Genetic Diversity

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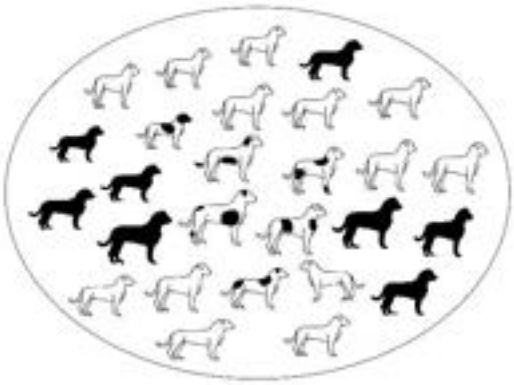
Genetic diversity is a concept that is universally embraced as necessary in the evolution and maintenance of dog breeds. What is the meaning of genetic diversity? How is it measured or determined? What are the methods and consequences of gene pool manipulation to achieve and maintain genetic diversity?



Diverse breed gene pools have differences between breed lines and dogs to allow improvement through selection.

Genetic diversity is important because it allows for variability within a breed's gene pool. **Genetic variability is important in selection because if there is no variation for a particular trait or disease, then there can be no improvement through selective breeding.** Genetic improvement requires genetic variability between dogs.

Some people concerned with genetic diversity recommend preventing homozygosity (the pairing of "like" genes). This recommendation derives from the Species Survival Plan (SSP) rescue programs designed for endangered species. The basis for this recommendation is to breed the least related individuals together to prevent the homozygosity of all disease-related genes. Commercial genetic testing companies can easily compute homozygosity measurements from DNA samples and promote them as genetic diversity panels; reported as inbreeding coefficients (ICs). These DNA derived ICs are correlated with deep pedigree-based ICs.

What does homozygosity indicate, and what does breeding for heterozygosity (the pairing of "unlike" genes) achieve in dog breeding? To understand these questions, we need to understand the genetic differences between species and dog breeds.

Genetic differences between species and dog breeds

The obvious difference between species and breeds is natural versus artificial selection. Natural selection in a species always selects for fitness and reproductive traits in a natural environment. Natural species are maintained if they can thrive and reproduce. Artificial selection which is used to create breeds is toward any conformational, behavioral and health characteristics that are being selected for, and away from those being selected against. Artificial selection is hopefully positive towards genes for quality and health. However, artificial selection can also directly select for genes and traits that are detrimental to health and fitness. Selection for extreme conformation is an example.

The process of speciation, the continued evolution of a species, causes divergence in the population or subpopulation. This divergence causes a loss of genetic diversity and creates unique population (gene pool) structure. These changes are not detrimental to the population if they continue to improve the fitness of the species. The same must be accepted for dog breed populations. They should be allowed to change and evolve if those changes allow for increased fitness (quality and health) and the ability to reproduce. There are plenty of undesirable traits and diseases that breeds strive to lose, and their loss causes a loss of genetic diversity.

There are many examples of natural species with very limited genetic diversity and high levels of

homozygosity with no negative health or reproductive consequences. Some of these are common species, like the Northern Elephant Seal.[1] Others are geographically isolated species, like Sable Island Horses[2] or Channel Island Foxes.[3] Population genetics calculations suggest that these populations have lost their genetic diversity due to homozygosity and will eventually go extinct. However in reality, these populations are robust and expanding because deleterious genes are not at a high frequency. This is not to say that homozygosity should be a goal of breeding. **It does show that homozygosity by itself does not cause disease and poor health, and is not necessarily deleterious to a population.** What is deleterious is the accumulation of disease-associated genes.

Natural selection requires large populations and genetic drift to improve species. With artificial selection, breeds do not require a large population size for genetic improvement. Few dog breeds fulfill the population thresholds determined for natural species to be able to survive. **However, few breeds exhibit inbreeding depression requiring SSP-like rescue programs.** Most dog breeds are robust, and only require continued reproduction and selection for quality and health. Breeds with small populations look like populous breeds did earlier and just need proper selection and population expansion.

What is homozygosity, and what does it tell you?

