

Responsible Breeding Management of Genetic Disease

Jerold S Bell DVM, Department of Clinical Sciences, Tufts Cummings School of Veterinary Medicine, N. Grafton, MA. jerold.bell@tufts.edu

Breeders and Breeding

Breeders of dogs desire to produce the best with their matings. However, breeding has become more complicated today, and more people with intact dogs are becoming "breeders". It is up to other breeders, breed associations, and veterinarians to educate prospective breeders on understanding breed characteristics, historical selection parameters, and the continuous evolution of health testing to promote healthy breeding practices.

Adding to the complexity of breeding is the expansion of planned cross-breedings (designer breeds) to produce offspring. Therefore, the discussion is no longer between pure-bred and cross-bred, but between purposely-bred and random-bred dogs.

There is a general misconception that mixed-breed dogs are inherently free of genetic disease. This may be true for rare, breed-related disorders; but the common genetic diseases that are seen across all breeds are seen with the same frequency in mixed-breeds. A mixed-breed dog with hip arthritis has no less a case of hip dysplasia than a pure-bred dog. The only difference is that conscientious breeders test and label their dogs as dysplastic prior to the onset of clinical signs. I do not see a difference between the relative frequencies of old pure-bred dogs versus old mixed-breed dogs with hip arthritis requiring arthritis pain medication.

Testing for inherited hypothyroidism (for thyroglobulin autoantibodies by Michigan State University) shows 10.7% of 55,053 tested mixed-breed dogs to be affected. The average percentage of affected dogs for all pure breeds is 7.5%. This does not tell us that mixed-breed dogs are more prone to autoimmune thyroiditis: More mixed-breed dogs are tested based on clinical signs. However, these results show us that this hereditary disorder is seen frequently in both pure-bred and mixed-breed dogs. To those that feel that this disorder is not genetic, we look at the historical breed predilections for the disorder. Those breeds with the highest genetic propensity for autoimmune thyroiditis remain high over the years (example: 31.4% of English Setters tested), and those breeds with the lowest propensity remain low (example: 1.1 % of French Bulldogs). Selection based on thyroid testing (and in the future direct genetic tests for liability genes) should reduce the frequency of this disorder.

The most common inherited disorders for all dog breeds according to the AKC Canine Health Foundation are: cancer, eye disease, epilepsy, hip dysplasia, hypothyroidism, heart disease, autoimmune disease, allergies, patellar luxation, and renal dysplasia. With the exception of renal dysplasia, all of these genetic conditions are routinely seen in mixed-breed dogs.

There are some defective disease-causing genes that mutated so long ago, that the mutation (and its associated disease) is found in evolutionary divergent breeds. The same ancestral autosomal recessive mutation for the progressive rod cone degeneration (prcd) form of progressive retinal atrophy (PRA) is shared by over 17 diverse breeds, including the American Cocker Spaniel,

Australian Cattle Dog, Chinese Crested, Kuvasz, Labrador Retriever, and Toy Poodle. The list of affected breeds continues to grow as more are discovered with the same defective gene. The question is not, "Which breeds carry this defective gene during their development", but "Which breeds did not lose this defective gene during ancestral development."

It is also not surprising that prcd-PRA affected dogs (who must receive the defective gene from both parents) have been identified in Labradoodles (Labrador x Poodle crosses), and Cockapoos (Cocker Spaniel x Poodle crosses). Labradoodles are also being diagnosed with hip dysplasia, elbow dysplasia, and inherited Addison's disease; all recognized disorders in both parent breeds.

So, if breeders desire to produce the best with their matings, the basic question becomes; "Who IS a reputable breeder?" For purposely-bred dogs, It IS those breeders who perform genetic testing for breed-susceptible disorders. Official test results should be made available to prospective breeders, and the pet and breeding-stock purchasing public. It doesn't matter whether a breeder is a large commercial breeder, or only breeds once. In today's environment, not testing for documented breed-related hereditary diseases is irresponsible breeding.

Responsible breeding also involves knowledge of how best to use the results of genetic testing. For pure-breeds there are concerns about the breadth of the available gene pool and genetic diversity. Genetic test results should be used to benefit the overall health of breeds, not to limit it. A discussion of these issues, and breeding recommendations for genetic disorders based on different modes of inheritance are included in the proceedings of the 2007 Tufts' Canine & Feline Breeding and Genetics Conference: www.vin.com/tufts/2007.

