

## **Norwich Terriers, 5-21**

### **Title: Paroxysmal Dyskinesia in Norwich Terriers**

Breeders of Norwich Terriers have been long aware of a seizure disorder in the breed, affecting about 1% of our dogs according to the two most recent breed health surveys. Our Health Committee is about to launch a new survey, and we expect to again see a small group of our terriers affected by neurological problems. Many Norwich Terriers suffering from seizure episodes have been diagnosed by veterinarians and veterinary neurologists as having “idiopathic epilepsy.” A diagnosis of idiopathic epilepsy does not answer the question of the causes of the disease, nor its pathology. Thus, when a Norwich is diagnosed with idiopathic epilepsy, it means that the precise nature of the disorder has not been well described and classified in the veterinary literature, and therefore the dog is diagnosed as having a recurrent seizure disorder (epilepsy) of unknown causes (idiopathic).

So far there have been two epilepsy studies conducting DNA analysis on the samples from Norwich Terriers but they have not identified a gene or complex of genes associated with seizures in the breed. The first effort was headed by Dr. Gary Johnson’s lab at University of Missouri in 2009 collecting samples of affected Norwich Terriers and control samples for their Canine Epilepsy Network (CEN). In spite of several announcements of breakthroughs in describing the genetic component of epilepsy in other breeds, the Norwich Terrier genome did not yield progress in mapping seizure disorder in our breed. However, CEN is involved in sample-sharing and is continuing to store its DNA collection and make it available to other researchers working on genetics of epilepsy.

The last time Norwich terrier samples were used in such research was a study by Dr. Hannes Lohi at the University of Helsinki in Finland. The study team worked with DNA samples from several breeds alongside those from the Norwich Terrier: Lagotto Romagnolo, Australian Shepherd, Vizsla, and Finnish Spitz, among others, and they found mutation LGI2 responsible for canine epilepsy in Lagotto Romagnolo dogs. Currently, there are no further plans to work with Norwich Terrier samples. Although no correlation has been found in genetic studies comparing any of the suspect regions in other breeds of dogs suffering from epilepsy with the Norwich Terrier genome; it is our hope that it is a matter of time when a breakthrough happens. And we are inching our way to the answers.

The first scientific paper on the seizure condition affecting Norwich Terriers was not a genetic breakthrough but a result of data compilation. The study was based on owners' questionnaires, pedigrees and other records submitted by the owners of affected Norwich Terriers in Great Britain (DeRisio 2016).<sup>1</sup> The conclusion of the study was that 1) the majority of the affected dogs were related and 2) the condition was a paroxysmal dyskinesia characterized by sustained muscular hypertonicity in the pelvic limbs, lumbar region, and thoracic limbs, impairing posture and locomotion without loss of consciousness.

Paroxysmal movement disorders are typically characterized by intermittent attacks of abnormal involuntary movements. The term "paroxysmal" indicates a well-defined onset and termination of clinical manifestations. In other words, the dog behaves normally, without lasting effects between the episodes. The episodes are transient and characterized by hyperkinetic movement.

There have been some breakthroughs in understanding the genetics of paroxysmal movement disorders in people. Most primary forms of these disorders occur as sporadic or

familial cases with autosomal dominant inheritance (Garone 2020)<sup>2</sup>. But how to advance the progress towards finding the genetic component of epilepsy in a tiny breed? We might have to wait for that for a while, but meanwhile we can continue expanding our knowledge of the condition and its environmental components.

What is appearing increasingly more likely is that the seizure disorder affecting Norwich Terriers might be metabolic in nature. Owners of Norwich Terriers suffering from PD have been long reporting that a diet change reduces the frequency of seizure episodes, sometimes dramatically. By trial and error over the years, Norwich terrier owners discovered that tweaking protein sources affects frequency of seizures in the affected dogs. The diet involves either refraining from certain kind of protein, or protein rotation between single-protein foods. Most owners who changed their dog's diet reported a subsequent improvement with a reduction in frequency of episodes. To make things confusing, it seems to be a different offending protein for individual dogs.

A point of reference for dietary factor is paroxysmal dyskinesia affecting border terriers, and termed Spike's Disease. Spike's Disease is a type of paroxysmal dyskinesia specific to border terriers. The affected dogs are sensitive to gluten, unlike Norwich Terriers that appear to be sensitive to protein, however the pattern of the disease is similar in that once an offending allergen is eliminated from the diet; the severity of the condition is lessened. It was found that the border terriers with the seizure disorder had much higher levels of gluten antibodies compared to healthy border terriers. The antibody levels decreased after the start of a gluten-free diet, and were back to a normal level nine months later. Furthermore, dogs stopped having PD episodes.<sup>3</sup>

Additionally, owners of the affected Norwich Terriers should avoid “generic” environmental factors shown to affect epileptic dogs. Studies illuminated that seizure-precipitating factors are common in dogs with epilepsy. The most frequently recognized seizure precipitants consisted of stress-related situations, sleep deprivation, and hormonal factors.<sup>4</sup>

There might be other factors involved too. There is a currently an ongoing study, funded by the Canine Health Foundation, that is looking at an association between epilepsy and inflammatory gastrointestinal disease. Several nervous system disorders in humans have been linked to alterations in gut microbial populations. The researchers at North Carolina State University are trying to find an answer to a question whether a similar link exists in canines. This current CHF grant is headed as “Is Gut Dysbiosis Associated with Canine Idiopathic Epilepsy?” The study is primarily interested in a difference in microbiome of the dogs suffering from grand mal seizures and other unaffected dogs living in the same household and fed the same diet. Norwich Terriers with their paroxysmal dyskinesia episodes are not prime candidates for the study, but we might still benefit from the study results.

In the meantime, we are eager to spark interest in any researcher that would like to help us find more answers. We have DNA samples, a well described movement seizure disorder, an anecdotal dietary link, a small gene pool and a very eager community of Norwich Terrier owners willing to put effort in our search for a genetic breakthrough.

Contributed by Magda Chiarella, Norwich Terrier Club of America Health Committee

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<sup>1</sup> De Risio L., Forman O.P., Mellersh C.S. and Freeman J. (2016), Paroxysmal Dyskinesia in Norwich Terrier Dogs. *Movmnt Disords Clncl Practice*, 3:573-579. Doi:10.1002/mdc3.12334.]

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<sup>2</sup> Garone, Giacomo (2020), Clinical and Genetic Overview of Paroxysmal Movement Disorders and Episodic Ataxias, *Int J Mol Sci.* 2020 May; 21(10): 3603. Published online 2020 May

<sup>3</sup> Lowrie M et al (2015). The clinical and serological effect of a gluten-free diet in border terriers with canine epileptoid cramping syndrome, *Journal of Veterinary Internal Medicine* 29(6): 1,564-1,568

<sup>4</sup> Forsgård, J. A., Metsähonkala, L., Kiviranta, A. M., Cizinauskas, S., Junnila, J., Laitinen-Vapaavuori, O., & Jokinen, T. S. (2019). Seizure-precipitating factors in dogs with idiopathic epilepsy. *Journal of veterinary internal medicine*, 33(2), 701–707. <https://doi.org/10.1111/jvim.15402>