2016 AAFP Guidelines for the Management of Feline Hyperthyroidism

Clinical context: Since 1979 and 1980 when the first reports of clinical feline hyperthyroidism (FHT) appeared in the literature, our understanding of the disease has evolved tremendously. Initially, FHT was a disease that only referral clinicians treated. Now it is a disease that primary clinicians routinely manage. Inclusion of the measurement of total thyroxine concentration in senior wellness panels, as well as in diagnostic work-ups for sick cats, now enables diagnosis of the condition long before the cat becomes the classic scrawny, unkempt, agitated patient with a bulge in its neck. However, earlier recognition of the problem has given rise to several related questions: how to recognize the health significance of the early presentations of the disease; how early to treat the disease; whether to treat FHT when comorbid conditions are present; and how to manage comorbid conditions such as chronic kidney disease and cardiac disease with treatment of FHT. The 2016 AAFP Guidelines for the Management of Feline Hyperthyroidism (hereafter referred to as the Guidelines) will shed light on these questions for the general practitioner and suggest when referral may benefit the cat.

Scope: The Guidelines explain FHT as a primary disease process with compounding factors, and provide a concise explanation of what we know to be true about the etiology and pathogenesis of the disease. The Guidelines also:

- Distill the current research literature into simple recommendations for testing sequences that will avoid misdiagnosis and separate an FHT diagnosis into six clinical categories with associated management strategies.
- Emphasize the importance of treating all hyperthyroid cats, regardless of comorbidities, and outline the currently available treatments for the disease.
- Explain how to monitor the treated cat to help avoid exacerbating comorbid diseases.
- Dispel some of the myths surrounding certain aspects of FHT and replace them with an evidence-based narrative that veterinarians and their practice teams can apply to feline patients and communicate to their owners.

Evidence base: To help ensure better case outcomes, the Guidelines reflect currently available, evidenced-based knowledge. If research is lacking, or if a consensus does not exist, the expert panel of authors has made recommendations based on their extensive, cumulative clinical experience.

Feline hyperthyroidism: an overview

Feline hyperthyroidism (FHT) first became evident about 35 years ago, when the initial reports appeared in the literature.1,2 It was apparent that this was a ‘new’, not just an undiagnosed, disease because pathological studies within the prior decade showed a very low incidence of thyroid adenomas in cats.1,6,7 The prevalence of FHT has steadily increased worldwide since those first reports, and the disease is now diagnosed in 1.5–11.4% of older cats around the world.3,8–11 FHT is the most common endocrine disorder in middle-aged or older cats in the US,3,12 where its prevalence is up to 10% of cats older than 10 years.3 Clinical reports from the early 1980s described what is now known as the classic,
Iodine (¹³¹I) therapy in the tinely offering radioactive Research centers began rou-

of these other forms. 

has increased the recognition 

Guidelines) in feline geriatric screening panels 

emerged. The inclusion of total serum thyrox-

goiter) and ‘subclinical’ hyperthyroidism 

were cardiorespiratory diseases. 13 In the 

(Figure 1). The most important comorbidities 

were autonomous.17,18 To date there are no 

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Diagnosis

Because thyroid hormone affects various body systems, the clinical presentation of a hyperthyroid cat can include a variety of signs. No single clinical presentation is pathognomonic for FHT. Also, as FHT is being diagnosed earlier in its progression, clinical signs may be subtle in many cats. For this reason, diligence in obtaining historical and physical exam findings in middle-aged to older cats is important. Many of these patients will have comorbidities that can complicate diagnosis or treatment.

Presenting signs, differential diagnoses and diagnostic confirmation

The classic signs of FHT are weight loss, polyphagia, polyuria, polydipsia, increased vocalization, agitation, increased activity, tachypnea, tachycardia, vomiting, diarrhea and an unkempt hair coat (Figure 2). Differential diagnoses for cats with clinical signs similar to hyperthyroidism should include diabetes mellitus, gastrointestinal malabsorption or maldigestion, neoplasia (especially gastrointestinal lymphosarcoma), chronic kidney disease (CKD) and parasitism.

A definitive diagnosis of FHT requires demonstration of persistently elevated thyroid hormone concentrations (T4, or T4 plus free T4 by equilibrium dialysis [fT4ed]) occurring concurrently with one or more of the typical clinical signs.

Signalment, history and physical examination

The classic presentation for a hyperthyroid cat is a patient that is greater than 8 years of age, is active, has a good appetite and demonstrates some weight loss. The owner may also notice some degree of polyuria indicated by the need to clean the litter box more often. Behavioral patterns such as drinking from a dripping faucet or from drip containers used for indoor plants may suggest the cat is thirsty.

During the examination, owners of hyperthyroid cats will often make comments such as:
- ‘I think my cat is senile.’
- ‘My cat is starving all the time.’
- ‘My cat feels great and is acting like a kitten again.’
- ‘I can’t believe this cat is 16 years old.’
- ‘My cat is losing weight because it is so much more active.’
- ‘The diet is finally working.’

If a suspicion of FHT exists, asking the following questions when obtaining the patient’s history may elicit answers that increase the index of suspicion for the disease:

Pertinent questions during history-taking
- How often do you see your cat drink water? Has this changed?
- How often are you cleaning the litter box? Has this changed? Are urine clumps larger?
- Have there been any changes in defecation habits?
- How is your cat sleeping?
- Has your cat been more active or has it displayed any new behaviors?
- Is your cat vocalizing more often?
- How is your cat eating? Do you notice any vomiting or diarrhea?
Some FHT cases are clear-cut: they conform to the classic clinical signs described for hyperthyroidism and are supported by laboratory T4 results and the patient’s history. However, FHT often has a more ambiguous presentation, complicated by concurrent disease or clinical laboratory incongruities. In an effort to help practitioners clarify the diagnostic and therapeutic challenges of FHT, the Panel has developed a new, simplified approach that encompasses a range of six distinct case presentations from overt FHT to no clinical evidence of the disease. By using the outcome of the physical exam, patient history and minimum database, a clinician can assign a cat to one of six diagnostic categories, as described below and summarised on page 404.

