PURINA PRO PLAN

GREAT DANE Update

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Genetic & Gut Bacteria Link to Bloat in Great Danes

LEADS TO RISK ASSOCIATION TEST

Bloat Genetic Test Available for Great Danes

Breeders and owners of Great Danes can learn whether their dog carries a high-risk gene variant, or allele, predisposing them to developing gastric dilatation-volvulus, or bloat. Based on groundbreaking research at the Fred Hutchinson Cancer Research Center, the test identifies seven mutations in three different genes containing risk alleles associated with bloat.

Available through VetGen, a veterinary genetic disease research and detection service for purebred animals in Ann Arbor, Michigan, the test costs $65. For more information, you may call 800-483-8436 or 734-669-8440 or email vetgen@vetgen.com.

Great Dane breeder Nikki Riggsbee of Valrico, Florida, knows about bloat. She recognizes the signs of the life-threatening condition and understands the urgency of getting a dog that is bloating to a veterinarian for emergency care.

Late one night her 5-year-old female show champion fawn Dane, "Cecelia" (CH McEmn's High Maintenance Woman), began dry heaving, a telltale sign of bloat. "The signs are very consistent," says Riggsbee, who has bred Danes under the McEmn prefix since 1980. "They have dry heaves and bring up white foam and yellow stringy mucous. Their abdomen feels tight and hard."

Knowing time was of the essence, Riggsbee rushed Cecelia to an emergency veterinarian 45 minutes away, bypassing two clinics on the way to get to one where there was a veterinarian experienced in treating bloat. "Recognition, quick action and access to an experienced veterinarian is required for survival," she says. "You

CH McEmn's High Maintenance Woman ("Cecelia") bloated when she was 5 years old. After a gastropexy, or stomach-tacking procedure, was performed during emergency surgery, she lived a long, healthy life.

need to find a veterinarian long before you need one."

Cecelia was stabilized and treated for shock. She was given intravenous fluids and a tube was inserted into her mouth going to her stomach to relieve the pressure from the gas. The Great Dane was then taken to surgery, where her stomach was untwisted and checked for dead tissue, which can occur when the blood supply is cut off, and for blood clots in her spleen. Fortunately, Cecelia's stomach tissues and abdominal organs were healthy.

A gastropexy was performed as part of the emergency bloat surgery. The procedure involves tacking the stomach to the right side of the abdominal wall to prevent the stomach from shifting or twisting in the future. Riggsbee was able to take Cecelia home several hours later.

Gastric dilatation-volvulus (GDV), more commonly known as bloat, is a disorder affecting large- and giant-sized, deep-chested dogs. Gastric dilatation is when the stomach fills like a balloon with gas, and gastric dilatation with volvulus is when the gas-filled stomach twists 180 degrees clockwise on its side, cutting off any escape for the gas through the esophagus or duodenum.

GDV happens so fast that dogs can die within two hours of the first signs. As the gas builds in the stomach, a dog becomes increasingly uncomfortable. Signs include pacing, panting, retching unsuccessfully, and standing with a hunched back. Clinical signs include a distended abdomen, pale gums, and a weak, rapid pulse. Shock may occur when the vena cava, the large vein carrying deoxygenated blood back into the heart, becomes blocked from the stomach's twisting.

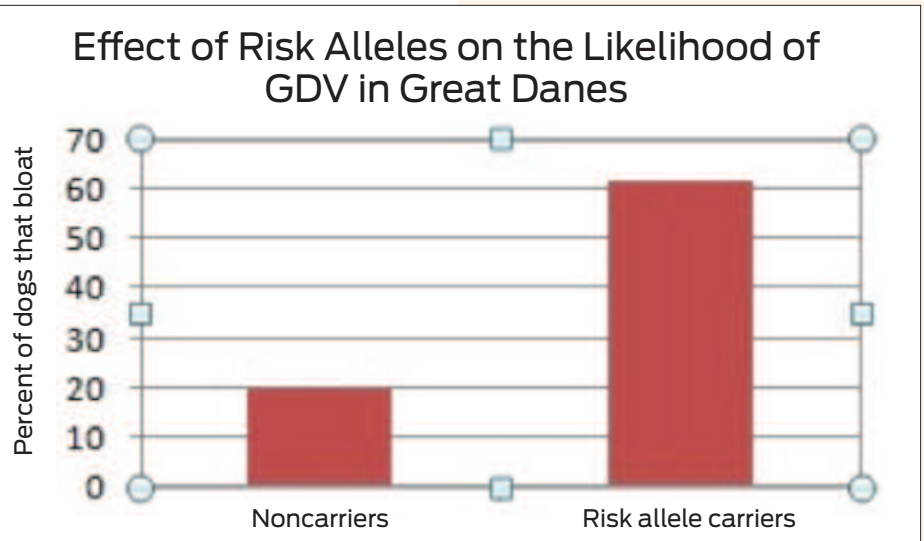
Great Danes have the highest risk of bloat of any breed, with an estimated 37 percent experiencing GDV during their lifetime. The majority die without emergency veterinary care. Although GDV has been recognized in dogs for more than 100 years, little is known about what causes it.

