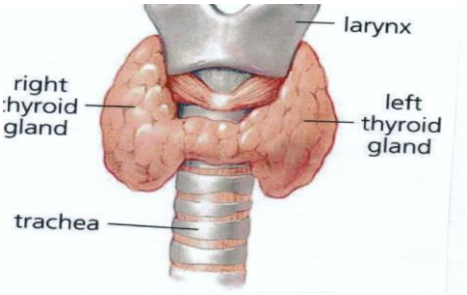
A Coat of Many Colors

Thyroid Disease Is Often Misunderstood and Misdiagnosed

By Robin K. Nelson, DVM

1. **What is the thyroid gland and why is it important?**

   The thyroid is a small gland located in the neck region on both sides of the trachea or windpipe. Basically the thyroid serves as a "volume dial" for metabolism.



It produces two forms of thyroid hormone. T3 is the active hormone which regulates metabolism at the cell level. T4 is the inactive form created to circulate in the bloodstream. When circulating levels of T4 begin dropping, the pituitary gland at the base of the brain produces a substance called thyroid stimulating hormone or TSH. This hormone triggers the thyroid gland to make and release more T4. When T4 is absorbed into tissue cells, it is converted to T3 for use.

Virtually every organ in the body is affected when thyroid hormone is low.

1. **What is canine hypothyroidism?**

   It is the natural deficiency of thyroid hormone. Hypothyroidism is the most common hormone imbalance of dogs. It is frequently misunderstood, misdiagnosed, and mistreated. The term hypothyroidism should be reserved for the end stages of thyroid disease when the dog's thyroid gland is no longer capable of producing sufficient hormones to sustain clinical health.

2. **What causes hypothyroidism?**

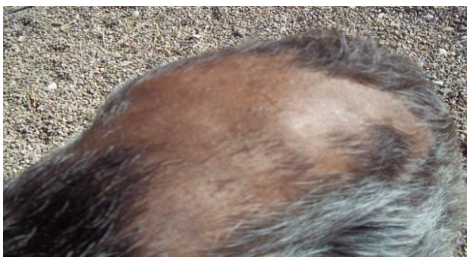
   Ninety-five percent (95%) of hypothyroidism is caused by an immune reaction in the dog's thyroid gland. Inflammation of the thyroid gland appears in early adulthood and progresses for several years in many affected breeds. Initiating factors are unknown, but the response is the appearance of thyroid antibodies directed mainly at thyroglobulin, a protein produced by and used entirely within the thyroid gland. In some cases, antibodies are also directed at the thyroid hormones T3 and T4.

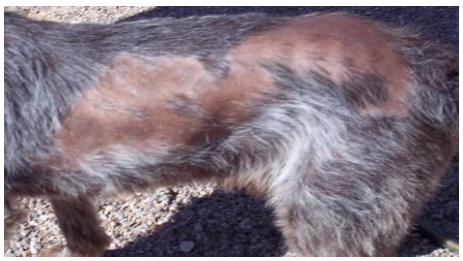
   Stresses can affect onset or severity, but only dogs that have the genetic potential can develop autoimmune thyroiditis. Eventually, the autoimmune response results in irreversible destruction of the thyroid glands, an inability to make thyroid hormones, and finally development of clinical signs of hypothyroidism.

3. **What does hypothyroidism look like?**

   Observable clinical signs appear after 75% or more of the thyroid gland has been destroyed.

   Abnormal skin is a common clinical finding. Dogs suffer hair loss presenting with a rat tail, a bald area around the collar, or failure of hair growth after clipping. Recurring skin infections or ear infections are common. Seborrhea is often a problem as the skin thickens, becomes scaly and greasy, and malodorous. The skin can also be very pruritic or itchy. Dry and brittle coats or shorter, puppy-like coats may also be observed with hypothyroidism.

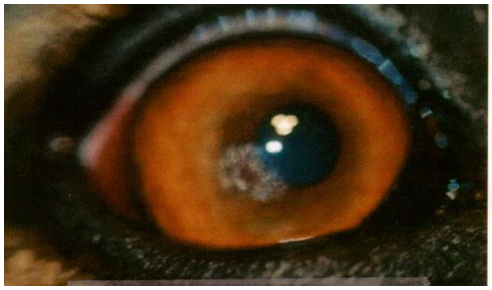




NGWPR Long-term Foster Dog "Hope" prior to treatment.

Hope after one month's treatment.

