

Researchers Aim to Isolate Gene for Tricuspid Valve Dysplasia

Canine researchers have taken a big step toward identifying the gene that causes the most common heart condition in Labrador Retrievers, tricuspid valve dysplasia. Having located the chromosome that contains the defective gene, the scientists now are working to isolate the gene so a genetic test can be developed for determining dogs that are carriers.

Kathy Wright, DVM., a canine cardiologist, and her team of scientists at the Comparative Cardiovascular Catheterization Laboratory in the Division of Cardiology at Cincinnati Children's Hospital, have studied 234 Labrador Retrievers with tricuspid valve dysplasia (TVD) during the past two years. The dogs represent 12 different bloodlines.

The first major discovery by the team was learning that CFA 9 is the chromosome housing the gene causing this serious and sometimes life-threatening heart condition in Labs. "Isolating the specific gene in that region of CFA 9 is the next step," Wright says. "Once that is accomplished, a DNA test can be developed for that genetic mutation."

Potentially, in the future, breeders will be able to take dogs to the veterinarian for a simple blood test to determine whether they carry the condition. This will help breeders make informed breeding decisions and reduce the incidence of TVD in Labrador Retrievers.

Understanding TVD

Tricuspid valve dysplasia (TVD) in dogs is a congenital heart condition. In medical terms, dysplasia means a malformation; TVD is a condition in which the heart's tricuspid valve forms improperly during embryonic development. Like the human heart, a dog's heart is divided into two halves. The tricuspid valve is in the right half between the right atrium and the right ventricle. Its job is to prevent the back flow of oxygen-depleted blood as it flows from the right atrium to the right ventricle on its way to becoming oxygenated once again by the lungs via the pulmonary artery.

Made up of irregularly shaped flaps, the tricuspid valve forms a barrier when blood tries to work its way back into the right atrium as the right ventricle contracts. In utero, these flaps are adhered to the ventricle wall. Normally, cellular degeneration takes place and the flaps are detached. In dogs with TVD, this degeneration does not take place and the flaps remain connected to the ventricle wall, hampering the valve from doing its job of preventing the blood's back flow. Blood is then regurgitated, or leaked, back into the right atrium, increasing the workload of the right side of the heart.

Depending on the severity of the malformation, the regurgitation can range from a small amount to a significant leak. In severe cases, the right side of the heart must work harder to compensate for the deficient tricuspid valve, causing an increase in pressure in the veins and a decrease in blood flow to the left side of the heart. Over time in severe cases, right-sided congestive heart failure sets in and, although medical intervention can help slow the heart failure, eventually the animal will die.

Although all dogs are at risk, tricuspid valve dysplasia is seen more often in large breeds, such as the Labrador Retriever, German Shepherd Dog, Great Dane, Borzoi and Weimaraner. Signs of TVD vary, depending on the severity of malformation. Mildly affected dogs may have no outward signs of the condition and live normal, healthy lives. Moderately affected dogs often will not show any signs for several years.

"This condition is not all gloom and doom like some of the literature suggests," Wright says. "One of the dogs in our study that has been identified with severe TVD is 6 years old and shows no signs. Another dog in the group is moderately affected by it, and he's 14."

However, in severe cases, the animals will usually develop signs of right-sided heart failure: a distended abdomen due to ascites, or fluid buildup, cool limbs, and intolerance of exercise. Some dogs may faint or collapse as a result of an abnormal heart rhythm.

"Usually owners notice one of two things," points out Wright. "They think their animal is getting fat, but actually they're seeing the fluid that is accumulating in the dog's abdominal region. Or they see that their dog is slowing down, acting lazy or more fatigued."

If these signs are apparent, an owner should contact his or her veterinarian for assistance in slowing the progression of heart failure. "Often, a case of TVD that demonstrates clinical signs as a puppy or young adult dog goes hand in hand with a second condition, such as a hole in the ventricle or an obstruction. These are considered worst case scenarios, and heart failure can set in quickly," Wright says.

Identification & Treatment

If a Lab's TVD is severe enough to cause health problems, a veterinarian should be able to detect the signs of the valve's malformation during a physical exam. Usually a heart murmur can be heard with a stethoscope, but noise in the exam room, a wiggling puppy or even panting can keep the vet from hearing the telltale murmur.

Occasionally, the valve's dysfunction not only causes an audible murmur but also creates a palpable buzzing sensation called a "thrill" that can be felt by placing a hand on the right side of the chest. When a thrill and/or a murmur is detected in a young Lab, ultrasound and chest X-rays should be performed to determine if TVD is present.

Through ultrasound, also called echocardiogram, the veterinary cardiologist would expect to see a noticeably enlarged right atrium in moderate or severe TVD cases. The size of the right atrium may even be larger than the rest of the heart. Enlargement of the right side of the heart occurs as the right atrium expands to accommodate the increase in blood volume as it leaks back through the faulty valves. Ultrasound I would also show irregularities in the location, shape, motion and attachment of the valve leaflets. Blood regurgitating back into the right atrium could also be seen by color flow Doppler.

