

# **Feline Hyperthyroidism**

Patty Lathan, VMD, MS, DACVIM

## **Etiology**

Feline hyperthyroidism is the most common endocrinopathy in cats, and is caused by excessive production of thyroid hormones (T3 and T4). It is usually caused by benign adenomatous hyperplasia or adenoma, and is bilateral in most cases (approximately 80%). Thyroid carcinoma is rare (1-2% of cases), but may develop in cats treated with methimazole long-term.

The prevalence of hyperthyroidism has increased significantly since the first cases were reported in 1979, and epidemiologic studies have demonstrated that its incidence has increased at a rate greater than that of other geriatric diseases. The underlying cause is unclear, but likely multifactorial. Iodine-deficient diets and goitrogens, such as soybean isoflavones and bisphenol A (found in the can lining of pop-top canned foods), have been implicated.

## **Diagnosis**

Hyperthyroidism is generally a disease of older cats, with a mean age of 13 years. Common clinical signs include weight loss, polyphagia, and hyperactivity. Conversely, some cats (~10%) present with the apathetic form of the disease, in which they are less active and have decreased appetite. The reason for this presentation is unclear, but it may be due to concurrent disease or very chronic hyperthyroidism. Whereas cats diagnosed with hyperthyroidism used to be noticeably underweight on physical examination, clinicians' ability to diagnose the disease earlier, combined with the prevalence of obesity in the feline population, has led to the diagnosis in many cats that are either overweight or in apparently good body condition, although most have lost weight. A palpable thyroid nodule is suggestive of hyperthyroidism, but may also be present in cats without the disease. About half of hyperthyroid cats have cardiac abnormalities, including tachycardia, murmur, and gallop rhythm.

Definitive diagnosis of hyperthyroidism usually relies upon an increased total T4 concentration. However, a minimum database, including complete blood count, serum biochemistry, and urinalysis, is recommended to help identify concurrent disease. Since hyperthyroidism causes an increase in the glomerular filtration rate, it is critical to evaluate the renal values. Treatment of hyperthyroidism may unmask underlying renal disease or exacerbate renal disease that is already present. Other abnormalities associated with hyperthyroidism include mild erythrocytosis (probably due to increased erythropoiesis), increased phosphorus due to altered bone metabolism, and increased ALT and ALP. However, an increased ALT >500 U/L may be suggestive of concurrent hepatic disease and require further investigation.

Thyrotoxic cardiomyopathy is not uncommon in cats with hyperthyroidism, and this author rarely performs an echocardiogram on hyperthyroid cats with only a murmur but no clinical signs of cardiac disease. If the murmur does not resolve following normalization of the T4, an echocardiogram may be warranted at that time. Blood pressure measurement and fundic exam

are, however, evaluated in each patient. Most cases of mild hypertension will resolve with normalization of the T4, but if the hypertension is severe (>200 mm Hg) or causing retinal lesions (tortuous vessels, retinal hemorrhage) or other clinical signs, anti-hypertensive therapy is indicated.

T3 measurement is insensitive for the diagnosis of hyperthyroidism, and is not routinely used. Total T4 concentration is increased in >90% of hyperthyroid cats. However, in approximately 10% of affected cats, total T4 is within the upper half of the reference range. This can be due to mild disease, daily fluctuation of T4 into and out of the reference range, or to non-thyroidal illness. In these cases, a repeat total T4 will often be increased. Alternatively, a free T4 (by equilibrium dialysis) may be evaluated. An increased free T4 (ED) is more sensitive for the diagnosis of hyperthyroidism than a tT4, but less specific. This means that the free T4 (ED) is more likely to be increased in a mildly hyperthyroid cat or one with concurrent illness. However, the fT4(ED) is also more likely than the tT4 to be increased in a euthyroid cat with non-thyroidal illness. Diagnostic accuracy is improved when the tT4 is evaluated together with a fT4(ED). A patient with a tT4 in the upper half of the reference range, and with a fT4(ED) above the reference range, is very likely to be hyperthyroid. Conversely, a euthyroid patient with concurrent illness and a high fT4 is likely to have a tT4 concentration in the lower half of the reference range.

