BOXER CARDIOMYOPATHY

by: Wendy Wallner, DVM

What is Boxer cardiomyopathy? Boxer cardiomyopathy as we know it consists primarily of an electrical conduction disorder which causes the heart to beat erratically (to have an arrhythmia) some of the time. If the erratic beats occur infrequently and singly, the dog will probably not have symptoms of heart disease. If the erratic beats occur in sequence, weakness, collapse or sudden death may result. These arrhythmias may or may not be detected by listening to the heart with a stethoscope.

Whether or not they are detected depends on the frequency of the abnormal rhythm. If frequent, they can easily be heard with a stethoscope. The arrhythmia usually consists of VPCs (ventricular premature contractions) that are heard as an extra beat or a skipped beat that do not have a corresponding pulse. To identify these, the listener must therefore have one hand on the stethoscope holding it to the chest and one hand feeling for a pulse (usually at the femoral artery on the inside of the hind leg). In the normal functioning heart, there is a pulse for every beat that is heard.

When a VPC occurs, a beat is heard through the stethoscope (and it sounds like a stutter as it is not in the normal rhythm sequence of the sinus beats), but there is no pulse to go with it. These VPCs have a characteristic pattern on an ECG and this is the way they are confirmed. Often this is the first abnormality noticed in a boxer with cardiomyopathy. Usually the dog is having no symptoms of heart disease when these are noticed by a veterinarian during a routine exam. If the frequency of these irregular beats increases, the animal may suffer "fainting" spells (called syncopal episodes). This happens because these abnormal beats do not pump the blood effectively (no corresponding pulse) to the vital organs like a normal beat does and the brain becomes oxygen deprived while the abnormal beats are occuring.

Usually when an animal faints, they are having what is known as a run (several in a row) of VPCs. If the heart corrects itself, the animal regains consciousness in a matter of seconds to minutes. If the run of VPCs continues, this is termed ventricular tachycardia and can lead to the development of ventricular fibrillation which is fatal if the rhythm is not converted. This ventricular fibrillation (V-fib) is the cause of sudden death in most boxers with cardiomyopathy. There is no blood being pumped through the body when the animal is in V-fib.

Cardiomyopathy can also be responsible for sudden death associated with anesthesia. Now, just because a boxer has VPCs does not absolutely mean it has cardiomyopathy IF there is another disease process at work. I have seen animals with severe infection or cancer have VPCs that resolved completely once the infection was cleared or the malignancy removed. If, however, VPCs are seen in an otherwise healthy boxer, one

would have a high index of suspicion for cardiomyopathy because of the prevalence of the disease in the boxer breed.

Some boxers with cardiomyopathy will enter another phase of disease where the ventricles of the heart start to dilate. At this time it is unclear whether this is a progression of the electrical conduction disorder, a separate disease more like that seen in other large breed dogs, or a subset of boxer CM that is not necessarily a progression of the previously arrhythmic dogs. With this condition, the walls of the heart become thin, the heart muscle weakens and these animals can show symptoms of heart failure such as coughing (from lung congestion) and/or fluid retention in the abdomen (ascites) depending on which side of the heart is most affected.

In time as the heart becomes very enlarged it begins to be an inefficient pump and dogs so affected may require numerous medications to keep the heart functioning well enough to sustain life. Still, most boxers affected with cardiomyopathy will ultimately die of their arrhythmia, not of congestive heart failure. The only way to definitively make the diagnosis of cardiomyopathy is to have a veterinary pathologist evaluate tissue samples from the heart muscle after death.

How is it diagnosed? The best way to evaluate a boxer for arrhythmia is to use a 24 hour ECG called a Holter monitor. While an ECG can pick up arrhythmias if they are very frequent, the Holter is much better at doing so. It will tell you if your dog has VPCs, whether they are frequent or infrequent, single or multiple, from a single focus in the heart or from several sites.

Not enough boxers have been studied to know if a small number of VPCs may be normal, but what is known is that most boxers that go on to die of cardiomyopathy have many VPCs in a 24 hour period (hundreds to thousands) and that they have runs of ventricular tachycardia. The Holter monitor allows us to identify dogs who may have problems due to these runs of VPCs. For example, most asymptomatic animals have single VPCs interspersed with their normal beats throughout the 24 hour period. If a Holter shows many clusters or runs of VPCs, this means that this animal may be at higher risk for syncope or sudden death and can affect how the dog is treated (with anti-arrhythmic drugs, for example).

