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MEGAESOPHAGUS

A Top Health Concern in Great Danes



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GREAT DANE PUPPIES WITH MEGAESOPHAGUS MAY BENEFIT FROM NEW TREATMENT

“As with any heritable trait in a breed with a lot of genetic diversity, some lines see megaesophagus very frequently and others never report seeing it.”

Neil O’Sullivan, PhD, co-chair of the Health and Research Committee of the Great Dane Club of America

It had been 33 years since Sterling Moffat had produced a puppy with megaesophagus. Not a condition easily forgotten, she recognized the clinical signs right away in a 5-week-old blue male puppy from her 2018 litter.

“He regurgitated his food and had a bullfrog throat,” says Moffat of Lyme, New Hampshire, who has bred Great Danes under the Sterling prefix since 1973. “Milk came out of his nose as he nursed. He was not thriving as puppies

should, and there was an odd sloshing or clicking sound in his throat.”

Megaesophagus is one of the top health concerns in Great Danes, says Neil O’Sullivan, PhD, co-chair of the Health and Research Committee of the Great Dane Club of America.

Although no statistics are available, Great Danes are cited in a [survey of owners](#) conducted from December 2014 to May 2015 as one of the breeds most often affected by congenital megaesophagus.



“Wabi-Sabi” at 6 weeks of age had just begun showing clinical signs of congenital idiopathic megaesophagus.

“As with any heritable trait in a breed with a lot of genetic diversity, some lines see megaesophagus very frequently and others never report seeing it. It is a serious challenge in the breed, and since the affected puppies are typically diagnosed at 3 to 5 weeks of age, the burden has been heavy for breeders,” Dr. O’Sullivan says.

Congenital idiopathic megaesophagus, which is usually diagnosed around weaning, literally means “a huge esophagus.” The esophagus is a long, slender muscular tube that carries food from the mouth to the stomach, but in puppies with megaesophagus the enlarged tube fails to contract normally thus hindering the transit of food. Swallowing depends on the synchronized constriction of the esophagus with the opening and closing of the lower esophageal sphincter (LES) that separates the esophagus from the stomach.

“The LES in a normal dog relaxes and opens in response to swallowing, which increases pressure in the esophagus,” explains Jillian Haines, DVM, MS, DACVIM, associate professor in small animal internal medicine at Washington State University. “In dogs with megaesophagus, the LES does not open appropriately to allow the passage of food out of the esophagus and into the stomach.”

As a result, food is trapped in the esophagus until it is regurgitated. Unlike vomiting, regurgitation happens suddenly and effortlessly. Regurgitation usually occurs soon after a puppy eats but can also happen hours later. Regurgitated food does not contain stomach bile, though it may be partially digested from salivary enzymes.

Puppies with megaesophagus may cry from pain as the esophagus stretches when food is trapped. They also may cry from being hungry due to most of the food they eat never reaching the stomach. Moffat’s puppy,

LEARN MORE AT CANINE UPRIGHT BRIGADE

The homepage of the [Canine Upright Brigade](#) website promises that megaesophagus is not a death sentence and things will get better. A comprehensive resource for owners of dogs with megaesophagus due to various conditions, Canine Upright Brigade offers information, inspiration and provides support including assistance with veterinary expenses and supplies such as a Bailey chair to qualified dog owners. A private Facebook group with over 9,000 members offers real-time mentorship and opportunities to share experiences.

whom she named “Wabi-Sabi” after the Japanese philosophy of finding beauty in imperfection, was malnourished and smaller than his littermates.

Moffat took Wabi-Sabi to the veterinarian, who took barium radiographs of the esophagus. Liquid barium, a metallic compound that shows up on radiographs, appears as a bright ball in the stomach of normal puppies. In puppies with megaesophagus, the barium may pool and balloon at the LES. In some affected puppies, the barium stops midway down the esophagus due to a constricting ring anomaly of the blood vessels of the heart known as persistent right aortic arch. These cases require surgical treatment.

The radiographs taken of Wabi-Sabi’s esophagus showed the barium stopping at the LES, confirming a diagnosis of megaesophagus. Left untreated, puppies like Wabi-Sabi often die from malnutrition or pneumonia secondary to aspirating regurgitated food. Prognosis for resolution of congenital megaesophagus in puppies traditionally is 20 to 40 percent. If puppies receive proper nutrition and care, some outgrow the condition.

NOVEL TREATMENT FOR MEGAESOPHAGUS

Medical management of megaesophagus is challenging. Medications that are effective in stimulating esophageal movement in humans

A GENETIC STUDY OF MEGAESOPHAGUS IN GREAT DANES

The genetic cause(s) of congenital idiopathic megaesophagus (CIM) likely varies on a breed-by-breed basis. Geneticist Leigh Anne Clark, PhD, associate professor at Clemson University, has been studying the disorder in Great Danes and German Shepherd Dogs.

