

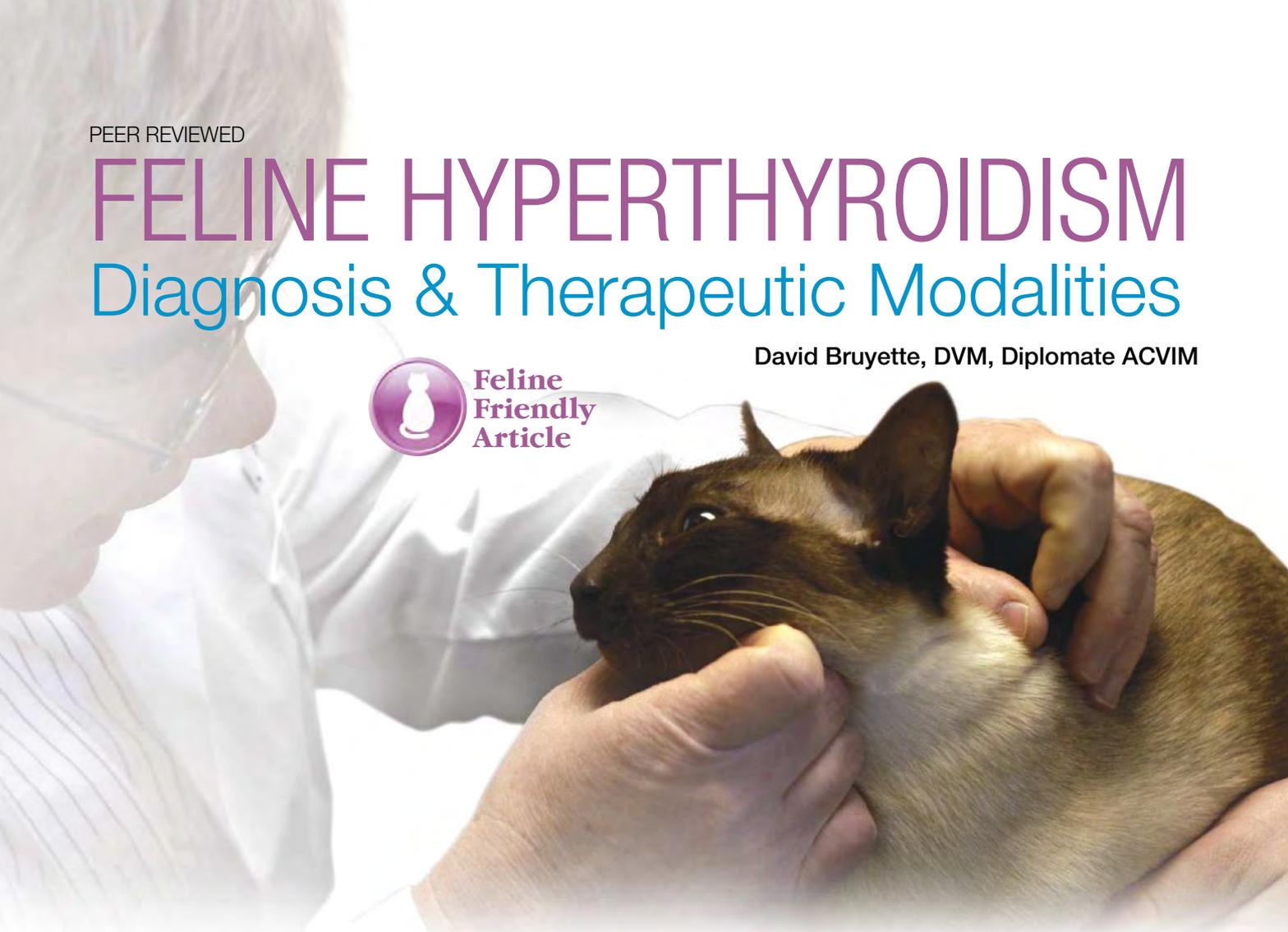
FELINE HYPERTHYROIDISM

Diagnosis & Therapeutic Modalities

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Feline
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Article



Hyperthyroidism is recognized as the most common endocrinopathy of older cats. Despite worldwide occurrence, though, its pathogenesis remains unclear.

