

Dilated cardiomyopathy (DCM) in Great Danes:

The cardiologist-researcher's view

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We have been working with the Great Dane community since 2008, looking at the prevalence and natural history of dilated cardiomyopathy (DCM) in Great Danes. First of all, this was funded by the EU in a large, European study called the LUPA project, which investigated the genetic basis of a number of canine diseases, and DCM was just one work-package of this, and Great Danes one of the breeds which we followed. Prior to this (1996 – 2002), and during the LUPA project, I also worked with the Newfoundland community investigating DCM in that breed, research which resulted in my PhD and British Heart Foundation funding for a post-doc attempting to identify the gene or genes involved in DCM, which was not successful. The LUPA project used a different strategy, called GWAS (genome wide association study) to identify markers of DCM by comparing the genetic code of healthy dogs and DCM dogs within each breed. Sadly, for Great Danes and Newfoundlands, we have still not elucidated the genetic cause of DCM. Evidence for Dobermanns and Irish Wolfhounds suggests that it is genetically complex, and multiple genes may play a role in the susceptibility to DCM within a single breed.

So what is DCM? DCM is a condition where the heart muscle fails to pump normally, especially the left side of the heart (the left ventricle is the main pumping chamber of the heart). Therefore, the left ventricle gets more dilated, rounded rather than being elliptical, and walls are relatively thin compared to the chamber dilation. Eventually, since blood is not effectively pumped out of the heart, pressures build up in the heart chambers, and so fluid dams back in the circulation. If the left side of the heart fails, this fluid dams back into the lung tissue, causing pulmonary oedema, resulting in difficulty breathing. If the right side of the heart fails, free fluid accumulates in the body cavities (ascites, pleural effusion). These signs are called congestive heart failure, and treatment is essential to get rid of the surplus fluid and to alleviate symptoms. Treatment is also directed to improve pump function, reduce

workload of the heart and to counteract the neurological and hormonal activation with perpetuates and worsens congestive heart failure and worsens heart muscle function.

We can see the heart changes by ultrasound – called echocardiography (echo). We can also screen by echo for early changes which may eventually lead to DCM, such as a more dilated left ventricle than normal for the breed, sex and weight of the dog, or reduced pump function (so called “equivocal” changes, since we only prove they lead to DCM by monitoring them over time). Echo can identify clear DCM, but prior to any symptoms of congestive heart failure developing (called preclinical or “occult” DCM). It is important for the individual dog to recognise this, as we know certain medication (Pimobendan) can delay progression of the disease, although no treatment cures it. Of course, screening is also necessary to attempt to reduce prevalence of the disease, but identifying it as early as possible in breeding dogs, to reduce the risk of transmission to progeny. However, DCM is an acquired disease, and so many dogs have been bred prior to DCM being diagnosed. This is always difficult in a condition which may be late in onset in some dogs, without a method to allow a very early diagnosis (given the absence of genetic tests at this time).

Our research with Great Dane DCM has developed our knowledge and understanding about the family basis of DCM, evidence for inheritance and natural history of the condition as it develops over several years (by repeat assessments ever 12 – 24 months). The Kennel Club Charitable Trust and the Great Dane Breed Council generously funded the work with Great Danes, between 2009 – 2014, and after that, the Great Dane Breed Council, various Great Dane Clubs and a number of private benefactors made generous donations to allow us to continue assessment of Great Danes to continue the research.

Our research, and the results of a questionnaire which went out to the Great Dane community in 2015, showed that a number of Great Danes were suffering from sudden death; these deaths were in an outwardly healthy Great Dane, and could be during sleep or during exercise. In some of these Great Danes which we had screened, we knew they had abnormal heart rhythms so we believe that the arrhythmias are the cause of death, if they degenerate into ventricular fibrillation and cardiac arrest. In some Great Danes, this was at a young age, prior to any screening assessment with us. Other arrhythmias may also be identified. Atrial fibrillation (AF) is a very fast, chaotic, irregular rhythm which generally occurs in dogs with advanced heart disease. But some Great Danes (and other giant breeds) may have AF at slow

heart rates without any significant echo changes in the heart. It is important to identify this and to consider converting it or controlling the heart rate if and when this becomes necessary as the rapid heart rate can result in deterioration in heart muscle pump function.

This led to us applying for a further grant from the Kennel Club Charitable Trust and the Great Dane Breed Council, which they generously awarded in October 2016, as well as some funds generated by an “Great Dane registration fee” the first time a dog was included. This new study was to look for abnormal heart rhythms (arrhythmias) and the association with current or future development of DCM. We did this by 24 hour ECG recording of the heart rhythm (called Holter monitoring). In addition, we investigated the role of blood tests for cardiac biomarkers to see if these could identify Great Danes with heart disease; if they were sufficiently sensitive and specific, a simple blood test could be used for “pre-screening” to identify those Great Danes who should undergo the “gold-standard” screening of echo and Holter.

So, with this current tranche of funding, we are able to recruit and screen the following eligible Great Danes:

- Great Danes of over 12 months old, considered healthy by their owners. They will have the cardiac biomarker blood tests done, and a Holter monitor fitted for 24 hours. The dog’s own veterinary surgeon is able, if he/she and the practice is willing, to fit the Holter and to take the blood samples and submit to IDEXX laboratories. The Holter analysis and laboratory analysis costs are covered by the grant. To be able to recruit more Great Danes in different geographical areas, the Great Dane UK association has generously funded another two Holter units to the two already funded by the Great Dane Breed Council. For Danes attending their own veterinary surgeon, we will send out the Holter equipment and full instructions for fitting and removing it, and for the blood sampling.
- “Full” screening in Great Danes of 4 years of age or older. These should also be considered healthy by their owners (or suspected to have DCM by the owner or the veterinary surgeon). As well as a physical examination, a blood sample to check on general health and thyroid function is carried out. Cardiac biomarkers will also be checked. Echocardiography will be used to check for DCM or other abnormalities. In

addition, the Holter monitor will be fitted. For this full screening, each Great Dane will need to be able to attend our small animal teaching hospital in the Wirral.

