

## Chronic Kidney Disease/Hyperthyroidism/Iodine 131: *Considerations and therapeutic options that enhance our success*

Even though about 35% of hyperthyroid cats have some degree of renal insufficiency, most are candidates for I131. Chronic kidney disease (CKD) isn't caused by hyperthyroidism, nor does it inevitably preclude treatment with I131. But it does necessitate screening hyperthyroid cats for CKD, carefully assessing their candidacy for I131, and setting up the best protocol for each individual's post I131 care.

### Screening Hyperthyroid Cats for CKD

#### A Urinalysis comes first:

We require a urinalysis in every cat we evaluate for hyperthyroidism, because it reveals the earliest signs of CKD and detects infections that may be silently destroying renal tissue. Most cats with CKD fail to concentrate urine (SG<1.040) before they have elevations in BUN and creatinine, especially with thyroid disease.

Decreases in SG, as well as signs of pu/pd, are usually due more to renal insufficiency than to hyperthyroidism. Microalbuminuria can be seen with hyperthyroidism and CKD.

Note: Uretic diets and SQ fluids can both cause urine dilution, so let us know if either influenced your sample. If you are unable to get a UA at your practice, we'll obtain one and will send the results to you when your patient is at FHTC for the pre-treatment consultation.

#### The Blood Work:

Although both the **BUN and Creatinine values may be "masked"** by the increased glomerular filtration rate (GFR) associated with hyperthyroidism, the creatinine seems to be more so, and therefore has less meaning in the hyperthyroid cat. In other words, it is entirely possible for the creatinine to appear normal ( $\leq 1.8 \mu\text{g/dl}$ ) in the face of thyroid disease, despite a high BUN and low S.G.. This isn't fully understood, but contributing factors may include: decreased muscle mass causing lower creatinine levels, or increased food consumption in polyphagic cats can result in higher BUN levels.

Because most hyperthyroid cats have "beefy" RBC production with high hematocrits, even a slightly low Hct  $\leq 30$  is considered significant and may be a sign of non thyroidal illness. For example, cats in moderate CKD may have erythropoietin deficiency, but the anemia may be masked by hyperthyroidism.

**Electrolyte derangements** such as hyperphosphatemia, hypokalemia, and hypercalcemia are also signals that the kidneys are in more advanced, rather than early, failure.

#### The Physical Exam Counts:

Kidneys are often smaller, firmer and more irregular in more advanced stages of renal degeneration. These patients are also more likely to be dehydrated.

### Levels of CKD Affect Candidacy for I131

When screening hyperthyroid cats for I131 candidacy at FHTC, we classify their **renal function** as **no CKD, early** (stages 1 to early 2), **moderate** (stages 2+ to 3), or **end-stage CKD** (stage 4).

#### No CKD (normal)

Hyperthyroid cats with UA SG's  $\geq 1.040$  along with **normal BUN and creatinine values** usually have normal renal function. Barring other non-thyroidal illness, **they are typically good candidates for I131.**

#### Early CKD

Those with SG's  $\leq 1.040$ , probably have **some insufficiency**, even if not yet azotemic, or the azotemia is 'masked' by thyroid disease. If the SG is still above 1.018 and little or no azotemia (BUN $\leq 40$ ) is evident, they are often still in early stages (1-2) of CKD. Although CKD is somewhat unpredictable, these cats may have a few more years of a decent quality life as the renal changes are usually gradual. **We typically treat these cats with I131**, as long as the owners can accept the fact that their aging cat has another disease they'll still need to manage even after the thyroid disease is cured. The vast majority of CKD cats that we treat fall into this category and do well after treatment.

#### Moderate CKD

Hyperthyroid cats that are **moderately azotemic** (BUN $\geq 40$ ) with UA SG's  $\leq 1.018$ , +/- other signs of renal failure, are often heading into upper stage 2, if not 3, CKD. If the hyperthyroidism is very mild, one option for these cats would

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be to ignore it, or to partially correct the hormone level with a small dose of methimazole once a day. Rarely, y/d® seems to be a reasonable compromise for some of these cats with relatively short expected lifespans.

On the other hand, the hyperthyroidism may be too severe to ignore, the cat can't tolerate the methimazole, and won't eat the y/d®. Also, some owners wish to invest in the best chance this cat has for a better quality life, for whatever amount of time he/she has left. Moderately azotemic cats may not be ideal, or even 'good' candidates, but elimination of the hyperthyroidism via **I131 is still their best medical option** for a longer and more comfortable life. **We do treat some of these cats with I131**, and are happy to counsel you about your patient's candidacy on a case by case basis.

