From the Health and Genetics Committee

Another Fatal Genetic Disease of Golden Retrievers: Hypertrophic Cardiomyopathy

In 2020, the Health and Genetics Committee wrote an article about fatal genetic diseases in Golden Retrievers. This 2025 update to that article follows the identification of another potentially fatal genetic disease, Golden Retriever hypertrophic cardiomyopathy (HCM).

Cardiomyopathy is a disease of heart muscle. The two major types of cardiomyopathy are dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM). In DCM, the heart muscle is stretched thin and does not pump blood well. In HCM, the heart muscle is thicker than normal and does not pump blood well. While heart failure can occur with both DCM and HCM, these are different diseases.

Golden Retriever HCM is a type of cardiomyopathy that can be caused by a recently described genetic mutation in cardiac troponin-1 (CTn1) in Golden Retrievers (Rivas et al, 2025). Troponin is part of a protein complex in cardiac muscle necessary for proper muscle function. In HCM, the heart muscle is abnormal and is thickened, particularly in the left ventricle. In humans, a similar point mutation in the comparable human gene has been implicated in human HCM cases (Cava et al, 2021). HCM in dogs often causes heart murmurs and exercise intolerance, and sudden death is possible (Schoeber et al, 2022). In the recently described Golden Retriever HCM, carriers of the mutation had no observable changes on echocardiograms even with detailed measurements, a finding consistent with this being an autosomal recessive disease. In all cases described, affected Golden Retrievers inherit a mutated CTn1 from each parent. Golden Retrievers that have one copy of the mutated CTn1 do not develop HCM but are carriers (Rivas et al, 2025). As with other autosomal recessive conditions, affected puppies can be avoided by following one very basic rule: Two carriers for the same recessive disease should not be bred to each other.

Genetic diversity within the breed is the major means for preventing genetic diseases where the genes that cause the disease are not yet described and/or a DNA test is not commercially available. DNA tests can prevent breeding carriers to each other when the DNA variant causing the disease has been described. A DNA test for Golden Retriever HCM is commercially available at NC State Veterinary Hospital https://hospital.cvm.ncsu.edu/services/small-animals/genetics/golden-retriever-hcm/. With the publication of the mutation causing HCM, it is likely the test will be available from additional laboratories soon. Prudent use of DNA testing also can help maintain genetic diversity by allowing carriers of autosomal recessive condition to be bred to normal clear dogs without risk of producing puppies affected with that condition. As we all adjust to another fatal genetic disease, it is important to remember that **1)** there are no known issues associated with breeding a carrier of an autosomal recessive condition to a normal/clear dog; **2)** that all dog carry some genetic conditions; and **3)** new (de novo) inheritable mutations occur in both dogs and humans and while most are benign some have major inheritable effects (Acuna-Hidalgo et al, 2016; Zhou et al, 2025). For these reasons we aren't ever going to eliminate all genetic diseases but prudent use of DNA testing enables us to avoid some bad crosses while maintaining genetic diversity.

Below is the summary information on the some of the other described fatal autosomal recessive diseases of Golden Retrievers and at the end of this article, we have included the take-away.

Neuronal Ceroid Lipofuscinosis (NCL) is an inherited fatal disease of Golden Retrievers. NCL came to the attention of Golden Retriever owners because of an affected Golden Retriever named Lexi and the efforts of Ron and Pat Rubrecht who diligently sought diagnoses for affected dogs and helped prevent future cases (Hubbs and Rubrecht, 2019). You can read the remarkable and courageous story of Lexi, her owner and breeders online http://grca.org/wp-content/uploads/2019/05/Hubbs-NCL5a2.pdf. Goldens with NCL are normal at birth but start to show signs of neurologic disease between one and two years of age (Meinman et al. 2022). NCL is progressive, fatal and some very successful Goldens are carriers of this disease. Additional information on Golden Retriever NCL is available at www.CanineGeneticDiseases.net/GoldenNCL/. Our hearts go out to the affected Goldens and their owners.

Hypomyelinating polyneuropathy (HPN) of Golden Retrievers was first described in 1989 in two Golden Retriever littermates. Recently, three different genetic causes for Golden Retriever HPN have been described. Golden Retriever HPN affects peripheral nerve myelin, the protective coating of nervous tissue. Affected Golden Retrievers developed neuromuscular weakness with multiple muscles affected (Cook et al, 2023). Before three years of age, all affected Golden Retrievers were euthanized due to this condition. Each of these dogs had mutations in genes associated with peripheral nerve disease in humans. One of these dogs had a heterozygous mutation in a gene known to cause a similar disease in humans – the mutation was considered likely to be de novo (new in that dog) and was not believed to be a concern for the breed. Two of the affected Goldens were unrelated to each other and had the same homozygous mutation in the MTMR2 gene, indicating autosomal recessive inheritance. Another affected Golden had a homozygous mutation in SH3TC2, also indicating autosomal recessive inheritance. DNA testing for Golden Retriever HPN is commercially

available from the veterinary genetics laboratory at UC Davis https://vgl.ucdavis.edu/test/congenital_hypomyelinating_polyneuropathy.

