

QUESTIONS AND ANSWERS ABOUT TOLLERS AND THYROID DISEASE

PART 1: TOLLERS, THYROID DISEASE AND THE MSU THYROID STUDY

Q: Are there any recommendations for preparing my dog for the thyroid test?

A: Yes, please read below.

Most dogs in a breeding program should be tested for thyroid function before breeding. Recent vaccinations can interfere with the TgAA test, so avoid testing a dog within 3 months of vaccination. It might be wise to consider testing dogs when you do the OFA hip certification since most females are hip tested while not in estrus. The following recommends will help you prepare your Toller for the thyroid test:

- Fasting preferred
- Age to screen – prebreeding and yearly up to age 4, then every other year until 8 years.
- Vaccinations can change the TgAA levels so wait 3 months after vaccinating a dog
- Steroid drugs will interfere with test results
- Sulfonamides decrease circulating thyroid hormones and thus cause an elevation in TSH
- Antihistamines may interfere
- Consider doing the test when you OFA hip test.

Q: At what age should I test my dog for thyroid disease?

A: Autoimmune thyroiditis has a variable onset, but it is usually seen between 1 to 5 years of age, but varies from breed to breed. The TgAA portion of the blood test can detect the disease as early as one year of age. Dogs negative at two years of age can become positive at 6 years of age. Ideally, all dogs should be tested before breeding. Since the majority of dogs tested with the disease have a positive blood test by 4 years of age, annual testing for the disorder for the first four years is recommended followed by testing every other year until the age of 8 years. One single negative blood test will not guarantee that the animal will never develop thyroid disease.

Q: What does the MSU premium thyroid test panel include?

A: The premium thyroid test offered by the MSU study combines the OFA certification tests as well as additional thyroid function tests. They are listed below with the normal range values.

<u>MSU Thyroid Panel</u>	<u>Thyroid Test Component</u>	<u>Normal Range</u>
OFA Certification	Free T4 by Dialysis (FT4D)	6-42 pmol/L
Thyroid Tests by MSU	Thyroid Stimulating Hormone (cTSH)	0-37 mU/L
	Specific Thyroglobulin Autoantibody (TgAA)	< 10% negative 10-15% inconclusive > 25% positive
	Additional Thyroid Function	
Tests done by MSU	Total Thyroxine (TT4)	15-67 nmol/L
	Total Ti-iodothyronine (TT3)	1.0-2.5 nmol/L
	Free (unbound) T3 (FT3)	4.5-12.0 pmol/L
	T4 Autoantibody (T4AA)	< 20
	T3 Autoantibody (T3AA)	< 10

Q: What percentage of sporting dog breeds are affected with autoimmune thyroiditis?

A: Michigan State University data of sporting breeds with autoimmune thyroiditis (% affected) are:

English Setter	32.4%	
German Wirehaired Pointer	20.5%	
<i>Nova Scotia Duck Tolling Retriever</i>	<i>18.5%</i>	
Pointer	17.6%	Sporting breeds with a higher than average %
Cocker Spaniel	16.1%	
English Cocker Spaniel	15.5%	
Golden Retriever	14.7%	
Chesapeake Bay Retriever	14.5%	
Irish Setter	14.0%	
Brittany	13.6%	
Gordon Setter	13.2%	
Vizsla	10.3%	
German Shorthaired Pointer	9.8%	Sporting breeds with % similar to all breed averages
<u>English Springer Spaniel</u>	<u>8.2%</u>	
Labrador Retriever	6.7%	
Flat-Coated Retriever	4.6%	Sporting breeds with lower than average %
Irish Water Spaniel	3.9%	

PART 2 – GENERAL INFORMATION ABOUT THYROID DISEASE

Q: What are the symptoms of hypothyroidism?

A: Common symptoms include:

- Lethargic behavior such as a lack of interest in play, frequent napping, tiring out on long walks
- Weight gain, sometimes without an apparent gain in appetite
- Bacterial infections of the skin
- Dry skin
- Hair loss, especially on the trunk or tail (“rat’s tail”)
- Discoloration or thickening of the skin where hair loss has occurred
- Cold intolerance/seeking out warm places to lie down
- Slow heart rate
- Chronic ear infections
- Severe behavioral changes such as unprovoked aggression, seizures, anxiety and/or compulsivity
- Depression

Q: What are the stages of hypothyroid disease and usual age of onset?

