What is Degenerative Myelopathy?

Degenerative myelopathy (DM) is an insidious, progressive disease that results in destruction of tissue within the spinal cord, usually in middle aged or older dogs. Since one of the most important functions of the spinal cord is to conduct signals from the brain to the nerves controlling the hind limbs, the principal clinical feature (visible symptom) of degenerative myelopathy is poor control over hindlimb function. Dogs with degenerative myelopathy show a lack of coordination in both hind limbs, together with a degree of muscle weakness. Commonly these dogs will knuckle over on both paws, cross hind limbs (especially when turning in tight circles) and swing hind limbs wide or take abnormally long strides. Diagnosis of the disease requires magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) tap to exclude other common spinal cord disorders such as intervertebral disc extrusion (slipped discs). There is currently no available cure for DM. The disease inevitably progresses over a variable period of time – anywhere from 6 months to 3 years. Ultimately, affected dogs lose the ability to walk in both hind limbs. At this point, most owners elect for euthanasia.

A New Problem in Chesapeake Bay Retrievers?

Veterinary neurologists are familiar with DM because it is a common problem in German Shepherd dogs. From time to time sporadic cases have also been seen in other breeds. However, we are now seeing a growing number of Chesapeake Bay Retrievers with the condition. Knowing that this disease is strongly associated with particular breeds, it is possible that DM has a strong genetic component in CBRs as well. As yet we do not understand the cause; meaning, we do not have enough data to ascertain whether the problem is due to a defect within a single gene or defects in multiple genes acting in concert. More data and pedigrees need to be collected from dogs affected with DM to ascertain whether the problem is worth investigating further to try and locate a genetic component in the CBR breed.

Trying to Eliminate the Disease

As a result of these concerns, the School of Veterinary Medicine at the University of Pennsylvania, in association with the ACC Health Committee and the ACC Charitable Trust has initiated a project that will try to establish the underlying genetic defect responsible for the condition. Importantly, once the gene (or genes) involved are known, a simple blood test may be developed that can be used in any individual to diagnose the condition and to identify those dogs that are potentially carriers of the gene(s) involved. In this way it should be possible to remove dogs with the defect from the breeding population if necessary.
**How Will the Project Work?**

This project has been broken down into phases in order to prioritize the initial needs of the project. Phase 1 of the project will survey the number of diagnosed cases or potential cases of DM that have been seen in the CBR breed, and collect samples and pedigrees only from those affected dogs. If there are enough cases to warrant further investigation (as judged by the ACC Health Committee along with our colleagues at U-Penn), then Phase 2 will be to collect blood samples from both affected and unaffected dogs. In Phase 3, DNA from both affected and non-affected dogs will be sequenced to identify the culprit gene(s) underlying the condition and develop a diagnostic test to identify other affected dogs and carriers.

During Phase 1, the ACC Health Committee highly encourages collection of DNA samples on any and all dogs that have a definitive diagnosis of DM. This will help us identify and document cases of DM within the breed. Obtaining DNA is simple – a small amount of blood is taken from the dog, from which the DNA can later be extracted and sequenced. Since other diseases can mimic DM, it is important that owners with affected dogs have a definitive diagnosis made – either following MRI study including CSF collection (through a referral center), or by having a post-mortem examination performed once a dog is euthanized. Only dogs that have a definitive diagnosis made can ultimately be included in Phase 3 of the study. In order for the project to succeed, we need to get information on as many affected dogs as possible. Thus, in Phase 1 of the study our aim will be to collect as many samples and pedigrees as possible from affected dogs. If you have a dog with DM, and are interested in participating in the study please contact us so that we can send you appropriate information on what is needed to participate. If you have a dog that you think may have DM, feel free to contact us if you need more information on how to get a definitive diagnosis for him/her.

After Phase 1 is over, the ACC Health Committee will evaluate whether there is significant interest in the Chesapeake Bay Retriever community to proceed with Phases 2 & 3 of the study. This evaluation will include reviewing information on whether there are a significant number of positively identified or potentially DM affected dogs in the gene pool. If Phase 1 shows that it is in the best interest of the breed to continue investigating this disease in CBRs, then we will proceed to Phases 2 & 3 of this study. Phases 2 & 3 would include collecting DNA samples on affected dogs, their relatives, and unrelated dogs, in order to gather enough data to accurately study a genetic component of this disease in the CBR breed.
How is Genetic Testing Done?

Traditional methods used to identify the genes underlying particular diseases involve pedigree analysis – analyzing the pedigrees of as many affected and non-affected littermates as possible in an attempt to establish the mode of inheritance underlying the disease. Once this has been done, however, identifying the gene involved still relies on ‘trial and error’ – looking at a large number of suspect genes and sequencing each to find a possible mutation that causes the genetic defect. This is particularly slow, and may not identify the culprit gene. However, since the recent completion of the canine genome project, it is now possible to search for defective genes in a particular population using what are known as ‘Single Nucleotide Polymorphisms’ or SNiPs for short. Using this method, DNA from affected and non-affected dogs is sequenced, and areas of chromosomes that are associated with inheritance of the disease can be tracked over time. This then allows us to ‘home in’ on the region of the chromosome of interest and start hunting for particular genes in that area.

How Does Confidentiality Work in a Genetics Study?

Although it is crucial to the success of this study to involve pedigree collection along with the DNA sample collection, this information will be kept strictly private (as indicated by initialing a confidentiality statement when submitting the DNA sample). Because Phase 2 & Phase 3 of this study require samples from both affected dogs and their relatives to be examined, those members of the ACC Health Committee closest to the study and researchers at U-Penn will need to keep track of the samples/pedigrees. It goes without saying that any breeder with an affected dog is likely to be concerned at the implications for their breeding program. Again, for this reason no dog names will be made public at any stage of the project, unless owners specifically request this on the sample collection sheet. It is also to be remembered that any affected dog has inherited the culprit gene(s) almost certainly from an ancestor several generations ago, and that the culprit gene(s) is/are now widespread within the breed. If you have an affected dog, you are not alone, and there will be other breeders and owners with affected dogs too.

What do I do if I think I have a dog with DM?

For this project, we have identified a list of people who will be the first port of call for owners who think they have a dog with DM. First, if at all possible, try to obtain video footage of your dog doing the following:

1) walking towards and away from the camera on a leash in a straight line;
2) walking from left to right in a straight line in front of the camera
3) walking on a leash in a tight circle, first to the left and then to the right;
4) walking on a leash up and down stairs;
5) walking over an obstacle (eg a small box that has to be stepped over).
What do I do if I think I have a dog with DM? (cont.)

Secondly, it is important to get advice from one of the contacts listed below. If your dog may have DM, ideally a diagnosis should be made following referral to a veterinary neurologist. Alternatively, if you are sure your dog has DM and you decide to have it euthanized, please request a post mortem exam from your own vet to confirm the diagnosis. Most importantly, if you wish your dog to be part of the project, you will need to have blood collected by a veterinarian, and sent, together with a copy of the pedigree and a filled-out collection form to our colleagues at the University Of Pennsylvania College Of Veterinary Medicine. These forms and addresses can be obtained by calling one of the Health Committee contacts listed below. Alternatively, you will also be able to find this contact information and forms for samples by visiting the ACC website health page at:

http://www.amchessieclub.org/health.html

Contacts:

If you have any questions, need the forms to fill out, or you think you may have a dog with DM, please contact:

Dr Briedi Gillespie, 509-335-2819
Or e-mail Dr. Gillespie at: btreece@vetmed.wsu.edu

Most importantly, as a group, we can beat this debilitating disease, but only if we all work together.