- Some of the financial support for the project is through a registration fee (£50) for each new Great Dane recruited into the study, so each owner needs to be willing and able to pay this. In addition, some veterinary surgeons may need to charge owners for their time and consumables in taking the blood samples or fitting Holters etc., but we encourage veterinary surgeons to contribute to the research by providing this service free of charge if they are able to.

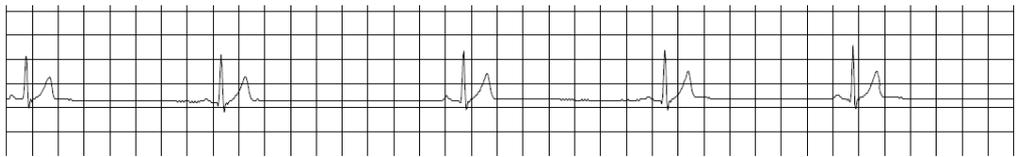
Acknowledgements

Hannah Stephenson was a colleague who was a researcher with the LUPA project and she was instrumental in gaining the trust and the enthusiasm of the Great Dane community in the early years, when she worked with us. She remains involved with the Great Dane research but is busy with her ambulatory cardiology service and her young family.

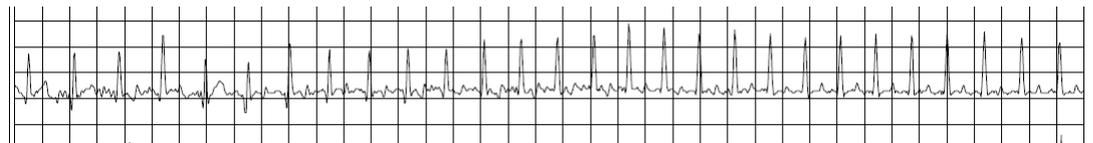
Joan Toohey, one of our hospital receptionist team, is well known by the Great Dane community and she has helped with the administration of the Great Dane DCM projects, with publicity, fund-raising, recruitment and booking in dogs for our assessment here, and for us to send Holter units out to. I am indebted to her for her help and enthusiasm. I am also indebted to my cardiology team, present and past, for their help and support of this project.

All the Great Dane community, for your support and participation. However, none of this research would have been possible without the generous contributions of many members donating as individuals, through their clubs, societies and associations, and via the Great Dane Breed council, going back over 10 years. This includes the registration fee which was been recently introduced. The Kennel Club Charitable Trust would not have awarded the grants they have, without this demonstration of the support of the Great Dane community and the Great Dane Breed Council. We are proud to continue to work with the Great Dane community to help improvement in the health and longevity of this magnificent breed.

Some Holter images of the different heart rates and heart rhythm (ECG)



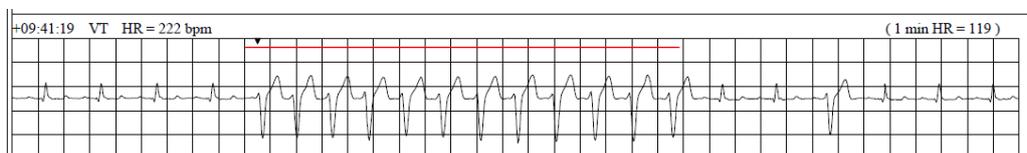
Normal ECG complexes, at slow heart rate (35 beats a minute), during sleep. (One channel)



Normal ECG complexes, at fast heart rate (200 beats a minute), during exercise, showing regular rhythm. (One channel)



Mostly normal ECG complexes but one abnormal, called a ventricular premature complex (VPC; red circle), premature compared to the underlying rhythm. This VPC is just single, but they can occur 2 together (couplet) or 3 together (triplet) (more serious when grouped). A healthy dog should have fewer than 50 VPCs over the 24 hours. (Three simultaneous channels).



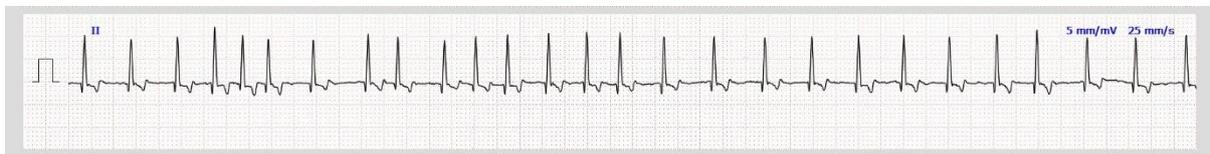
Some normal complexes, and then a paroxysm of abnormal ventricular complexes, called ventricular tachycardia (red line). This is called ventricular tachycardia. There is another abnormal complex (single VPC) 4th complex from the end. This dog was on antiarrhythmic medication but sadly, still suffered a sudden death.

ECG showing “lone” atrial fibrillation (AF) in a Great Dane



The heart rate is not fast (100 beats a minute), but it is very irregular. This dog was completely asymptomatic. AF can be due to stretch of the upper chambers of the heart (the atria) but echo did not show major changes other than reduced pump function in this dog.

ECG showing fast AF in a Great Dane with advanced DCM and congestive heart failure



The heart rate was very fast, at about 240 beats a minute, and very irregular. This dog showed signs of shortness of breath, coughing and exercise intolerance with the advanced stage of his DCM.