

Genetics based selection pressure to breed better, healthier dogs

Jerold S Bell

Tufts Cummings School of Veterinary Medicine, North Grafton, MA

The ability to apply selective pressure to breeding dogs to improve the genetic health of offspring begins with an understanding of the selection tools that we have available to us, as well as the ethical responsibilities to use these tools in assisting with breeding decisions.

Ethical responsibilities regarding genetic disease

As veterinary medical professionals, we are at the front lines of improving the genetic health; of our patients, of breeds, and of all dogs and cats. For most genetic diseases, we know how to either prevent their occurrence, or at least lessen the possibility of producing offspring with genetic disease. This can occur through the genotypic testing of the parents (identification of parents carrying liability genes for genetic disease), phenotypic testing of the parents (identification of parents affected with genetic disease), or pedigree analysis (identification of carrier risk based on the knowledge of carrier or affected relatives).

The genetic improvement of dogs and cats will only occur through selective breeding. However, the responsibility for this improvement lies not just with the breeder; but also with the veterinarian, the breed organizations, and the general public. Inherent in these responsibilities is the acknowledgement that breeding without genetic testing is irresponsible, and unethical. Genetic testing is health quality control. It is no longer acceptable for a breeder to choose two individuals and breed them together without regard to genetic disease control.

There is an active debate and inquiry into the genetic health of dog breeds. Several reports offer similar recommendations of; avoidance of selection for extreme phenotypes, the use of genetic testing to select for healthy breeding animals, and modification of breeding practices. The Kennel Club in the UK has initiated a program entitled, "Fit For Function, Fit For Life". At the heart of the program is the belief that all dogs should be able to see, walk, and breathe freely. Extreme phenotypes that the Kennel Club is addressing include the brachycephalic syndrome, excessive skin or eye conformation predisposing to disease, extreme conformation predisposing to lameness, and unstable temperament. The Kennel Club at their 2012 Crufts dog show had six Best of Breed winners (Bulldog, Pekingese, Clumber Spaniel, Mastiff, Neopolitan Mastiff and Basset Hound) be disqualified from moving on to the group competition due to their failing a veterinary inspection. The Kennel Club also has an Accredited Breeder Scheme to identify breeders that do health testing and adhere to specific breeding standards.

Some breed organizations and agencies have embraced the belief that close breeding is the cause of impaired breed health, and have adopted protocols and programs that restrict close breeding. The Kennel Club in the UK recently adopted a "Mate Select" program that lists health test results, but also seeks to find a mate that is the least related through pedigree analysis; i.e., outbreeding to produce the lowest inbreeding coefficient and the most heterozygosity. Mars Veterinary has a Optimal Selection® panel that selects prospective mates based on genotypic heterozygosity. This process is akin to a Species Survival Plan (SSP) that is utilized when attempting to "rescue" an endangered species. It is using the tool of the inbreeding coefficient as the goal of breeding.

The vast majority of dog and cat breeds do not show evidence of genetic depletion as seen in endangered species, such as; low reproductive success, and increased stillborn and neonatal mortality. Recommendations to outbreed (only breed to those least related) homogenizes breeds and erases the genetic difference between individuals. It is a self-limiting process. It requires that matings be done between individuals who are different from each other. However, eventually there will be no more "lines" with differences. Everyone will be in the center, and no one at the periphery. If a genetic disease or deleterious trait comes up, there will be no "other line" to breed and get away from it. Breed gene pool diversity requires distinct lines in order to create selective pressure.

Prudent breeding practices allow some linebreeding, some outbreeding, and even occasional inbreeding; with different breeders maintaining breeding lines or crossing lines as they see fit. It is the

different opinion and breeding actions of breeders that maintain breed diversity. This is not something that can be legislated or regulated.

When breeds have issues with genetic diseases, the only way to improve their gene pool is through selection against the specific diseases and their associated liability genes. The types of matings (linebreeding or outbreeding) have no bearing on controlling deleterious genes, or the genetic health of breeds. Pure and pedigreed breeds are only endangered if breeders ignore selection for healthy breeding stock.

Genetic registries

In the United States, several genetic registries have been established to assist breeders with genetic disease control. The Canine Eye Registry Foundation or CERF (<http://www.vmdb.org/cerf.html>) is a closed database showing only normal eye examination results by ACVO boarded veterinarians. The not-for profit Orthopedic Foundation for Animals (OFA: www.offa.org) has semi-open registries for hip dysplasia, elbow dysplasia, autoimmune thyroiditis, congenital cardiac disease, patella luxation, and other genetic diseases. From the OFA web portal you can look up individual dogs, and their health testing status. This is Facebook for dogs; each with their own web pages and information.

