



Canine Hypothyroidism

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P Profile

Definition

- Hypothyroidism is an endocrinopathy caused by decreased production of thyroid hormone.

Systems

- Because most cells in the body are affected by thyroid hormone, hypothyroidism can affect most organs.
- Common signs are related to the dermatologic system and decreased metabolic rate.

Genetic Implications

- Lymphocytic thyroiditis is heritable in beagles and borzois; heritability is suspected in other breeds.
- Congenital hypothyroidism is an inherited autosomal recessive trait in rat terriers, toy fox terriers, and giant schnauzers.

Incidence/Prevalence

- Approximately 1 in 200 dogs is affected.^{1,2}

Signalment

Breed

- Golden retrievers, Doberman pinschers, and spaniels are predisposed.^{1,2}
- There may be regional differences.
- Multiple breeds are predisposed to lymphocytic thyroiditis and likely predisposed to hypothyroidism,³ but any breed may develop hypothyroidism.

Age & Range

- Mean age is 7 years (range, 0.5–15 years).
- Hypothyroidism secondary to lymphocytic thyroiditis appears to develop at a younger age than idiopathic thyroid atrophy.

Sex

- Spayed and neutered dogs are at increased risk compared with intact dogs.

Causes

- Primary hypothyroidism, the most common form, results from destruction of the thyroid glands.
- Secondary hypothyroidism, caused by decreased thyroid-stimulating hormone (TSH) release from the pituitary, has rarely been reported.
- Tertiary hypothyroidism, caused by hypothalamic dysfunction, has not been proven in dogs.
- Congenital hypothyroidism from thyroid peroxidase deficiency has been seen in rat terriers and toy fox terriers. Giant schnauzers also develop congenital hypothyroidism, probably from TSH or thyrotropin-releasing hormone (TRH) deficiency.

Pathophysiology

- Adult-onset hypothyroidism is typically caused by lymphocytic thyroiditis or idiopathic thyroid atrophy.
- Lymphocytic thyroiditis is characterized by infiltration of the thyroid gland by lymphocytes, plasma cells, and macrophages.
 - Eventually, fibrous connective tissue replaces parenchyma.
- Idiopathic thyroid atrophy is characterized by thyroid parenchyma being replaced by adipose tissue.
 - Fibrosis and inflammation are minimal.
 - Idiopathic thyroid atrophy may be the result of thyroiditis.
- Thyroid carcinoma is a rare cause of hypothyroidism, which does not develop until at least 75% of the thyroid has been destroyed.

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Signs

- Common metabolic signs include weight gain, lethargy, and weakness; cold intolerance or heat-seeking behavior; and mental dullness.
- Dermatologic changes are common (see **Dermatologic Signs**).
- Neurologic dysfunction is uncommon and resolves with levothyroxine supplementation.
 - Peripheral neuropathy may result in exercise intolerance, ataxia, weakness, conscious proprioception deficits, and hyporeflexia.
 - Recent studies suggest that abnormalities in the limbs are more related to muscle than nerve.⁴
 - Cranial nerve dysfunction (V, VII, VIII) and peripheral and central vestibular disease have been reported.
 - Seizures are rare.
- Cardiac abnormalities (eg, weak apex beat, bradycardia) are uncommon.
- Reproductive abnormalities include periparturient mortality and lower birth weight in pups born to hypothyroid bitches,⁵ and inappropriate galactorrhoea in females.⁶ Decreased fertility is not well documented in hypothyroid bitches. Decreased libido and fertility have been reported in males of other species; however, decreased fertility

was not documented in a study of ¹³¹I induced hypothyroidism in male dogs.⁷

- Ocular changes may include corneal lipid deposits, lipemia retinalis, uveitis, secondary glaucoma, and keratoconjunctivitis sicca.
- Laryngeal paralysis and megaesophagus have been reported, but no causal relationship has been proven.
- Myxedema coma is very rare.

Dx Diagnosis

Differentials

- Dermatologic abnormalities could be caused by hyperadrenocorticism and alopecia X.
- Metabolic signs could be caused by many other disease processes.

Laboratory Findings

- CBC, serum biochemistry profile, and urinalysis are indicated to rule out other diseases before thyroid-specific tests are conducted.
- Mild nonregenerative anemia is common.
- Most hypothyroid dogs have fasting hypercholesterolemia and hypertriglyceridemia.
- Alkaline phosphatase (ALP) and alanine aminotransferase (ALT) may be slightly elevated.

