



Dachshund

Update

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Cord1-PRA Genetic Testing Recommended for Miniature Dachshunds

Almost as soon as Dawn DiBari brought “Sunshine” home, she knew something was wrong with the 4-year-old Miniature Long-haired Dachshund’s vision. The dog took a long time to focus his eyes, and he gravitated to the walls of rooms instead of the middle — sure signs he couldn’t see well.

“I was told he was shy, but I could tell by the way he looked at me there was a problem,” says DiBari of West Palm Beach, Fla. “If I went down to the floor instead of standing, it seemed he could see me and would respond.”

DiBari decided to have Sunshine tested for genetic eye disease. Less than a month after buying the Dachshund, DiBari learned that Sunshine has a gene mutation that puts him at risk for developing progressive retinal atrophy (PRA).

PRA is an inherited eye condition. Eight different forms of the disease have been discovered, but more are likely to exist. A progressive disease that usually leads to blindness, PRA affects both eyes simultaneously. Unfortunately, there is no treatment, no cure and no way to stop or reverse the damage.

The good news about PRA is that dogs adapt well, and the disease is painless. Since the disease generally progresses slowly, dogs are able to compensate for vision loss with their acute hearing and olfactory senses. Owners who keep furniture in fixed locations help their dogs stay mobile and independent.

Difficult to Distinguish

PRA has been diagnosed in Miniature and Standard Dachshunds of Smooth, Longhaired and Wirehaired varieties. The different sizes and coat varieties of the seventh most popular breed registered by the American Kennel Club complicate determining all forms and causes of PRA in Dachshunds.

Two forms of PRA are known to affect Dachshunds: cone-rod dystrophy 1-PRA (cord1-PRA) and cone-rod dystrophy PRA (crd-PRA). Gene mutations for both diseases have been discovered in recent years. A genetic test is available for cord1-PRA, and a test

for crd-PRA, already available in Europe, is expected soon in the United States.

Mutations in different genes cause the different forms of PRA — all which have similar clinical signs. The disease affects individual dogs differently; thus, even in dogs of the same bloodline with the same form of PRA, the age of onset and rate of disease progression can vary widely.

“Some dogs show signs of PRA in their first year, while others may not develop signs until later in life,” says Gregory M. Acland, B.V.Sc., DACVO, professor of medical genetics at Cornell University’s Baker Institute for Animal Health. “Some dogs die before the disease becomes evident, which accounts for why some owners unknowingly breed dogs with PRA. On the other hand, though the disease generally progresses slowly with loss of vision over years, some dogs go completely blind within months.”

Clinical signs of PRA include: dilated pupils, a glow from the back of the eyes, sticking close to an owner in dimly lit environments, slow movement, reluctance to go outside at night, and walking along the walls of a room rather than crossing through the center. Dogs also commonly stumble on steps and bump into objects.

There are no definitive statistics on the prevalence of PRA, but the disease is believed to affect several breeds of dog as well as mixed breeds and cats, says Acland, who has been studying PRA for decades. Some forms appear to be breed-specific, while others affect several breeds.

In Dachshunds, the genetic mutation

for cone-rod dystrophy 1-PRA was discovered by researchers at the Animal Health Trust in Suffolk, England. This form of PRA affects Miniature Long-haired Dachshunds — like Sunshine — as well as Miniature Smooth Dachshunds and English Springer Spaniels. The mutation was found in the RPGRIP1 gene, which codes for a key protein in photoreceptor cells.

The genetic test for cord1-PRA was developed in 2007 and is available through U.S. genetic test laboratories as well as the Animal Health Trust.

Cord1-PRA recently was also detected in Miniature Wirehaired Dachshunds via testing at VetGen veterinary genetics service in Ann Arbor, Mich. Crossbreeding between varieties contributes to the disease spreading to other varieties, says Robert Loechel, chief scientific officer at VetGen.

The mutation for cone-rod dystrophy PRA in Standard Wirehaired Dachshunds was discovered in 2008 by researchers at the Norwegian School of Veterinary Science in Oslo, Norway. A deletion in the gene nephronophthisis 4, also known as nephroretinin or NPHP4, results in a truncated protein that affects other proteins in the retina.

“The cord1-PRA and cone-rod dystrophy PRA vary considerably in the age of onset and rate of progression,” says Acland. “We believe it is possible there may be different forms of cord1-PRA. Although cord1-PRA is associated with the RPGRIP1 gene mutation, it is not necessarily caused

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Breeding Implications for Cord1-PRA* in Dachshunds			
	Normal/Clear	Carrier	Affected
Normal/Clear	All Normal/Clear	50% Normal/Clear 50% Carrier	All Carrier
Carrier	50% Normal/Clear 50% Carrier	25% Normal/Clear 50% Carrier 25% Affected	50% Carrier 50% Affected
Affected	All Carrier	50% Carrier 50% Affected	All Affected

* Cord1-PRA has an autosomal recessive form of inheritance, thus an affected dog receives a copy of the gene mutation from both his sire and dam.

Cord1-PRA Genetic Testing

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by it. In fact, the cord1-PRA test can yield false positive results."

