Multidrug Resistance 1

Other Names: Ivermectin sensitivity, MDR1 gene defect, Multidrug sensitivity, MDR1

Affected Genes: ABCB1

Inheritance: Autosomal Incomplete Dominant

Mutation: chr14:13726596-13726599 (tel:13726596-13726599) (canFam3): 4 bp deletion (del AGAT)

Common Symptoms

Multidrug resistance 1, also called MDR1, is an inherited condition affecting several breeds of dogs, especially herding dogs such as the toy Australian shepherd. The Mutation (/glossary/#Mutation) in the *ABCB1* gene associated with MDR1 causes dysfunction of P-glycoprotein, which is responsible for removing certain drugs and toxins from the body. Clinical signs are most commonly associated with distribution of the drug in the central nervous system. MDR1 is inherited in an autosomal incomplete dominant manner in dogs meaning that dogs only need to inherit one copy of the mutated gene to be at an increased risk of developing adverse reactions to certain medications. Though adverse reactions to certain drugs are most commonly seen in dogs having two copies of the mutated gene, Carrier (/glossary/#Carrier) dogs can also experience drug sensitivities and dosages need to be adjusted accordingly. Thus, dogs that have one or two copies of the mutation are considered at-risk for adverse drug reactions. If an at-risk dog is treated with one of several common drugs (see below*), they are at risk of developing neurologic symptoms that could range from tremors, excess salivation, anorexia, and blindness to coma and even death. Because of the defective ability to metabolize specific drugs, these drugs can be lethal even at low doses. The MDR1 mutation does not cause adverse effects in dogs unless the dog is exposed to these drugs. Therefore, veterinarians should be notified when a dog is at risk for multidrug resistance 1 prior to administration of any medications.

***Drugs known to cause neurological signs related to the MDR1 mutation:**
Acepromazine, butorphanol, doxorubicin, emodepside, erythromycin, ivermectin, loperamide, milbemycin, moxidectin, rifampin, selamectin, vinblastine and vincristine

In addition to this list, there are many other drugs known to be removed from the central nervous system via the P-glycoprotein mechanism in humans. However, reports of neurological dysfunction related to drugs other than those listed here are scarce in dogs. Please consult your veterinarian when giving drugs to known multidrug resistance 1 carriers, affected dogs, or untested dogs of breeds commonly affected with this condition.

Breed-Specific Information for the Toy Australian Shepherd

Toy Australian shepherd is included as a breed susceptible to multidrug resistance 1 because of its close relatedness to the miniature Australian shepherd breed, which is known to develop this disease due to Mutation (/glossary/#Mutation) of the *ABCB1* gene. The frequency of the causal mutation in the general toy Australian shepherd population is unknown.

Testing Tips

Genetic testing of the *ABCB1* gene in toy Australian shepherds will reliably determine whether a dog is a genetic Carrier (/glossary/#Carrier) of multidrug resistance 1. Multidrug resistance 1 is inherited in an autosomal incomplete dominant manner in dogs meaning that dogs only need to inherit one copy of the mutated gene to be at an increased risk of developing the disease. Though adverse reactions to certain drugs are most commonly seen in dogs having two copies of the mutated gene, carrier dogs can also experience drug sensitivities and dosages need to be adjusted accordingly. Thus, dogs that have one or two mutant copies of the gene are considered at-risk for adverse drug reactions. When carriers of this Mutation (/glossary/#Mutation) are bred with another dog that also is a carrier of the same mutation, there is risk of having affected pups. For each pup that is born to this pairing, there is a 25% chance that the puppy will inherit two copies of the mutation and a 50% chance that the puppy will inherit one copy of the mutation and, in either case, may be susceptible to having adverse drug reactions. Reliable genetic testing is important for determining breeding practices. Because symptoms do not appear unless dogs are exposed to certain drugs, genetic testing should be performed before breeding. In order to eliminate this mutation from breeding lines and to avoid the potential of producing affected pups, breeding of known carriers is not recommended. Toy Australian shepherds that are not carriers of the mutation have no increased risk of having affected pups when bred to a dog that is also clear for this mutation.

There may be other causes of this condition in dogs and a normal result does not exclude a different mutation in this gene or any other gene that may result in a similar genetic disease or trait.

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