An X-ray of the chest would clearly show right atrial and ventricle enlargement in moderate or severe cases, but not in mild cases. In some cases of TVD, the right side of the heart becomes so large that it pushes the left heart farther to the left, as seen on X-ray. Another test that can be performed is electrocardiography, or EKG. A Labrador with TVD may have abnormalities of the heartbeat, also called atrial arrhythmias, which the EKG can detect.

Although a Lab may be clinically identified with TVD as a result of ultrasound, X-ray or EKG tests, it may be years before signs develop, or they may not develop at all. Even when the TVD is severe, a dog sometimes will not show outward signs of the condition until the animal is in congestive heart failure. If and when that happens, treatment strategies are usually aimed at controlling the signs brought on by the failing heart.

At that point, an owner should limit the dog's exercise to avoid overburdening the already weakened heart. A low-sodium diet may be recommended. Digoxin can be administered to control atrial arrhythmia. Minimizing fluid retention is key to the animal's comfort. Diuretics are typically prescribed to help reduce fluid.

Sometimes, however, a dog's belly becomes so distended that removing the accumulated fluid is necessary. Drug therapy helps delay the fluid from building up again, but it does not halt the swelling. Periodic removal of the fluid is often required. Unlike dogs with left heart failure, dogs experiencing right heart failure normally feel good between procedures to remove excess fluid. Unfortunately, the period between these procedures eventually becomes so short that owners often choose euthanasia.

Today, surgery to replace or repair the defective valve is not considered a viable option. Several veterinary medical centers are working on surgical procedures but results are not yet favorable. "It is important for owners to remember that although severe *NO* can eventually be fatal, many dogs do well and experience good quality of life for an extended period of time once their signs appear," Wright says. "Paying close attention to your animal's signs and communicating with your veterinarian are essential to keeping the dog comfortable for as long as possible."

Controlling TVD in Labradors

Now that Wright and her colleagues have proved that TVD is an inherited condition, making good breeding decisions is crucial in the fight to reduce the prevalence of TVD in Labrador Retrievers. Dogs that are affected should not be used for breeding. Future breedings of their sire and dam to each other also should not be repeated. Unfortunately, clinical signs of TVD often do not appear until after an afflicted dog is of breeding age, so owners may unknowingly breed a dog bearing the genetic marker for TVD.

The best way to avoid this, says Wright, is to have any Labrador that is being considered for breeding purposes screened for the condition by ultrasound. "I recommend that Lab breeders have a veterinary cardiologist perform an echocardiogram on their dogs," urges Wright. "TVDO often brings about subtle changes and the condition can be difficult to identify, so you're better off consulting someone who is used to looking at the right side of the heart."

Other ways to help reduce the incidence within the Labrador breed are by communicating with new owners about the condition and alerting owners of sires and dams and littermates of dogs who are identified with TVD, as well as those who are researching heart condition in canines (see "How Owners of Labrador Retrievers Can Help," below). Meanwhile, Wright and her colleagues are hard at work to pinpoint the gene responsible for TVD so that someday soon a simple blood test at your veterinarian's office will show if your puppy is free of the most common heart condition in Labrador Retrievers.

How Owners of Labrador Retrievers Can Help

Kathy Wright, D.V.M., a veterinary cardiologist, is seeking more Labradors for her research into tricuspid valve dysplasia (TVD), a congenital and sometimes fatal heart condition in dogs. If you have a Lab with TVD and are willing to send a blood sample and pedigree. or better yet, have a complete cardiovascular examination performed on your dog and their dose relatives, contact Wright at:

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Phone: (513) 636-4395

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E-mail: kathy.wright@chmcc.org

In addition. the Orthopedic .Foundation for Animals (OFA) at the University of Missouri-Columbia maintains a registry of purebred dogs with congenital cardiac conditions. Through its huge database, OFA allows breeders to look at the genetic health of whole families of dogs. For more information or an application, contact OFA at:

Orthopedic Foundation for Animals

2300 E. Nifong Blvd.

Columbia, MO 65201

Phone: (573) 442-0418

Fax_(573) 875-5073

<http://www.offa.org>

Heart-to-Heart Collaboration

You wouldn't expect to see four-legged patients getting treatment at a hospital for children, but in Cincinnati this unusual combination has produced some very exciting results. Veterinary cardiologist Kathy Wright heads a clinic for dogs on the campus of Cincinnati Children's Hospital.

There she and her colleagues have been treating and studying Labrador Retrievers with tricuspid valve dysplasia. "This unusual collaboration of veterinary clinic within a children's hospital actually makes a lot of sense," explains Wright. "We're studying a congenital heart condition in dogs that correlates very closely to Ebstein's Anomaly, a rare congenital heart condition in humans."

The scientific team is getting close to pinpointing the gene that causes tricuspid valve dysplasia in Labs. Once found, it is hoped that locating the corresponding gene responsible for Ebstein's Anomaly in humans would be relatively simple. "By studying Labradors," Wright explains, "we're able to look at an essentially isolated population with a higher incidence of affected individuals than in the human population. That makes the research easier and, hopefully, quicker."

Wright and the other canine scientists at Cincinnati Children's Hospital hope they will soon know exactly which gene is responsible for causing the most common heart condition in the most common breed of dog, having far-reaching impact on the lives of both man and man's best friend.