Genetic Test Results and Genetic Registries

For direct genetic tests, official test results of the parents, and/or the offspring (tested prior to placement) should be made available to prospective breeders or purchasers of pet or breeding dogs. For some breed associations, the results of genetic testing are available in on-line, publicly accessible databases.

For disorders where there is no direct genetic test available, the knowledge of phenotypic test results (for affected, or carrier status if possible) should be made available in open health database registries. For most of these disorders, it is only through the open reporting of affected dogs that knowledge of disease risk can be identified through the test results or health status of close relatives.

The Orthopedic Foundation for Animals (OF A: www.offa.org) maintains semi-open health registries for testable genetic disorders. Applications for all of the hereditary disorders in their databases include a check-off to openly report ALL test results; both normal and abnormal. For many breeds of dogs tracking hip dysplasia for example, over one-third of the applicants check the box for open reporting. It is important that as breeders and veterinarians we encourage open reporting of health results. The days of stigmatizing conscientious, health-testing breeders who have produced dogs with hereditary disease are gone. No one wants to produce affected offspring from their matings, and no one should be blamed if this occurs (unless the breeder is not doing the recommended health testing). It should be everyone's goal to produce healthy offspring, but this is not possible if the only available health information is about normal dogs,

but not abnormal dogs. Once the majority of owners are initialing the box for open reporting, the OFA can change it to a check-off box for not reporting abnormal test results.

The Canine Health Information Center (CHIC: www.caninehealthinfo.org) was established by the AKC Canine Health Foundation and the OFA to assist breeds with managing breed-specific genetic disorders. The AKC national breed clubs determine the recommended testable disorders for the breed (whether tests of the phenotype or the genotype). If an owner is contemplating breeding their dog, they can look up the recommended genetic tests to perform in their breed. Veterinarians can also assist prospective breeders by looking up and discussing the recommended genetic tests for the breed. Prospective breeding dogs can be researched, and their genetic test results, as well as that of their close relatives can be studied.

The benefit of the CHIC system is that dogs gain CHIC certification by completing their health testing, regardless of their test results. CHIC is about health consciousness, not health perfection. As more tests for defective genes are developed, every individual is likely to carry some deleterious genes.

Veterinarians should ask for pedigrees and results of parental or early age health testing of pure-bred and cross-bred puppies on first presentation to their clinics. If the test results were not provided to the owner, many can be immediately searched in on-line databases like OFA or CHIC. A lack of available test results shows that the puppy was not purchased from a health conscious breeder, and it may be liable to develop genetic disease. The general public must be educated to become informed "consumers" when purchasing puppies. They should spend as much time researching the purchase of what will become a member of their family for 10+ years, as they do purchasing home appliances. Breeder health guarantees that provide for replacement of puppies with genetic disease are often worthless; as few pet owners will be willing to give up a member of their family once an emotional bond has been established.

Example: Cerebellar Abiotrophy (Ataxia) in Scottish Terriers

The Scottish Terrier Club of America (STCA) has provided all of the tools necessary to determine genetic risk of carrying the defective gene causing the autosomal recessive genetic disorder cerebellar abiotrophy (CA), or for producing affected puppies. CA is a degenerative neurological disease that causes slowly progressive incoordination from several months to several years of age. The defective gene is old, and widespread in the Scottish Terrier gene pool worldwide.

The STCA has an area on their website entitled CA Central (www.stca.biz/GrandCentral) where a list of all confirmed CA affected dogs and their pedigrees is listed. The club maintains an on-line searchable pedigree database (www.stca.biz/pedigrees) that includes identification of all dogs with obligate CA risk. They also have a relative risk analysis calculator in CA Central that allows breeders to calculate the CA carrier and affected risk of dogs and of proposed matings.

The STCA has funded several studies to identify the autosomal recessive defective gene causing CA, and its members and breeders hope to some day have a genetic test for carriers. However,

CA Central allows their breeders to minimize their current risk of producing Scottish Terriers affected with cerebellar atrophy, and reduce the frequency of the defective gene now, while waiting for a genetic test to be developed.

Health testing and the knowledgeable use of test results is now an important requirement for responsible breeding. Breeders, veterinarians, and breed organizations must educate the general public of the need to check for health testing in their dog purchases. As this happens, the overall genetic health of purposely-bred dogs will improve.