Thyroid-Specific Diagnostics

- Total T₄ (TT₄) concentration is a sensitive but nonspecific screening test; values are low in most patients.
 - Additional testing (free T₄ [fT₄], TSH) is recommended before diagnosing hypothyroidism.
 - Euthyroid dogs may have low TT₄ levels because of individual variation, nonthyroid illness, or drug administration.
 - Euthyroid sight hounds and sled dogs often have levels below the reference range, leading to inaccurate diagnosis.
- Measurement of fT₄ by equilibrium dialysis is a more accurate indicator of thyroid function than TT₄, as fT₄ (not bound to proteins) is the active form.
 - It is also less affected by nonthyroid illness when compared with TT₄.
 - Measurement of fT₄ without an equilibrium dialysis step offers no diagnostic benefit over TT₄.
- Because of decreased negative feedback, TSH concentrations are often elevated in hypothyroid dogs.
 - Increased TSH in conjunction with decreased TT₄ or fT₄ is specific for hypothyroidism; however, up to 33% of hypothyroid dogs have normal TSH concentrations.
- Measurement of T₃ concentrations is less accurate than measurements of TT₄ and fT₄.
- The TSH stimulation test evaluates thyroid reserve.
 - Lack of increase in T₄ concentration 4–6 hours after TSH administration is standard for diagnosis of hypothyroidism, but the expense of human recombinant TSH limits the test's clinical usefulness.
- The TRH stimulation test is less straightforward, less reliable, and more difficult to obtain than the TSH stimulation test.
- Of dogs with hypothyroidism, antithyroglobulin antibodies (ATAs) are found in ~35%, anti-T₃ antibodies in 34%, and anti-T₄ antibodies in 15%.

Dermatologic Signs

- Alopecia, seborrhea, and pyoderma
- Bilaterally symmetric alopecia in areas of increased wear (eg, lateral thorax, tail)
- Slow regrowth of clipped hair
- Dry and brittle hair coat
- Hyperpigmentation, hyperkeratosis, myxedema, and otitis externa
- Increased incidence of pyoderma, folliculitis, generalized demodicosis, and *Malassezia* infections as a result of immunosuppression

ACTH = adrenocorticotropic hormone, ATAs = antithyroglobulin antibodies, fT₄ = free thyroxine, TRH = thyroid-releasing hormone, TSH = thyroid-stimulating hormone, T₃ = triiodothyronine, T₄ = thyroxine, TT₄ = total thyroxine



A 2-year-old neutered Labrador retriever with classic signs of myxedema (cutaneous mucinosis) and failure to regrow fur clipped several months before presentation for severe lethargy, heat-seeking behavior, and reluctance to rise.



Severely thickened skin, particularly in the eyelids and forehead.



Hyperpigmentation on the abdomen. Metabolic signs improved significantly within the first week of therapy, but the dermatologic signs took several months to resolve.

- ❑ Antibody presence is not diagnostic of hypothyroidism; <20% of euthyroid dogs with ATAs develop hypothyroidism signs within 1 year.
- In patients with consistent signs, CBC results, and serum biochemistry findings, begin by measuring TT₄ concentration. If value is low, fT₄ and TSH concentrations are measured. A low fT₄ concentration with an increased TSH concentration is approximately 86% accurate for diagnosis.
- ❑ As some hypothyroid patients will have TSH concentrations within reference range, therapeutic trial is recommended in patients with low fT₄ and strong clinical suspicion.
- While owners may avoid additional diagnostics beyond decreased TT₄ concentration, treatment without appropriate diagnostics should be

avoided. Cost of treatment is expensive over time, and inappropriate diagnosis may lead to delayed diagnosis of another disease.⁸

Drug Interference with Thyroid Testing

- Several medications can affect thyroid hormone concentrations⁹; these drugs (except sulfonamides) rarely cause clinical hypothyroidism but can interfere with test results.
- ❑ Glucocorticoids decrease TT₄, fT₄, and sometimes TSH in a dose-dependent manner.
 - Such testing should be avoided when steroids are administered.
- ❑ Phenobarbital can cause decreased TT₄ and fT₄ and slightly increased TSH but does not cause clinical hypothyroidism.
- ❑ Sulfonamides block T₃ and T₄

Therapeutic Trial

- A therapeutic trial with levothyroxine may be indicated in patients with consistent clinical signs, no other significant illness, and equivocal test results.
- Owners should be instructed to monitor a specific clinical sign or lesion for improvement during the trial.
- Some conditions respond to levothyroxine even in euthyroid animals.
- If a clinical response is evident, therapy should be discontinued and the patient observed for recurrence.
- If signs recur, hypothyroidism is confirmed.

