

**Dog Tips** 

# New: A Promising Treatment for Often-Fatal Eating Disorder

This swallowing disorder can lead to regurgitation, aspiration pneumonia, failure to thrive, and tragically, euthanasia in many cases, so any hope for an effective treatment is welcome news. Researchers have found a surprising treatment to help dogs successfully outgrow the condition.

#### Analysis by <u>Dr. Karen Shaw Becker</u>

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#### STORY AT-A-GLANCE

- Megaesophagus (ME) is a potentially fatal swallowing disorder in dogs that inhibits the movement of food and water into the stomach, resulting in regurgitation, aspiration pneumonia, and failure to thrive
- Congenital megaesophagus, which is present at birth, most often reveals itself when a puppy is weaned to solid foods at about four weeks of age; acquired megaesophagus usually occurs in older pets and is almost always secondary to another condition
- Recently, researchers at Clemson University uncovered a genetic variation linked to development of congenital ME in German Shepherd dogs, a breed predisposed to the condition; they also developed a genetic test breeders can use to reduce the risk in future litters
- Also recently, researchers at Washington State University studied sildenafil (Viagra) as a treatment for ME, and found that dogs with moderate disease have better success on the drug than dogs with more severe symptoms
- In acquired megaesophagus, the underlying cause must be identified and treated, if possible, to cure or control the condition; however, in some cases, no cause for the disorder can be found

Megaesophagus (ME) is a swallowing disorder in dogs characterized by an enlarged esophagus that can't efficiently move food into the stomach, resulting in regurgitation, aspiration pneumonia, failure to thrive, and tragically, in many cases, euthanasia.

"The literature tells us that many dogs with the disease die from aspiration pneumonia or are humanely euthanized due to poor quality of life within eight months of diagnosis," says Dr. Jillian Haines, a veterinarian at Washington State University.<sup>1</sup>

The good news, which I'll share shortly, is that recent research conducted by Haines and colleagues has uncovered a promising treatment for this often-fatal eating disorder.

# **Congenital Megaesophagus Shows Itself Very Early**

Megaesophagus can be congenital or acquired, but the congenital form is much more common. Congenital idiopathic megaesophagus (CIM) most often reveals itself when a puppy is weaned from mother's milk to solid foods at about four weeks of age.

A 2022 Clemson University study uncovered a genetic variation linked to the disorder in German Shepherd Dogs, a breed predisposed to the congenital (from birth) idiopathic (no known cause) form of the disease. Their findings were published in PLOS Genetics.<sup>2</sup>

Other breeds predisposed to megaesophagus include the Fox Terrier, Great Dane, Irish Setter, Labrador Retriever, Dachshund, Miniature Schnauzer, Newfoundland, and the Shar-pei. Researchers don't yet know if the same genetic variation present in the German Shepherd is what causes the disease in other breeds. According to Sarah Bell, lead author of the Clemson study:

"They don't have swallowing activity. When the puppies swallow food, it just sits in their esophagus and doesn't trigger those sequential contractions that normally occur to help push the food into the stomach. Because a dog's esophagus is horizontal instead of vertical like ours, gravity doesn't aid the transportation of food into the stomach."

Puppies with megaesophagus must be fed sitting upright in a sort of doggy highchair (called a **Bailey chair**) so that food and water makes it into their stomachs, and they must remain in the chair for up to 30 minutes after finishing their meal.

Thankfully, some pups outgrow the condition, but many others require lifelong symptom management involving upright feedings, small liquid meals given several times a day, gelatin cubes, and medication.

As part of the study, researcher Leigh Ann Clark, an associate professor in Clemson's Department of Genetics and Biochemistry and colleagues developed a genetic test for the disease that German shepherd breeders can use to reduce the risk that future litters will develop the condition.

# Male Puppies Twice as Likely to Develop the Condition

The Clemson team performed a genome-wide scan to identify genes associated with the disorder and discovered an association on canine chromosome 12 with a variant within melanin concentrating hormone receptor 2 (MCHR2), which influences appetite, weight, and the way in which food moves through the gastrointestinal (GI) tract. The researchers suspect an imbalance of melanin-concentrating hormones plays a role in CIM.

The study also showed that male puppies are at twice the risk of females for developing the disease, perhaps because higher estrogen levels allow food to pass to the stomach more efficiently.

"What they've found in people is that estrogen has the effect of relaxing the sphincter that connects the esophagus to the stomach," explained Bell. "By having more estrogen, the smooth muscle there is naturally more likely to open. This increases the motility of food into the stomach."

According to the Clemson researchers, the presence of the MCHR2 variant coupled with the dog's sex can predict whether a puppy will develop a megaesophagus with 75% accuracy. Owners can swab their dog's gums and submit the sample to genetic testing companies to learn which variant(s) their dog inherited, and breeders can use the test to reduce the number of pups born with the disease while preserving genetic diversity.

### **Promising Treatment for Megaesophagus Discovered**

Sildenafil is the generic name for the active ingredient in Viagra. Researchers at Washington State University's College of Veterinary Medicine discovered that liquid sildenafil relaxes the smooth muscle of the lower esophagus, allowing it to open to let food pass to the stomach. Besides some rare gastrointestinal (GI) irritation, no side effects were observed in dogs given the dose used in the study.<sup>4</sup>

According to Clark at Clemson, sildenafil increases the number of dogs who successfully outgrow CIM and no longer need a Bailey chair. While sildenafil is most well-known as a treatment for erectile dysfunction, it's also used to treat high pulmonary blood pressure in both humans and dogs.