Recently, measurement of TSH has been evaluated for diagnosis of hyperthyroidism. The most commonly used assay is the canine assay, which has a lower limit of detection (0.03 ng/mL) that is too high to differentiate between hyperthyroid cats and some normal cats. Whereas 98% of hyperthyroid cats have a TSH lower than the limit of detection, 30% of euthyroid cats also have a TSH below the limit of detection.

Nuclear scintigraphy is useful in confirming hyperthyroidism, differentiating whether unilateral or bilateral disease, identifying ectopic (intrathoracic tissue), and differentiation of carcinoma vs. adenoma. It can also be used to help calculate dose of I-131 for treatment.

## **Treatment**

Current treatments include medical, radioactive iodine, and dietary options. Thyroidectomy is much less common now that radiation therapy is available.

In the United States, medical therapy generally consists of methimazole administration. Methimazole inhibits thyroid hormone synthesis by inhibiting the enzyme thyroid peroxidase. The medication is relatively inexpensive and is reversible, which is advantageous if the patient has renal disease. However, this means it must also be given for the life of the patient, and the long-term monitoring cost should be factored into the cost of treatment. There are also several potential side effects associated with methimazole therapy. Gastrointestinal upset (vomiting, diarrhea) is the most common of these (in approximately 10% of patients), and should resolve with discontinuation of the medication. Following discontinuation, the drug can usually be restarted at a lower dose and gradually increased. Facial excoriation is uncommon but generally

requires discontinuation of the medication. Neutropenia, thrombocytopenia, and hepatotoxicity are the most life-threatening of the side effects but are usually reversible if caught in time. This means that regular monitoring of the CBC and serum chemistry (q2 weeks x 3 months) is recommended.

Transdermal methimazole administration is also possible in patients that will not tolerate oral medication, or for owners that don't want to deal with pilling their cats. The pluronic lecithin organogel (PLO) formulation appears to be effective in most cats, although there are some cats that don't respond to it as well as they would to the pill. It also appears to cause fewer GI side effects than the oral formulation. Keep in mind, however, that the effects of this gel on humans (including children) have not been evaluated. Thus, it might not be ideal to use on a cat in a household with a child who frequently handles the cat and may get the medication on his/her skin.

Interestingly, although only 1-2% of cats with hyperthyroidism have a carcinoma at diagnosis, up to 20% of cats that have been treated for 4 or more years with methimazole may develop thyroid carcinomas.

Radioactive iodine is a definitive therapy for hyperthyroidism and is currently the treatment of choice in hyperthyroid cats with normal renal function. I-131 is injected IV or SQ, and then the I-131 is concentrated in the hyperactive thyroid tissue. Beta particles from the I-131 then travel short distances (<2 mm) and destroy the hyperactive tissue. Thus, normal tissue is usually spared. This is a very effective therapy, and most cats have a normal T4 3 months following treatment. However, some (10-20%) patients develop clinical hypothyroidism, diagnosed with concurrent low tT4 and increased TSH. Iatrogenic hypothyroidism is associated with the development of azotemia and decreased survival in some cats, and supplementation of levothyroxine improves survival.

Dietary therapy is another option for the treatment of hyperthyroid cats. This diet is severely iodine restricted, and since iodine is necessary for thyroid hormone synthesis, should result in decreased thyroid hormone synthesis. Studies have been promising, provided that the cat will eat the diet, and that it is the ONLY diet that the cat eats. Although euthyroid cats can eat the diet, they MUST be supplemented with a normal iodine-containing diet. In one study, although T4 concentrations normalized in most cats receiving the diets, there was not an overall increase in body weight or decrease in heart rate, so optimal clinical control is unlikely.

The prognosis for hyperthyroid cats is variable and dependent upon the cat's physical condition at diagnosis, in addition to concurrent disorders. One study showed a median survival of 2 years with methimazole treatment, and 4 years with I-131 therapy.