Comparing statistics for ECG and Holter, it becomes evident why the Holter is superior in detecting subtle arrhythmias. The average 3 minute ECG provides the cardiologist with only 240 beats compared with 90,000 to 110,000 on the average Holter tape. Studies from human medical literature claim that individuals with more than 3000 VPCs in 24 hours have a 29% chance of having a normal random ECG, those with 1000-3000 VPCs in 24 hours have a 50% chance of having a normal random ECG and those with less than 300 VPCs have almost a 100% chance of having a normal random ECG. This is why so many affected boxers have normal random ECGs. ECG data is meaningless unless it

is abnormal!

Why not use Echo? Since boxer CM is a disease characterized primarily by arrhythmias, Echo is not the method of choice to make a diagnosis of CM. An echocardiogram is useful to determine if the heart is contracting properly. It will also help detect and identify the source of any murmurs that may have been heard on auscultation with a stethoscope by allowing visualization of the heart valves and blood flow patterns through those valves. It can be used to rule out the inherited condition of sub-aortic stenosis (SAS) which is known to affect the boxer and can also lead to sudden death.

It can also show whether or not there is any enlargement of the heart chambers or any thinning (as seen in dilated cardiomyopathy) or thickening (as seen in hypertrophic cardiomyopathy) of the heart muscle walls. It is not a good tool for detecting an arrhythmia, unless the arrhythmia is very frequent. Most boxers with CM will have normal echocardiograms unless they also have SAS or have the type of CM (progression, different disease or subset?) that causes dilatation of the ventricles.

What about supplementing with L-Carnitine? It has been shown that dogs on commercial diets have adequate amounts of L-carnitine in their plasma and that 80% of dogs with cardiomyopathy that have a deficiency of L-carnitine in the heart muscle have normal to increased L-carnitine levels in their blood. Although there has been a correlation between two sibling boxers with dilated cardiomyopathy and a response to supplementation with the L-carnitine, many more boxers have shown no improvement with supplemental L-carnitine. The two sibling boxers were found not to have a deficiency of carnitine in the diet, but most likely had an inability to utilize the carnitine present in their blood and to transport it into the heart cells where it must be actively concentrated so that it can be used for fatty acid metabolism, generation of energy and detoxification of certain metabolic compounds.

These dogs most likely had an inherited defect of the membrane transport of L-carnitine. While supplementation with L-carnitine improved the contractility of these dogs and caused a temporary improvement, it did not decrease their arrhythmias. One of these dogs eventually died due to ventricular arrhythmia, the other due to an apparent sudden onset of Addison's disease. Both parents were also affected with CM, but died before treatment with L-carnitine could be evaluated. (Keene, 1991)

Historical Perspectives This condition was identified and defined by Dr. Neil Harpster back in the late 60s and early 70s. The first paper was published in 1983 and was the result of examination of 64 boxers over a 15 year period with varying presentations of the condition. He described it as being quite different from other large and giant breed cardiomyopathies as had been characterized in the Doberman and Great Dane in that the hearts of the affected boxers showed an absence of dilitation of the ventricles, the

dogs rarely suffered from atrial fibrillation and the heart muscle showed extensive changes histologically on post mortem exam.

The disease was characterized as a cardiomyopathy based on the human nomenclature which calls myocardial disorders for which no specific cause can be found "primary cardiomyopathies". Because the dogs that Harpster studied were closely related, he proposed an inherited origin for the condition. In the original group of 64 dogs studied, Dr. Harpster found a slight male predisposition (57.8%) and an age range of 1-15 years with only 15.6% of the dogs less than 6 years of age and 25% over the age of 10. The average age at the time of diagnosis was 8.2 years. (In a 1991 report which added another 48 dogs to the original study, the average age at diagnosis dropped to 6.9 years.)

Dr. Harpster divided the 64 dogs into 3 categories based on the clinical features of their disease. The first category included dogs who had no clinical signs of disease. The second group had occasional episodes of fainting or weakness usually after a stressful event but were otherwise completely normal. The third group included dogs with signs of heart failure. The most common finding on the physical exams of all of these dogs was the presence of a cardiac arrhythmia. ECG findings consistently showed ventricular premature beats (VPCs) occurring singly, in pairs and in runs and episodes of ventricular tachycardia. The portions of ECG which did not show these abnormal beats appeared normal.

