



# Chihuahua Owners Urged to Contribute to Epilepsy Research in the Breed

hihuahua breeder Frieda Kane found her 5-year-old female, CH Guichon's Tika Toy ("Tika"), shaking out of control. Kane felt her heart beating fast as she ran to the dog.

"I had just let the dogs inside, and she was missing. When I found her, I thought she was choking, so I picked her up. Then, all of a sudden, she went limp in my arms. I thought she had died," recalls Kane of Durham, N.C.

Tika had not died. She had suffered a seizure, her first as far as Kane knew. "That was my first experience with a dog having a seizure," Kane says. "It's very unnerving to see your dog go through one."

For the next two and a half years, Kane stood by while Tika had many more seizures. Despite twice daily treatments of Phenobarbital, Tika experienced some severe seizures. Though the Phenobarbital helped keep the seizures in control most of the time, Tika still had them every five to six weeks.

"One time, she had a seizure that completely flipped her body over," Kane says. "The seizures began getting more intense."

Then one day, Tika experienced a seizure that lasted over 45 minutes and from which she never regained consciousness. After a discussion with her veterinarian, Kane decided it was best to euthanize her retired champion though the dog was only 7 ½ years old.

According to a health survey conducted in 2009 by the Chihuahua Club

of America (CCA), Chihuahua breeders on average report having about two dogs affected by seizures. One breeder reported having 20 Chihuahuas from 30 litters that suffered seizures. Forty-five percent of the survey participants had bred or owned a Chihuahua with seizures of unknown origin.

Epilepsy is a complex disease believed to affect from 2 to 4 percent

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of dogs. It occurs more commonly in about 30 breeds, which are affected significantly more than the 0.5 to 5 percent of all dogs. The good news is that epilepsy is successfully controlled in more than two-thirds of dogs, and the majority of seizures are not lifethreatening and do not require emergency treatment.

"Epilepsy has only recently come to the forefront as a health concern in Chihuahuas that needs research and funding," says Cathleen Cogan Bird, chair of the CCA Health Related Issues Committee. "We're working to learn more about the disease incidence by encouraging breeders to share their experiences with epilepsy. We will be conducting another breed health survey later this year. Updates on the survey will be available on the parent club website (www.chihuahuaclubofamerica.com). We want to educate owners and breeders about epilepsy and provide resources so they can participate in research."

#### A Collaborative Research Effort

A collaborative international research group, the Canine Epilepsy Research Consortium, has been working since 1999 to advance understanding about epilepsy. Researchers at the University of Missouri and the University of Minnesota organized the consortium, which is made up of veterinary and human clinicians, neurologists and geneticists. The investigators share samples, data and resources.

At the University of Missouri, researchers focus on identifying the genetic risk factors for epilepsy. Their goal is to develop a DNA test to help breeders make selective breeding decisions by identifying which dogs have the potential to develop the disease and which healthy ones are carriers.

The knowledge may also contribute to effective treatments for dogs suffering from epilepsy. They have collected DNA samples from more than 10,000 dogs representing 112 breeds. The national parent club is encouraging Chihuahua breeders and owners to submit DNA samples from affected dogs and their relatives.

Gary Johnson, D.V.M., Ph.D., leads the epilepsy research at the University of Missouri. "The most useful DNA samples for epilepsy research are those from affected dogs and their littermates, sires and dams, and grandsires and granddams," he says. "A copy of the dog's pedigree allows us to assemble extended family groups for the research. We use an online seizure survey (www.canine-epilepsy.net) to collect information as well."

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## How to Submit DNA Samples for Epilepsy Research

Chihuahua owners and breeders are urged to submit DNA samples of dogs that experience seizures and their relatives for analysis by researchers at the University of Missouri College of Veterinary Medicine. Participation will help the researchers identify specific gene sequence variations in Chihuahuas.

For information about participating, please visit the websites of the Chihuahua Club of America at www.chihuahuaclubofamerica.com and the Canine Epilepsy Project at the University of Missouri at www.canine-epilepsy.net. Please contact Liz Hansen, Project Coordinator of the Animal Molecular Genetics Laboratory at the University of Missouri, for more information at 573-884-3712 or HansenL@missouri.edu. The Canine Epilepsy Project is supported by grants from the AKC Canine Health Foundation, National Institutes of Health, individual parent clubs and private donations.

### **Epilepsy Research**

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Though much still is unknown about the genetics of epilepsy, the researchers are making progress. The complexity of the research is impacted by the probability that epilepsy could be a polygenic disease in which several genes interact to cause seizures. The investigators have conducted genomewide association studies of more than 100 dog breeds. Genomewide analysis helps to identify good candidate genes that may contain gene mutations.

The majority of differences in the chromosomes of individual dogs are single nucleotide polymorphisms (SNPs), which are a change of one nucleotide or letter in the DNA sequence. Although some SNPs have functional effects that alter the biology of any animal, the majority of SNPs have no biological significance but can be used as markers to identify the chromosomal region carrying a mutation.

