Genetics of Deafness in Dogs

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Congenital deafness in dogs (or other animals) can be acquired [caused by intrauterine infections, ototoxic drugs like gentamicin, liver disorders, or other toxic exposures before or soon after birth] or inherited. Inherited disorders most commonly can be caused by a gene defect that is either autosomal dominant, autosomal recessive, sex-linked, mitochondrial, or may involve multiple genes (more on this later). It is usually impossible to determine the cause of congenital deafness unless a clear problem has been observed in the breed, or carefully planned breedings are performed. In this article I will discuss what is currently known about the genetics of deafness in dogs so that breeders can make the best informed decisions possible when attempting to reduce or eliminate deafness.

Congenital deafness has been reported for more than 100 dog breeds, with the list growing at a regular rate (see list); it can potentially appear in any breed but especially in those with white pigmentation of skin and hair. Deafness may have been long-established in a breed but kept hidden from outsiders to protect reputations. The disorder is usually associated with pigmentation patterns, where the presence of white in the hair coat increases the likelihood of deafness. Two pigmentation genes in particular are often associated with deafness in dogs: the merle gene (seen in the collie, Shetland Sheepdog, Dappled Dachshund, Harlequin Great Dane, American Foxhound, Old English Sheepdog, and Norwegian Dunkerhound among others) and the piebald gene (Bull Terrier, Samoyed, Greyhound, Great Pyrenees, Sealyham Terrier, Beagle, Bulldog, Dalmatian, English Setter). However, not all breeds with these genes have been reported to be affected. The deafness, which usually develops in the first few weeks after birth while the ear canal is still closed, usually results from the degeneration of part of the blood supply to the cochlea (the stria vascularis). The sensory nerve cells of the cochlea subsequently die and permanent deafness results. The cause of the vascular degeneration is not known, but appears to be associated with the absence of pigment producing cells known as melanocytes in the stria. All of the functions of these cells are not known, but one role is to maintain high potassium concentrations in the fluid (endolymph) surrounding the hair cells of the cochlea; these pigment cells are critical for survival of the stria and the stria is critical for survival of the hair cells. A different form of congenital hereditary deafness is seen in the Doberman, which is also accompanied by vestibular (balance) disturbance; this deafness results from a different mechanism where hair cell death is not the result of degeneration of the stria but is instead the primary pathology. Deafness may also occur later in life in dogs from other causes such as toxicities, infections, injuries, or due to aging (presbycusis); most of these forms of deafness do not have a genetic cause in animals and thus do not present a concern in breeding decisions, but a newly-identified form of adult-onset hereditary deafness is now recognized in Border Collies and Rhodesian Ridgebacks.

The prevalence of congenital deafness in different breeds is seldom known because of the limited number of studies (see table). In the Dalmatian, where the prevalence is highest, 8% of all dogs in the US are bilaterally deaf and 22% are unilaterally deaf; rates are lower in Europe. In the English Setter, English Cocker Spaniel, Australian Cattle Dog, and Bull Terrier, where fewer numbers of dogs have been hearing tested, the prevalence appears to be about one third to one half that of Dalmatians. Unilateral or bilateral deafness is found in 75% of all white Norwegian Dunkerhounds, but the prevalence in normal-color dogs is

unknown. Other breeds with a high prevalence are the Catahoula and Australian Shepherd. The prevalence of all types of deafness in the general dog population is low, reported to be 2.56 to 6.5 cases per 10,000 dogs seen at veterinary school teaching hospitals, but these data predate the availability of hearing testing devices and so are much lower that actual values. Recognition of affected cases is often difficult, because unilaterally deaf dogs appear to hear normally unless a special test (the brainstem auditory evoked response, BAER) is performed; facilities to perform the BAER are usually only available at veterinary schools (see list). It should be noted that a unilaterally deaf dog can be as great a genetic risk for transmission of deafness to its offspring as is a bilaterally deaf dog, so BAER testing of puppies from affected breeds is important.