GROUP 1: Classic clinical disease
Cats with uncomplicated clinical hyperthyroidism and elevated T4
These are cats with one or more clinical signs consistent with FHT that have an elevated T4 and no identifiable concurrent disease. T4 is above the laboratory reference interval in FHT cases. The Panel recommends that reference laboratory testing be utilized for diagnosis and monitoring of FHT so that precise serum hormone levels can be followed throughout treatment and to avoid quality control discrepancies. Ideally, for purposes of consistency, monitoring should be performed at the same reference laboratory. If in-clinic testing is performed for geriatric screening and significant changes are noted in thyroid hormone levels, obtain confirmatory testing at a reference laboratory.

Complete blood count (CBC) findings are generally unremarkable, although macrocytosis may be present. Cats with marked anemia may suffer from a comorbidity and further work-up should be performed. Serum chemistry findings often include elevated serum alanine transference (ALT) or alkaline phosphatase. Serum ALT levels can be markedly elevated.

If liver enzymes do not normalize after successful treatment for FHT, further diagnostic work-up is warranted. Azotemia may suggest dehydration or underlying renal failure. Urinalysis results are variable, although the urine specific gravity may be less than 1.030 due to primary polydipsia or inability to concentrate the urine due to hyperthyroidism.

Management of Group 1 cats consists of treatment for their hyperthyroid disease (see pages 406–410).

GROUP 2: Possible FHT with probable non-thyroidal disease
Cats with clinical hyperthyroidism and normal T4
Cats in this category have clinical signs suggestive of FHT along with T4 within the laboratory reference interval.

The Panel recommends the following approaches for Group 2 cats:
- Further testing for FHT should consist of T4 and fT4ed assays measured 2–4 weeks after the initial blood screening. A T4 value in the upper half of the reference interval combined with an elevated fT4ed supports a diagnosis of hyperthyroidism.
- If the T4 and fT4ed are both within the reference interval the cat should be evaluated for non-thyroidal disease (see right).
- If no concurrent illness is found and FHT is still suspected, further testing is warranted, including triiodothyronine (T3) suppression testing, serum TSH concentration in conjunction with T4 and T4ed, or thyroid scintigraphy.

GROUP 3: Enlarged thyroid without clinical FHT
Cats without clinical hyperthyroidism, T4 within the reference interval, but with enlarged thyroid gland(s)
Monitor clinical signs in these cats and repeat a serum T4 assay in 6 months.

GROUP 4: Subclinical FHT
Cats without overt clinical hyperthyroidism, but with an elevated T4 and with some physical exam findings suggestive of hyperthyroidism
Repeat the T4 test in 1–2 weeks. If serum T4 is still elevated, treat the cat for FHT. While no data exist for the best way to manage Group 4 cats, the consensus of the Panel is to treat these cats for hyperthyroidism. If a repeat T4 is normal, then re-evaluate the patient in 6 months with a complete physical exam and a T4 assay.

GROUP 5: Clinical FHT with confirmed non-thyroidal disease
Cats with clinical hyperthyroidism confirmed by elevated T4, and one or more concurrent diseases
Hyperthyroid cats are commonly middle-aged or older and often have concurrent diseases (see right). But because FHT is a serious disease that can result in rapid deterioration of the patient, the Panel recommends the treatment of all diagnosed cats, including those animals with comorbidities. Appropriate monitoring and careful management of concurrent diseases will optimize the patient’s health.

GROUP 6: Clinically normal
Cats with no clinical signs of hyperthyroidism and no palpable thyroid nodule but with an elevated T4 on screening lab test
Because falsely elevated T4 values may occur, repeat the T4 test preferably using radioimmunoassay or chemiluminescent enzyme assay. If the T4 is now normal, monitor the cat and retest T4 every 6 months, or sooner if clinical signs develop. If the T4 is elevated, treat for FHT.
Palpably enlarged thyroid glands are suggestive, but not necessarily indicative, of clinical hyperthyroidism.

A thorough physical exam is important because findings in hyperthyroid cats can vary significantly. Classically, weight loss and muscle loss, affecting the epaxial muscles especially, is notable. The cat may appear unkempt (Figure 2). Palpably enlarged thyroid glands are suggestive, but not necessarily indicative, of clinical hyperthyroidism. Heart murmurs and arrhythmias are often auscultated in FHT. Abnormal size, shape or consistency of the kidneys or intestinal tract may suggest comorbidities.

The identification of hypertension in cats with FHT is critical for their health. Monitoring blood pressure in suspect and diagnosed cats at every visit is optimal. Because systemic blood pressure can be difficult to assess in a cat out of its normal environment, performing a complete fundic exam may determine whether hypertensive retinopathy is present (Figure 3). Monitoring blood pressure and retinal anatomy throughout treatment of FHT is important because, if hypertension does not resolve with control of FHT, the cat will require additional diagnostic testing for such conditions as chronic renal disease, diabetes mellitus, hyperaldosteronism and hyperadrenocorticism, as well as need specific antihypertensive management. Additionally, some cats can develop hypertension after re-establishment of euthyroidism.

