

# East Anglian Collie Association



## Multi-drug Resistance (MDR1)

It is now widely accepted that some Collies appear to be hypersensitive to certain toxins (natural or drug-induced) and are more prone to stress-related problems.

The problem first came to light in 1983 when several Collies died from Ivermectin poisoning and, since then, the veterinary profession has accepted this drug should never be given to Collies. More recently a Rough Collie died from eating horse faeces (Ivermectin is used for worming horses and any excess drug passes out with their faeces).

Researchers have since found that approximately 60% of Rough and Smooth Collies appear to be susceptible not only to Ivermectin, but to a wide range of other drug substances. The MDR1 (multi-drug resistant) gene is responsible for ensuring the body's natural P-glycoprotein functions normally by protecting the body from both environmental toxins and administered toxins eg drugs, and acting as a transport mechanism moving substances from cell to cell. P-glycoproteins are normally extensively distributed in the blood-brain and blood-testes barriers as well as major organs such as the liver, kidneys, intestines and placenta. When they are present in the intestinal tract three things normally happen – the substance may be metabolised; it may enter the circulatory system; or it may be passed out of the large intestine with the faeces.

In MDR1-affected dogs the function of the P-glycoprotein is compromised and so toxins may leak into the major organs. If these compounds leak across the blood-brain barrier, they enter the central nervous system causing toxic reactions such as excessive salivation, Ataxia, blindness, coma, respiratory problems and even death.

Because of a lack of the p-glycoprotein transporter in the body, an MDR1-affected dog also tends to have a deficiency of Cortisol (a steroid hormone produced by the Adrenal glands). Cortisol is responsible for stress management and the maintenance of an efficient immune system, and a deficiency can therefore lead to stress-related problems such as colitis or inflammatory bowel disease.

### Mode of Inheritance

An MDR1 **Clear** dog (normal or +/+) receives a healthy MDR1 gene from each of its parents and can therefore only pass on healthy genes to its offspring. The healthy + genes are dominant and such animals do not exhibit drug toxicity.

A '**Carrier**' (+/-) is a dog that has received a normal [dominant] MDR1 gene from one of its parents, and a defective gene [recessive] from the other parent which is 'carried' by the dominant + gene. Please bear in mind that a carrier can pass either a normal or a defective genes onto its offspring resulting in approximately 50% of the puppies inheriting a defective MDR1 gene. Theoretically the 'carrier' animal should not be susceptible to drug toxicity but unfortunately the dominance of the MDR1 + gene has been found to be incomplete as some 'carrier' animals also appear to be susceptible to high doses of those drugs that cause problems in MDR1-affected dogs, that is, those with two defective MDR1 genes (-/-).

An **Affected dog** (-/-) receives a defective or mutant MDR1 gene from both its parents,



so such dogs are double recessive and **will** display toxic reactions to a wide range of drug compounds (see list below). In 2007 a genetic test was made available for MDR1 and so It is extremely important that breeders try and use Normal (+/+) dogs in their breeding programmes so as to eliminate the defective MDR1 genes as soon as possible.

If you have an MDR1-affected Collie (-/-) you could be in a position to save its life by providing your veterinary surgeon with a copy of its MDR1 Certificate and the list of drug compounds that your Collie should never be given. Of those vets who have already been asked to put MDR1 test results onto a Collie's records, all have been aware of the Ivermectin problem but have had no idea about the broad spectrum of drug compounds that can severely threaten an MDR1-affected dog. Please note there are usually alternative, safe drugs your Collie could be given instead.

## Testing procedure

DNA is usually collected on buccal swabs and submitted to any of the following testing laboratories:

**Animal Genetics UK** (*test currently costs £32.00/dog*)

**Genomia** (Czech Republic)

**Laboklin** UK Ltd (*test currently costs £48.00/dog, inclusive of VAT*)

All offer good discounts for testing 5 or more dogs

- **Please refer to the Laboklin web site for the current list of suspect drugs.**
- **Please note, Laboklin and Animal Genetics submit results to the KC if requested on the order forms. Copies of test certificates from other labs must be submitted to the KC by the dog's owner.**
- **Ensure you put your dog's KC registered name on the order form and provide your vet with a copy of the MDR1 test result so it can be added to the dog's veterinary record.**

Pat Hutchinson, Health Coordinator, EACA ©2015