

## Referring a Patient for Radioactive Iodine Therapy

Radioactive iodine therapy is still the treatment for feline hyperthyroidism that offers the highest cure rate of all available treatment options. In addition, it has been used to treat cats for over 30 years, so has a well-established safety record. At OSU, we can schedule up to 2 cats a week for radioactive iodine treatment. (Radioiodine appointments are scheduled on Mondays.) The estimate for radioactive iodine treatment at OSU is \$950-1250. This includes the exam, radioactive iodine administration, and three to five days of hospitalization. We have assembled the following FAQ to aid you in screening your hyperthyroid feline patients prior to referral so the procedure can be as smooth as possible for both you and your client.

### *1. What initial screening tests are required before a cat may be considered for radioactive iodine therapy?*

A physical exam, complete blood count, serum biochemistry, total T4, urinalysis, blood pressure, and methimazole trial are required for all cats prior to radioactive iodine therapy. These tests are considered necessary to diagnose hyperthyroidism and to screen for significant co-morbidities including renal disease. Pre-treatment urine concentration is not a reliable indicator of which cats will develop post-treatment azotemia.<sup>1</sup> Therefore, a methimazole trial to determine renal function during the euthyroid state is required. Additional testing (e.g. cardiology evaluation, thyroid scintigraphy) may be considered on a case-by-case basis, but is not routine.

Cats should be relatively stable before being considered for radioiodine therapy. Cats that have clinically significant co-morbidities may not be good candidates for treatment, considering the length of boarding and minimal monitoring and treatment capabilities during the immediate post-treatment hospitalization. Cats who require more than once daily monitoring or require medications that cannot be hidden in food are excluded from treatment.

### *2. What about cats that cannot tolerate methimazole?*

For cats that do not tolerate methimazole then a trial with Hill's Prescription Diet y/d may be considered. Euthyroidism must be induced and then maintained for four weeks. See guidelines for the methimazole trial below for the definition of euthyroidism and follow-up diagnostic testing. Alternatively, these cats could undergo a more in-depth work-up (e.g. GFR study) to try to better assess the risk of post-treatment azotemia. Please contact the Small Animal Medicine Service at OSU prior to referral to discuss patients that cannot tolerate methimazole or will not eat y/d.

### *3. How should the methimazole trial be performed?*

Methimazole does not block the release of preformed thyroid hormone, therefore there is a delay before serum T4 concentrations fully normalize after beginning treatment. We recommend starting methimazole (1.25-2.5 mg/cat) on a twice daily basis. Twice daily methimazole is preferable to once daily, as euthyroidism is reached more quickly.<sup>2</sup> The dose should be titrated every 2 weeks until euthyroidism is achieved. For the purposes of a methimazole trial, euthyroidism is defined as a T4 within the lower half of the reference range. Euthyroidism should then be maintained for 4 weeks as the degree of azotemia appears to stabilize by that point.<sup>3</sup> A renal profile and urine specific gravity should then be performed to determine if there is reasonable renal function.

### *4. What defines reasonable renal function?*

Creatinine levels will usually increase compared to the initial values following a return to euthyroid status.<sup>4</sup> This is theorized to occur secondary to an increase in muscle mass once hyperthyroidism is corrected and a decrease in GFR.<sup>5</sup> Reasonable renal function is defined as a serum creatinine within normal reference limits for the

diagnostic laboratory. Cats that develop an asymptomatic, mildly elevated creatinine during the methimazole trial may still be considered for radioactive iodine therapy on a case-by-case basis. Please contact the Small Animal Medicine Service at OSU prior to referral to discuss these patients.

*5. When should methimazole be discontinued prior to radioactive iodine therapy?*

Methimazole does not directly affect the iodide pump; therefore it does not interfere with the uptake of radioactive iodine into the thyroid adenoma. Time of discontinuation of methimazole prior to radioactive iodine administration has been shown to not affect the treatment response.<sup>6</sup> Therefore, some facilities do not routinely discontinue methimazole prior to treatment. However, use of methimazole up until the day of radioactive iodine treatment may lead to an increased risk of iatrogenic hypothyroidism. When hyperthyroidism is treated, TSH levels increase.<sup>7</sup> This will increase the activity of normal, nonadenomatous thyroid tissue, increasing the uptake of radioactive iodine into these tissues.<sup>8</sup> In addition, there is a “rebound effect” in normal thyroid tissue where radioactive iodine uptake is enhanced between 4 and 9 days after discontinuation of methimazole.<sup>9</sup> Therefore, we recommend a 2 week washout of methimazole prior to treatment with radioactive iodine.

For some cats, discontinuation of methimazole for 2 weeks prior to radioiodine treatment will not be feasible. These cats may have hypertension that becomes unmanageable despite medical therapy once hyperthyroidism recurs or may develop intractable gastrointestinal signs. Some cats with chronic, severe hyperthyroidism are at increased risk of a “thyroid storm” with discontinuation of the methimazole. In these select cases, methimazole may be used up until the day of radioiodine treatment. Please contact the Small Animal Medicine Service at OSU prior to referral to discuss patients you think may benefit from continued methimazole therapy up until the day of radioiodine therapy.

*6. When is a pretreatment cardiac workup required?*

The incidence and severity of cardiac manifestations of hyperthyroidism has decreased over time as recognition of hyperthyroidism occurs earlier in the course of the disease.<sup>10</sup> Based on the overall low prevalence of clinically relevant echocardiographic changes, routine screening of all cats prior to radioactive iodine therapy is low yield and is not recommended.<sup>11</sup> However, cardiac evaluations are offered for all cats identified with a heart murmur. Cardiac evaluations are only required for cats identified with dyspnea or an arrhythmia (including tachyarrhythmia >220 bpm) as these cats may require immediate intervention for their cardiac disease. The cardiac consultation can be performed the same day as the appointment with the Internal Medicine service. The cost for the cardiac consultation is an additional \$300-500.