A: Subclinical thyroiditis or Stage 1 can be detected with a positive TgAA in the majority of dogs.

Once the disease progresses, outward signs of hypothyroidism can surface. The usual symptoms include weight gain, sluggishness, skin and hair problems including hair loss, weakness, cold intolerance, aggression and infertility. To see what the expected laboratory values would be at various stages of thyroid disease, please refer to Table 1.

<u>Stages of Hypothyroid Disease</u>	<u>Usual Age of Onset</u>
Stage 1 – Subclinical thyroiditis	2-3 years old
Stage 2 – Subclinical hypothyroidism	3-5 years old
Stage 3 – Hypothyroidism	6-7 years old

Table 1. Stages of Thyroid Disease and thyroid test result.

<u>DOG'S THYROID CONDITION</u>	<u>TEST: TgAA</u>	<u>cTSH</u>	<u>FREE T4</u>	<u>TOTAL T4</u>
Normal	negative	normal	normal	normal
Early thyroid disease	positive	normal	normal	normal
Subclinical thyroid disease	positive	high	normal	normal
Clinical thyroid disease	positive	high	low	low
End-stage thyroid disease	negative	high	low	low

Q: What does it mean when TgAA is the only abnormality?

A: This most likely reflects the presence of subclinical thyroiditis. Long before a dog becomes hypothyroid, laboratory tests can detect autoantibodies to thyroglobulin, a large protein synthesized by the thyroid glands. The presence of elevated TgAA levels confirms thyroiditis, promotes early recognition of this disorder and facilitates genetic counseling. False positive results can occur if the dog has been vaccinated recently, so be sure to wait to thyroid test a dog until 3 months after vaccinating. It is very important to note, that dogs with equivocal results or an abnormal reading should be retested in 3 to 6 months.

Q: If my Toller has elevated TgAA levels will he become hypothyroid?

A: He has an increased risk for sure, but no guarantee he will become hypothyroid.

Interestingly, in one study 171 dogs with TgAA positive results 50% showed no symptoms, about 25% showed symptoms of Stage 1, about 14% showed symptoms of Stage 2 and about 15% showed symptoms of Stage 3 hypothyroidism.

Of the 50 % of dogs to have TgAA positive tests with no symptoms, it was found that within a year, 1 in 20 became hypothyroid, 1 in 5 had early or partial failure of the thyroid and 6-15% became TgAA negative. Therefore, some dogs subsequently test normal and others may progress with the disease in varying degrees. **This demonstrates the need to retest dogs that are TgAA positive who appear healthy.**

The limited research to date shows some dogs are able to tolerate lifelong lymphocytic thyroiditis without ever developing hypothyroidism. And some dogs will have elevated levels of TgAA for a long time before developing hypothyroidism. For these reasons, it is important to understand that elevated TgAA levels do not necessarily indicate hypothyroidism is present or guarantee it will ever fully develop. The MSU study will help define the occurrence of autoimmune thyroiditis in Tollers and the variable aspects of the disease.

Q: How is hypothyroidism treated?

A: Fortunately the treatment is relatively easy and inexpensive, and hypothyroidism usually does not compromise a dog's quality of life. The preferred treatment for most cases of hypothyroidism is giving synthetic levothyroxine twice a day initially, and then perhaps only a daily dose is required. A positive response to treatment is usually seen within one week. Periodic monitoring is needed and adjustments in dosage may be necessary. The prognosis is generally good and many dogs live long and productive lives with this disease.

Q: Where can I go to read further about thyroid disease?

