



**Internal Medicine Service**  
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## Hyperthyroidism in Cats: Diagnosis and Treatment

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Hyperthyroidism is recognized as the most common endocrinopathy of older cats. Despite worldwide occurrence, the pathogenesis of feline hyperthyroidism remains unclear. Traditional methods of managing feline hyperthyroidism include thyroidectomy, anti-thyroid medications, and radioactive iodine. Recent studies document that another option now exists for hyperthyroid cats; feeding a limited-iodine food normalizes thyroid hormone concentrations and alleviates clinical signs of hyperthyroidism. Surgery and radioactive iodine are designed to provide permanent solutions, whereas, oral anti-thyroid drugs and nutritional management control hyperthyroidism and are needed daily to achieve/maintain their effect. All management options are effective and each has its pros and cons. It's important to discuss all options with pet owners so the appropriate management can be selected for each hyperthyroid cat. The good news for owners of hyperthyroid cats is that a number of treatment options exist to help manage this common endocrine disorder. Our job as veterinarians is to tailor the treatment to meet the goals of both the patient and client in a manner that is effective, safe and financially sound.

### Diagnosis

Diagnosis most often is based on the presence of one or more typical clinical signs and increased serum total thyroxine ( $T_4$ ) concentration. However, up to 10% of all hyperthyroid cats and 40% of those with mild disease have serum  $T_4$  values within reference range.<sup>1,2</sup> The diagnosis of hyperthyroidism should not be excluded on the basis of a single normal serum  $T_4$  value, especially in a cat with typical clinical signs, a palpable thyroid nodule and serum  $T_4$  in the upper half of the normal range.<sup>3</sup> In these cases, serum free  $T_4$  ( $fT_4$ ), measured by equilibrium dialysis, may provide an alternative means of diagnosing hyperthyroidism in cats with normal serum total  $T_4$  values. Studies document that up to 20% of sick euthyroid cats can have increased  $fT_4$  concentration.<sup>4</sup> Therefore, it is most appropriate and reliable to interpret the two values together. Mid-to-high reference range total  $T_4$  and increased  $fT_4$  concentration is consistent with hyperthyroidism. In contrast, low total  $T_4$  and increased  $fT_4$  values are usually associated with non-thyroidal illness.



*"Sir," an 11-year-old Tabby with hyperthyroidism, has been on the y/d diet for 2 years.*

### Management Options

Once hyperthyroidism has been diagnosed, all management options (thyroidectomy, radioactive iodine, anti-thyroid drugs, nutritional management) should be discussed with pet owners. All options can be  $\geq$  90% effective for controlling hyperthyroidism when used appropriately. The selected management option will differ for each cat based on several considerations (**Table 1**). Radioactive iodine therapy is considered the gold standard for treatment of hyperthyroidism; however, most pet owners currently opt for medical management. Until recently, this included oral or transdermal anti-thyroid drugs. Now nutritional management using a limited-iodine food is another option for cats with hyperthyroidism.

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### Nutritional Management

Production of thyroid hormone requires uptake by the thyroid gland of sufficient amounts of iodine, which is provided by dietary intake. The only function for ingested iodine is for thyroid hormone synthesis.<sup>5</sup> This observation led to the hypothesis that limiting dietary iodine intake could be used to control thyroid hormone production and potentially manage hyperthyroidism in cats. After more than a decade of research and development, a limited-iodine therapeutic food (Hill's® Prescription Diet® y/d™ Feline) containing < 0.3 ppm (mg/kg) iodine on a dry matter basis (DMB), is now available as an option for managing cats with hyperthyroidism.

### Iodine Content of Commercial Cat Foods

Iodine occurs naturally in many ingredients typically used in the manufacture of commercial pet foods (particularly fish, shellfish and fresh meats) and unless steps are taken to strictly control the iodine content of ingredients, the final iodine concentration in pet foods varies widely.<sup>6-9</sup> Commercial cat foods in New Zealand had iodine amounts ranging from 0.19 to 21.2 ppm in one study whereas in Germany a range of 0.22 to 6.4 ppm was reported.<sup>6,10</sup> Evaluation of 28 canned cat foods in the US revealed an iodine content ranging from 1.09 to 52.3 ppm (mean = 7.83) and 14 dry cat foods contained iodine amounts ranging from 1.34 to 5.94 ppm (mean = 2.77).<sup>9</sup> Based on these studies, the amount of iodine is much higher in many canned foods compared with dry foods and variability of iodine content is much greater in canned food.<sup>6,9-10</sup>

Multiple feeding trials have been conducted in a research colony using over 100 cats with naturally occurring hyperthyroidism to determine the safety and effectiveness of limited dietary iodine in the management of the disease. The results of all studies support that a therapeutic food with dietary iodine ≤ 0.3 ppm iodine (dry matter basis) provides a safe and effective management option for cats with naturally occurring hyperthyroidism. Serum total thyroxine concentrations return to the normal range within 4 to 12 weeks of initiating nutritional management and 90% hyperthyroid cats maintained on the limited-iodine food as the sole source of nutrition become euthyroid.

