

## Canine Hypothyroidism

### Features

This endocrinopathy is most often associated with primary thyroid dysfunction caused by lymphocytic thyroiditis or idiopathic thyroid atrophy. It is common in dogs, with highest incidence in middle-aged to older dogs. Young adult large and giant-breed dogs are also occasionally affected. Congenital hypothyroidism is extremely rare.

A variety of cutaneous symptoms can be seen. Alopecia on the bridge of the nose occurs in some dogs. The hair coat may be dull, dry, and brittle. Bilaterally symmetrical alopecia that spares the extremities may occur, with easily epilated hairs. Alopecic skin may be hyperpigmented, thickened, or cool to the touch. Thickened and droopy facial skin from dermal mucinosis, chronic seborrhea sicca or oleosa, or ceruminous otitis externa may be present. Seborrheic skin and ears may be secondarily infected with yeast or bacteria. In some dogs, the only symptom is recurrent or antibiotic-resistant pyoderma or adult-onset generalized demodicosis. Pruritus is not a primary feature of hypothyroidism and, if present, reflects secondary pyoderma, *Malassezia* infection, or demodicosis. Non-cutaneous symptoms of hypothyroidism are variable and may include aggression, lethargy or mental dullness, exercise intolerance, weight gain or obesity, thermophilia (cold intolerance), bradycardia, vague neuromyopathic or gastrointestinal signs, central nervous system involvement (e.g., head tilt, nystagmus, hemiparesis, cranial nerve dysfunction, hypermetria), and reproductive problems (e.g., decreased libido, prolonged anestrus, infertility). Puppies with congenital hypothyroidism are disproportionate dwarfs with short limbs and neck relative to their body length.

### Top Differentials

Differentials include other causes of endocrine alopecia and seborrhea, superficial pyoderma, *Malassezia* dermatitis, and demodicosis.

### Diagnosis

1. Rule out other differentials
2. Hemogram and serum biochemistry panel: nonspecific findings may include a mild, nonregenerative anemia, hypercholesterolemia, or elevated creatine kinase
3. Dermatohistopathology: usually, nonspecific endocrine changes or findings consistent with pyoderma, *Malassezia* dermatitis, or seborrhea are seen.

If present, dermal mucinosis is highly suggestive of hypothyroidism, but this can be a normal finding in some breeds (e.g., Shar pei)

4. Serum total thyroxine (TT<sub>4</sub>), free thyroxine (fT<sub>4</sub>) by equilibrium dialysis, and endogenous thyroid-stimulating hormone (TSH) assays: low TT<sub>4</sub>, low fT<sub>4</sub>, and high TSH are highly suggestive of hypothyroidism, but false-positive and false-negative results can occur, especially with TT<sub>4</sub> and TSH. For example, although TT<sub>4</sub> is a good screening test, it should not be used alone to make a diagnosis because its serum level can be artificially increased or decreased by several factors, such as nonthyroidal illness, autoantibodies, and drug therapy (Table 9-1)

### Treatment and Prognosis

1. Any secondary seborrhea, pyoderma, *Malassezia* dermatitis, or demodicosis can be treated with appropriate topical and systemic therapies.

TABLE 9-1

### Factors and Drugs That May Affect Total Thyroxine (TT<sub>4</sub>) Serum Levels in Dogs

Reduced TT <sub>4</sub> Values	Increased TT <sub>4</sub> Values
Normal hourly fluctuations	Normal hourly fluctuations
Nonthyroidal illness	Recovery phase of illness
Prolonged fasting	Age <3 months
Age >7 years	Obesity
Breed = Greyhounds	Autoantibodies
Autoantibodies	Diestrus, pregnancy
Phenobarbital	Estrogen
Furosemide	Progesterone
Glucocorticoids	Insulin
Sulfonamides	Narcotic analgesics

### Nonsteroidal Anti-inflammatories (e.g., Rimadyl, Etogesic)

Salicylates  
Tricyclic antidepressants  
Phenylbutazone  
Mitotane  
General anesthesia

NOTE: When hypothyroidism is suspected, both TT<sub>4</sub> (total T<sub>4</sub>) and fT<sub>4</sub> (free T<sub>4</sub> [by equilibrium dialysis]) should be measured. Compared with TT<sub>4</sub>, fT<sub>4</sub>—the small portion of thyroxine that is not protein bound—is less affected by nonthyroidal illness, autoantibodies, and drug therapy; the exception is sulfonamides.