Traditional therapeutic measures for managing feline hyperthyroidism include:

- Thyroidectomy
- Antithyroid medications
- Radioactive iodine.

Recent studies have documented another therapeutic option for hyperthyroid cats—a **limited-iodine diet**, which helps normalize thyroid hormone concentrations and alleviate clinical signs.

All therapeutic options are effective, with their own pros and cons.

- **Surgery** and **radioactive iodine** provide permanent treatment for feline hyperthyroidism.
- **Oral antithyroid drugs** and **nutritional management** must be administered daily to control hyperthyroidism if a permanent solution is not chosen.

DIAGNOSIS

Diagnosis of feline hyperthyroidism is based on:

- Presence of one or more clinical signs (see **Clinical Signs of Feline Hyperthyroidism**)
- 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 the reference range.^{1,2}

- Hyperthyroidism should not be excluded based on 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 reference range.³
- In these cases, serum free T_4 , measured by equilibrium dialysis (ft_4ED), may provide an alternative approach to diagnosis. Studies document that up to 20% of sick euthyroid cats can have increased ft_4 concentrations.⁴
- Therefore, it is appropriate and reliable to interpret the 2 values together:
 - » Mid to high serum total T_4 and increased ft_4 concentration is consistent with hyperthyroidism.
 - » Low serum total T_4 and normal or increased ft_4 values are usually associated with nonthyroidal illness.

MANAGEMENT OPTIONS

Methods of managing feline hyperthyroidism include:

- **THYROIDECTOMY** provides a permanent solution.
- **RADIOACTIVE IODINE** is considered the gold standard for treatment.
- **ANTITHYROID MEDICATIONS** are often oral and needed daily to achieve and maintain their effect.
- **LIMITED-IODINE DIETS** normalize thyroid hormone concentrations and alleviate clinical signs of hyperthyroidism.

Clinical Signs of Feline Hyperthyroidism

- Weight loss and poor hair coat
- Aggressive or “cranky” behavior
- Periodic vomiting
- Polyuria and polydipsia
- Increased appetite, activity, restlessness, and heart rate
- Occasionally, difficulty breathing, weakness, and depression

All management options can be ≥ 90% effective for controlling hyperthyroidism when used appropriately. The selected management option will differ for each cat based on several considerations (Table).

Radioactive iodine therapy is considered the gold standard for treatment of hyperthyroidism; however, most pet owners currently chose medical management with oral or transdermal antithyroid drugs. An additional option—nutritional management using a limited-iodine food—is now available for cats with hyperthyroidism.

RADIOACTIVE IODINE

Radioactive iodine therapy is often considered the best option for many hyperthyroid cats because:

- A single treatment has the potential to eliminate a benign thyroid tumor or abnormal thyroid tissue.
- Extra-thyroidal thyroid tissue, which may occur in 10% to 20% of hyperthyroid cats, is treated.
- No general anesthesia is required
- Reported side effects are minimal.

The goal of treatment is to restore euthyroidism with the smallest possible single dose of radioactive iodine, while avoiding development of hypothyroidism.⁶ Controversy exists as to the best method

of calculating the optimum dose for individual cats.^{5,6}

Cats should be in stable condition prior to radioiodine therapy; those with clinically significant cardiovascular, renal, gastrointestinal (GI), or endocrine (eg, diabetes mellitus) disease may not be good candidates, especially due to the required boarding time after treatment.⁵

Mechanism of Action

After administration, radioactive iodine is actively concentrated by the thyroid gland, with a half-life of 8 days.

- It 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 is expected.

Posttreatment Hypothyroidism

Based on the majority of reported cases, posttreatment hypothyroidism is transient and generally uncommon (2%–7% of cases); even fewer cats have clinical signs or appear to require thyroid hormone replacement.^{7–11} However, in 1 study, up to 30% (50/165 cats) were hypothyroid 3 months after radioiodine therapy; of these:

- 56% (19/34 hypothyroid cats with available information) had clinical signs of hypothyroidism.
- 52% (23/44 cats) were given thyroid hormone supplementation.¹²

Since hypothyroidism has been associated with azotemia and decreased survival time in previously hyperthyroid cats, thyroid hormone replacement may be needed in some cats, especially those with concurrent kidney disease.¹³ Owners should be advised of this possibility, particularly if their motivation for this particular treatment is to avoid long-term medical therapy.

