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Update on Canine Degenerative Myelopathy

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Historically, in veterinary medicine, the clinical diagnosis of canine degenerative myelopathy was a diagnosis of exclusion – if the symptoms were consistent with Degenerative Myelopathy and spinal imaging, and CSF were normal, DM was considered the most likely diagnosis. There was, however, no confirmatory test.

In the past three years we have fortunately seen real breakthroughs in our understanding of this all-too-common disease. At long last, we are able to make a near-certain diagnosis of the disease ante mortem. Although there is

still no effective treatment for DM, the magnitude of the recent advance in diagnosis cannot be over-emphasized. Without an understanding of the cause of a disease, proposed treatments are at best an educated guess.

Understanding the Cause:

Why was the cause of DM such a mystery for many years? Some of that answer relates to science and some to logistics. Pathologically, DM is characterized by symmetrical loss of both myelin and axons in the thoracolumbar spinal cord without any signs of inflammation. Coupled with the knowledge that the disease is slowly progressive, nutritional, toxic or genetic etiologies would be most likely. Equine DM is in part a nutritional disease, but nutrition in dogs with DM didn't seem to be any different than dogs without DM. Toxin seemed plausible, but none could ever be identified. Some postulated the disease was immune-mediated despite the lack of inflammation in path samples, but the lack of response to prednisone and other immunomodulatory medications made this unlikely. That left a genetic etiology on the table. In some ways, this theory made sense – the disease was seen most characteristically in certain breeds of dogs – German shepherds, collies, and boxers, Chesapeake Bay retrievers. The onset of disease in middle aged to older dogs was an argument against a genetic cause.

Logistically, DM was a hard disease to study as well. The diagnosis relied upon histopathology of the thoracolumbar spinal cord. Removing the TL spinal cord from a dog post-mortem is a very time-consuming process. It also did not help that dogs typically would not be euthanized until months to even years after the diagnosis was made. Maybe if the dog was diagnosed at a university teaching hospital and died in-hospital, pet owners would have been happy to allow a necropsy and the removal of the cord for study. Months later, when the dog's time had finally come, most owners did not enthusiastically volunteer to bundle their non-ambulatory 90 pound dog into the car for a three-hour drive to the university for euthanasia and necropsy.

DM sat was a problem waiting for an answer, when slowly things started to change in the world of veterinary neurology. More neurologists became available in private practices, which meant many dogs with DM were now located physically closer to their neurologist, making it harder for them to be lost to follow-up. When the time came to euthanize the dog, not only was it more likely the dog would be near its neurologist, but also that the neurologist was equipped to actually remove the spinal cord post-mortem.

At the same time, on a scientific level, molecular genetics was advancing by leaps and bounds. The University of Missouri College of Veterinary Medicine decided to make a big push to study genetic diseases of animals.

SOD2: Shortly thereafter, a young veterinary neurologist, Joan Coates, joined Missouri's faculty and she decided to tackle the DM question. She assembled a team of researchers in clinical neurology, neuropathology and genetics, invited all veterinary neurologists to participate in her project, and spent years communicating with breed organizations, breeders and individual pet owners. Eventually, she had enough DNA samples from dogs with histopathologically confirmed DM to start her genetic studies. She discovered that dogs with DM have a mutation in a gene known as SOD2.

Would a mutation in the SOD1 gene make sense for dogs with DM? Yes, absolutely. "SOD1" stands for superoxide dismutase 1.This is a gene responsible for repairing oxidative damage to cells. What types of cells are most likely to be affected by oxidative damage? Any cell containing a high amount of lipid. Myelin has high lipid content. Myelin-rich white matter in the nervous system would be expected to be one of the most sensitive tissues in the body to oxidative damage ¬¬– the exact pathology seen in dogs with DM.

It would even make sense that DM doesn't manifest until later in life, as it would take many years to accumulate enough oxidative damage to become symptomatic. It explains why dogs with DM don't respond to treatment ¬– by the time they show symptoms, the damage is already done.

Finally, Dr. Coates checked to see if there were any known diseases in other species caused by mutation of the SOD1 gene. It turned out that there is a human disease caused by SOD1 mutation – a rare spinal cord variant of Lou Gehrig's disease – and has similar symptoms and clinical course to canine DM. Everything started to make sense – DM is the result of inheriting two bad copies of the SOD1 gene. Since this discovery in 2010, many dogs that tested positive for DM have since passed away and dozens of these have been necropsied. Only one has turned out to not have DM, supporting the validity of the test.

Degenerative Myelopathy Testing:

Genetic testing for DM is now available through the Animal Molecular Genetics Laboratory at the University of Missouri. Either blood samples or

cheek swabs may be submitted. The cheek swabs are a little cheaper, but the blood samples contain much more DNA. DNA is banked by the lab when blood samples are submitted but not with cheek swabs. Therefore blood samples are preferred whenever possible, as they contribute to the overall study of the disease. A sample submission form and instructions are attached. Interpreting a DM test is straightforward if you understand what the test tells you. Two bad copies of the gene means the dog will likely develop the disease during its natural lifespan.

Other causes of a TL myelopathy could be present, so ideally spinal MRI +/- spinal tap are necessary to exclude other diseases. On practical grounds, most pet owners would be reluctant to perform spinal surgery on a DM positive dog, so the gene test alone may make sense for a lot of patients.

Finding a Cure:

The next step in DM research is to look for a cure. The best hope will be to start treatment before a dog is symptomatic, so eventually early testing of dogs of affected breeds may be recommended. Dr. Coates is collaborating on clinical trials to treat the human form of DM and hopefully some of this work will spill over into veterinary medicine soon.

Prognosis:

Current management recommendations for DM center around maintaining a sufficient degree of physical fitness to allow dogs to better compensate for their neurologic impairment. We typically recommend a formal physical rehabilitation program with a veterinarian whose practice is dedicated to rehabilitation. This currently seems to be the biggest factor in keeping these dogs functional for as long as possible, and most rehab vets are experts at managing and recommending various assistive devices such as slings, booties and carts as needed. It is also important to micromanage the dog's overall health and stress levels, as it seems periods of physiological or psychological stress are accompanied by decline (often transient) in neurologic function in dogs with DM. It seems to be very easy to upset the apple cart in DM dogs. Antioxidant therapy and good nutritional support may be helpful in these patients, but may actually be the least important factor in affected patients.

Antioxidants Used in the Management of DM

Vitamin E:	**1000-2000 IU per day**
Vitamin C:	**1000-2000 mg per day**
B-complex:	**High potency 2 capsules per day or stress formulation 1 capsule per day**
Selenium:	**100 (small dog) to 200 (large dog) ug/day. Excessive doses are toxic.**
Aminocaproic Acid:	**250 mg/mL suspension, mix 2 ml with 1 ml chicken broth and give q8h**

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- See more at: http://www.asgvets.com/canine-degenerative-myelopathy/#sthash.Ua6scFI8.dpuf

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