



ISSUES IN ENDOCRINOLOGY

Canine Hypothyroidism: Diagnosis and Treatment

Johanna Heseltine, DVM, MS, DACVIM (Small Animal Internal Medicine), Clinical Assistant Professor Texas A&M University College of Veterinary Medicine & Biomedical Sciences, College Station, Texas

Hypothyroidism is a common endocrine disease of dogs. It occurs when the thyroid glands fail to produce adequate amounts of the hormones thyroxine (T₄) and triiodothyronine (T₃). Primary hypothyroidism resulting from idiopathic thyroid gland atrophy or immune-mediated lymphocytic thyroiditis is the most common diagnosis. Uncommon causes of canine hypothyroidism include congenital disease resulting from dyshormonogenesis of thyroid hormone, abnormal thyroid-stimulating hormone (TSH) production, or abnormal thyroid gland development.¹

Thyroid hormones are involved in a wide variety of metabolic processes, and low thyroid hormone levels result in a constellation of clinical signs and laboratory abnormalities that characterize hypothyroidism. Multiple hormone tests are required to make a diagnosis. The diagnosis should never be based on low T₄ concentration as a sole finding.

FIRST STEP: MAKING AN ACCURATE DIAGNOSIS

Veterinarians find diagnosing hypothyroidism—which can affect any breed (at left and right)—is tricky because many canine diseases mimic the disorder.

CLINICAL PRESENTATION

Hypothyroidism typically affects middle-aged dogs, although it has been reported in younger and older dogs. Any breed can be affected. Clinical signs (**BOX 1**) may be nonspecific, which can result in overdiagnosis of this disorder; lethargy and weight gain are common.^{2,3} Clinical signs may have an insidious onset and may not be noticed by the owner. Hypothyroidism often causes hair coat changes, including bilaterally symmetric, nonpruritic alopecia over the trunk or areas of wear, post-clipping alopecia, and a dull, lusterless hair coat (**FIGURE 1**). Skin changes may include scaling, seborrhea, hyperpigmentation, and recurrent infections (pyoderma or otitis externa).^{2,3}



FIGURE 1. Dog with hypothyroidism—note the excessive body weight, dull hair coat, and scaling.



Rare clinical signs and syndromes that have been associated with hypothyroidism include megaesophagus, vestibular dysfunction, facial nerve paralysis, and atherosclerosis.^{4,5,8}

BOX 1 Clinical Signs Commonly Associated With Canine Hypothyroidism²⁻⁷

- Signs related to decreased metabolic rate
 - Lethargy or dull mentation
 - Inactivity or unwillingness to exercise
 - Weight gain
 - Cold intolerance or heat seeking
- Dermatologic changes
 - Symmetric, nonpruritic hair loss
 - Post-clipping alopecia
 - Dry, dull hair coat
 - Scaling
 - Hyperpigmentation
 - Recurrent pyoderma or otitis externa
- Uncommon**
- Incoordination
- Ocular signs
 - Lipid corneal deposits
- Peripheral nervous system signs
 - Facial nerve paralysis
 - Laryngeal paralysis
 - Polyneuropathy
 - Other
- Vestibular signs
- Megaesophagus or esophageal dysmotility
- Cardiovascular abnormalities
 - Bradycardia
 - Exacerbation of other cardiac signs
 - Atherosclerosis
- Reproductive effects
 - Periparturient mortality
 - Lower birth weights
- Myxedema coma
 - Depressed mental status
 - Altered thermoregulation
 - Bradycardia
 - Hypoventilation
 - Thickened skin

DIAGNOSTIC PROCESS

Dogs should be tested for hypothyroidism only when the disease is strongly suspected based on the patient's history and physical examination findings (**BOX 1**). Complete blood count and serum biochemistry panel results may heighten clinical suspicion for hypothyroidism. Hypothyroidism can be misdiagnosed when testing is performed only because a dog is overweight or because a T4 concentration is included with a standard biochemistry panel.

A stepwise approach is helpful in accurately diagnosing canine hypothyroidism (**FIGURE 2**).

Step 1: Evaluate Minimum Database Results for Supportive Findings

Results from a complete blood count, serum biochemistry panel, and urinalysis are helpful to rule out concurrent disorders that could affect thyroid test results. However, none of the abnormal results that may be seen on these tests are specific for hypothyroidism.

Approximately 75% of hypothyroid dogs have elevated cholesterol levels.^{2,3} While mild hypercholesterolemia alone should not prompt testing for hypothyroidism, it supports a suspicion of hypothyroidism. Liver enzymes may be mildly elevated. A mild, nonregenerative anemia is present in about 30% to 40% of hypothyroid dogs.^{2,3} The urinalysis typically shows no abnormalities. Dilute urine, if present, should prompt investigation for concurrent illness or another cause of clinical signs.