The SNP chips allow the researchers to focus on a small area of the canine genome by comparing profiles of affected and healthy dogs. The regions of difference help to distinguish the location of disease genes, and then the researchers can evaluate the genes and surrounding DNA sequence.

"So far, we have not generated strong evidence for the locations of any epilepsy genes," Johnson says. "We are exploring other strategies and hope to generate whole genome sequences with DNA from epileptic dogs."

#### Identifying the Cause of Seizures

Determining the exact nature of seizures can be challenging since there are many causes. This is why it is important to get a thorough diagnostic workup. Testing to eliminate other causes may include physical and neurological examinations, a complete blood panel, liver and thyroid testing, and screening for infectious diseases and toxins.

Seizures can occur secondary to diseases, such as a brain tumor or infection, metabolic disorders like hypoglycemia, some types of liver diseases, an abnormally formed brain, head injuries, or exposure to poisons. Hypoglycemia is a condition that occurs when the body does not produce glycogen as quickly as needed. In Chihuahuas and other toy and small breeds, there is a shorter timeframe for the conversion of glycogen into glucose to supply the brain and other tissues with fuel.

"The hard thing to understand about epilepsy is that while some breeds are prone to seizures due to hypoglycemia, or low blood sugar seizures, this is not the cause of all seizures in these breeds. It's important to figure out why a dog has seizures and to rule out various factors," says Liz Hansen,

Project Coordinator of the Animal Molecular Genetics Laboratory at the University of Missouri.

When the origin of seizures cannot be determined, dogs are considered to have idiopathic epilepsy (IE). A biochemical defect in brain cells or the brain environment is believed to cause IE. About 66 percent of dogs with IE experience their first seizure from 1 to 3 years of age.

These dogs may experience focalonset or generalized tonic-clonic seizures. Focal seizures are called partial seizures because they involve

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a limited part of the brain and may be observed as twitching of one side of the face or body. In contrast, a generalized seizure affects the entire brain at once. When focal seizures progress to generalized seizures, it is called generalized seizures with focal onset.

Most seizures are not life-threatening and do not require emergency treatment. Phenobarbital and potassium bromide are the most commonly prescribed treatments for dogs with seizures due to their safety, affordability and high rates of success. Some dogs need both medications to control seizures. If a dog still is not getting adequate seizure control with Phenobarbital and potassium bromide, other medications may be substituted or added to a dog's medication regimen.

Treatment generally is not needed for dogs that suffer infrequent seizures, only one or two a year, unless the seizures involve five minutes or more of unconsciousness or occur in clusters, meaning multiple seizures in a 24-hour period. Severe seizures that last longer or occur in clusters may require emergency treatment.

Carla R. Soto of Morgantown, N.C., breeds Chihuahuas under the Hardwin prefix. She is like the majority of people who responded to the parent club's 2009 health survey and reported having two Chihuahuas that suffered from seizures. "Sunny" (CH Winhaven Davlyn Thunder Buster), who is now 7 years old, has had infrequent seizures since he was 3 years old and takes no medication. "Sam" (Davlyn Major Hardwin's Sam I Am), who is 8 years old, also takes no medication.

Recalling Sunny's first seizure, Soto says, "It was frightening. I was sitting in my chair at the computer, and he was under the chair. I heard an odd thumping noise. When I looked down he was thrashing around, his eyes were bulging, and his head was twisted oddly back toward his tail."

Initially, Soto thought her dog was choking and began performing the Hemlich maneuver. As the Chihuahua began to relax, Soto thought perhaps she had dislodged something he may have choked on. She did not relate the behavior to a seizure.

When Sunny had a second seizure, Soto and her husband grabbed the dog and rushed him to the veterinarian. When they were just one highway exit away from the veterinary clinic, Sunny relaxed in Soto's lap. After describing the two incidents to the veterinarian, they learned Sunny most likely was experiencing seizures.

Today, Sunny still has occasional seizures, although they occur less frequently and are less intense. "I am not as worried about his seizures anymore," she says. "The veterinarian explained to me that he's not in pain and doesn't realize what is happening."

Soto's experience with Sunny helped prepare her for recognizing seizures when Sam developed them at age 4. "Sam's seizures are mild compared to what Sunny experienced," says Soto. "His eyes dilate and become fixed on something, and he drools, shakes his head and stiffens his front legs."

The challenging part of idiopathic epilepsy to Soto is that the seizures occur for no apparent reason. "I can't pinpoint anything that sets them off," she says. "My dogs eat the same food and do not seem to have any stressors. They just randomly occur."

Though much still is unknown about epilepsy, the University of Missouri researchers along with the Canine Epilepsy Research Consortium investigators are making progress. By contributing DNA samples and supporting information about pedigrees, Chihuahua breeders and owners will help shed light on idiopathic epilepsy in the breed.

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