Genetic Analysis
The Benefits of Informed Decision-Making

Christine M. Scruggs, VMD

Breeders today face a wide array of genetic testing and computer programs to aid them in their search to create the "perfect" dog of a particular breed. The variety and types of testing available, as well as pedigree analysis, can be confusing to the well-seasoned exhibitor, much less the novice breeder just beginning to learn about conformation, temperament, and genetics. Genetics itself is a field in flux – new discoveries are constantly being published as research yields exciting results in both human and canine genetics. The Canine Genome Research Project parallels the Human Genome Research Project in its attempt to characterize the vast amount of genetic information within the canine and human populations, respectively. Individual researchers seek to characterize specific genes or genetic disorders in order to reduce or eliminate them from the population. A breeder, then, must continually be informed about the latest research in his or her breed, the testing available for that breed, and what to do with the information once it has been obtained.

Currently, there are both phenotypic (appearance or expression) and genotypic (DNA) tests available for all three varieties of poodle. Examples of phenotypic testing include: patellar luxation testing, x-rays looking for evidence of Legg-Calve-Perthes disease, and hip and elbow x-rays all offered by the Orthopedic Foundation for Animals (OFA), hip x-rays through PennHIP, echocardiogram for heart defects, eye exams for progressive retinal atrophy, cataracts, corneal dystrophy, and entropion offered through the Canine Eye Registration Foundation (CERF), thyroid panels to check for hypothyroidism, skin punch biopsies for sebaceous adenitis (SA), blood chemistries* to check for juvenile renal disease, Addison's disease (hypoadrenocorticism), Cushing's disease (hyperadrenocorticism), etc. Examples of genotypic testing include the Optigen DNA test for PRA in miniature and toy poodles, and the von Willebrand's DNA test offered by VetGen for all three varieties. There are several ongoing research projects including those to identify DNA markers for Addison's disease, SA, PRA in the standard poodle, and epilepsy. As can be seen, phenotypic testing is much more common and available than genotypic testing.

The difference between phenotypic testing and genotypic testing is that phenotypic testing predicts the likelihood of an individual expressing a gene by the appearance of the individual's structure, i.e. conformation of the hips in an x-ray or appearance of the retina in an ophthalmic exam. Phenotypic testing does not predict if the animal is a carrier of the genetic defect in question, only if it is affected, or expressing the gene. Genotypic testing, on the other hand, involves using markers to identify actual genes, both dominant and recessive, of a particular disease. This means that the individual can be identified as either clear (does not carry the gene), carrier (does not express but does carry the gene), or affected (both expresses and carries the gene). Of course, an affected animal can also be determined through phenotypic appearance, or actual expression of the gene. Genotypic testing is highly useful in that puppies can be identified as affected earlier than the actual expression of the gene (such as PRA which may not be expressed until 3 years of age or older), and carriers and clears can be identified such

that breedings can be planned to avoid producing affecteds. Phenotypic testing is useful in identifying trends within a family, and trying to reduce producing affecteds through pedigree analysis and judicious breeding.

When evaluating your breeding program and making decisions concerning traits which you seek to strengthen or reduce within your kennel, remember that most traits cannot be changed or fixed within a single generation. If you seek to concentrate on a single trait, such as PRA, remember that in concentrating on eradicating that one trait, you may lose others by limiting your gene pool and reducing your choices. For instance, now that there is a DNA test for PRA, you could, theoretically, eradicate the disease from the population by only breeding clears to clears. However, this would be extremely detrimental to the breed in general, because in only breeding the clear individuals, you will put a "bottleneck" or severe reduction in genetic diversity within the breed. However, through judicious breeding you can reduce the incidence of affected individuals. You can breed clear individuals to any other individual – even an affected dog if it has an overwhelming number of other traits you are seeking to improve. Understand that breeding a clear to an affected will result in every puppy being a carrier. Any puppy from such a breeding should only be bred back to a clear individual if the breeder desires to avoid producing affected puppies. Carriers can be bred back to clears to produce 50% clear and 50% carrier. Carriers can be bred to carriers to produce 25% clear, 50% carriers, and 25% affected. And, if desired, carriers can be bred to affecteds to produce 50% carriers and 50% affected (obviously, the least likely choice besides affected to affected which would produce 100% affected puppies). This example is only valid in the case of a simple recessive, and would not apply if there are multiple genetic influences on a particular trait (such as hip dysplasia).

