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Congenital Heart Disease

Miranda Levin Claymore Columns, Recommended Health Tests Tricuspid Valve Dysplasia, Ventricular Septal Defect

Photo by Margory Cohen.

Thankfully, congenital heart disease is rare in Deerhounds, but it does occur.

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DEERHOUND CLUB
Gezondheid – Hartproblemen bij de hond

In Deerhounds, we normally think of heart disease as arising late in life, mostly as a manifestation of dilated cardiomyopathy. But Deerhounds also can be born with a defective heart. The medical term for "present at birth" is congenital. An individual born with a congenital heart defect is said to suffer from congenital heart disease.

The heart is a complex organ with four chambers and four valves, all of which must work together perfectly to adequately circulate blood. Making a heart requires the embryo to follow a sophisticated genetic blueprint for cell growth, differentiation, and remodeling. Heart development occurs early in prenatal life so that the heart can supply the young embryo/fetus with the oxygen and nutrients necessary to grow and develop.

Congenital heart disease arises when a mistake occurs during development. Sometimes the mistake is in the genetic blueprint for making a heart. Other times, the blueprint is fine, but the mistake occurs in carrying out the plan.

The more complicated a process is, the more opportunities exist for mistakes. Given its complexity, it is a small miracle that the heart almost always develops correctly and that congenital heart disease is rare in all species. Of course, we only see the congenital defects that are compatible with life. Embryos with more severe heart defects die early and are resorbed.

Thankfully, congenital heart disease is rare in Deerhounds. The two Deerhound Health Surveys conducted by the SDCA in 1996 and 2011 surfaced only five reports of what might have been congenital heart disease. Two reports were heart murmurs in a 1-year-old male and a 2-year-old female, which can be a clue that a congenital heart defect is present. The other three reports were two males and a female that had leaky mitral valves (one of the four valves in the heart) discovered when they were 2½, 4, and 5½ years old, respectively. Given the age of these three dogs, it is impossible to know if the leaky valves were congenital or due to some illness later in life.

During more than 30 years in the breed, I know of only a few Deerhounds confirmed to have congenital heart disease. Two cases are recent, and both owners are happy for me to share their experiences. But before I do, I will provide a primer on the heart and heart murmurs.

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Heart Anatomy and Terminology

The heart is two pumps fused side by side that share a common wall called the septum. One pump, called the right heart, receives blood from all over the body and pumps it to the lungs. The other pump, called the left heart, receives blood from the lungs and pumps it throughout the body. Together, they circulate blood in a figure 8 pattern – from the right heart through the lungs and back to the left heart, and then from the left heart throughout the body and back to the right heart.

Each side of the heart has two chambers. The upper chamber, called the atrium, receives blood and has a thin elastic wall so it can swell. The lower chamber, called the ventricle, pumps blood and has a thick, muscular wall. The left ventricle wall is thicker than the right ventricle wall because it takes more work to push blood throughout the body than just to the lungs.

Each atrium and ventricle are separated from each other by a valve, called the atrioventricular (AV) valve. The right AV valve has three leaflets (flaps) and so is called the tricuspid valve. The left AV valve has only two leaflets and so is called the bicuspid valve. The left AV valve also is called the mitral valve because it reminded early anatomists of a bishop's hat, or miter.

Heart Murmurs and Congenital Heart Disease

The first hint that a dog might have congenital heart disease almost always comes when a veterinarian hears a heart murmur during a routine examination. A heart murmur is the sound blood makes when it is churning instead of flowing smoothly through the heart – like the difference between a quietly flowing river and one tumbling over rocks. Through a stethoscope, a murmur can sound like radio static or the rush of wind through grass.

How loud the murmur is, where on the chest it can be heard, and when during the heartbeat it occurs are all clues about what sort of heart defect might be responsible. It takes training and experience to detect soft murmurs. Loud murmurs often can be felt as a "thrill" or vibration by placing a hand gently on the side of the dog's chest. This is especially true in Deerhounds and other breeds with narrow chests, large hearts, and little body fat.

