

## Topic 10: White Shaker Disease Syndrome

Lindsey Buracker and John Robertson

### Introduction and Overview

White Shaker Disease Syndrome (WSDS) is a neurologic disease seen primarily in dogs with white coats, particularly in West Highland White Terriers, Maltese Terriers (Bagley, et al., 1993), and Samoyeds (Cummings, et al., 1986). The disease presents with a very unique generalized **tremor**, in young (5 months to 3 years old) dogs of either gender (Yamaya, et al., 2004). The National Institutes of Neurological Disorders and Stroke defines tremor as “unintentional, somewhat rhythmic, muscle movement... involving one or more areas of the body: (Source: <http://www.ninds.nih.gov/disorders/tremor>). There have been numerous cases of WSDS in breeds of dogs without a white coat (Dachshund, among others) (Yamaya, et al., 2004), and in the adult years of their life. Therefore, the terms “shaker dog syndrome”, “white shaker disease” and “little white shaker dog” have been used as synonyms of WSDS (Yamaya, et al., 2004). The cause of the disease is not known and there is little research being done on this condition in any breed.

Because there are several neurologic and neuromuscular diseases that can produce tremor and incoordination, it is essential that the Westie owner immediately get a thorough evaluation of their dog and that an accurate diagnosis is made.

### Symptoms and Diagnosis

WSDS is characterized by a relatively sudden onset of constant tremors over the entire body, which includes the head and eyes. A tremor is a characteristic, abnormal set of repetitive movements that occurs when opposing muscle groups alternately contract and relax (Smith and Thacker, 2004). Uncontrolled eye movements, referred to as *opsoclonus*, consist of rapid, involuntary, multidirectional (horizontal and vertical) rapid eye movements.

The tremors are exaggerated by excitement, handling, forced locomotion, and high levels of stress (Summers, et al., 1995). Although some dogs with WSDS may have constant tremors, they are alert and responsive to their owners and environment. These dogs generally show no deficit in cranial nerve function, such as facial touch sensation or dilation/constriction of the pupils. In some instances, tremors may be severe enough to cause an ataxic or wobbly uncoordinated gait, or cause hypermetria, shown as overreaching with the legs when walking forward (a form of ataxia)(Smith and Thacker, 2004).

There are other diseases that can manifest as tremors, all of which must be ruled out before appropriate treatment can be administered (Smith and Thacker, 2004). Exposure to toxic substances such as moldy food, lead

poisoning, organophosphate poisoning, various inflammatory or infectious diseases of the nervous system, and epileptic patients can all show signs of tremors. These possibilities are ruled out by performing an electrophysiological evaluation of nerve function and nerve biopsy. After a variety of baseline tests are performed to eliminate the aforementioned possibilities, those dogs with normal test results and typical signs are diagnosed with WSDS.

Occasionally, a head tilt may be seen. Unfortunately, head tilt is seen with other central or peripheral neurologic disorders and can even be seen with ear problems. The association of head tilt and WSDS should be established by thorough examination and by elimination of other potential causes (Smith and Thacker, 2004).

Westies also suffer another neurologic disease that is not related (as far as we know now) to WSDS and which must be considered in the differential diagnosis since it may present as tremors at a young age. Krabbe disease, or globoid cell leucodystrophy (GCL), is a neurologic disease in which nerve cells accumulate material inside of the cells, due to a deficiency of a specific enzyme, needed for normal cell metabolism.

West Highland white and Cairn terriers are the two breeds most affected by GCL, which is inherited as an autosomal recessive trait (Parker, et al., 1995, Wenger, et al., 1999). Clinical signs tend to appear beginning around 3 months of age. Dogs may die from the disease in less than a year or may be euthanized due to poor quality of life (Parker, et al., 1995). Common clinical signs include ataxia of the hindlimbs, muscle wasting, head and body tremors, and even blindness. In many dogs, there is also a substantial degenerative change in the peripheral and autonomic nervous systems (Summers, et al., 1995). In the brain of affected dogs, pathologists have noted gray discoloration, firmness of the cerebral cortex, and ventricular dilation, reflecting tissue loss (Summers, et al., 1995). The brains of affected dogs appear reduced in size, with a notable decrease in the amount of white matter (Summers, et al., 1995).

GCL is one of a number of diseases called "storage diseases" in which intermediate metabolites build up within cells. GCL is caused by deficient galactocerebrosidase activity (GALC), and is a severe disorder of the peripheral and central nervous system. When the enzyme GALC is defective, psychosine, a metabolite highly toxic to myelin-forming oligodendrocytes and Schwann cells accumulates. Myelin makes up most of the white matter in the central nervous system and is also present in the peripheral nervous system. Myelin is essential for normal functioning of nerve fibers in both systems; hence the neurological deterioration from myelin breakdown found in this disorder. This leads to severe neurological symptoms such as progressive blindness, seizures, and eventually death.

Deficiency of galactocerebrosidase has been demonstrated not only in the brain but also the liver and kidneys of affected dogs (Fletcher et al., 1972, Yunis, et al., 1976, Wenger, et al., 1999).

To determine if a dog is affected with GCL, a blood sample is collected and analyzed by polymerase chain reaction (PCR) for the enzyme deficiency (Cifti, et al., 2000). Although not done commonly, examination of a nerve biopsy using electron microscopy may aid in reaching a diagnosis and MRI can also be useful (Cozzi, et al., 1998; Wenger, et al., 1999).

Krabbe disease has been reported in humans, dogs, mice, monkeys, and sheep (Fletcher, et al., 1972). In humans diagnosed in infancy, death usually occurs before 2 years of age, but the disease has also been identified later in life. Canine GCL most closely resembles the late-onset form in human patients and unfortunately there is no effective treatment (Yunis, et al., 1976).