- synthesis and long-term administration can cause clinical hypothyroidism with increased TSH.
 - Reversed by discontinuation.
- ❑ Potassium bromide does not appear to affect thyroid function.
- ❑ Aspirin decreases TT₄ and fT₄ concentrations.
- ❑ Carprofen, meloxicam, and deracoxib do not appear to significantly affect thyroid function.

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Imaging

- Ultrasonography demonstrates decreased echogenicity and smaller-than-average (volume and cross-sectional area) thyroid lobes in hypothyroid versus euthyroid dogs.

Tx Treatment

Inpatient or Outpatient

- Almost all hypothyroid dogs are outpatients. Patients with myxedema coma (rare) are treated with IV levothyroxine and supportive therapy.

Rx Medications

- Oral levothyroxine supplementation is initiated at 0.02 mg/kg q12h. Dose may be based on surface area for larger dogs (0.5 mg/m²).
 - Patients that respond to therapy and have appropriate TT₄ concentrations can be switched to q24h therapy but may require q12h dose if response is not maintained.
- Administration with food decreases bioavailability.
- Brand name or FDA-approved generic products are recommended, as bioavailability varies among products.
 - The patient should be maintained on the same product, or dose adjustment may be needed.
- The oral liquid formulation of levothyroxine (Leventa, leventa.com) has higher bioavailability than the pill formulations and can be administered q24h.

Precautions

- Because thyroxine increases cardiac oxygen demand, initial dose should be decreased by 25%–50% in patients with cardiomyopathy.¹⁰

- Treatment of hypothyroidism may precipitate an Addisonian crisis in patients with undiagnosed hypoadrenocorticism.
 - Before initiating levothyroxine therapy, hypoadrenocorticism should be ruled out with a baseline cortisol and/or ACTH stimulation test in patients with consistent signs or bloodwork (especially electrolyte) abnormalities.

↑ Follow-up

Patient Monitoring

- Concentrations of TT₄ should be assessed 4 weeks (sooner in patients with clinical signs of hyperthyroidism) after initiation of levothyroxine therapy or dose adjustment.
- Adjustments should be made based on both TT₄ concentrations and clinical response to therapy.
 - Once an appropriate treatment is established, TT₄ concentrations should be measured q6mo.
- Trough (premedication) TT₄ concentrations should be in the middle of the reference range, and peak (4–6 hours after medication) concentrations should be in or just above the reference range.
 - Peak concentration is often measured alone in patients on q12h dosing.
 - Both values are needed in patients on a q24h regimen.
 - Appropriate peak concentration in conjunction with low trough concentration suggests need for q12h dosing.
 - Another goal of therapy is normalization of TSH concentration if it is increased at time of diagnosis.
- Clients may note an increase in the dog's energy level in 1–2 weeks of

instituting therapy, but weight loss and dermatologic changes are not usually obvious for at least a month, and hair regrowth can take several months.

- Neurologic changes may initially improve rapidly initially, but full resolution can take several months.

Complications

- Lack of therapeutic response is common with an incorrect diagnosis based on only a low TT₄ value.
- Other possibilities include decreased GI absorption, poor compliance, and concurrent unidentified skin problems (eg, flea hypersensitivity, atopy).

***** In General

Relative Cost

- CBC, serum biochemistry profile, urinalysis, TT₄, fT₄, and TSH: \$\$–\$\$\$
- Monitoring and medication: \$\$/year

Cost Key

\$ = up to \$100
 \$\$ = \$101–\$250
 \$\$\$ = \$251–\$500
 \$\$\$\$ = \$501–\$1000
 \$\$\$\$\$ = more than \$1000

Prognosis

- Excellent with a good quality of life. ■ **cb**

See Aids & Resources, back page, for references & suggested reading.

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