

# NEUROAXONAL DYSTROPHY

-by Colleen Kirby ( Miracol Papillons )  
Acknowledged by Dr. Urs Giger



There's been talk about a new disease in Papillons that's has everyone concerned. That disease is known as Neuroaxonal Dystrophy or NAD. Unfortunately, it is not new. This disease has been in our breed for many years. These past several years we've seen diagnosed case in the United States. It is also seen in Japan and likely elsewhere.

Diagnosing the disease proves to be very challenging. The only way to accurately diagnose NAD is through necropsy and pathology of the Central Nervous System. MRI has not been proven to be helpful in the early diagnosis of NAD premortem. Upon necropsy the brain and spinal cord often look grossly normal, but the histopathology under the microscope reveals the debilitating changes. As other disorders may mimic the signs and no biochemical or molecular test is yet available, examination by an experienced pathologist is crucial in reaching an accurate diagnosis of NAD.

## What exactly is NAD and what are the symptoms ?

Neuroaxonal Dystrophy is a hereditary, neurodegenerative disease . The disease affects the nerve axons in the brain and other parts of the body. NAD is apparently associated with an abnormal build up of substances throughout the nervous system which prevents them from working the way they should. Spheroids form on the nerve endings going to the muscle, skin and to the eyes.

Pedigree analysis suggests a simple autosomal recessive trait. That means both parents must carry a copy of the mutated allele (gene) in order to produce an affected puppy. If there are 4 puppies in a litter, on average you will see one affected puppy, two clinically unaffected puppies which are carriers (like their parents) and one unaffected puppy that has two normal alleles. Unfortunately the gene involved has not yet been determined.

An affected puppy may start showing signs as early as 6 weeks of age. Often you will find a clumsy puppy or one that is just not as advanced in motor skills as his/her siblings. This may disappear and then reappear when the puppy is around 9-11 weeks of age. At that time you will see pelvic limb ataxis starting to take place along with hypermetria (high-stepping overreaching an intended goal or object.) The puppy stumbles and is easily knocked over. When running with excitement you may see a buckling or spastic action in the rear. They become fearful of slippery surfaces, and their rear legs will slide out from under them. Fine head tremors may be observed.

By 12-14 weeks of age the rear ataxis gets worse. They start standing with a wider base. The front end may start showing signs of ataxis as well. Their limbs become very stiff and when the puppy is lifted they often cross their legs. You may see a scrambling or panicky response as they can appear like they feel unsafe off the ground. The menace reflex (test of stabbing a finger toward the eye) has deteriorated or diminished as well.

By 15-18 weeks these puppies experience a very hard time. Many are unable to stand any longer, or if they are able, they are not standing for long. Intention tremors begin and it is starting to get difficult for the puppy to eat from a bowl.

By 19 weeks and beyond, glossoplegia ( paralysis of the tongue ) and dysphagia ( difficulty with swallowing ) start to affect the puppy. A very common secondary problem with NAD is aspiration pneumonia due to getting food in the wrong pipe. If pneumonia is not overwhelming them, you will continue to see the puppy struggle to maintain an upright position even when lying down. You may notice whole body tremors to the point of almost vibrating when awake. The puppy may need to be propped up to feel a little more comfortable. At this point their vision starts to deteriorate and they may even begin to lose their hearing. Some owners and breeders elect euthanasia for their affected puppies due to the observed progressive fatal condition.

While their physical condition worsens, they are emotionally aware of everything. You will probably still be greeted with a wagging tail and a puppy who wants to be a puppy and tries to mouth toys. When they are still able to drag themselves along, they even attempt to get away from their urination or defecation.

Generally, before the puppy dies, the tremors almost completely stop. Their limbs are not nearly as stiff as in the beginning stages of the disease and righting themselves is nearly impossible. In addition, they appear to be completely blind. They have lost almost all of their muscle tone and their nutritional condition is usually fair to poor. Eventually they die from pneumonia and/or deterioration of the brain. Puppies that have been diagnosed with NAD in the United States over the past 6 years have lived anywhere from 3 to 7 months.

### Are there known treatments for this disease ?

There are no known specific or symptomatic treatments or cures for Neuroaxonal Dystrophy and supportive care is all that can be offered. Prednisone has been unsuccessful in several puppies. Pain medication does not appear to be needed as we don't believe this to be a painful disease. When the limbs begin to stiffen, massaging and stretching them appears to be beneficial. Methocarbamol has been given to help with muscle relaxation, but it too does not seem to be very helpful. Many puppies are started on antibiotics ranging from Clavamox to Baytril for the treatment and prevention of pneumonia.

Keeping the puppy hydrated is vital and often having them drink from a bowl is not enough or forced water intake may result in aspiration, thus puppies have been given subcutaneous fluids.

Dairy products are usually avoided as this seems to contribute to the congestion. Too liquid of a diet also should be avoided as they can more easily aspirate. Using canned food with a bit of water has been the most beneficial way to feed NAD puppies.

### Where do we go from here ?

A study is being conducted by Dr. Urs Giger at the University of Pennsylvania, School of Veterinary Medicine. So far, Dr. Giger has seen several affected Papillon puppies. He has collected blood and serum along with tissue samples of the affected and is working toward finding the disease causing gene mutation or at least a marker for this disease.

This work is being done in collaboration with others. It is hoped the research will enable us to test our dogs to find out who is a carrier, who is at risk becoming ill and who is not and can safely be used for breeding.

If you have produced a puppy with NAD or signs similar to the above described disease or suspect you may have a carrier, own a dog related to a carrier please send samples and pedigree for the study to :

Dr. Urs Giger/NAD Papillon  
School of Veterinary Medicine  
University of Pennsylvania  
3900 Delancy Street  
Philadelphia, PA 19104-6010, USA

### Keeping an open mind

Neuroaxonal Dystrophy is an early, rapidly progressive debilitating neurological disorder. It's most frightening to those that have had to personally watch a puppy suffer. There have been many supporters for the blood collection and affected have been donated to the study.

We need to keep discussing NAD openly and to contribute samples from affected and related dogs.

-by Colleen Kirby ( Miracol Papillons )  
Acknowledged by Dr. Urs Giger