Homozygosity is the pairing of "like" genes in gene pairs. All genes come in pairs – one from the sire and one from the dam. If the sire and dam share a common ancestor, then the same genes can be passed down through both parents and pair up in the offspring. The effect of homozygosity is that it causes uniform expression (I.e., trait, characteristic, or disease) in all individuals inheriting the homozygous gene pair. There are positive genes that you want to select for (and create homozygosity), as well as deleterious or disease-causing genes that you want to select against.

To understand what homozygosity measurements represent, we must understand how homozygosity purposefully develops in a breed. Purebred dog breeds were created through artificial selection for specific tasks or traits. Through constant selection towards these breeding goals, breed characteristics reproduce uniformly through generations.

For a breed to reproduce uniformly, it requires homozygosity of genes. The genes that cause mammals to be mammals are homozygous, the genes that cause dogs to be dogs are homozygous, and the genes that cause a Gordon Setter to be a Gordon Setter are homozygous.

It does not take intense linebreeding to create homozygosity. Constant selection for certain traits will increase the frequency and homozygosity of their causative genes. **Creating homozygosity of genes for desirable traits and against disease-associated genes is the measurable result of selective breeding.** Mars Wisdom Panel computations show that mixed-breed dogs have on average 53% homozygosity and purebred dogs 63% homozygosity. This increase in homozygosity is not deleterious to breeds unless it causes increased expression of genetic disease.

Endangered species survival is based solely on producing viable offspring. This underscores the importance of SSP programs to prevent the homozygous expression of disease-associated recessive genes. Published metadata from Mars show that mixed-breed dogs carry statistically higher frequencies of 152 testable disease-associated genes than the combined tested purebred dog populations.[4] It is the population diversity of mixed breed dogs that reduces the expression of these recessive diseases. Linebreeding in mixed breed dogs would be expected to produce more recessive genetic disease than it does in purebred dogs. (Common complexly inherited genetic diseases are seen routinely in mixed-breed dogs.) Selection for health occurs in purebred dog matings. Selection for health diminishes the frequencies of disease associated genes and increases the homozygosity of health-related genes.

Diversity Breeding

Diversity breeding enthusiasts recommend SSP-type mating plans and only outbreeding (matings between dogs less related than the average in the population). What does outbreeding do to breed genetic diversity? If you take a group of dogs and only breed them to the least related in the group, you will have lower homozygosity. If you take the same group of dogs and do linebreedings (matings between dogs more related than the average in the population) you will have higher homozygosity. Have you changed the population or the genetic diversity of the breed? No. It is the same group of dogs with the same genes. Breeding for heterozygosity does not improve or change genetic diversity. It only masks the expression of recessive or additive genes; both positive and deleterious.

Does breeding for heterozygosity improve breed health? Embark studied data from the Morris Animal Foundation Golden Retriever Lifetime Study and found that on average, a 10% increase in inbreeding coefficient of the mother (not the litter IC, which was not studied) decreased litter size by 1 puppy.[5] This puppy loss would be expected to be the result of homozygosity of embryologically fatal recessive genes.

Every breed and breed family has different frequencies of deleterious recessive and additive genes in their background. The effects of linebreeding are going to be different in each situation. If a breed or family shows higher frequency of genetic disease with linebreeding, then more intense outbreeding and purposeful selection against those specific diseases is necessary to diminish the causative gene frequencies. If deleterious genes causing breed-related disease are old and dispersed in the gene pool, then those diseases are just as likely to be expressed with outbreeding. Direct selection against those diseases is the only way to reduce their incidence.

Some advocate for heterozygosity of major histocompatibility complex (MHC) genes that regulate the immune system. However, all peer-reviewed published studies on immune-related, immune-mediated, and auto-immune diseases identify specific MHC liability genes, and not general MHC homozygosity or diversity.[6-9]

Breed genetic diversity involves selecting individuals for breeding from the breadth of the gene pool, not the types of matings that they are involved in. With an expanding breed population, the average relationship (IC based on a set number of generations) between individuals in one generation will be lower than in the previous generation. This is why (in the absence of popular sire effect or other diversity limiting parameters) generational inbreeding coefficients over time go down in well managed breeds. However, the breeders of these breeds are all doing different types of matings (outbreedings, linebreedings, etc.) based on their needs and their selection preferences to improve the health and quality of their dogs.

