



# Feline Occult Hyperthyroidism

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## **P** Profile

Hyperthyroidism is caused by usually bilateral (70%) adenomatous hyperplasia of the thyroid gland. Hyperthyroidism occurs in middle-aged to older (> 6 yr) cats; there is no breed or sex predilection. Hyperthyroidism occurs more frequently in indoor cats and those consuming a canned fish-based diet or diets containing liver flavor and giblets. The disease is common in certain coastal areas of the United States as well as in England and Australia, but is uncommon in Japan, France, and South Africa.

## **HISTORICAL AND PHYSICAL EXAMINATION FINDINGS**

Historical findings include weight loss in conjunction with polyphagia, restlessness and increased activity, respiratory distress, weakness, vomiting, diarrhea, unkempt appearance or overgrooming, and such behavioral changes as aggression and inappropriate elimination. The most common physical examination finding is goiter (**Figure**). Other physical examination findings may include tachycardia, panting, hyperthermia, anxiety and overactivity, mydriasis, and long toenails. On rare occasions, cardiac arrhythmia, gallop rhythm, or systolic murmurs may be found on auscultation. Common laboratory findings can include leukocytosis with eosinophilia, erythrocytosis, increased liver enzymes (alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase), and mild azotemia. Low serum cholesterol is an uncommon finding, and urinalysis is often unremarkable.



Palpating to identify goiter in a cat with suspected hyperthyroidism

## **Dx** Basic Diagnosis

Hyperthyroidism can be diagnosed in approximately 90% of cats simply by measuring total serum concentrations of  $T_4$  (**Table**). However, this article focuses on the other 10%—those cats with occult hyperthyroidism that have clinical signs suggestive of hyperthyroidism (polyphagia, polydipsia, polyuria, weight loss, goiter) but exhibit normal serum total  $T_4$  concentrations at the time of examination. These cats may be challenging to diagnose for three reasons: 1) the hyperthyroidism may be mild or in the early stages, 2) the cat might have another nonthyroid illness that is suppressing total  $T_4$  into the normal range, and 3)  $T_4$  levels tend to fluctuate (on a daily basis or perhaps even more frequently).

## **EARLY OR MILD HYPERTHYROIDISM: Repeat the $T_4$**

Middle-aged and older hyperthyroid cats that present with weight loss and/or goiter but otherwise seem normal may be difficult to diagnose in the **early stages of disease**. Resting serum concentrations of both  $T_4$  and  $T_3$  are above the normal range in most cats with hyperthyroidism; however, some cats with hyperthyroidism (up to 10%) have serum concentrations of  $T_4$  that are within the mid- to high-normal range. Because many hyperthyroid cats with normal serum concentrations of  $T_4$  have relatively early hyperthyroidism, it is likely that the thyroid hormone concentrations will eventually increase into the thyrotoxic range if the disorder remains untreated. Thyroid hormone concentrations in cats with mild hyperthyroidism may fluctuate into the normal range in some cats, suggesting that a diagnosis of hyperthyroidism cannot be excluded on the basis of the finding of a single normal to high-normal serum  $T_4$  or  $T_3$  result alone. In cats with clinical signs consistent with hyperthyroidism and in cats with palpable thyroid nodules, more than one serum  $T_4$  determination could be required to confirm a diagnosis. Therefore, **the first step should always be to repeat the basal  $T_4$  measurement**; the second serum  $T_4$  determination should be made at least 1 to 2 weeks later. *An elevated serum  $T_4$  concentration is diagnostic of hyperthyroidism. However, a single serum  $T_4$  level in the normal range in*

continues

$T_3$  = triiodothyronine;  $T_4$  = thyroxine; TRH = thyroid-releasing hormone; TSH = thyroid-stimulating hormone



The typical appearance of a thin, unkempt cat with long nails may not be present in the cat with early or mild hyperthyroidism.

*a cat with hyperthyroid signs does not rule out the disease.*

Because hyperthyroidism has become more common and recognized in its early stages, serum free  $T_4$  concentrations have recently been shown to be more diagnostic of early or "occult" hyperthyroidism. If the repeat  $T_4$  test is also equivocal, then free  $T_4$  is the next test indicated.