Information is the key to a successful breeding program. The more information you have on how certain traits are inherited and the trends of the expression of these traits within your breed, the better you can focus your breeding program and obtain your goals within your kennel. Remember that interpretation of the standard for a breed is highly subjective; obtaining consistency within your own kennel such that when a fancier sees one of your dogs and says, "oh yes, I recognize that as an XYZ poodle" is the goal of many breeders. Obtaining consistency while maintaining health, temperament, and conformation is what it is all about. The goal to reach this consistency is not one to strive for within a generation or two, but over many generations and many years. In today's atmosphere of immediate gratification, the fact of long-term commitment and concise definition of goals can sometimes get lost by the wayside. Also, the fact that long-term breeders are a veritable fount of information is sometimes ignored.

So, once you have defined your goals and hopefully obtained the advice of experienced breeders within the fancy, what next? Well, first and foremost, obtain all of the genetic testing available for your breeding animal that is possible. For toy breeders this would include DNA testing for PRA, patellar luxation evaluation, registration and evaluation with CERF for eye abnormalities, and some breeders include thyroid and cardiac evaluations. Hip problems and von Willebrand's disease do not seem to be as much a problem within the toy poodle population, although some breeders also test for these diseases as well. Miniature breeders usually include CERF and PRA testing for the eyes, hip x-rays, patellar evaluation, thyroid panels, and an echocardiogram to detect heart abnormalities. Standard breeders typically include hip x-rays (either through PennHIP or OFA), CERF (unfortunately DNA testing for PRA is not yet

available for the standard variety of poodle), von Willebrand's factor DNA test, sebaceous adenitis punch biopsy, and may run a thyroid panel to check for hypothyroidism. Current research is being conducted on Addison's and Cushing's disease, as well as epilepsy and other genetic problems; such testing may be available to one or more of the poodle varieties in the future.

Now that you have all the genetic testing available done on your dog or bitch, how do you decide to whom to breed? For example, say you have a bitch to breed and you are in search of the best dog to sire her puppies. First and foremost, you want to breed to a dog that will most complement your own bitch and one whom the owner has completed all genetic testing and found satisfactory. This means you must evaluate your bitch with an objective eye, recognizing the qualities which you would most like to improve or maintain, and those qualities which you would like to reduce or eliminate. In evaluating such qualities you need to know where they came from, and how strong they are within your line versus the line you will be introducing into your kennel. This is where pedigree analysis is imperative. The more information you have on each generation, and the more generations available to your knowledge base, the more you will be successful in predicting whether a particular breeding will produce the qualities you desire. In analyzing a pedigree it is not sufficient to scan over three generations and determine the strengths of the sire and dam. At least six to ten generations will provide the necessary database in determining the qualities that are strong versus weak within an individual. Whether or not such a large pedigree is available, it is also important to evaluate the puppies already produced by the dog to determine what sort of traits he tends to reproduce consistently (and keep in mind the bitch contributes 50% of the genes too!) and to evaluate his immediate relatives (siblings, half-siblings, cousins) to determine their strengths and weaknesses.

Pedigree analysis is only successful if breeders are open and honest about both the strengths and weaknesses within their lines and are willing to divulge that information. This is where talking to long-term breeders can be very useful. Breeders who have been producing puppies for 20 or 30 years or more have a wealth of knowledge about their breed. Learning as much as possible about the pedigree of a sire, even 10 generations back, can make a huge difference in deciding to whom to breed your bitch. For instance, in the first three generations you may not see any inbreeding, i.e. every dog and bitch bred appear to be entirely unrelated. Go back four or five generations, however and you may discover that the great –grandparents were, in fact, brother to sister or father to daughter matches. If you scan a 10 generation pedigree a single dog may appear over and over in the later generations, but perhaps only once in the three generations. This is called the "popular sire effect". This single dog will have much more influence on future generations if he appears multiple times within an extended pedigree. If this dog has traits which you wish to strengthen within your own line, wonderful – you would like to perform this match. If, however, this dog does not have traits which you would like to reproduce, perhaps you would reconsider the match. So you see, if the "popular sire" appears only once in the three generation pedigree of the dog you are considering, you may not pay much attention to that, thinking – how much influence will he really have? But if you scan a ten generation pedigree and the "popular sire" appears 50 times or more, you realize that his degree of influence may be quite large. To quote Dr. Jerold Bell, "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."