For any cat that you suspect is hyperthyroid, obtain a minimum database both to diagnose FHT and identify any potential comorbidities. Include a CBC, serum chemistry, urinalysis and T4 assay. Definitive diagnosis of FHT may require additional testing using fT4ed and TSH with T4, use of 99Tc scintigraphy (Figure 4) or a T3 suppression test. Chest radiographs, echocardiography and abdominal imaging will further evaluate the extent of non-thyroidal disease.
Managing hyperthyroid cats with concurrent CKD

Panel members have observed that many clinicians believe that an elevated T4 supports renal function. Recent literature suggests that treatment of FHT while avoiding hypothyroidism is desirable in cats with renal insufficiency (Figure 5). The Panel recommends treatment of hyperthyroid patients regardless of concurrent disease (eg, Group 5 cats). This includes cats with pre-existing CKD and those that develop azotemia after initiation of FHT treatment. These patients will require careful monitoring in order to achieve and maintain a euthyroid state while at the same time preventing hypothyroidism or mild hyperthyroidism.

Treatment recommendations differ depending on the degree of underlying renal disease. Therefore, it is important to fully determine the renal status of the patient prior to initiating FHT treatment. The Panel recommends using the staging guidelines set out by the International Renal Interest Society (IRIS), including determination of blood pressure and urine protein quantification. Note that cachexia will affect the serum urea nitrogen level (elevated due to increased protein turnover) and creatinine level (decreased due to loss of muscle mass). Recording a body condition score and muscle condition score at each physical exam will help to document progressive changes.

Managing the cat that is non-azotemic at initiation of treatment for hyperthyroidism

The Panel recommends the same monitoring for non-azotemic hyperthyroid cats as for Group 1 cats. Azotemia may develop subsequent to treatment of FHT. If that occurs, survival time decreases significantly. Avoid causing iatrogenic hypothyroidism. Evaluation of serial concomitant creatinine, T4 and TSH tests may help to determine whether T4 supplementation is necessary. Utilize the IRIS guidelines for staging and treatment, including management of hypertension and proteinuria if those abnormalities do not resolve upon returning to euthyroidism.

Keeping cats with azotemia ‘a little bit’ hyperthyroid to increase renal perfusion and lower creatinine levels is deleterious. This approach can exacerbate renal damage while giving a false sense of security based on an artificially lowered creatinine level. Elevated T4 causes increased beta-adrenergic activity and activation of the renin–angiotensin–aldosterone system, leading to increased cardiac output, volume overload, sodium retention, renal hypertension and glomerular sclerosis, ultimately progressing to, or worsening, CKD.

Managing the cat that is azotemic at initiation of treatment for hyperthyroidism

Cats that are identified as hyperthyroid with concurrent renal azotemia fall into the Group 5 category and should be monitored accordingly. Comorbidity of azotemia with FHT is common.

The Panel recommends treating FHT in cats with pre-existing CKD. Treat both diseases...
concurrently. Manage IRIS stage 1 and 2 cases as though they are non-azotemic. If the patient responds favorably and renal function is stable using a reversible treatment, then consider an irreversible FHT treatment. If a permanent treatment for FHT is pursued, careful monitoring and aggressive kidney support may be required during the period of regeneration of previously suppressed normal thyroid tissue.

Typically the thyroxine nadir occurs 2 weeks after radiiodine treatment, with T4 normalization occurring around 4 weeks after treatment. Supplementation with levothyroxine during this period will resolve iatrogenic hypothyroidism and may be necessary in clinically hypothyroid patients. However, this treatment will also suppress pituitary TSH, which is needed to stimulate regeneration of atrophied thyroid tissue. In such cases, it is imperative to establish euthyroidism in order to avoid renal hypertension and further glomerular damage, while at the same time avoiding iatrogenic hypothyroidism. Just as in those cats that develop azotemia after treatment of FHT, the evaluation of serial concomitant creatinine, T4 and TSH tests may help to determine whether T4 supplementation is necessary. The Panel generally recommends testing post-surgical and post-radioiodine patients at 30, 60, 90 and 180 days after treatment.

Managing hyperthyroid cats with concurrent heart disease

Concurrent heart disease is common in hyperthyroid cats, and may or may not be a direct effect of FHT. As with other concurrent diseases, first correct the hyperthyroidism and then evaluate the heart disease once the cat is euthyroid. Correction of the thyrotoxicity and systemic hypertension can improve cardiac disease in some cats. For several months following successful resolution of the hyperthyroid state there can be echocardiographic abnormalities that both emerge and resolve. Serially evaluate cats with documented echocardiographic changes prior to achieving euthyroidism, as well as cats with emerging clinical signs. N-terminal probrain natriuretic peptide (NT-proBNP) values increase in cats with FHT and in cats with hypertrophic cardiomyopathy (HCM), but typically decrease within 3 months of achieving a euthyroid state. If NT-proBNP remains elevated after 3 months, further evaluate the cat for HCM.

The goal of therapy is to restore euthyroidism, avoid hypothyroidism and minimize side effects of treatment.

Novly diagnosed, unregulated hyperthyroid cats with concurrent congestive heart failure (CHF) require simultaneous treatment for both diseases as well as regular monitoring of CHF status as the cat becomes euthyroid.

Treatment modalities

Hyperthyroidism in cats is a life-threatening disease requiring prompt veterinary attention. After establishing a diagnosis of FHT, the clinician and client are faced with multiple treatment options. The choice of therapy often depends on factors such as the cat’s age, comorbidities, treatment cost, availability of treatment options, and the clinician’s recommendation and expertise. The goal of therapy is to restore euthyroidism, avoid hypothyroidism and minimize side effects of treatment. In general, treat all cats diagnosed with FHT and monitor prudently.