The Canine Health Information Center or CHIC (www.caninehealthinfo.org) is an open health database that has been established by the AKC Canine Health Foundation and the Orthopedic Foundation for Animals. National parent clubs decide to enroll in the CHIC program, and determine the testable genetic disorders for their breed. (For example, hip evaluation, CERF examination, and thyroid testing.) Owners, breeders, and prospective owners can search online for dogs in the OFA/CHIC database, and view their test results. If a dog completes the recommended testing panel, it receives a CHIC number regardless of whether it passes all of the tests. CHIC is about health consciousness, not health perfection. As more testable disorders are identified, few dogs will be normal for all tests. The Kennel Club in the UK has similar Health Breeding Schemes and a searchable Health Tests Results Finder to look up individual dogs. A similar listing of tests is not currently available for cats, however breed related diseases are found on the Feline Advisory Bureau (FAB-UK) website: www.fabcats.org/breeders/inherited_disorders.

Responsibilities of veterinarians

With each hereditary disorder, we as a veterinary profession are being called upon to determine what is “normal”, what is “abnormal”, and what screening tests can be performed to allow selection away from disease causing phenotypes. Care must be taken, so that selective pressures are not so severe that they limit genetic diversity in the breed gene pool.

When a client makes an initial puppy or kitten appointment, we should examine all of the paperwork provided by the breeder or pet store. This includes not only the prior medical care, but the registration paperwork that lists the sire and dam. On receiving the paperwork, the health test requirements for the breed can be identified, and the health test results of the parents searched. If test results are not available on the web-based registries, ask the owner if the breeder provided them with verification of each of the required genetic test results on the parents; i.e., a copy of the official test results from the testing agencies. If no verified test results are available, then the puppy or kitten was not bred by a health conscious breeder. There is no expectation of genetic health in your patient, and you and the owner can only hope for good health.

When a client is planning on breeding a dog, you can look up the pre-breeding health test requirements. You can provide many of the tests yourself (radiographs, thyroid profile, or cheek swab or blood samples for genetic tests). For eye examinations or heart examinations by a cardiologist, you can assist your client by providing information on local health screening clinics. You must emphasize the ethical responsibility of pre-breeding genetic testing, or a decision to not breed their animal. Genetic testing is a requirement, not a choice.

If a client is looking to purchase a purebred or designer-bred dog, you should counsel them on the behavioral and genetic expectations for the selected breeds. Provide them with the genetic health test

requirements. Ensure they understand that they should only purchase a pet from parents that have verified results of their breed-specific required health tests.

Responsibilities of breeders

It is the ethical responsibility and obligation of all breeders to perform the available required pre-breeding genetic health tests on prospective breeding stock. A breeder is anyone that plans a mating between two animals. These include matings between two members of the same breed, or crosses between two members of different breeds (designer matings). The most common genetic diseases of; canine hip and elbow dysplasia, valvular heart disease, patella luxation, eye disease, and hypothyroidism occur at similar frequencies in mixed-breed versus pure-bred populations. If two animals are purposely bred, then the breed-specific genetic testing for each parent is required.

Most genetic tests only need to be done once in the prospective breeding animal's lifetime. Others (eye examinations, phenotypic heart examinations, thyroid profile, etc.) should be repeated, depending on the breed specific age of onset of the disorder, and age requirement for diagnosis.

If a breeder is not willing or able to have the prescribed pre-breeding genetic tests performed, then they should find a different hobby or profession. Cats and dogs are living beings. It is not ethical to forgo the obligation of genetic testing.

Everyone loves their breed, and their own breeding stock. The more genetic tests that are developed, the greater chance there is of identifying an undesirable gene in an animal. Conscientious breeders understand that negative test results limit their breeding options. With direct gene tests, they can use carriers when bred to normal testing mates. For disorders without direct gene tests, they may have to choose a normal relative, as opposed to one they were planning on using in the next generation. Matings should be planned that prevent or minimize the risk of producing genetic disease, but do not limit the genetic diversity of the breed.

