

Feline Hyperthyroidism

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1 Hyperthyroid cat.

P Profile

Definition

- Hyperthyroidism is a hypermetabolic state caused by excessive production and secretion of thyroid hormones.

Systems

- Hyperthyroidism can affect all body tissues directly or indirectly as a result of secondary hypertension.

Signalment

- Mean age of affected cats is 13 years (range, 4–24 years).¹
- Two case control studies reported greater risk for female cats.^{2,3}

Causes

- The majority of hyperthyroid cats have benign adenomatous nodular hyperplasia, similar to toxic nodular goiter in humans.
- Both lobes of the thyroid gland are typically involved.

Risk Factors

- Case control studies have identified risk factors such as iodine deficiency, iodine content of canned food, cat litter, fish, liver- or giblet-flavored canned food, fire-retardant chemicals, and bisphenols in pop-top cans.⁴
- At a molecular level, decreased expression of inhibitory G proteins associated with the thyrotropin receptor has been found in adenomatous thyroid tissue.
 - This could contribute to excess secretion of thyroid hormone.

Signs

- Clinical signs include weight loss and poor body condition (87%; **Figure 1**), polyphagia (49%), vomiting (44%), polyuria and polydipsia (36%), diarrhea (15%), weakness (12%), and voluminous stool (8%).⁵
 - Restlessness (40%), skin changes (36%), and respiratory signs (23%) are also common.¹
 - Lethargy and anorexia (7%)⁵ may be seen with concurrent disease (eg, occult hyperthyroidism).¹
- Physical examination findings include palpable thyroid nodule (83%; **Figure 2**), weight loss (65%), heart murmur (54%), tachycardia (42%), and increased nail growth (6%).⁵
 - Less common abnormalities include retinal hemorrhage, retinal vessel tortuosity, retinal detachment, dyspnea, and ventral neck flexion.^{1,5}



2 Visible thyroid nodule in neck.

Diagnosis

Definitive

- Diagnosis should be pursued based on supportive signalment, history, and examination findings.
- Hyperthyroidism is usually diagnosed by documenting elevations in serum concentrations of total thyroxine

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(TT₄), a highly specific and sensitive test for the diagnosis of feline hyperthyroidism.

- The serum T₄ level alone will be diagnostic in over 90% of hyperthyroid cats.
- Measurements of total triiodothyronine (TT₃) concentrations are not helpful and have no role in the diagnosis of hyperthyroidism, as 30% of hyperthyroid cats have a normal TT₃.
- If hyperthyroidism is suspected and TT₄ is within the reference range, consider rechecking the TT₄ concentrations up to several weeks later, as concentrations may fluctuate in and out of normal range.
 - A high-normal TT₄ in a middle-aged to older cat is suspicious for hyperthyroidism.
 - Concurrent disease may also suppress thyroid levels (effect of nonthyroidal illness).¹
- Additional tests to consider include measurement of free T₄ (fT₄) concentration (See **Free T₄**), T₃ suppression testing, and nuclear scintigraphy.
- The T₃ suppression test involves administration of 25 µg of liothyronine PO q8h for 2 days.
 - On the morning of day 3, a third dose of 25 µg should be administered.
 - Blood should be drawn at baseline and 2 to 4 hours after administration of the final pill for measurement of TT₃ and TT₄.
 - Hyperthyroid cats have a TT₄ concentration >2 µg/dL.

- Healthy cats have a TT₄ concentration <1.5 µg/dL.
- Values between 1.5 and 2 µg/dL are nondiagnostic.
- The T₃ suppression test is useful for diagnosis of mild hyperthyroidism when TT₄ and fT₄ are nondiagnostic; however, consistent owner administration of pills for 3 days is difficult and failure could result in a false-positive diagnosis.
- Nuclear scintigraphy is typically performed at specialized centers (eg, university hospitals, referral facilities).
 - Technetium-99m is commonly used; it is trapped and concentrated in the thyroid and has a short half-life.
 - Uptake is compared with uptake in the zygomatic salivary glands.⁶
 - Ectopic (<5% of hyperthyroid cats) and metastatic tissue can also be detected.

Differential

- Differential diagnosis includes renal disease, diabetes mellitus, GI lymphoma, exocrine pancreatic insufficiency, inflammatory bowel disease, liver disease, and heart disease.