Among the theories about what causes bloat, owners historically have suspected their dogs gulp atmospheric air when eating. A study published in 2013 in the *Journal of Veterinary Internal Medicine* found otherwise. The researchers examined the stomach gas of 10 dogs admitted to an emergency clinic for GDV surgery and concluded the gas is due to bacterial fermentation similar to the fermentative bloat that occurs in cattle. In an earlier study, these researchers showed that the stomach contents of a dog with GDV continue to expand and bubble in a plastic container until the top pops off.

Groundbreaking research at the Fred Hutchinson Cancer Research Center in Seattle has found a genetic link to bloat in Great Danes that is believed to predispose them to developing GDV by causing an imbalance in the bacterial population of their gut. The study will be published later this year in the *American Journal of Veterinary Research*. The AKC (American Kennel Club) Canine Health Foundation contributed to funding that supported the genetic portion of the study.

Understanding High-Risk Alleles

The research has provided insights indicating that the imbalance, or dysbiosis, believed to occur in the gut microbiome of Great Danes that have bloated is caused by specific genes in the major



The lifetime risk of bloat in Great Danes is 62 percent for dogs that carry one or more of three identified risk alleles compared to 20 percent for dogs that do not carry a risk allele.

histocompatibility complex (MHC). This complex helps a dog's immune system distinguish itself from pathogenic bacteria and viruses and protects beneficial bacteria in the gut from being targeted for destruction. Bloat is a complex disease. Although a dog may be genetically predisposed to developing GDV, nongenetic factors also contribute to whether a dog actually bloats.

"We found a report indicating a strong correlation between inflammatory bowel disease (IBD) and bloat," explains lead investigator Michael A. Harkey, PhD. "This suggested to us a preexisting condition in the gut contributes to bloat. Since IBD is linked to immune system genes, it seemed logical that risk genes causing this gut imbalance lead to chronic low-level IBD. We hypothesized that these coexisting conditions may have the same root cause."

The Great Dane study involved looking at a group of dogs that have survived bloat through surgical intervention and a control group that never bloated. The researchers sequenced five immune genes from each dog looking for genetic variations associated with bloat. They determined that three gene variants, or alleles, contribute to bloat in Danes, and dogs carrying at least one of the risk alleles had a threefold higher risk of developing bloat than those that do not carry a risk allele.

"Sixty-two percent of Danes carrying a risk allele had to undergo emergency surgery to survive a bloat episode," says Dr. Harkey. "Potentially, this information will help breeders and owners trying to decide if their dogs should have gastropexy surgery or if dogs should be bred. Our ultimate goal is to develop diagnostic and therapeutic strategies to minimize the occurrence of bloat."

The study yielded significant evidence showing that the MHC genes DLA88 and DRB1 play a role in predisposing a dog to bloat. A recently discovered variant of the DLA88 gene, called 05101, was found to be three times more frequent in Danes that bloated than in those that had not bloated. Another DLA88 variant, known

as 1001, shows up seven times more often in healthy control dogs than in the bloat group, thus it is believed to have a protective effect against bloat. Related to the DRB1 gene, the 1201 variant shows up in dogs that have bloated two times more than in control dogs.

"These alleles cannot be considered as the only cause of bloat," Dr. Harkey emphasizes. "Rather, we think they predispose a dog to bloat, and that this dog is more likely to react to environmental, emotional or dietary triggers. There also may be other genes that act in concert with these risk alleles to produce bloat."

