history and other examination findings. Genetic testing in the future may also help us tailor treatments to specific individuals, as dogs with particular genetic mutations may respond differently to different treatments. It is important to understand, though, that not all genetic tests are equally valuable. Some genetic tests do not look directly for the genes of interest (which can be difficult to identify) but instead look for linkage markers, or more easily identified DNA mutations that are thought to be present along with the gene of interest. These tests can be useful in some situations but are more likely to give false results than tests that look directly for a particular gene.

There are many things we do not understand about glaucoma, although we now realize we need to think beyond "plumbing." As our knowledge of this disease increases in coming years, our testing and treatment options promise to increase as well. ■

Dr. Stephanie Pumphrey received her DVM at the Tufts Cummings School of Veterinary Medicine. She is currently an ophthalmology resident at Tuft's Foster Hospital for Small Animals.

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The PBGVCA Health Committee urges you to take advantage of the AKC Canine Health Foundation's (CHF) educational podcasts about canine health. The "Genome Barks" Podcast Series features a wide variety of canine health topics, including lectures from the AKC's highly successful Breeders' Symposia, in-depth discussions by CHF-funded researchers and interviews with other canine health experts. The podcasts are released every two weeks and are available for direct download at www.genomebarks.com or Apple's iTunes store.

WHAT OFFA HAS TO OFFER! from Carolyn Randel, Health Committee

Have you looked at the OFFA website lately? If not please take a look.

There are so many areas to this site. Not only can you look for the health test results for PBGVs, but you can find a listing of those that have qualified for a CHIC certificate. The number of DNA tests available for the various breeds is also very impressive. Plus, there is a calendar that lists various health clinics that are being offered around the country.

There is too much to print here so take the time to look at the wealth of information that is given on this site.

The web address is www.offa.org.