

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

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.

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!

This is a disease that primarily affects the electrical system of the heart so the best way to test for it is a 24 hour Holter monitor. 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.

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

HOWEVER, the identification of VPCs do 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), 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.

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

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. There are 141 DIFFERENT mutations in these 8 genes. 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.

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. They have not been identified in people yet.

Our results in the boxer also suggest that multiple genes could work together to impact the severity of the disease in the dog. We hope to soon understand about these other factors in the dog.

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. This DOES NOT mean that they develop it earlier, it means that when they do develop the VPCs they tend to have more of them.

So far we have tested 1690 dogs, 53% were negative, 41% were positive heterozygotes and 6% were positive homozygotes. Only 80 Holter monitor readings were submitted to correlate with the test results.

Of these 80, only 13 of them were from dogs that were 6 years of age or older (ARVC age group). 10/13 were positive for the mutation and had an average of 4,856 VPCs

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

Therefore, as with any genetic information, we recommend ALWAYS using test results to guide your decisions about breeding rather than using them as an absolute recommendation for all dogs. Do not make drastic decisions. Each dog and each family line should be considered individually, 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.

**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.

**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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