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PURINA Pro Club

Great Dane Update

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Scientists Hope to Study Addison's Disease in Great Danes

Though Great Danes are not among the breeds generally identified as having a genetic condition known as Addison's disease, scientists hope to learn more about its prevalence in the breed in a study in which the Great Dane Club of America currently is helping to recruit volunteers.

Addison's disease — sometimes called the "Great Pretender" because it mimics many other illnesses — may occur suddenly and severely, or symptoms may wax and wane. Addison's disease is sometimes confused as inflammatory bowel disease, hepatic or liver disease, or acute kidney failure, says Anita Oberbauer, Ph.D., professor of animal science at the University of California-Davis and longtime researcher of Addison's disease.

Breeds more commonly known to have Addison's disease in their bloodlines include: Standard Poodles, Bearded Collies, Portugese Water Dogs, Leonburgers, Rottweilers, West Highland White Terriers, and Wheaten Terriers. The Health and Welfare Committee of the Great Dane Club of America (GDCA) hopes to gather enough participants to study the heritability of Addison's disease in Great Danes.

"There is an anecdotal sense that Addison's disease is a growing problem in the breed," says J.P. Yousha, chair of the GDCA Health and Welfare Committee. "In at least one article about the condition, Great Danes were listed among the top breeds that can develop Addison's. We hope to identify at least 50 related Great Danes with Addison's whose owners are willing to participate in a study to identify the gene that passes the disease from one generation to the next."

"It's important to note that information about breeders or owners who volunteer to be part of the study will be kept confidential through a numbering system," Yousha says.

Joining Ongoing Research

Yousha is sending information about potential study participants to Oberbauer at the University of California-Davis. Through Oberbauer's studies of Addision's disease in several breeds, she has discovered that the condition seems to be regulated by a single gene inherited in an autosomal recessive pattern.

"This means that for Addison's to be passed on, both the sire and dam have to carry a recessive gene for the disease," Oberbauer says. "If one parent is heterozygous — having one dominant and one recessive gene for the disease — and the other parent is homozygous recessive — carrying two recessive genes — 50 percent of the litter will be carriers of the disease. The other 50 percent will be homozygous recessive and have the disease themselves. In the case of two heterozygous parents, 25 percent of their offspring will be affected, 50 percent will be carriers, and 25 percent will be normal."

Oberbauer explains that it is important to study different breeds because a generalization cannot be made that the mutation for Addison's disease appears on the same gene in every breed of dog.

"It's believed that breeds derived from common ancestors typically show the same mutations," Oberbauer says. "So even if a mutation happened long ago, it comes down consistently through breeds. However, if you have a spontaneous mutation in the same gene but at a different location, a totally different pattern of inheritance can result."

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"Lola" Wins Best in Futurity

A 12—month-old, fawn-colored-black mask Great Dane named "Lola" (Rojon's Keepsake) was the winner of the 2003 Best in Futurity at the Great Dane Club of America's National Specialty in October in Orlando, Fla. Lola was bred by Paula Heller of Dadeville, Ala., and Ray Cataldi Jr. of Round Lake, Ill., and is owned by Nancy Welsh of Pittsburgh, Pa., and handled by Cataldi. She was among 315 Great Danes competing for Best in Futurity.

Lola, winner of the 2003 Great Dane Club of America's Best in Futurity, poses with, from left, Purina Area Manager Carol Grossman, Futurity judge Nancy Lerch, co-breeder and handler Ray Cataldi Jr., and former GDCA president Robert Edison.

Whelped Sept. 23, 2002, Lola is one of eight puppies in her litter, four of which are being shown in conformation. The breeding was out of Heller's dam, CH Rojon's Romantique, and sired by CH Sarmac's I've Arrived. Describing the Futurity winner, Welsh says, "Lola is outgoing, alert and interested in everything."

As the breed club's Futurity winner, Lola also took home the *Purina Pro Plan* Futurity Alliance trophy. Offered in select AKC national parent breed clubs, the Futurity Alliance awards funding to the Great Dane Club of America based on the number of futurity-nominated litters and puppies. Additional funding is provided for puppies that ultimately earn conformation championship titles. The program is intended to support breeders who take part in the breed club's Futurity competition. The funding supports the club's health research and education endeavors. ■

Addison's Disease

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The goal of her research is to find a genetic marker for Addison's disease in each breed, Oberbauer says. These discoveries will facilitate development of DNA tests, which will enable breeders to make informed decisions. Ultimately, carrier dogs could be bred to clear dogs without producing affected puppies, and testing of offspring would allow breeders to retain clear puppies in their breeding program.

Understanding Addison's Disease

Addison's disease is the common name for hypoadrenocorticism or adrenal insufficiency. Adrenal glands sit on top of the kidneys where they secrete hormones directly into the bloodstream. Each gland has two distinct parts. The outer region, or adrenal cortex, secretes corticosteroid hormones, which have important effects on a dog's metabolism, blood chemistry, coat and body shape. The inner region, or adrenal medulla, is part of the sympathetic nervous system, the body's first response and defense against physical and emotional stress, Oberbauer says.