> "We expect that bloat is caused by an accumulation of several gene variants that together create a predisposition to bloat."
>
> Michael A. Harkey, PhD, of the Fred Hutchinson Cancer Research Center

Analyzing the Gut Microbiome

The two-part study included an analysis of the gut microbiome, or the gut bacterial population, of each dog using rapid sequencing of bacterial DNA from stool samples to identify and quantify the thousands of species of bacteria in the gut. Led by Meredith Hullar, PhD, the goal was to identify bacterial species that were unusually high or low in the Danes that bloated compared to the ones that did not bloat.

"We detected profound changes in the composition of the microbiome of Danes that survived bloat," says Dr. Hullar. "For example, the two most abundant phyla of bacteria in the gut microbiome, *Bacteroidetes* drops and *Firmicutes* increases in dogs that have bloated. Since these two phyla account for over 70 percent of the bacteria in the gut, this is a change that could have significant effects on health and potentially cause bloat."

Additionally, the link between a dog's genes and dietary fiber intake was found to cause an altered metabolism potentially associated with GDV. "We found that dogs with GDV have a significantly lower intake of dietary fiber than non-GDV control dogs," Dr. Hullar explains. "Our findings suggest a diet containing more complex fiber may provide some preventive measures against GDV. At the moment, we cannot say 'how much' fiber is important."

If future studies show that interventions such as probiotics or a high-fiber diet help rebalance the gut microbiome, these potentially could help prevent bloat and block the genetic predisposition to bloat. "There is much yet to learn," Dr. Hullar says. "We know that changes in the bacterial population of the gut microbiome can have serious effects on health."

Hoping for Therapeutic Results

Although the researchers say they have just scratched the surface in understanding bloat, their work already has produced a genetic tool for Great Dane breeders and owners to use to screen their dogs to determine whether they are at risk for bloat. As the research continues, therapeutic answers may result, which could lead to preventives for dogs that carry the disease genes.

"We chose to initiate this study with Great Danes because of their extremely high incidence of bloat," Dr. Harkey says. "It is important to note that the genetic links found so far do not fully account for all dogs that bloated in this study. We expect that bloat is caused by an accumulation of several gene variants that together create a predisposition to bloat."

As for Cecelia, Riggsbee's female Great Dane who bloated late in the night, though she was one of an estimated 37 percent of Danes that experience bloat, the emergency surgery and preventive gastropexy procedure ensured she did not bloat again. ■

Purina appreciates the support of the Great Dane Club of America and particularly Neil O'Sullivan, PhD, chair of the GDCA Health and Research Committee, in helping to identify topics for the *Purina Pro Plan Great Dane Update* newsletter.

Purina Pro Plan Incorporates NATURAL Formulas Into Existing Platforms

Purina Pro Plan is integrating existing NATURAL formulas, as well as adding new formulas, to the already strong FOCUS, *SPORT* and *SAVOR* platforms. Containing no artificial colors, flavors or preservatives and no poultry byproduct meal, the formulas are made without corn, wheat or soy, and include grain-free options. Additionally, two new formulas made without corn, wheat, soy, artificial colors or flavors, or poultry byproduct meal will be added to the BRIGHT MIND platform. Look for the formulas this summer.

LEARN MORE

Handlers stack Standard Poodles during judging at the Poodle Club of America National Specialty in April at the Purina Event Center in Gray Summit, Missouri.

Purina Event Center Adds Amenities

Record-setting entries at the Poodle Club of America National Specialty, held in April at the Purina Event Center in Gray Summit, Missouri, helped confirm to club officials that holding the event in the Midwest after many years in the East was a good move. Recent upgrades to the classy dog show venue include improved cellphone reception, expanded Internet service to support live streaming, and an enhanced Wi-Fi connection with increased bandwith that allows for easy photo and video sharing on social media. Video monitors throughout the facility allow exhibitors to watch the action in the show rings in real time. Located about an hour from St. Louis, the Purina Event Center, which was custom built to support the dog fancy, opened in 2010.

TAKE A VIDEO TOUR

Upcoming Events

Check out upcoming Purina-sponsored show and sporting events at venues across the country. These events are great opportunities to meet dog enthusiasts, canine experts and Purina representatives who can answer questions about *Purina Pro Plan* dog food and *Purina Pro Club*.

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