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Gene Pools

MAINTAINING AND IMPROVING BREEDS

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In order to understand how to maintain breeds, we have to understand the genetic forces that shape them. Natural species evolve through natural selection. Any genetic changes within a population that improve the chance of survival and ability to reproduce in the populated environment will be at an advantage and thrive. This results in a loss of genetic diversity through the disadvantaged. This loss is not detrimental to the population as it is directly related to increasing its superiority.

Dog breeds develop through artificial selection for desired phenotypes – what you can see in the dogs. These can include conformation, behavior, working ability and health. Most breeds originally started from either a small population of related founders, or as a population of unrelated dogs that conformed to a working or conformational phenotype. Some breed lines will be discarded over time due to genetic defects, or an inability to adhere to a standard. Regardless of the breed origin, generations of reproduction within a small population produce homozygosity (the fixation of gene pairs) through close breeding. This is what causes breeds to reproduce themselves with each generation.

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Genetic studies of dog breeds show that they lose on average 35% of their genetic diversity through breed formation. Genetic studies also document the increased homozygosity found in dog breeds. **Low effective population size (low number of founders) and high deep-pedigree inbreeding coefficients (homozygosity) are a natural and expected consequence of breed development.**

Breeds differ from natural populations in that only a small percentage of dogs reproduce to create the next generation. In a population sense, this represents a genetic bottleneck with each generation. Individuals chosen for breeding should represent the quality traits of the breed. Quality traits should not be lost through the absence of selection or the abandonment of quality lines.

> *"The popular sire syndrome is the single most influential factor in restricting breed gene pool diversity"*

Population expansion is an important aspect of breed maintenance. If the offspring of small population breeds are generally healthy their population can grow and expand. They are at stages of breed development where more populous breeds were earlier in their development. Breeders of small population breeds need to mentor their puppy buyers to expand their breeder base as well as the number of dogs.

Population expansion allows the creation of new "family lines." A larger population allows average relatedness of breeding pairs (based on recent generations) to be less than the prior generation. Population contraction is detrimental to breed maintenance due to the loss of quality breeding lines and genetic diversity. **Healthy breed gene pools require expanding, or large, stable populations.**

There are times when a lot of breeding is going on and registrations are increasing, and times (such as the recent past) when less breeding is going on. However, it is the offspring that reproduce (regardless if from prolific or limited-breeding parents) that contribute their genes to the next generation. Breeding quality dogs from different "lines" and areas of the gene pool prevents the loss of genetic diversity.

The popular sire syndrome is the single most influential factor in restricting breed gene pool diversity. When a breed is concentrating on a specific sire or multi-generational sire line, other quality male lines are abandoned. This causes a loss of genetic diversity to the breed gene pool in exchange for a rapidly increasing influence of the popular sire. Now is an important time to use frozen semen of quality dogs from the past to expand gene pools. Stored DNA (such as from the OFA CHIC repository) or semen can be used for breed-specific genetic testing that might not have been previously available.

All individuals carry some deleterious genes, which can increase in frequency with natural as well as artificial selection. More "lines" of naturally occurring species have died off due to genetic disorders or diminished fitness than those that have survived. As individuals propagate, deleterious mutations can become breed-related disease if they are disseminated and increase in frequency.

Studies show that some breeds have more issues of specific genetic diseases with linebreeding and others do not. This depends on the genetic load of deleterious recessive genes in the gene pool. **The genetic health of dog breeds is not a direct function of homozygosity, genetic diversity, or population size; but of the accumulation and propagation of specific disease liability genes.**

Artificial selection to maintain breeds requires active selection against deleterious genes. This is easier with dominant or additive genes, as the genotype is observed in the dog's phenotype. For recessive deleterious genes, selection involves the development and use of genetic tests that reveal the carrier state, or the identification of lines with carrier risk.

Some hereditary disorders and disease-predisposing phenotypes have been actively selected for by breeders. The most evident and widespread is the brachycephalic obstructive airway disorder, seen in extremely short-muzzled breeds. Other extreme phenotypes include excessive skin, excessive skin folds, excessive hind limb angulation, excessive size, excessive coat, dome-shaped skulls, and eyelid abnormalities. **It is important that breed standards and selection practices specifically avoid selection for extreme phenotypes that cause**

disease liability. For the show ring, judges' education should be directed towards rewarding moderation of disease-related extreme phenotypes.