Step 2: Screen With a T4 Concentration

Total T4 concentration is a useful screening test for hypothyroidism. The sensitivity of this test for the diagnosis of canine hypothyroidism is reported to be 89% to 100%.⁹⁻¹² If the T4 concentration is well within reference range, it is very likely the dog is euthyroid and further thyroid testing is not required. Free T4 (fT4) and thyroid-stimulating hormone (TSH) are evaluated only if the T4 concentration is low (**FIGURE 2**). Combined T4, fT4, and TSH testing is not recommended at this stage and may add unnecessary expense since a normal T4 concentration effectively rules out hypothyroidism.

However, a T4 concentration below reference range is not diagnostic for hypothyroidism. In addition to normal daily fluctuations, several medications have



BOX 2 Drugs That Alter Canine Thyroid Hormone Function or Test Results¹³⁻²⁰

- Prednisone (high dose)
- Phenobarbital
- Trimethoprim-sulfamethoxazole
- Aspirin (high dose)
- Clomipramine
- Thyroxine supplementation

BOX 3 Euthyroid Sick Syndrome

This syndrome refers to a condition in which nonthyroidal illness suppresses the concentration of circulating thyroid hormones. The mechanism is complex and likely involves changes in hormone distribution and metabolism and altered binding of hormones to proteins.

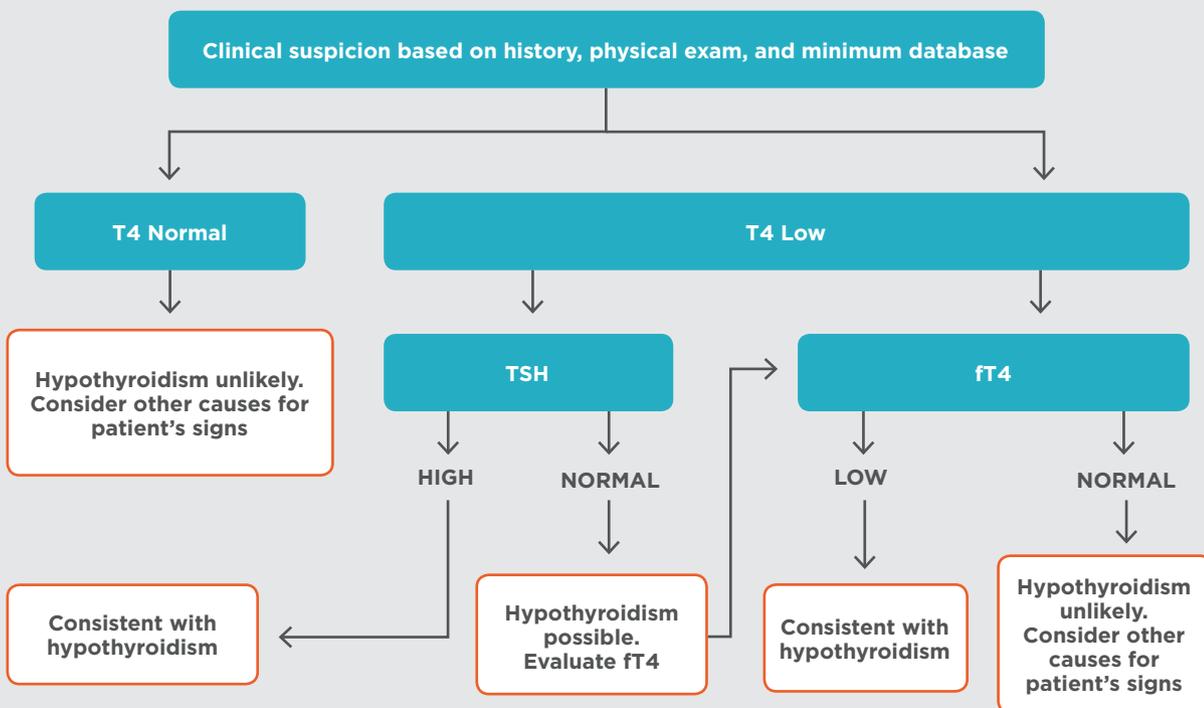
been demonstrated to lower the serum T4 concentration of dogs (BOX 2), and some also affect fT4 and TSH concentrations. Certain drugs, such as trimethoprim-sulfamethoxazole, can have direct effects on the pituitary-thyroid axis and result in hypothyroidism.¹³ Furthermore, nonthyroidal illnesses can alter thyroid hormone metabolism and result in the euthyroid sick syndrome (BOX 3). Concentrations of fT4 are less likely to be affected by concurrent illness, but if the illness is severe enough, fT4 can also be low.^{21,22} Therefore, thyroid testing should not be

performed in dogs that are systemically ill. If a dog with a concurrent illness is tested for hypothyroidism, test results should be interpreted with caution.