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2. Levothyroxine 0.02 mg/kg PO should be administered every 12 hours until symptoms resolve (approximately 8-16 weeks). Some dogs can then be maintained with 0.02 mg/kg PO every 24 hours; others require lifelong twice-daily dosing to maintain remission.
3. Dogs with concurrent heart disease should be started on levothyroxine more gradually. Treatment should begin with 0.005 mg/kg PO every 12 hours; dosage should be increased by 0.005 mg/kg every 2 weeks until 0.02 mg/kg every 12 hours is being administered.
4. After 2 to 4 months of therapy, the serum  $TT_4$  level should be measured 4 to 6 hours after medication administration and should be in the high normal to supranormal range. If the level is low or within the normal range and minimal clinical improvement has been seen, the dosage of levothyroxine should be increased and the serum  $TT_4$  level checked 2 to 4 weeks later. If the level is  $>7.5$  mg/dL, the levothyroxine dose should be reduced.
5. If signs of thyrotoxicosis from oversupplementation (e.g., anxiety, panting, polydipsia, polyuria) occur, the serum  $TT_4$  level should be evaluated. If the level is markedly elevated, medication should be temporarily stopped until adverse effects abate; it should then be reinstated at a lower dose or a less frequent dosage schedule.
6. The prognosis is good with lifelong replacement thyroxine therapy, although hypothyroidism-induced neuromuscular abnormalities may not completely resolve.



**FIGURE 9-37 Canine Hypothyroidism.** An obese Rottweiler with hypothyroidism. Note that the hair coat lacks the bilaterally symmetrical alopecia that is considered characteristic of this disease.



**FIGURE 9-38 Canine Hypothyroidism.** Generalized truncal alopecia in an adult collie.



**FIGURE 9-39 Canine Hypothyroidism.** Mild alopecia on the bridge of the nose may be an early lesion of hypothyroidism.



**FIGURE 9-40 Canine Hypothyroidism.** Alopecia and hyperpigmentation with no evidence of secondary superficial pyoderma on the trunk.

## Canine Hyperadrenocorticism (Cushing's disease)

### Features

Spontaneously occurring hyperadrenocorticism is associated with the excessive production of endogenous steroid hormones (principally glucocorticoids, but sometimes mineralocorticoids or sex hormones) by the adrenal cortex. The disease is caused by a hyperfunctioning adrenal tumor (15%-20% of cases) or pituitary tumor (80%-85% of cases). Pituitary-dependent hyperadrenocorticism (PDH) is caused by the excessive production of adrenocorticotrophic hormone (ACTH), usually from a pituitary microadenoma or macroadenoma. Iatrogenically induced disease occurs secondary to excessive administration of exogenous glucocorticoids. Iatrogenic hyperadrenocorticism can occur at any age and is common, especially in chronically pruritic dogs and dogs with immune-mediated disorders that are controlled with long-term glucocorticoids. Spontaneously occurring hyperadrenocorticism is also common and tends to occur in middle-aged to older dogs, with an increased incidence noted in Boxers, Boston terriers, Dachshunds, Poodles, and Scottish terriers.