Regular breed health surveys should be conducted by breed clubs to monitor for the presence and changing prevalence of genetic disorders. The OFA offers on-line health surveys for breeds. **Breed genetic health should be judged on breed health surveys that document the occurrence of genetic disease.**

Parent breed clubs should determine realistic pre-breeding genetic screening requirements based on the prevalence and severity of testable disorders in the breed. **Health testing requirements should be listed in the OFA CHIC and AKC Bred with H.E.A.R.T. program websites.**

Without direct selection against genetic disorders, the genetic health of breeds will decline. Breeders who refuse to do pre-breeding health screening should be directed to find a different hobby or profession that they can actually be good at. It is not ethical to breed dogs without selection for genetic health. **Selection of healthy breeding stock is the most important aspect of maintaining breeds.**

Each breeder must prioritize their selection for positive traits and against disease traits with each mating. Some breeders feel that genetic screening will reduce the genetic diversity of breeds. **The proper use of genetic screening actually increases breeding choices by allowing quality dogs at higher-risk of carrying disease liability genes to be bred:**

- Quality carriers of testable disease-causing recessive genes should be bred to normal testing mates and replaced for breeding with quality, normal testing offspring.
- Quality dogs with a less desirable phenotype (such as fair or even mild hip dysplasia in breeds with high frequencies of dysplasia) should be bred to dogs with desirable phenotypes (good or excellent hips) and replaced for breeding with offspring whose phenotype is better than the parent.
- Quality non-affected dogs from lines expressing disorders that do not have genetic tests (such as epilepsy) should be bred to mates from families or litters not expressing the disorder and replaced for breeding with a quality, healthy offspring.

In small population breeds with high frequencies of genetic disorders, breeders are often "frozen" from breeding for fear of producing disease. This causes continued breed decline due to population contraction. Breed improvement requires selection of the best breeding choices in matings that can reduce the frequency of genetic disease. As the population and breeding choices expand, the ability to reduce the frequency of disease expands with it. **Breed improvement involves; 1) selection of breeding dogs, 2) appropriate pairing of mates, 3) breeding, and 4) replacement of less desirable breeding dogs with more desirable offspring.**

An unfortunate development in dog breeding is recommendations designed for the preservation of rare and endangered species. These involve outbreeding (reducing homozygosity and average inbreeding coefficients) and increasing minor gene or chromosome segment frequencies. Dog breeding requires diverse lines, and not a homogenized and randomized outbred population. Outbreeding will not reduce the frequency of breed-related genetic disease, as the causative genes are already dispersed in the breed gene pool. Genetic selection for quality and against undesirable traits is what causes homozygosity and reduces the frequency of minor genes and chromosomal segments. Blindly selecting for them without knowing their effect could significantly reverse selection-based breed improvement. **Homozygosity is synonymous with pure breeds. It is not inherently correlated to impaired genetic health, and does not have to be artificially controlled.**

Expanding populations with different breeders undertaking different types of matings and selecting on different lines, while monitoring and selecting against genetic disease provides for a healthy, diverse breed gene pool.

Official genetic screening results should be made available to prospective breeders, and to the pet and breeding-stock purchasing public. This is facilitated through open genetic health databases like the OFA. It doesn't matter whether a breeder is a large commercial breeder, or only breeds once. It is no

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longer acceptable to say that genetic disease "just happens." In today's environment, not testing for documented breed-related hereditary diseases is irresponsible and unethical breeding. **Breed-specific pre-breeding health screening should become as universal as equine pre-purchase examinations.**

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BREED MAINTENANCE AND IMPROVEMENT REQUIRES:

- A large or expanding breed population
- Avoidance of the popular sire syndrome
- Avoidance of extreme phenotypes that can produce disease liability
- Monitoring of health issues in the breed
- Constant selection for quality and health

Pedigree Analysis and How Breeding Decisions Affect Genes

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To some breeders, determining which traits will appear in the offspring of a mating is like rolling the dice - a combination of luck and chance. For others, producing certain traits involves more skill than luck - the result of careful study and planning. As breeders, you must understand how matings manipulate genes within your breeding stock to produce the kinds of offspring you desire.

When evaluating your breeding program, remember that most traits you're seeking cannot be changed, fixed or created in a single generation. The more information you can obtain on how certain traits have been transmitted by your animal's ancestors, the better you can prioritize your breeding goals. Tens of thousands of genes interact to produce a single individual. All individuals inherit pairs of chromosomes; one from the mother, and one from the father. On the chromosomes are genes; so all genes come in pairs. If both genes in a gene pair are the same gene (for instance, “aa” or “AA”) the gene pair is called homozygous. If the two genes in a gene pair are unlike (for instance, “Aa”) the gene pair is called heterozygous. Fortunately, the gene pairs that make a cat a cat and not a dog are always homozygous. Similarly, the gene pairs that make a certain breed always breed true are also homozygous. Therefore, a large proportion of homozygous non-variable pairs - those that give a breed its specific standard - exist within each breed. It is the variable gene pairs, like those that control color, size and angulation that produce variations within a breed.