When prospective breeding stock has a carrier or affected test result, you should counsel your client to release this information to the listing health registry. If negative test results are not made available, then other breeders will not be able to ascertain the disease risk of their own breeding stock to make informed breeding decisions. As opposed to the stigma that used to be attached to the appearance of genetic disease, the stigma now rests on those that hide the occurrence of genetic disease. Dealing with genetic disorders is a community effort.

When making breeding decisions, breeders can search the health registry websites for genetic test results on prospective mates. If test results are not available on animals that have already been bred, then it must be assumed that they are affected or carriers. Otherwise the results would be available.

When selling a kitten or puppy, breeders should provide new owners with full documentation of the health test results (copies of official test results) on the parents. If early direct genetic testing was done on the puppies, these results should be provided. It is not enough to say that the testing was done. If testing was done then the breeder has the paperwork, and it should be provided. It must be impressed upon the public that health consciousness is one of the most important considerations when getting a puppy or kitten. Health guarantees that provide for replacement of puppies or kittens with genetic defects are not a replacement for health testing. Such a guarantee is of little value, as no one wants to part with their family member once the emotional bonds have been made. A puppy or kitten is not a toaster.

Responsibilities of breed organizations/parent clubs

It is the responsibility of the breed club to conduct regular breed health surveys to monitor the health of the breed. If breed-related disease is present, it is up to the breed club to promote and fund research to identify phenotypic and genotypic tests that can be used by breeders to improve the genetic health of the breed.

For dog breeds, the parent club should work with CHIC, the Kennel Club, or other national agencies to select the required and recommended genetic testing that should be performed before dogs are bred. Breeders should be counseled to perform pre-breeding health testing.

Parent clubs should review their breed standards and select against morphological changes that promote disease, morbidity, or mortality. They should counsel their breeders against breeding to extreme standards that can promote disease, and should educate judges to select against morphology that promotes disease.

The parent club should also scientifically monitor if significant health issues are being caused by a lack of genetic diversity. If so, they should be open to scientific measures that can increase genetic diversity, including opening of the stud book, or even controlled crossbreeding programs.

Responsibilities of the general public

When a consumer gets a purposely-bred kitten or puppy, the emotional aspect of adding a new member to the family often overwhelms the rational aspect of this important decision. Acquiring a new pet should not be an impulse decision. The new pet will hopefully be with the family for the next 10 to 15 years. The public should spend as much time researching this decision as they do when purchasing a new car or a refrigerator.

Prospective owners need to research whether a specific breed is suitable for them and their home. They also need to research the breed-specific health testing requirements for the selected breed. Whether purchasing from a private breeder, one found on the internet, or a pet store, the parental health testing results for both parents should be available. If they are not available, then just walk away – regardless of how cute the puppy or kitten.

Statements of testing by the breeder, or on a breeder website are not sufficient to document health test status. If the testing has been done, the breeder will be happy to provide the official documentation that they are a health conscious breeder. Health guarantees that provide replacement for pets with genetic disease do not eliminate the need for genetic testing. If a breeder states that they do not have the health test documentation, but offer a guarantee of genetic health, the prospective owner should walk away. The breeder has not fulfilled their ethical responsibility and obligation of health testing.

The general public is the engine that drives the pet breeding industry. If the general public demands puppies from health tested breeding stock, then the market will change to favor health conscious breeders. If people can easily sell pets to the public on a website without any health tests being done, then there is no market force to change the situation to improve the genetic health of cats and dogs. It is the public's choice of where they get a puppy or kitten. It is the general public's obligation to document genetic health testing from breeders.

All genetic disease is not preventable. However, the frequency of genetic diseases can be significantly decreased, if not eliminated by valid testing and breeding selection in purposely bred dogs and cats. It is time to put an end to the excuse of ignorance of the breeder, veterinarian, or general public in their roles and responsibilities to improve the genetic health of dogs and cats. It is up to all of us to educate each other about producing genetically healthy cats and dogs, and call for the documentation of health testing of all breeding stock.

Genetic tests

Genetic tests vary on what they are able to identify, and therefore how they can be used in managing genetic disease. To understand how we can use genetic tests, we have to understand the types of tests that are available, what they can tell us, and their limitations.

Phenotypic tests

Some tests measure the phenotype, or what can be seen in the animal. This may not directly relate to the genotype, or the genes regulating the defect that you are trying to manage. Screening for cataracts, auscultating for heart murmurs, hip and elbow radiographs, thyroid profiles, urinalysis for crystals or metabolites, skin biopsy for sebaceous adenitis, and observations on behavioral traits are all tests of the phenotype. Most tests of the phenotype only identify affected individuals, and not carriers of disease liability genes.