Four common treatment options for FHT are available: treatment with radioactive iodine, medical management with methimazole or carbimazole, surgical thyroidectomy and dietary therapy using an iodine-restricted food. Rarely used therapies include percutaneous ethanol or thermal ablation of the cat’s thyroid. The four principal treatments are discussed in turn in the following sections of the Guidelines. Each modality has advantages and disadvantages, as summarized on page 407 and also described elsewhere.

Common treatment approaches

Most clinicians recommend definitive therapy with radioactive iodine or thyroidectomy, especially if the cat is fairly young and otherwise healthy. However, in the case of geriatric cats, cats with concurrent non-thyroidal disease (especially CKD), and cats whose owners decline definitive therapy, the long-term administration of the antithyroid drugs methimazole and carbimazole or an iodine-restricted diet are options. In addition, pretreatment with methimazole or carbimazole to restore euthyroidism prior to surgery is a common practice for cats. Hyperthyroid cats at increased risk of complications, including those with cardiovascular disease or severe hyperthyroidism, may benefit from treatment with methimazole or beta-adrenergic antagonists before definitive treatment with radioactive iodine or surgery.
### Radioactive iodine

Experts generally agree that radioiodine is the treatment of choice for most cats with FHT. The distinct advantages of ¹³¹I treatment include:

- The potential to eliminate benign thyroid tumors or hyperplastic thyroid tissue with a single treatment.
- Treatment of functional extrathyroidal tissue, which may occur in 10–20% of cases.²¹,⁵⁸
- No general anesthesia.
- Minimal side effects.

### Oral or transdermal medication

- Response rate ≥95% while on medication
- Small pills, liquid or topical gel
- Requires no hospitalization
- No risk of permanent hypothyroidism
- Reversible if kidney function declines

### Surgical thyroidectomy

- ≥90% cure rate if both glands are removed
- 35–60% cure rate if one gland is removed
- Cures disease within 1–2 days
- Relapse rate 5% if bilateral procedure; ≤30% if unilateral
- Requires no special equipment
- Most general surgeons can perform

### Dietary therapy

- Only a change in diet is required
- Response rate ≥82% while on diet
- Safe in cats with renal insufficiency

### Advantages and disadvantages of feline hyperthyroidism treatments

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<tr>
<th>TREATMENT</th>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
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<tr>
<td>Radioactive iodine</td>
<td>- Kills abnormal cells in any location</td>
<td>- Requires special license and facility</td>
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<tr>
<td></td>
<td>- Cure rate ≥95%; most successful treatment for carcinoma</td>
<td>- Hospitalization varies from 3 days to 4 weeks depending on dose cat receives</td>
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<td></td>
<td>- Relapse rate 5%</td>
<td>and regional regulations</td>
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<td></td>
<td>- Simple treatment – one injection or oral capsule</td>
<td>- Owner cannot visit</td>
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<td></td>
<td>- Serious side effects are rare</td>
<td>- Cat is under ‘house arrest’ for 2 weeks after discharge</td>
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<td></td>
<td>- Limited testing needed after successful treatment</td>
<td>- Owner must collect wastes for 2 weeks after discharge</td>
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<td></td>
<td>- Minimal risk of permanent hypothyroidism</td>
<td>- Owner cannot cuddle cat for long intervals for 2 weeks after discharge</td>
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<td></td>
<td>- Preferred treatment for humans</td>
<td>- Not reversible</td>
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<tr>
<td>Oral or transdermal medication</td>
<td>- Response rate ≥95% while on medication</td>
<td>- Relapse rate 100% when off medication</td>
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<td></td>
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<td>- Daily medication (usually twice daily) for the rest of the cat’s life</td>
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<tr>
<td>Surgical thyroidectomy</td>
<td>- ≥90% cure rate if both glands are removed</td>
<td>- Frequent lab tests to monitor effectiveness and safety</td>
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<td></td>
<td></td>
<td>- Drug reactions occur in up to 25% of cats; facial itching, vomiting, liver failure, abnormal blood cell levels and bleeding episodes may occur</td>
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<td></td>
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<td>- Tumor continues to grow and may become malignant</td>
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<td>- General anesthesia in a cat with a compromised cardiovascular system is risky</td>
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<tr>
<td>Dietary therapy</td>
<td>- Only a change in diet is required</td>
<td>- May damage parathyroid gland and cause a transient or permanent calcium crisis</td>
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<td></td>
<td>- Requires hospitalization</td>
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<td></td>
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<td>- Not reversible</td>
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<tr>
<td></td>
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<td>- Most cats require stabilization first with medication</td>
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<td></td>
<td></td>
<td>- Voice or purr may change</td>
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<tr>
<td></td>
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<td>- Requires no special equipment</td>
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<td>- Most general surgeons can perform</td>
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Over the life of the cat, the cost of treating uncomplicated FHT is similar whether radioactive iodine, medication or surgery is chosen. The cost of feeding y/d each year is approximately the same as the total cost for any of the other three treatments. The cost of radioiodine or surgery is borne up front, while the costs of oral antithyroid drug therapy and food are separated over time. Owners should be encouraged to discuss any financial concerns with their family veterinarian.

