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DACHSHUND Update

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LAFORA DISEASE IN MINIATURE WIREHAIRS

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AWARENESS OF LAFORA DISEASE

IN MINIATURE WIREHAISED DACHSHUNDS COULD AID PREVENTION

Miniature Wirehaired Dachshund breeder Dianne Graham of Pulaski, Virginia, learned about Lafora disease five years ago when she discovered an English dog in her dog's pedigree was affected. Two of her bitches tested as carriers of the autosomal recessive condition that

was first recognized in Mini Wirehairs in the U.K. more than three decades ago. Graham quickly realized that few U.S. breeders knew about Lafora.

A late-onset progressive myoclonic epilepsy seen in dogs around 7 years of age, Lafora disease at its peak in 2013 affected



GENOTYPE RESULTS FOR LAFORA DISEASE (AUTOSOMAL RECESSIVE INHERITANCE)

P/P Positive/Positive	Affected dogs have two copies of the mutant gene that causes the condition and will develop the disease.
P/N Positive/Negative	Carrier dogs have one copy of the normal gene and one copy of the mutant gene. They will not develop the disease but will pass a mutant gene on to about half of their offspring.
N/N Negative/Negative	Clear dogs have no copies of the mutant gene responsible for the condition and will neither develop the condition nor pass it on to their offspring.

up to 10 percent of Miniature Wirehaired Dachshunds in the U.K. and 42 percent were carriers. Gradually, after a genetic test became available in 2012 to owners and breeders, disease incidence began to decrease. [In 2017, only 3 percent of Mini Wirehairs in the U.K. were affected and 26 percent were deemed carriers.](#)

Graham made it her mission to educate North American breeders about the incurable condition that eventually claims the lives of all affected dogs. She began a database to record the testing results of North American Miniature Wirehaired Dachshunds and investigated the history of affected dogs in America.

“As far as I know, there haven’t been any recent affected dogs with Lafora disease in the U.S.,” Graham says. “The only dog I am aware of was brought to Canada in the late ‘80s as a 5-year-old Champion. He started showing signs when he was 7 years old and was put down when he was in his teens. His frozen semen was later tested, and he was found to be affected.”

FAMILY OF MINI WIRE-HAIRS SHARES LAFORA

A different scenario took place in Miniature Wirehaired Dachshunds in the U.K., where for decades before the gene mutation for Lafora disease was discovered, breeders had produced litters in which some dogs later in life showed signs of epilepsy. They suspected it was a hereditary condition, though the late onset of clinical signs meant that most dogs had already been bred when it became apparent they were affected.

In the 1990s, veterinary neurologists Clare Rusbridge, BVMS, PhD, DipECVN, FRCVS, of the University of Surrey in Guildford, England, and Sue Fitzmaurice, BVSc, MRCVS, DACVIM (Neurology), of The Ralph Veterinary Referral Centre in Marlow, Buckinghamshire, England, found an extended family of Miniature Wirehairs in which the disease was clearly inherited. They sent pedigree information and DNA from those dogs to Berge A. Minassian, MD, of The Hospital for Sick Children at the University of Toronto in

“As far as I know, there haven’t been any recent affected dogs with Lafora disease in the U.S.”

Dianne Graham, Miniature Wirehaired Dachshund breeder, Pulaski, Virginia

Canada, who was studying a similar inherited, severe form of progressive myoclonic epilepsy in humans that occurs in late childhood or adolescence.

Dr. Minassian identified the *Epm2b* gene mutation for Lafora disease in the Mini Wirehairs in 2005 and matched it to the human Lafora disease mutations in the *EPM2A* gene and the *EPM2B* gene. Affected dogs, as well as affected people, inherit two copies of the gene mutation. The *Epm2b* gene mutation in dogs results in the intracellular accumulation of abnormal glycogen phosphatase laforin, a protein essential for making normal structured glycogen.

Affected dogs are not able to convert starch into sugar, so insoluble glycogen builds up in

their cells into large accumulations called Lafora bodies. The gene mutation disables the gene from controlling laforin and from protecting tissue against carbohydrate accumulation. As the Lafora bodies gradually grow, they have a neurotoxic effect in the central nervous system.

When Lafora bodies amass within the nerve cells of the brain, the cells start to malfunction and degenerate causing neural problems such as twitching, jerking and sometimes seizures. As the disease progresses, the dogs experience other neurological problems, including dementia and difficulty walking. Besides brain tissue, Lafora bodies are found in muscles, skin, liver, and heart. Although Lafora disease appears as progressive myoclonic epilepsy, it is actually a glycogen metabolism disorder.

Besides Miniature Wirehaired Dachshunds, the disease is found in Basset Hounds and Beagles, with all three breeds sharing the same single mutation that leads to near-absent expression and loss of function of the gene. The canine mutation consists of a variable expansion of a dodecamer repeat sequence in the *Epm2b* gene.

Originally, gene sequencing options were limited, as the traditional method of polymerase chain reaction (PCR)-based sequencing was unreliable for detecting carriers. At The Hospital for Sick Children, Dr. Minassian and his team used a Southern blot test to identify the mutation and to provide DNA screening of dogs using blood samples.