The method of genetic transmission of deafness in dogs is usually not known. There are no recognized forms of sex-linked deafness in dogs, although this does occur in humans. The disorder has been reported to have an autosomal recessive mechanism in the Rottweiler, Bull Terrier, and Pointer, but these suggestions are not reliable because the reports were published before the availability of BAER testing and the ability to detect unilaterally deaf dogs. Studies of the Pointer used a highly inbred research population ("anxious" Pointers), which can obscure the mode of inheritance. Some references state that deafness transmission in most other breeds is autosomal dominant, but this is false, as will be discussed below. Pigment-associated inherited deafness is not restricted to dogs. Similar defects have been reported for mice, mink, pigs, sheep, horses, cattle, cats, ferrets, rabbits, llamas, alpacas, and humans. Deafness in blue-eyed white cats is common, first mentioned in Darwin's *Origin of Species*. Blue eyes, resulting from an absence of pigment in the iris, is common with pigment-associated deafness but is not, in and of itself, an indication of deafness or the presence of a deafness gene; however, in several breeds (Dalmatian, English Setter, English Cocker Spaniel, Bull Terrier), dogs (and cats) with blue eyes are statistically more likely to be deaf. Waardenburg's syndrome, a human condition, presents with deafness, a stripe of white in the hair and beard, blue or different colored eyes (even in Blacks and Asians), no pigment behind the retina, and minor structural deformities around the nose and eyes. This is an autosomal dominant disorder with incomplete penetrance, which means that individuals that inherit the disorder may not show all components of the syndrome - i.e., they may not be deaf. Incomplete penetrance of a defect greatly complicates the determination of mode of inheritance. **At present** there is no documentation that incomplete penetrance is a factor in any canine deafness, except perhaps that deafness can affect one or both ears.

In simple Mendelian genetics, each dog carries two copies of each gene, one from each parent. The possible outcomes of breedings can be demonstrated with tables showing the genotype of both parents and the possible combinations in their offspring. If deafness is carried as a theoretical simple autosomal recessive gene (d), the breeding of two hearing carriers (Dd) (Table 1) will result, **on average**, in 25% affected dogs (dd), 50% hearing carriers (Dd), and 25% free of the defect (DD). It must be emphasized that these percentages reflect average breeding outcomes and not necessarily every individual litter. The breeding of a carrier to a dog free of the defect (Table 2) will result in no affected dogs but 50% carriers and 50% free. The breeding of an affected dog to a carrier (Table 3) will result in 50% affected, 50% carriers, and no free. Finally, the breeding of an affected dog to a dog free of the defect (Table 4) will result in 100% carriers and no affected or free.

If instead the deafness is carried as a simple autosomal dominant gene (D), the breeding of an affected dog (Dd) to a free dog (dd) (Table 3) would result **on average** in 50% affected and 50% free. Dogs with the genotype DD would be unlikely to occur unless two deaf dogs had

been bred. All of the above assumes that incomplete penetrance is not acting. If more than one gene (recessive and/or dominant) is involved in producing the deafness, the possible combinations become much more complicated. In humans more than 50 different autosomal recessive or dominant deafness genes or loci have been identified. The children of two deaf parents with two different recessive deafness can be unaffected but carry both genes. If deafness in dogs results from more than one recessive gene, the possible outcomes of breedings are more numerous and determination of the mechanisms of transmission will be difficult.

As stated above, deafness can be associated with the merle (dapple) gene, which produces a mingled or patchwork combination of dark and light areas overlayed on the basic coat color. This gene (*M*) is dominant so that affected dogs (*Mm*) show the pigmentation pattern, which is desirable in many breeds. However, when two dogs heterozygous with merle (*Mm*) are bred, 25% will end up with the *MM* genotype (i.e., Table 1). These dogs usually have a solid white coat and blue irises, are often deaf and/or blind, and may be sterile. Breeders in these dog breeds know not to breed merle to merle. In this case the deafness is neither dominant nor recessive, but is linked to a dominant gene that disrupts pigmentation and as a secondary effect produces deaf dogs.

