

UK CASE STUDY

In 2003 a UK kennel lost a very promising youngster, who, if he had been tested, may have survived. It was confirmed that he ate grass from a cow field and the cows had recently been treated with a particular worm dose.

In 2004, as part of Mealey/Neff's original research, the kennel had all its dogs DNA tested for MDR-1, but unfortunately they did not inform their Vet that one of these was double negative and in 2008, another loss!

Had the Vet been informed, this Collie was a Double Negative (-/-) perhaps the treatment would have been different. **The owner knew the status but had not informed their vet!** This kennel owner now has the genetic status of all its dogs recorded with their vet, please follow this example so that you do not repeat this error.

NOTES:

*Presented at the MDR 1 Seminar
Sponsored by Rough Collie Breed Council
and supported by Smooth Collie Club of GB – English Shetland Sheepdog Club
Border Collies – Australian Shepherd Club of UK
12 February 2011*



The ROUGH COLLIE BREED COUNCIL

established 1966
www.roughcolliebreedcouncil.org.uk

MULTI DRUG RESISTANCE 1 (MDR-1) GENE

ITS SIGNIFICANCE TO SUSCEPTIBLE BREEDS

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WHAT IS MDR-1

An allergic reaction to drugs is no stranger to man or beast and it has long been recognised that Rough Collies, along with Smooth Collies, are particularly sensitive to a range of sedatives, tranquillisers and anaesthetics. It is now known that Australian Shepherds, Border Collies, Old English Sheepdogs, Shetland Sheepdogs, Long Haired Whippets, Silken Windhounds together with a number of regional sheepdog varieties and newly developing breeds are also affected.

MDR-1 - Multi-Drug Resistance is **NOT** a life threatening disease, it is a statement that your dog, due to a genetic disorder, can if given or prescribed certain drugs (*Not only Ivermectin*) react to them in unexpected ways and in some cases these drugs may be lethal!

MDR-1 is a Protein (*P_Glycoprotein*) which is responsible for pumping out drugs and toxins from the brain. Animals which do not possess this protein are unable to prevent the toxins from drugs and other disorders permeating the brain.

It appears to be predominating in those pastoral breeds known to be descended from the early British Herding dogs. Full details of those breeds affected can be found on the Rough Collie Breed Council web-site. www.roughcolliebreedcouncil.org.uk/drug_sensitivity.html

MDR-1 is also prevalent in the human race.



some incidence of drug sensitivity. Once analysed the results revealed a pre-existing mutation of the **MDR-1** gene in the wider Collie family, possibly dated early to mid nineteenth century, which confirmed what many Collie enthusiasts had long suspected.

The American research team's findings were published as recently as 2004, and the DNA test perfected by the research team made available, in both America and Europe, during 2007, therefore the significance of the MDR-1 mutation has yet to be fully evaluated. There are those who believe that this is far in excess of currently accepted knowledge, sighting the fact that when given as a cocktail of drugs the effects are far more serious, while others prefer to deny its relevance.

Whatever your belief, the knowledge that a DNA test exists, can only assist veterinarians in their choice of treatment options, this of greatest importance when deciding the treatment for more serious conditions such as cancer and heart disease.

The European scientific team working in Germany are still actively investigating the effects of abnormalities in the Multi Drug Resistance gene complex, together with its production of P-glycoprotein, on humans and it is believed that their finding will also apply to the canine species, but time is required before speculative theory can be translated into irrefutable fact. Until this happens breeders are urged to DNA test all breeding stock, taking the results into consideration when choosing a suitable mate, and owners are encouraged to insist that their veterinary advisors not only add their pet's genetic **MDR-1** status to their medical records, but to also fully research the problem before treating any Collie related animal.



HOW IT WAS DISCOVERED

Early in the 1980s a new class of anti-parasitic preparations for large animals, based on the active ingredient, *Ivermectin*, became available for general veterinary use and although not licensed for use on dogs veterinary practitioners were not slow in discovering its usefulness when treating persistent cases of parasitic infestations, so that it quickly became the drug of choice especially when mange was diagnosed.

Shortly after *Ivermectin's* introduction to the veterinary armory rumours began to circulate about its adverse side-effects when administered to Rough Collies. When a well known Italian breeder lost four of her valuable Rough Collies after an *Ivermectin* based drug was administered as a wide spectrum anti-parasitic preventative to her kennel suspicions became facts which were widely circulated by breeders throughout the world. However the veterinary profession as a whole remained sceptical despite Merck Sharp and Dohme Ltd [MSD], who manufactured the drug used in the Italian case, issuing the following advice — '*Ivermectin is known to have an adverse effect on certain breeds of dog*' — in three letters written to the editor of 'The Veterinary Record'. A more detailed warning included in the drug's packaging was not introduced until after at least one more serious breeding kennel lost several valuable animals.

