

An allergic reaction to drugs is no stranger to man or beast, and it has long been recognised that Rough Collies are particularly sensitive to a range of sedatives, tranquillisers and anaesthetics, although many in the veterinary profession have and continue to pour scorn on such claims.

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 armoury 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 discover 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 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.

A large number of drugs are known to be controlled by the MDR-1 gene in man although there is insufficient data available to be specific about the way these drugs may affect dogs carrying the double mutant (-/-) MDR-1

gene, but it is now recognised that more than fifty substances are known, suspected, or have the potential to cause problems with these dogs and this list is being extended almost daily. These drugs, although not necessarily licensed for dogs in the UK, are used to treat a wide spectrum of canine ailments including cancer, heart disease and pain relief, in addition to anti-parasitic and anti-histamines preparations which sparked off the original research.

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.

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 not surfacing until one of the problem drugs are administered for an unrelated health condition, the solution is to avoid these drugs which is perfectly possible.