Hypothyroid dogs are often **obese** or have a difficult time losing weight. They can be **lethargic**, or appear "mentally dull," lacking desire to work or play.Some hypothyroid dogs don't show obvious skin or behavior changes. **Non-regenerative anemia and high cholesterol levels** may raise suspicion of thyroid disease. Elevated cholesterol(found in 65-80% of hypothyroid dogs) and circulating fats can lead to changes in the eye**. Corneal dystrophy** is an abnormality of the clear covering of the eye. It can appear as a small white spot or circle on the eye's surface. Severe forms can lead to painful ulceration.



Corneal Dystrophy can lead to painful ulceration.

Without adequate thyroid hormone, nerves do not conduct electrical impulses normally. Neurological signs such as **general weakness**, listlessness, poor coordination, **seizures**, or even **unexplained, non-painful lameness** can suggest hypothyroidism. Focal nerve problems associated with hypothyroidism include facial paralysis appearing as a droopy eye or lip, and vestibular disease presenting with a head tilt, bizarre eye motion and balance disruption.

Hypothyroidism can affect the heart causing **bradycardia** (slow rate) or an abnormal rhythm.
Other conditions suspected to be associated with hypothyroidism include megaesophagus (digestive tract problems),laryngeal paralysis (difficulty breathing), and new or unexplained aggressive behavior.

Aberrant behavior associated with thyroid dysfunction includes **unprovoked aggression towards other animals and/or people**, seizure disorders, erratic temperament, fearfulness, and phobias**.**

Current evidence supports a significant relationship between thyroid dysfunction and dog-to-human aggression.

If hypothyroidism is recognized and treated appropriately, outcome follow-ups show significant behavioral improvement. Contrary to popular belief, evidence-based medicine has shown hypothyroidism has very little effect on canine reproduction.

4. What does testing for hypothyroidism involve?

Testing for thyroid disease isn't simple or perfect. True hypothyroidism is a multisystemic disorder and all suspected cases require a general medical workup including a CBC, health profile, and urinalysis. Appropriate thyroid evaluation requires more than just a total measure of T4 (circulating thyroid hormone).Testing for hypothyroidism must include checking for autoantibodies. Measuring autoantibodies is the best available way to diagnose hereditary hypothyroidism. 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. Autoantibodies indicate autoimmune thyroiditis. For months to years antibodies attack and gradually destroy normal thyroid tissue.

Autoantibodies are an indication of immune-mediated thyroid disease NOT a measure of thyroid function. Some dogs with autoantibodies never become hypothyroid. There has been controversy in recent years concerning the possible contribution routine vaccination might make to the origin of thyroiditis in dogs. Low-grade false positive results can occur if a dog has been vaccinated recently, especially with rabies vaccine.

Discordant test results are common when interpreting a thyroid panel. They may reflect intermediate stages of thyroid disease. Metabolic, infectious, endocrinologic, and cancerous illnesses can all cause low thyroid hormone values. Dogs on seizure medications, (phenobarbital or potassium bromide), prednisone or other corticosteroids, nonsteroidal anti-inflammatory drugs used for injury or arthritis pain, separation anxiety medication like clomipramine, or sulfonamide antibiotics can all have abnormally low total T4. It is best to measure T3, T4, TSH, autoantibody levels, and consider clinical signs and clinicopathologic abnormalities prior to deciding whether to treat a dog for hypothyroidism.

6. What does the OFA thyroid profile show?

Importantly, the OFA profile measures autoantibodies to thyroid hormone proteins. This information allows us to diagnose hereditary autoimmune thyroiditis at an early stage. Actual T3 and T4 levels show whether or not a significant enough amount of thyroid tissue has been destroyed to require oral thyroid supplement. The serum free T4 is arguably

the most accurate test of thyroid gland function and carries the highest priority of the thyroid hormone tests. It is least likely to be influenced by nonthyroid illness. TSH, if elevated, supports the diagnosis of hypothyroidism.

7. **Why repeat a thyroid profile?**
   Unfortunately, hypothyroidism seldom demonstrates obvious clinical signs
   before 3-5 years of age, so dogs are well into the showing and breeding years.
   Because of the variable onset of the presence of thyroid autoantibodies, periodic testing is necessary. Dogs that are normal at one year of age may test positive for autoantibodies at six years of age. The majority of affected dogs will have autoantibodies by four years of age.
   The OFA thyroid-registry database suggests annual testing for immune-mediated thyroid disease for the first 4 years. Any test showing significant levels of thyroid autoantibodies confirms a diagnosis of hereditary hypothyroidism.