“The genetic complexity of megaesophagus relates to some risk factors that may be shared across breeds and other factors may be unique to a breed,” Dr. Clark says.

Dr. Clark is the lead investigator of research to identify genetic risk factors contributing to gastrointestinal motility disorders in Great Danes. The [two-year study](#), funded by the AKC Canine Health Foundation and sponsored by the Great Dane Club of America Charitable Trust, aims to determine if there is a genetic link between CIM and gastric dilatation-volvulus (GDV), or bloat.

Based on her earlier work in Great Danes, Dr. Clark is studying a narrow region of chromosome 6 that was shown to be a risk factor for CIM. Meanwhile, she is searching for additional genomic regions that contribute to CIM to determine if there is an association between CIM and GDV due to shared genetic risk factors impacting gastrointestinal motility.

CIM is an esophageal disorder in which poor contractility causes enlargement of the esophagus. GDV is characterized by gas filling the stomach like a balloon — gastric dilatation — and then twisting 180 degrees clockwise cutting off an escape for the gas through the esophagus or duodenum — gastric dilatation-volvulus.

Dr. Clark is generating genetic profiles from Great Danes using a new genetic processing technology called low-pass whole genome sequencing (LP-WGS). The three-step process starts with LP-WGS followed by imputing missing data and then conducting genome-wide association analyses with millions of genetic variants.

“We’ve performed the low-pass sequencing on 83 Great Danes,” she says. “This process produces a large amount of data that will take us closer to the causal mutation.”

The findings in Great Dane also are being compared with Dr. Clark’s earlier work in German Shepherd Dogs showing an association between megaesophagus and a region of chromosome 12.

Great Dane breeders and owners are encouraged to help advance the research. For more information about participating in the study, contact [Sarah Murphy](#) at Clemson University. Note that DNA samples are needed from:

- Dogs greater than 5 years of age with no history of megaesophagus or bloat, as well as no known relatives (parents, littermates or offspring) diagnosed with megaesophagus or bloat. Priority is given to dogs that have not had prophylactic gastropexy.
- Dogs that have survived a bloat episode.
- Dogs that have been diagnosed with idiopathic megaesophagus, not due to persistent right aortic arch (PRAA), as a puppy via a barium radiograph or other X-ray method.

are not effective in dogs because the canine esophagus is made of striated muscle rather than smooth muscle as in humans. Similarly, medications used to treat acid reflux or vomiting are not effective as they stimulate the LES to remain closed.

Owners of affected puppies turn to feeding their dog in an upright position so gravity can help push the food downward. Special feeding chairs, called [Bailey chairs](#), can be fitted to an individual dog. After completing a meal, a dog stays in the chair for about 10 to 20 minutes, though sometimes even this doesn’t work.

“In many dogs with megaesophagus, the LES does not open at the appropriate time or sufficiency,” Dr.

Haines explains. “Even with upright feedings, food is retained within the esophagus that is later regurgitated.”

Breeders may choose to euthanize affected puppies rather than face an uncertain survival. That’s what Moffat did 33 years ago. “I had a necropsy done on an affected puppy,” she says. “His esophagus looked like a bag full of food that took up his entire chest.”

Moffat had hope that a new treatment could potentially help Wabi-Sabi. “I had heard there was a new treatment and told my veterinarian I wanted to try using sildenafil (Viagra®),” she says. “She looked at me like I had two heads. I went home and forwarded the research article to her. After looking into it, she agreed we should try it.”

Published in *Veterinary Record* in April 2017, a clinical trial performed by researchers at the University of Parma in Italy showed successful treatment of puppies with oral sildenafil citrate. Their study included 21 puppies, the majority of which were Great Danes, with congenital megaesophagus.

Ranging from 22 to 45 days of age, the puppies were randomly assigned to a group that received two times a day a sildenafil liquid mixture at a rate of 1 milligram per kilogram (0.45 milligram per pound) or a placebo. All puppies were held in an upright position for 10 minutes following each feeding.

“We thought that sildenafil might be effective by relaxing the lower esophageal sphincter smooth muscle,” explains lead researcher Alessandro Menozzi, DVM, PhD, associate professor of veterinary pharmacology and toxicology at the University of Parma. “This could facilitate the passage of food into the stomach and relieve the pressure on the esophageal wall.”

The results were immediate. “The number of regurgitation episodes were notably decreased in puppies of the sildenafil treatment group after the first dose,” Dr. Menozzi says. “Regurgitation episodes ceased almost completely after 10 days of sildenafil administration, and no relapses were observed up to one month after the end of the treatment. The puppies without sildenafil continued to regurgitate, though the rate of regurgitation gradually decreased.”

The puppies receiving sildenafil also gained significantly more weight. Radiographs of their esophagus taken at the start and finish of the study showed that the esophageal diameter had narrowed significantly; in contrast, the esophageal diameter had grown even larger in the placebo group puppies. No side effects of sildenafil were noted.

