

## Alternative Treatments Studied for Dobermans with Dilated Cardiomyopathy



Dilated cardiomyopathy (DCM) in Doberman Pinschers is a challenging disease in which to identify dogs that will develop a severe case and die, and those that will be mildly affected despite testing positive in genetic screening.

An inherited, irreversible heart muscle disorder that affects Dobermans more than any other breed, DCM can cause ventricular arrhythmia, or erratic heartbeats, and sudden death. Normal heartbeats are interrupted by rapid beats that fire too closely together, subsequently shorting out the heart, and the dog faints. About one-third of these dogs have no prior signs of the disease until they die. Some dogs recover, yet some die suddenly.

Dobermans with DCM also can develop congestive heart failure when the heart dilates to compensate for the weakened heart muscle. This causes the heart to hold a greater volume of blood, while its thinned walls continue to weaken. Fluid may back up in the dog's heart, lungs and abdomen. Signs of pulmonary edema include coughing, rapid breathing and lethargy. By the time the characteristic clinical signs, such as weakness, lethargy and coughing, appear, the disease may be advanced and the prognosis grim. Since the congestive heart failure form of the disease is often not diagnosed until dogs are around 7 ½ years old, they may have already been bred when DCM is discovered. Fifty percent of dogs with congestive heart failure die within months. Affected dogs usually appear normal until the heart muscle is no longer able to pump adequate amounts of blood to the body.

Due to the prevalence of the disease in the breed, the Doberman Pinscher Club of America recommends that dogs receive an echocardiogram screening when they are between 1 and 2 years of age, along with a baseline Holter monitor test. Dogs in breeding programs should be tested every six months. These tests help to identify the disease sooner when treatment can help slow its progression, ease clinical signs and improve quality of life.

These diagnostic tests should be used together because while one test may produce normal results, the other may pick up on an abnormality or vice versa. For example, an echocardiogram examines the structure of the heart and detects functional abnormalities at a single segment of time, while the Holter monitor provides information about the heart's electrical activity over an entire day. Together, these tests help to identify dogs that might later experience sudden death or develop structural disease if not already present.

DCM is different in every breed and can occur in mixed-breed dogs as well. Other breeds affected by DCM include Afghan Hound, Boxer, Dalmatian, Golden Retriever, Irish Wolfhound, Labrador Retriever, Newfoundland, Old English Sheepdog, Portuguese Water Dog, Saint Bernard, and Scottish Deerhound. Cocker Spaniels can develop the condition related to a nutritional deficiency. DCM affects male and female Dobermans equally. Individual dogs vary in the age of onset, rate of disease progression and frequency of sudden death versus congestive heart failure. Environment and lifestyle factors could play a role as well. Affected

dogs benefit from drug therapy, which offers palliative care but does not alleviate the long-term effects of the disease.

Here is a review of two experimental treatments. One involves the use of adult bone-marrow stem-cell therapy by ReGena-Vet Laboratories, a startup biotech in Davis, California, and the other is investigating the use of a nucleoside triphosphate that transfers energy to cells to maintain viability and increase heart function.

### **Stem-Cell Therapy May Aid Healing**

An active obedience competitor, “Sonny” showed no hint of being ill when he was diagnosed with DCM two years ago at the age of 5. He enthusiastically performed high jump retrieves and broad jumps during training and at trials.

Owner Carol Stephens of Kodak, Tennessee, was taken aback by the diagnosis. “Sonny was never short of breath or seemed faint or weak,” she says. “The veterinarian placed him on medications, and we began taking him every six months for cardiology follow-up examinations. Meanwhile, we continued to train and compete in obedience, as he showed no signs of the disease.”

About a year after Sonny was diagnosed with DCM, Stephens attended a presentation on the use of stem-cell therapy to treat canine diseases by Richard Vulliet, DVM, PhD, professor of molecular biosciences at the University of California-Davis, and founder of ReGena-Vet Laboratories. Stephens shared information about Sonny’s condition and diagnosis of DCM with Dr. Vulliet, who thought the dog could be a good candidate for stem-cell therapy.

The DCM disease process in Dobermans starts when cardiomyocyte cells in the heart die prematurely and noncontractile fibrotic cells replace them. As the heart muscle loses its contractile cells, it is unable to adequately pump blood to the body. Stem-cell therapy provides a potent dose of anti-inflammatory, antifibrotic, proangiogenic cells that home to the damaged tissues to help them heal.

These mesenchymal stem cells (MSCs) from adult bone-marrow stem cells are injected into a dog’s bloodstream. Their ability to release therapeutic growth factors and cytokines gives them a local paracrine effect, meaning they are able to impact cell-to-cell signaling. Although the body already has some circulating stem cells to help repair itself when injury or disease occurs, there are not enough stem cells to offset the damage of chronic heart failure.