The hair coat often becomes dry and lusterless, and slowly progressing, bilaterally symmetrical alopecia is common. The alopecia may become generalized, but it usually spares the head and limbs. Remaining hairs are easily epilated, and alopecic skin is often thin, hypotonic, and hyperpigmented. Cutaneous striae and comedones may be seen on the ventral abdomen. The skin may be mildly seborrheic (fine, dry scales), bruise easily, and exhibit poor wound healing. Chronic secondary superficial or deep pyoderma, dermatophytosis, or demodicosis is common and may be the client's primary complaint. Calcinosis cutis (whitish, gritty, firm, bonelike papules and plaques) may develop, especially on the dorsal midline of the neck or ventral abdomen, or in the inguinal area.

Polyuria and polydipsia (water intake > 00 mL/kg/day) and polyphagia are common. Muscle wasting or weakness, a pot-bellied appearance (from hepatomegaly, fat redistribution, and weakened abdominal muscles), increased susceptibility to infection (conjunctival, skin, urinary tract, lung), excessive panting, and variable behavioral or neurologic signs (expanding pituitary tumor) are often present.

### Top Differentials

Differentials include other causes of endocrine alopecia, superficial pyoderma, demodicosis, and dermatophytosis.

### Diagnosis

1. Hemogram: neutrophilia, lymphopenia, and eosinopenia are often seen
2. Serum biochemistry panel: an elevated alkaline phosphatase enzyme level is typical. There may also be mildly to markedly elevated alanine transaminase activity, as well as elevated cholesterol, triglyceride, or glucose levels
3. Urinalysis: the specific gravity is usually low, and there may be bacteriuria, proteinuria, or glucosuria
4. Urine cortisol/creatinine ratio: usually elevated. A nonspecific screening test that is not diagnostic by itself because false-positive results are common (stress-induced, seen with many other illnesses). To minimize the effects of stress, a home-collected urine sample should be used, instead of one obtained at the veterinary hospital
5. Dermatohistopathology: often shows nondiagnostic changes consistent with any endocrinopathy. Dystrophic mineralization (calcinosis cutis), thin dermis, and absent erector pili muscles are highly suggestive of hyperadrenocorticism, but these changes are not always present
6. Abdominal ultrasonography: may demonstrate adrenal tumor or hyperplasia
7. Computed tomography (CT) or magnetic resonance imaging (MRI): may detect a pituitary mass
8. Adrenal function tests:

Adrenocorticotrophic hormone (ACTH) stimulation test (cortisol): an exaggerated poststimulation cortisol level is highly suggestive of endogenous hyperadrenocorticism, but false-negative and false-positive results can occur. In iatrogenic cases, an inadequate response to ACTH stimulation is typical. *Note:* Reconstituted cosyntropin (ACTH solution) can be stored frozen at  $-20^{\circ}\text{C}$  in plastic syringes for up to 6 months with no adverse effects on its bioactivity

ACTH stimulation test (17-hydroxyprogesterone): exaggerated basal and poststimulation 17-hydroxyprogesterone levels may be seen in endogenous hyperadrenocorticism, but false-negative and false-positive results can occur. 17-Hydroxyprogesterone, a progestin, is an adrenal gland-produced precursor of cortisol

Low-dose (0.01 mg/kg) dexamethasone suppression test: inadequate cortisol suppression is highly suggestive of endogenous hyperadrenocorticism, but false-negative and false-positive results can occur. Suppression at 4 hours followed by escape from suppression at 8-hour sampling is characteristic of PDH

High-dose (0.1 mg/kg) dexamethasone suppression test: used to help differentiate between adrenal neoplasia and pituitary-dependent hyperadrenocorticism. A lack of cortisol suppression is suggestive of adrenal neoplasia, whereas cortisol suppression suggests pituitary disease

Endogenous ACTH assay: used to help differentiate between adrenal neoplasia and pituitary-dependent hyperadrenocorticism. An elevated ACTH level is suggestive of pituitary disease, whereas a depressed ACTH level is suggestive of adrenal neoplasia

### Treatment and Prognosis

1. Any concurrent infections (e.g., pyoderma, demodicosis, urinary tract infection) should be treated with appropriate therapies.
2. Treatment of choice for iatrogenically induced cases is to progressively taper, then discontinue glucocorticoid therapy.
3. Treatment of choice for adrenal neoplasia is adrenalectomy.
4. Dogs with inoperable adrenal tumors or metastases may benefit from mitotane or trilostane therapy.