There are ways to measure the genetic diversity of a population. One method is to measure the average inbreeding coefficient (or Wright’s coefficient) for a breed. The inbreeding coefficient is a measurement of the genetic relatedness of the sire and dam. If an ancestor appears on both the sire and dam’s side of the pedigree, it increases the inbreeding coefficient. The inbreeding coefficient gives a measurement of the total percentage of variable gene pairs that are expected to be homozygous due to inheritance from ancestors common to the sire and dam. It also gives the chance that any single gene pair can be homozygous.

The types of matings that you choose for your breeding animals will manipulate their genes in the offspring, affecting their expression. Linebreeding is breeding individuals more closely related (a higher inbreeding coefficient) than the average of the breed. Outbreeding involves breeding individuals less related than the average of the breed. Linebreeding tends to increase homozygosity. Outbreeding tends to increase heterozygosity. Linebreeding and inbreeding can expose deleterious recessive genes through pairing-up, while outbreeding can hide these recessives, while propagating them in the carrier state.

Most outbreeding tends to produce more variation within a litter. An exception would be if the parents are so dissimilar that they create a uniformity of heterozygosity. This is what usually occurs in a mismating between two breeds, or a hybrid, like a Cockapoo. The resultant litter tends to be uniform, but demonstrates "half-way points" between the dissimilar traits of the parents. Such litters may be phenotypically uniform, but will rarely breed true due to the mix of dissimilar genes.

One reason to outbreed would be to bring in new traits that your breeding stock does not possess. While the parents may be genetically dissimilar, you should choose a mate that corrects your breeding animal's faults but complements its good traits. It is not unusual to produce an excellent quality individual from an outbred litter. The abundance of genetic variability can place all the right pieces in one individual. Many top-winning show animals are outbred. Consequently, however, they may have low inbreeding coefficients and may lack the ability to uniformly pass on their good traits to their offspring. After an outbreeding, breeders may want to breed back to individuals related to their original stock, to attempt to solidify newly acquired traits.

Linebreeding attempts to concentrate the genes of specific ancestors through their appearance multiple times in a pedigree. It is better for linebred ancestors to appear on both the sire's and the dam's sides of the pedigree. That way their genes have a better chance of pairing back up in the resultant offspring. Genes from common ancestors have a greater chance of expression when paired with each other than when paired with genes from other individuals, which may mask or alter their effects.

Linebreeding on an individual may not reproduce an outbred ancestor. If an ancestor is outbred and generally heterozygous (Aa), increasing homozygosity will produce more AA and aa. The way to reproduce an outbred ancestor is to mate two individuals that mimic the appearance and pedigree of the ancestor's parents.

Inbreeding significantly increases homozygosity, and increases the expression of both desirable and deleterious recessive genes through pairing up. If a recessive gene (a) is rare in the population, it will almost always be masked by a dominant gene (A). Through inbreeding, a rare recessive gene (a) can be passed from a heterozygous (Aa) common ancestor through both the sire and dam, creating a homozygous recessive (aa) offspring.

The total inbreeding coefficient is the sum of the inbreeding from the close relatives (first cousin mating), and the background inbreeding from common ancestors deep in the pedigree. Such founding ancestors established the pedigree base for the breed.

Knowledge of the degree of inbreeding in a pedigree does not necessarily help you unless you know whose genes are being concentrated. The relationship coefficient, which can also be approximated by what is called the *percent blood* coefficient, represents the probable genetic likeness between the individual whose pedigree is being studied, and a particular ancestor. It is a measurement of the average percentage of genes the individual and the ancestor should have in common.

We know that a parent passes on an average of 50% of its genes, while a grandparent passes on 25%, a great-grandparent 12.5%, and so on. For every time the ancestor appears in the pedigree, its percentage of passed-on genes can be added up

and its "percentage of blood" estimated. In many breeds, an influential individual may not appear until later generations, but then will appear so many times that it necessarily contributes a large proportion of genes to the pedigree.

The average inbreeding coefficient of a breed is a measurement of its genetic diversity. When computing inbreeding coefficients, you have to look at a deep pedigree to get accurate numbers. An inbreeding coefficient based on 10-generation pedigrees is standardly used, but requires a computerized pedigree database to compute.

The average inbreeding coefficient for a breed will be based on the age and genetic background of the breed. A mating with an inbreeding coefficient of 14 percent based on a ten generation pedigree, would be considered moderate inbreeding for a Labrador Retriever (a popular breed with a low average inbreeding coefficient), but would be considered outbred for an Irish Water Spaniel (a rare breed with a higher average inbreeding coefficient).

Most breeds start from a small founding population, and consequently have a high average inbreeding coefficient. If the breed is healthy and prolific, the breadth of the gene pool increases, and the average inbreeding coefficient can go down over time. Some dog breeds were established on a working phenotype, and not on appearance. These breeds usually start with low inbreeding coefficients due to the dissimilar backgrounds of the founders. As certain individuals are linebred on to create a uniform physical phenotype, the average inbreeding coefficient can increase.