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It is important to understand that a heart murmur in a young puppy does not necessarily indicate a congenital heart defect. Many puppies have a soft murmur that is due to mild blood turbulence and is not associated with a congenital heart defect. This is especially true for large and giant breed dogs like Deerhounds. These so-called "innocent murmurs" usually disappear within the first year of life. But if the pup has any signs of heart trouble or the murmur is loud, then further investigation by a veterinary cardiologist is in order.

It also is important to understand that a heart murmur first detected in an adult dog may be due to congenital heart disease. In such cases, although the heart defect and resulting murmur were present from birth, they went undetected. While a loud murmur is hard to miss, a soft one can go unheard, particularly if there is background noise or if the dog is squirming or panting while the veterinarian is listening to the heart. The paper by Pugliese et al. (2021) gives an excellent description of how to do a proper heart examination with a stethoscope and how to evaluate and describe any murmur heard.

Tricuspid Valve Dysplasia (TVD) in a Deerhound

Margory Cohen's boy, Thane, was discovered to have a heart murmur during a routine wellness examination when he was 5 months old. A follow-up ultrasound examination by a veterinary cardiologist showed that he had TVD.

The cardiologist graded Thane's TVD as moderate on a 3-grade scale (mild, moderate, severe). She put him on pimobendan, a drug to strengthen his heart, and enalapril, a drug to ease the workload on his heart. (The latter drug was later changed to benzapril.)

When I began writing this column, Thane seemed to be doing well. As Margory put it in an email to me, "He eats great, runs hard, breathes hard as one would from the zooms and flight they do, and never coughs." Sadly, just before this column went to press, Thane died suddenly at home one morning . He was 3 weeks short of his first birthday.

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What is TVD?

Dysplasia is a medical term for abnormal growth or development. In TVD, it is the tricuspid valve in the right heart that develops abnormally. This valve opens to allow blood to flow from the right atrium into the right ventricle, and it closes when the right ventricle contracts to pump blood to the lungs.

A dysplastic tricuspid valve does not close completely, allowing some blood that should go to the lungs to leak back (regurgitate) into the right atrium. As a result, the right ventricle must work harder to pump blood to the lungs. Over time, the right ventricular wall will thicken, just like any muscle that works harder. If the tricuspid valve leaks badly, then the resulting regurgitation can cause the right atrium to balloon and even lead to right heart failure.

In which breeds does TVD occur?

TVD has been identified most often in Labrador retrievers, and I write more about that later. But it also has been seen in many other breeds. Papers have reported TVD in 11 breeds (Parker et al., 2006; Oliveira et al., 2011) and in 15 breeds (Favril et al., 2018). We can now add Scottish Deerhound to the list.

At what age is TVD usually discovered?

For 18 dogs of various breeds, the median age at which TVD was identified was 8 ½ months (Saunders 2021). However, the oldest age was 13 years, underscoring the need to consider congenital heart disease even in an old dog with a heart murmur.

Prognosis and treatment for TVD

How TVD affects a dog depends on the degree of valve malformation. Dogs with a mildly or even moderately malformed tricuspid valve routinely live normal lifespans. But dogs with a severely malformed tricuspid valve typically develop symptoms of congestive heart failure and may also develop heart arrhythmias.

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Cardiologist Kate Meurs explained the prognosis for dog with TVD like this in a 2018 article in *Today's Breeder* magazine:

"Some dogs can live with the disease their whole life and only be mildly affected. Other dogs will be unresponsive to medications and live a much-shortened life span. Each dog is a little different, and so much depends on the quality of care and how severely malformed the tricuspid valve is."

There is no cure for TVD, short of valve replacement surgery, which is not a routine option for dogs. On the other hand, TVD is not a progressive disease like cardiomyopathy. In other words, the valve problem present at birth does not go away, but it also does not get worse with time.

If a cardiologist believes that TVD should be treated, then she will use drugs that strengthen the heart, drugs that reduce the heart's workload, and/or drugs that alleviate symptoms of heart failure, if such symptoms develop.