Stephens began working with Dr. Vulliet and her veterinary cardiologist at home, Rebecca Gompf, DVM, MS, DACVIM-Cardiology, of the University of Tennessee in Knoxville, in providing care for Sonny. Dr. Gompf examines Sonny’s heart at six-month follow-up examinations using Holter monitoring and echocardiogram testing.

ReGena-Vet processes Sonny’s stem cells at no cost, thanks to funding support from the Doberman Pinscher Club of America (DPCA) Foundation. “The Foundation got involved in supporting stem-cell therapy research as a treatment option for DCM because of the good results seen in humans with diseases of the heart and orthopedic injuries,” says Dr. May Jacobson, chair of the grants committee. “So far, we have provided \$25,000 for this work.”

“Just after a few weeks of injections, I noticed an increase in Sonny’s activity and appetite,” Stephens says. “He became more playful and initiated play with other dogs. He was bouncy and happy, behaviors he hadn’t shown in years.”

Dr. Vulliet stresses that stem-cell therapy is not without risk, though he is encouraged because data from laboratory animal studies demonstrate bone marrow stem cells can help in DCM. Among his goals for the future, he plans to conduct a clinical trial with enough patients to achieve a statistical significance.

“This still is an experimental treatment that is evolving — not a miracle — and no procedure is without risk,” cautions Dr. Vulliet. “For example, in Dobermans with DCM, anesthesia to collect bone marrow from which we obtain stem cells can increase the risk of a fatal arrhythmia in some dogs.”

Now in his 14th month of stem-cell therapy, Sonny continues to do well. “Sonny is happy, active and keeping up with the younger dogs in our household,” Stephens says. “Each cardiology visit shows improvement in his heart, with the most recent echocardiogram showing that his left ventricle had reduced in size. We are hoping that Sonny will be the Doberman that proves stem-cell therapy can give a diseased dog a long, happy life.”

### **Novel Treatment Shows Promise**

A [study published in January 2016](#) has shown success in treating DCM with a novel therapy, 2-Deoxyadenosine triphosphate (dATP), by helping to increase the heart’s ability to contract normally.

The study led by researchers at the University of Washington in Seattle and the University of Guelph in Ontario, Canada, involved adding a special form of adenosine triphosphate (ATP), dATP, to heart muscle removed from dogs with end-stage DCM. Not only did the dATP-treated muscles contract better than the ATP-treated muscles, they also contracted at a level equal to the heart muscle of normal functioning dogs.

DCM is a disease characterized by weak contraction and dilation of the heart. Heart muscle cells require ATP for energy for contraction and relaxation, but in dogs with heart failure, the ATP turnover rate, an estimate of how much ATP is used and remade, is abnormally low.

“The work thus far has only been performed in vitro in the laboratory to canine heart muscle cells,” says Lynne O’Sullivan, DVM <https://www.purinaproclub.com/resources/dog-articles/health/alternative-treatments-studied-for-dobermans-with-dilated-cardiomyopathy>

The work thus far has only been performed in vitro in the laboratory to create heart muscle cells,” says Lynn O’Sullivan, DVM, DVSc, DACVIM-Cardiology, faculty cardiologist at Ontario Veterinary College at the University of Guelph. “Although it is too early to use this technique in dogs, studies in other species have shown that gene therapy may be used to produce increased dATP in heart cells. Not as simple as giving an oral pill, gene therapy involves delivering a benign virus into the heart or heart vessels that carries genetic information to heart muscle, resulting in an increase in the enzyme responsible for producing dATP.”

In [related research](#), Dr. O’Sullivan aims to determine the clinical usefulness of a blood test combined with novel cardiac ultrasound parameters in helping to predict the outcome for Dobermans diagnosed with DCM. “We want to better understand the changes occurring to heart function as the disease progresses,” she says.

Although DCM is a complex disease, these alternative experimental treatments may one day offer hope to Doberman Pinschers and those who love them.

Efforts to study the disease and to educate owners and breeders about DCM are helping to advance progress.

Purina appreciates the support of the Doberman Pinscher Club of America and particularly Dr. May Jacobson, chair of the DPCA Health Research Evaluation Committee, who helped to identify this topic for the *Purina Pro Plan Doberman Pinscher Update* newsletter.

### **DPCA Includes Cardiac Testing in CHIC Program**

Due to the high prevalence of dilated cardiomyopathy, an irreversible genetic heart disease, in the breed, the Doberman Pinscher Club of America (DPCA) has designated cardiac testing as part of the Orthopedic Foundation for Animals’ (OFA) [Canine Health Information Center](#) (CHIC) certification requirements.

DPCA requires an OFA advanced cardiac database exam performed by a board-certified veterinary cardiologist. The exam must include basic auscultation, an echocardiogram and Holter monitor testing.

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