Linked-marker based tests

Some defective genes can be linked to a genetic marker, which could be tested for. Linked-marker based tests do not identify the defective gene, but a marker that lies close on the chromosome. If a crossover occurs between the marker and the defective gene during reproduction, the marker will no longer be linked to the defective gene. False positive and false negative results will occur. Due to this phenomenon, linkage test results must be compared with results from other family members to determine whether they correlate with the known genotype of relatives. Linked marker tests include those for cerebellar ataxia in Italian Spinone and primary hyperparathyroidism in Keeshond.

Direct mutation based tests

Direct gene tests are specific for mutations and are a direct measurement of the genotype. They can identify affected, carrier, and normal individuals. These can be run at any age, regardless of the age of onset of the disorder. Most direct gene tests identify a mutation that is causative for a genetic disorder. These genes are 100% penetrant, and an affected genetic test result is 100% correlated with clinical disease. However, some direct genetic tests identify a mutation that causes an increased susceptibility for genetic disease. These **susceptibility alleles** can be part of polygenic/complexly inherited traits, or the cause of incomplete penetrance of (assumed) simple Mendelian traits.

Degenerative myelopathy is considered a complexly (polygenic) inherited disease. An autosomal recessive susceptibility gene has been identified that is homozygous (two abnormal copies) in all DM affected dogs. However, a large proportion of individuals in these breeds are homozygous for this gene and do not become affected. They are considered “at risk”, but not genetically affected. In the Wire Fox Terrier, there is a 91% allele frequency in the breed; however no Wire Fox Terrier has even been diagnosed with degenerative myelopathy. In the Boxer, less than 0.5% of dogs develop the disease. Testing Boxers for the DM susceptibility gene shows 39% testing carrier, and 43% testing homozygous “at risk” for the susceptibility gene. This is an example of a genetic test with **low penetrance**; indicating that the homozygous state is poorly predictive of clinical disease. There are additional (unidentified) genes that must also be present to produce clinical DM. This test is useful in ruling out a diagnosis of DM in homozygous normal and carrier dogs. However, selecting against 82% (“at risk” and carrier dogs) of the Boxer gene pool when making breeding decisions - when the vast majority will not produce the disorder - is detrimental to the genetic diversity of the breed. Similar situations occur in other breeds susceptible to DM. In these breeds, breeding dogs should NOT be selected against or have their mating choices altered due to carrier or homozygous “at risk” status of DM unless there is knowledge of close (first or second degree) relatives diagnosed with clinical degenerative myelopathy.

Some breeders feel that any carrier or “at risk” dogs should only be bred to homozygous normal testing dogs. However, requiring that all mating be performed with dogs from only 18% of the population (following the Boxer example) would tremendously skew the breed’s gene pool and restrict genetic diversity. This is unnecessary for an extremely low prevalence disease. With genetic tests for lowly penetrant defective genes, selection should only be considered for dogs with families that contain clinically affected individuals. This recommendation should significantly reduce the frequency of clinical disease, as well as the frequencies of other contributory alleles.

Other examples of low prevalence but high allele frequency diseases are cord1 PRA in English Springer Spaniels (42% “at risk”, 38% carrier, ~1-2% disease prevalence) and Miniature Dachshunds, and rcd4 PRA in Gordon Setters and Irish Setters. With rcd4 PRA, the average age of clinical diagnosis of the disease is around 10 years of age. However, this is the average age that clinically affected dogs are recognized; not the average age when all homozygous dogs become affected. The actual average “age of onset” of this late-onset disease may be in the teens; when many dogs will already be deceased. Now that Gordon Setters are being tested worldwide, many dogs who are homozygous for the defective gene with normal vision are being identified. With an approximately 30% carrier rate in the small Gordon Setter gene pool, selection against the gene must necessarily be gradual so as to not restrict the breed’s genetic diversity.

Other susceptibility genes are found to occur at a greater frequency in affected animals, but **are not present in all affected animals**. An example is the susceptibility gene for perianal fistula/anal furunculosis in German Shepherd Dogs. Dogs with the susceptibility haplotype (specific sequence of 3 DLA genes) have a 5.0X odds ratio for the disease versus those without the haplotype. This risk factor occurs whether the susceptibility haplotype is heterozygous or homozygous; though homozygous dogs develop the disease at an earlier age. Another example is the genetic test for Pug Dog Encephalitis, a painful, fatal disease affecting 1-2% of Pugs. Dogs homozygous for a susceptibility haplotype have a 15.6X odds ratio for developing the disease, but dogs heterozygous for the susceptibility haplotype have no greater risk.