Diversity breeder enthusiasts look at the graph of a breed's average ICs over time and say, “Well if decreasing average ICs represent a healthy breed then why not just plan matings with lower ICs?” It sounds reasonable.

However, the impact of everyone outbreeding causes the homogenization of breeds, so differences between "lines" disappear. If outbreeding between the two most unrelated dogs, their offspring make those lines related. The next mating must be to a dog unrelated to the two original lines and now these three lines are related in the offspring. Continued matings in additional generations to unrelated dogs becomes more difficult as dogs become homogenized and related to each other. If everyone outbreeds, it disrupts the ancestral pedigree structure of breeds that was based on selection. It removes the genetic differences between dogs that are necessary for genetic improvement through selective breeding.

Outbreeding proponents state that molecularly identified low frequency gene variants and genetic markers should be selected for and increased in breeds (without knowing what the associated genes code for). It is more likely that those low frequency markers are the result of generations of selection against specific undesirable traits and diseases.

Heterozygosity should not be a selected goal. **Heterozygosity and homozygosity measurements are tools and not goals.** They can be utilized in different situations to bring in novel genes and traits, or to create uniformity of existing genes and traits. Increased homozygosity should also not be a breeding goal. Inbreeding coefficients should only increase due to purposeful linebreeding for quality and health.

Homozygosity measurements are not a measurement of individual or population health or vitality. The only way to measure breed health is through breed health surveys that document clinical disease and reproduction parameters. Homozygosity is not inherently correlated to impaired genetic health and does not need to be artificially controlled. Managing breeds requires breed conservation efforts, not species survival plans.[10]

Practical aspects of gene pool diversity

Based on AKC statistics, on average only 10.4% (for populous breeds) to 13.9% (for smaller population breeds) of dogs within a breed reproduce to create the next generation of dogs. **This represents a genetic bottleneck with each generation in every purebred dog population.** It emphasizes the fact that breeders must utilize the breadth of the gene pool background in selecting dogs for breeding, and judiciously select dogs with the best health and quality.

Genetic diversity also exists in dogs from the same breed on different continents. Molecular genetic studies show that breed subpopulations diverge and can be differentiated, even though all members of the breed descended from the same breed founders. While there may be subtle differences in selection for conformation between continents/kennel clubs, this genetic diversity can be utilized in matings.

Frozen semen from quality dogs several generations back are another source of genetic diversity. Many breed clubs have created club-owned frozen semen repositories for breeders who do not wish to retain semen or continue to pay for their storage. Knowledge of the dog's health and qualities are important in their use. DNA testing can be performed on a semen sample.

Having a stable or expanding breed population size is important to maintain genetic diversity. Diminishing breed population size can cause a loss of gene pool diversity. If a breeder is retiring from breeding, their line should be maintained. **New owners should be mentored to become health-conscious breeders to grow the population, especially in small population breeds.**

Each breed has its own unique history, genetic makeup and gene pool structure that will require different efforts to improve its health and quality. **There is no simple solution (just outbreed) or one way of breeding (just linebreed) that maintains a healthy gene pool.** The most important aspect of gene pool diversity is maintaining the breadth of the breed's gene pool. Unique family lines should not be abandoned, and gene pool narrowing popular sire effects should not sideline other genetically unique male lines. The most robust breed gene pools have everyone doing something a little different. In each generation based on the particulars of the breed, if everyone practices health-conscious breeding, if some breeders are outbreeding, some linebreeding on one line, others linebreeding on another line, and there is no popular sire effect, then the health and genetic diversity of the breed is being maintained.

