Feline Hyperthyroidism – Ensuring Treatment Success
Todd L. Towell, DVM, MS, DACVIM

Abstract:

Hyperthyroidism is a disease of older cats consequently many patients have concurrent diseases. Indeed therapy for hyperthyroidism is often associated with unmasking of concurrent chronic kidney disease. Selecting the appropriate therapy for hyperthyroid cats with concurrent conditions is challenging. Traditional management options for feline hyperthyroidism include thyroidectomy, anti-thyroid medications, and radioactive iodine. All three modes of therapy are effective but none are without risks. Recent studies document that a fourth option now exists for hyperthyroid cats. Feeding a low-iodine food decreases thyroid hormone concentrations and alleviates clinical signs of hyperthyroidism in cats. For any individual patient with multiple diseases the clinician must weigh the pros and cons of managing each disorder and decide which one has the greatest impact on longevity and quality of life.

Traditional Therapies for Hyperthyroidism

Anti-thyroid Medications

The thioureylene anti-thyroid drugs (methimazole, carbimazole and propylthiouracil) are the most common medical management of both human and feline hyperthyroid patients because of their reliable ability to inhibit the synthesis of thyroid hormones and thereby lower serum thyroid hormone concentrations. These drugs do not affect the trapping of inorganic iodide by, or the release of preformed hormones from the thyroid gland. They are widely recommended to stabilize hyperthyroid cats prior to surgery and are the only drugs that can be used chronically for management of hyperthyroidism.¹

Chronic administration of anti-thyroid medications has the advantage of being readily available, requiring no special facilities, and being reasonably inexpensive, at least initially. Almost all cats are potential candidates unless thyroid carcinoma is suspected. Anesthesia and hospitalization are avoided. On the other hand, daily administration of medication is required. A real risk of poor compliance by the owner in regularly administering or the cat in accepting the medication exists. Noncompliant patients typically relapse within 24-72 hours after the last dose.² Lack of compliance impacts both efficacy and cost because it compels more frequent monitoring. Propylthiouracil is no longer recommended because it is associated with an unacceptably high incidence of serious hematologic complications in both healthy and hyperthyroid cats. Methimazole is licensed for use in hyperthyroid cats in many countries (Felimazole®, Dechra Limited). Carbimazole, as a controlled-release formulation (10 or 15 mg tablets) was recently licensed for cats in Europe (Vidalta®, Schering-Plough). Methimazole and conventional carbimazole tablets for human use are also available. Carbimazole and methimazole can also be formulated in a pluronic lecithin organogel (PLO) for transdermal application with reasonable efficacy. However there are no transdermal products approved for use in hyperthyroid cats. Custom formulation increases expense of therapy and stability of the product is not guaranteed. While many cats have been successfully managed long term on oral therapy the risk of adverse reactions should not be overlooked.
Most adverse reactions associated with methimazole or carbimazole occur within the first 3 months of therapy. Reported reactions include vomiting with or without anorexia and depression, self-induced excoriations of the head and neck, and mild to serious hematologic complications. These hematologic complications include agranulocytosis and thrombocytopenia either alone or concurrently and more rarely immune mediated hemolytic anemia. Occurrence of these serious hematologic side effects has led to the recommendation of performing screening tests (complete blood count (CBC) and platelet count) every 2 weeks initially. If this monitoring is cost prohibitive testing if and when clinical signs develop and prior to surgery is appropriate. Hepatic toxicity, characterized by marked increases in the liver enzyme activities and bilirubin concentration, has been described in less than 2% of cats treated with methimazole. Cessation of therapy is required if either serious hematologic or hepatic reactions develop. Serum antinuclear antibodies develop in approximately 50% of cats treated with methimazole for longer than 6 months, usually in cats on high-dose therapy (>15 mg/day). Although clinical signs of a lupus-like syndrome have not been reported, decreasing the daily dosage is recommended. Comparable studies have not yet been reported for carbimazole. However given carbimazole’s conversion to methimazole a similar effect is expected.