Many owners and breeders ask what tests should be done in their cats and dogs. The answer depends on whether the cat or dog is going to be a pet, or be used for breeding. For a pet, it is only important to know that it is not going to be affected by a health related disorder. For breeding animals, it is important to know if they carry disease liability genes that they can pass on to their offspring.

Genetic counseling for pet animals

The vast majority of our patients are not breeding animals, but they still require genetic counseling for inherited disorders. We counsel owners of large-breed puppies to feed lower calorie foods to provide for a more uniform growth rate and better joint development. We understand the nutritional counseling needs for FUS cats and obese “pre-diabetic” cats.

The hallmark of genetic disease is our ability to predict its occurrence before its onset, allowing us to alter its morbidity or mortality. We need to be knowledgeable about what genetic tests are available, and in what patients they should be run. Patients from breeds with an incidence of von Willibrand’s disease should be tested early in life, so that measures can be taken to prevent excessive hemorrhage during surgery or injury. Patients at risk of carrying the *mdr-1* mutation should be tested early in life, before drug treatment.

In high risk breeds, individual animals should be genetic tested (or verified results documented on parents) before purchase. These include Maine Coon Cats for the autosomal dominant hypertrophic cardiomyopathy gene, and Persian and Himalayan cats for autosomal dominant polycystic kidney disease.

We need to understand the temporal periods when genetic testing will be most accurate, and allow for intervention. Puppy hips should be palpated with a gentle Ortolani procedure at each vaccine visit, and again at spaying or neutering under anesthesia. Juvenile interventional surgery will only benefit those with significant subluxability prior to major growth (for pubic symphysiodesis) or the development of osteoarthritic changes (for triple pelvic osteotomy).

Genetic testing for hypothyroidism is based on the presence of thyroglobulin autoantibodies. A dog with normal TgAA levels on two tests at least two years apart between two and six years of age is phenotypically normal. However, TgAA levels should not be measured within two to three months post-vaccination, as a transient iatrogenic rise can occur during this period.

Genetic counseling for breeders

The goal of genetic counseling is to effectively manage the spread of defective genes, while preserving the health and genetic diversity of the population. Genetic counseling recommendations are geared toward preventing the production of affected animals, and reducing the production of carriers. At the same time, recommendations should allow the continuation of breeding lines, to preserve the genetic diversity of the population.

Historically, genetic counseling has ranged from recommendations to not repeat a mating and outbreed, to recommendations to eliminate all relatives of affected animals from the breeding pool. Neither of these two extremes serves the best long-term interest of breeds. Outbreeding can prevent the production of affected animals, but it will propagate and further disperse detrimental recessive genes.

Recommendations for breeding should be based on genetic test results or knowledge of carrier or affected relatives if genetic tests are not available. The testable disorders for each breed should be

discussed with your clients. For dogs, breed-specific genetic test recommendations are available at the CHIC website (www.caninehealthinfo.org).

There are no breeding recommendations that will fit every situation. Protocols for genetic counseling and breeding management of genetic disorders can be based on the known (or unknown) mode of inheritance, and the availability and type of genetic tests. Genetic tests should be used to increase the breeder's options for breeding, and not limit them.

In the case of a **simple autosomal recessive disorder** for which a direct genetic test for carriers is available, the recommendation is to test breeding-quality stock, and breed quality carriers to normal-testing individuals. This prevents affected offspring from being produced. The aim is to replace the carrier breeding-animal with a normal-testing offspring that equals or exceeds it in quality. As each breeder tests and replaces carrier animals with normal-testing animals, the problem for the breed as a whole diminishes.

With a genetic test, breeders can positively determine if an individual is a carrier of a defective gene. The typical response of a breeder on finding that their animal is a carrier is to remove it from a breeding program. If a majority of breeders do this, it puts the breed's gene pool through a genetic bottleneck that can significantly limit the diversity of the breed. The goal of genetic testing is to allow the superior genes of a breeding individual to be propagated, even if the animal is a carrier. One defective gene that can be identified through a genetic test out of tens of thousands of genes, is not a reason to stop breeding. If an owner would breed an individual if it tested normal for a genetic disease, then a carrier result should not change that decision. A direct genetic test does not alter WHO gets bred, only WHO THEY GET BRED TO.