The advantages/disadvantages chart may be downloaded from www.catvets.com/hyperthyroidism for use with clients, and is also available as supplementary material at http://jfms.com. DOI: 10.1177/1098612X16643252
Physiologically stable cats respond best. Those with clinically significant cardiovascular, renal, gastrointestinal or endocrine disease (e.g., diabetes mellitus) may not be good candidates for this approach, especially in the light of the time necessary for isolation after treatment.44

After administration, the thyroid gland actively concentrates $^{131}$I. Although $^{131}$I has a physical half-life ($t_{1/2}$) of 8 days, the biological $t_{1/2}$ is much shorter; generally 1.5–4 days. $^{131}$I emits both beta particles and gamma radiation. The beta particles are responsible for the majority of tissue destruction, but are only locally destructive, traveling a maximum of 2 mm. Therefore, no significant damage to adjacent parathyroid tissue, atrophic thyroid tissue or other cervical structures occurs. The main limitations to widespread use of radioactive iodine are the requirement for special licensure and isolation of the cat for variable periods after treatment. This can range from 3 days to 4 weeks depending on regional radiation regulations and the dose administered.65

**Expected outcomes**

The goal of treatment is to restore euthyroidism with the smallest possible single dose of $^{131}$I, while at the same time avoiding development of hypothyroidism.44 Controversy exists as to the best method of calculating the optimum $^{131}$I dose for individual cats.44,65 No dose selection method guarantees a successful dose. In spite of the various dose selection methods, however, the success rate of a single $^{131}$I treatment is very high – over 95% in most studies.14,44,66,67 T4 declines into the reference interval by 4–12 weeks post-treatment.44,68 Complete resolution of clinical signs of FHT may take several months. The 5% of cats that do not achieve euthyroidism with one dose of $^{131}$I are usually those with larger tumors, more severe clinical signs, higher T4 values or carcinomas.67 Cats that do not have carcinomas generally respond favorably to a second dose of $^{131}$I.50,58 Conventional low dose $^{131}$I fails to cure thyroid carcinomas because malignant cells do not concentrate iodine as efficiently as do hyperplastic or adenomatous cells.68 A very high dose of $^{131}$I, or a combination of surgical debulking and high dose $^{131}$I, is the most successful option for the treatment of thyroid carcinoma.24,68

Depending on the treatment dose of $^{131}$I, up to 75% of cats may become hypothyroid for some interval post-therapy.48,69–71 Because $^{131}$I predominantly damages hyperactive cells, permanent post-treatment hypothyroidism is an uncommon sequela.44 Cats treated with higher doses of $^{131}$I may suffer damage to normal thyroid cells and are more likely to experience post-treatment hypothyroidism that may require hormone replacement.72 In 2–7% of cases it is transient, causes no clinical signs and the cat requires no supplementation with thyroid hormone.14,69–71 Up to 30% of cats remain hypothyroid 3 months after radiiodine treatment, with approximately half of those exhibiting clinical signs or experiencing a worsening of renal function and requiring hormone supplementation.73 Hyperthyroid cats with carcinomas that receive high doses of $^{131}$I are at the greatest risk of clinical hypothyroidism post-therapy.68

Thyroid hormone replacement may also be needed in cats with concurrent kidney disease. Advise owners of this possibility, particularly if their motivation is to avoid long-term oral medication.

**Medical therapy**

Antithyroid drugs can be used long term as a sole treatment or short term to stabilize the patient before any surgery or anesthesia or if radioiodine therapy is not immediately available.44,74,75 A methimazole trial prior to $^{131}$I or bilateral surgery may predict the risk of significant renal compromise after definitive therapy for FHT.

Two pharmacologically active ingredients are available as licensed veterinary drugs for treatment of hyperthyroidism, methimazole (Felimazole; Dechra Veterinary Products)76 and carbimazole (Vidalta; MSD Animal Health). Carbimazole is not currently available in the US but is utilized in other countries. It is a metabolite of methimazole that has a similar mechanism of action as well as side effects; dosing is similar as well.77 Methimazole acts by blocking thyroid peroxidase, thus inhibiting biosynthesis of thyroid hormones.78 As in humans, methimazole is thought to accumulate in the thyroid glands of cats.78,79 In healthy cats, oral methimazole is well absorbed and the pharmacokinetic parameters are not significantly altered by hyperthyroidism.78

Methimazole should be started at a dose of 1.25–2.5 mg per cat twice daily (q12h). Twice daily dosing is associated with less serious side effects than a higher dose once daily (q24h).44,78–80 After the cat becomes euthyroid with q12h dosing, giving the total daily dose q24h may maintain euthyroidism and increase owner compliance.80,81 Transdermal methimazole preparations, when available, can be useful for uncooperative cats. In such cases, the same or a slightly higher starting dose than for the oral route should be used.80

Most hyperthyroid cats are euthyroid within 2–3 weeks of commencing treatment with antithyroid drugs,44,65,82,83 and so T4 should be

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**Thyroid storm**

Thyroid storm is a rare, but life-threatening, complication of FHT. It results from a rapid increase in serum thyroid hormone. Causes include damage to the thyroid gland during $^{131}$I therapy or vigorous thyroid gland palpation, abrupt withdrawal of antithyroid medication, anesthesia, exacerbation of NTD or a stressful event. If you anticipate the occurrence of a possible event, using a beta-adrenergic antagonist, such as atenolol at 6.25 mg/cat q24h, as a prophylactic treatment at least 24 h prior to the event will effectively prevent clinical signs.63

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**Radioactive iodine is the treatment of choice for most hyperthyroid cats.**
monitored after that time period. If the cat is still hyperthyroid, methimazole dose adjustments can be made in increments of 1.25–2.5 mg/day until euthyroidism is achieved. When maintenance doses in excess of 10 mg/day are required, compliance should be questioned. If T4 drops below the lower end of the reference interval, the methimazole dosage should be reduced in decrements of 1.25–2.5 mg/day and the T4 and renal parameters rechecked in 1 week. Treatment with transdermal methimazole can utilize a similar scheme as for oral methimazole. In cases of local skin irritation, switching to oral administration should be considered.