A: For further information please refer to the following articles:

- International Symposium on Canine Hypothyroidism: <http://www.akcchf.org/research/articles/whitepapers/96hyp.pdf>
- Thyroid Study in Welsh Springer Spaniels http://www.artwork.net/cok13/thyroid_study.htm
- Hypothyroidism: <http://www.canadaguidetodogs.com/greatdane/danearticle2.htm>
- What's the Big Deal about the Little Thyroid: <http://www.gdhfa.org/ThyroidLaBrie.htm>
- Is Hypothyroidism Really the Leading Canine Genetic Disease: <http://www.offa.org/issue1.pdf>
- Canine Autoimmune Thyroid Disease and Symptoms of Hypothyroidism: <http://www.canine-epilepsy-guardian-angels.com/ThyroidDisease.htm>

PART 3. BREEDING RECOMMENDATIONS

Q: Why is the TgAA test important to breeders?

A: The TgAA test can be a useful tool for breeders. The original concept behind measuring TgAA was to determine which dogs should not be used for breeding among the breeds in which the condition is known to be inherited, or suspected to be inherited. The incidence of autoimmune thyroiditis is higher in sporting dogs. The Toller has a higher than normal risk for developing this disorder, so the TgAA test can help breeders screen their stock and breed accordingly to help reduce the incidence.

Q: What are commonly accepted breeding recommendations?

A: Experts at the Symposium on Canine Hypothyroidism held at the University of California – Davis in 1996 had the following suggestions for breeding. The work-up for a breeding dog should include the following laboratory tests: total T4 (TT4), free T4 measured by equilibrium dialysis (fT4ed), thyroglobulin autoantibodies (TgAA) and canine thyroid stimulating hormone (cTSH).

* In an apparently healthy dog, normal results indicate no current thyroid disease, and breeding may proceed. If there is a family history of hypothyroidism, the tests may be repeated annually.

* A dog that has normal lab results but shows clinical signs of hypothyroidism should be withheld from breeding and the tests should be repeated in two to six months. Other causes for the clinical signs should be pursued.

* If the results of the apparently healthy dog's tests are abnormal, there is some potential risk in breeding. The experts recommend waiting and retesting the dog in three to six months.

* Abnormal results in conjunction with clinical signs of hypothyroidism warrant treatment and avoiding breeding the affected dog.

Please note that experts do not say TgAA positive dogs WITHOUT signs of hypothyroidism should be removed from breeding. They recommend these dogs be utilized in a breeding program carefully and breed to dogs testing TgAA negative. However if the dog has signs of hypothyroidism, experts advise a stay on breeding.

The MSU study provides an inexpensive opportunity for breeders to thyroid test their dogs. Ideally, all breeding stock should be tested before breeding. Since the prevalence of autoimmune thyroiditis is yet to be well defined in the Toller, the thyroid tests should be used in the context of the overall breeding plan. Carefully consider whether the dog should be used in a breeding program as you normally would. It would be prudent to recommend dogs with high TGAA be bred to dogs that are negative for TGAA and/or tested clear (normal T4 and TSH levels) for thyroid disease as older dogs. This would be like the breeding recommendations for PRA utilizing a Pattern A dog to a carrier (B) or affected dog (C).

Since there is no absolute proof at this time that autoimmune thyroiditis is the cause for all hypothyroidism in Tollers, it seems reasonable to breed a dog with elevated TgAA albeit cautiously, until more is known about how lymphocytic thyroiditis progresses in Tollers and what the inheritance is. As the breeder, you must decide if the value of this dog's total makeup outweighs the risk of furthering a condition like lymphocytic thyroiditis in our breed. Hopefully with more definitive research, clearer direction will be on the near horizon.

From the research evidence thus far, if the dog is negative for TGAA after 6 years and there is no elevation of the T4 and TSH, the dog will probably not develop autoimmune thyroid disease. Dogs positive for TGAA should have a T4 and TSH run annually to monitor thyroid function. If and when the clinical signs develop the dog should be put on thyroid supplementation and breeding this dog should be seriously reevaluated.

PART 4 – OFA THYROID CERTIFICATION

Q: What are the OFA thyroid test components?

