

## **A Summary of the Latest Findings of Juvenile Cardiomyopathy in the Toy Manchester Terrier**

**By Regina R. Allen DVM**

In March 2013, a study conducted by Dr. Carolyn Legge et. al. at the University of Prince Edward Island, *Histological Characterization of Dilated Cardiomyopathy in the Juvenile Toy Manchester Terrier*, was published in the journal *Veterinary Pathology*. This study was the first analysis of the disease at the tissue level, and is the first complete description of this form of heart disease. This research marks a significant milestone in understanding juvenile cardiomyopathy in Toy Manchester Terriers, and will hopefully lead to the detection and prevention of the disease in the future. The study and its recommendations are summarized below.

Dilated cardiomyopathy is the most prevalent form of cardiomyopathy in the dog, and is most common in specific breeds. Although most cases are adult-onset occurring in young to middle-aged animals, there are several breeds with a juvenile form of the disease, including Portuguese Water Dogs and occasionally Doberman Pinschers. Dilated cardiomyopathy is characterized by dilation and impaired function of the left or both ventricles of the heart, leading to heart failure and death. The over-representation of this disease in certain breeds suggests a genetic basis.

A new and rapidly progressive form of dilated cardiomyopathy has recently been recognized in juvenile Toy Manchester Terriers. These dogs appear healthy prior to dying suddenly, males and females are represented equally, and the dogs are typically less than one year old. The sudden death of the dogs in the study without pre-mortem clinical signs suggests that they died of a sudden fatal arrhythmia. Stress associated with surgery, anesthesia, and/or exertion may have triggered these arrhythmias that lead to sudden death in susceptible individuals. Cryptorchid males were over-represented in this study, whether or not they were castrated, suggesting an undefined association, possibly genetic, between cryptorchidism and juvenile cardiomyopathy. These characteristics are similar to the form of juvenile cardiomyopathy in Portuguese Water Dogs, but the visible cardiac changes in Toy Manchester Terriers are significantly different.

Cardiac weight data suggests mild cardiomegaly (enlargement). However, because the results were mild in Toy Manchester Terriers, it is assumed that sudden death occurred before major dilative changes occurred. The microscopic changes in the hearts of the dogs in this study were uniform, with cardiac muscle cells replaced by fibrous material, a chronic change that takes weeks to occur. Additionally, acute cell necrosis (death) and mineralization were present, which indicates a mixture of acute and chronic lesions, indicating repeated waves of heart cell injury and repair.

Despite the chronic lesions and indications of heart cell injury and repair, none of the study dogs had symptoms of heart disease prior to sudden death. This combination of microscopic lesions, absence of overt heart disease, and sudden death is unique to dogs with juvenile cardiomyopathy. However, there are some similarities between these features and those of adult Dobermans and Boxers who die of occult (asymptomatic) dilated cardiomyopathy. Adult Dobermans and Boxers who died suddenly of cardiomyopathy had microscopic changes consistent with those found in Toy Manchester Terriers.

Sudden death in Doberman Pinschers and Boxers with the same lesions as Toy Manchester Terriers are caused by fatal arrhythmias. The same cause may be postulated for Toy Manchester Terriers. The cycles of heart cell injury and repair and resulting in microscopic fibrous changes to the heart cells create pro-arrhythmic substances that result in sudden death. In the study, the right ventricle of the heart was most affected by these microscopic changes, which could provide insight to the possible cause of the disease.

Examination of the hearts and other tissues from the Toy Manchester Terriers in this study did not reveal evidence of valvular heart disease, vascular disorders, or other disease that could account for the visible and microscopic changes described in the study. No infectious agents were identified by microscopy, and the tissues were negative for parvovirus antigen. In addition to viral infection, autoimmune disease and other causes of cardiac injury should be considered as factors inciting sudden arrhythmias and death of Toy Manchester Terriers in this study.

Heritability and modes of transmission of dilated cardiomyopathy have been established in many affected breeds. The presence of a distinct form in this relatively rare breed suggests that genetic factors contribute to cardiac disease in Toy Manchester Terriers. The narrow gene pool and presence of microscopic heart muscle lesions among close relatives is further evidence for a genetic cause. The prevalence in various regions of Canada and the United States suggests that an environmental cause is **not** to blame. Affected close relatives and a high inbreeding coefficient are consistent with a recessive or multigenetic mode of inheritance. Dominant or X-linked modes of inheritance are unlikely due to lack of transmission from parent to offspring (i.e. affected dogs die before they are old enough to be bred) and the prevalence in females, respectively.

Further work is necessary to identify a specific genetic cause of this form of cardiomyopathy in the Toy Manchester Terrier. The collection of tissues and DNA samples from affected dogs is crucial to obtain a sample size large enough to perform a genetic association study. Multiple affected related individuals could help determine the mode of inheritance. Additionally, a larger collection of samples could provide an insight into the interactions between genetic and environmental factors in the development of the disease.

To summarize, this ground-breaking paper describes a previously unrecognized form of juvenile-onset dilated cardiomyopathy. Further investigations should include electrocardiographic and echocardiographic evaluation of juvenile Toy Manchester Terriers to detect electrical abnormalities or other heart dysfunction. Further pedigree analysis and eventual genetic testing is needed to confirm that this disease is heritable in the Toy Manchester Terrier.