Because diagnosing hypothyroidism is not an emergency, sending samples out to a reference laboratory is advisable. Since additional confirmatory tests are required, it is helpful to collect and hold extra serum when collecting for the T4 test.

It is important to remember that “normal” reference ranges for T4 do not apply to sighthounds, as healthy dogs of these breeds have lower T4 concentrations than other breeds.^{23,24}

FIGURE 2. Approach to canine thyroid testing.



**TABLE 1** Test Results for Diagnosis of Canine Hypothyroidism^a

HORMONE	CONCENTRATION
Total T4	Low
Free T4	Low
TSH	High or normal

^aTo confirm the diagnosis, all 3 results must be obtained.

Step 3: Confirm With an fT4 or TSH Concentration

When a dog suspected to have hypothyroidism has a low total T4 concentration, fT4 and/or TSH concentrations must be evaluated to help confirm or refute the diagnosis (**TABLE 1**). If the TSH concentration is high, hypothyroidism can be diagnosed. However, 13% to 38% of hypothyroid dogs have normal TSH concentrations,^{10-12,25} so a normal TSH concentration does not exclude the diagnosis. Because of this limitation, it is often helpful to evaluate fT4 and TSH simultaneously as confirmatory tests. If the fT4 is low, a diagnosis of hypothyroidism can be made.

If T4 is low and fT4 is within reference range, hypothyroidism cannot be diagnosed, and the clinician should consider other differentials for the dog's clinical signs.

T3 concentrations vary widely and are not diagnostically useful.

Approximately 75% of hypothyroid dogs have elevated cholesterol levels.^{2,3} While mild hypercholesterolemia alone should not prompt testing for hypothyroidism, it supports a suspicion of hypothyroidism.

TREATMENT

Initiating Therapy

Studies have shown that most dogs can be regulated with once-daily levothyroxine,^{26,27} usually initiated at 0.02 mg/kg PO q24h. Some clinicians begin with twice-daily administration of levothyroxine (0.02 mg/kg PO q12h) and attempt to reduce the dosing to once daily, once clinical signs are well controlled. Lethargy often improves after a few weeks. Most clinical signs improve within 4 to 6 weeks, although dermatologic changes take months to resolve.

Monitoring and Adjusting Therapy

After 4 weeks of therapy, blood is collected 4 to 6 hours post-pill for T4 measurement. (T4 can be measured as early as 2 weeks after starting or adjusting therapy,²⁶ but waiting until 4 weeks allows for assessment of improvement in clinical signs at the same visit.) The post-pill T4 concentration should be at the upper end of the reference range or slightly above (<6 mcg/dL). Laboratory reference ranges for "initial" T4 concentrations and "post-pill" concentrations may be different, so careful sample labeling and interpretation are important.

If the post-pill T4 concentration is below the target concentration, the dose of levothyroxine should be increased by 25%. The T4 concentration is then rechecked in 2 to 4 weeks. The dose is gradually increased until the post-pill T4 concentration is within the target range. Similarly, if the post-pill T4 concentration is too high, the dose should be decreased by 25% and the concentration rechecked. Once an effective dose has been established, the interval between monitoring visits is increased to every 6 months.

Treatment Failure and Adverse Effects

Treatment failure is uncommon. Possible reasons for failure to achieve the targeted T4 concentration include owner noncompliance in administering medication or patient refusal to swallow the pills. Variable gastrointestinal absorption of levothyroxine is also considered to be a possible cause.²⁸ If a target post-pill T4 concentration has been achieved and clinical signs are not controlled, the dosing frequency should be increased to twice daily. Additionally, the diagnosis of hypothyroidism should be reconsidered. If the diagnosis of hypothyroidism is definitive and the dog's



T₄ concentration is well controlled, consider whether a concurrent disorder could be causing clinical signs.

Dogs are generally resistant to the effects of excessive levothyroxine supplementation. However, clinical signs such as polyuria/polydipsia and hyperactivity may develop.²⁶

SUMMARY

Thyroid testing should be carried out only when patients are suspected of having thyroid disease. Measurement of T₄ concentration is helpful to rule out hypothyroidism but should not be solely relied on to confirm the diagnosis. Combined testing that includes the serum T₄ concentration along with fT₄ and/or TSH levels is needed for definitive diagnosis and will help decrease the possibility for misdiagnosis of hypothyroidism. Since lifelong therapy is required, it is appropriate to achieve a definitive diagnosis before starting therapy. **TVP**

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Johanna Heseltine

A clinical assistant professor at Texas A&M University, Johanna Heseltine received her DVM from the University of Saskatchewan and then completed a rotating small animal internship at the University of Prince Edward Island. She completed her master's degree and small animal internal medicine residency at Virginia Tech and is a Diplomate of the American College of Veterinary Medicine (small animal internal medicine). Dr. Heseltine has held faculty and teaching positions and worked in private specialty practice. She is interested in a broad range of internal medicine disorders of small animals.