Again, knowledge is the key to success. Remaining informed about current research and genetic testing available (both phenotypic and genotypic) as well as learning as much as possible about the ancestors of your dogs and those to whom you breed, will provide a strong foundation from which to build. A breeder needs to have a clear idea of those traits which he/she wishes to strengthen or reduce within his/her own line and then performing judicious breedings to reach these goals. A combination of inbreeding or line breeding to strengthen traits, mixed with outcrossing to bring in new or reduce undesirable traits will only be successful if the breeder makes informed decisions about each and every pairing of a sire and dam. The more DNA tests that are available, the more a breeder can make "safe" decisions and avoid producing puppies affected with an undesirable trait, such as PRA. And until such DNA tests are available for a particular trait, use of phenotypic testing and pedigree analysis will provide information of trends within a line, and likelihood of reproducing a particular trait. The informed breeder will make decisions to improve his/her line, and produce puppies with qualities he/she desires in searching for the "perfect" dog.

* Blood chemistries can only determine if an animal is currently affected by renal disease, Addison's disease, or Cushing's disease. There are no available tests at this time to predict whether an individual will have or produce such traits in the future.

GLOSSARY

Addison's disease:	Hypoadrenocorticism, or lack of cortisol secretion from the adrenal glands. Can be life threatening.
Cataracts:	A partial or complete opacity of the lens and/or its capsule in the eye. Complete opacity can lead to blindness.
Corneal dystrophy:	Opacities in the center or periphery of the cornea, which can have varied appearances and may or may not progress. Complete opacity can lead to blindness.
Cushing's disease:	Hyperadrenocorticism, or overproduction of cortisol secretion from the adrenal glands. There are three forms of this disease.
Echocardiogram:	Ultrasound of the heart, showing structures within the heart and surrounding vessels.
Entropion:	Turning of the eyelids inward, toward the cornea. Can cause damage to the cornea over time and in severe cases.
Epilepsy:	Seizures, either mild or severe unexplained by toxin ingestion or other cause. Considered heritable in some breeds of dogs.
Genotype:	Actual genes producing a trait are determined. DNA analysis.

Hypothyroidism:	Underproduction of thyroid hormone. Can produce a variety of symptoms; easily treated with thyroid supplementation.
Inbreeding:	Usually considered to be breeding within immediate relatives – in other words, father to daughter, mother to son, sister to brother.
Juvenile renal Disease:	Acute renal failure at a young age, usually before 2 years of age. Considered genetic in origin although not currently characterized. Fatal.
Legg-Calve-Perth's Disease:	Joint disease caused by loss of blood supply to the femoral head of the hip joint. Subsequent remodeling results in pain and stiffness similar to hip dysplasia. Believed to have a genetic basis, not currently characterized.
Line breeding:	Usually considered to be breeding within the line of a pedigree but not immediate relatives. For example, breeding two cousins or uncle to niece.
Outcrossing:	Usually considered to be breeding two completely unrelated individuals within a three generation pedigree.
Patellar luxation:	when the patella, or knee cap, slips out of joint to either side. Can result in "locking" of the knee joint, lameness, and arthritis. May need surgical correction.
Phenotype:	Actual physical expression of a gene. For example blue eyes are the expression of two recessive genes for blue.
Progressive retinal Atrophy:	A group of diseases affecting the retina, or reflective layer at the back of the eye. Can be progressive over time and usually leads to blindness.
Sebaceous adenitis:	A disease causing disruption and atrophy of the sebaceous glands in the skin. Can lead to hair loss, infections and severe discomfort. Considered to be a possible recessive, but current mode of inheritance not completely characterized.
Von Willebrand's Disease:	Underproduction of a clotting factor necessary to form blood clots. Can lead to severe bleeding and death.