TABLE. FELINE HYPERTHYROIDISM: THERAPEUTIC MANAGEMENT OPTIONS

Therapeutic Option	Advantages	Disadvantages
Antithyroid Drugs	<ul style="list-style-type: none"> • Routinely available • Reversible • Costs spread out over time 	<ul style="list-style-type: none"> • Not curative (controls T₄ and signs) • Daily administration needed • Drug side effects
Limited-Iodine Food	<ul style="list-style-type: none"> • Routinely available • Reversible • Costs spread out over time 	<ul style="list-style-type: none"> • Not curative (controls T₄ and signs) • Cat can only eat a single food
Radioactive Iodine	<ul style="list-style-type: none"> • Cures current tumor • Single treatment • Effective for ectopic tissue • Side effects uncommon 	<ul style="list-style-type: none"> • High initial costs • Limited availability • Hospitalization required • Irreversible*
Thyroidectomy	<ul style="list-style-type: none"> • Cures current tumor 	<ul style="list-style-type: none"> • High initial costs • Requires anesthesia and hospitalization • Risk of postoperative hypocalcemia • Irreversible*

* Important consideration; procedure may negatively affect renal function in cats with kidney disease

Limitations

The main limitation to widespread use of radioactive iodine is the requirement for special licensing and isolation of the cat after treatment, which can range from several days to several weeks depending on state or local radiation regulations and the dose administered.⁶

ANTITHYROID DRUGS

Antithyroid drugs are commonly used for treatment of hyperthyroidism in cats.¹⁴⁻²¹ 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.⁶ Almost all cats are potential candidates unless thyroid carcinoma is suspected.

Mechanism of Action

If administered appropriately, antithyroid drugs reliably inhibit the synthesis of thyroid hormones and, thereby, lower serum thyroid hormone concentrations. These drugs do not affect the thyroid gland's ability to trap inorganic iodide or release preformed hormones.

Administration

The antithyroid drugs used most often in cats are methimazole and carbimazole; both can be given orally or formulated for transdermal application.

- Custom formulation of transdermal products may increase expense of therapy and there is no guarantee of product stability.
- However, results of a recent prospective study showed that once daily treatment for 12 weeks with transdermal methimazole in a novel lipophilic vehicle was as effective as twice-daily carbimazole administered orally.¹⁴

Side Effects

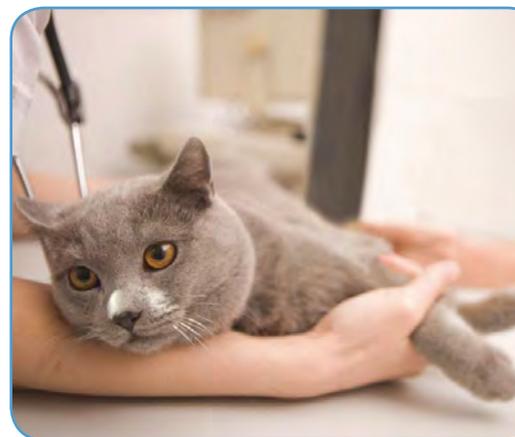
While many cats are successfully managed long-term with antithyroid drugs, it is important to monitor for side effects associated with their use.^{15,18,19,21}

- In the study with the largest number of cats, 18% had side effects associated with methimazole; a more recent study revealed that 44% of 39 cats had side effects.^{15,19}
- In 44 cats receiving carbimazole for 1 year, 44% had associated side effects, with GI signs (decreased appetite, vomiting, diarrhea) being most common.
- In another study, 13% of 39 cats treated with carbimazole experienced side effects.¹⁸

Determining what percentage of side effects are caused by the drug versus another factor, such as concurrent disease, is difficult.²¹

Most adverse reactions occur within the first few weeks to months after beginning therapy and include depression, inappetence, vomiting, and self-induced excoriations of the head and neck (facial pruritus).

