

Genetic Testing: Genotype versus Phenotype

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With each variety of the poodle, standard, miniature, and toy, there are various genetic tests available. This article will describe the types of tests available for each variety, whether they are genotypic or phenotypic tests, and current research being conducted for each variety. The second article in the series will describe how to utilize each test within a breeding program to hopefully maximize the health of the breed. Genetic tests can be divided into two categories, 1) genotypic testing which utilizes DNA analysis involving gene markers to describe the actual genetic makeup of the individual, and 2) phenotypic testing which utilizes the appearance or actual physical expression of a gene to determine the status of an individual.

There are very few genotypic tests available for the poodle breed at this time. DNA tests which are available include progressive retinal atrophy (PRA) for toy and miniature poodles (not currently offered for standards), von Willebrand's disease for all three varieties, and neonatal encephalopathy for standard poodles. The DNA test will determine whether an individual is clear (cannot pass on a deleterious gene), carrier (does not have the disease itself but can pass it on to offspring) or affected (both has the disease and can pass it on to offspring). The DNA test is the gold standard for genetic testing in any breeding program. However, it can take many canine generations and a significant amount of time, money, and research to isolate and identify the specific area on the DNA strand which results in the expression of a particular disease. If there is not a human counterpart for a canine disease, funding for research may be woefully inadequate. Even if funding is not an issue, having breeders contribute to researching the disease by providing information and samples from affected dogs in their kennel can be difficult.

There are more genetic tests available of the phenotypic type. These tests do not determine the genetic makeup of the individual, but rather describe the actual expression of the gene or genes involved in the trait in question. For instance, in people brown eyes are more common than blue eyes. But people with brown eyes can carry the gene for blue eyes, even though they do not have blue eyes. If two people who carry the gene for blue eyes have a child, there is a 25 % chance that the child will have blue eyes even though both of the parents, by appearance, have brown eyes and neither of the parents have blue eyes. Phenotypic tests rely upon the appearance of the individual resulting from the expression of the genes, but do not identify whether the individual may carry other genes which would result in a different appearance in the offspring.

Phenotypic tests available for toy poodles include pelvic x-rays for Legg Calve Perthes (LCP) disease, hind limb x-rays for patellar luxation (as well as palpation and manipulation of the joint by a veterinarian), CERF exam for optic nerve hypoplasia, cataracts, and other eye abnormalities, thyroid panel for hypothyroidism, and an echocardiogram or ultrasound of the heart for patent ductus arteriosus. Phenotypic tests for the miniature poodle include an ACTH stimulation test for Addison's disease, x-rays of the pelvis and hind limbs for hip dysplasia, LCP, and patellar luxation respectively,

evaluation of the patella by a veterinarian, CERF for optic nerve hypoplasia and cataracts, skin punch biopsies for sebaceous adenitis, thyroid panel for hypothyroidism, and an echocardiogram for patent ductus arteriosus. The typical phenotypic tests for the standard poodle include an ACTH stimulation test for Addison's disease, low or high dose dexamethasone test for Cushing's disease, abdominal ultrasound evaluation of the adrenal glands for both diseases, pelvic x-rays to evaluate for hip dysplasia, thyroid panel for hypothyroidism, CERF to evaluate for PRA, cataracts, optic nerve hypoplasia and other eye abnormalities, skin punch biopsies for sebaceous adenitis, and an echocardiogram for patent ductus arteriosus.

Phenotypic tests describe the appearance of an individual at a single point in time. Some phenotypic tests, such as the OFA and PennHIP tests for hip dysplasia, are considered predictive in the development of a particular disease in that individual, and are only performed once in the lifetime of the dog. Other phenotypic tests, such as the CERF exam, SA skin punch biopsy, etc. are recommended to be performed yearly, as they are not predictive and a normal test one year does not mean the same individual will remain normal in future years.

In toy poodles, pelvic x-rays for LCP are considered predictive after 12 months of age and according to the current database do not need to be repeated. The veterinary evaluation for patellar luxation is also at 12 months of age or older. CERF exams for toys are typically conducted before breeding and anywhere from 12 months of age onward. CERF exams are not considered predictive, and are recommended to be repeated yearly for the lifetime of a dog if the dog is used in a breeding program. Thyroid testing for toys includes a thyroid panel evaluating various hormones involved in thyroid function. The thyroid test is also recommended to be repeated yearly. Finally, in toys the echocardiogram can be used to identify abnormalities of the heart. For some diseases, such as patent ductus arteriosus and single echocardiogram can identify affected animals and does not need to be repeated. Other cardiac diseases require repeat testing, yearly or otherwise, to monitor the status of a breeding individual.

The miniature poodle is very similar to the toy in phenotypic testing available and/or recommended. These tests include those for LCP, patellar luxation, CERF, thyroid disease, and an echocardiogram. Like the toy poodle, the miniature need only be evaluated at 12 months of age or older for LCP and patellar luxation, and needs yearly repeated tests for the remainder. Other phenotypic tests which may be conducted for a miniature poodle include an ACTH stimulation test to identify Addison's disease and an SA skin punch biopsy to identify sebaceous adenitis affected individuals. Both of these tests only identify whether an individual is clear of the disease at a single point in time and are not predictive in any manner. These tests are recommended to be repeated either yearly or otherwise depending upon a variety of factors.