There is no specific level or percentage of inbreeding that causes impaired health or vigor. If there is no diversity (non-variable gene pairs for a breed) but the homozygote is not detrimental, there is no effect on breed health. The characteristics that make a breed reproduce true to its standard are based on non-variable gene pairs. There are pure-bred populations where smaller litter sizes, shorter life expectancies, increased immune-mediated disease, and breed-related genetic disease are plaguing the population. In these instances, prolific ancestors have passed on detrimental recessive genes that have increased in frequency and homozygosity. With this type of documented inbreeding depression, it is possible that an outbreeding scheme could stabilize the population. However, it is also probable that the breed will not thrive without an influx of new genes; either from a distantly related (imported) population, or crossbreeding.

Fortunately, most breeds do not find themselves in the position of this amount of limited diversity and inbreeding depression. However, the perceived problem of a limited gene pool has caused some breeders to advocate outbreeding of all individuals. Studies in genetic conservation and rare breeds have shown that this practice actually contributes to the loss of genetic diversity. By uniformly crossing all “lines” in a breed, you eliminate the differences between them, and therefore the diversity between individuals. Eventually, there will not be any “unrelated line” to be found. Everyone will have a mixture of everyone else’s genes. This practice in livestock breeding has significantly reduced diversity, and caused the loss of unique rare breeds.

A basic tenet of population genetics is that gene frequencies do not change from generation to generation. This will occur regardless of the homozygosity or heterozygosity of the parents, or whether the mating is an outbreeding, linebreeding, or inbreeding. This is the nature of genetic recombination. Selection, and not the types of matings used affect gene frequencies and breed genetic diversity.

If two parents are both heterozygous (both Aa) for a gene pair, on the average, they would produce 25% AA, 50% Aa, and 25% aa. (These are averages when many litters are combined. In reality, any variety of pairing up can occur in a single litter.) If a prolific male comes out of this litter, and he is homozygous aa, then the frequency of the “a” gene will increase in the population, and the frequency of the “A” gene will decrease. This is known as the popular sire syndrome. Of course, each individual has thousands of genes that vary in the breed, and everyone carries some deleterious recessive genes. The overuse of individual breeding animals contributes the most to decreased diversity (population bottlenecks), and the increased spread of deleterious recessive genes (the founders effect). Again, it is selection (use of this stud to the exception of others), and not the types of matings he is involved in that alters gene frequencies. Breeders should select the best individuals from all lines, so as to not create new genetic bottlenecks.

Decisions to linebreed, inbreed or outbreed should be made based on the knowledge of an individual's traits and those of its ancestors. Inbreeding will quickly identify the good and bad recessive genes the parents share, based on their expression in the offspring. Unless you have prior knowledge of what the offspring of milder linebreedings on the common ancestors were like, you may be exposing your litters (and buyers) to extraordinary risk of genetic defects. In your matings, the inbreeding coefficient should only increase because you are specifically linebreeding (increasing the percentage of blood) to selected ancestors.

Don't set too many goals in each generation, or your selective pressure for each goal will necessarily become weaker. Genetically complex or dominant traits should be addressed early in a long-range breeding plan, as they may take several generations to fix. Traits with major dominant genes become fixed more slowly, as the heterozygous (Aa) individuals in a breed will not be readily differentiated from the homozygous-dominant (AA) individuals. Desirable recessive traits can be fixed in one generation because individuals that show such characteristics are homozygous for the recessive genes. Individuals that pass on desirable traits for numerous matings and generations should be preferentially selected for breeding stock. This prepotency is due to homozygosity of dominant (AA) and recessive (aa) genes. However, these individuals should not be overused, to avoid the popular sire syndrome.

Breeders should plan their matings based on selecting toward a breed standard, based on the ideal temperament, performance, and conformation, and should select against the significant breed related health issues. Using progeny and sib-based information to select for desirable traits, and against detrimental traits will allow greater control.

THE ASPECT OF POPULATION SIZE ON HEALTHY BREEDING IN DOG BREEDS

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A large number of individual dogs in a breed population allow greater choices when making breeding decisions. Multiple breed "family lines" support greater breed diversity; the genetic difference between individuals in the breed. When selecting on several different traits or disorders, a large population should allow for several choices of mates that fulfill different selection preferences. A goal of all breeds is to grow and maintain a large, diverse and healthy population.