Ventricular Septal Defect (VSD) in a Deerhound

Ken Cheatham's 9-year-old male Deerhound, Koh-i, was discovered to have a heart murmur during a routine wellness examination when he was about a year old. At the time, Ken lived in Alaska where a single veterinary cardiologist served the entire state, flying from town to town. When Ken eventually got Koh-i to the cardiologist, an ultrasound exam showed the murmur was due to a VSD. Koh-i began taking pimobendan and has lived a normal, healthy life that included lure coursing and agility trials.

What is a VSD?

A VSD is simply a hole in the septum shared by the right and left ventricles. It allows blood to flow between the two ventricles. At first, blood always flows from left to right because the left ventricle is a stronger pump than the right ventricle. With each beat, the left ventricle pushes blood not only throughout the body but also into the right ventricle.

A VSD increases the workload on the left heart in two ways. First, the blood that is pushed into the right ventricle is pumped to the lungs and then returns right back to the left heart. Second, some of the blood that the left ventricle

intends to send to the body gets shunted into the right ventricle, and so the left ventricle has to work harder to deliver enough blood to the body.

Over time, the left ventricular wall will thicken. If the VSD leaks badly, then the resulting demand on the left ventricle can lead to left heart failure. In addition, the extra blood being pumped to the lungs by the right ventricle can cause the blood vessels leading to the lungs to thicken. The resulting back pressure on the right ventricle can become great enough to cause blood to flow through the VSD in the opposite direction, from right heart to left heart, which is a life-threatening situation.

VSDs can vary in size and can be separated into categories based on their location in the septum. It is important to remember that the loudness of the resulting heart murmur typically is inversely related to the size of the VSD (Bellsham-Revell and Ferasin, 2020). That's because the murmur is simply the sound of blood churning as it squirts through the VSD. The smaller the hole, the faster the blood will move through it, and the greater the churning.

In which breeds does VSD occur?

VSD has been identified in dozens of dog breeds and in mixed breed dogs. Different papers have reported VSD in 8 breeds (Parker et al., 2006), in 15 breeds and mixed breed dogs (Patterson 1968), in 29 breeds and mixed breed dogs (Bomassi et al., 2015), and in up to 60 breeds (!) (Oliveira et al., 2011). We can now add Scottish Deerhound to the list.

At what age is a VSD usually discovered?

For 56 dogs of various breeds, the median age at which a VSD was identified was 9 months (Saunders 2021). But the oldest dog was almost 12 years old when its VSD was found.

Prognosis and treatment for a VSD

A VSD does not worsen with time. For that reason, the prognosis depends completely on how large the VSD is. Dogs with small VSDs and no symptoms at the time the VSD is discovered almost always live normal healthy lives without any treatment (Bomassi et al., 2015). Dogs with larger VSDs may

benefit from taking pimobendan to help their heart work better, but I can find no study comparing long-term health and survival with and without this medication.

Dogs that have symptoms of heart failure at the time the VSD is discovered have a guarded prognosis even with medical treatment. On the other hand, if the VSD is successfully closed by surgery, then the dog is cured, and the prognosis is excellent.

What Causes Congenital Heart Disease?

When a dog is discovered to have congenital heart disease, this is one of the first questions its owner and breeder ask. Unfortunately, there is rarely an answer. In almost every instance of congenital heart disease in dogs and humans, the cause remains unknown. This is true even though a lot of research time, effort, and money have gone into looking for possible causes, particularly in humans.

Studies have suggested many factors that can affect heart development and might increase the risk of congenital heart disease. These factors can be grouped into three categories:

1. Exposure of the mother to some harmful substance during pregnancy, such as an infectious agent, environmental pollutant, prescription or illegal drug, or toxin
2. A nutritional imbalance or deficiency in the mother during pregnancy
3. A genetic variant that the embryo/fetus inherited from its father or mother.