### End-stage CKD

**We don't advise I131 therapy for hyperthyroid cats in end-stage CKD.**

Cats with isosthenuria, severe azotemia (BUN $\geq$ 70), and other clinical and laboratory signs of overt renal failure are simply too compromised to regain their health regardless of elimination of the thyroid disease. We worry about the owners of these cats spending money and raising their hopes for their cat's recovery to no avail. Low-dose methimazole is typically the best option for this group of cats.

## Treatment Goals and Plans for Recovery

Our **GOALS** with I131 therapy are to:

1. **Obliterate the thyroid tumor(s)**
2. **Avoid methimazole and y/d®**

The thyroid adenoma(s) or adenocarcinoma(s), present in every HT4 cat, are destroyed in the vast majority of cats treated with I131 after a single injection, thereby eliminating the need for ongoing treatment with other modalities.

However, about 3-5% of hyperthyroid cats have thyroid tumors that do not absorb I131 very well, referred to as poor radioiodine uptake ability (RIU). These cats require a second treatment to destroy all remaining hyperactive thyroid cells.

Conversely, 3-5% of all cases we treat will need thyroid hormone supplementation after the hyperthyroidism is resolved, either because insufficient normal tissue remains or it can't reactivate.

**Whether a cat needs a second treatment with I131 or requires thyroid hormone supplementation, the therapy is considered successful if the hyperactive tissue is ultimately obliterated, thereby eliminating the hyperthyroidism.**

## Management POST I131

How well CKD cats do after successful I131 treatment depends in part upon how they are managed medically and at home.

**The keys to restoring health in CKD cats after the hyperthyroidism is eliminated are:**

1. **Correction of low thyroid hormone levels**
2. **Management of CKD long term**

We monitor and correct low **thyroid hormone levels** more assertively in cats with CKD as they are less tolerant of the hypothyroid state than are cats with no kidney disease.

Hypothyroidism, T4  $\leq$ 1.25  $\mu$ g/dl, may cause a decrease in glomerular filtration, which could accentuate the azotemia and lead to more rapid decline.

Continued **management of the renal failure** is also crucial for recovery. We explain to your client that ongoing management of the CKD will be needed at home as the kidneys gradually fail to do their 'jobs', those in early insufficiency requiring less intervention than those in moderate failure. We encourage them to continue this conversation with their primary veterinarian and suggest that timely rechecks with you are more important than ever.

## Protocols for CKD Cats Post I131

After I131, we approach the management of cats in EARLY CKD differently than we do those in MODERATE CKD. We will fax a letter to you, the referring veterinarian, with one of two **protocols based on EARLY vs MODERATE CKD**. This letter, familiar to most of you, details:

1. Approximate **LEVEL (EARLY vs MODERATE)** of renal disease
2. **Interpretation of lab changes** post I131 (expected corrections or "unmasking" BUN, Cr)
3. **Thyroid hormone supplementation** guidelines (why, when, how much)
4. **Other considerations** for treating cats with renal disease long term

The primary difference in the following **protocols for EARLY or MODERATE CKD** involves the timing of thyroid hormone supplementation.

### EARLY CKD Protocol

If the urine specific gravity is dilute (<1.040), but the BUN is normal to mildly elevated (BUN 35-45), we express a concern about the possibility of decreased renal reserves to the owner.

We advise the client that thyroid hormone supplementation may be necessary if the thyroid hormone falls below normal and remains low after I131.

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We do not automatically initiate thyroid hormone supplementation prior to the first recheck post I131 in cats with early CKD.

### Indications for Thyroid Hormone Supplementation Post I131 in EARLY CKD

If the T4 drops below 1.25  $\mu\text{g}/\text{dl}$  by the 1 month recheck post I131, we advise supplementation, especially if the renal values have worsened.

Sometimes the T4 is temporarily low at the first recheck, and then increases to normal as the remaining thyroid tissue reactivates. If the cat is doing well clinically and the renal values have not worsened significantly, you may be able to wait and recheck all values again in 2 months before starting l-thyroxine supplementation.

If the T4 is still low 3 months out from I131, supplementation may be necessary indefinitely. Fortunately this occurs in less than 10% of the CKD cats we treat.

An elevated cTSH level may prove the hypothyroidism, and indicates a need for supplementation.

Note: We typically have canine (there is no feline) TSH's run at Michigan State University.

Occasionally, months down the line, if the residual thyroid tissue regenerates some, it may be able to produce enough thyroid hormone, making supplementation no longer necessary.

If you decide to reevaluate at some point, to see if your patient actually still needs hormone supplementation, discontinue the l-thyroxine 14 days prior to lab work to get a meaningful result.

Note: We use Leventa® (Schering Plough®), a liquid l-thyroxine that is palatable for cats. Give 0.1 mg=0.1 ml/cat/day either on an empty stomach or with a very small amount of food. 1 bottle contains 30 ml=300 doses, and is stable for 12-18 months in the refrigerator.