As the number of breeds reporting adverse reactions increased and additional drugs, several of which were licensed for canine use, were added to the list of suspect preparations, two groups of veterinary scientists began investigating the origin of this apparent problem. Early observations showed affected dogs had an elevated concentration of the offending substance in their central nervous system, when this fact was linked to the discovery that genetically modified laboratory mice, being used in quite independent research into the necessity of the Multi Drug Resistance-1 [MDR-1] gene, quickly died when treated with an '*Ivermectin*' based spray for a mite infestation, the American based team, headed by Dr Katrina Mealey and Dr Mark Neff, gained the necessary breakthrough in isolate the cause of this problem.

In order to take this research forward a DNA test was perfected, with swabs collected internationally from a wide selection of apparently unrelated breeds, mostly pastoral and hounds, which had reported

HOW TO TEST

MDR-1 Testing can be carried out at any age from 6 weeks onward, and although currently it can be costly, hopefully in time, with more people making use of the system, it could reduce.

The approximate turn around for obtaining results is 7 days from a simple swab test or blood sample.

SWAB TEST: This can be taken by the owner and involves Buccal Swab taken from inside the cheeks. The sample is then forwarded to a laboratory with appropriate named identification

BLOOD TEST: This should be taken by a Veterinary Surgeon, and involves from 0.5 – 1.0 ml of blood, which again should be identified. The advantage of this method being samples can be retained by the laboratory for the lifetime of the dog. In the future, with more DNA testing for other problems, perhaps this is a route to consider

Either way it is preferable to have the sample correctly and officially identified as the Kennel Club now require for most KC Health Scheme Results to be confirmed by use of a Micro-Chip,

Although a swab test is perfectly acceptable, there are some who will always try and avoid the truth by submitting results from animals other than the one in question!

KC APPROVED LABORATORIES

Laboklin – Europe

<http://www.laboklin.co.uk/>

Genomia Laboratory – Eastern Europe

<http://www.genomia.cz/en/test/mdr1/>

Veterinary Clinical Pharmacology Lab – USA

<http://www.vetmed.wsu.edu/depts-VCPL/>

TEST RESULTS RECEIVED - WHAT NEXT ?

Once the laboratory has tested the sample, the status of the dog will be recorded as follows:

- /- Double Negative – thus more prone to reaction
- +/- Carrying one negative gene – also prone to reaction
- +/+ Clear, none carrier

At present, there are no proven links between MDR-1 and any other health problem but with the advances in medicine, both Canine and Human there is always a possibility that this may change.

DANGEROUS DRUGS

The Rough Collie Breed Council, representing all the Rough Collie Breed Clubs, includes several pages on its web-site advising on all health matters <http://www.roughcolliebreedcouncil.org.uk/health.html> including MDR-1, and receives regular updates concerning the possible use of other “**Dangerous**” drugs.

The list of drugs which may affect our dogs is growing daily making it impossible to reprint all those known here.

A summary of known drugs may be found on information sheets supplied by testing laboratories, or by research through the internet

These drugs are roughly divided into 3 groups, A,B & C.

Class A drugs are those which should not be used on MDR1 affected animals

Class B drugs are those to be used under Veterinary supervision

Class C drugs should only be used in the permitted application and dosage



THE WAY FORWARD

It is up to individual breeders and owners to test through any of the recognised outlets and to inform **not only the Veterinary Profession** but prospective purchasers of stock and other breeders when considering breeding programmes.

Vets are more than helpful if they are made aware that certain drugs should not be administered and in many cases, can and do offer alternative treatments.

The Rough Collie Breed Council, on behalf of its Member Clubs, would like to assure all owners of affected breeds that even those graded double negative [-/-] after a DNA test regularly live long happy healthy lives.

The side effects of this drug sensitivity do not surface until one of the problem drugs are administered for an unrelated health condition, the solution is to avoid these drugs which is perfectly possible.

SHOULD BREEDING RESTRICTIONS BE IMPOSED ?

With the advantages of modern genetic testing there appears no need to restrict breeding only to Clear/Clear (*i.e.* +/+) animals. Breeders can use the knowledge gained from modern techniques to improve the health status of the breed while retaining the breed qualities already attained. To do otherwise could leave a breed with little resemblance to its Breed Standard.