**Mitotane:** One should give 50 mg/kg PO every 24 hours with food for 7 to 14 days. An ACTH stimulation test is performed every 7 days. If inadequate cortisol suppression persists, one should increase the mitotane dosage to 75 to 100 mg/kg/day for an additional 7 to 14 days, monitoring with ACTH stimulation tests weekly. When adequate adrenal suppression is demonstrated, maintenance mitotane therapy is initiated as described below (see Number 7)

**Trilostane:** Therapy should be initiated and maintained as described below (see Number 8)

- 1 5. An effective treatment (where available) for PDH is microsurgical transsphenoidal hypophysectomy. This procedure requires a highly skilled neurosurgeon and specialized veterinary facilities that have access to advanced pituitary imaging techniques. Postoperative complications may include hypernatremia, keratoconjunctivitis sicca, diabetes insipidus, and secondary hypothyroidism.
6. The traditional medical treatment of choice for PDH is mitotane 50 mg/kg PO administered every 24 hours with food. The daily dosage is continued until the basal serum or plasma cortisol level normalizes and does not increase following ACTH stimulation. Control is usually achieved within 5 to 10 days of initiation of therapy, so the patient should be closely monitored with ACTH stimulation tests performed every 2 to 3 days. Monitoring

water and food intake before and during induction may be useful. Water and food intake often markedly decreases when adequate adrenal suppression has been achieved. If signs of adrenal insufficiency (e.g., anorexia, depression, vomiting, diarrhea, ataxia, disorientation) develop, mitotane therapy should be stopped and hydrocortisone 0.5 to 1.0 mg/kg PO every 12 hours administered, until symptoms resolve.

7. To maintain remission following mitotane induction, mitotane PO with food 50 mg/kg should be administered once weekly, or 25 mg/kg twice weekly. Dogs that relapse during maintenance therapy should be reinduced with daily mitotane for 5 to 14 days or until recontrolled, then maintained with 62 to 75 mg/kg once weekly, or 31 to 37.5 mg/kg twice weekly. A great deal of patient variability occurs, requiring close monitoring.
8. An alternative medical treatment for PDH is trilostane (not currently available in the United States). At this writing, its optimal dosing regimen has not yet been determined, but many investigators are using the following protocol:
  - Dogs <5 kg: give 30 mg PO with food q 24 hours
  - Dogs between 5 and 20 kg: give 60 mg PO with food q 24 hours
  - Dogs between 20 and 40 kg: give 120 mg PO with food q 24 hours
  - Dogs >40 kg: give 240 mg PO with food q 24 hours
 One can assess efficacy by monitoring clinical signs and evaluating results of ACTH stimulation tests 10 days, 4 weeks, and 12 weeks after the start of therapy, then every 3 months thereafter. ACTH stimulation tests should be performed 4 to 6 hours after trilostane dosing. A post-ACTH cortisol level <150 nmol/L (but >20 nmol/L) is usually consistent with good control. However, optimal clinical control has also been reported with post-ACTH cortisol concentrations between 150 and 250 nmol/L, so blood work results should always be interpreted alongside clinical signs. If the dog is not clinically well controlled and post-ACTH cortisol concentrations are >150 nmol/L, the dose of trilostane should be increased. Dose adjustments should be made in increments of 20 to 30 mg/dog. A wide range of trilostane doses to induce and maintain remission have been reported in dogs, with the therapeutic dose for most dogs being between 4 and 20 mg/kg/day. Some dogs may require twice-daily dosing if duration of effect is inadequate. Clinical signs such as polydipsia/polyuria/polyphagia often start to improve within the first 10 days of treatment,