Congenital myasthenic syndrome (CMS) of Golden Retrievers was first described in four puppies from California in a paper published in 2020 (Tsai et al, 2020). All four puppies were related and had the same breeder. At least two of the affected puppies were the result of a dog being bred to his daughter. Three of the four puppies ended up being euthanized and the other was lost to follow-up.

Beginning at weaning age, CMS affected puppies display weakness and exercise intolerance. CMS is a diagnosis for a spectrum of conditions affecting the interaction of peripheral nerves and the muscles. In people, 32 different types of CMS have been described. Golden Retriever CMS is attributed to a recessive mutation in COLQ (collagen-like tail subunit of asymmetric acetylcholinesterase) inherited from each parent. This COLQ mutation has not been found in unrelated Golden Retrievers, dogs of other breeds or wild canids. However, CMS in Labrador Retrievers is caused by a different mutation in the COLQ gene (Rinz et al 2014. We know that it was not detected in the unrelated Golden Retrievers (<100) tested but it could easily exist in some other bloodlines. The UC Davis website indicates that the frequency of CMS in Golden Retrievers is currently being investigated. The Embark website indicates that the CMS mutation is very rare in Goldens, with >99% testing normal/clear for CMS https://embarkvet.com/resources/genetic-health-testing-for-golden-retrievers/.

Recessive diseases are most common when closely-related dogs are bred to each other. The original description of NCL in Golden Retrievers involved two litters of puppies resulting from the breeding of a sire and dam who each had the same mother (i.e. they were half-siblings) (Gilliam et al 2015). NCL became a problem for the breed as a whole due to the unintended selective use of some highly successful NCL carriers for breeding that increased the chance of two carriers being bred to each other. Similarly, Golden Retriever CMS was identified in puppies produced in inbred Golden Retrievers and the two affected Goldens with pedigrees available were from a father to daughter breeding (Tonomuro et al, 2015). In short, narrowing the gene pool whether intentional or not, increases the chance for autosomal recessive disease.

Golden Retriever HCM, HPN, CMS and NCL are not alone. There are other fatal genetic diseases lurking out there in the canine genome. A few have been discovered and more will undoubtedly be discovered. More than 150 genetic variants for diseases affecting dogs are known today and two in five dogs have at least one copy of one of those genes (Donner et al, 2018). The genes causing canine diseases are being described at an increasing rate. Many of the existing tests are for single gene disorders – diseases like NCL and CMS where that genetic change is usually sufficient by itself to cause disease (Gilliam et al, 2015). In the future, it is likely that DNA tests will be developed for DNA variants that interact with other genes, environmental factors and/or age to increase the risk for disease. These are multifactorial diseases where a single gene is not sufficient to cause the disease. Hemangiosarcoma may be among those diseases since a chromosomal region is associated with increased susceptibility, but no single gene has been implicated (Tonomura et al, 2015). In addition, there are diseases that are carried on the X chromosome and tend to be passed from the dam to her male offspring. Finally, there are diseases that are inherited only through direct maternal lineage – the mitochondrial disorders that are carried within the cytoplasm of the dam's eggs. In short, the number genes associated with diseases of Golden Retrievers and the number of DNA tests will continue to increase. The good news is that DNA testing may help guide breedings so that bad crosses are avoided. The key is to use the tests wisely – automatic exclusion of carriers should be avoided as that can affect genetic diversity which is the main protection from the multitude of genetic diseases whose genetic causes are not yet discovered.

A final word of caution – all tests have error rates. A correctly controlled DNA test is very accurate. However, quality control is crucial – an inaccurate DNA test can cause a lot of problems for a breeder. Errors can happen at any stage – collection of the DNA, conduct of the test and reporting of the findings. In humans, direct-to-consumer raw genetic testing is available for a large number of ancestry or health-related conditions. In one report, 40% of the health-related positive tests on the raw direct-to-consumer test results were found to be false positive (the test indicated that the mutation was present when it was not) by subsequent more carefully controlled medical DNA testing (Tandy-Connor et al, 2018). In short, the quality of DNA testing matters. In addition, DNA mutations that cause disease in one breed will not always cause disease in a different breed (Moses et al, 2018). As a result, an international effort summarized online by the Harmonization of Genetic Testing in Dogs (HGTD) https://dogwellnet.com/ctp/, was recently established to provide an international database on the testing laboratories, the genetic tests, and each breed's DNA test. These are early days in the process of providing public information but owners should remember that the quality is more important than the cost of a DNA test.

The Take-Away:

- Prudent use of DNA testing can prevent disease in Golden Retrievers.
- NCL testing is extremely important for Golden Retriever breeding dogs.
- DNA testing is only helpful when a high-quality testing laboratory conducts the test.

- DNA testing for diseases that do not affect Golden Retrievers is not recommended because genetic background (breed) influences the effect of a DNA variant.
- Many new DNA tests are anticipated in the future and all Golden Retrievers likely carry some potentially harmful recessive mutations.
- Automatic exclusion of carriers from breeding based on carrier status for recessive genes is not recommended; genetic diversity is important for breed preservation.
- Two carriers for the same fatal recessive disease should not be bred to each other.

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