Circulating thyroid hormones can either be bound to carrier proteins or free (unbound) in the plasma. Most commercial  $T_4$  and  $T_3$  assays measure total concentrations, both free and protein-bound. Because only the free fraction of thyroid hormone is available for entry into the cells, free  $T_4$  determina-

tions may provide a more consistent assessment of thyroid gland status than total  $T_4$  concentrations. The finding of a high free  $T_4$  concentration (despite mid- to high-normal levels of  $T_4$ ) in a cat with a consistent history (e.g., weight loss despite good appetite) and physical examination findings (e.g., palpable thyroid nodule) supports the diagnosis of early occult hyperthyroidism. However, measurement of free  $T_4$  levels does have the potential for false-positive results (see next section).

**NONTHYROID ILLNESS WITH SUSPECTED HYPERTHYROIDISM:**

**Free  $T_4$**

In hyperthyroid cats with **moderate to severe concurrent nonthyroid illness**,

such as renal disease, diabetes mellitus, systemic neoplasia, primary hepatic disease, or other chronic illnesses, normal serum thyroid hormone concentrations may be found at the time of initial evaluation. Since severe nonthyroid illness would be expected to decrease serum thyroid hormone concentrations into the low to undetectable range in sick cats without concurrent hyperthyroidism, concomitant *hyperthyroidism should be suspected in any middle- to old-aged cat with severe nonthyroid illness and normal serum  $T_4$  concentrations, especially if signs of hyperthyroidism are also present.*

Free  $T_4$  concentrations seem to be much less affected by concurrent nonthyroid illness and may more accurately reflect true thyroid status. Occasionally, however, cats with nonthyroid illness (particularly those with gastrointestinal disease that affects serum binding proteins for  $T_4$ ) that do *not* have hyperthyroidism have high free  $T_4$  concentrations for reasons that are unclear. Therefore, to avoid misdiagnosing hyperthyroidism, free  $T_4$  should always be evaluated in conjunction with the total  $T_4$  concentration. In general, the combination of a high free  $T_4$  value with a low total  $T_4$  concentration ( $< 20$  nmol/L or  $< 2.5$   $\mu$ g/dl) is indicative of nonthyroidal illness, whereas a high

**TESTS FOR HYPERTHYROIDISM IN CATS**

TEST	PROTOCOL	REFERENCE RANGE IN CATS	COMMENTS
<b>Serum total <math>T_4</math></b>	Serum sample, refrigerate or freeze, stable at room temperature	1.2–4.8 $\mu$ g/dl (15–62 nmol/L)	Diagnoses approximately 90% of cases of hyperthyroidism in cats, especially with repeat testing
<b><math>T_3</math> suppression test</b>	Collect serum sample for $T_3$ and $T_4$ analysis; then administer 7 doses of synthetic $T_3$ at a dosage of 25 $\mu$ g Q 8 H. Collect a sample for $T_3$ – $T_4$ analysis 4 hours after administration of last $T_3$ dose.	50% reduction in $T_4$ ; $T_3$ analysis is to ensure compliance with administering $T_3$ medication	See text
<b>TRH stimulation test</b>	Administer 0.1 mg/kg TRH IV; collect samples before and 4 hr after administration	Stimulation to at least twice baseline values of total $T_4$	See text
<b>Free <math>T_4</math> by dialysis</b>	Collect a single serum sample	1.21–3.4 ng/dl (15.6–44 nmol/L)	—
<b>Thyroid scintigraphy</b>	Administer mTch-99; scan thyroid gland	—	Limited availability

free  $T_4$  value with a high-normal  $T_4$  concentration ( $>25$  nmol/L or  $>3.0$   $\mu\text{g/dl}$ ) is suggestive of hyperthyroidism.

## **Dx** Advanced Diagnosis

### **TESTING FOR OCCULT HYPERTHYROIDISM**

#### **Thyroid Hormone (Triiodothyronine) Suppression Test**

If a thyroid nodule cannot be palpated or if another illness is known to be present, the diagnosis of hyperthyroidism should be confirmed with  $T_3$  suppression or thyroid scintigraphy, which remain the gold standards for diagnosis of occult hyperthyroidism in cats. Inhibition of pituitary TSH secretion by high circulating concentrations of thyroid hormone is a characteristic feature of normal pituitary-thyroid regulation. Administration of  $T_3$  decreases TSH secretion in normal cats; this can be detected by a decrease in serum  $T_4$  concentrations. In contrast, when thyroid function is autonomous, as in cats with hyperthyroidism, administration of thyroid hormone has little or no effect on thyroid function because TSH secretion has already been chronically suppressed.

