

TFT Genetics
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Part 4: Patellar Luxation; Progressive Retinal Atrophy; Autoimmune Thyroiditis

Introduction

In previous essays I have discussed basic genetic principles (Part 1); Congenital Hypothyroidism with Goiter - CHG (Part 2); and Demodectic Mange, Legg-Calve Perthees, and von Willebrand's Disease (Part 3). In this essay I will discuss some other genetic disorders (or in some cases multifactorial disorders with a genetic component). Specifically, I will discuss Patellar Luxation, Progressive Retinal Atrophy, and Autoimmune Thyroiditis.

Patellar Luxation

Patellar luxation is fairly common in small dogs including the Toy Fox Terrier. The quadriceps tendon (above the patella), the patella, and the patellar tendon (below the patella) should all be aligned. The patella moves within the trochlear groove. Ideally, the groove should be deep enough so as to not allow medial or lateral dislocation during flexion and extension. However, when the connective tissue is too loose and/or the groove is too shallow, such dislocation (i.e. luxation) can occur. Mild forms can go unnoticed because the animal can extend the leg and restore normal positioning and function without manual manipulation. More severe forms require manual intervention to restore normal gait. Very severe forms can become permanent. The more severe forms can be readily observed by anyone looking carefully. Milder forms can be observed by manual manipulation. There have been no clear, definitive studies that indicate that this condition is inherited. However, health survey information and anecdotal reports from conscientious breeders suggest that at least a genetic predisposition, if not a direct inheritance, is likely. Ideally, every breeding dog (or potentially breeding dog) should be tested. Dogs can be tested at any age by any competent veterinarian, but are only added to the OFA database if the testing is done when the animal is 12 months old or older. When looking at the OFA form, it has check boxes to indicate if the animal is normal or luxated. If luxated, it can be assigned a grade (1, 2, 3 or 4) and it can be indicated if the luxation is unilateral or bilateral, intermittent or permanent, medial or lateral. Currently, there are no statistics available on the OFA website for TFTs but, at the time of this writing, the database had last been updated in December 2002 so an update may be forthcoming soon. Any dog with Grade 3 or 4 should definitely not be bred. Grade 2 animals should also probably not be bred. Since Grade 1 animals have few if any problems until well into old age, they may be useful in a breeding program but their offspring should be closely monitored. One caution is that if a genetic predisposition exists, it is unclear that offspring inheriting the predisposition will be limited to luxation of the same grade as the parent(s). Therefore, it is unknown if a mating between animals where one or both parents are Grade 1 will produce offspring with luxation no worse than Grade 1 or whether such a mating can produce offspring with more severe forms of patellar luxation. Until that information is known it is impossible to make an informed recommendation for breeders concerning the breeding of animals with mild (Grade 1) luxation. Only careful testing and vertical pedigree analysis can answer these questions and, so far, at least to my knowledge, no one has yet undertaken such a study in TFTs. If anyone is aware of such a study, I would like to hear about it.

Progressive Retinal Atrophy (PRA)

Progressive Retinal Atrophy (PRA) is actually a group of related disorders that result from deterioration of the retina resulting in eventual blindness. In all breeds except the Siberian Husky (where it is believed to be an **X-linked recessive** disorder), it is apparently the result of an **autosomal recessive** gene and thus requires the mating of two **carriers** to produce an affected animal. Even then, only 25% of the offspring of such matings should be affected. The number of affected TFTs and of asymptomatic (clinically normal) carriers is unknown but is probably small. Dogs with early onset PRA should not be bred. Elimination of the disorder would require that the parents of any dog with PRA be removed from the breeding program and all other offspring of that cross be tested (preferably prior to breeding). Testing is by electroretinogram (ERG) which can detect PRA long before noticeable symptoms appear. ERG involves placing a contact lens on the eye and 2 electrodes on the head and then flashing a bright light into the eye, which results in a distinctive measurable electrical signal. The strength of the signal determines if the PRA exists (weakened signal) or not. However, even though testing can be done before symptoms appear, it is possible to miss the condition if the electrical abnormality is not yet measurable. A DNA test that can detect clinically normal carriers has been developed for some breeds but has not yet been tested in TFTs. Unless it can be shown that the incidence of PRA in TFTs is actually not small, I would not recommend routine (ERG) testing at this time. Careful recordkeeping to identify affected individuals and, by inference, asymptomatic carrier parents is sufficient for now.