We know that most individuals carry some unfavorable recessive genes. The more genetic tests that are developed, the greater chance there is of identifying an undesirable gene in your patient. History has shown that breeders can be successful in reducing breed-wide genetic disease through testing and making informed breeding choices. However, 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 males 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 breeding 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 animal. Genetic test results should be used to benefit the overall health of breeds, not to limit it.

For autosomal recessive disorders without genetic tests, breeders can still reduce the carrier risk in their matings. A quality individual that is found to be a carrier can be retired from breeding and replaced with a quality, lower-risk offspring. In this way, the carrier risk can be cut in half. By repeating this vertical mating scheme (breeding once to a low-risk mate and replacing with an offspring), you are maintaining the good genes of the line, reducing the carrier risk with each generation, and replacing, not adding to the overall carrier risk in the breeding population. The problem with recessive disorders without carrier tests is the propagation and dissemination of unapparent carriers in the gene pool. Multiple offspring should not be placed in breeding homes. An open health registry that is supported by the parent club makes it easier for breeders to objectively assess the carrier risk of prospective breeding animals. By determining the average carrier-risk for the breeding population, breeders can select matings that have a projected risk that is lower than the breed average. Using relative-risk assessment as a tool, breeders should replace higher-risk breeding animals with lower-risk offspring that are equal to or better than their parents in quality. A negative aspect of pedigree analysis is that it selects against families, regardless of an individual's normal or carrier status. On the other hand, it allows for the objective risk assessment and continuation of lines that might otherwise be abandoned due to high carrier-risk. An example of an open health database and relative risk analysis program is cerebellar abiotrophy in the Scottish Terrier (www.stca.biz/GrandCentral/CACentral-CA.asp).

Autosomal dominant genetic disorders are usually easy to manage. Each affected animal has at least one affected parent, but it can be expected that half of the offspring of an affected animal will be free

of the defective gene. With disorders that cause death or discomfort, the recommendation is to not breed affected animals. To produce the next generation of a line, a normal full-sibling of an affected animal can be used, or the parent that is normal can be used. A problem with some autosomal dominant disorders is incomplete penetrance, where some individuals 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 individuals are at risk of carrying incompletely penetrant dominant genes.

For **sex-linked (also known as x-linked) recessive defective genes**, selecting a normal male for breeding loses the defective gene in one generation, regardless of his relationship to affected and carrier relatives. Carrier, affected, or high risk females should not be used, due to the high risk of producing affected male offspring. 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. Without a test for carriers, you can use relative-risk assessment to breed him to a female that is at low risk of being a carrier. This prevents affected offspring, and a quality son can be selected for replacement. **Rare sex-linked dominant disorders** are managed the same way as autosomal dominant disorders. The difference is that affected males will always produce all affected daughters.

Most **complexly (polygenic) inherited disorders** have no tests for carriers, but do have phenotypic tests that can identify affected individuals. These disorders require knowledge of the affected or normal status of full-sibs to prospective breeding animals. Open health genetic registries like the Orthopedic Foundation for Animals database provide such information (www.offa.org). Individuals whose siblings are normal and whose parents' sibs are normal have the greatest chance of carrying a low genetic load for the condition. This breadth of pedigree analysis is more important than normalcy in the depth of pedigree (parents and grandparents only.) Affected individuals can be replaced with a normal sib or parent, and bred to a low-liability mate. Breeders can replace the higher risk parent with a quality, lower risk offspring, and repeat the process. For **disorders without a known mode of inheritance or carrier test**, breeders should be counseled to use the same control methods as with polygenic disorders.

It is distressing to breeders when we confirm a genetic disorder. As veterinary professionals, we can offer positive and practical genetic counseling recommendations to maintain breed lines and genetic diversity, and improve the overall health of breeds. The total elimination of defective genes will probably be impossible for most breeds. The use of these guidelines can assist breeders in making objective breeding decisions for genetic disease management, while continuing their breeding lines. The individual breeder can use genetic tests to; 1) identify carriers, 2) work to breed away from the defective gene(s), and 3) ensure (through testing) that the defective gene(s) is not reintroduced in future matings. Each breeder will have their own rate of progress, depending on the frequency of the defective gene(s) in their own breeding animals, and which desirable individuals are carriers.