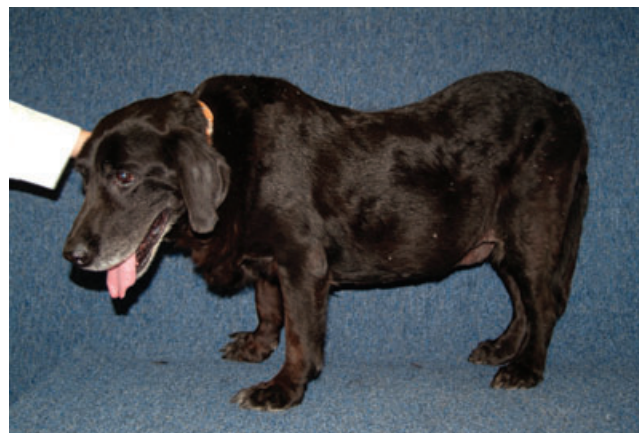
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but alopecia and other skin changes may take 3 or more months to improve. If signs of adrenal insufficiency (depression, inappetence, vomiting, diarrhea) develop at any time during therapy, or if post-ACTH cortisol concentrations (measured 4-6 hours after trilostane dosing) are  $<20$  nmol/L, trilostane should be stopped for 5 to 7 days, then reinstated at a lower dose. *Note:* Although trilostane appears to be well tolerated by most dogs, sudden death has been reported in dogs with concurrent heart problems. Trilostane is also contraindicated in pregnant and lactating dogs, dogs with primary hepatic disease, and dogs with renal insufficiency.

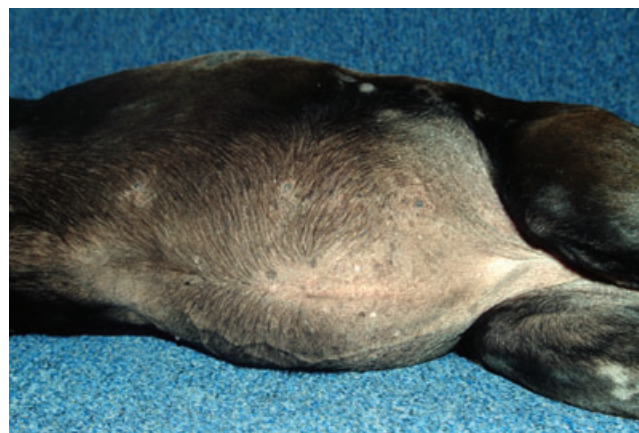
2. 9. Other alternative, but less consistently successful, medical treatments for PDH include the following: Ketoconazole 15 mg/kg PO with food q 12 hours  
Selegiline (L-deprenyl) 1-2 mg/kg PO q 24 hours
3. 10. For calcinosis cutis, adjunctive topical treatment with dimethyl sulfoxide (DMSO) gel every 24 hours may help resolve the lesions. During DMSO therapy, serum calcium levels should be monitored periodically because hypercalcemia is a potential adverse effect of this treatment.
11. The prognosis ranges from good to poor, depending on the cause and severity of the disease, with the average survival time for dogs with PDH being approximately 2.5 years after diagnosis.



**FIGURE 9-11 Canine Hyperadrenocorticism.** An adult Labrador demonstrates the typical potbellied appearance. Generalized muscle wasting, which causes the abnormal posture, is also seen. Note that the hair coat is generally in good condition and does not demonstrate bilaterally symmetrical alopecia.



**FIGURE 9-12 Canine Hyperadrenocorticism.** An adult Labrador with an adrenal tumor, demonstrating severe muscle wasting that causes the abnormal body confirmation.



**FIGURE 9-13 Canine Hyperadrenocorticism.** Same dog as in Figure 9-12. The potbellied appearance and alopecia are apparent.



**FIGURE 9-14 Canine Hyperadrenocorticism.** Same dog as in Figure 9-12. Generalized seborrhea sicca can be secondary to numerous underlying diseases but was caused by hyperadrenocorticism in this dog.