To perform the  $T_3$  suppression test in cats, draw a blood sample for determination of basal serum concentrations of total  $T_4$  and  $T_3$  (Table). Centrifuge the blood sample, remove the serum, and keep it refrigerated or frozen. Instruct the owner to administer oral  $T_3$  (liothyronine [Cytomel—Jones Medical Industries, St. Louis, MO]) on the following morning at a dosage of 25  $\mu\text{g}$  3 times daily for 2 days. On the morning of the third day, the owner gives a seventh 25- $\mu\text{g}$  dose of liothyronine and brings the cat to the veterinary clinic within 2 to 4 hours for serum  $T_4$  and  $T_3$  determinations. *When the  $T_3$  suppression test is performed in normal cats, there is a marked decrease in serum  $T_4$*

*concentrations after exogenous  $T_3$  administration. In contrast, when the test is done in cats with hyperthyroidism—even those with only slightly high or high-normal resting serum  $T_4$  levels—minimal if any suppression of serum  $T_4$  concentrations is seen. Cats with hyperthyroidism have postliothyronine serum  $T_4$  values greater than 20 nmol/L (approximately 1.5  $\mu\text{g/dl}$ ), whereas normal cats and cats with nonthyroid disease have  $T_4$  values less than 20 nmol/L.*

Serum  $T_3$  concentrations can be used to monitor owner compliance with giving the drug. If inadequate  $T_4$  suppression is found but serum  $T_3$  values do not increase after treatment with liothyronine, problems with owner compliance should be suspected and test results should be considered questionable.

#### **Thyrotropin-Releasing Hormone Stimulation Test**

In clinically normal cats, administration of TRH causes increased TSH secretion and serum  $T_4$  concentrations, whereas in cats with hyperthyroidism, the TSH and serum  $T_4$  response to TRH is blunted or absent. The TRH stimulation test is performed by collecting blood for serum  $T_4$  and  $T_3$  determinations before and 4 hours after intravenous administration of 0.1 mg/kg TRH (Relefact TRH—Hoechst-Roussel Pharmaceuticals, Somerville, NJ; Thypinone, Abbott Diagnostics—Abbott Park, IL) (Table). Many cats become transiently ill after TRH injection, manifesting vomiting, salivation, urination, and defecation after administration of TRH. Thus, the test is an in-hospital procedure and is less desirable than the  $T_3$ -suppression test or thyroid scintigraphy. Cats with mild hyperthyroidism show little if any increase in serum  $T_4$  values after administration of TRH, whereas a consistent increase of serum  $T_4$  concentrations (approximately 2-fold) occurs after TRH administration in both clinically normal cats and those with

## **Dx** at a glance

### **WHAT TO DO**

Diagnosis may be achieved after any given step, precluding the need for succeeding steps.

1. Submit serum sample for total  $T_4$  analysis
2. Repeat  $T_4$  measurement 1-2 weeks later
3. Submit sample for free  $T_4$  analysis (False-positive results sometimes occur for unknown reasons; evaluate in conjunction with total  $T_4$  test results, Steps 1 & 2)
4. Conduct  $T_3$  suppression test (Owner compliance is a limiting factor.)
5. Perform either:
  - TRH stimulation test (Induces transient illness; evaluate patient before use.)
  - OR
  - Thyroid scintigraphy

nonthyroid disease. The relative increase (percentage increase) in serum  $T_4$  concentration after administration of TRH is the most sensitive criterion for predicting whether cats are hyperthyroid. An increase in serum  $T_4$  less than 50% is consistent with mild hyperthyroidism. *Cats with hyperthyroidism have lost the normal pituitary-thyroid axis suppression associated with negative feedback; therefore, there will not be an increase in serum total  $T_4$  values after TRH stimulation.* ■

See Aids & Resources, back page, for references, further reading, and contacts.

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