All breeds originate from a small population of either related dogs or dogs who share a common conformational, behavioral, or working phenotype. Through selection, a breed standard is developed. Individual dogs that do not adhere to the standard or who demonstrate deleterious traits or disorders are purged from breeding. Those individuals who demonstrate and propagate desirable characteristics will have an increasing influence on the gene pool through multiple generations of descendants. Once breed characteristics are fixed in the population, it can go through an expansion stage where the population grows.

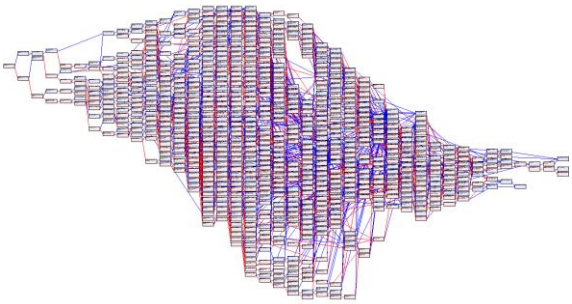

Fig. 1: Pedigree of a typical purebred dog (individual at the left). Breed founders appear at the right, and the breed goes through a purging stage, and then expansion stage.

All breeds will have several influential ancestors that appear far back in pedigrees, but pass on a high percentage of their genes to every individual in the breed. For example, all Bichons Frises share on average 17.5% of their genes with Pitou (born in 1924), which is between the contribution of a grandparent and great-grandparent. He does not appear on average until the 16th generation, but appears over 4 million times in every Bichon pedigree and 38% of his alleles have been retained in the breed population. Bearded Collie Bailie of Bothkennar was born in the 1940s, and contributes 32.6% of his genes to every modern Beardie.

This process of breed evolution causes a loss of genetic diversity through the purging of undesirable individuals and the concentration of genes of influential ancestors. All breeds are partial clones of their influential ancestors. This is an expected consequence of breed evolution and is not detrimental to the breed.

Genetic disorders can be due to ancient disease liability genes that preceded breed formation and are shared by many breeds, or by recent mutations that cause breed-specific disease. These can originate from a random mutation and be propagated through breed ancestors. Conversely, genes causing genetic disorders can be linked on a shared chromosome to a selected trait (ex., hyperuricosuria and Dalmatian spotting), or genetic disorders can be caused by direct selection for disease-causing phenotypic traits (ex., brachycephalic obstructive airway disease).

IS POPULATION SIZE DIRECTLY CORRELATED TO BREED HEALTH?

Evidence from registration figures and valid breed health surveys show that the size of a population does not determine whether the breed will suffer from higher frequencies of genetic disease. There are many large population breeds with high frequency genetic disorders, and many small population breeds that show excellent health. In a small population breed, individual mating choices and individual litters have a greater effect on the breed frequency of disease liability genes because they represent a larger percentage of the total gene pool. **It is the lack of selection for genetic health in either large or small population breeds that allows the propagation of genetic disorders.** Breed genetic health depends on selection against disease liability genes regardless of the size of the population.

DOES A LARGE POPULATION AUTOMATICALLY CONFER GENETIC DIVERSITY?

When analyzing entire breed population databases back to founders, every dog breed - regardless of its population size – has the same findings; high homozygosity and low effective population size (minimum number of ancestors explaining the complete genetic diversity of a population). These are necessary and expected consequences of breed formation and evolution. As a breed gene pool expands, the average recent generational relationship (inbreeding and kinship) between mates can decrease. However, the average total generational relationship between dogs back to founders does not decrease. Breeds with small populations look the same as breeds with large populations did much earlier in their evolution and development.

In both large and small population breeds, genetic diversity can be lost if breeders do not utilize dogs from the breadth of the gene pool. This is most evident in the popular sire syndrome. This can be compounded when a popular sire is replaced by a popular son, who is replaced by a popular grandson, and the entire breed truncates on a single popular sire line. This causes a loss of genetic diversity from the breadth of the gene pool that would be propagated from other quality male lines.

Another issue with popular sires is that their genetic contributions can only be evaluated after their prolific breeding period is over, and their genes have already been disseminated throughout the gene pool. Many recently identified genetic disorders that rise in frequency in a breed are caused by genes carried by popular sires. This is different from an influential ancestor, whose qualities and influence are constantly evaluated every generation. If an influential ancestor's descendants are not producing quality, then they are not bred and the ancestor's influence diminishes. With the popular sire syndrome a breed population may expand in numbers, but if breeding is concentrated in only a portion of the gene pool genetic diversity will diminish.

Some breeds may lack enough health and vitality from the start, and these breeds collapse and do not progress beyond the purging stage of development. Other breeds may have a robust and growing population, but due to other factors experience a population contraction and decline that could significantly eliminate the genetic diversity present in the gene pool. The recent economically induced decline and then rise in AKC

registrations is not detrimental to a breed as long as it was a temporary slowing, and not a loss of breeding lines. Frozen semen is also an important hedge against the loss of diverse lines. Population contraction is a serious detriment to breed genetic diversity if it includes the loss of diverse within-breed lines. In extreme cases, a breed may require opening up its stud book to bring new genes into its gene pool. However most current dog breeds show acceptable genetic diversity and only require health conscious breeding and population expansion to maintain their gene pools.