SIGNS OF LAFORA DISEASE

Among the initial signs of Lafora disease in Miniature Wirehaired Dachshunds, [owners participating in a breed health survey reported the following](#). The average age of onset for the dogs in the survey was 6.94 years, with most dogs living a few years after diagnosis.

- Myoclonus, or sudden twitches or jerks, of the neck and limbs was the most common sign, affecting 78 percent of dogs. Myoclonus may be spontaneous or a reflex action triggered by sudden noise, bright light, sudden movement, or flickering visual stimuli.
- Hypnic jerks, the type of sudden jerks people experience as they fall asleep, was the second most common sign, occurring in 52 percent of dogs.
- Generalized tonic-clonic seizures were the third most common sign, affecting 41 percent of dogs.
- Less common signs included focal seizures characterized by “jaw smacking,” “fly catching” or panic attacks.
- Later signs include dementia, blindness, aggression to people and dogs, deafness, and fecal and urinary incontinence due to loss of housetraining.



U.K. DACHSHUND LOVERS JOIN FORCES

The gene mutation discovery for Lafora disease united members of the Wirehaired Dachshund Club of the U.K. to work together to educate breeders about the estimation of breeding probability of the recessive condition. The goal was to eradicate the disease from the breed.

Efforts to develop a commercial test for the gene mutation would not be easy since PCR sequencing — the more common and affordable type of genetic testing — was not possible to identify carriers. The Southern blot method required a blood sample, took months to process and cost around \$300.

With help from the Dachshund Breed Council and The Kennel Club Charitable Trust, the Wirehaired Dachshund Club raised

more than 40,000 pounds (\$52,000) toward the development of a DNA test and for a subsidy program to enable breeders to screen their dogs. After the test became available at The Hospital for Sick Children in 2012, breeders could take advantage of the subsidized testing program if they agreed not to breed carrier or affected dogs.

Further, the Wirehaired Dachshund Club asked The Kennel Club to require DNA testing for Lafora disease for Miniature Wirehairs bred by the club's Assured Breeders, a designation for breeders who adhere to good breeding practices for their breed. [Results for every dog tested would be published on The Kennel Club's health test website.](#)

"The DNA test is now an official requirement under The Kennel Club's Assured Breeder program,

"If we are concerned with breeding healthy dogs, we should be aware of Lafora and the opportunity to test our dogs to ensure the disease does not affect dogs here."

Kenneth Levison, treasurer,
Dachshund Club of America

and no responsible breeder in the U.K. would breed Miniature Wirehairs without knowing the Lafora status of the parents,” says Ian Seath, chair of the Dachshund Breed Council.

To convince breeders who were not part of the Assured Breeders program, Seath and other members of the Dachshund Breed Council presented data on the disease. “It was a much more powerful message to state the number of Mini Wirehair puppies born over a particular time period and the percent that we expect to be affected by Lafora disease because they were bred from untested parents,” Seath says.

In 2010, it was estimated that from 5 to 10 percent of Minia-

ture Wirehairs in the U.K. were affected with Lafora, possibly as many as 500 dogs, with 50 to 100 affected dogs born a year, Seath says. “The proportion of litters that could potentially produce an affected puppy was estimated to be about 55 percent,” he says.

After the Wirehaired Dachshund Club began holding Lafora screening sessions two times a year, with 50 to 60 dogs screened per session, the number began to decrease. Between 2012 and 2017, more than 700 Miniature Wirehairs were DNA tested for Lafora. With a goal of zero dogs affected, the [Wirehaired Dachshund Club of England continues to monitor test results and post them online quarterly.](#)



Caution about the risk of the disease spreading to other varieties is important, says Seath. “We have found no carriers of the mutation in Standard Wires in the U.K.,” he says. “But, we have reports that a Miniature Smooth Dachshund from the U.S. is a carrier. This dog was bred from two Miniature Wire-hair parents. The fact that U.S. and Fédération Cynologique Internationale breeders can cross the coats means Lafora could spread to other varieties.”

Although Lafora originated in dogs in the U.K., the disease could become a problem in America, Seath cautions. “Some of the U.K. carrier dogs were used at stud, and it would be surprising if the mutation was not also in U.S. pedigrees with U.K. dogs in the background,” he says.

EASIER DNA TESTING AVAILABLE TODAY

Fortunately, testing for Lafora is easier today. The Hospital for Sick Children no longer offers the test; however, two European diagnostic testing laboratories perform the service. Laboklin performs the Southern blot test previously used in Canada, and Genomia uses PCR testing that can be done from a cheek swab. Both labs provide testing results in two to three weeks.

In the U.S., Kenneth Levison, treasurer of the Dachshund Club of America (DCA), says, “At this point, the board of DCA is looking for additional information and waiting on the availability of genetic testing in this country before making genetic testing recommendations. If we are



concerned with breeding healthy dogs, we should be aware of Lafora and the opportunity to test our dogs to ensure the disease does not affect dogs here.”

Graham, who had two bitches test as carriers, says, “I won’t breed to an outside dog unless I study the pedigree. It has been a hard road to eliminate this from my line. I finally have a male that tested clear. Every affected dog is someone’s much-loved pet, and they may have to live with the epileptic fits associated with Lafora disease for six to 10 years. That’s a hard price to pay when you consider how easy it is to screen dogs prior to breeding.” ■

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