

# Canine Thyroid Registry

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### Background Information

Autoimmune thyroiditis is the most common cause of primary hypothyroidism in dogs and is recognized as a heritable condition. Predisposed dogs are born with normal thyroid function and generally grow and develop in a normal manner. Evidence of an immune reaction in the thyroid glands begins to appear sometime in early adulthood in most affected dogs. The initiating factors remain unknown, but part of the response is the appearance of thyroid autoantibodies directed at thyroglobulin and sometimes the thyroid hormones, T4 and/or T3. Eventually the autoimmune response results in irreversible destruction of the thyroid glands, an inability to make thyroid hormones, and finally, development of clinical signs of hypothyroidism. This pathologic process may extend for several years in many affected dogs. Thus detection of positive thyroid autoantibodies early in the course of the disease serves to identify dogs at increased risk of becoming hypothyroid in the future.

Because of the variable onset of the presence of autoantibodies, periodic testing will be necessary. Dogs that are negative at 1 year of age may become positive at 6 years of age. Hence, dogs should be tested every year or two in order to be certain that they have not developed the condition. Since the majority of affected dogs will have autoantibodies by 4 years of age, annual testing for the first 4 years is recommended. After that, testing every other year should suffice. Unfortunately, a negative at any one time will not guarantee that the dog will not develop thyroiditis.

The registry data can be used by breeders in determining which dogs are best for their breeding program. Knowing the status of the dog and the status of the dog's lineage, breeders and genetic counselors can decide which matings are the most appropriate for reducing the incidence of autoimmune thyroiditis in the offspring.

### General Procedures

Purposes - To identify those dogs that are phenotypically normal for breeding programs and to gather data on the genetic disease - autoimmune thyroiditis.

Examination and Classification - Each dog is to be examined by an attending veterinarian and have a serum sample sent to an OFA approved laboratory for testing according to the available application and general information instructions. The laboratory fee will be determined by the approved laboratory. Check with the referral laboratory for special requirements for sample handling and tests for registry purposes.

Certification - A certificate and breed registry number will be issued to all dogs found to be normal at 12 months of age. Ages will be used in the certification process since the classification can change as the dog ages and autoimmune disease progresses. The OFA fee is \$15.00 and no charge will be made for re certification at a later age. It is recommended that reexamination occur at ages 2, 3, 4, 6 and 8 years.

Preliminary evaluation - Evaluation of dogs under 12 months of age can be performed for private use of the owner since a few dogs are already positive at that age. However, certification will not be possible at that age.

Dogs with autoimmune thyroiditis - All data, whether normal or abnormal is to be submitted for purposes of completeness. There is no OFA fee for entering an abnormal evaluation of the thyroid in the data bank. Information on results determined to be positive or equivocal will not be made public without the explicit written permission of the owner or agent.

Thyroid abnormalities fall into several categories - Two types will be defined by the registry.

#### Autoimmune Thyroiditis Idiopathically Reduced Thyroid Function

Autoimmune thyroiditis is known to be heritable.

Those dogs with laboratory results that are questionable - therefore, not definitive, will be considered as equivocal. It is recommended that the test be repeated in 3-6 months.

#### Classification

The method for classifying the thyroid status will be accomplished using state of the art assay methodology.

#### Indices of thyroiditis:

Free T4 by dialysis (FT4D) - This procedure is considered to be the "gold standard" for assessment of the thyroid's production and cellular availability of thyroxine. FT4D concentration is expected to be decreased in dogs with the thyroid dysfunction due to autoimmune thyroiditis.

Canine Thyroid Stimulating Hormone (cTSH) - This procedure helps determine the site of the lesion in cases of hypothyroidism. In autoimmune thyroiditis the lesion is at the level of the thyroid and the pituitary gland functions normally. The cTSH concentration is expected to be abnormally elevated in dogs with thyroid atrophy from autoimmune thyroiditis.

Thyroglobulin Autoantibodies (TgAA) - This procedure is an indication of the presence of the autoimmune process in the dog's thyroid.