Piebald is a recessive allele of the *S* gene, where the dominant allele is expressed as a solid color. Three recessive alleles are recognized: Irish spotting (s^i), piebald (s^p), and extreme white piebald (s^w). These gene alleles affect the amount and distribution of white areas on the body, with the three displaying increasing amounts of white in the order listed. Genetic transmission of deafness in dogs with the recessive alleles of this pigment gene, such as the Dalmatian (which is homozygous for s^w), is less clear. Deafness in Dalmatians does not appear to be autosomal dominant, since deaf puppies result from hearing parents. It does not appear to be a simple recessive disorder, since we have bred pairs of deaf Dalmatians and obtained bilaterally hearing and unilaterally hearing puppies, when all should have been deaf if the disorder was recessive. These findings might be explained by a multi-gene cause - the presence of two different autosomal recessive deafness genes, or a syndrome with incomplete penetrance. Further studies will be required to determine the mechanisms. Several candidate genes known to cause pigment-related deafness in humans or other species have been eliminated as the possible cause of pigment-associated deafness in Dalmatians. Whole-genome screens will hopefully identify the cause in this and other breeds.

Recent studies have shown that deafness in Dobermans, which do not carry the merle or piebald genes, results from direct loss of cochlear hair cells without any effects on the stria vascularis. Vestibular (balance) system signs, including head tilt and circling, are seen, and the deafness, which is usually bilateral, is transmitted by a simple autosomal recessive mechanism. A similar pathology has been described for the Shropshire Terrier, a breed that may no longer be in existence.

So what should breeders do when deafness crops up? The most conservative approach would be to not breed the affected animal and not repeat the breeding that produced deafness. It is frequently recommended (i.e. Dalmatian Club of America) that bilaterally deaf puppies should be euthanatized by breeders, since they can make poor pets, are difficult to train, can be prone to startle biting, may die from misadventure (cars), and require excessive care. There is considerable controversy on this point, and there is no question that many people have successfully raised deaf dogs. For every story of a problem deaf dog there seems to be a story of one that was successfully raised. Unfortunately, there is no way to predict how a deaf

puppy will turn out. Unilaterally deaf dogs can make good pets but should not be bred. When deafness is uncommon in a breed, affected dogs should not be bred, but this does not mean that all related dogs are a risk and must be retired from breeding. An understanding of simple autosomal recessive and dominant patterns, as explained above, can allow the breeder to make better informed decisions (even though we do not yet know the mechanism of inheritance) and likely avoid future deaf animals without sacrificing a breeding line that has been shaped over many years. However, extreme caution must be used when line breeding of dogs related to deaf dogs, whether the deafness is unilateral or bilateral. To make these decisions in an informed manner for breeds with known deafness, it is important that advantage be taken of hearing testing facilities at veterinary schools. Unilaterally deaf dogs cannot be detected by other means, and these dogs **will** pass on their deafness genes.

For more details and a more technical discussion, see: Strain G.M. (2015) The genetics of deafness in domestic animals. *Fronteers in Veterinary Science* 2:29. (https://www.frontiersin.org/articles/10.3389/fvets.2015.00029/full). This article is available on-line and is free.

Russian translation: https://animalso.com/ru/dogs-deafness-genetics/ courtesy of Animalso.

Tables:

Theoretical outcomes of breeding of two carriers of a recessive deafness gene (d).

Table 1	Dd	
Dd	DD	Dd
	Dd	dd

Theoretical outcomes of breeding a carrier and a dog free of the recessive deafness gene.

Table 2	DD	
Dd	DD	DD
	Dd	Dd

Theoretical outcomes of breeding a carrier and an affected dog with the recessive deafness gene.

Table 3	Dd	
dd	Dd	dd
	Dd	dd

Theoretical outcomes of breeding an affected dog and a dog free of the recessive gene.

Table 4	DD

dd	Dd	Dd
	Dd	Dd

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