Autoimmune Thyroiditis

According to some, hypothyroidism is not uncommon in dogs including TFTs. About 80% of hypothyroidism is of the form “autoimmune thyroiditis” in which the body’s immune system fails to recognize the thyroid as “self” and produces antibodies (TgAA) that attack thyroid tissue reportedly leading to progressive loss of function. Recognition of this condition is difficult because symptoms are fairly general and include such things as weight gain; neurological, ocular, gastrointestinal, or cardiovascular problems; anemia; impairment of bone development; sluggishness; hair loss; cold intolerance; loss of libido; and infertility. Furthermore, not all affected animals will show all of these signs. In fact, some argue that because of the general nature of these symptoms and the observation that often they do not resolve when supposed hypothyroid dogs are put on thyroid hormone therapy, the observed signs and symptoms may not be the result of hypothyroidism at all. However, it is not clear that this supposed non-responsiveness is because the animals are not hypothyroid or because the thyroid hormone measured (total T3, total T4) is non-predictive of thyroid disorder or treatment response. Even if we assume that there is some percentage of reported cases that are not actually due to hypothyroidism, it may be true, and is at least reported as such, that at least some cases do exist. In those cases, the most obvious sign may be hair loss but the most problematic for breeders is probably the loss of libido and the infertility problems. If you have a dog showing any of these signs, especially hair loss and/or fertility problems you should probably suspect hypothyroidism and have the animal tested. Testing currently involves running a complete thyroid panel including T3/T4/TSH and TgAA. The latter (TgAA) is specific for autoimmune thyroiditis. This test will only detect symptomatic individuals and will not detect presymptomatic individuals or asymptomatic carriers. The mode of inheritance appears to involve a single, **autosomal recessive** gene. No DNA test for affected individuals or carriers has been developed. Therefore, carriers can only be detected when affected offspring are produced from normal parents. The lack of a DNA test for carriers coupled with the late onset in some affected individuals makes elimination of the disorder difficult. Fortunately, treatment is fairly simple and inexpensive requiring daily doses of thyroid hormone. Successful treatment will eliminate the signs. If treatment is unsuccessful and infertility persists then either the disorder has essentially become self-eliminating (or at least self-limiting) or it was not the result of a hypothyroid condition.

Summary

Of the three disorders discussed in this essay none can actually be tested for the existence of carriers in TFTs. Carriers can only be identified when two clinically normal dogs produce affected offspring. These three disorders also share the common feature of variable age of onset including some individuals who will show no noticeable signs until well-past breeding age. This makes elimination difficult. Of the three, the one of most concern to breeders and their clients is, and probably should be, patellar luxation. This disorder has an apparently moderately high incidence in TFTs and should be monitored vigilantly. The structural nature of the disorder, coupled with the potential severity of the abnormality, suggests that there probably needs to be an extensive study, including comprehensive vertical pedigree analysis, done to determine the frequency and severity of the problem. The OFA database can help with this but only if breeders take advantage of its existence and have their dogs tested. The situation is complicated by the fact that luxation can occur in genetically normal dogs as a result of trauma. This injury-related incidence of luxation is not heritable and animals in which luxation is the result of injury should be excluded from any pedigree analysis. Furthermore, they pose no problems as breeding dogs. Unfortunately, the tendency has been to consider all cases of patellar luxation as genetic. Conscientious breeders need to honestly evaluate the cause of any luxation in their breeding stock. Only such honesty can produce the trust necessary to accept the word of a breeder when they indicate that a particular case is trauma-related rather than genetic. Progressive Retinal Atrophy appears to be relatively uncommon in TFTs and vigilant observation by conscientious breeders is probably all that is required at this time. Autoimmune Thyroiditis is not life-threatening and can, in most cases, be successfully treated. In cases involving infertility that cannot be successfully treated by thyroid hormone therapy, the disorder essentially becomes self-limiting.