



UNIVERSITY OF MINNESOTA

<https://z.umn.edu/leonberger>

LEMP Genetic Test Result Interpretation

Clear (LEMP-N/N): A **clear** dog has no copies of the LEMP mutation (this is also referred to as being homozygous normal or free of the known mutation causing leukoencephalomyelopathy). A clear dog cannot produce LEMP affected (D/D) offspring.

Carrier (LEMP-D/N): A **carrier** dog has one copy of the LEMP gene mutation (this is also referred to as being heterozygous). **A carrier dog is a healthy dog, and is not at risk of developing LEMP.** LEMP carriers will, on average, pass the LEMP gene mutation on to half of their offspring; they can produce LEMP-D/D (affected/susceptible) offspring if mated to another carrier or affected dog.

Affected/Susceptible (LEMP-D/D): An **affected/susceptible** dog has two copies of the LEMP gene mutation (this is also referred to as being homozygous affected). LEMP-D/D dogs often develop leukoencephalomyelopathy at or before 3 years of age and clinical signs are characterized by slowly worsening gait abnormalities, especially spontaneous knuckling, dragging of the paws and hypermetria of the thoracic limbs, and a characteristic pattern on magnetic resonance imaging (MRI). Affected dogs show corresponding gross lesions in the cervical spinal cord white matter that may extend to the thoracic spinal cord, as well as to the brain; peripheral nerve and muscle biopsies are unremarkable. Spinal reflexes of affected dogs are mostly normal. In the progressive clinical course of the disease, affected dogs may become increasingly immobile within a few months. Like many diseases of the CNS, there is no effective treatment for LEMP. Since in most cases the dog is not in pain, but is strongly restricted in its quality of life, owners are encouraged to ask a veterinarian for advice. LEMP-D/D dogs will pass one copy of this mutation on to all of their offspring.

Further Information on LEMP

We are testing for a specific DNA variant in a specific gene; therefore this can be referred to as a gene mutation test. This situation is different from other types of genetic tests that describe only the identification of a DNA marker that could be very far away from the true disease gene, and not be as highly predictive as desired. The LEMP mutation is inherited in a **partially penetrant autosomal recessive** manner. Autosomal recessive means that two copies of the mutation are required to show signs of disease; partially penetrant means that among genetically affected dogs (LEMP-D/D) not all will show obvious clinical signs in their lifetime.

We have designated the letter D to indicate the mutant form of the LEMP gene and N to indicate the normal form of the gene. A dog's particular combination of N or D forms of the gene is known as its genotype. The genotype of a clear dog is designated as N/N, they have no copies of the LEMP mutation; a carrier dog is designated as D/N. Both clear (LEMP-N/N) and carrier (LEMP-D/N) dogs do not develop the LEMP disease, but could still show clinical signs of other unrelated neurologic diseases (e.g. polyneuropathy, disc disease). The genotype of leukoencephalomyelopathy affected/susceptible dogs is D/D. The LEMP disease often shows a juvenile onset (before 3 years of age) and is characterized by a generalized progressive ataxia.

Below are the chances any given puppy in a litter from the indicated mating will have the genotype of N/N, D/N or D/D. **Matings that produce, or are comprised of an LEMP-D/D dog are not recommended and are shown in red.**

LEMP genotypes of parents	Average probability LEMP-N/N puppies	Average probability LEMP-D/N puppies	Average probability LEMP-D/D puppies
N/N x N/N	100%	0%	0%
N/N x D/N	50%	50%	0%
N/N x D/D	0%	100%	0%
D/N x D/N	25%	50%	25%
D/N x D/D	0%	50%	50%
D/D x D/D	0%	0%	100%

Breeding Recommendations

In general, LEMP-D/D dogs should not be used for breeding. We **do not** recommend exclusion of LEMP carrier (D/N) dogs from the breeding population. We **do** recommend avoiding matings that have the potential to produce affected (D/D) offspring. As long as one of the two parents is LEMP clear (N/N), affected offspring will not be produced.

In a global group of more than 5,000 Leonbergers which have been submitted to our laboratories, ~14% were carrier (D/N) dogs. Immediately eliminating all D/N dogs from breeding may have negative consequences for the genetic diversity of the breed. If you prefer a D/N dog for your breeding program, you should keep them for future breeding.

Within the Leonberger breed LPN1, LPN2, LPPN3 and LEMP genotypes must all be considered when selecting breeding pairs. LPN2 affected dogs (both D/N & D/D) are not recommended to be bred. Within in each mating pair, at least one parent should be should be LEMP clear (N/N), LPN1 clear (N/N), and LPPN3 clear (N/N).

One final word of caution

We were able to identify a causative genetic mutation for one form of LEMP in Leonbergers. While all LEMP affected Leonbergers to date have tested LEMP-D/D, it is important to remember that this LEMP test is diagnostic for only one form of leukoencephalomyelopathy. Thus, it is still possible that affected offspring with a different genetic form of leukoencephalomyelopathy could occur, even from a mating of two dogs that both have been tested LEMP-N/N. To that end, we also recommend that both dogs in a breeding pair be free of any signs of neurological disease, regardless of genotype. Nonetheless this LEMP test will help to prevent this severe form of leukoencephalomyelopathy and therefore reduce significantly the frequency of this fatal disorder in the Leonberger breed.