The standard poodle does not have a problem with patellar luxation or LCP, and individuals of this variety are not usually evaluated for these diseases. The standard poodle is recommended to have pelvic x-rays at 2 years of age or older, to determine the status of the hip joint for dysplasia. There is also PennHIP available for evaluation of the

hip joint, which can be done as young as 16 weeks, but usually performed at 12 months or older. Like the miniature poodle, the standard may have yearly or more frequent ACTH stimulation and SA punch biopsy tests, to determine the status of the individual at a particular moment in time. Other yearly tests include the thyroid panel and CERF exam. Less common tests are the low dose dexamethasone suppression test for Cushing's disease, and the echocardiogram to check for patent ductus arteriosus and other cardiac conditions.

Overall, it is obvious that having a DNA test for all the diseases which affect the poodle would be the gold standard in an ideal world. Unfortunately, breeders do not have DNA tests available for most diseases. Relying on phenotypic testing is better than no testing at all, however interpretation and use of this type of testing in a breeding program must be conducted judiciously. Depending on the reliability and predictability of the phenotypic test, some are more accurate than others. The next article will focus on utilizing both genotypic and phenotypic testing in a breeding program, to decrease the percentage of deleterious genes within the poodle population. Please note that all the tests mentioned in this article for the different varieties may not be used in all breeding programs, and may be financially (or otherwise) prohibitive in some cases. Each breeder must make his or her own choices in utilizing available tests within their breeding programs. However, it would be ideal if ALL breeders would publish the results of the tests they do utilize, so that the breeding community as a whole could work together to improve the noble poodle.

Glossary

ACTH stimulation test – a blood chemistry test conducted to evaluate the function of the adrenal glands. Used most frequently to identify individuals affected with Addison's disease.

Addison's disease – otherwise known as hypoadrenocorticism, this disease results from the malfunction of the adrenal glands and low level of essential hormones which regulate important body functions. Can be life threatening.

Adrenal glands – a pair of glands which produce cortisol and other hormones essential to regulation of important body functions, including heart rate, electrolyte balance, kidney function, etc.

Cataracts – thickening, clouding and discoloration of the lens of the eye, which can lead to blindness.

CERF – stands for canine eye registration foundation. A registry for ophthalmologic diseases or normal individuals once examined by a board certified ophthalmologist.

Cushing's disease – otherwise known as hyperadrenocorticism, this disease results from the malfunction of the adrenal glands and a high level of regulatory hormones which can interfere with normal body functions. Usually not immediately life threatening, but can decrease life expectancy if not treated.

Echocardiogram – ultrasound of the heart to determine heart function, appearance, and to evaluate for cardiac diseases such as patent ductus arteriosus, etc.

Genetic affected – an individual which carries a deleterious gene and expresses that gene in appearance.

Genetic carrier – an individual which carries one copy of a deleterious gene but does not express that gene in appearance (i.e. appears “normal”).

Genetic clear – an individual which appears normal and does not carry any copies of a deleterious gene. This individual will not reproduce the disease for which he/she is clear.

Genotype – the actual genetic makeup of an individual – often expressed as the DNA of the individual.

Dominant gene – only one copy of the gene is necessary for an individual to be affected with the trait of concern.

Legg Calve Perthes disease – a malformation of the hip joint in which the blood supply to the joint is affected and the femoral head (or “ball” of the “ball and socket” hip joint) becomes malformed. Results in lameness and pain.

Low or high dose dexamethasone suppression test – used to characterize or identify Cushing’s disease in an individual.

Neonatal encephalopathy – a disease currently only identified in the standard poodle, resulting in abnormal brain development and death in a puppy.

Optic nerve hypoplasia – disease of the eye in which the optic nerve does not develop normally and results in blindness.

Patellar luxation – disease of the stifle (knee) joint in which the patella (kneecap) dislocates out of the joint socket. Can result in permanent lameness if severe and not corrected.

Patent ductus arteriosus – disease of the heart in which the ductus arteriosus, a conduit which is present and open before birth for blood to bypass the non-functional lungs, does not close at birth as it should. This results in oxygenated blood mixing with non-oxygenated blood, turbulence in the heart, and other cardiac effects.

Progressive retinal atrophy – disease of the eye in which the retina degenerates over time. Initially leads to night blindness and progressively leads to total blindness.

Phenotype – physical expression of a gene or trait. The appearance of an individual as an expression of his/her genes.

Recessive gene – requires two copies of the gene for an individual to express the trait of concern.

Sebaceous adenitis – disease of the skin which can lead to hair loss, skin infections, odor and other affects.

Von Willebrand’s disease – disease of a clotting factor in the blood which can lead to bleeding disorders and become life-threatening if severe.