The Golden Retriever Club of America, Inc.

From the Health & Genetics Committee

Progressive Retinal Atrophy in Golden Retrievers

Inherited eye diseases are common in dogs. In the US, guidance on inherited eye diseases of dogs is provided by the Genetics Committee of the American College of Veterinary Ophthalmologists (ACVO). For purebred dogs, the guidance is updated regularly and published in The Blue Book: Ocular Disorders Presumed to be Inherited in Purebred Dogs which is available online (6). The GRCA Code of Ethics guidelines specifically states that Golden Retrievers that have been used for breeding should receive annual eye exams by a veterinary ophthalmologist throughout their life, with normal results being recorded in an online registry meeting specific criteria (4). The online registry that currently meets those criteria is the Companion Animal Eye Registry (CAER) operated by the Orthopedic Foundation for Animals (5). This article is about Progressive Retinal Atrophy (PRA), a gradually worsening disease of the visual cells in the retina, which is located at the back of the eye. PRA is one of the conditions where an unequivocal recommendation against breeding clinically affected dogs is noted the Blue Book.

What is Progressive Retinal Atrophy (PRA)?

PRA is the name for a clinical condition of dogs that is characterized by generalized progressive degeneration of the photoreceptor cells of the retina leading to blindness. This disease is progressive and is NOT retinal dysplasia (which is a development condition of the retina that is present at birth).

There are several different forms of PRA but in most forms the retina will appear normal in young dogs, with retinal degeneration followed by blindness developing with age. Because PRA generally develops in mature dogs, affected dogs could be bred before the condition is detected, either by a routine ophthalmologic examination or when blindness develops. However, for many dog breeds, there are now genetic tests for many common forms of PRA affecting that breed. The genetic tests allow detection of dogs that are at risk for developing PRA before the eye disease can be detected. These genetic tests can also identify PRA carriers, dogs that have the potential to produce puppies affected by PRA, and can aid in the selection of appropriate mates for those dogs.

Several different genetic mutations can cause PRA in dogs and some of these mutations affect only one breed; other mutations can occur in multiple breeds (8-10). With regard to breeding considerations, forms of PRA that are presumed to be inherited can be viewed as falling into two very broad categories: 1) PRA where the genetic cause has not yet been identified; and 2) PRA where the genetic cause has been identified and there is a

DNA test. In dogs in general, there are autosomal recessive, autosomal dominant, and sex-linked forms of PRA. However, most forms of PRA are inherited as an autosomal recessive condition – which means that affected dogs need to inherit a defective gene from each of their parents. With a recessive condition, the parents will have normal vision if they have one normal allele.

There are three types of PRA in Golden Retrievers where the gene causing the PRA has been identified. These are *prcd*-PRA, GR_PRA1 and GR_PRA2. There is a genetic test of each of these forms of PRA. At least one other form of PRA is believed to have a genetic cause that has not yet been identified. The mutation that causes *prcd*-PRA is one of the most common deleterious mutations in dogs and the genetic mutation causing it has been identified in at least 30 different breeds (1). The genetic mutation that causes *prcd*-PRA in dogs also causes one form of retinitis pigmentosa and blindness in humans (9). The genetic mutations that cause GR_PRA1 and GR_PRA2 have only been described in Golden Retrievers (2; 3).

Because each of the mutations known to cause PRA are simple autosomal recessives, certain well-defined rules of inheritance apply:

1. A Golden Retriever that is clinically affected with *prcd*-PRA, GR_PRA1 or GR_PRA2 has inherited a disease allele from each of its parents. Both the sire and the dam of a clinically affected dog are carriers (or affected) and are likely to have passed a copy of the deleterious gene to other offspring. Testing for the disease allele identifies those Goldens that have the deleterious gene and whether they are genetically carriers or affected.
2. A Golden Retriever that has one PRA allele and one normal allele is a PRA carrier. At least one of its parents is a carrier (possibly both), and some of their siblings may also be carriers (or affected, if both parents are shown to be carriers).
    a. Carriers bred to carriers or affecteds can produce affected puppies (Figure 1).
    b. Carriers bred to DNA tested normal/clears (both alleles are normal) should not produce puppies affected with *prcd*-PRA but may produce carriers (Figure 2).

The Health & Genetics Committee recommends that close relatives of Goldens that are affected or carriers of any form of PRA be DNA tested for that form of PRA unless they are direct descendants of dogs DNA tested as normal/clear. Carriers should only be bred to Goldens that have been DNA tested as normal/clear for that form of PRA, and any offspring sold with full registration should be DNA tested and their status disclosed before ownership transfer. In addition to relatives of carriers and affected Goldens (and their prospective mates), owners may wish to DNA test frequently used stud dogs. Owners may want to test their Goldens for a variety of other reasons as well. Tests for *prcd*-PRA, GR_PRA1 and GR_PRA2 are widely available from multiple providers of DNA tests. However, it is important to remember that laboratory errors can occur and the quality of the testing laboratory should be considered. DogWellNet has a site that provides some quality indicators for commercial laboratories that may be helpful in selecting a laboratory https://dogwellnet.com/index.php?app=dwlabs&module=search&controller=labs. If DNA

test results for *prcd*-PRA, GR_PRA1 and/or GR_PRA2 are submitted to the Orthopedic Foundation for Animals (OFA) with the recording fee, OFA will issue a registry number.