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UNDERSTANDING BREEDS AS POPULATIONS

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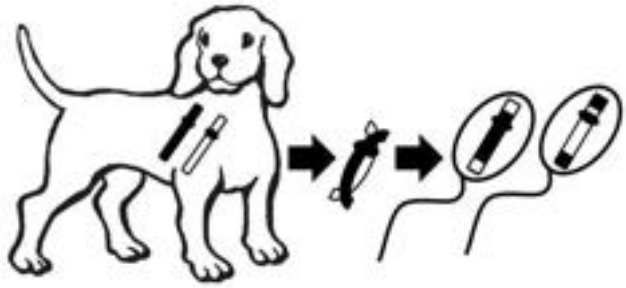
Dog breeds are like different ethnic populations of people. All people on earth are humans (Homo sapiens), but we are not all closely related. Ethnic populations originally arose due to geographic isolation. There are some mutated genes (and hereditary diseases) that are shared by different ethnic populations. These mutations occurred a long time ago in distant ancestors that preceded population migrations and the separation of ethnic populations. In some ethnic populations certain common genetic diseases occur at a higher frequency (like high blood pressure and diabetes). Some ethnic populations are prone to certain genetic diseases that are seen very rarely in other populations.

The same thing occurs in purebred dog populations. Dog breed populations are like early isolated human populations. The most common genetic diseases that are seen by veterinarians every day in practice are due to ancient liability genes that originated in ancestors that preceded the separation of breeds. They occur in both purebred and mixed breed dogs. These include allergies, hip dysplasia, heart disease, cruciate ligament disease, slipping kneecaps, cataracts, hereditary cancers and others. Breed-specific genetic disorders are due to more recent mutations. For many genetic disorders, validated genetic tests are available to identify carriers. For others, genetic screening and medical history differentiate normal from affected dogs.

BREED FORMATION & CHROMOSOMAL INHERITANCE

Breeds were formed by selecting for a working, behavioral and/or conformational standard. Dogs that did not adhere to a standard or were unhealthy were discarded. Those that did adhere were used for breeding. As only a small number of dogs are used to produce the next generation, rapid change can occur in the breed's genetic background. Dogs that embody and produce health and quality were considered superior to the standard and their offspring were used more frequently. Their genes were retained and propagated in the breed gene pool. Dogs that produced offspring that were unhealthy or inferior to a standard were not used. Their influence and that of their ancestors was diminished.

Dogs have 39 pairs of chromosomes – one in each pair from its sire and one from its dam. Dogs used for breeding supply one chromosome from each pair to every offspring. Due to chromosomal crossovers during meiosis producing sperm or eggs, each chromosome can include a mixture of chromosomal segments from its two parents. When genes are selected, the chromosomal segment (haplotype block) containing the gene is inherited along with many other “linked” genes in the segment. Selection for positive traits will cause the inheritance of a chromosomal segment from the parent(s) containing causative genes. Selection against deleterious traits or diseases will cause the loss of a chromosomal segment containing causative genes. As meiotic crossovers occur producing sperm and eggs through the generations, the size of the chromosomal segment containing genes under positive and negative selection can get smaller.



Chromosomal crossover during meiosis forming sperm or eggs can mix maternal and paternal segments on each chromosome.

As ancestors and dogs who pass on positive traits to the breed are linebred on (appearing in both the sire and dam's sides of the pedigree) this can cause haplotype blocks to pair up - causing runs of homozygosity (ROH). Even without close linebreeding, selection for positive traits will increase their homozygosity having originated from distant ancestors. Breed-defining genes would be expected to be collected in runs of homozygosity due to selection over time.

Deleterious (primarily recessive) mutated genes can accumulate in the background of the breed gene pool. These accumulate primarily because they are not expressed in the heterozygous (carrier) state. Deleterious genes can increase in frequency if linked to positively selected genes, or through genetic drift. An increasing frequency of breed-related disease will be due to homozygosity of deleterious recessive or additive liability genes. Individual liability genes can cause embryonic death (thus resulting in smaller litter size or infertility), increased neonatal death, or breed-specific genetic disease. This is due to the expression of specific deleterious genes and not a general result of increased homozygosity.

If disease liability genes are linked in haplotype blocks to positively selected genes, then dogs that demonstrate the positive traits and do not carry the disease-liability genes should be selected for breeding. These dogs can occur due to phenocopies (selected traits due to other genetic causes), or due to meiotic chromosomal crossovers that break the linkage between the positive and disease-liability genes. If the positive and deleterious genes cannot be separated due to tight linkage (adjacent genes or even multiple effects of the same gene) then this is not a healthy breed standard. The standard may need to be changed, achieved through other selected genes or possibly through crossbreeding.