Of the 64 dogs in the original study, only 18 were presented for necropsy. All of the hearts had extensive and diffusely distributed changes in the myocardium (heart muscle tissue). The changes included the presence of cells that are not normally seen in heart muscle, the replacement of muscle tissue by fibrous tissue (scarring) and infiltration of fat into the muscle tissue. (Harpster, 1983,1991)

The Present While Dr. Harpster saw equal numbers of each of the 3 categories of boxer CM, we now seem to see more boxers in the first 2 categories and very few with signs of congestive heart failure. Dr. Kate Meurs at The Ohio State University, currently the most active researcher in regard to boxer CM and the recipient of the recent ABC/AKC grant, has placed that number at probably less than 10%. This may be due to increased awareness of the condition on the part of boxer owners and veterinarians and an increasing number of "normal" or at least asymptomatic boxers being critically evaluated for the presence of arrhythmias.

A few years ago, upon my appointment to the ABC's Health and Research Committee, I came up with a protocol for heart testing for boxers. These guidelines were published in the ABC News Bulletin in December of 1996. The recommendations were as follows:

- Minimum Heart Screening for boxers involved in breeding programs and/or

performance events:

- Age 1 year: auscultation by a board certified veterinary cardiologist (If arrhythmia detected - Holter exam; if murmur detected - Echocardiogram) Rationale: One year is the accepted time for clearance of sub-aortic stenosis. This auscultation screening could be performed at the national specialty and at individual breed club's specialty shows for a nominal fee. Any dogs with murmurs would be referred to a cardiologist in their area for further workup.

- Age 2 years: Holter monitor, auscultation (Echo if murmur detected) Rationale: The 2 year check would occur before the animal was used for breeding (at least extensively) and would be useful in detecting dogs with early arrhythmias before they are bred. In some dogs, arrhythmias have been detected as early as 12 weeks of age.

- Age 5 years: Holter monitor, auscultation (Echo if murmur detected) Rationale: By 5 years, many animals would show signs of arrhythmia if they were going to develop CM, since the arrhythmia often precedes clinical disease by several years.

The main purpose of these screens was to develop a database which could be analyzed and related to causes of death in dogs so that some sort of standardized system of interpreting the holter results could be determined. Not only would it help to identify and eliminate dogs with SAS from breeding programs, it would also help identify and eliminate those asymptomatic boxers with very large numbers of VPCs. It was never intended to eliminate any and all dogs with VPCs from breeding programs. There simply is not enough information available to use the results in this manner.

If large numbers of boxers are not holtered and followed over time, there never will be a database large enough to provide meaningful holter results. If this is the case, we are at the mercy of the only other test that will identify boxer CM - a genetic marker for the disease. Unfortunately, this type of test can take decades to establish. Since we know that the hallmark of boxer CM is arrhythmia and that the Holter is the best tool to detect arrhythmia, it is the only method we currently have to try to evaluate our breeding stock before they have produced offspring.

While there currently are no concrete numbers to identify normal vs. abnormal dogs, the Holter is still extremely important in identifying those grossly abnormal dogs with hundreds or thousands of VPCs who are asymptomatic and would otherwise be unknowingly reproduced. Until many Holtered dogs have been followed into old age and their medical histories analyzed and causes of death determined, we will not know the true significance of lower numbers of VPCs. We can, however, use all information obtained through Holter testing responsibly by slanting a breeding program toward those boxers that seem less affected.

References Harpster NK: Boxer Cardiomyopathy. In Kirk RW (ed): Current Veterinary Therapy VIII. Philadelphia, WB Saunders, 1983, pp 329-337.

Harpster NK: Boxer Cardiomyopathy - A Review of the Long-Term Benefits of Antiarrhythmic Therapy. In Veterinary Clinics of North America: Small Animal Practice - Volume 21, No. 5, September 1991, pp 989-1004.

Keene BW: Myocardial L-Carnitine deficiency in a family of dogs with dilated cardiomyopathy. JAVMA 198:647, 1991.