



Canine MDR-1 Gene Mutation

What is the MDR-1 gene?

The MDR-1 gene (also known as Multi Drug Resistance-1 gene or ABCB-1 gene) encodes P-glycoprotein. This protein is responsible for pumping many drugs and other toxins out of the brain.

What does it mean if my dog has a mutant MDR-1 gene?

Dogs that have a mutation in this gene have a defective protein pump and cannot eliminate certain medications out of their brain as a normal dog would. Because of this defect, these dogs are more likely to have adverse reactions to certain medications, even when given at normal doses. If not considered, certain drugs can lead to serious side effects.

What are the breeds most commonly affected by this mutation? Dogs most commonly affected are often herding breed dogs and include Collies, Border Collies, Shetland Sheepdogs (Shelties), Australian Shepherds, Old English Sheepdogs, English Shepherds, German Shepherds, Long-haired Whippets, Silken Windhounds and McNabs.

Can mixed breed dogs have the MDR-1 mutation?

YES! The MDR-1 mutation has been identified in many mixed breed dogs - even dogs that don't look like herding breed dogs. Ideally, mixed breed dogs should be tested for the mutation before receiving the listed medications.

What are the drugs that are affected by the MDR-1 mutation?

- **Drugs that have been suggested or documented to cause problems in dogs with the MDR-1 mutation:** acpromazine (tranquilizer/sedative/preanesthetic agent); butorphanol (analgesic, pre-anesthetic agent); erythromycin (antibiotic); loperamide (antidiarrheal); selamectin, ivermectin, milbemycin and moxidectin (antiparasitic agents); rifampin (antibiotic); doxorubicin, vinblastine and vincristine (chemotherapy agents)
- **Drugs that appear to be safely tolerated by dogs with the MDR-1 mutation (but are known to be pumped out by the MDR-1 encoded protein):** ciclosporin/cyclosporine (immunosuppressive agent); digoxin (cardiac drug); doxycycline (antibiotic, immunomodulatory agent)
- **Drugs that appear to be safely tolerated by dogs with the MDR-1 mutation (but may be pumped out by the MDR-1 encoded protein):** morphine, buprenorphine and fentanyl (opioid analgesics and pain medications)

Note: Many other drugs have been reported to be pumped by P-glycoprotein in humans, but there is currently no data stating whether these drugs are or are not pumped by canine P-glycoprotein

What heartworm prevention products can I use if my dog has the MDR-1 mutation?

Fortunately, the dose of ivermectin, selamectin, milbemycin and moxidectin in the commercial heartworm preparations are low enough to be used safely even in dogs with the MDR-1 mutation. Therefore, any of the monthly heartworm preventatives (administered at the label dose) can be used.

How do I know if my dog has the MDR-1 mutation?

The only way to know for sure if a dog has the mutant MDR-1 mutation is to have the dog tested. If your dog is a herding breed dog and has already reacted to one of the listed drugs, he/she likely has the mutation. If your dog hasn't reacted or if you aren't sure, your dog should be tested due to the potential risk of adverse reactions.

What do the MDR-1 test results mean?

This is a DNA mutation test. It will determine whether or not a dog has the MDR-1 mutation and, if it does, whether it has one copy ("heterozygous") or two ("homozygous") of the abnormal gene. The test report will provide you with the genotype for your dog, generally listed as Normal/Normal, Normal/ Mutant or Mutant/Mutant. Dogs with even one copy of the mutation should be considered somewhat sensitive to listed drugs. If your dog carries the mutation, provide a copy of the test results and a copy of the listed drugs to veterinarians treating your dog and let them know your dog may not have these drugs or might require alternations in dosages of these drugs.

How can I have my dog tested for this MDR-1 mutation?

There are two ways to have a DNA test done: Blood sample (EDTA) – more reliable and faster results: 2 mls of blood sample can be collected by your veterinarian and submitted to the Veterinary Clinical Pharmacology Laboratory at Washington University. Cheek swab: You can order a test kit directly through the Veterinary Clinical Pharmacology Laboratory at Washington University. Instructions can be found at <http://www.vetmed.wsu.edu/depts-VCPL/test.aspx>.

What if I have a herding breed dog and I decide not to test my dog for the mutation - Should I be concerned with the medications given?

Yes. If you know your dog is a herding breed or a herding breed cross, you may choose to manage your dog as potentially affected by the MDR-1 mutation and you should discuss the potential medication risks and benefits with your veterinarian.

How old must a dog be before it can be tested?

A dog can be tested at any age with the blood test or as soon as it is weaned from its mother with the cheek swab.

If my dog carries the MDR-1 mutation, can he/she pass on the mutant gene to their offspring? Yes.

The DNA test results should assist you with breeding decisions.

For more information, please refer to the Veterinary Clinical Pharmacology Laboratory at Washington University website: <http://www.vetmed.wsu.edu/vcpl/>