DO OUTBREEDING PROGRAMS IMPROVE GENETIC DIVERSITY AND GENETIC HEALTH?

Conservation geneticists versed in rare and endangered species have designed species survival plans (SSPs) that call for outbreeding; mating together animals that are least related to each other. The purpose of SSPs is to prevent the homozygous expression of deleterious recessive genes. However, natural species and artificially selected breeds have completely different, and in many instances completely opposite selection pressures and desired outcomes. SSPs call for using all available individuals in breeding and only outbreeding. Dog breeding calls for selection, which requires differences between prospective mates and therefore genetic diversity between individuals.

Outbreeding homogenizes the population by removing the genetic difference between individuals in the breed and making everyone “alike”. If two unrelated parents are bred together, the offspring make the two lines related. If an offspring is then outbred to a further unrelated line, their offspring make all of the lines related. Outbreeding is a self-limiting process as there will eventually be no unrelated dogs. In order to have selective pressure for positive traits and against negative traits or disorders, there must be variation and genetic differences between individuals in the gene pool. This requires distinct family lines that are eliminated by outbreeding programs.

Thus, the basic conceptual point is, “What constitutes genetic diversity?” Is it the diversity within each dog (heterozygosity through outbreeding)? Or is it the diversity between each dog (maintaining diverse family lines)? **These two concepts are diametrically opposed to each other and breeders and breed organizations must decide which is in the best interest of their breeds.**

The genes causing common breed-specific genetic disorders have already been dispersed in breed gene pools. Therefore the chance of breeding two carriers together is based on the frequency of the deleterious gene(s) in the population, and not necessarily the type (outbreeding or linebreeding) of mating. Outbreeding propagates deleterious genes in the carrier state and randomizes the occurrence of genetic disease; the same as is seen with common genetic disorders in mixed-breed dogs. **The only way to select against specific genetic disorders is to specifically select against the causative or liability genes through direct genetic testing or phenotypic genetic screening.**

ADDITIONAL FACTORS IN SMALL POPULATION BREEDS

Small population breeds have added issues because each mating has a much greater influence on the entire gene pool. If a breed has particular hereditary disorders at a higher frequency, mates should be selected that can minimize or lower the risk of producing these disorders. A quality higher risk dog (closely related to affected) can be bred to a lower risk dog and replaced with a lower risk offspring. As this process is repeated, the carrier risk and deleterious gene frequency will diminish in the population. As most disorders are complexly inherited and have no tests for carriers, carrier risk must be based on knowledge of phenotypic pedigree depth (parents and grandparents) and breadth (littermates and littermates of parents).

Some breeders in small population breeds are afraid to breed and possibly cause more disease. However if no breeding is going on, the breed will certainly become extinct. Mates must be selected that reduce the risk of producing genetic disorders. Breeders need to do their best to select for health and quality and then see what they produce.

In small population breeds a greater number of offspring should be placed in breeding homes to expand the population. However, breeders of some small population breeds try to constrain breeding and limit it only to themselves. This is a shortsighted attitude. Breeders should recruit and mentor puppy buyers to become thoughtful breeders. As a population expands, the choices of mates increase and the average recent relatedness of mates will decrease. Decreasing average recent generational inbreeding coefficients is a natural consequence of expanding populations utilizing the breadth of their gene pools. It does not need to be artificially manipulated. Breeders all doing something a little different with their mating choices – i.e., which individuals they are selecting, the types of matings utilized, etc. – is what maintains breed genetic diversity. With health conscious breeding, there are greater choices available to produce healthier offspring.

CONCLUSIONS

All breeds require expanding or large, stable breeding populations. Mates should be selected that represent the breadth of genetic diversity in the gene pool. It is mate selection and not the types of matings that they are involved in (linebreeding or outbreeding) that maintains genetic diversity.

Large and small population breeds show the same population indices of; high homozygosity, low effective population size, and high relationship to influential ancestors. The difference between large and small populations is in the available choice of breeding individuals.

Health conscious selection through breed-appropriate genetic screening of prospective breeding individuals is the most important aspect of improving and maintaining the genetic health of any breed, regardless of its population size.

The Effects of Genetic Testing: Constructive or Destructive?

By Jerold S. Bell, DVM, Tufts Cummings School of Veterinary Medicine
(This article originally appeared in the June, 2001 issue of the AKC Gazette)

Every breed has genetic disorders. Finding tests that identify carriers of the genes which cause these disorders is a goal in all breeds. Once a genetic test is found, however, it is a double-edged sword: Its use can enable breeders to improve a breed or devastate it.

