

## Neuronal Degeneration in Great Pyrenees: Genetics and Breeding Decisions

Research conducted at the College of Veterinary Medicine, University of Minnesota.

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For those of you who were unable to attend the Health Committee's talk at the 2017 National Specialty on April 13<sup>th</sup>, Dr. Ekenstedt's slides are provided, and a brief summary below captures the most important points.

A newly recognized nervous system disorder, characterized by widespread degeneration in the central nervous system (brain and spinal cord) has surfaced in the Great Pyrenees breed. It has been named 'Neuronal Degeneration', or NDG. Affected dogs have ataxia – such as difficulty walking on slippery surfaces – from a very young age. NDG is slowly progressive over several years, and will eventually lead to the dog not being able to walk at all.

Dr. Ekenstedt's talk discussed how breeders jumped into action to discover the genetic cause of this disease; they did all the right things to solve this puzzle quickly, including rallying owners of affected dogs and related dogs to submit samples for DNA. The talk included discussion of the fact that **all** dogs (and all people, and all mammals!) have mutations (typically at least a dozen) "lurking" in their genomes, particularly recessive mutations just like NDG. The way NDG was dealt with is a perfect model for how to cope with these situations when they arise (and they will, in any breed of dog). Rather than use denial or blaming tactics, the best way to solve these problems when they arise, is to be transparent, since they can (and will!) happen to anyone. The only way to avoid recessive diseases with any success is to breed dogs together that do not share any ancestors at all...and we know this is nearly impossible to do within today's purebred dogs.

The talk included discussion about the genetic tools that are now available for dogs which cover the entire canine genome, and can rapidly test multiple dogs simultaneously (called "SNP arrays"). Using these tools on the samples we obtained (cases and their unaffected relatives), we were able to rapidly identify the area of the genome that is associated with NDG. From there, we were a little lucky, because there was a perfect candidate gene within the region that causes the nearly-identical disease in humans when it is mutated! We sequenced this gene in the affected dogs and were able to identify a four letter deletion. Case/affected dogs have two copies of this deletion, whereas normal dogs can have no copies of the deletion or one copy of the deletion (totally normal dog, but a carrier of the deletion that can pass it on to offspring). The University of Minnesota Canine Genetics Laboratory now offers this genetic test to Great Pyrenees breeders and owners to aid diagnosis and to guide breeding decisions.

The most important take-home point from the talk is which breedings are okay in terms of NDG. It is VITAL to consider the health of the entire breed population when making these choices! Obviously you should avoid any breedings that produce affected puppies (for example, breeding two carriers to each other). But it is unnecessary – and actually HARMFUL to the breed - to eliminate all carriers from the gene pool! The carrier rate is somewhere around 12% (perhaps a little lower), and eliminating 10-12% of the gene pool is only going to create new genetic bottlenecks (in other words – new problems!). Every dog has ~20,000 genes, and you do not want to throw out a dog with 19,999 great genes that just happens to be a carrier at one of them (in this case, NDG, which we can actually test for!). It is recommended that great dogs who

happen to be carriers should be bred in order to retain all their other great genes – just breed them to a clear dog, so you don't produce any affected puppies. All the puppies will either be clear or carriers – test the litter so you know who's who. Then, slowly, over time (you do NOT need to do it in one generation!), replace the breeding stock with the clear dogs. If the first and even the second time around the best dog in the litter happens to be a carrier, fine, keep them and breed them to another clear dog. Eventually the best dog will also be a clear dog. This approach slowly removes the mutated version of the gene from the Great Pyrenees breed without causing any catastrophic new problems. In summary: keep great carrier dogs in the gene pool, breed them to clear dogs, test the puppies, and slowly, over several generations, replace carriers with (great) clear dogs.

For more information, see our laboratory's website:

<https://www.vetmed.umn.edu/departments/veterinary-and-biomedical-sciences/research/canine-genetics-lab>

Here is the link specifically to the NDG page:

<https://www.vetmed.umn.edu/departments/veterinary-and-biomedical-sciences/research/canine-genetics-lab/genetic-testing/neuronal-degeneration>

Finally, we are always happy to answer any questions you might have about NDG. Email us at: [ndginfo@umn.edu](mailto:ndginfo@umn.edu).