Three studies were designed to determine the magnitude of iodine control necessary to return newly diagnosed cats to a euthyroid state;<sup>11</sup> the maximum level of dietary iodine that maintains cats in a euthyroid state;<sup>12</sup> and the effectiveness of a therapeutic food formulated based on the previous studies to control naturally occurring hyperthyroidism in cats.<sup>13</sup> In summary, results of these studies demonstrated that a food with 0.17 or 0.32 ppm iodine (DMB) maintained normal thyroid hormone concentrations in hyperthyroid cats, helping to further define the range of iodine effective for managing hyperthyroidism. We have treated 22 cats to date with feline y/d with follow-up data for at least 6 months. All of the cats found at least one form of the diet (dry or canned) to be palatable. Nineteen of 22 (86%) cats experienced clinical improvement with normalization of their TT4 concentrations. Of the three cats that failed to achieve remission, 2 cats were discovered to be eating foods other than y/d and when the owners switched them to y/d exclusively remission of hyperthyroidism was achieved. One cat (5%) failed to respond to dietary therapy and was subsequently treated with 131-I.

We are currently conducting a prospective study evaluating the efficacy of feline y/d in managing feline hyperthyroidism to include monitoring of thyroid function (TT4, fT4ED, TSH), clinical signs, body weight, renal function and blood pressure pre and post-treatment. The study should be completed in 2013.

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### Newly Diagnosed Patients

After confirming the diagnosis and performing a thorough patient evaluation, nutritional management should be discussed along with other options for managing hyperthyroidism. If selected as the management option, gradual transition to the limited-iodine food (Hill's® Prescription Diet® y/d™ Feline) over at least 7 days is recommended. It is very important to counsel owners so they understand that success of nutritional management depends on the limited-iodine food being the sole source of nutrition for their cat.

The first recheck evaluation should be done 4 weeks after completing the transition to y/d Feline (i.e., once the cat has eaten y/d exclusively for 4 weeks) and as a minimum should include physical examination and measurement of T<sub>4</sub>, BUN, serum creatinine, and urine specific gravity. All cats should have decreased T<sub>4</sub> concentrations compared with baseline and many will have returned to normal by the 4-week evaluation. Clinical improvement including weight gain, improved hair coat and decreased tachycardia/cardiac murmur also may be noted by the first evaluation. Clinical signs should continue improving by the next re-evaluation at 8 weeks and most cats will be euthyroid. Some cats require slightly longer to become euthyroid; however, it's expected that 90% will have normal T<sub>4</sub> concentrations if the limited-iodine food is their sole source of nutrition.

If euthyroidism is not achieved within 4 to 12 weeks, a thorough history is indicated to confirm that only the limited-iodine food is being fed.

### Long-Term Monitoring

Once a euthyroid state is achieved, it's appropriate to continue patient monitoring indefinitely. For stable patients without concurrent disease, evaluation (including T<sub>4</sub>) can be done every 6 months during the recommended wellness examination; it's acceptable to monitor more often if the clinician believes it's indicated based on clinical judgment of individual patients/owners. Hyperthyroid cats with concurrent diseases generally should be evaluated at least every 3-4 months.

### Feeding Limited-Iodine Foods to Healthy Cats

Feeding a limited-iodine food to healthy cats for up to 1 year has not been associated with any ill effects. Twelve cats randomly assigned from a group of 42 adult cats (14 neutered males and 28 spayed females) ranging in age from 1.6–13.6 years (mean = 8.1 years) were fed a food with iodine amounts of either 0.15–0.17 ppm or 0.22–0.24 ppm.<sup>14</sup> No physical examination abnormalities were noted and serum T<sub>4</sub>, T<sub>3</sub>, and free T<sub>4</sub>, and results of CBC and serum chemistries were within normal limits for the duration of the study.

The minimum iodine requirement for healthy cats has not been clearly established and there is a discrepancy between recommendations of the Association of American Feed Control Officials (AAFCO) and National Research Council (NRC). In the most recently reported study, iodine requirement was estimated to be 0.46 mg of iodine per kg (or ppm) of diet for adult cats.<sup>14</sup> The authors indicated that for adult cats, the level of dietary iodine necessary to cause clinical signs of iodine deficiency (e.g., thyroid hypertrophy, poor hair coat, myxedema, lethargy) and/or changes in thyroid hormone profiles must be < 0.15–0.17 ppm I DMB (lowest level fed in this study) because none of these changes were observed.<sup>14</sup>

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### Managing Hyperthyroid Cats with Concurrent Kidney Disease

Chronic kidney disease (CKD) and hyperthyroidism are more likely to be diagnosed in older cats so it's not surprising that many hyperthyroid cats have CKD. Untreated hyperthyroidism complicates the diagnosis of CKD because it's associated with increased glomerular filtration rate (GFR) and therefore often masks biochemical markers of CKD. Regardless of the therapeutic modality (methimazole, surgical thyroidectomy, or radioiodine), decreased GFR, increased serum urea and creatinine concentrations and development of overt clinical signs of kidney disease have been reported after successful treatment of hyperthyroidism.<sup>4,15-20</sup> The presence of underlying CKD may affect the prognosis - one study documented a shorter survival time in hyperthyroid cats with azotemia.<sup>21</sup> However, two recent studies comparing survival of cats that developed azotemia with those that did not after treatment of hyperthyroidism found no significant difference between the two groups if cats did not become hypothyroid post-treatment.<sup>22,23</sup>