- GI signs are less common with transdermal administration of methimazole.¹⁶
- Mild to serious hematologic complications, including agranulocytosis and thrombocytopenia either alone or concurrently and, more rarely, immune-mediated hemolytic anemia, may also occur.
- Hepatic toxicity with marked increases in bilirubin concentration and hepatic enzyme activity has been described in less than 2% of cats treated with methimazole.
- 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.⁶



Cessation of therapy is required if serious hematologic or hepatic reactions develop.

THYROIDECTOMY

Thyroidectomy for treatment of feline hyperthyroidism has become rare due to the availability of other therapeutic options.

NUTRITIONAL MANAGEMENT

A limited-iodine therapeutic food containing < 0.3 ppm on a dry matter basis (DMB) is now available as an option for managing cats with hyperthyroidism (Prescription Diet y/d Feline, hillsvet.com).

Mechanism of Action

Production of thyroid hormone requires sufficient dietary iodine. The only known function for ingested iodine is for thyroid hormone synthesis.⁵ 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.

Research Studies

Multiple feeding trials to determine the safety and effectiveness of limited dietary iodine in the management of feline hyperthyroidism were conducted in a research colony (over 100 cats) with naturally occurring hyperthyroidism.

- Study results showed that a therapeutic food with

dietary iodine \leq 0.3 ppm iodine (DMB) provided a safe and effective management option for cats with naturally occurring hyperthyroidism.

- Serum total thyroxine concentrations returned to a normal range within 4 to 12 weeks of initiating nutritional management and 90% of the hyperthyroid cats maintained on the limited-iodine food as the sole source of nutrition became euthyroid.

Three studies were designed to determine the:

- Magnitude of iodine control necessary to return newly diagnosed cats to a euthyroid state²²
- Maximum level of dietary iodine that maintains cats in a euthyroid state²³
- Effectiveness of a therapeutic food formulated (based on the previous studies) to control naturally occurring hyperthyroidism in cats.²⁴

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 amount of iodine that effectively manages hyperthyroidism.

A prospective study, which should be completed in 2013, is evaluating the efficacy of a limited-iodine diet in managing feline hyperthyroidism relative to pre- and posttreatment:

- Monitoring of thyroid function (T_4 , fT_4 ED, TSH)
- Clinical signs
- Body weight
- Renal function
- Blood pressure.

To date, over 150 cats with naturally occurring hyperthyroidism have been managed successfully by feeding a limited-iodine food, most for 2 to 3 years and some cats for as long as 6 years.

Administration

If the limited-iodine food is selected as the management option for a client's hyperthyroid cat, gradual transition to the food over a mini-

HYPERTHYROID CATS WITH CONCURRENT KIDNEY DISEASE

Because chronic kidney disease (CKD) and hyperthyroidism are often diagnosed in older cats, it is not surprising that many hyperthyroid cats have CKD.

Diagnosis of CKD is complicated by untreated hyperthyroidism because hyperthyroidism is associated with increased glomerular filtration rate (GFR) and, therefore, often masks biochemical markers of CKD.

Decreased GFR, increased serum urea and creatinine concentrations, and overt clinical signs of kidney disease have been reported after successful treatment of hyperthyroidism, regardless of therapeutic modality (methimazole, thyroidectomy, or radioactive iodine).^{4,30-33}

Prognosis may be affected by the presence of underlying CKD (see **Effects of CKD in Cats with Hyperthyroidism**).

Treatment options, especially those that are irreversible (thyroidectomy, radioactive iodine), should be considered carefully because it is impossible to consistently predict which cats will (1) develop overt CKD after hyperthyroidism treatment or (2) experience progression of kidney disease.

Feeding a therapeutic renal food is the only intervention shown to improve quality of life and prolong survival time in cats with naturally occurring CKD, regardless of the option chosen to treat hyperthyroidism.^{34,35}

A limited-iodine food is a reasonable choice for managing cats with concurrent hyperthyroidism and CKD, especially those that do not have advanced kidney disease associated with uremic signs.