A: The OFA thyroid certification includes 3 separate thyroid function tests. The first two thyroid tests help determine if thyroid disease is present. The TgAA test is a marker that reveals if the dog has inherited thyroid disease. Therefore it is important to make certain that thyroid testing include the TgAA test – especially for prescreening breeding animals. The three components include:

FT4D – Free T4 by dialysis is one of the best tests for thyroid screening because it is not affected by non-Thyroidal illness as much as Total T4 values. It is considered the “gold standard” for assessing thyroid Hormone production and availability of thyroxine. FT4D is expected to decrease in dogs with thyroid dysfunction due to autoimmune thyroiditis.

cTSH – Canine Thyroid Stimulating Hormone. This is a test for thyrotropin which is the hormone produced by the pituitary gland and regulates the production of thyroid hormones (T4 and T3). This test 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 high in dogs with thyroid atrophy from autoimmune thyroiditis.

TgAA – Thyroglobulin Autoantibody. Detects early autoimmune thyroiditis and the presence of the autoimmune process in the dog's thyroid. This is a marker for dogs that have inherited thyroid disease.

Q: What are the OFA certification categories and corresponding lab values?

A: For certification purposes, the OFA has the following categories with corresponding laboratory value interpretations. If your dog is not determined to be normal, an OFA certificate will not be issued. For equivocal results or an abnormal test, the test should be repeated in 3 to 6 months.

a. Normal

FT4D within normal range
cTSH within normal range
TgAA negative

c. Positive compensative autoimmune thyroiditis

FT4D within normal range
cTSH greater than or equal to normal range
TgAA positive

b. Positive autoimmune thyroiditis

FT4D less than normal range
cTSH greater than normal range
TgAA positive

d. Idiopathically reduced thyroid function

FT4D less than normal range
cTSH greater than normal range
TgAA negative

e. All other results are considered equivocal

Q: How does a dog obtain an OFA Thyroid Registry number?

A: Certification is possible for any dog over 1 year of age. A certificate and breed registry number will be issued to all dogs found to have normal thyroid results. It is recommended that the thyroid tests be repeated at 2,4,6, and 8 years of age. Ages will be used in the certification process since the classification can change as the dog ages.

The MSU study results can be submitted to the OFA for thyroid certification with the appropriate paperwork and \$15.00 fee. Laboratories listed below can also provide OFA certification. Each dog tested should have a veterinarian ship the blood sample, the OFA application, and the OFA fee to an OFA approved laboratory. The OFA application can be obtained by calling 573-442-0418 or by contacting the website at <http://www.offa.org>

Q: What Laboratories are currently certified by OFA?

A: The US and Canadian approved laboratories are listed below. The OFA laboratory certification process includes quality control, quality assurance and reagent certification. Labs will not release results to an individual, only to a veterinarian, if the sample is to be used for OFA certification purposes.

Endocrine Diagnostic Section

Diagnostic Center for Population & Animal Health
4125 Beaumont Road, Room 122
Lansing, MI 48910-8104
517-353-0621

New York State Animal Health Diagnostic Laboratory

College of Veterinary Medicine, Cornell University
Upper Tower Rd.
Ithaca, NY 14853
607-253-3673

Texas Veterinary Medical Diagnostic Laboratory

1 Sippel Rd.
College Station, TX 77843
979-845-3414

Animal Health Laboratory

Laboratory Services Division
University of Guelph
Door P2 Bldg. 49, McIntosh Lane
Guelph, Ontario, N1G 2W1
CANADA
519-824-4120 ext. 54501

Veterinary Diagnostic Laboratory

Attn: Sample Handling
College of Veterinary Medicine
University of Minnesota
1333 Gortner Ave.
St. Paul, MN 55108
612-624-0761

Vita-Tech

1345 Denison St.
Markham, Ont, L3R 5V2
CANADA
1-800-667-3411

University of California

Veterinary Medical Teaching Hospital
Clinical Pathology, Chemistry, Room 1017
1 Garrod Drive
Davis, CA 95616
530-752-7380

Antech Diagnostics*

1111 Marcus Ave.
Suite M28
Lake Success, NY 11042
800-872-1001

*only the Lake Success, NY location of Antech has
been certified to process OFA thyroid panels