The reported occurrence of azotemia after treatment of hyperthyroidism ranges from 15 to 49%.<sup>15,19-21,24</sup> Iatrogenic hypothyroidism has been reported to decrease GFR in human patients.<sup>25</sup> Post-treatment iatrogenic hypothyroidism has been reported in cats after radioiodine therapy and bilateral thyroidectomy, which constituted the predominant therapeutic modalities in previous studies.<sup>24</sup> In one recent study, cats with iatrogenic biochemical hypothyroidism were almost twice as likely to develop azotemia post-treatment as euthyroid cats.<sup>22</sup> The hypothyroid cats with azotemia had shorter survival times than cats without azotemia, whereas, consistent with previous reports, there was no difference in survival times of euthyroid cats with or without azotemia.

It's not possible to consistently predict which cats will develop overt CKD after treatment of hyperthyroidism or have progression of their kidney disease. This should be considered when deciding on treatment options, particularly those that are irreversible (thyroidectomy, radioactive iodine). Regardless of the option selected for managing hyperthyroidism, it's important to remember that the only intervention shown to improve quality of life and prolong survival time in cats with naturally occurring CKD is feeding a therapeutic renal food.<sup>26,27</sup> Until recent availability of limited-iodine food, nutritional recommendations have not generally been considered for hyperthyroid cats without azotemia. In cats with compromised renal function, but without azotemia (IRIS Stage 1), the decrease in GFR associated with normalizing serum T<sub>4</sub> levels may be sufficient to prevent effective clearing of protein metabolic by-products (BUN and creatinine) when dietary intake of protein and phosphorus is high. This could contribute to the occurrence of post-therapy azotemia in hyperthyroid cats.

Based on the nutrient profile, y/d Feline is a reasonable choice for managing cats with concurrent hyperthyroidism and CKD, especially for cats that do not have advanced kidney disease associated with uremic signs. When compared with typical feline foods available in the marketplace, y/d Feline contains controlled amounts of phosphorus, sodium, and high-quality/highly digestible protein; in addition it is supplemented with omega-3 fatty acids. Over a 10-year period, 108 cats with naturally occurring hyperthyroidism have been managed at the Hill's Pet Nutrition Center where limited-iodine food is the option of choice for managing hyperthyroid cats. Almost all of these cats had normal values for BUN and creatinine prior to beginning nutritional management of hyperthyroidism and a few were classified as having IRIS Stage I CKD (e.g., persistently low urine specific gravity). Acute azotemia or increasing BUN or creatinine values has not been observed as serum T<sub>4</sub> concentrations become normal in these cats, which have been followed from 3 months to five years. In many of these cats, serum creatinine

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concentrations have decreased after feeding the limited-iodine food, which is an unexpected finding. In our work with 22 cats with hyperthyroidism treated with feline y/d, 4/22 cats (18%) were azotemic (IRIS Stage 1 and 2 CKD) prior to starting the diet. All 4 cats experienced normalization of their BUN and creatinine within 30-150 days along with normalization of their TT4's. One potential explanation is that the expected decrease in GFR associated with normalizing serum T<sub>4</sub> may be offset by the nutrient profile of the limited-iodine food which is similar foods for mature adult cats or cats with early CKD. Additional study is needed to better understand the effects of using limited-iodine food on hyperthyroid cats with concurrent kidney disease.

### Conclusions/Summary

Hyperthyroidism is the most common endocrine disease of older cats worldwide. While the pathogenesis is unclear, several effective management options are available. All should be discussed with pet owners, including pros/cons, so that the best option can be selected for individual patients and their owners. Feeding a limited-iodine food is now available as an option for effective management of hyperthyroid patients. When fed as the sole source of nutrition, approximately 90% of hyperthyroid cats become euthyroid within 4 to 12 weeks. To date, over 150 cats with naturally occurring hyperthyroidism have been managed successfully by feeding a limited-iodine food, most for 2-3 years and some cats for as long as 6 years. ■

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**Table 1. Advantages/disadvantages of options for managing cats with hyperthyroidism**

Option	Advantages	Disadvantages
Thyroidectomy	Cures current tumor	High initial costs Requires anesthesia Hospitalization required Risk of post-operative hypocalcaemia Irreversible*
Radioactive Iodine	Cures current tumor Single treatment Effective for ectopic tissue Side effects uncommon	High initial costs Limited availability Hospitalization required Irreversible*
Anti-Thyroid Drugs	Routinely available Reversible Costs spread over time	Not curative (controls T <sub>4</sub> and signs) Daily administration needed Drug side effects
Limited-Iodine Food	Routinely available Reversible Costs spread over time	Not curative (controls T <sub>4</sub> and signs) Cat can only eat a single food

\*Important consideration due to potential for worsening renal function in cats with kidney disease