Investigation of the potential heritability of persistent right aortic arch in Greyhounds

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To further investigate the birth of 4 pups with PRAAs in 3 different litters born of 2 different sets of parents in the kennel of this report, relevant pedigrees were reviewed (Fig 1). Within the overall racing Greyhound population, 61% of dogs are completely outbred (ie, the sire and dam have no ancestors in common), with only 39% having some degree of inbreeding. Furthermore, the subset of racing Greyhounds used as breeding stock is 95% outbred. The mating pair described first in this report (that produced litters in May 1997 and January 2001) was considered part of this breeding stock subset; by use of a computer program, an inbreeding coefficient of 0% was calculated for mating of that pair of dogs. The inbreeding coefficient is the probability that 2 alleles in the offspring for any given gene are identical by descent (as opposed to random chance) and is calculated by examining 6 previous generations for inbreeding. Because most undesirable traits are thought to be recessive, the higher the inbreeding coefficient for a given mating, the more likely a defect may be evident in the resultant offspring. The second mating pair of this report had an inbreeding coefficient of 0.39%. Although the dogs of this mating are included in the subset (5%) of breeding Greyhounds with some level of inbreeding, this degree of inbreeding can be considered miniscule. For comparison, a mating between 2 dogs with 1 common grandparent is 1.6%. Overall, it can be concluded that the 4 puppies with PRAAs of this report were no more inbred than any typical racing Greyhound.

Nonetheless, subjective evaluation of the pedigrees illustrated a number of first generation dogs directly shared by all sixth generation descendant puppies. Additionally, both parents of the 1 affected puppy in the litter born in September 2001 were traced to 2 great, great grandparent sibling males, in the fifth generation. In combination, these data support the theory that PRAA in that puppy was an inherited defect, despite the statistical finding that the inbreeding coefficient for that mating was no larger than that among the breeding population as a whole.

After evaluating the environment in which these dogs were bred, it did not appear likely that a teratogen had resulted in these puppies' vascular defects. Both bitches had not been administered any medication; they had received only a supplement containing calcium, potassium, and vitamins during pregnancy, which was given to all pregnant bitches at this kennel. The kennel facility was free from industrial runoff, and the quality of the well water was tested. Since the birth of the puppies with PRAAs, the owners of the kennel...
have not altered its management or breeding practices and there has not been any reoccurrence of PRAA or other defects in the puppy population.

Congenital heart defects represent one of the most commonly reported malformations in dogs, affecting approximately 1% of animals epidemiologically. The 6 most common heart defects have all been proven to be heritable through genetic studies: patent ductus arteriosus, pulmonic stenosis, subaortic stenosis, ventricular septal defect, tetralogy of Fallot, and PRAA. The incidence of these heart diseases is highest among purebred dogs, and in the case of PRAA, epidemiologic studies, as well as breeding studies, have proven German Shepherd Dogs and Irish Setters genetically predisposed to its development.

However, not all congenital heart defects are caused by genetic inheritance. Generally, when a defect that is not common to a specific breed is detected, it is thought most likely to be non-genetic in origin. As a result, the clinician and breeder alike may reasonably attribute the defect to errors in development or a spontaneous genetic mutation, and not recommend against future matings between that sire and dam. However, if a repeat breeding produces the same defect in the offspring, it cannot easily be dismissed as a spontaneous development and further investigation is warranted.

Whether the occurrence of PRAA in these Greyhounds should be considered congenital or heritable remains a matter of debate. The mode of inheritance of PRAA, along with the other 6 most common heart defects, is complex and polygenic in its basis. Initially, investigation of the heritability of heart defects such as PRAA began with epidemiologic studies, the results of which indicated that purebred dogs are more prone to development of heart defects than are mongrel dogs. In familial breeding studies involving matings between 2 individuals of the same breed with similar heart defects, not only was there a high frequency of congenital heart disease in the offspring but also the type of heart defect detected in those puppies was identical or closely related to that of the parents. The results of further investigations fitted polygenic models of inheritance, in which the genes act additively to increase embryologic susceptibility to the development of a specific heart defect.

At present, research is underway to identify the locations of genetic defects (such as PRAA) in the canine genome. One approach involves comparative genetic research. In humans, 80% of conotruncal heart defects, including aortic arch abnormalities, have been associated with deletion of the chromosome 22q11 region (also known as the DiGeorge region). However, comparative mapping of the DiGeorge region has ruled out its linkage to conotruncal heart defects in dogs. Another approach in genetic research is detection of cosegregation of microsatellite DNA markers with the disease trait. This technique is most applicable to clinical veterinary medicine because it relies on case identification. By comparing the genome of affected animals with unaffected siblings and parents, a candidate gene may be identified. However, the limiting factor with this approach is accurate diagnosis and establishment of proper sample size. For example, assuming PRAA to be a simple dominant or recessive disease trait in the Greyhounds described in this report, it would be necessary to examine the
genomes of at least 20 affected dogs, their siblings, and parents. With a sample size of only 3 affected living puppies in this report, such an approach was not possible. Furthermore, PRAA appears to be a complex trait that involves the combined effects of genes at more than 1 locus and would require an even larger database of affected dogs and their families for investigation. Any such research undertaking would require long-term data input from breeders and extensive genetic analyses. Without doubt, there is a need for coordinated reporting of the occurrence of genetic defects and analysis of the basis of their heritability. Until such information is available, recommendations regarding the potential heritability of many congenital defects will largely be made on the basis of opinion or limited personal experience.

References

Pedigree information provided by the National Greyhound Association, Abilene, Kan.