What is L-2-hydroxyglutaric aciduria ?

L-2-HGA (L-2-hydroxyglutaric aciduria) in Staffordshire Bull Terriers is a neurometabolic disorder characterised by elevated levels of L-2-hydroxyglutaric acid in urine, plasma and cerebrospinal fluid.

L-2-HGA affects the central nervous system, with clinical signs usually apparent between 6 months and one year (although they can appear later). Symptoms include epileptic seizures, "wobbly" gait, tremors, muscle stiffness as a result of exercise or excitement and altered behaviour.

The mutation, or change to the structure of the gene, probably occurred spontaneously in a single dog but once in the population has been inherited from generation to generation like any other gene. The disorder shows an autosomal recessive mode of inheritance: two copies of the defective gene (one inherited from each parent) have to be present for a dog to be affected by the disease. Individuals with one copy of the defective gene and one copy of the normal gene - called carriers - show no symptoms but can pass the defective gene onto their offspring. When two apparently healthy carriers are crossed, 25% (on average) of the offspring will be affected by the disease, 25% will be clear and the remaining 50% will themselves be carriers.

The mutation responsible for the disease has recently been identified at the Animal Health Trust. Using the information from this research, we have developed a DNA test for the disease. This test not only diagnoses dogs affected with this disease but can also detect those dogs which are carriers, displaying no symptoms of the disease but able to produce affected pups. Carriers could not be detected by the tests previously available which involved either a blood or urine test detecting elevated levels of L-2-hydroxyglutarate or magnetic resonance imaging. Under most circumstances, there will be a much greater number of carriers than affected animals in a population. It is important to eliminate such carriers from a breeding population since they represent a hidden reservoir of the disease that can produce affected dogs at any time.

The test is available now and information on submitting samples is given below.

CLEAR: the dog has 2 copies of the normal gene and will neither develop L-2-HGA, nor pass a copy of the L-2-HGA gene to any of its offspring.

CARRIER: the dog has one copy of the normal gene and one copy of the mutant gene that causes L-2-HGA. It will not develop L-2-HGA but will pass on the L-2-HGA gene to 50% (on average) of its offspring.

AFFECTED: the dog has two copies of the L-2-HGA mutation and is affected with L-2-HGA. It will develop L-2-HGA at some stage during its lifetime, assuming it lives to an appropriate age.

Carriers can still be bred to clear dogs. On average, 50% of such a litter will be clear and 50% carriers; there can be no affected produced from such a mating. Pups which will be used for breeding can themselves be DNA tested to determine whether they are clear or carrier.

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