**Side effects of methimazole**
The most severe, but rare, side effects observed with methimazole are hepatopathy and marked blood dyscrasias (severe leukopenia, anemia and thrombocytopenia). Gastrointestinal upset, lethargy and facial pruritus (Figure 6) occur at variable frequency. Occurrence, frequency and severity of side effects have not been shown to be dose related. Gastrointestinal upset may be less frequent with transdermal preparations. Most side effects appear within the first 4–6 weeks of therapy and are less common after 2 or 3 months of treatment.

**Expected outcomes**
Overall, almost all hyperthyroid cats treated with methimazole will experience successful control of their disease. T4 responds to methimazole administration within 1 week of treatment. However, clinical response to therapy may not be seen until T4 is maintained within the reference interval for 2–6 weeks. Because methimazole does not destroy hyperplastic or adenomatous thyroid tissue, abnormal tissue will progressively grow over time if methimazole is used as a long-term treatment. The size, volume and number of functional thyroid nodules will increase proportionally with the duration of disease, so that the dose of methimazole necessary to control thyrotoxicosis may need to be progressively increased. Eventually, some cats will not tolerate the dose of methimazole necessary to control FHT or will become completely resistant to methimazole therapy, necessitating the need to explore alternative treatment methods.

**Surgical thyroidectomy**
Thyroidectomy is an established surgical technique that may be curative. Surgical options include bilateral thyroidectomy with an intracapsular or extracapsular approach, unilateral thyroidectomy (reserved for cats with true unilateral disease) and staged bilateral thyroidectomy. Surgery and anesthesia are sometimes associated with substantial procedural morbidity and mortality. Hypocalcemia occurs in a widely varying range (6–82%) of thyroidectomy patients, depending on the surgical method chosen. In cats that have had unilateral or bilateral thyroidectomy with careful preservation of the parathyroid glands, hypocalcemia may be mild and transient, and not require treatment. Severe hypocalcemia associated with hypoparathyroidism may be transient (lasting days, weeks or months) or permanent. Other complications of thyroidectomy include Horner’s syndrome, laryngeal nerve paralysis and recurrence of hyperthyroidism.

If the surgeon fails to remove all abnormal thyroid tissue, the cat will require revision surgery. Tc imaging prior to surgery will decrease the number of subtotal thyroidectomies by revealing multinodular disease and bilateral involvement. Imaging will also identify cats with ectopic tissue or a large goiter that descends through the thoracic inlet into the chest.

In cats with substernal disease, surgical removal may be difficult. Approximately 4–9% of hyperthyroid cats have adenomatous tissue in ectopic sites (sublingual or substernal sites are most common), which a surgeon would likely miss at surgery.

**Expected outcomes**
Surgical thyroidectomy is associated with a high rate of both short- and long-term success, with most studies showing >90% of cats achieving euthyroidism postoperatively, with a relapse rate approaching 5% within 3 years. The success of the procedure is highly dependent on presurgical stabilization of the patient and the surgeon’s expertise. Because of the short T1/2 of T4 in cats, euthyroidism after successful thyroidectomy usually occurs within 24–48 h of surgery. Unilateral thyroidec tomy is associated with transient hypothyroidism that resolves within 1–3 months as remaining thyroid tissue recovers function. Bilateral thyroidectomy may result in clinical hypothyroidism that requires hormonal supplementation. Persistence or recurrence of post-surgical hyperthyroidism is associated with incompletely removed abnormal tissue.
Dietary therapy

Production of thyroid hormone requires uptake by the thyroid gland of sufficient amounts of dietary iodine. The only function of ingested iodine is for thyroid hormone synthesis. This finding led to the hypothesis that limiting dietary iodine intake could be used to control thyroid hormone production and potentially manage FHT. A restricted-iodine diet (Hill’s Prescription Diet y/d Feline; Hill’s Pet Nutrition) containing 0.2 ppm (mg/kg) iodine on a dry matter basis is currently available for the management of FHT.

Expected outcome

With good client compliance, 75% of cats have significantly reduced T4 and improvement of clinical signs within 28 days of starting the diet. Normalization may require up to 180 days in cats with severe elevations in T4, and some fail ever to reach euthyroidism. In a 1 year study, 83% of hyperthyroid cats went into remission on the diet. A limitation of a restricted-iodine diet is lack of palatability, affecting up to 12% of cats studied. Also, dietary management may be difficult or contraindicated in the following scenarios:

- Patients in multi-cat households.
- Hyperthyroid cats with concurrent disease requiring other nutritional management.
- Cats taking compounded flavored medications or supplements that contain iodine.
- Indoor–outdoor cats.

The long-term consequence of a restricted-iodine diet in hyperthyroid cats is unknown. The iodine concentration of the restricted diet (0.2 ppm) is lower than the iodine requirement of euthyroid adult cats (0.46 ppm). This may not cause problems because cats fed an even more iodine-restricted diet (0.17 ppm) for 1 year did not show signs of deficiency.

In addition to efficacy in restoring euthyroidism, three studies showed reductions in serum creatinine concentrations together with stable or increasing bodyweights in hyperthyroid cats eating the iodine-restricted diet. The mechanisms behind these effects are currently unknown.

A cat may undergo surgical excision of a thyroid tumor while on an iodine-restricted diet, but if an owner subsequently wants the cat to undergo radioiodine therapy, the optimum withdrawal time from the diet is unknown. Limited-iodine diets increase iodine uptake in the autonomous thyroid glands of hyperthyroid cats. Further studies are necessary to determine whether consumption of a limited-iodine diet changes sensitivity of the thyroid gland to radioiodine treatment.

Monitoring hyperthyroid patients

Monitor all cats with hyperthyroidism, both to control the disease effectively and to avoid iatrogenic hypothyroidism. Close monitoring of hyperthyroid cats as they become regulated will allow for recognition of comorbidities and exacerbation or improvement of already identified concurrent disease.

