

ARDS in Dalmatians

- *The author, dr.Tyge Greibrokk, has been professor of analytical chemistry at the University of Oslo in Norway since 1986. He is the head of a major research group, international editor of a scientific journal, he has supervised more than 120 masters and Ph.D. students and he is the author/coauthor of about 250 scientific publications, including papers on methods for DNA-analysis and one paper on inherited deafness among Dalmatians.*

Introduction

Adult Respiratory Distress Syndrome (ARDS) appeared as a symptom of a genetic defect (ref.1) among Dalmatians in Finland (and once in Denmark) in the years 1987-1997. In Finland 6 litters were affected, the last in 1997, with a total of 17 dogs thought to be suffering from the disease. All the 17 dogs died or were euthanized. Early on, indications for an inherited disease were found by dr. A.-K. Järvinen and coworkers in Finland and studies of the pedigrees of the affected litters soon pointed towards the bitch O'Soul Escada as the probable source of a genetic defect. The damage to her genes is thought to have been caused by a point mutation. Several of the descendants from Escada were extensively used in breeding and the results (concerning ARDS) appeared to be in accordance with an autosomal recessive mechanism of inheritance. Although there has been no test matings to ultimately prove this mechanism, the national breed clubs in Finland, Norway and Denmark and the health committee of the Danish Kennel Club have accepted the recessive inheritance hypothesis based on strong circumstantial evidence.

A study utilizing simple statistical methods for estimating the number of affected dogs that would be expected in Finland, starting with the first litter after Escada in 1977 (the O'Soul K-litter), ending with all the litters registered in 1997, including all the litters in between (in Finland), supported the hypothesis of a recessive inheritance (ref. 2).

Probability of inheriting the defect gene

A dog which has inherited the recessive defect gene is called a carrier. A carrier cannot become ill, unless both parents carried the bad gene. If a carrier is mated to a non-carrier, the probability for a puppy of inheriting the mutant gene is 50% (1/2). Since we in most cases do not know who the actual carriers are, we can only talk about statistical probabilities for inheriting the defect gene. This means that in the next generation (the 2. generation after a known carrier) the statistical probability for being a carrier is 1/4, in the 3. generation 1/8, in the 4. generation 1/16, in the 5. generation 1/32, in the 6. generation 1/64, in the 7. generation 1/128 and so on. All this assumes that the other parent is outside the ARDS lines. Thus, from the 7. generation on, the probability of being a carrier is less than 1%.

A recessive gene in the population will by constant "dilution" (mating each new generation with non-carriers) soon become no health problem, as long as new carriers are not produced. As a matter of fact point mutations are quite common and a national population may contain many defective recessive genes, which are not known, appearing only by extensive in-breeding. This is the reason why small populations are bound to give genetic problems and why it is important not to reduce the genetic variation more than absolutely necessary.

Probability of provoking the disease

Recessive inheritance means that the illness can only be caused by parents both carrying the disposition for the defect. In average, 25% of the puppies (1/4) after two carriers will become ill, 25% will be free of the gene, while 50% will inherit the gene without becoming ill. It is important to be aware of that this is the statistical average of large numbers. Thus, in a small litter it is very likely that no defects will be found. The way of calculating the statistical probabilities of provoking the disease, in mating two dogs which both have an ARDS background, is to multiply the two probabilities. If a 7. generation dog is mated with a 6. generation dog, the probability of provoking ARDS is 1/128 multiplied with 1/64, which is close to 0.01%. For all practical purposes this is outside the danger zone.

Recommendations to the breeders

In 1993 the discussion of means to stop the ARDS threat, spread from Finland to Norway and Denmark. The breed clubs made some preliminary recommendations, until further knowledge could be obtained. The author of this article, who by the way had no breeding on the ARDS lines, argued for taking rapid measures, in accordance with the expectations of recessive inheritance. The discussion soon centered on the potential losses by eliminating too many good dogs from breeding, versus the risk of spreading the mutant genes. After extensive discussions with veterinarians that were familiar with inherited diseases, it became clear that the specialists would not give direct advice on exactly where to stop breeding, because they had little knowledge of other potential problems that could be provoked by limiting the population too much. Everybody agreed on, however, that parents, littermates and direct offspring of afflicted dogs should not be used in breeding. Further measures were left to the breed clubs to decide. The recommendations which finally were made, met no opposition when this author discussed the situation with geneticists at a conference of inherited canine diseases in UK in 1994. Later, when the situation had become less urgent concerning immediate measures, the recommendations (in Denmark, Finland and Norway) were strengthened in order to prevent new carriers from being imported.

Current rules/recommendations in breed clubs

Several breed clubs have rules/recommendations for their breeders concerning ARDS. In general these recommendations are equivalent with those recommended by the European Cooperation of Dalmatian Clubs (ECDC), that the first 5 generations after a known carrier shall not be used in breeding.

In Denmark, imported dogs must not be closer than 7 generations after a carrier. Several clubs also recommend that the sum of generations of the parents of a litter should be at least 12 (6+6), 13 (6+7) or 14 (7+7 or 6+8)).

According to the opinion of this author, more breed clubs could assist their breeders by making recommendations for breeding. Such recommendations should probably vary in different countries, according to the size of the potential problem. It is important that the information is balanced, not resulting in hysteria and war between breeders. Furthermore it should be made clear that it is up to the breeders how long the ARDS will continue to be with us as a potential problem. By continued breeding on dogs close to carriers, the ARDS threat will stay with us. By breeding away from the carriers, the problem can be solved in a few years, as demonstrated by the development in the Nordic countries.

Possibility of identifying a carrier

In theory it is possible to develop methods to identify the carriers by analyzing their DNA. However, the site of the mutant gene on the DNA is not known, and blood samples are available anymore. Current methods cannot resolve the problem, unless new research is directed towards developing more information. Unfortunately, such research is very expensive, probably too expensive for the limited resources of the breed clubs in Europe. The possibility of developing a DNA-test for checking the absence/presence of a carrier in the near future, is therefore not high. Consequently it would be wise to use the information which already is available today.

Getting information

Information on theoretical carriers was calculated by the author for ECDC and is available on the web side (ref. 3). Dalmatian owners/breeders seeking the "ARDS-status" of their dog(s) may also contact the author, with a copy of the pedigree(s).

References

- 1) A.-K. Järvinen, E. Saario, E. Andresen, I. Happonen, S. Saari and M. Rajamäki, Lung injury leading to respiratory distress syndrome in young Dalmatian dogs, *J. Vet. Int. Med.* 9 (1995) 162-168
- 2) T. Greibrokk, Inheritance of the disposition for ARDS among Dalmatians, ECDC meeting, Kolding, Denmark, August 1999
- 3) www.ecdc.org