#### Certification

##### Normal

FT4D Within normal range  
cTSH Within normal range  
TgAA Within normal range

##### Positive autoimmune thyroiditis

FT4D Less than normal range  
cTSH Greater than normal range  
TgAA Positive

##### Positive compensative autoimmune thyroiditis

FT4D Within normal range  
cTSH Greater than normal range or equal to normal range  
TgAA Positive

##### Idiopathically reduced thyroid function

FT4D Less than normal range  
cTSH Greater than normal range  
TgAA Negative

All other results are considered equivocal

#### Laboratory Certification

The laboratory certification process will include quality control, quality assurance and reagent certification.

Laboratories may apply and if successful will be approved to perform analyses for OFA thyroid certification. A site visit by a qualified veterinary endocrinologist chosen by OFA will be required and

continued quality assurance and quality control will be necessary to maintain certification. Fully certified status can be obtained by passing the site visit and passing the results of the first OFA quality assurance assay test.

## Clinical Signs of Hypothyroidism

### General Clinical Signs

Lethargy  
Exercise Intolerance  
Obesity  
Mental Dullness

### Cold Intolerance

### Cardiovascular Signs

Abnormally low heart rate (bradycardia)

### Cardia arrythmias

### Neurological Signs

Weakness  
Knuckling  
seizures  
Ataxia  
Facial Nerve Paralysis

### Gastrointestinal Signs

### Diarrhea

Constipation

### Blood Disorders

Anemia  
Elevated cholesterol levels  
Coagulation irregularities

### Vestular Signs

### Circling

### Reproductive Functions

Cycle irregularities  
Prolonged anestrus  
Cycle cessation  
Diminished libido  
Low birth weights  
Spontaneous abortions  
Excessive lactation (galactorrhea)  
Testicular atrophy

### Skin Problems

Alopecia  
"Rat" tail  
**Dry, brittle coat**  
Pigment changes in skin and coat  
Seborrhea  
Chronic otitis externa  
Skin thickening (myxedema)  
**Poor wound healing**  
Persistent infection (pyoderma)

### Eye Problems

Fatty deposits of the cornea  
Corneal ulceration  
Uveitis

## Behavioral Changes Associated with Thyroid Dysfunction in Dogs

by W. Jean Dodds, DVM and Linda P. Aronson, DVM

In North America, the principal reason for pet euthanasia stems not from disease, but undesirable behavior. While this abnormal behavior in dogs and cats can have a variety of medical causes, it also can reflect underlying problems of a psychological nature.

Inheritance has been shown to play an important role in the behavior of both animals and humans. The role of inheritance in behavior was reviewed by Plomin (Science 248:183-188, 1990), who pointed out that the genetic influence on behavioral disorders rarely accounts for more than half of the phenotypic expression of behavioral differences. Each of the multiple genes involved has a small effect on behavior. Development and application of newer techniques in molecular biology offers the promise of identifying the DNA marker sequences

responsible for behavioral variation. However, behavior is the most complex phenotype because it reflects not only the functioning of the whole organism but also is dynamic and changes in response to environmental influences. With respect to animal behavior, applied behavioral genetics was first studied several thousand years ago because animals were bred and selected for their behavior as much as their conformation. The results can be attested to by the dramatic differences in behavior and physique among various dog breeds. Today these breeds have a great range of genetic and behavioral variability.

Many investigators in recent years, have noted the sudden onset of behavioral changes in dogs around the time of puberty. Most of the dogs have been purebreds or crossbreds with an apparent predilection for certain breeds. For a significant proportion of these animals, neutering does not alter the symptoms and in some cases the behaviors intensify. The seasonal effects of allergies to inhalants and ectoparasites such as fleas, followed by the onset of skin and coat disorders including pyoderma, allergic dermatitis, alopecia, and intense itching, have also been linked to changes in behavior.

Another interesting association which has been increasing in frequency is the link between thyroid dysfunction and aberrant behavior. Typical clinical signs include unprovoked aggression towards other animals and/or people, sudden onset of a seizure disorder in adulthood, disorientation, moodiness, erratic temperament, periods of hyperactivity, hypo-attentiveness, depression, fearfulness and phobias, anxiety, submissiveness, passivity, compulsiveness, and irritability. After the episodes, a majority of the animals were noted to behave as if they were coming out of a trance-like state and were unaware of their previous behavior.

A similar association between behavioral and psychologic changes and thyroid dysfunction has been recognized in humans since the 19th century, and more recently has been noticed in cats with hyperthyroidism. In a recent human study, 66% of patients with attention deficit-hyperactivity disorder were found to be hypothyroid, and supplementing their thyroid levels was largely curative.