Without genetic tests, the number of dogs that can be identified as carriers is low, even though many dogs may be suspected of being carriers because they have relatives that are known to be affected. Without tests, though, genetic-disease control involves breeding higher-risk dogs to lower-risk dogs. Dog breeds have closed gene pools; in other words, the diversity of genes in a given breed is fixed. The number of dogs removed from consideration for breeding based on concerns regarding a specific genetic disease is usually low, and therefore does not greatly alter the breed's gene pool, or diversity.

A genetic test that should be used to help maintain breed diversity should not result in limiting it.

However, once a genetic test is developed that allows breeders to positively determine if a dog is a carrier of a defective gene, many owners are likely to remove carrier dogs from their breeding stock. Although doing so is human nature, this temptation must be overcome. Any quality dog that you would have bred if it had tested normal should still be bred if it tests as a carrier.

Any quality dog that you would have bred if it had tested normal should still be bred if it tests as a carrier.

In such circumstances, carriers should be bred to normal-testing dogs. This ensures that affected offspring will not be produced. Carrier breeding stock should be subsequently replaced with normal-testing offspring that exceeds it in quality. If the only quality offspring is also a carrier, then use that offspring to replace your original carrier. You have improved the quality of your breeding stock, even though the defective gene remains in this generation. It is certainly true, though, that the health of the breed does depend on diminishing the carrier frequency and not increasing it. You should therefore limit the number of carrier-testing offspring that you place in breeding homes. This does not mean, however, that you should prevent all of them from being bred. It is important to carry on lines. A genetic test that should be used to help maintain breed diversity should not result in limiting it.

Consider All Aspects

We know that most dogs carry some unfavorable recessive genes. The more genetic tests that are developed, the greater chance there is of identifying an undesirable gene in your dog. Remember, however, that your dog is not a single gene, an eye, a hip, or a heart. Your dog carries tens of thousands of genes, and each dog is a part of the breed's gene pool. When considering a breeding, you must

consider all aspects of the dog - such as health issues, conformation, temperament and performance - and weigh the pros and cons. When a good-quality dog is found to carry a testable defective gene, there is a better option than removing that dog from your breeding program. That option is to breed it, so that you can keep its good qualities in the gene pool, and then replace it in your program with a normal-testing dog.

There are breeders who contend that no more than 10 percent of carrier dogs should be removed from breeding in each generation. Otherwise, they say, the net loss to the gene pool would be too great. In fact, *less than 10 percent of all dogs in a breed are ever used for breeding*. Dog breeds do not propagate according to what is known as the Hardy-Weinberg equilibrium, where all members of a group reproduce and pass on their genes to the next generation. Breeders already place tremendous pressure on their gene pools through selective breeding decisions. Indeed, breeders who focus their selective pressure on the more elusive traits in their dogs, rather than on testable and predictable single-gene conditions, are right to do so.

The Dangers

It is important that breed clubs educate their owners on how genetic tests should be properly interpreted and used. History has shown that breeders can be successful in reducing breed-wide genetic disease through testing and making informed breeding choices. You should remember, however, that there are also examples of breeds that have actually experienced more problems as a result of unwarranted culling and restriction of their gene pools.

These problems include: reducing the incidence of one disease and increasing the incidence of another by repeated use of stud dogs known to be clear of the gene that causes the first condition; creating bottlenecks and diminishing diversity by eliminating all carriers of a gene from the pool, instead of breeding and replacing them; and concentrating on the presence or absence of a single gene and not the quality of the whole dog.

Breeders are the custodians of their breed's past and future. "Above all, do no harm" is a primary oath of all medical professionals. Genetic tests are powerful tools, and their use can cause significant positive or negative changes. Breeders should be counseled on how to utilize test results for the best interests of the breed.

Breeding Strategies for Managing Genetic Traits

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With each new generation of dogs, breeders ask, "How can I continue my line and improve it?" Aside from selecting for conformation, behavior and ability, breeders must consider how they are going to reduce the incidence of whichever genetic disorders are present in their breed. There are no answers that will fit every situation. There are, however, guidelines you can follow to preserve breeding lines and genetic diversity while reducing the risk of producing dogs that carry defective genes, or are affected with genetic defects.

Autosomal Recessive Disorders

In the case of a simple autosomal recessive disorder for which a test for carriers is available, the recommendation is to test your breeding-quality stock, and breed carriers to normal-testing dogs. The aim is to replace the carrier breeding-animal with a normal-testing offspring that equals or exceeds it in quality. You don't want to diminish breed diversity by eliminating quality dogs from the gene pool because they are carriers. As each breeder tests and replaces carrier dogs with normal-testing dogs, the problem for the breed as a whole diminishes.