The first two categories can be lumped together as “environmental risk factors,” while the third category can be called “genetic risk factors.” Most researchers today believe that a pup’s or baby’s chance of being born with a heart defect is governed by the interplay among multiple factors rather than by a single factor (Lage et al., 2012; Suluba et al., 2020).

Environmental risk factors

When it comes to environmental risk factors for congenital heart disease, I can find no studies in dogs. But there are plenty of studies in humans.

Researchers have investigated the relationship between congenital heart disease and maternal virus infections (for example, Ye et al., 2019), maternal exposure to environmental contaminants (for example, Nicoll 2018), maternal exposure to prescription and illegal drugs (for example, Lynch and Abel, 2015) maternal stress (Joshi et al., 2020), and maternal nutrition (for example, Yang et al., 2020). A recent study (Nie et al., 2020) even found that babies born to mothers with "proximity to greenness" during pregnancy had a lower risk of congenital heart disease, possibly because of "improved air quality, enhanced physical activity and social interaction, and reduced mental fatigue and stress." (If you are curious about how "greenness" was measured, as I was, then see Note 1 at the end of this article.)

Prescription drugs are a special case worth discussing. Before the FDA will approve any human drug for marketing, that drug must be tested in pregnant animals of two species (typically rats and rabbits) for its ability to cause birth defects of any sort, including congenital heart disease. On the other hand, FDA does not require that veterinary drugs be tested in pregnant animals before approval. Consequently (and paradoxically), when it comes to pregnant dogs, more is known about the safety of human drugs than about the safety of veterinary drugs.

Genetic risk factors

For genetic risk factors, there not only have been many studies in humans (Lage et al., 2012; Suluba et al., 2020; Diab et al., 2021) but also studies in dogs. These include epidemiology studies across many breeds (Parker et al., 2006; Oliveira et al., 2011; Brambilla et al., 2020) and studies of a single type of congenital heart disease (Famula et al., 2002; Ontiveros and Stern 2021).

For TVD, a heritable risk factor has been confirmed in Labrador retrievers, but the responsible genetic variant(s) have not been identified. A 2002 study of 234 Labs from 12 bloodlines reported that a genetic risk factor for TVD resided on chromosome 9 and that TVD was inherited as an autosomal dominant trait with variable penetrance (Famula et al., 2002). But a subsequent larger study of less closely related Labs found no risk variant for TBD on chromosome 9. The current consensus is that TVD in Labs involves multiple genetic risk factors, possibly interacting with one or more environmental factors, and that the inheritance pattern is complex.

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The terms “variable penetrance” and “complex inheritance pattern” reflect the fact that, in Labs that inherit one or more TVD risk variants, the degree of disease severity is unpredictable. In some dogs, TVD will be severe and life-shortening. Other dogs will have a heart murmur and mild regurgitation that never causes symptoms. Still other dogs will be completely normal in every evaluable way but carry the risk variant, as evidenced by their ability to produce pups with TVD.

TVD also has been reported to be heritable in Dogue de Bordeaux in Israel, where the limited data available suggest an autosomal recessive mode of inheritance (Ohad et al., 2013). I can find no studies that have tried to identify a genetic risk factor in this breed.

Finally, a recent UK study raised the possibility that Border Collies are at increased risk of TVD (Navarro-Cubas et al., 2017). The authors suggested that future studies should try to identify a mode of inheritance and potential genetic risk factor for TVD in this breed.

For VSD, a heritable risk factor has been confirmed in Keeshonden (Patterson, 1968). But multiple genetic variants are involved, which collectively influence VSD occurrence (Werner et al., 2005).

Implications of Congenital Heart Disease

The discovery of a congenital heart defect in a Deerhound has implications for the dog’s owner and the dog’s breeder.