Laboratory Findings/Imaging

Minimum Database

- In cats with hyperthyroidism, results of CBC should show normal to elevated RBCs (21%), PCV (47%), and mean corpuscular volume (44%).⁴
- Alkaline phosphatase (75%) and alanine transaminase (71%) activities

will be mildly elevated.⁴

- Urine specific gravity ranges from 1.009–1.050 (mean, 1.031).⁴
- Fructosamine concentrations are decreased below the normal range in 50% of hyperthyroid cats because of accelerated protein turnover.
 - Fructosamine may not be useful to monitor diabetes or distinguish between stress hyperglycemia and diabetes with concurrent hyperthyroidism.
- Thoracic radiographs may show cardiomegaly, pulmonary edema, or pleural effusion.
- Abdominal radiographs can rule out concurrent conditions and identify small kidneys.

Ancillary Testing

- Echocardiography and electrocardiography can determine whether cardiac changes represent primary cardiac disease or changes secondary to hyperthyroidism are potentially reversible.
- Blood pressure measurement should be part of the evaluation.
 - In a study of hypertensive cats with ocular abnormalities, hyperthyroidism was found to be an uncommon cause; however, many cats with hyperthyroidism have concurrent renal disease that can contribute to hypertension.
 - Consider treatment if repeated measurements of systolic blood pressure are >160 mm Hg and if there is evidence of end-organ damage.

Treatment

- Hyperthyroidism can be treated with radioactive iodine and surgery or controlled with drug therapy or a therapeutic diet.
 - Radioactive iodine is generally the best therapy but may be unavailable and/or unaffordable for owners.
- Treatment is tailored to the needs of each cat, household, and owner.

Free T₄

- fT₄ represents the unbound portion of thyroxine and is the hormonally active portion (<1% of the total).
- Measurement is only recommended using a dialysis technique that separates the bound from the unbound fraction.
- Up to 8% of clinically ill, nonhyperthyroid cats also have increased fT₄ concentrations.

fT₄ = free thyroxine, T₃ = triiodothyronine, T₄ = thyroxine, TT₃ = total triiodothyronine, TT₄ = total thyroxine

Methimazole

- Is readily available, reliable, convenient, and inexpensive short-term, but is potentially toxic, requires daily administration, and disease control is dependent on compliance.
- Competes for iodine with tyrosine residues on thyroglobulin and prevents the coupling of diiodotyrosine and monoiodotyrosine.
 - This prevents formation of T₄ and T₃.
- Typical starting dose is 2.5 mg q12h, but some mildly affected cats may be controlled with 1.25 mg q12h or 2.5 mg q24h.
- Adverse effects are dose related.
 - Less than 5% of adverse effects (ie, leukopenia, thrombocytopenia, hepatopathy) are life threatening.
 - Other side effects include eosinophilia, lymphocytosis, self-induced excoriations (up to 15%), positive ANA, vomiting, and anorexia (up to 20%).
 - Vasculitis may be the cause of the skin excoriations (Figure 3).
 - Agranulocytosis is thought to be immune-mediated.
- Treatment goal is to have TT₄ concentrations in the low-normal range within 1 month.
 - If TT₄ is not decreasing, rule-outs include problems medicating the cat, infrequent or inadequate dose, and thyroid carcinoma (rare).
- There are various formulations of methimazole:

- Can be formulated as a lecithin gel for transdermal use in cats that are difficult to pill.
- Felimazole (dechra-us.com) is a coated pill available in 2.5 mg and 5 mg sizes and is FDA-approved for use in cats.

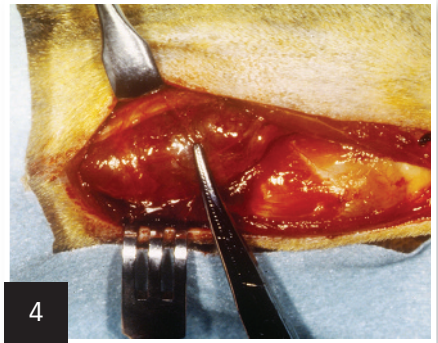
Radioactive Iodine

- Curative therapy, noninvasive, with rapid response.
 - Disadvantages include expense, availability, and need for short-term hospitalization.
- Cats need to be monitored for hypothyroidism and azotemia post-treatment.
- Actively taken up by hyperplastic thyroid tissue.
 - Destroys the diseased tissue and spares the atrophied normal tissue.
- Dose range is typically between 3.5 to 5.4 mCi administered PO, SC, or IV.
- Hospitalization varies widely, depending on the agency licensing the facility.
- Treatment is successful in 94% of cats.
 - 2% of cats become hypothyroid, 1.5% remain hyperthyroid, and 2.5% relapse within 1–6.5 years of treatment.