Dachshunds may even be affected by other forms of PRA, Acland continues. "PRA has been observed in several Dachshunds of all varieties that is not associated with the RPGRIP1 mutation, the NPHP4 mutation or the prcd (progressive rod cone degeneration) mutation that causes PRA in many other breeds," he says. "These cases may represent one or more disease-causing mutations. My laboratory and those of many of my colleagues are working to identify as many of the genetic causes for PRA in dogs as possible."

Pathogenesis & Genetic Testing

Progressive retinal atrophy is a disease-causing degeneration of the retina, the tissue at the back of the eye that converts light into electrical impulses. These impulses are sent to the brain and interpreted as images. The retinal tissue is made up of light receptor, or photoreceptor, cells called rods and cones. Rod cells function in low light by detecting shapes and motion. Cone cells operate in bright light, perceiving definition and color.

Owners May Submit Samples for PRA Research

Owners of Dachshunds diagnosed with progressive retinal atrophy (PRA) are encouraged to submit blood samples for genetic research under way at the Cornell University Baker Institute for Animal Health. For information, please call 607-256-5600.

Dogs with PRA experience a progressive loss of photoreceptor cells. In rod cone dystrophies, rod cells are generally affected first, causing loss of night vision. As the disease progresses, cone cell function diminishes, eventually leading to complete blindness. With cone rod dystrophies, cone cells are lost earlier. Some forms of PRA cause photoreceptor cells to develop abnormally.

An eye examination that includes an ophthalmoscopy and electroretinogram can detect PRA, although usually not until after signs appear. In an ophthalmoscopy, a veterinarian uses an instrument to examine the retina and look for late stages of PRA. An electroretinogram (ERG), which is performed when a dog is under anesthesia, measures electrical signals from the retina and is used for diagnosing early PRA.

Clinical signs of disease include a decrease in the size and number of retinal blood vessels and changes in reflectivity of the eyes. Breeds at risk for eye diseases, such as PRA, should have Canine Eye Registration Foundation (CERF) tests prior to breeding.

Testing for Cord1-PRA

Miniature Dachshunds are at risk for developing cone-rod dystrophy 1-PRA, which is also known as cord1-PRA. This type of PRA affects how a dog sees in bright light and his ability to perceive definition and color. Eventually, many dogs become blind. Testing for the genetic eye disease can be performed at any age with a cheek swab DNA test. For information about having your dog tested, please contact these veterinary testing laboratories:

VetGen Veterinary Genetics Service
Ann Arbor, Mich.
\$75 for testing
www.vetgen.com
800-483-8436

Animal Health Trust
Suffolk, England
\$77 for testing
Swab.request@aht.org.uk
011-44-1638-555621

University of Missouri
College of Veterinary Medicine
Animal Molecular Genetics Laboratory
Columbia, Mo.
\$40 for testing
www.caninegeneticdiseases.net
573-884-3712

Board-certified veterinary ophthalmologists perform CERF eye tests, which cover 25 conditions and diseases.

The many forms of PRA combined with other potential causes of vision loss can make diagnosis difficult. Some dogs with PRA have been known to develop cataracts, which can be mistakenly diagnosed as the cause of a vision deficit. The unpredictable cause of PRA makes it easy to unknowingly breed a dog with the disease.

Genetic testing is key to reducing the incidence of PRA, although at this time a genetic test is only available for cord1-PRA in Miniature Dachshunds. Genetic testing of dogs before breeding can help limit the production of carriers and affected dogs.

Shannon Glines of Bellaluna Dachshunds in Atascadero, Calif., had a cord1-PRA test performed on her finished conformation champion, "Jack," a Miniature Longhaired Dachshund. When positive test results came back, Glines changed her plans for breeding the dog.

Experts advise breeders that carrier and affected dogs can remain in the gene pool to help maintain genetic diversity and desirable characteristics; however, these dogs only should be bred with tested clear dogs. Their offspring also should be tested before being bred.

"Testing of dogs at risk of being carriers or affected with PRA will allow breeders to rapidly eliminate the risk of producing affected dogs and gradually remove causative mutations from the gene pool," Acland explains. "If a two or three generation approach is undertaken, then elimination of a disease can be achieved without losing valuable breeding lines."

Jack had a CERF examination last summer and was cleared of signs of PRA. The result gives Glines hope. "Perhaps Jack will be at risk but never truly affected," she says.

Meanwhile, DiBari's male Miniature Longhaired Dachshund Sunshine is not so lucky. His CERF test revealed signs of PRA. "Sunshine has good

and bad days," DiBari says. "Some days he recognizes me and my voice. Other times he has no idea who I am."

The experience has made DiBari an advocate for both DNA and CERF testing. "DNA testing is just as important as CERF testing," she says. "The CERF test shows what is happening now, but the DNA test is an invaluable tool to help breeders breed responsibly and prevent PRA in our Dachshunds.

"It also is a tool to help owners be aware of the possibility of blindness in their dog and look for signs. This will help them to accommodate for changes in their dog's sight."

As DiBari wrote on a Web page dedicated to Sunshine, "I don't want anyone to go through what Sunshine and I are going through." ■

Purina appreciates the support of the Dachshund Club of America and particularly Charlotte Borghardt, chairwoman of the DCA Health Committee, in helping to identify topics for the *Purina Pro Club Dachshund Update* newsletter.

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