

## Genetic disorders in dogs

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There has been a shift over the last few years in the profile of diseases that veterinarians encounter in the dog. Improvements and developments in antibiotics, antihelminthics and more effective vaccines have controlled many of the infectious diseases that have caused problems in the past. As a result, there has been a relative increase in diseases that have a genetic basis.

In excess of 350 inherited diseases, or diseases where inheritance is thought to play a part, have now been recognised in the dog. Of these, we know the precise mode of inheritance in approximately 55% of cases, and of these approximately 70% (around 140 distinct conditions) are the result of a single recessive mutant gene. Of the rest, a small percentage result from a single dominant mutation and the rest represent complex or polygenic conditions, where more than one gene requires to be mutated, usually in a recessive fashion, in an affected dog. Unfortunately, many of the inherited diseases that exercise breeders' minds the most, like hip dysplasia, epilepsy auto-immune diseases, heart disease and cancer, are polygenic in nature.

One of the major challenges facing present-day dog breeding is to address, control and eradicate these inherited diseases. Unfortunately, as the figures above show, the vast majority results from recessive mutations and this makes control much more difficult. This is because clinically normal dogs can in fact be carriers of the mutation. Although carriers will not become clinically affected, and are consequently therefore very difficult to identify, they will pass on a mutant version of a disease-causing gene to some of their offspring. In this way, carriers act like silent genetic reservoirs of the mutation dripping mutant genes into the gene pool causing the breed frequency to increase. Ultimately a point will be reached where the probability that two carriers will mate and produce one or more affected offspring becomes high.

Identifying carriers before mating is key to a breeder's efforts to control the spread of inherited disease. At the moment, the only way that carriers can be identified for most of these conditions is to use traditional pedigree analysis. Take a condition that results from a single recessive mutant gene, like Progressive Retinal Atrophy in the Labrador. If a litter is born to clinically normal parents having one or more affected puppies, then both parents are obligate carriers. Unfortunately, this kind of analysis can miss a number of carriers, for example, the carrier frequency may be low so that the chances of two carriers mating to produce an affected offspring will be low. Similarly, two carriers could mate but, by chance they don't actually produce an affected puppy.

If progress is to be made we need a more reliable method of identifying carriers so that breeders can take this into account when developing their breeding programmes. Fortunately, recent progress of the canine genome project has provided detailed genetic maps of canine chromosomes which will help scientists to identify the genetic mutations that cause these inherited diseases. Once a mutant gene has been identified, a simple DNA test can be developed to identify the presence of a mutant gene in an individual dog. Such developments greatly add to the armoury that a breeder can use to address inherited disease. By testing all potential breeding stock before they are mated a breeder will know whether they have a genetically clear dog, a carrier or, perhaps an affected, and take note of this when deciding whether to breed from the tested dog or not.