The mechanism whereby diminished thyroid function affects behavior is unclear. Hypothyroid patients have reduced cortisol clearance, and the constantly elevated levels of circulating cortisol mimic the condition of an animal in a constant state of stress, as well as suppressed TSH output and production of thyroid hormones. In humans and seemingly in dogs, mental function is impaired and the animal is likely to respond to stress in a stereotypical rather than a reasoned fashion. Chronic stress in humans has been implicated in the pathogenesis of affective disorders such as depression. Major depression has been shown in imaging studies to produce changes in neural activity or volume in areas of the brain which regulate aggressive and other behaviors. Dopamine and serotonin receptors have been clearly demonstrated to be involved in aggressive pathways in the CNS. Hypothyroid rats have increased turnover of serotonin and dopamine receptors, and an increased sensitivity to ambient neurotransmitter levels. In dogs with aberrant aggression, a large collaborative study at Tufts University has shown a favorable response to thyroid replacement therapy within the first week of treatment, whereas it took about three weeks to correct their metabolic deficit. Dramatic reversal of behavior with resumption of previous problems has occurred in some cases if only a single dose is missed. A similar pattern of aggression responsive to thyroid replacement has been reported in a horse.

Tables 1 and 2 summarize results of complete thyroid diagnostic profiling on 634 canine cases of aberrant behavior, compiled by the authors in collaboration with Drs. Nicholas Dodman, and Jean DeNapoli of Tufts University School of Veterinary Medicine, North Grafton, MA.

Table 1. Canine Aberrant Behavior \*

Total No. Cases	Purebreds	Mixed Breeds	Thyroid Dysfunction	Euthyroid
634	568	66	401	233

- Mean Age, 3.7 years (Range 0.5-12 years). Median Age, 2.5 years.

Table 2. Most Commonly Represented Breeds with Thyroid Dysfunction and Aberrant Behavior\*

Breed	Thyroid Dysfunction	Aggression	Seizures	Fearful	Hyperactive
Golden Retriever	50/73	12/16	22/30	4/6	1/6

German Shepherd	34/53	10/22	14/16	3/7	2/2
Akita	27/38	24/33	0/1	0	0/2
Labrador Retriever	8/30	6/11	12/16	2/15	0/3
Shetland Sheepdog	14/25	3/6	2/3	2/4	3/3
Collie	8/9	0	7/7	0	0
English Setter	4/6	1/1	0	1/3	1/2
Other Purebreds	217/334	89/135	72/93	10/15	5/16
Mixed Breeds	39/66	11/27	16/23	4/5	1/8
Totals	401/634	156/251	145/189	25/55	13/42
	63%	(62%)	(77%)	(47%)	(31%)

\* Some dogs had more than 1 abnormal behavior.

Numerator = Thyroid Dysfunction. Denominator = Aberrant behavior

\*Ninety percent (568 dogs) were purebreds and 10% were mixed breeds.

\*There was no sex predilection found in this case cohort, whether or not the animals were intact or neutered.

\*63% had thyroid dysfunction as judged by finding 3 or more abnormal results on the comprehensive thyroid profile

\*The major categories of aberrant behavior were: aggression (40% of cases), seizures (30%), fearfulness (9%), and hyperactivity (7%); some dogs exhibited more than 1 of these behaviors.

\*Thyroid dysfunction was found in 62% of the aggressive dogs, 77% of seizing dogs, 47% of fearful dogs, and 31% of hyperactive dogs.

\*Outcomes of treatment intervention with standard twice daily doses of thyroid replacement were evaluated in 95 cases. Of these, 58 dogs had greater than 50% improvement in their behavior as judged by a predefined 6-point subjective scale (34 were improved >75%), and another 23 dogs had >25 but <50% improvement. Only 10 dogs experienced no appreciable change, and 2 dogs had a worsening of their behavior. When compared to 20 cases of dominance aggression treated with conventional behavioral or other habit modification over the same time period, only 11 dogs improved >25% and of the remaining 9 cases, 3 failed to improve and 3 were euthanized or placed in another home. These initial results are so promising that complete thyroid diagnostic profiling and treatment with thyroid supplement, where indicated, is warranted for all cases presenting with aberrant behavior.