### MODERATE CKD Protocol

Hyperthyroid cats that are **moderately azotemic** ( BUN $\geq$ 45 ), with UA SG's <1.018, +/- other signs of renal failure, are often heading into upper stage 2, if not 3, CKD.

**Azotemic cats in MODERATE CKD** require a different approach than those in EARLY CKD.

In cats with moderate renal failure, even transient hypothyroidism following I131 can contribute to renal function decline. A lower-than-normal GFR associated with iatrogenic hypothyroidism (IH) not only unmask, but can accelerate the progression of the renal failure. Therefore, even transiently low thyroid hormone levels must be prevented in this group. We no longer wait for the initial rechecks to determine a need for supplementation in azotemic cats.

**In order to prevent even a temporary T4 trough in azotemic cats, we begin thyroid hormone supplementation as soon as the T4 level is expected to drop off.**

Studies show that thyroid hormone level decrease significantly in 77% of cats 6 days after I131 therapy. Therefore, we have the owners begin l-thyroxine 6 days post I131 in these cats.

We dispense Leventa® to the owner at their initial appointment with us, the day of the I131 treatment, with instructions to give 0.1 mg once daily. The 0.1 ml can be put inside the cat's cheek, or given in a small amount of food.

**We prepare the owner for the fact that their cat may very well need oral hormone replacement for life.**

The 1-month post I131 recheck is done while the cat is on the thyroid hormone supplement. The T4 may be elevated from supplementation at this time. This is generally not a problem. Our goal is to destroy the thyroid tumor(s), and to prevent a T4 trough, not to perfect the T4 immediately. We can start decreasing the supplement until the desired T4 range of 1.25 to 2.5  $\mu\text{g}/\text{dl}$  is met.

Sometimes the T4 continues to be, or becomes higher than we'd like on the Leventa®, in which case we may discontinue it and recheck the T4 value 2 weeks later to see if supplementation is still necessary.

### Managing the CKD: Other Considerations

Along with curing the hyperthyroidism with I131, and correcting low thyroxine levels as needed afterwards, the CKD must be managed long term to optimize your patient's recovery.

**Considerations for managing renal failure patients include:**

1. Check BP and correct if hypertensive
2. SQ fluids prn to correct dehydration (correct hypertension prior to fluid administration)
3. Check Hct and initiate erythropoetin if anemic (<30)
4. Renal failure diets only if BUN >60, and only if they'll eat them well

Note: We do not suggest feeding CKD cats protein-restricted diets until the azotemia reaches an 'unlivable' level, usually over 60 mg/dl. Obligate carnivores require meat protein for energy and to rebuild muscle. Hyperthyroid cats suffer from muscle wasting, making this even more important. Heart muscle damaged from thyrotoxicity is more likely to remodel and repair if the cat eats a lot of meat-based proteins found in canned and raw cat diets.

5. Potassium: supplement if K+ <4.0
6. Cobalamine Q 2 weeks (low in many azotemic +/- HT4 cats)
7. Phosphorus binders if hyperphosphatemic
8. Appetite stimulants (mirtazapine), antiemetics (Cerenia®), H2-receptor blockers Note: Renal clearance of mirtazapine is poor in CKD cats, so doses higher than 1.0 mg/cat Q 3 days may cause more agitation in some cats. (over)



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## **INSIDE: Chronic Kidney Disease/Hyperthyroidism/Iodine 131 - *Considerations and therapeutic options that enhance our success***

9. Urinalyses at all rechecks. UTI's in older cats are more likely related to pyelonephritis than simple cystitis, so C/S and longer term antibiotics are indicated.

### **What should we be telling our clients about I131 therapy in hyperthyroid cats with CKD?**

I131 therapy remains the treatment of choice for most hyperthyroid cats with early insufficiency, and occasionally for those in moderate stages of renal failure. If the cat has significant thyroid disease, it is still best to destroy the thyroid tumors and eliminate the thyroid disease, even if it means supplementing with l-thyroxine afterwards, a small price to pay for better health.

Veterinarians should avoid telling clients that treating their cats with I131 assures them that no oral medication(s) will be necessary. Not only do some of these cats need thyroid hormone supplementation after I131, but they require medical management of their CKD as well.

As always, we're here to help you screen your hyperthyroid cats with CKD for candidacy for I131 treatment. We will assist you to set up a protocol specifically designed for each individual to help ensure their recovery from hyperthyroidism and stabilization of their CKD for as long as possible.

If you have any questions about this information or have a case you'd like to discuss, please feel free to call us!

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### **Upcoming Newsletters:**

Etiology of Hyperthyroidism and Why Some Cats Go 'Round Again • Other Considerations: Optimizing Recovery After I131  
Methimazole Trials: What Are They Good For?

*We're available to consult about these topics any time – please contact us if you have any questions.*

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