Thoughts for Consideration Regarding Genetic Testing

It is very likely that all dogs carry several deleterious recessive genes. DNA tests allow us to breed PRA carriers responsibly, so that the chance of an affected puppy is greatly reduced, while gradually reducing the prevalence of the genes causing PRA in Golden Retrievers. It is also important to remember that "for a dog to have a lasting influence on the breed, it must be an extraordinarily successful individual" and to avoid the knee-jerk reaction of inappropriately removing excellent dogs from the gene pool just because we now have a way to identify their carrier status for a form of PRA. Also, rapid elimination of carriers can narrow the gene pool so that other harmful recessive genes are concentrated, thus potentially causing more harm than good. Therefore, many breeders working with affected lines will choose to breed carriers to normal/clear individual and test the offspring that may be used for breeding while others will only breed normal/clear to normal/clear. Both approaches are responsible.

Genetic tests for for *prcd*-PRA, GR_PRA1 and/or GR_PRA2 are among the many DNA tests available today. Goals for achieving a healthier breed over the long term as more genetic tests become available include: honesty; open communication of genetic problems; rational use of the PRA tests and other emerging DNA tests to prevent producing affected Golden Retrievers; tolerance of those with different breeding strategies that still produce healthy puppies; acceptance that many dogs will carry abnormal genes, but an understanding that genetic tests allow us an opportunity to produce homozygous normal individuals gradually without loss of quality. A rational informed approach to genetic testing will pave the way for the extraordinarily successful individual of the future to be as good or better in their performance/conformation as we could have ever envisioned in the past, but increases the likelihood that the descendants from successful lines also contribute good health to the Golden Retrievers' future.

An article on DNA Health Testing Summary Guidance is also available in the Health & Research Section of the GRCA website https://grca.org/about-the-breed/health-research/ and the AKC Canine Health Foundation has a detailed review available on the current state of genetic testing https://www.akcchf.org/educational-resources/library/articles/CANINE_GENETIC_TESTING_07-28-2020_FINAL_with-links.pdf

The Importance of CAER Exams

Yearly CAER eye examinations are critical to detecting cases of clinical PRA because *prcd*-PRA GR_PRA1 and GR_PRA2 are not the only cause of PRA in Golden Retrievers. Indeed, after each of these causes of PRA in Golden Retrievers had been identified, the genetic cause of ~9% of PRA cases in Golden Retrievers had not yet been identified. Guidelines from the American College of Veterinary Ophthalmologists on PRA are clear: "Breeding is not advised for any animal demonstrating bilaterally symmetric retinal

degeneration (considered to be PRA unless proven otherwise)”(6). In addition, there is no DNA test for some other very important eye diseases of Golden Retrievers, such as pigmentary uveitis, that can be identified in CAER examinations (7). Therefore, for Goldens that have ever been bred, breeders should continue yearly examinations throughout their lives, and the examination findings should be registered with OFA if the dogs are clear. Whether or not the owner chooses to register with OFA, if the CAER form is used, the frequency of eye diseases is recorded by ACVO. This does not disclose the identity of affected dogs unless owners chose to do so and enables GRCA to follow trends in eye disease in the breed. In addition, if dogs with clinically normal eyes are registered with OFA, breeders can check to be sure that ancestors of their puppies had clinically normal eyes into late adulthood.

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Figure 1

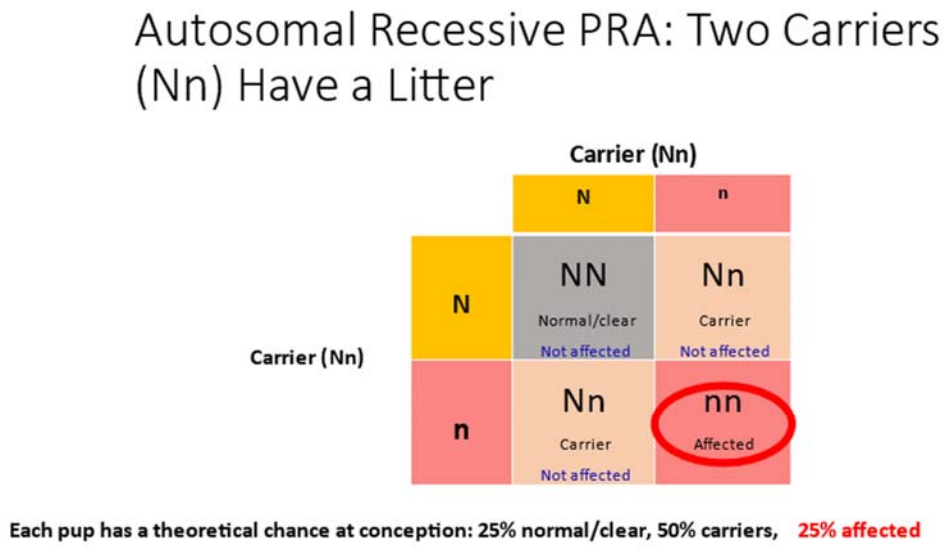

Figure 2