“Fortunately, all the enrolled puppies fully recovered after the end of the clinical trial and no longer needed any further treatment,” Dr. Menozzi says. “Thirty days after the conclusion of the trial those in the sildenafil group had only sporadic regurgitation episodes, and after two to three months, they were completely healthy.

“Congenital idiopathic megaesophagus is probably related to delayed development of neurons controlling the motility of the esophagus, thus affected puppies have a good chance to fully recover over time. Sildenafil treatment has the goal of improving the clinical signs and hastening the recovery. It also minimizes the risk of aspiration pneumonia, the main cause of death in these puppies together with euthanasia.”

NEW OUTLOOK FOR AFFECTED PUPPIES

Unlike the reduced episodes of regurgitation seen immediately in the treated puppies at the University of Parma, Moffat did not see quick results



At 10 months of age, Wabi-Sabi, right, had caught up in size to his littermates, including his sister, “Phaedra.”

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with Wabi-Sabi. "This may have been because he was treated with a tablet form of sildenafil," she says.

"The biggest variable affecting the success of sildenafil is its ability to get the drug into the stomach for absorption," explains Dr. Haines. "Just like food and water can get retained in the esophagus, so can the medication."

A [recent study at Washington State](#) (see Abstract G104) found short-term success giving dogs with megaesophagus liquid sildenafil. "We found that giving liquid sildenafil diluted to a 5-milliliter volume in an upright position followed by a meal resulted in good delivery of the drug into the stomach," Dr. Haines says.

"The liquid sildenafil moved to just above the LES or directly into the stomach in a small number of dogs. When a meal was given, the LES relaxed to move the liquid through to the stomach though not enough

to allow the meal through. Once the sildenafil is in the stomach, it can begin working to relax the LES."

Dr. Haines speculates that the timing of dosing is linked to success. The Italian study used twice-daily dosing based on published studies in humans and cats. "Dogs with megaesophagus may eat many meals a day," she says. "The sildenafil would therefore only be effective for two of the meals."

After changing to a liquid mixture of sildenafil and giving it three times a day right before meals, Moffat began to see improvement in Wabi-Sabi. "The nighttime regurgitation continued for a few weeks before it resolved, but the daytime regurgitation pretty much stopped," she says. "He began to gain weight, and by 8 1/2 weeks of age, he was almost caught up to his littermates."

At age 4 months, Wabi Sabi was doing well. "When I was sure he was stable, I let him go to a home," Moffat



As an adult dog, Wabi-Sabi, renamed "Cos" by his new owner, no longer needs medications or special feeding accommodations for megaesophagus.

says. “At that time, he was still getting sildenafil and was eating from an elevated feeder.”

Wabi Sabi — now called “Cos” (Sterling’s Wabi-Sabi v. Bgdawgs) — appears healthy. “His new owner had him radiographed at 7 months of age and his esophagus was normal so she weaned him off the sildenafil,” says Moffat. “At 1 year, he was radiographed because he ate a sock and was still normal. He is now 3 years old and lives a normal life with no medications or special feeding accommodations.”

Although sildenafil is still in the early stages of research, it may not be a cure-all for congenital megaesophagus. “Sildenafil is likely most effective in dogs with moderate disease severity and less retention of food material,” Dr. Haines says. “Dogs that have severe disease are often retaining a lot of food and liquid in the esophagus. This material blocks the sildenafil from reaching the stomach to be effective. However, I have still seen improvement in these dogs with longer term use.”

Dr. Haines became interested in megaesophagus as a veterinary resident when she adopted a mixed-breed dog with the condition. “Every dog with this disease is different,” she says. “What works for one dog may not work at all for another. Owners should work with their veterinarian to find the best treatment for their dog.”

She also advocates optimism. “Many dogs recover and go on to live full lives with megaesophagus. During an initial diagnosis, dogs may be feeling their worst and likely a feeding plan has not yet been developed. I encourage owners to stay positive during this first phase. With some time and consistent care, dogs will hopefully improve.”

Dr. Haines should know. “When I got ‘Cake,’ we still thought of megaesoph-



agus as a death sentence. I figured I was giving her a loving home for the last few months of her life. However, that was not Cake’s plan. She was a fighter, so I decided to fight with her. The entire hospital rallied around us, and Cake thrived,” she says. “Cake lived eight great years with the disease before passing away in 2020 from cancer.”

Although there is much to learn about effective treatments for dogs with congenital megaesophagus, sildenafil provides a promising possibility. ■

Purina appreciates the support of the Great Dane Club of America, particularly Dr. Daryl Pitts and Dr. Neil O’Sullivan, co-chairs of the GDCA Health and Research Committee, in helping to identify topics for the *Great Dane Update*.

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