

Can We Fix a Broken Heart? Dilated Cardiomyopathy in the Great Dane

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We have known for some time that dilated cardiomyopathy occurs with increased frequency in the Great Dane in comparison to some other dog breeds. Despite this there has been very little research in to this disease in Great Danes. We have been screening dogs at the University of Liverpool for the last 3 years, and we are starting to build up a better picture of DCM in the UK population. This started with the LUPA project, which is still aiming to identify the genetic mutation responsible for DCM in a number of dog breeds. We have also received funding from the Breed Council and the Kennel Club to continue this research. This talk will aim to summarise the main characteristics of DCM in all dogs, and discuss some of the findings of our research so far.

The normal heart

The heart is one of the most important organs in the body. It consists of four main chambers, the atria (or receiving chambers) and the ventricles (or pumping chambers). The left side of the heart pumps blood around the body, and the right side of the heart pumps blood to the lungs, where the blood picks up oxygen. Normal heart function is required for nutrients and oxygen to be delivered to the tissues of the body, and for waste products to be removed.

Dilated cardiomyopathy

Dilated cardiomyopathy is a disease of the heart muscle which affects a number of large and giant breed dogs, people, cattle, hamsters and even turkeys! The disease is characterised by:

- 1 Dilation and rounding of the heart chambers (particularly the left ventricle and the left atrium)
- 2 Impaired pumping ability (contractility) of the heart
- 3 Thinning of the heart muscle

Ultimately, the dilated and poorly contractile heart is unable to pump blood efficiently around the body. There is a very long phase when a dog will show no clinical signs of heart dysfunction, or may show only very mild signs (such as slowing at exercise, or taking longer to recover from exercise than normal). This phase is the preclinical phase of DCM.

Dilated cardiomyopathy is usually an adult-onset disease, so dogs often do not show signs until they are older. In our experience, most Great Danes show signs from 6 years or older, with some not developing any signs until 8 or 9 years of age or older. Some never show signs of having the disease at all, and may die of other diseases.

The most commonly reported signs of DCM in Great Danes are those of congestive heart failure. Congestive heart failure occurs when there is high pressure in the chambers of the heart, and blood 'backs up' in the lungs or in the blood vessels of the body. The high pressure inside the vessels causes fluid to leak out in to the surrounding tissue. In DCM, left-sided heart failure is more common, where fluid builds up in the lungs. This is called pulmonary oedema. Dogs with congestive heart failure will show signs of severe exercise intolerance, cough or difficulty breathing.

Inheritance of DCM

A group of researchers in the USA have published pedigrees of dogs suggesting that the inheritance of DCM in Great Danes is X-linked recessive. This would mean that male dogs were much more likely to develop the disease (see genetics notes). We are not sure if this is the case in the UK.

In other dog breeds (Dobermanns, Newfoundlands) the disease is thought to be autosomal dominant – it appears in every generation of a pedigree and in equal numbers of male and female dogs. Clearly, the advice regarding breeding of dogs with DCM varies greatly depending on how the disease is inherited. This is one of the most important things to establish in our population of dogs, even before a genetic test becomes available.

The LUPA project is currently running tests on samples collected here in the UK and in the rest of the world, to try and determine the genetic mutation or mutations responsible for DCM in Great Danes. These are in the early stages, but we are hopeful that we have found a significant locus.

DCM in UK Danes

We have now screened over 100 Great Danes as part of our research. In most cases these dogs have been presumed healthy by their owners and were being screened as normal dogs. We have identified approximately 20% of the dogs screened as having DCM. This is a worryingly high prevalence. Most dogs have been 6 or older, but some of the more recent dogs have been younger (disease identified in dogs as young as 4). A number of dogs are coming back for repeat scans every year, which is giving us vital information on the progression of the disease.

The other vital information that we gain by screening Great Danes over time is that we build up a picture of what is normal for Danes on heart scans. For example, some of the measures of contractility that are published for dogs in general, do not always hold true for Great Danes, and they may have slightly abnormal contractility that is of no clinical significance. We have also found differences in the normal values for male and female Great Danes.

Sudden Death in Great Danes

Sudden death occurs in other breeds that develop dilated cardiomyopathy, particularly in Dobermanns. In this breed, dogs can develop ventricular arrhythmias, or more 'classical' DCM with heart failure, or both. Some dogs die suddenly at young ages without ever having shown signs of the disease. Sudden death and heart failure due to DCM can occur in the same families, and there are differences between males and females in the development of disease.

Sudden death is a problem that we have recently started investigating in more detail, as there were increasing reports of this problem in UK Danes. The Breed Council recently purchased a Holter monitor (ECG recorder), which is giving us vital information about ventricular arrhythmias which we think may be the underlying cause of many sudden death cases. The Holter records an ECG for 24 hours, and we can therefore identify the number and severity of ventricular arrhythmias. A normal dog should have fewer than 20 extra beats (VPCs) in 24 hours. Anything over 100 VPCs in 24 hours is considered abnormal and we often recommend treatment when there is over 1000 VPCs in 24 hours.

We have also received hearts from some dogs that have died suddenly. This is absolutely

vital to our research and we are so grateful to everyone that has contributed.

Can We Fix a Broken Heart?

Unfortunately, dilated cardiomyopathy is an incurable disease, but we can give dogs medication to prolong their life, and improve their quality of life. Once a dog is in heart failure, there are numerous medications that may be of benefit. It is likely your dog would be prescribed:

- 1 A diuretic (e.g. furosemide) to reduce fluid build-up in the tissues
- 2 An ACE-inhibitor (e.g. Fortekor®, Vasotop®) to reduce salt and water retention that occurs in heart failure, and to dilate the blood vessels, reducing the work the heart has to do
- 3 Vetmedin to improve the pumping ability of the heart

Other drugs that you may receive include Prilactone (a drug that reduces scar tissue in the heart), or drugs to control abnormal heart rhythms such as digoxin or diltiazem.

We now have evidence from a study in Dobermanns and a lot of evidence from people that giving a dog an ACE-inhibitor BEFORE it develops clinical signs of disease can prolong the time to onset of clinical signs. We therefore now suggest that this treatment is given to any dog with preclinical DCM.

If a dog is identified as having ventricular arrhythmias, we can give medications to try and reduce the number of arrhythmias that they are having. Most often we use a drug called sotalol. We hope that these drugs will reduce the likelihood that a dog will die suddenly of their arrhythmias, but definite evidence for this effect is lacking.

Ultimately, reducing the number of dogs developing DCM will be the best way of controlling the disease. We face numerous, peculiar challenges when trying to reduce the incidence of DCM in Danes. Firstly, at the moment, we cannot test for the disease in young dogs, and therefore animals may be bred from before a diagnosis is made. Furthermore, we do not yet definitively know the mode of inheritance of the disease, and further research is needed to investigate whether dogs with ventricular arrhythmias, and dogs with DCM, have the same disease. In addition, some dogs may die of other causes before they ever show signs of the disease, and therefore may be considered to be 'normal' if they never had a heart scan.

Myself and all of my colleagues involved in DCM research are very grateful to everyone who has participated in our study so far, and urge more people to bring dogs for screening – remember, the age limit is now only 4 years old! We hope to be using the Holter monitor much more in the future as well. Any information that you can provide about dogs with sudden death or DCM will always be appreciated and will help further our understanding of this disease in Danes.

If you have any questions, or want to be involved in the research, contact me on 0151 795 6100 or hmc79@liv.ac.uk.