Dr. Jerold S. Bell is a Clinical Associate Professor, and Director of the Clinical Veterinary Genetics Course for the Tufts Cummings School of Veterinary Medicine. He was trained in genetics and genetic counseling at Michigan State University, and the University of Missouri. His DVM is from Cornell University. Dr. Bell is a lecturer to all-breed and individual breed dog clubs. He has published numerous articles on breeding and genetics in the AKC Gazette. He is the project administrator of genetic disease control programs for national parent clubs, and practices small animal medicine at Freshwater Veterinary Hospital in Enfield, CT. He and his wife breed Gordon Setters.

Jerold Bell: Responsible Breeding Management of Genetic Disease – conference notes
Speaking to us as a veterinarian, not just a scientist or breeder. *see attached handout*

2007 Tufts Canine & Feline Breeding & Genetics conference : www.vin.com/tufts/2007

Who is a breeder? – Anyone who breeds a dog. Before, people considered: breed history, selection parameters & characteristics. The genteel society carefully decided breeding stock based on what they were bred to do.

Many more breeding, more rushed society “less time” to make decisions.

Differences in types of dogs: Pure-bred, Designer breed (crosses between two pure-bred dogs), Random-bred

The majority of the puppies he sees in his practice are “designer breeds” The myth is that they are “healthier” than pure-breds.

For this discussion – purposefully bred dogs vs randomly bred dogs.

Are designer breed dogs and mixed breed dogs healthier – NO, not in his practice. More issues with hip arthritis in older mix bred dogs. For example, 7.5% of pure bred dogs test positive for thyroid issues, whereas 10.7% of mixed breed dogs.

As breeders, we can control the health of our dogs, by carefully selecting our breeding stock.

Top 10 Canine Health Concerns:

1. Cancer
2. Eye disease (Cataracts, PRA, etc)
3. Epilepsy

4. Hip dysplasia
 5. Thyroid
 6. Cardiovascular issues
 7. Autoimmune
 8. Allergies
 9. Patellar luxation
 10. Renal dysplasia
- Dr Bell sees as much in mixed breed dogs as in pure bred dogs. Same with the Top 10 research priorities.

Who is a reputable breeder? (See attached handout)

It is a roll of the dice when breeding, but now the dice are loaded. It is our responsibility to do genetic testing. Selection alters maintains genetic diversity, not breeders. Overuse of popular sire pushes aside other quality males that should be contributing to the gene pool.

Breeders are the custodians of their breeds, and their gene pool. Above all, do no harm. Breeders must be counseled to use genetic tests for the best interests of their breed.

Genetic Test Results

Direct genetic tests: Test of the genotype. Only need to know the results of the breeding stock to make breeding decisions. Phenotypic tests, linkage tests, no test for carriers, complex or unknown mode of inheritance – need to know results of littermates, family, etc.

With tests for carriers: Breed quality carriers to genetically normal mates. Replace carrier parents with quality genetically normal offspring. This eventually “cleans” the gene pool.

Without genetic tests, the effect on selection on the gene pool is minimal. With genetic tests, if everyone decides not to breed carriers, it can have a significant limiting effect on the gene pool. “Do not throw the baby out with the bath water” BREED TO A NORMAL

Breeders must consider all aspects such as health, temperament, etc

Without test:

Breed higher risk individuals to lower risk individuals. Replace the higher risk individual with its lower risk offspring. Repeat until the risk is minimal.

Open Health Database – As long as we keep problems ‘secret’ we will not be able to deal with them.

Breeders need to be informed about the problems occurring in the offspring they produce. They should also maintain contact with the owners of the puppies they produce to keep track of problems that are created.

When seeing a new puppy in his clinic, he asks the owner to bring all paperwork, he goes on the OFA website and looks the parents up to see what testing has been done. This is an education opportunity and allows the owners to know what to expect for the health of their new puppy.

CHIC is not about health normalcy, it is about health consciousness. No need to test normal, but just test. OFA is now a database manager. OFA's depth of information allows for better research for breeders to make informed decisions on selection.

It is important to report both abnormal and normal results for the future of your particular breed. You can go to OFA's website and get a form to release abnormal results on past dogs.

Open databases are vital to the health and future of our breeds. Examples: Scottish Terriers, Bernese Mountain Dogs.

How can we educate the public?

- Make them more informed consumers of dogs and puppies

- Able to discern responsible breeders.

- Knowledgeable about genetic testing

- Recognize that price and quality should be linked (b/c of testing, medical care, etc)