Addison's disease occurs when the adrenal cortex produces insufficient amounts of the corticosteroid hormones cortisol and aldosterone. Cortisol regulates a number of physiological processes, including metabolism, regulating stress, reproduction and the immune system function, Oberbauer says. Aldosterone is important in regulating electrolyte levels in the blood.

Three types of Addison's disease are recognized: primary, atypical and secondary, she says. Primary and atypical are most likely caused by immune-related damage to the adrenal glands. Secondary is caused by tumors, defects of the pituitary gland or long-term steroid use.

"Most dogs with the disease are diagnosed with primary Addison's, which means there is a slow degradation of the adrenal cortex over time," Oberbauer says. "Eventually, there is nothing left of the organ to produce cortisol and aldosterone. The dog's mineral balance and metabolism are disrupted, and that's why the symptoms are so diffuse."

Addison's disease can only be identified when an adrenocorticotropic hormone (ACTH) stimulation test is performed — which means if veterinarians don't test for Addison's, they won't find it.

"Testing puppies does not indicate whether they have Addison's disease," Oberbauer says. "Puppies with the disease may still be producing adequate levels of cortisol and aldosterone, but those levels will decrease over time."

Typically Addison's disease develops in a dog's "middle age," between the ages of 4 and 6, but it can appear in dogs as young as 1 year old or as old as 12 years old, Oberbauer says. "Most literature on the disease says Addison's occurs more often in females than males, but our studies have shown equal numbers of affected males and females in every breed we're studying."

A Case Study

Bobbie Palsa knows firsthand about Addison's disease in Great Danes. Her black Dane, Catherine, was diagnosed at the age of 3. "Catherine's first symptom was limping on her right hind leg," she says. "We thought perhaps she had bumped it in the yard or around the house. Then she started acting like she was weak in her hind end, and she would muscle herself up with her front end when she got up from lying down. Then one night she got up off an armchair, and her hind leg collapsed under her."

At first Catherine's veterinarian diagnosed early arthritis and prescribed Rimadyl. Her limp got better, but her appetite decreased. Within a week, she was eating nothing at all. "Our veterinarian ran blood work and a urine analysis, and the only element out of line was her potassium level, which was at the high end of normal," Palsa says. "Fortunately, he consulted with a colleague, Dr. Deborah Greco, who is a canine endocrinologist. She suggested he run the ACTH stimulation test. That gave him the diagnosis of Addison's disease."

Unlike other dogs with Addison's that take years to diagnose or those that die without ever being diagnosed, Catherine began receiving treatment just three weeks after her symptoms appeared. Even in that relatively short time, however, she went from weighing 126 pounds to 99 pounds. Because of gastrointestinal bleeding, she had to be given fluids and a drug to coat her stomach.

"To replace the hormones she wasn't producing, our veterinarian immediately put Catherine on a monthly hormone injection and a daily dose of prednisone," Palsa says. "She began feeling better almost immediately, and she continues in good health today. She's 7 years old, weighs 148 pounds and still plays like a puppy."

Managing Addison's Disease

Catherine's medication regimen is typical of those prescribed by veterinarians for dogs with Addison's disease. "Dogs with primary Addison's disease are generally treated with medicine that replaces the aldosterone that the body does not make," Oberbauer says. "Dog owners may either give their dog a daily oral medication, or their veterinarian may administer a monthly injection. Dosage and frequency is determined by body weight, and then adjusted by monitoring electrolyte levels. The initial adjustment period takes one to four months, followed by quarterly monitoring once the dosage is established."

Glucocorticoids, such as the prednisone Catherine was given, are prescribed to replace the cortisol. "Typically, a veterinarian will start a dog on a high dose, with a gradual reduction in the dosage as the dog stabilizes," Oberbauer says.

Both types of medication are given at doses to accommodate everyday stress. "Under unusually stressful situations, however, dogs with Addison's disease are unable to produce the extra cortisol provided by healthy adrenal glands," Oberbauer says. "During these times, a veterinarian may prescribe glucocorticoid supplementation. An owner's awareness of situations that trigger stress in their dog is vital so that stressors can be avoided, minimized or additional medication can be provided."

Research Opportunity

"It's true that the Great Dane breed has larger and more common health problems than Addison's disease, but we have an opportunity to work with Dr. Oberbauer to determine the prevalence of the condition in our breed and how the disease is inherited," Yousha says. "It's truly an opportunity to try to eliminate one more disease from our breed while contributing to the overall scientific knowledge about canine Addison's disease." ■

Study of Addison's Disease in Great Danes

The Great Dane Club of America is seeking Great Dane families in which at least one member has been diagnosed by a veterinarian as having Addison's disease.

The information provided may be used in a potential research study into the genetics and heritability of the disease in Great Danes. A minimal population of 50 affected dogs is necessary for the study at the University of California-Davis.

It is important that close relatives of Danes submitted to be part of the study are available to be included. Ideally, an owner or breeder will also be able to provide the health status of approximately five close family members (such as parents, siblings, offspring). Confidentiality is assured, as all dogs will be assigned numbers for the study.

If you have or know of owners of Great Danes that could help explore Addison's disease in the breed, please contact:

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