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Strategies for Managing Genetic Traits, Speaker Jerold S. Bell, DVM

Summary prepared by Diana Engelbart, Nirmankaya Cattery

All cats have genetic characteristics. Some of these traits may contribute to award-winning cats and some may, unfortunately, lead to genetic disease. In his presentation, Dr. Bell gave an overview of modes of inheritance, availability of genetic tests, and how those test results should be used. He discussed what the spread of defective genes means to a breeding program and considerations for working with gene-pool size and the importance of diversity in a breed.

The primary goals of a breeder should be to maintain and enhance the quality of the breed, both in conformation to the standard and in genetic health. Further, breeders should manage genetic disease with the goal to first produce unaffected cats and then decrease the frequency of carriers of the defective genes.

To effectively manage genetic traits, the breeder must understand the mode of inheritance of the trait under consideration. Modes of inheritance are either simple, involving just one gene, or complex in which more than one gene is involved. Simple inheritance is the easier to manage. Examples of traits that display simple inheritance are: progressive retinal atrophy and polycystic kidney disease.

Tests that are available to the breeder may include PCR tests for the gene itself, linkage-based tests, and phenotypic tests. Direct genetic tests will provide direct answers. The challenge to the breeder is to use the test result to improve the breed and not to impact the breed negatively. Linkage-based tests are very useful, but may provide false negatives and false positives. Phenotypical tests may identify affected individuals, but do not identify carriers of defective genes.

A genetic disease may be widespread, either with a high-frequency of the disease occurring in the population, or with a low one. Widespread, high-frequency genetic diseases can put a breed at risk. Recent or emergent mutations need aggressive control so that they can be quickly eliminated from the gene pool and not pose a lingering threat.

The size and diversity of a breed's gene pool is also a factor in considering an effective strategy to control genetic disease. One must use genetic tests wisely to avoid damage to the breed. Draconian measures, such as extensive spaying and neutering, may result in more harm than good by decreasing the breed's diversity.

There are four basic scenarios in managing genetic traits and those scenarios are based on modes of inheritance.

In the first scenario. the trait is passed along by a recessive gene, and there are two subcategories: a test exists to identify carriers or no test exists. If a test exists for carriers, then the following strategy should be used to bring the breeding group to a condition of health. In the first generation, carriers of excellent quality should be bred to cats of equally excellent quality that are normal genetically. The carrier

parent should be replaced in the breeding program by a genetically normal offspring. In future generations, selection should be made against carriers for breeding. Note that in this scenario, a carrier does not develop disease and is otherwise healthy.

If no test is available, a vertical mating system should be used. Replace a known carrier or high-risk cat with quality offspring. Breed the quality offspring to a low risk mate, and replace them with their quality offspring. Repeat this approach to ensure maintaining good genetic qualities while reducing the risk of detrimental attributes.

In order to make this approach more effective, a relative/recurrence risk analysis should be performed. It is vital that the recessive mode of inheritance be known. An open health registry should be used. This means openness not only among breeders but also between breeders and owners needs to be in place.

The benefits of this approach are that the risk can be lowered, the risk can be understood, and means to deal with the problem can be rationally understood. However, this approach also has the danger that entire families, or lines, may be selected against unnecessarily and that selection may be made against both carrier and normal cats.

In the second scenario, the defective gene causing disease is dominant. In this scenario, affected cats should be replaced with normal siblings, parents, or older offspring. Genetic testing should be used to identify normal and affected individuals, so that appropriate breeding choices can be made. In the case of a dominant gene, there is still the opportunity to harvest the good genes from the individual through wise breeding choices.

In the third scenario, the trait is passed along via sex linkage. The basic strategy for dealing with this mode of inheritance is to breed and replace affected the males and carrier or high risk females with normal males or prior-born normal male offspring. Only normal males should be used, as carrier females will produce affected males.

In the fourth scenario, the genetic trait is based on a number of genes (i.e., it is polygenetic), or there is an unknown mode of inheritance. In this case, the breeder needs to understand the phenotypic breadth of the pedigree. This includes the status of the littermates of potential breeding stock, as well as the littermates of parents. This provides the most information possible on the range of genes involved, and again requires an open health database. Breedings need to be examined to determine which offspring are affected and which are not. Both parents will contribute to the severity of the problem. Only through careful analysis will it be possible to select the most appropriate breeding stock.

Ultimately, in order to overcome genetic problems within a breed, it will be necessary to know the bad as well as the good. Along with the databases and other tools, it will be of utmost importance to drop the stigma attached to these genetic problems. Breeders must share information freely.

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