Canine Degenerative Myelopathy

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In 1973, Dr. Averill first described a degenerative disease of unknown cause affecting the spinal cord in the older German Shepherd Dog. Degenerative (progressive) myelopathy (disease of the spinal cord) is a disease of the spinal cord causing progressive weakness in the hind limbs. Though most commonly reported in German Shepherd Dogs, high disease prevalence also exists in other breeds, such as Cardigan and Pembroke Welsh Corgis, Rhodesian Ridgebacks, Chesapeake Bay Retrievers and Boxers. While the cause has been unknown, an increasing number of cases reported in families of pure bred dogs have raised concerns for an underlying genetic predisposition.

What is degenerative myelopathy?

Degenerative myelopathy is a progressive disease of the spinal cord in older dogs. The disease has an insidious onset typically between 8 and 14 years of age. It begins with a loss of coordination (ataxia) in the hind limbs. The affected dog will wobble when walking, knuckle over or drag the feet. This can first occur in one hind limb and then affect the other. As the disease progresses, the limbs become weak and the dog begins to buckle and has difficulty standing. The weakness gets progressively worse until the dog is unable to walk. The clinical course can range from 6 months to 1 year before dogs become paraplegic. If signs progress for a longer period of time, loss of urinary and fecal continence may occur and eventually weakness will develop in the front limbs and flaccid paralysis in all limbs. Another key feature of DM is that it is not a painful disease.

We do know that the disease begins with the spinal cord in the thoracic (chest) region. If we look under the microscope at that area of the cord from a dog that has died from DM, we see degeneration of the white matter of the spinal cord. The white matter contains fibers that transmit movement commands from the brain to the limbs and sensory information from the limbs to the brain. This degeneration consists of both demyelination (stripping away the insulation of these fibers) and axonal loss (loss of the actual fibers), and interferes with the communication between the brain and limbs.

How is degenerative myelopathy diagnosed?

Degenerative myelopathy has been a diagnosis of elimination. We look for other causes of the weakness using diagnostic tests like myelography and MRI. When we have ruled them out, we end up with a presumptive diagnosis of DM. The only way to confirm the diagnosis is to examine the spinal cord under the microscope when a necropsy (autopsy) is performed. There are characteristic degenerative changes in the spinal cord typical for DM and not some other spinal cord disease.

What else can look like degenerative myelopathy?

Any disease that affects the dog's spinal cord can cause similar signs of loss of coordination and weakness. Since many of these diseases can be treated effectively, it is important to pursue the necessary tests to be sure that the dog doesn't have one of these diseases. The most common cause of hind limb weakness is herniated intervertebral disks. When herniated, disks can cause pressure on the spinal cord and weakness or paralysis. Short-legged, long back dogs are prone to slipped disks. A herniated disk can usually be detected with X-rays of the spine and myelogram or by using more advanced imaging such as CT scan or MRI. Other diseases we should consider include tumors, cysts, infections, injuries and stroke. If necessary, your veterinarian can refer you to a board certified neurologist who can aid in diagnosing degenerative myelopathy. A directory to a neurologist near you can be found at www.acvim.org under the *"Find a specialist near you"* link.

How do we treat degenerative myelopathy?

There are no treatments that have been clearly shown to stop or slow progression of DM. Although there are a number of approaches that have been tried or recommended on the internet, no scientific evidence exists that they work. The outlook for a dog with DM is still grave. Efforts are being made to improve quality of life such as good nursing care, physical rehabilitation, pressure sore prevention, monitoring for urinary infections, and ways to increase mobility through use of harnesses and carts.

What is the cause of degenerative myelopathy?

We feel that genetics play an important role in the disease since it is common in certain breeds of dogs and follows stereotyped pattern with age of onset and clinical signs. With the completion of the first draft of the canine gene map, we have used that map to find the gene(s) responsible for DM. ***Drs. Joan Coates and Gary Johnson at the Animal Molecular Genetics Laboratory of the University of Missouri and Drs. Claire Wade and Kerstin Lindblad-Toh at the Broad Institute of MIT/Harvard and their colleagues have identified a DNA mutation that is a major risk factor for development of DM in dogs***. The mutation found in the superoxide dismutase 1 (SOD1) gene has similarities to some forms of ALS (Lou

Gehrig's disease) in people. We call this a risk factor because not all dogs that are homozygous for the mutation will get the disease. We are doing additional mapping studies to determine why that is. Thus, we describe the inheritance pattern as autosomal recessive with incomplete penetrance. Dogs must have 2 copies of the mutation to be at risk for developing DM.

How do we interpret the genetic test?

A DNA test based on the *SOD1* mutation is commercially available (www.caninegeneticdiseases.net or www.offa.org/dnatesting/). The dogs homozygous for the mutation are *at-risk* for developing DM and will contribute one chromosome with the mutant allele to all of their offspring. The heterozygotes are DM carriers that are unlikely to or rarely will develop clinical DM but could pass on a chromosome with the mutant allele to half of their offspring. The normal homozygotes are unlikely to develop DM and will provide all of their offspring with a protective normal allele. The DM-associated SOD1:c.118A allele has been detected in at least 100 different dog breeds (manuscript in preparation). It remains to be seen whether or not mutant homozygotes are at risk of developing DM on all of these different genetic backgrounds. Additionally, it will be important to continue the histopathologic examination of spinal cords from DM suspects of various breeds to confirm the diagnosis and identify breeds that are susceptible to DM.

The "A" allele is very common in some breeds. An overly aggressive breeding program to eliminate the dogs testing A/A or A/G might be devastating to the breed as a whole because it would eliminate a large fraction of the high quality dogs that would otherwise contribute desirable qualities to the breed. Thus, a realistic approach when considering which dogs to select for breeding would be to consider dogs with the A/A or A/G test result to have a fault, just as a poor top-line or imperfect gait would be considered faults. Dogs that test A/A (AT RISK) should be considered to have a worse fault than those that test A/G. Dog breeders could then continue to do what conscientious breeders have always done: make their selections for breeding stock in light of all of the dogs' good points and all of the dogs' faults. Using this approach over many generations should substantially reduce the prevalence of DM while continuing to maintain or improve those qualities that have contributed to the various dog breeds.

How can I help?

If you have a dog that might be affected, please visit our website, www.caninegeneticdiseases.net or contact us directly (Ms. Liz Hansen - HansenL@missouri.edu or Dr. Joan Coates – CoatesJ@missouri.edu). We can help you in determining whether or not your dog is affected. In return, we would ask your help in collecting the samples and information necessary to continue understanding the genetic cause of this disease. Your ongoing support will be necessary to achieve our goal.