As breeds develop and reproduce to a standard, their genetic difference from other breeds increases. Runs of homozygosity for breed-defining traits and quality genes is a positive development, even though it results in a loss of genetic diversity from genes that do not reproduce a standard or maintain health. The genetic diversity between breeds is large. This is why pure breeds can be separated by their DNA signatures. Breed subgroups (conformation versus working or breed populations on different continents) can also be differentiated based on their DNA. This can provide an important source of breed genetic variation if needed. The genetic diversity within the breed should be small, so that the breed reproduces itself to a healthy standard. This is the “big picture” of genetic diversity in dog breeds.

The fine detail of genetic diversity within a breed concerns maintaining a healthy phenotype and reproductive ability. Dogs from the breadth of the gene pool should be used for breeding as long as they represent health and quality. Restricted genetic diversity is not an issue in pure breeds, unless there is no alternative direction to go for health and quality.

DIFFERENCES BETWEEN BREEDS AND SPECIES

The force of species evolution is natural selection - the ability to thrive and reproduce within the species’ environment. Artificial selection that could be detrimental to species survival is not an issue in the wild. Genetic isolation can create subspecies (often with multiple isolation events) and can cause random genetic changes due to genetic drift.

Endangered species can share several population parameters with breeds. Their population size is usually small, and they have a closed population. In many instances, there is a limited foundation base (founder genome equivalent). Endangered species can experience decreased fertility and ability to thrive due to both genetic and environmental variation.

Genetic disease in endangered species occurs primarily through genetic drift. This is the random accumulation of disease liability genes in the absence of selection. As carriers of recessive and additive disease liability genes are healthy, they are not selected against and their genes are propagated in the offspring. Who reproduces in the population is random, and if carriers reproduce, the liability genes are passed on. When recessive disease liability genes pair up, or when additive genes combine to cross a threshold, clinical disease results.

Species survival plans (SSPs) were developed by population geneticists working with rare and endangered species who have a limited number of available breedable individuals. With the assumption that avoidance of homozygosity of deleterious recessive genes provides for the healthiest and robust offspring, SSPs are designed to mate the most unrelated individuals together (through pedigree or molecular genetic markers). This hopefully limits the expression of recessive disease-causing genes. SSPs also work to maintain the breadth of genetic diversity (evaluating the rareness or commonness of genetic background) in the species population. The only individual selection in SSP systems is to not breed unhealthy animals. However, if an unhealthy animal represents a unique genetic background it could still be used in matings to maintain genetic diversity. The goal of an SSP is successful reproduction with the production of healthy, live offspring representing the diverse background of the species.

Purebred breeding requires constant (artificial) selection for positive traits including health, and against negative traits and disorders. Without constant selection for specific breeding goals and their associated genes, the health and quality of the offspring will decline. The ability of selective pressure to create change in the population is limited by the amount of variation that is present for the selected trait in the breed. Selecting for heterozygosity as a goal and mating the least related parents together, erases the differences between dogs in the breed that are required for selection. This limits the ability to apply selective pressure for improvement. As a breeder selects for more goals in any mating, the amount of selective pressure for each individual goal diminishes. I.e., it is easier and more productive to select for one to three goals at one time than for eight or nine goals. Any selective pressure (selection goal) that is not specifically directed toward health and quality will diminish the selective pressure for both.

SSP breeding systems are not appropriate for pure breeds. Only outbreeding for the most heterozygous dogs randomizes the positive and deleterious genes in the gene pool. Breed-specific genetic disorders are caused by liability genes that are already dispersed in the breed's gene pool. Outbreeding will not decrease the frequency of these genes in the population. The clinical occurrence and frequency of such disorders will not diminish based on outbreeding versus linebreeding. The disorder will just appear randomly in offspring from different matings. Outbreeding and linebreeding are tools, not goals. There are specific reasons for using either in planned matings.