Surgical Thyroidectomy
Surgical thyroidectomy is a relatively simple and curative procedure often considered the preferred treatment option. However, to decrease the cardiac and metabolic complications associated with anesthetizing hyperthyroid cats, prior medical management and control of the thyrotoxicosis are required. Once euthyroidism has been achieved, the main surgical considerations are whether to perform a unilateral or bilateral thyroidectomy, the type of technique to use, and the potential postoperative complications. Involvement of both of the thyroid lobes occurs in approximately 70% of hyperthyroid cats necessitating bilateral thyroidectomy. In 15% of cats with bilateral disease one thyroid lobe appears grossly normal and if left in situ will result in recurrence of hyperthyroidism with a year. Recurrence is also more likely in cats with ectopic thyroid tissue which requires nuclear imaging facilities to diagnose. Hypoparathyroidism resulting in hypocalcaemia is the most significant potential postoperative complication. This generally arises only if the parathyroid glands are injured, devascularized, or inadvertently removed during a bilateral thyroidectomy. Mild hypocalcaemia develops in most cats post bilateral thyroidectomy, but treatment is not necessary unless clinical signs develop. Fortunately hypoparathyroidism is rarely permanent, and recovery of parathyroid function may occur days to months after surgery. Serum levels of thyroid hormone typically fall below the reference range for weeks to months after surgery. Historically the recommendation has been that thyroxin supplementation is not necessary unless clinical signs of hypothyroidism occur. However, a recent study suggests that asymptomatic iatrogenic hypothyroidism is a risk factor for progression of chronic kidney disease in these patients. Treating biochemical hypothyroidism in the absence of clinical signs may be appropriate. Owners should be advised of this possibility particularly if the impetus for surgical therapy was to avoid the need for long term oral medication.

Radioactive Iodine
Nearly 20% of hyperthyroid cats have multiple areas of hyperfunctional and / or intrathoracic thyroid tissue making surgical thyroidectomy ineffective. Radioiodine treatment is
often considered the best option for many cats since it has the potential to cure the disease with a single treatment, is not dependent on the location of the hyperfunctional thyroid tissue, no general anesthesia is required and side effects are minimal. Markedly elevated pretreatment T4 levels, increasing size of goiter and the severity of clinical thyrotoxicosis as well as preexisting kidney disease all potentially adversely affect the response to this therapy.1

Like stable iodine, 131I, is actively concentrated by the thyroid gland. It has a half-life of 8 days and emits both β-particles and γ-radiation. The β-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 is expected. The aim of therapy is to restore euthyroidism with the smallest possible single dose of radiation while avoiding the development of hypothyroidism.1 Controversy exists as to the best method of calculating the optimum dose for an individual cat. Approximately 30% of cats are estimated to become hypothyroid greater than 3 months after radioactive iodine therapy. As previously mentioned, therapy for asymptomatic hypothyroidism may decrease the risk of progressive chronic kidney disease. Owners should be advised of this possibility particularly if the motivation for 131I therapy was to avoid the need for long term oral medication.

The main limitation to widespread use of radioactive iodine is the requirement for special licensing and the isolation of the cat for variable periods after treatment. This can range from several days to several weeks depending on state or local radiation regulations and, particularly, the dose.1

Effect of Treatment on Kidney Function:

Chronic kidney disease (CKD) is common in cats over 15 years of age. The typical age of onset of hyperthyroidism is 12 to 13 years of age. Therefore it is not uncommon for hyperthyroidism and CKD to occur concurrently in geriatric cats. Hyperthyroidism complicates the diagnosis of chronic kidney disease as it increases glomerular filtration rate (GFR) and therefore may mask the biochemical markers of CKD. Regardless of therapeutic modality (methimazole, surgical thyroidectomy, or radioiodine) decreased GFR, increased serum urea and creatinine concentration and development of overt clinical signs of renal disease have been reported after successful treatment of hyperthyroidism.3-9 The presence of underlying CKD may affect the prognosis. One study documents a shorter survival time in hyperthyroid cats with CKD.10 While another study comparing the survival of cats that developed azotemia with those that remained nonazotemic after treatment of hyperthyroidism found no significant difference between the two groups; mean survival time of 595 days compared with 584, respectively.11

The reported incidence of azotemia after treatment of hyperthyroidism is 17–49%.3,4,7,8,10,12 One study of predominately medically treated hyperthyroid cats documented a lower percentage (15%) of progression to azotemia.12 One explanation for this decrease is inadequate control which may not have normalized GFR sufficiently to unmask underlying CKD. However, the authors postulate that the lower incidence of post treatment azotemia could be related to a low incidence of biochemical hypothyroidism in these medically treated cats. Iatrogenic hypothyroidism has been reported to decrease GFR.13 Post treatment iatrogenic hypothyroidism has been reported in cats after radioiodine therapy and bilateral thyroidectomy, which constitute the predominant treatment modalities in previous studies.12
In one recent study, cats with iatrogenic biochemical hypothyroidism were almost twice as likely to develop azotemia post treatment as euthyroid cats. The hypothyroid cats with azotemia had shorter survival times than non-azotemic cats whereas consistent with previous reports there was no difference in the survival times of euthyroid cats with and without azotemia. The authors suggest that the results of this study indicate iatrogenic biochemical hypothyroidism, even in the absence of clinical signs, contributes to the development of azotemia and reduced survival times after treatment of hyperthyroidism. Based on this study even asymptomatic cats with iatrogenic biochemical hypothyroidism post therapy for hyperthyroidism may benefit from thyroid hormone supplementation to maintain euthyroidism.

