Genetic Testing and Counseling: A Trojan Horse for Dog Breeds?

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Disease-causing genes are searched for by researchers, and the resulting genetic tests are desired by breeders. Once obtained, it is a double-edged sword: Its use can enable breeders to improve a breed or devastate it.

Dog breeds have a closed stud book, which means that there is a finite amount of polymorphic genes and genetic diversity present. They can only lose genes, not gain them through selective breeding.

The primary reaction of a breeder discovering that their breeding stock carries a defective gene is to retire it from breeding. As researchers, we often recommend using a genetic test to eliminate carriers from breeding.

Widespread elimination of all carriers of a high frequency gene can place a strong negative pressure on a gene pool. This can act to decrease the genetic diversity of the breed, cause a loss of other quality genes, and increase the frequency of other defective genes through genetic bottlenecks.

We know that most individuals carry some unfavorable genes. The more genetic tests that are developed, the greater chance that a breeder will identify an undesirable gene in their breeding stock. Making breeding decisions based on a single testable gene is inappropriate**. Any quality individual that would have been bred if it had tested normal should still be bred if it tests as a carrier.** Prospective breeding animals represent the quality of the gene pool. We should be offering genetic counseling recommendations that eliminates defective genes, but maintains breed lines and genetic diversity.

The best way to utilize genetic tests is to breed quality carriers to normal-testing mates, and replace them with quality, non-carrier offspring. This prevents affected offspring, while maintaining breed lines and genetic diversity in the breed.

Genetic Counseling and Control of Genetic Disease

The primary goal of domestic animal breeding is to maintain and enhance the quality of the breed. This is well understood in livestock production breeding, but often overlooked in dog breeding. Breeders must consider all relevant aspects, which may include various health issues, conformation, temperament, and working ability. Health and diversity issues are important, but they must coincide with, and not replace selection for quality.

The goals of genetic counseling are to:
1) prevent the production of additional affected individuals
2) decrease the frequency of the defective gene(s)
3) maintain a genetically diverse pure-bred population

Genetic counseling recommendations need to take into account the dynamics and epidemiology of both the breed gene pool, and the defective gene(s). Rare or low frequency defective genes require more stringent selective pressure to prevent their spread. High frequency (breed-wide) defective genes require more pragmatic management that does not adversely affect the gene pool.

Genetic Counseling Recommendations
-Selection against a **single gene trait with a test for carriers** is based on the individual. Breeders only have to know the results of the individuals they plan on breeding.
-Selection against **disorders that lack a test for carriers, complexly inherited disorders, or disorders with an unknown mode of inheritance**, require knowledge of the carrier or affected status of related animals.

Autosomal recessive disorders:
With a valid genetic test for carriers, breeders should mate quality carriers to normal-testing individuals, and replace the carrier parent with a quality, normal-testing offspring. Carrier-testing offspring should be selected against for breeding. In this way breeders can prevent affected offspring, while eliminating the defective gene from their breeding stock in one generation.

Without a genetic test for carriers, knowledge of the affected or carrier status of relatives is important. This requires testing for the affected phenotype, knowledge of pedigree backgrounds, and relative risk pedigree analysis. An **open health database** is the best method for objectively disseminating this information. Breeders should mate quality, higher-risk individuals to lower-risk individuals. Replace the higher-risk individuals with their lower-risk offspring. Repeat the process in the next generation. If the majority of breeders plan matings with a carrier-risk below the average of the breed, then the frequency of the defective gene will diminish in the population. This has been successfully done in many breeds.

Relative Risk Pedigree Analysis: With simple autosomal recessive genes and no test for carriers, knowledge of affected and carrier relatives can provide an objective risk assessment. Relative risk is the **minimal risk** based on known risk from the pedigree. The positive aspect of relative risk pedigree analysis is that it objectifies risk relative to the population. It allows breeders to understand their own risk, and that of their proposed matings. It allows breeders with higher-risk breeding stock to lower their risk through planned matings. The negative aspect of relative risk pedigree analysis is that it selects against entire families, based on relatives with risk. It selects against both carrier and normal individuals. However, without carrier tests it is an effective tool to reduce the frequency of both affected and carrier individuals, and has been successfully used in many breeds.

X-linked (sex-linked) recessive disorders: Replacing affected and carrier individuals with normal male relatives will lose the defective gene in one generation. Avoid breeding high carrier-risk females, as half of the male offspring from carrier females will be affected.

Autosomal dominant and X-linked dominant disorders: Quality affected individuals should be replaced for breeding with a normal-testing parent, sibling, or prior-born offspring. Ideally you do not want to breed affected individuals, as half of their offspring will be affected.

Complexly inherited (polygenic) disorders, and familial disorders with no known mode of inheritance: The knowledge of affected relatives is important in determining risk status. Open health database registries can provide this important information. Three factors should be considered:

1) Complexly inherited disorders should be viewed as threshold traits. A number of genes must combine to cross a threshold to produce an affected individual.

2) Increased response to selection can be attained by attempting to break down the phenotype into measurable traits that may be more directly linked to the underlying genes. Example: Measuring joint laxity, acetabular depth, or liability to secondary boney changes in hip dysplasia.

3) The most important method to manage complexly inherited disorders is to select for **breadth of pedigree normalcy.** Phenotypically normal individuals with normal or mostly normal littermates have the greatest chance of carrying normal genes. Phenotypically normal individuals with affected littermates have a greater chance of carrying a genetic load of disease-causing genes. Normal parents who have a preponderance of normal littermates provide even greater confidence. An open health database that shows genetic test results of close relatives can provide this information.

Genetic tests are powerful tools, and as with any tool require an instruction manual for their proper use. When these tests are available to breeders, genetic counseling advice should be provided that allows their use to be beneficial, and not detrimental to the breeds.