# ABCF MESSENGER

Official Newsletter of the American Boxer Charitable Foundation, Inc.
Virginia Zurflieh, Editor



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***From the editor**: This issue of the Messenger features updates from Dr Joan Coates on DM and Dr Kate Meurs on ARVC. Dr Coates' update includes the latest statistics on the prevalence of the DM mutation in the boxer breed -- **72%!** -- plus links to further information. For those who missed the "live" presentation, a link to a recording of Dr Meurs' Oct 19 "webinar" appears just above her report.*

*The final entry in this issue is a memorial to the late Anna Rosenstreich of Hexenhaus Boxers in New Zealand and Western Australia, whose family paid tribute to their beloved mother's 'Life with Boxers' by making a generous donation to the ABCF Memorial Endowment Fund. Our heartfelt thanks go to Daniela, Gabi, Michael and Silvia.*

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## Canine Degenerative Myelopathy


Joan R. Coates DVM, MS, Diplomate ACVIM (Neurology)
Associate Professor Veterinary Neurology and Neurosurgery
University of Missouri, College of Veterinary Medicine


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.

**Results on genetic testing for the Boxer breed so far…**

As of 10/1/2010, we have tested 1987 Boxers. The genotype total includes 251 clears (12.6%), 608 carriers (30.6%), and 1128 (57%) AT RISK. The allelic frequency takes into account the number of chromosomes with the mutation. **The allelic frequency is 72% in the population of Boxers tested.**

**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. We are in great need of spinal cord tissue samples from older (> 10 years) UNAFFECTED dogs. These samples will help us compare the abnormalities seen in the spinal cord of DM dogs. We have a kit available to help with tissue collections. Your ongoing support will be necessary to achieve our goal.

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*This update from Dr Kate Meurs was originally published to the Showboxer-L email list, and was prefaced by an emotional plea to Boxer owners to use the ARVC-1 test in conjunction with Holter testing to obtain the most comprehensive test results. For those who missed Dr Meurs' live "webinar" on October 19, a recording will be available on the WSU website (*http://www.vetmed.wsu.edu/deptsVCGL/index.aspx*) within a week or so. During the online seminar, Dr Meurs responded to a number of interesting and sometimes provocative questions about ARVC and the ARVC-1 test; and provided an excellent explanation, illustrated with slides, of why it is of the utmost importance to have your Boxer's Holter report (cassette or digital) read by a cardiologist, not just a computer.*

## Update on Boxer Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

Dr Kathryn M. Meurs, DVM, PhD, Diplomate ACVIM (cardiology)
meurs@vetmed.wsu.edu

Boxer ARVC is an adult onset heart muscle disease that can lead to sudden death or the development of congestive heart failure where the dog starts to cough or becomes short of breath.

**o** This is an inherited disease, but it is adult onset. The average age where the clinical signs may be observed or a Holter monitor becomes abnormal is 6 years of age. However, this is widely variant. Some dogs will show it younger and some, not until they are much older!

**o** This is a disease that primarily affects the electrical system of the heart so the best way to detect the abnormal electrical system is a 24 hour Holter monitor (cassette or digital). Since the disease is adult

onset and can start at varying ages, we recommend that Holtering be started at 3 years of age and repeated ANNUALLY. A single Holter reading that is normal at one point in the dog's life does not mean that it can never have ARVC. It simply means that it does not at this time.

**o** Findings on the Holter that suggest a diagnosis of ARVC are ventricular premature complexes (VPCs).

**o** HOWEVER, the identification of VPCs does not mean that ARVC has been diagnosed. There are many other things that can cause VPCs in dogs including inflammation of the heart muscle from certain viruses (parvovirus, etc), other parasites (Chagas), and tumors, including tumors in other body organs. Particularly if a Boxer is less than 3 years of age with VPCs it is less likely that his VPCS are due to ARVC.

**o** We have identified a genetic deletion for a gene that functions by holding cardiac cells together. This is very similar to what is known about the disease in human beings and much of what we know about the disease in humans may be applicable to the dog.

**o** In humans there are 8 different genes that can cause the development of ARVC. Each one, all by itself can lead to the development of ARVC. Therefore, it is very likely that there is more than one mutation in the Boxer dog that may lead to the disease in some lines of dogs. This does not mean that testing for the one known one is useless since it does give you some information to plan your line around, it just means there may be more than one.

**o** ARVC is a disease of variable penetrance. This means that some individuals with the genetic mutation will not show the disease until they get older and that some individuals with the mutation will NEVER show the disease. In humans there are cases of IDENTICAL TWINS with the mutation where one twin develops severe heart disease and one does not. This suggests that although the mutation affects the heart, it may require certain environmental or other genetic factors to develop the severe form of the disease. We may or may not soon understand these other factors in the dog. They have not been identified in people yet. We hope to soon start a study to look at some potential factors. I may be contacting some of you to ask if you would be willing to participate.

**o** In our study we found that dogs that were homozygous for the mutation (2 copies of the abnormal gene) had a more severe form of the disease based on Holter findings (more VPCs)--and NEW INFORMATION --are more likely to develop a weak heart muscle and heart failure. This DOES NOT mean that they develop it earlier (this does not mean they will always get it but are more likely to be severe).