"If you look at the literature, there are no drugs we can use to manage megaesophagus. Sildenafil is the first to target these mechanisms and reduce regurgitation, which is big because that's what ultimately kills these dogs," said WSU's Haines.

"It opens the lower esophageal sphincter for 20 minutes to an hour, which works really well for dogs because we only want that to open when they are eating." <sup>5</sup>

## **Dogs With Moderate Disease Do Best With Sildenafil**

The WSU team used video fluoroscopy (a moving x-ray) to monitor first liquid, and later, blended wet food as it traveled down the esophagus of study participants. Ten dogs with megaesophagus were involved in the research. They were given either a placebo or sildenafil for two weeks, then no drug for a week, then the drug they weren't given in the first two weeks for another two weeks.

The dogs' owners kept a record of regurgitation episodes, without knowing whether their pet was taking the test drug or placebo. Interestingly, while the researchers noted no significant difference between the two drugs during the 30-minute video fluoroscopy, 9 out of the 10 owners reported reduced regurgitation during the two weeks their dog received liquid sildenafil.

"In many cases, the owners were able to figure out which drug was sildenafil because it was working," Haines said.

The dogs also gained an average of a little more than 2 pounds by the study's end.

"Moderately affected dogs that were regurgitating frequently but not excessively seemed to see the most dramatic results," Haines said. "I actually prescribed sildenafil to several of those patients after the study, and they are still using it today."

Unfortunately, dogs with severe megaesophagus symptoms showed less positive results, probably because it was harder to get the drug into their stomachs for absorption.

"I think sildenafil will be life-changing and lifesaving for a lot of dogs," Haines said. "This research helps support its use and hopefully will encourage more people to use it."

## **Potential Causes of Acquired Megaesophagus**

As I mentioned earlier, megaesophagus can be congenital or acquired. The acquired form usually occurs in older pets and is almost always secondary to certain other conditions including autoimmune neuromuscular disease (myasthenia gravis), Addison's disease, and hypothyroidism. It can also be caused by a problem in the esophagus like a foreign body, inflammation, or a tumor, as well as by exposure to toxins including organophosphates.

In acquired megaesophagus, it's crucial that an underlying cause be identified and treated, if possible, in order to cure or control the condition. In some cases, no cause for the disorder can be found and it's determined to be idiopathic.

A few years ago in Australia, over 100 dogs fed Advance Dermocare dog food by Mars developed megaesophagus. To my knowledge, no causal link between the food and the disease was established, but as it turned out, a similar problem had occurred earlier in Latvia with a different dog food, and it was discovered that many dogs from around the world had been affected by this strange condition linked to ultraprocessed kibble.<sup>6</sup>

Based on what I know about how dry pet food is manufactured, it's possible an unknown toxic byproduct of the extrusion process is the culprit. For example, we know that advanced glycation end-products (AGEs) are a byproduct of processed pet food. AGEs are compounds that form as the result of what is known as the Maillard reaction.

When heat-processed proteins join with carbohydrates, the biochemical result is a compound that can cause widespread inflammation and damage in the body.

Advanced glycation end-products have been extensively studied in humans and have been shown to exacerbate diabetes and interfere with kidney function. AGEs have also been linked to aging, Alzheimer's disease, cancer and more recently, neurologic disease such as intervertebral disc disease and autoimmune diseases.<sup>7</sup>

Since acquired megaesophagus is often immune-mediated, a second possibility I've pondered is that something in the suspect foods triggers an overwhelming immune response that ultimately targets the esophagus. It seems to me that if there isn't an immune component, then a potential unidentified neuromuscular toxin in the food may be a culprit.

# **Treatment and Supportive Care**

If the megaesophagus is acquired and secondary to an underlying disease, that problem must be identified and resolved if possible.

In cases of congenital or acquired idiopathic megaesophagus, treatment is focused on symptom management and supportive care. There are a few drugs that are sometimes used in pets with megaesophagus, depending on the cause, but they aren't always effective.

Natural support is chosen by integrative or functional medicine vets depending on the root cause (immune-mediated ME is treated differently than organophosate exposure).

Eating and drinking obviously pose the biggest threat to pets with megaesophagus, because these are the activities that prompt episodes of regurgitation, which is what leads to lack of nutrients and aspiration pneumonia.

Pets with megaesophagus tend to do better with small, frequent meals fed by hand, with the head in an elevated position. With the body elevated, which means in a vertical position, gravity can do some of what the esophagus isn't doing.

Many owners of dogs with megaesophagus encourage their dogs to hold a sit position for 10 minutes after eating or drinking anything, to allow the food and water to eventually reach the stomach with the effect of gravity. As mentioned earlier, others use a Bailey chair.

Many veterinarians also recommend thickening agents be added to water to reduce the likelihood of recurrent aspiration episodes. Finding the best form of food to feed and method for feeding it is usually mastered through trial and error.

"We're learning to manage the disease, and we're adding on, in many cases, years to the time these animals get to spend here with their owners," says Haines.<sup>8</sup>

Managing a dog with megaesophagus is obviously time-consuming. But with the proper care, many pets live relatively normal lives with a disorder that used to be fatal in most cases.

#### **Sources and References**

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- <sup>7</sup> Shen, C. et al. Molecules 2020, 25(23), 5591
- <sup>8</sup> WSU Insider November 21, 2021