Regardless of the treatment method, evaluation of multiple parameters (see below) when monitoring newly diagnosed and treated hyperthyroid cats will optimize the cat’s healthcare.

What to monitor

- Improvement in the cat’s physical condition – weight gain, improved body condition score, improved hair coat, resolving tachycardia and resolving behavioral changes are all positive indicators of improved thyroid status.
- T4 – the goal in cats without renal insufficiency is a T4 value between 1 and 2.5 µg/dl (12.9–32.3 nmol/l) (normal range 1–4 µg/dl [12.9–51.6 nmol/l]).
- CBC – severe hematological side effects are possible but infrequent.
- Renal parameters – blood urea nitrogen, creatinine, urine specific gravity, phosphorus and potassium should be monitored. Glomerular filtration rate (GFR) stabilizes within about 1 month of achieving thyroid control.
- fT4ed – note this assay is not indicated as a sole monitoring parameter for hyperthyroidism.
- TSH testing – may be useful to evaluate for hypothyroidism.
- Other specific parameters for cats with known concurrent disease – gastrointestinal function testing, cardiac monitoring and urine culture.

Appropriate monitoring, along with careful management of concurrent diseases, will optimize the cat’s healthcare.

Initial follow-up testing after starting treatment is conducted at 2–4 weeks. Subsequent testing occurs 2–4 weeks after any change in dose. Stable, uncomplicated hyperthyroid cats are then monitored every 4–6 months via T4 assay, CBC, chemistry panel and urinalysis. Cats with concurrent disease may require other laboratory testing or imaging at a different monitoring interval. Clinical improvement in hyperthyroid cats can be expected when T4 levels are within the reference interval. However, to achieve adequate control in cats with renal insufficiency, serum T4 should be maintained in the upper half of the reference interval.

Prognosis

Although older studies report survival times of 2 years after diagnosis, more recent data show that cats without concurrent CKD have a median survival of up to 5.3 years. Thanks to better awareness of the disease, routine screening tests and a variety of readily available treatment options, the hyperthyroid cat will often live for an extended period in a properly managed case. Untreated FHT is a progressive disease that can lead to significant morbidity and mortality. Morbidity and
Various outdated perceptions exist regarding the treatment of FHT, especially if other diseases are being concurrently managed in the same patient. The most significant of these ‘myths’ are discussed here, along with evidence-based realities that should guide treatment.

**MYTH: Methimazole causes kidney damage**

**FACT:** Kidney damage is not a side effect of methimazole treatment. This myth may have originated due to confusion with pre-existing kidney disease that was being masked by the diuresis and cachexia created by the hyperthyroidism.

**MYTH: Treatment of hyperthyroidism in general can result in kidney disease**

**FACT:** Treatment of FHT does not cause kidney damage or renal failure regardless of treatment modality. Side effects of each treatment modality have been described in numerous texts, and none cause direct damage to the kidneys. Treatment of FHT by any means can ‘unmask’ pre-existing CKD, thereby giving the impression of causality where none exists.

**MYTH: Maintaining T4 slightly above the reference interval will help patients with comorbidities like CKD. This ‘renal-protective’ effect is assumed to be the result of improved appetite and increasing blood flow to the kidneys**

**FACT:** This myth is now known to be untrue. On the contrary, left untreated, even mild FHT can cause or exacerbate CKD and glomerular damage; hypertension and proteinuria are possible mechanisms. Early treatment can help reduce damage to the kidneys from hyperthyroidism. Furthermore, unregulated FHT induces a catabolic state that creates a false sense of security in the patient’s health and masks clinical signs of comorbid disease due to increased appetite and activity level. In addition to the negative energy balance created by the catabolic state, increased gastrointestinal transit times and malabsorption contribute to a negative energy balance.

**MYTH: Post-treatment T4 should be below the reference interval because producing a hypothyroid state does not harm cats. The patient is not clinically hypothyroid as long as the T4 is in the reference interval and the patient gains weight**

**FACT:** Cats can develop clinically significant hypothyroidism even if the T4 is within the reference interval. While treatment of hyperthyroidism does not cause or exacerbate renal disease and achieving a euthyroid state is beneficial to the patient, overtreatment (iatrogenic hypothyroidism) can cause progression of renal disease and increase patient morbidity and mortality. Newer data suggest that using canine endogenous TSH as a means of ruling out iatrogenic hypothyroidism can be beneficial in optimizing outcome. One study determined that 20% of cats treated for FHT were iatrogenically hypothyroid, and twice as many cats with elevated TSH were azotemic compared with cats without elevated TSH. The goal remains to establish a T4 in the lower half of the reference interval but to ensure a normal (non-elevated) TSH. The patient should show concurrent clinical improvement. Normalized T4 without improvement in clinical signs warrants further diagnostic evaluation.

**MYTH: Cats with creatinine levels within the reference interval do not have CKD**

**FACT:** Increased GFR and cachexia will artificially lower creatinine levels in spite of significant renal disease. Monitoring body condition score and muscle condition score will better evaluate whether sarcopenia has occurred. The Panel recommends using the IRIS guidelines for staging, monitoring and treating CKD.

**MYTH: Isolation after 131I administration is too stressful for the cat**

**FACT:** Although any time a cat is away from home it may experience stress, this stress is much less than the stress of the illness or other treatment. It is important to fully explain to the owner that any illness and treatment can be stressful and the risks of treatment must be weighed against the benefits. 131I may actually be the option best tolerated by the patient. Hospitalization for 131I is similar to what a cat experiences when boarding while the owner is on vacation. Often the cat is less stressed than the owner fears, and most cats tolerate the required post-treatment isolation reasonably well. Many facilities are addressing the environmental needs of cats with improved mental and physical stimulation during their stay. With availability of scintigraphy and a better understanding of dose titration of 131I, radiation safety can still be ensured with relatively short stays in the hospital. Many stays are shorter than would be required to treat some of the complications associated with poorly controlled FHT.