**Prognosis for Traditional Therapies:**
Several studies have estimated the survival time of cats after treatment for hyperthyroidism. The largest study, published in 1995, included over 500 cats evaluated prospectively and treated with radioactive iodine. The mean survival time was 24 months (range 2 weeks to 7 years). The percentage of cats alive at 1, 2, 3, and 4 years after treatment was 89%, 72%, 52%, and 34%, respectively. There are few studies that directly compare the outcomes of the different treatment methods. One retrospective study suggests that when cats with pre-existing kidney disease are excluded the median survival time in cats treated with methimazole alone (2 years) was significantly shorter than for those treated with radioactive iodine alone (4 years) or methimazole followed by radioactive iodine (~ 5 years). The shorter survival time in cats treated with methimazole may be related to owner/cat compliance, adverse drug reactions or may represent a bias in case selection for the different treatments. Cats referred for radioiodine therapy are generally younger and healthier than those that are not. The most common causes of death in cats treated for hyperthyroidism are malignancy and renal disease.

**Nutritional Management**
Three studies have documented the safety and efficacy of Hill’s Prescription Diet® y/d® Feline as the sole management in cats with naturally occurring hyperthyroidism. These studies were designed to determine the magnitude of iodine restriction necessary to return newly diagnosed cats to a euthyroid state; the maximum level of dietary iodine that will maintain cats in a euthyroid state and the efficacy of a therapeutic food formulated based on the previous studies to control naturally occurring hyperthyroidism in cats. The results of these studies support that a therapeutic food with dietary iodine levels at or below 0.32 ppm dry matter basis (DMB) provides an effective and safe therapy for cats with naturally occurring hyperthyroidism. Serum total thyroxine concentrations returned to the normal range within 8 to 12 weeks of initiating nutritional therapy in cats fed foods with ≤ 0.3 ppm iodine DMB. All hyperthyroid cats maintained on foods with ≤ 0.3 ppm iodine DMB as the sole source of nutrition remained euthyroid. In all of these studies biochemical features of renal function remained stable and no other biochemical abnormalities were observed.

**Nutritional Management of Hyperthyroid Cats with Concurrent Diseases**
Chronic kidney disease is the most common concurrent condition of hyperthyroid cats. Both diseases have increased prevalence in geriatric patients. Strong evidence supports the use of therapeutic renal foods, specifically Hill’s Prescription Diet® k/d® Feline, for the management
of IRIS Stage 2 cats with chronic kidney disease. However, if nutritional management for hyperthyroidism is desired in a patient with concurrent chronic kidney disease (IRIS Stage 1-3) y/d Feline may be an appropriate choice, particularly compared to commonly available maintenance foods. The nutrient profiles of select therapeutic and maintenance dry and wet foods are listed in Table 5. While not specifically designed to manage chronic kidney disease, y/d Feline is designed for mature cats. Phosphorus levels are almost half of that found in the representative grocery store foods. Transitioning to a therapeutic renal food and an alternative therapy for hyperthyroidism should be considered if cats are uremic or if a stable IRIS Stage 1-3 cat progresses.

Diabetes mellitus may also occur in cats with hyperthyroidism. Dietary therapy is also a cornerstone of the management of type II diabetes in cats. Recent studies suggest foods that contain 5% to 26% of calories from carbohydrates help maintain glycemic control in diabetic cats. The percent of calories from carbohydrates in y/d Feline (23% dry, 24% canned) falls within these guidelines.