   Dogs with autoantibodies, low T4, and high TSH have had thyroid destruction to the point of requiring treatment. Sometimes a thyroid profile is difficult to interpret and labeled "equivocal," especially early in the course of immune-mediated thyroiditis. The interpretation of results from baseline thyroid profiles in intact females is more reliable when they are tested in anestrus. Health screening should be performed 12- 16 weeks AFTER the onset of the previous heat cycle. Thyroid profiles should be repeated annually to monitor dogs on thyroid medication.

Indices of thyroiditis:

a) Free T4 (FT4) – this procedure is considered to the "gold standard" for assessment of the thyroid's production and cellular availability of thyroxine. FT4 concentration is expected to be decreased in dogs with thyroid dysfunction due to autoimmune thyroiditis.
b) 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.
c) Thyroglobulin Autoantibodies (TgAA) – This procedure is an indication of the presence of the autoimmune process in the dog's thyroid.

Certification

a. Normal
FT4 Within normal range
cTSH Within normal range
TgAA Negative

b. Positive autoimmune thyroiditis
FT4 Less than normal range
cTSH Greater than normal range
TgAA Positive

c. Positive compensative autoimmune thyroiditis
FT4 Within normal range
cTSH Greater than normal or equal to normal
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

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9. **How is hypothyroidism treated?**
   Because of its wide safety margin and efficacy, the treatment of choice is T4 hormone known as levothyroxine. Synthetic thyroid hormone replacement will need to be administered lifelong. The typical starting dose is .02mg/kg or .1 mg per 10 pounds administered orally twice a day. This is a much higher dose than is necessary in man because the oral absorption of levothyroxine is lower in dogs. Administering synthetic thyroid hormone should result in normal serum concentrations

of T3, T4, and TSH. Retesting a thyroid profile after 4-8 weeks of therapy confirms normal thyroid hormone levels have been achieved. A blood sample is drawn 3-7 hours after administering the levothyroxine. The thyroid medication may need to be adjusted based on retest results. In addition to providing thyroid supplementation for dogs showing typical signs of hypothyroidism, some veterinarians promote levothyroxine treatment in the early stages of autoimmune thyroiditis prior to T3 and T4 levels dropping below normal. Oral thyroid hormone may correct underlying thyroid imbalance, reduce the possible risk of developing other immune-mediated disorders, and hopefully control or prevent the thyroiditis from progressing to depletion and exhaustion of the thyroid gland.

10. **What is the prognosis for hypothyroidism?**
    The prognosis is excellent for return to normal function following adequate treatment in most hypothyroid dogs. With appropriate therapy, all the clinical signs and clinicopathologic abnormalities associated with hypothyroidism are reversible. The dog's general sense of well being and activity level will improve within weeks, but improvement in skin and cardiac function may take months.

11. **Why worry about canine hypothyroidism?**
    Though typically not fatal, hypothyroidism means a subnormal life, especially left undiagnosed or untreated. Immune-mediated thyroiditis, accounting for approximately 95% of the cases of hypothyroidism, is inherited. Early detection and appropriate breeding can reduce the incidence of hypothyroidism in offspring.

    Any test showing significant levels of thyroid autoantibodies confirms the diagnosis of hereditary thyroid disease. Studies of the mode of inheritance in dogs are inconclusive to date. Like hip dysplasia, it is likely polygenic. Laboratory and pedigree analyses of affected families show a progressive earlier age of onset of thyroiditis or clinical signs of thyroid dysfunction, along with an increased proportion of affected versus normal offspring in successive litters.

Knowing the status of a dog AND the status of the dog's lineage allows breeders to determine which breedings are most appropriate for reducing the incidence of autoimmune thyroiditis in the offspring.

Breeding normal testing dogs that have come from litters which have mostly tested normal is recommended.

Robin K Nelson is a veterinarian currently practicing in Omaha, NE. She has owned a GWP or two since 1980. In early 2000, Dr. Nelson read the article "Canine Hypothyroidism: Prevalence of Postive TgAA in Laboratory Samples from German Wirehaired Pointers" featured in a veterinary journal. Finding it interesting, she decided to run a thyroid profile on her seemingly normal GWP. Her dog's thyroglobulin autoantibodies were six times what they should be, providing evidence of ongoing thyroiditis. Dr. Nelson tested and medicated her GWP for 10 years gaining first-hand experience in managing hypothyroidism in German Wirehaired Pointers.Today, Dr. Nelson continues to be very interested as advances in genetics make it possible to better understand and hopefully prevent autoimmune thyroiditis.