**MYTH: The cost of 131I is prohibitive**

**FACT:** Over the life of the patient the cost of treating uncomplicated FHT is similar if one chooses radioactive iodine, medication or surgery. The cost of feeding y/d each year is approximately the same as the cost of any of the other three options. The cost of radiiodine or surgery is borne up front, while the costs of oral antithyroid drug therapy and dietary therapy are separated over time.

**MYTH: The cost of 131I is prohibitive**

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Mortality in the well-managed hyperthyroid cat are more strongly influenced by the presence and severity of the comorbid disease than by FHT itself. FHT secondary to thyroid carcinoma carries a slightly less favorable prognosis than hyperplasia or adenoma due to the pathology of neoplastic disease. However, with appropriate treatment, even cats with thyroid carcinomas often die from unrelated non-thyroidal illness than from consequences of their thyroid tumor.
Feline hyperthyroidism (FHT) is increasing in prevalence and is now the most common endocrine disorder in middle-aged and older cats, occurring in about 10% of US feline patients >10 years of age.

No one has verified any definitive cause, although epidemiological studies suggest both genetic and environmental influences.

Feline geriatric screening panels now routinely include serum T4, which allows detection of elevated T4 levels at an early stage in disease progression and helps enable timely diagnosis and intervention.

Because older age is a risk factor for FHT, clinicians should anticipate the presence of other age-related comorbidities such as heart disease, diabetes mellitus, gastrointestinal dysfunction and CKD in a certain percentage of hyperthyroid patients. FHT case presentations may be ambiguous due to the presence of concurrent diseases or diagnostic inconsistencies.

A systematic approach to FHT diagnosis will categorize suspected cases into one of six diagnostic groups, each of which has an associated management strategy.

The four common therapeutic modalities, implemented individually or in combination, are radioactive iodine, pharmaceutical therapy, surgical thyroidectomy and dietary therapy.

Because FHT is life-threatening, the Panel recommends treatment of all hyperthyroid cats with concurrent management of any comorbidities.

Overall success of management of FHT is 83–99%, depending on the patient’s clinical status and treatment modality. Radioiodine and surgery are potentially permanent cures for both adenomas and carcinomas. Methimazole/carbimazole and dietary therapy will control clinical disease in milder cases and in cats with significant comorbidities.

Regular monitoring of a hyperthyroid cat is important not only to assess therapeutic efficacy but also to detect iatrogenic hypothyroidism and to confirm comorbidities that become evident with resolution of the hyperthyroid state.

Morbidity and mortality in the well-managed hyperthyroid cat are more strongly influenced by the presence and severity of the comorbid disease than by FHT itself.

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SPECIAL ARTICLE / 2016 AAFP feline hyperthyroidism guidelines


Feline Hyperthyroidism

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Feline Hyperthyroidism

Feline hyperthyroidism is the most common endocrine disorder in middle-aged and older cats. It occurs in about 10 percent of feline patients over 10 years of age. Hyperthyroidism is a disease caused by an oversecrete thyroid gland that secretes excess thyroid hormone. Cats typically have two thyroid glands, one gland on each side of the neck. One or both glands may be affected. The excess thyroid hormone causes an overactive metabolism that stresses the heart, digestive tract, and many other organ systems.

If your veterinarian diagnoses your cat with hyperthyroidism, your vet should receive some form of treatment to control the clinical signs. Many cats that are diagnosed early can be treated successfully. When hyperthyroidism goes untreated, clinical signs will progress leading to marked weight loss and serious complications due to damage to the cat’s heart, kidneys, and other organ systems.

CLINICAL SIGNS
If you observe any of the following behaviors or problems in your cat, contact your veterinarian because the information may alert them to the possibility that your cat has hyperthyroidism.

- weight loss despite a normal or increased appetite
- increased urination, more urine in the litter box
- increased drinking or thirst
- defecation outside of the litter box
- increased vocalization
- restlessness, increased activity
- vomiting
- diarrhea
- rarely, lethargy and a lack of appetite
- poor hair coat, unkempt fur

DIAGNOSIS
Twice yearly examinations of your cat may allow early detection of hyperthyroidism, as well as other age-related diseases. During the physical examination your veterinarian may discover increased heart and respiratory rates, hypertension, a palpable thyroid gland, and loss of muscle mass. Routine screening of laboratory tests and blood pressure may detect abnormalities before clinical signs (bulleted list above) are advanced. Blood testing can reveal elevation of thyroid hormones to establish a diagnosis of hyperthyroidism. Occasionally, additional diagnostics may be required to confirm the diagnosis. Because hyperthyroidism can occur along with other medical conditions, and it affects other organs, a comprehensive screening of your cat’s heart, kidneys, and other organ systems is imperative.

MANAGEMENT AND TREATMENT OPTIONS
If your veterinarian diagnoses your cat with hyperthyroidism, he or she will discuss and recommend treatment options for your cat. Four common treatments for feline hyperthyroidism are available and each has advantages and disadvantages. The choice of therapy can depend on factors such as the cat’s age, other disease conditions, treatment cost, availability of treatment options, and your veterinarian’s recommendation.

For more information on feline hyperthyroidism, visit www.catvets.com/fht.

This was developed from the 2016 AAFP Guidelines for the Management of Feline Hyperthyroidism. ©2016 AAFP. All rights reserved.