Cats with evidence of hypertension or cardiac disease should be managed with appropriate therapies. Propranolol and atenolol are betablockers commonly used to symptomatically control tachycardia, polypnoea, hypertension, and hyperexcitability in hyperthyroid cats. They may be used in combination with nutritional therapy when rapid control of the clinical signs is desired. The concurrent use of anti-thyroid drugs is generally not necessary in cats with mild to moderate clinical signs. If severe clinical signs (emaciation, severe metabolic and cardiac dysfunction) are present and rapid reduction of serum thyroxine is desired anti-thyroid medications can be administered concurrently with the transition to y/d Feline. Monitoring in these cases is similar to the guidelines for transitioning hyperthyroid cats currently controlled with anti-thyroid medications (Figure 4) and should include serum T4 concentrations every 4 weeks until the values are within normal limits. Once the patient is euthyroid and has been eating y/d Feline exclusively for at least 2 weeks the anti-thyroid medication dose should be decreased or discontinued. The decision to discontinue or decrease the dose should be based on the individual response. Anti-thyroid medication should be discontinued if serum T4 concentrations are low normal to below the reference range. Routine recheck evaluations at 4 and 8 weeks after stabilization should include physical examination, T4, serum chemistries (BUN and creatinine) and urine specific gravity.

Certainly for any individual patient with multiple diseases the clinician must weigh the pros and cons of managing each disorder and decide which one has the greatest impact on longevity and quality of life. Additional information and recommendations for nutritional management of complicated clinical cases is available from the Hill's Veterinary Consultation Service. This service provides free total case management, nutritional counseling and product support for both domestic and international veterinary hospitals. The Veterinary Consultation Service can be contacted by phone at 1-800-548-VETS (8387) or by email through the www.hillsvet.com website.

**Adverse Effects of Nutritional Therapy**

Based on the studies completed to date, no adverse effects of nutritional therapy have been noted. In all cats treated to date biochemical features of renal function have remained stable and no other biochemical abnormalities have been observed. There have been no
reports of hypothyroidism or progression of kidney disease. Cats with IRIS stage 1 kidney disease have been managed with y/d Feline without progression of the disease. Hypothyroidism has not been reported in cats managed exclusively with y/d Feline.

**Conclusion:**

Hyperthyroidism is common older cats. While the pathogenesis of feline hyperthyroidism remains unclear a variety of treatment options are available. Traditional methods of managing feline hyperthyroidism include thyroidectomy, anti-thyroid medications, and radioactive iodine. All three modes of therapy are effective but none are without risk of side effects. Hill’s Prescription Diet® y/d Feline® is the first therapeutic food specifically formulated to manage hyperthyroidism in cats. Studies document that when y/d Feline is the sole source of nutrition 90% of hyperthyroid cats return to and remain euthyroid. Management of hyperthyroidism is now as safe and easy as feeding your cat.

---

* Data on file Hill’s Pet Nutrition, Inc.
Table 1. Nutrient Comparisons of Selected Dry Foods for Hyperthyroid Cats with Concurrent disease

<table>
<thead>
<tr>
<th>Key Nutritional Factor</th>
<th>Feline Dry Products</th>
<th>Feline Wet Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hill’s y/d</td>
<td>Hill’s g/d</td>
</tr>
<tr>
<td>Metabolizable Energy Kcal/kg</td>
<td>4,147</td>
<td>3,916</td>
</tr>
<tr>
<td>Protein*</td>
<td>8.2</td>
<td>7.9</td>
</tr>
<tr>
<td>Fat *</td>
<td>5.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Carbohydrate*</td>
<td>6.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Calcium†</td>
<td>215</td>
<td>163</td>
</tr>
<tr>
<td>Phosphorus†</td>
<td>150</td>
<td>135</td>
</tr>
<tr>
<td>Sodium†</td>
<td>58</td>
<td>72</td>
</tr>
<tr>
<td>Potassium†</td>
<td>188</td>
<td>184</td>
</tr>
<tr>
<td>Magnesium†</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Taurine†</td>
<td>77</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key Nutritional Factor</th>
<th>Feline Wet Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hill’s y/d</td>
</tr>
<tr>
<td>Metabolizable Energy Kcal/kg</td>
<td>1207</td>
</tr>
<tr>
<td>Protein*</td>
<td>8.2</td>
</tr>
<tr>
<td>Fat *</td>
<td>6.2</td>
</tr>
<tr>
<td>Carbohydrate*</td>
<td>7.5</td>
</tr>
<tr>
<td>Calcium†</td>
<td>207</td>
</tr>
<tr>
<td>Phosphorus†</td>
<td>141</td>
</tr>
<tr>
<td>Sodium†</td>
<td>58</td>
</tr>
<tr>
<td>Potassium†</td>
<td>207</td>
</tr>
<tr>
<td>Magnesium†</td>
<td>15</td>
</tr>
<tr>
<td>Taurine†</td>
<td>58</td>
</tr>
</tbody>
</table>

Nutrients expressed on as fed calorie basis: *= g/100 kcal; †= mg/ 100 kcal
References