- In cats with compromised renal function but no azotemia (IRIS Stage 1) being fed foods *high in protein and phosphorus*, decrease in GFR (associated with normalizing serum T_4 levels) may prevent effective clearing of protein metabolic by-products (blood urea nitrogen and creatinine).
- These factors could contribute to occurrence of posttreatment azotemia in hyperthyroid cats.
- The limited-iodine food contains *controlled amounts of phosphorus, sodium, and protein*; therefore, the nutrient profile of this food, which is similar to foods for cats with early CKD, may offset the expected decrease in GFR associated with a normalizing serum T_4 .
- Additional studies are needed to better understand the effects of using limited-iodine foods in hyperthyroid cats with concurrent kidney disease.

Effects of CKD in Cats with Hyperthyroidism

- A shorter survival time in hyperthyroid cats with azotemia has been documented.⁷
- The reported occurrence of azotemia after treatment of hyperthyroidism ranges from 15% to 49%.^{32-34,36,37}
- Two recent studies comparing survival of cats (after treatment for hyperthyroidism) that developed azotemia versus those that did not found no significant difference between the groups as long as the cats did not become hypothyroid posttreatment.^{38,39}
- Posttreatment iatrogenic hypothyroidism has been reported in cats after radioiodine therapy and bilateral thyroidectomy, which constituted the predominant therapeutic modalities in previous studies.³⁷
- Cats with iatrogenic biochemical hypothyroidism were almost twice as likely to develop azotemia posttreatment compared to euthyroid cats, according to 1 recent study.³⁸
 - » *Hypothyroid cats* with azotemia had shorter survival times than cats without azotemia.
 - » There was no difference in survival times of *euthyroid cats* with or without azotemia.

Iodine Content of Commercial Cat Foods

Iodine occurs naturally in many ingredients typically used when manufacturing commercial pet foods (particularly fish, shellfish, and fresh meats). Unless steps are taken to strictly control iodine content of ingredients, the final iodine concentration in pet foods varies widely.²⁵⁻²⁸

Commercial cat foods in New Zealand had iodine amounts ranging from **0.19 to 21.2 ppm** in 1 study, whereas in Germany, a range of **0.22 to 6.4 ppm** was reported.^{25,29} Evaluation of 28 canned cat foods in the U.S. revealed an iodine content ranging from **1.09 to 52.3 ppm**; 14 dry cat foods contained iodine amounts ranging from **1.34 to 5.94 ppm**.²⁸

Based on these studies:

- The amount of iodine is much higher in many canned foods compared to dry foods
- Variability of iodine content is much greater in canned foods.^{25,28-29}

mum of 7 days is recommended. It is very important for owners to understand that success of nutritional management depends on maintaining this food as the sole source of nutrition for their cats.

Follow-Up

The **first recheck evaluation** should:

- Take place once the cat has been eating the new food exclusively for 4 weeks
- Include, at minimum, a physical examination and measurement of T_4 , blood urea nitrogen, serum creatinine, and urine specific gravity.

All cats should have T_4 concentrations compared with previous baseline results; many will have returned to normal by the 4-week evaluation. Clinical improvements, such as weight gain, improved hair coat, and decreased tachycardia/cardiac murmur, may also be noted.

The **second recheck evaluation** should take place at 8 weeks.

- Clinical signs should show continued improvement by this evaluation.
- Most cats will also be euthyroid at this point; however, some cats require additional time.
- 90% of cats should have normal T_4 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.



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Long-Term Monitoring

Once a euthyroid state is achieved, it is appropriate to continue patient monitoring indefinitely.

- For stable patients without concurrent disease, evaluations (including T_4) can take place every 6 months during the recommended wellness examination.
- However, clinicians may schedule more frequent monitoring based on clinical judgment of individual patients/owners.
- Hyperthyroid cats with concurrent diseases generally should be evaluated at least every 3 to 4 months.

IN SUMMARY

Hyperthyroidism is the most common endocrine disease of older cats worldwide. While pathogenesis is unclear, several effective management options are available, including thyroidectomy, radioactive iodine therapy, and antithyroid medications. In addition, feeding a limited-iodine food is now an available option for management of hyperthyroid patients. All options should be discussed with pet owners to allow the best option to be selected for individual patients and their owners. ■

CKD = chronic kidney disease; DMB = dry matter basis; free thyroxine by equilibrium dialysis = ft_4ED ; GFR = glomerular filtration rate; GI = gastrointestinal; thyroxine = T_4 ; TSH = thyroid-stimulating hormone

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