Implications for Owners

The owner of a Deerhound with a congenital heart defect will be concerned chiefly with what the diagnosis means for her dog and herself. She will want to understand whether the dog needs treatment for the problem or instead will probably live a normal healthy life without intervention of any sort. If treatment is recommended, then she will want to understand what the treatment involves, what it will cost, how it is likely to benefit the dog, and how it might evolve over time. A veterinary cardiologist is generally the best person to provide this information. The owner of a dog diagnosed with a congenital heart defect also should inform the dog’s breeder.

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Implications for Breeders

The breeder of a Deerhound with a congenital heart defect will be concerned chiefly with whether the diagnosis reflects a heritable genetic risk factor that she should consider in her breeding program. Unfortunately, this question can rarely be answered.

If the breeder has heard that the same defect has shown up in other Deerhounds, or if the defect is reported to be heritable in other breeds, then a genetic risk factor is possible. But as discussed earlier, a heart defect in a single dog can result from a spontaneous mistake during development and not from an inherited risk factor.

With no way to know if a heart defect reflects a heritable risk factor, a breeder might take several approaches. She might decide to eliminate all the affected dog's relatives from her breeding program, just in case a heritable risk factor exists. In breeds with large populations, this approach might be justified, even if it eliminates good dogs from the breeding pool. But in a rare breed like Deerhounds, this approach might do more harm than good.

A breeder will want to screen (or re-screen) dogs in her breeding program for congenital heart disease by having an experienced veterinarian listen for a heart murmur, or even by having a veterinary cardiologist do a cardiac ultrasound evaluation. After she learned of Thane's diagnosis with TVD, his breeder, Johanna Hansen, told me she intends to take matters into her own hands – literally. She has bought a stethoscope and will learn how to use it to listen to her dogs' hearts. In this way, she can listen to the heart under optimum conditions: in a quiet room, when the dog is relaxed or even asleep. And she can do this as many times as she wants.

Finally, a breeder also will want to let owners of related dogs – at least siblings and sire – know about the congenital heart defect, so that those owners can screen their dogs.

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Note 1

Nie et al. (2020) measured "greenness" using NASA satellite image data, like this:

"We employed the Normalized Difference Vegetation Index (NDVI) to determine greenness. The derivation of NDVI was based on the land surface reflectance of the visible red and near-infrared parts of the electromagnetic spectrum. NDVI values range from −1 (representing no vegetation) to +1 (representing high-density forest cover). The annual average NDVI for the years 2003-2017 (referring to the period of study participants recruitment) was assessed from the MODerate-resolution Imaging Spectroradiometer (MODIS) satellite images at 500 m and 1000 m resolutions (https://search.earthdata.nasa.gov/)."

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Congenital heart disease is the medical term for a birth defect in the heart. Congenital heart disease occurs in all species, so it's not surprising that Deerhounds can be affected, too. Thankfully, birth defects in the heart are rare. I know of only a few cases in Deerhounds: tricuspid valve dysplasia (TVD) in one dog and a ventricular septal defect (VSD) in four.

The heart is complex and develops early in pregnancy. Studies (mainly in humans) suggest its development can be influenced by genetic variants inherited from either parent, by maternal nutrition, and by maternal exposure to viruses, pollution, toxins, drugs, and stress. Most experts now agree that heart defects likely have no single cause but instead occur when multiple risk factors intersect.

Investigating a possible genetic influence for any disease in a dog breed is challenging. First, one must figure out if the disease is heritable, which can be done only if there are multiple cases over multiple generations. For a rare disease in a rare breed, this first step is often impossible. Instead, genetic risk factors for a rare disease can be sought only in a breed or subpopulation with lots of affected dogs. If such an approach identifies a putative genetic risk factor, then one can screen for the presence of that factor in other breeds where the disease is rare.

For TVD, one or more heritable risk factors exists in Labrador retrievers and also might exist in some populations of Dogue de Bordeaux and Border collies. For VSD, multiple heritable risk factors exist in Keehsonden. Time will tell if this information leads to identification of a single genetic risk factor and its relative contribution to either defect.

The original article stated that Dr. Dillberger only knew of one VSD case–since that time, a few more cases have come to his attention, so this article has been updated accordingly. Ed.

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