IMPROVING BREED POPULATION HEALTH THROUGH HEALTH CONSCIOUS BREEDING

Purebred dog breeds were developed through artificial selection when dedicated breeders judiciously purged dogs and their genes from the breed gene pools if they were unhealthy or did not perform to a standard. Somewhere along the way, the responsibility to select for health and produce healthy offspring disappeared from dog breeding. Today, people just breed dogs and expect healthy offspring.

People decide which dogs get bred, and which get bred to each other. This is the difference between natural selection and artificial selection. If artificial selection does not select for health, then there can be no expectation of genetic health. If artificial selection selects for breed characteristics that impair health, then breed-related disease is the natural outcome. Dog breeding is all about selection.

In the planning of any proposed mating, the selection of healthy parents is paramount to the health of the offspring. A pre-breeding health examination includes phenotypic examination of the major organ systems for; musculoskeletal, cardiac, ophthalmologic, gastrointestinal, pulmonary, dermatologic and behavioral abnormalities. Medical history should be examined for episodic inherited disease that cannot be identified on examination; i.e., allergies, seizures, bloat, bladder stones, cruciate ligament disease, etc. Dogs demonstrating hereditary disease should be selected against for breeding.

Pure breeds can also have breed-specific genetic disease due to more recent mutations. For many of these there are breed-validated genetic tests that can identify causative or disease liability genes, or genetic screening to identify affected dogs. The OFA Canine Health Information Center (www.ofa.org) and the AKC Bred With H.E.A.R.T. program (http://www.akc.org/breeder-programs/akc-bred-with-heart-program/) both have breed-specific genetic testing requirements that have been determined by the parent breed club. All prospective breeding dogs should undergo a veterinary pre-breeding health assessment that covers screening and medical history evaluation for all common and breed-related genetic disorders. **If all breeders include pre-breeding genetic screening in mate selection, then America's dogs will be healthier.**

The advent of multiplex genetic panel testing (Mars Wisdom Health, Embark, etc.) provides genetic test results for over 180 canine traits and disorders. Unfortunately, most of the disease liability genes tested for in these panels are breed specific. **Unless the gene(s) have been validated to cause clinical disease in other breeds or mixed breeds, the test result may not have any significance in your dog.** In addition, the panel tests utilize SNPs (single nucleotide changes) instead of testing for a mutation, so false positive and negative results can occur. **Breeding decisions regarding breed-validated liability genes should be based on direct mutation and not SNP testing.**

Typical genetic counseling recommendations utilize the breeding of quality carriers to non-carrier dogs and replacing the carrier parent with a quality non-carrier offspring. In this way breeding lines (and breed genetic diversity) are not abandoned and testable disease liability genes can be lost in one generation. If a valid genetic test is not available then selection should be based on genetic screening and open health databases that identify relative risk of carrying disease liability genes.

Health conscious breeders are fulfilling their ethical responsibilities to produce healthier dogs. If a breeder is not willing or able to provide official health screening results for the parents of litters, then BUYER BEWARE! There will be no expectation of genetic health in the puppies. Without evidence of pre-breeding genetic screening, health guarantees that provide for a replacement of a family member once the emotional bonds have been made are worthless. It is only a piece of paper written to excuse a breeder from performing their ethical responsibility of pre-breeding health screening.

There are many conversations concerning issues with dog breeding in America. Many people prefer the predictable characteristics of purebred dogs. The "Adopt, Don't Shop" movement promotes rescuing a dog from a shelter instead of buying from a breeder. The fact is that there isn't even a fraction of rescue dogs available to provide canine companionship to America's families. This has created the "bred for rescue" industry. Dogs will continue to be bred so that they can be our faithful companions. **If any purebred or mixed-breed mating is being planned, health-conscious breeding through pre-breeding health examination, genetic screening and genetic testing should be performed.** If the public demands health-conscious breeding then the issue of genetic disease in dogs will change.

"All dogs deserve to live healthy lives." William J. Feeney, Chairman of the AKC Board of Directors.

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.

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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.

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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.

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Breeding Strategies for the Management of Genetic Disorders

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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.

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