Thyroidectomy

- Multiple techniques have been described to remove the thyroid glands (ie, extracapsular, intracapsular, modified intracapsular, and staged thyroidectomy; Figure 4)
- Approximately 80% of cats have

Serum TT₄ concentration is increased in more than 90% of cats with hyperthyroidism.



Surgical excision of a thyroid nodule.

bilateral involvement.

- Scintigraphy may be helpful to localize ectopic thyroid tissue and identify the approximately 5% of cats that do not benefit from surgery.
- Surgery is beneficial, curative, and usually permanent.
- Risks include damage to recurrent laryngeal nerves and hypoparathyroidism; disadvantages include anesthesia risks in cats with concurrent heart and kidney disease.
- Cats that become hypothyroid and azotemic postoperatively need to be treated.

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Methimazole drug reaction: (A) self-induced excoriation of face, (B) excoriations between the toes.





Follow-up

- Hypothyroidism is more likely to occur following definitive therapy and, if accompanied by azotemia, is associated with shorter survival time.⁷
- Kidney values and TT₄ should be monitored every 2–4 weeks for up to 3 months following therapy.
 - If azotemia is accompanied by hypothyroidism, institution of life-long replacement thyroxine therapy must be considered; this may help improve renal blood flow and glomerular filtration rate.⁸

Methimazole

- Check TT₄ concentrations, CBC, platelet count, and serum biochemistry profile q3–4wk for the first 3 months, then at 6 months and q6–12mo thereafter.
- Evaluate for evidence of drug reaction (ie, cytopenia, liver enzyme elevations), hypothyroidism, hyperthyroidism, and azotemia.

Prescription Diet

- Monitor TT₄ concentrations and serum kidney values 4 weeks after starting diet; TT₄ should be decreased after 4 weeks and normal within 8 weeks in 85% of cats.
- If concentrations remain elevated, evaluate diet history (including water source).

Surgery

- Monitor for hypocalcemia immedi-

ately after surgery, and for hypothyroidism and azotemia in the weeks and months following surgery.

- Supplement with levothyroxine if needed.

Radioactive Iodine

- Monitor for development of azotemia and hypothyroidism post therapy.
- Treat with levothyroxine as needed.



In General

Relative Cost

- Hyperthyroidism is a costly but rewarding disease to treat: \$\$\$\$\$

Cost Key

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

Prognosis

- Excellent for cats with uncomplicated hyperthyroidism.
- Varies for cats with severe hyperthyroidism or when concurrent disorders are present.
- Outcome will depend on successful management of thyroid complications and comorbid disease.
- Average survival after successful treatment is 2 years. ■ **cb**

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

Hyperthyroidism & Renal Disease

- As many as 33% of hyperthyroid cats have concurrent renal disease that will be unmasked with treatment.
- There is also evidence that hyperthyroidism itself may cause kidney damage^{11,12} that may not be reversible.
- No simple test can predict which cats will become azotemic following treatment.¹³
- Routine laboratory work will rule out pretreatment azotemia, but if the cat is nonazotemic, measurement of glomerular filtration rate is needed to better determine the development of posttreatment azotemia.
- It is uncertain how the development of azotemia affects survival, but studies have shown no significant difference between azotemic euthyroid versus nonazotemic euthyroid cats.^{7,14}
 - However, a recent study showed that the survival time of cats that became azotemic and hypothyroid following treatment was shorter than nonazotemic.⁷

TT₄ = total thyroxine

Nutrition Management

- Hill's Prescription Diet y/d Feline (Hillsvet.com) is an iodine-limited diet available for management of hyperthyroidism. Authors of clinical studies reported that limiting dietary iodine to <0.32 ppm (dry-matter basis) would decrease TT₄ concentrations to within the normal range within 8–12 weeks.^{9,10}
- For the diet to be effective, all other sources of iodine must be eliminated from the cat's diet.
- Newly diagnosed hyperthyroid cats can be switched from their regular diet over 1 week and—unless they are severely affected—treated solely with the diet.
- Cats already receiving methimazole can be transitioned to the diet; initial recommendations included slow transition off methimazole during diet introduction; current recommendations suggest abrupt withdrawal to prevent risk for hypothyroidism.
- To be effective, the diet must be fed throughout patient life.