



## Inflammatory Myopathy / Myositis (IM) Test Result Interpretation

**Clear (N/N):** A clear dog has no copies of the mutated IM gene (this is also referred to as being homozygous normal). However, this result does not rule out the possibility that a clear dog could have, or be a carrier for, a different myopathy mutation that this test cannot detect. IM clear dogs cannot produce IM affected offspring.

**Carrier (D/N):** A carrier has one copy of the mutated IM gene (this is also referred to as being heterozygous). To date, no carriers have shown signs of IM, however; having one copy of the mutated form of the IM gene does not rule out the possibility that a dog may have mild or no apparent signs of IM, or have a different myopathy caused by a mutation not detected by this test. IM carriers, on average, pass the IM gene mutation on to half of their offspring.

**Affected/Susceptible (D/D):** An affected dog has two copies of the IM gene mutation (this is also referred to as being homozygous affected). Affected dogs typically develop severe muscle disease before 1 year of age. Affected dogs will pass one copy of this mutation on to all of their offspring, and should not be used for breeding.

### Further Information

We are testing for a specific DNA mutation 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.

We have designated the letter D to indicate the mutant/deleterious (IM) form of the 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; this dog has no copies of the mutation, and cannot produce an affected (D/D) offspring. Dogs with the D/N genotype are carriers of the IM mutation; they can produce affected offspring when bred to another carrier, but are not yet known to be at risk of developing IM themselves. Dogs with the D/D genotype are affected with IM. All dogs with the D/D genotype to date have developed clinical signs of severe muscle disease before 1 year of age. These signs include: muscle tremors, pelvic limb stiffness, progressive weakness, and severe muscle atrophy. Serum creatine kinase activity was elevated in all affected dogs.

Inflammatory Myopathy is inherited in an autosomal recessive manner. Producing a puppy with IM caused by the mutant IM gene requires that both parents be either carriers (D/N) or affected (D/D). Below are estimates of the chance of a puppy with the affected D/D genotype being born from a litter produced by parents of all possible genotypes. **Matings that produce, or are comprised of an IM-D/D dog are not recommended and are shown in red.**

IM genotypes of parents	Average probability IM-N/N puppies	Average probability IM-D/N puppies	Average probability IM-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**

At this time we **do not** recommend exclusion of IM 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 IM clear (N/N), affected (D/D) offspring will not be produced.

In a population of ~150 Dutch Shepherds, ~8% were carrier (D/N) dogs. Immediately eliminating all D/N dogs from breeding may have negative consequences for the genetic diversity of the breed.

## **One final word of caution**

It is important to remember that this IM test is diagnostic for only one genetic form of myopathy and that our current state of knowledge does not allow us to state conclusively that no carrier dogs will develop signs of IM. Further, it is still possible that affected offspring with a different genetic form of myopathy could occur, even from a mating of two dogs that both have been tested N/N for the IM mutation. To that end, we also recommend that both dogs in a breeding pair be free of any signs of muscle disease, regardless of genotype, because this test can only detect one myopathy mutation.