

Scientists Seek the Genetic Cause of Hereditary Myopathy (as seen in the July 2003 Purina Pro Club magazine)

More and more, veterinarians are seeing Labrador Retrievers with an inherited health condition that weakens the muscles, making it difficult for a dog to walk. Autosomal recessive muscular dystrophy (ARMD), or hereditary myopathy, begins in puppies and climaxes at about 1 year old.

A 1-year-old Labrador with ARMD may not be able to climb stairs or walk farther than a few dozen feet. After that, the condition seems to stabilize, and a dog may gradually improve. Though there is no cure for ARMD, a scientist at Auburn University is working to develop a genetic test to help identify carriers.

Pattern of Inheritance

To be affected with ARMD, a dog must have two abnormal genes - one from each parent. A dog with only one abnormal gene does not show signs but is a carrier that will pass the health condition on to its offspring if bred with another dog with the same abnormal gene.

"The carriers are the silent reservoir of the health condition and are usually far more frequent," says Bruce F. Smith, VMD, PhD, associate professor of pathobiology at Auburn University College of Veterinary Medicine and director of molecular medicine at Auburn's Scott-Ritchey Research Center. "We have no idea of the carrier rate for ARMD, but I suspect that it may be 10 percent or greater, especially among field trial Labradors. We mostly see field trial Labradors with ARMD, and in fact, we know of a few very popular and successful field trial dogs that were carriers and resulted in the spread of the gene to many offspring."

To illustrate how ARMD spreads, Smith cites the example of a popular stud-dog carrier: "If he has 150 breedings a season and averages six puppies per breeding, the dog would produce about 900 puppies a year. Of these, 50 percent would be carriers. If he is bred for eight years, he could produce about 3,600 carriers." As the number of carriers increase, the number of dogs affected with ARMD also is likely to increase.

A carrier dam can have a significant impact on future generations, too. "One female Labrador had multiple litters over her career," Smith recalls. "She had her first affected puppy in her last litter, most likely because the breeder had been very careful to stay away from stud dogs with ARMD in their bloodlines. Nevertheless, she produced many carriers, some of which had produced puppies themselves by the time she was determined to be a carrier."

ARMD has not been identified in any other breed, but a similar health condition occurs in humans, forming a family of conditions known as LimbGirdle muscular dystrophy. Some of the canine gene research has been based on what is known about LimbGirdle muscular dystrophy in humans.

Genetic Research

Finding the gene that causes ARMD has been the focus since 1997 of Smith and Kyle Braund, a now-retired neuropathologist at the Scott-Ritchey Center. Braund, was the principle investigator of a two-year study funded by the AKC Canine Health Foundation, Auburn University Veterinary Sports Medicine Program and the Scott-Ritchey Research Center.

The study aimed to narrow the genes responsible for triggering ARMD by assessing whether dogs with ARMD lack certain proteins similar to what occurs in dogs with X-linked Duchenne-like muscular dystrophy, another type of genetic muscular disorder. "We couldn't find any proteins that were missing," Smith says.

When Braund retired in 1998, Smith took over as principal investigator and began focusing on finding genes at the molecular level. "We identified the most likely target gene that might be involved in this health condition," Smith says. "We began by sequencing the target gene from a normal dog and then

started sequencing that of an affected dog. If the target gene ends up not being the correct gene, we will then assemble pedigrees to map the trait against the completed canine genome sequence when it is finished next year."

Signs of ARMD

Identifying ARMD can be challenging, says Smith, who owns a Labrador Retriever with ARMD. "Unfortunately, there is no reliable test for ARMD," he says. "Before an actual determination can be made, several other muscle conditions must be ruled out"

A dog with ARMD is "not normal in terms of its ability to exercise," Smith says. "These dogs cannot run distances and should not be overstimulated by games such as fetch." Exercise, cold weather and excitement can aggravate the condition.

Affected dogs may have infections of the skin, eyes and ears with bacteria, fungi or yeast, and difficulty swallowing due to mega-esophagus. Such infections indicate that the dogs' "immune systems may be partly suppressed," Smith says. "But all of these infections can be treated, and owners of these dogs quickly learn to catch these problems and treat them aggressively."

Treatment of ARMD largely involves managing signs of the condition. For the most severely affected dogs, which are likely to have difficulty swallowing, Smith suggests feeding a soft gruel made from high-quality commercial food. He also recommends keeping the dog warm and minimizing stress.

"It can be a struggle to keep weight on an affected dog in the first year or two," Smith says. "However, the dog can switch to hard kibbles once it seems to be maintaining its weight. As the dog ages, it is important to watch its weight and feed to ideal body condition, not too heavy and not too thin."

While an affected dog generally lives a normal life span, the way a dog lives may not be normal. "These are definitely special need dogs," Smith says. "They require owners who have time to care for them. A number of owners have managed to keep and care for affected dogs; however, having one of these dogs in the house is not for everyone." Caring for a dog with ARMD requires the owner to form an active partnership with the veterinarian and may entail working with a neurological specialist as well.

Optimistic Future

"Having firsthand knowledge about what it's like to care for a dog with ARMD has been very helpful in studying the health condition," Smith says. "Over the years we have seen ARMD go from being a very rare occurrence to becoming quite common. The increase in the frequency has put some urgency in our work."

Concerns about how ARMD will affect future generations of the AKC's most-registered breed prompts continued studies to find a genetic test that will enable breeders to identify Labrador Retrievers that are carriers and remove them from their breeding program before they breed puppies that are carriers, or worse, affected by ARMD

Signs of ARMO

A Labrador Retriever puppy that shows any of the following signs particularly if the puppy appears aggravated by the cold, excitement or exercise - should be evaluated by a veterinarian for ARMD:

- Physical weakness
- Deficient muscle mass, particularly in the head, shoulders and hips
- Abnormal posture, such as an arched back
- Abnormal movement, particularly a "bunny hop" gait in the hind legs.
- Exercise intolerance

Muscle Disorders in Labrador Retrievers

ARMD is just one of several hereditary muscular disorders in Labrador Retrievers. Here are the others:

Exercise-Induced Collapse: Found primarily in young adult field Labrador Retrievers, this condition is characterized by weakness and eventual collapse after 5 to 15 minutes of strenuous exercise. The weakness starts in the rear limbs but progresses quickly to the front legs, causing a dog to have a wobbly gait and eventual collapse. After a few minutes a dog can usually return to normal activities.

Malignant Hyperthermia: Also known as canine stress syndrome, malignant hyperthermia is a potentially life-threatening health condition that results in excessive muscle contraction and rising body temperature when a dog is under general anesthesia, is stressed or has exercised.

X-Linked Duchenne-like Muscular Dystrophy: A disorder passed by bitches to male puppies, this condition is found in several breeds, not just Labrador Retrievers. Signs appear as early as 6 weeks old and include progressive weakness, stiff gate and muscular atrophy.

Familial Reflex Myoclonus: A rare condition that causes young puppies to exhibit sporadic muscle spasms that can progress to muscle stiffness.