(Source: [www.westierescueca.com/images/health2\\_sm.jpg](http://www.westierescueca.com/images/health2_sm.jpg))

The diagnosis of WSDS is generally made by history, age at onset and symptoms. Blood cytology, chemistry and x-rays, as well as a physical exam, are usually normal and have not proven valuable to aid in a diagnosis. A sample of cerebrospinal fluid may be collected for analysis, since an increase in the number of lymphocytes has been noted in some cases (Smith and Thacker, 2004). WSDS is rarely a fatal disease.

## **Causes**

Though the exact cause is not yet known, WSDS is most often associated with a mild central nervous system inflammation (nonsuppurative encephalomyelitis) (Smith and Thacker, 2004). The cerebellum is commonly affected and dysfunction of this part of the brain could be one of the initiators of the tremor. It is not known if the inflammation is the true cause or if there is an associated neurotransmitter abnormality in those dogs with WSDS. Further research should be done to rule out that possibility as well as an underlying virus as the cause of the tremors. There has also been some speculation that WSDS can be congenital in some breeds (West Highland White Terriers, Maltese Terriers, and Samoyeds).

## Treatment and Prevention

Early diagnosis is beneficial in treating dogs with WSDS, as many will respond in a few days to immunosuppressive levels of corticosteroids (anti-inflammatory drugs) (Yamaya, et al., 2004). Corticosteroids suppress the underlying disease process, whatever its origin. The tremors can be reduced with diazepam (Valium), which is used to diminish anxiety or modify behavior, as a muscle relaxant, or an anticonvulsant (Smith and Thacker, 2004). In some cases, dogs will have to remain on a low dose of corticosteroids for the duration of their life in order to remain free of signs of the disorder.

There are a few adverse affects that can occur from taking high doses of corticosteroids. Some of these include vomiting, gastrointestinal bleeding, ulcers, and diarrhea (Smith and Thacker, 2004). Even though the complications can be serious most can be managed clinically.

Unfortunately, since the underlying cause of WSDS is not yet known, there is no way to prevent the disease.

Some dogs experiencing tremors may convulse, and just before seizures may refuse to eat or seem disconnected with their environment. Affected dogs may need to be encouraged to eat and drink. Some owners have noted that hand feeding and raising food and water bowls off the floor is helpful (Swingle, C, 2008). Symptoms can lessen or resolve when the dog is relaxed or sleeping (Summers, et al., 1995). Some dogs respond well to being crated in a minimally dark room that is quiet during times of high stress.

In summary, WSDS is a disease that affects primarily white-coated dog breeds, including Westies. Clinical signs, including involuntary tremor, are seen in young dogs. An accurate diagnosis is essential in order to help affected dogs, which can be sustained with treatment. Further research is needed to determine the cause(s) of WSDS.

## References

Bagley, R, Kornegay, J, Wheeler, S, Plumer, S, Cauzinille, L, "Generalized tremors in Maltese: clinical findings in seven cases," Jour Amer Anim Hosp Assoc 29: 141-145, 1993

Ciftci K, Trovitch P, Applications of genetic engineering in veterinary medicine, Elsevier Science, Philadelphia, 2000

Cozzi F, Vite C, Wenger D, Victoria T, Haskins M, "MRI and electrophysiological abnormalities in a case of canine globoid cell leucodystrophy," Journ Small Anim Pract 39: 401-405, 1998

Cummings, J, Summers, B, DelaHunta, A, Lawson, C, "Tremors in Samoyed pups with oligodendrocyte deficiencies and hypomyelination," Acta Neuropath 71: 267-277, 1986

Fletcher, T, Kurtz, H, "Animal model for human disease: Globoid cell leukodystrophy," Am J Path 66: 375-378, 1972

National Institute of Neurological Disorders and Stroke "NINDS Tremor Information Page/Tremor Fact Sheet"

<http://www.ninds.nih.gov/disorders/tremor/tremor.htm>

Parker, A, "Little white shakers" syndrome: generalized, sporadic, acquired, idiopathic tremors in adult dogs. In J.D. Bonaguara and R.W. Kirk (eds) In J.D. Bonaguara and R.W. Kirk (eds) Kirk's Current Veterinary Therapy XII Small Animal Practice. pp. 1126-1127. W.B. Saunders Co., Toronto., 1995

Smith, K, Thacker, L, "Generalized temors: Identifying a White Shaker dog,"

<http://www.addl.purdue.edu/newsletters/2004/spring/tremors.htm>

Summers, B, Cummings, J, DelaHunta, A, "Degenerative diseases of the central nervous system," in Veterinary Neuropathology, Mosby-Year book, St. Louis, MO, 1995

Swingle, C , "White Shakers Syndrome", Westie Club of America,

<http://www.westieclubamerica.com/health/whiteshaker.html>.

Wenger, D, Victoria, T, Rafi, M, Luzi, P, Vanier, M, vite, C, Patterson, D, Haskins, M, "Globoid cell leukodystrophy in Cairn and West Highland White Terriers," J heredit 90: 138-142, 1999

Yamaya, Y, Iwakami, E, Goto, M, Koie, H, Watari, T, Tanaka, S, Takeuchi, A, Tokuriki, M, "A case of Shaker Dog Disease in a Miniature Dachshund," J Vet Med Sci 66: 1159-1160, 2004

Yunis, E, Lee, R, "The morphologic similarities of human and canine leukodystrophy," Am J Path 85: 99-114, 1976