For some disorders there are tests known as linkage-based carrier tests, which can generate a small percentage of false positive and negative results. When using these tests to make breeding decisions, it's advisable to first determine whether the results correlate with the test results and known genotypes of relatives.

When dealing with a simple autosomal recessive disorder for which no carrier test exists, breeders must assess whether each individual dog in their breeding program is at high risk of being a carrier. This requires knowledge of the carrier or affected status of close relatives in the pedigree. An open health registry that is supported by the parent club makes it easier for breeders to objectively assess these matters. By determining the average carrier-risk for the breeding population, breeders can select matings that have a projected risk which is lower than the breed average.

If breeding a dog that is at high risk of being a carrier, the best advice is to breed to a dog that has a low risk. This will significantly diminish the likelihood that affected dogs will be produced, and can reduce by up to half the risk that there will be carriers among the offspring. Using relative-risk assessment as a tool, breeders should replace higher-risk breeding dogs with lower-risk offspring that are equal to or better than their parents in quality. Relative-risk assessment allows for the continuation of lines that might otherwise be abandoned due to high carrier risk.

Breeding a dog only once and replacing it with an offspring allows breeders to improve their chances of moving away from defective genes and also limits the dissemination of defective genes. When dealing with disorders for which carriers cannot be identified, the number of offspring placed in breeding homes should be kept to a minimum.

Autosomal Dominant Disorders

Autosomal dominant genetic disorders are usually easy to manage. Each affected dog has at least one affected parent, but it can be expected that half of the offspring of an affected dog will be free of the defective gene. With disorders that cause death or discomfort, the recommendation is to not breed affected dogs. To produce the next generation of a line, a normal full sibling of an affected dog can be used, or the parent that is normal can be used.

A problem with some autosomal dominant disorders is incomplete penetrance. In other words, some dogs with the defective gene may not show the disorder. Roughly half their offspring, however, may be affected. If a genetic

test is available, this is not a problem. Otherwise, relative-risk assessment can identify which dogs are at risk of carrying incompletely penetrant dominant genes.

Sex-Linked Disorders

For sex-linked (also known as x-linked) recessive defective genes for which carrier tests exist, breeders should follow the same "breed and replace" recommendations as are outlined above in the discussion of autosomal recessive disorders. If there is no test, the defective gene can be traced through the pedigree. If a male is affected, he would have received the defective gene from his carrier mother. All of his daughters will be carriers, but none of his sons. By using relative-risk assessment to breed him to a female that is at low risk of being a carrier, you can prevent affected offspring, and select a quality son for replacement.

There are rare instances in which a female is affected with a sex-linked disorder. In such cases, she would have received the defective gene from both parents; specifically, an affected father and a mother who is either a carrier or is affected herself. If an affected female is bred, all the sons will be affected, and all the daughters would be carriers, so affected females clearly should not be bred. A normal male that is a littermate to an affected female, however, would be able to carry on the line without propagating the defective gene.

Sex-linked dominant disorders are managed the same way as autosomal dominant disorders are. The difference is that affected males will *always* produce all affected daughters.

Polygenic disorders

Polygenic disorders are those caused by more than one pair of genes. Most polygenic disorders have no tests for carriers, but they do have phenotypic tests that can identify affected dogs.

With polygenic disorders, a number of genes must combine to cross a threshold and produce an affected dog. These are known as *liability genes*. In identifying a dog's liability for carrying defective genes for a polygenic disorder, the breadth of the pedigree (that is, consideration of all siblings of individuals in the pedigree) is more important than the depth of the pedigree (consideration only of parent-offspring relationships.) A clinically normal dog from a litter that had one or no individuals affected with hip dysplasia (which is a polygenic disorder) is expected to carry a lower amount of liability genes than a dog with a greater number of affected littermates. This is why it is important to screen both pet and breeding dogs from your litters for polygenic disorders. Information on the siblings of the parents of potential breeding dogs provides additional data on which to base your breeding decisions.

Genetic disorders without a known mode of inheritance should be managed in the same way as polygenic disorders. If there are multiple generations of normalcy in the breadth of the pedigree, then you can have some confidence that there are less liability genes being carried. If a dog is diagnosed with a genetic disorder, it can be replaced with a normal sibling or parent and bred to a mate whose risk of having liability genes is low. Replace the higher-risk parent with a lower-risk offspring that equals or exceeds it in other aspects, and repeat the process.

Genetic tests are extremely useful tools to help manage genetic disorders. Even when there is no test, or a known mode of inheritance, much can still be done to reduce the incidence of affected and carrier animals. The use of these guidelines can assist breeders in making objective breeding decisions for genetic-disease management, while continuing their breeding lines.