*7. Is there a level of hypertension that would preclude treatment?*

There is substantial increased risk of hypertensive ocular injury and hypertensive encephalopathy at systolic blood pressures exceeding 180 mmHg.<sup>12</sup> Therefore, every effort should be made to decrease hypertension to below this level prior to radioactive iodine treatment with medical therapy (e.g. amlodipine, beta-blocker, ACE-inhibitor). Because of post-treatment isolation, there would be minimal intervention possible if the patient experiences an acute adverse hypertensive event. Difficult to manage hypertension is an indication for continuing methimazole up until the day of radioactive iodine treatment. However, it is recognized that the hypertension in some cats cannot be successfully managed until after they receive radioactive iodine therapy. Therefore, some cats with hypertension exceeding 180 mmHg may still be treated, but please contact the Small Animal Medicine Service at OSU prior to referral of these patients to discuss the case.

*8. When should a patient be rechecked following radioactive iodine therapy?*

Thyroid hormone concentrations normalize within two weeks of therapy in approximately 85% of cats.<sup>13</sup> Azotemia, if it develops, appears to stabilize within four weeks of therapy.<sup>3</sup> Hypertension can persist or may develop in the months following treatment as unmasked renal disease progresses.<sup>14</sup> Therefore, if the cat is doing clinically well at home, the first recheck is recommended four weeks post-treatment. At that time a physical exam, complete blood count, serum biochemistry, total T4, urinalysis, blood pressure should be performed. Please feel free to contact the Small Animal Medicine Service at OSU to discuss your patient’s follow-up labwork.

### 9. *When should persistent cardiac abnormalities be rechecked?*

Hyperthyroid-induced cardiac changes are largely reversible.<sup>15</sup> However, the absolute time to resolution of these changes has not been documented. Cardiac evaluations are recommended for all cats identified with a heart murmur or an arrhythmia (including tachyarrhythmia >220 bpm) that persists more than two months post-treatment.

### 10. *When should a cat be treated a second time with radioactive iodine?*

Approximately 5% of cats are persistently hyperthyroid post-treatment.<sup>13</sup> Most cats with persistent hyperthyroidism had large thyroid tumors, severe hyperthyroidism, and very elevated T4 concentrations.<sup>13</sup> If the hyperthyroid state persists for longer than three months after initial treatment, then a second radioactive iodine treatment is recommended.

## References

1. Riensche M, Graves T, Schaeffer D. An investigation of predictors of renal insufficiency following treatment of hyperthyroidism in cats. *J Feline Med Surg* 2008;10:160-166.
2. Trepanier L, Hoffman S, Kroll, M, et al. Efficacy and safety of once versus twice daily administration of methimazole in cats with hyperthyroidism. *J Am Vet Med Assoc* 2003;222:954-958.
3. Boag A, Neiger R, Slater L, et al. Changes in the glomerular filtration rate of 27 cats with hyperthyroidism after treatment with radioactive iodine. *Vet Rec* 2007;161:711-715.
4. van Hoek I, Lefebvre H, Peremans K, et al. Short- and long-term follow-up of glomerular and tubular renal markers of kidney function in hyperthyroid cats after treatment with radioactive iodine. *Domest Anim Endocrinol* 2009;36:45-56.
5. DiBartola S, Broome M, Stein B, et al. Effect of treatment of hyperthyroidism on renal function in cats. *J Am Vet Med Assoc* 1996;208:875-878.
6. Chun R, Garrett L, Sargeant J, Sherman A, Hoskinson. Predictors of response to radioiodine therapy in hyperthyroid cats. *Vet Radiol Ultrasound* 2002;43:587-591.
7. Graham P, Refsal K, Nachreiner R, Provencher-Boliger A. Measurement of feline thyrotropin using a commercial canine-specific immunoradiometric assay. *J Vet Intern Med* 2000;14:342 (abstract).
8. Fichetti A, Drost W, DiBartola S, et al. Effects of methimazole on thyroid gland uptake of <sup>99m</sup>Tc-pertechnetate in 19 hyperthyroid cats. *Vet Radiol Ultrasound* 2005;46:267-272.
9. Nieckarz J, Daniel G. The effect of methimazole on thyroid uptake of pertechnetate and radioiodine in normal cats. *Vet Radiol Ultrasound* 2001;42:448-457.
10. Fox P, Peterson M, Broussard J. Electrocardiographic and radiographic changes in cats with hyperthyroidism: comparison of populations evaluated during 1992-1993 vs, 1979-1982. *J Am Anim Hosp Assoc* 1999;35:27-31.
11. Weichselbaum R, Feeney D, Jessen C. Relationship between selected echocardiographic variables before and after radioiodine treatment in 91 hyperthyroid cats. *Vet Radiol Ultrasound* 2005;46:506-513.
12. Brown S, Atkins C, Bagley R, et al. Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med* 2007;21:542-558.
13. Peterson M, Becker D. Radioiodine treatment of 524 cats with hyperthyroidism. *J Am Vet Med Assoc* 1995;207:1422-1428.
14. Elliott J. Feline hypertension: diagnosis and management. Proceedings of the 27<sup>th</sup> World Small Animal Veterinary Association Congress; 2002 Oct 3-6; Granada, Spain.
15. Moise S, Dietze A. Echocardiographic, electrocardiographic, and radiographic detection of cardiomegaly in hyperthyroid cats. *Am J Vet Res* 1986;47:1487-1494.