Genetic diseases, particularly cardiac, are complex. Not all dogs with VPCs have ARVC and not all dogs with the mutation will show the clinical signs of ARVC.

Therefore, as with any genetic information, we recommend ALWAYS using test results to guide educated decisions about breeding. Do not make drastic decisions. The field of canine genetics is very new and the field of cardiac genetics is very complex. We are still learning how to best use these tools.

Here are some recommendations for testing:

Dogs that are positive for the test will not necessarily develop significant heart disease and die from the disease. Some dogs will develop a very mild form of the disease and will live quite comfortably, some may need treatment.

Removal of a significant number of dogs from the breeding population could be very bad for the Boxer dog breed. Remember that dogs that carry this mutation also carry other important good genes that we do

not want to lose from the breed.

**o** Positive Heterozygous (1 copy of the mutated gene and 1 copy of a normal gene) Dogs that are positive heterozygous should be carefully evaluated for signs of disease (Holter monitor and possibly an echocardiogram). If an arrhythmia (VPCs) is detected, possible treatment options should be discussed with your veterinarian. Adult dogs that do not show signs of disease and that have other positive attributes could be bred to mutation negative dogs. Puppies may be screened for the mutation and over a few generations, mutation negative puppies may be selected to replace the mutation positive parent and gradually decrease the number of mutation positive dogs in the population.

**o** Positive Homozygous (2 copies of the mutated gene) I recommend not breeding the homozygous dogs UNLESS they are exceptional members of the Boxer community and we need to be sure to maintain their positive attributes in the breed. Dogs that are homozygous for the mutation appear to have more significant disease and will certainly pass on the mutation. Therefore they should only be bred to a negative dog and over 2 generations of negative crosses a negative puppy could be selected as a replacement.

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## *Anna Rosenstreich, Hexenhaus Boxers*

In 2009, I received an email from Daniela Rosenstreich informing me that her mother, Anna Rosenstreich of Hexenhaus Boxers, New Zealand and Western Australia, had passed away shortly after being diagnosed with cancer. Daniela and her siblings wanted to make a significant donation to the Foundation as a tribute to their beloved mother who devoted a good deal of her life to our breed.

In response to my query, Daniela gathered an “album” of pictures (a painful trip down memory lane as can be imagined) and wrote a brief biography of Anna’s life with her Boxers. Please celebrate the life of this remarkable woman who loved, trained, cared for and developed her kennel “down under.”

We are honored that her family members Daniela, Gabi, Michael and Silvia chose to remember her by making significant donations to the American Boxer Charitable Foundation Memorial Endowment so that we may further our research to benefit our Boxers.

*Sharon Fosseen, Treasurer*
*American Boxer Charitable Foundation*

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*Biography and picture album* (http://tinyurl.com/hexenhausboxers ) *prepared by Daniela Rosenstreich to celebrate some of Anna’s achievements from her start in Boxers in 1972 through to her death in 2008.*

## Anna Rosenstreich, Hexenhaus Boxers

Anna Rosenstreich passed away on 3rd October 2008 after a brief battle with cancer. Anna had been breeding and showing Boxers since the early 1970s under the 'Hexenhaus' prefix, first in New Zealand, and then Western Australia.

Anna showing Ch Sigfrid vom Hexenhaus

Anna should be remembered for what she achieved with her boxers in a variety of arenas. From the start Anna focused on temperament and working ability and her boxers competed in obedience, utility, and tracking trials in New Zealand – it was (and still is) a relatively rare thing to see a Boxer in these events.

What made the Hexenhaus Boxers extra special was that the boxers Anna trialed in the highest level of obedience competition in New Zealand also carried conformation titles and Specialty in Show awards. Anna also helped others to be able to learn to work with their dogs – she was involved in obedience club administration and instructing for decades and is still fondly remembered at the Otago Canine Training Club. After the move to rural Western Australia it was harder for Anna to be involved in working events, but she continued to train and compete in local obedience club events.

Anna with granddaughter Isobel

Anna achieved great success as a breeder, with her home bred boxers doing very well in the conformation ring – both those she kept and showed herself, and those owned by others. Hexenhaus boxers appear in many other Boxer lines and Anna helped several breeders to get their start in the breed.

In her breeding program Anna stayed true to her idea of correct conformation and ignored passing fashions or convenient shortcuts. This meant the quality of her boxers was not always recognized by local all-breeds judges, but she had great success under international specialist judges, achieving Best in Specialty Show wins with several different home-bred Hexenhaus boxers over the years.

Anna with young Ch Fria vom Hexenhaus & Fausta vom Hexenhaus

However, Anna's dogs were never 'just' show or performance dogs. They were 100% part of her family. The love Anna had for boxers is probably best reflected in the fact that she seemed to value the photos and phone calls from happy puppy owners more than the show trophies that littered her home.

Given her devotion to the boxer breed, the Rosenstreich family chose to honour her memory with several bequests and memorial trophies, one of which was a major donation to the ABCF. Anna would have appreciated the fact that she will be able to continue to enhance the quality of life of Boxers for many years, thanks to the research the bequest will support.