OPTIMIZING RECOVERY FROM HYPERTHYROIDISM

The time before I-131 treatment until the thyroid disease resolves can be the most challenging for hyperthyroid cats.

These cats may be debilitated from hyperthyroidism and often have concurrent disease(s). Some cats simply have “too much other disease” to warrant I-131 therapy. Others will do fine after I-131, but may require ongoing management of any concurrent diseases to regain their health.

Important points to remember are that I-131 will resolve the hyperthyroidism, and the isotope does not cause radiation illness, but recovering from thyroid disease and stabilizing any non-thyroidal illness (NTI) takes time and conscientious medical management.

The Challenges:
Even if the cat’s thyroid disease has been more or less controlled on methimazole, when we discontinue it prior to radioiodine therapy, in order to maximize uptake of the isotope into the hyperactive thyroid tissue. Thus, the thyroid disease is temporarily uncontrolled before finally being resolved and the signs must be managed.

With ‘run-away-train’ metabolisms, hyperthyroid cats burn calories faster than they can eat them, and resort to catabolizing (breaking down) their own muscle. They also have extended changes in glucose and insulin metabolism making it difficult to rebuild muscle for awhile even after thyroid health is restored.

In addition to generalized weakness and muscle loss, hyperthyroidism can cause potassium wasting, dehydration, vomiting, diarrhea, poor cobalamin absorption, and hormonal mental distress. Signs of cardiovascular disease, such as hypertension, tachycardia, arrhythmias, and sometimes even pleural effusion, may be influenced or entirely due to thyrotoxicity.

Non-thyroidal illnesses such as CKD, primary GI disease (IBD, LSA), infections, periodontal disease, HCM, pancreatitis, or diabetes mellitus often complicate matters. If chronically ill, these cats may have weakened resistance to bacterial infections, and viral or parasitic residents may ‘flare’.

Optimizing Recovery
Once your patient’s candidacy for I-131 therapy is established we encourage plans to:

- stabilize the cat as much as possible before travel to our facility,
- manage their signs of both hyperthyroidism and NTI’s during hospitalization for I-131
- and for continued guidance by their primary care veterinarian after they return home to their owner’s care.
Thyroidal or Non-Thyroidal Illness (NTI?)

Statistical Correlation and What Really Matters

It may be difficult to differentiate which signs are due to HT4 and which are related to NTI.

Some signs have a high statistical correlation to thyroid disease. For example, tachycardia is most likely related to thyroid hormone elevation in HT4 cats, so it’s pretty safe to assume that the heart rate will decrease when the thyroid hormone normalizes. Likewise, thyroid nodules (adenomas, adenocarcinomas) are almost invariably productive, and we know that the thyroid hormone levels will return to normal after the hyperactive tissue is no longer functional.

Other signs of illness have no statistical correlation to thyroid disease, hence, there’s an equally good chance they are caused by something else.

Heart murmurs, for instance, are not statistically correlated to HT4; therefore, HM’s may or may not disappear after resolution of the thyroid disease.

Most gastroenteric signs, such as vomiting and diarrhea, have no statistical correlation to hyperthyroidism. We now believe that gastroenteritis in hyperthyroid cats often has a primary etiology, such as IBD or LSA, and is simply aggravated by thyroid disease. An exception might be the cat with very high thyroid hormones, which may cause both vomiting and diarrhea. If GI signs continue after the T4 normalizes, further diagnostics for a non-thyroidal etiology should be pursued.

Regardless of the underlying cause of the signs, they must be treated in order to improve the patient’s recovery.

When Do We Treat: Before or After T4 Normalization?

Veterinarians are often reluctant to assign treatments until known to be absolutely necessary, because it’s tough to pill cats, medications may have side effects, and they need to be monitored, typically by laboratory testing which adds expense.

Waiting to see which signs disappear once the T4 normalizes may be ok in some relatively robust cats with low-level symptoms.

On the other hand, frail patients require more aggressive management to prepare them for travel and hospitalization at our facility, and ultimately, to recover.

Which issues require intervention depend upon the severity of the disease, thyroidal or concurrent illness, as well as the cat’s general condition. For example, hypertension should be controlled before travel, but moderate liver enzyme elevations don’t usually require immediate intervention. Cats with cardiac failure require immediate stabilization, whereas diagnostics for chronic enteritis may be postponed until the thyroid disease is resolved, and excluded from the etiology differential.

No Overnight Cure: How Long Before the Hyperthyroidism is Resolved?

We advise your clients that the I-131 doesn’t eliminate the thyroid tumor(s) overnight. The thyroid hormones must decrease before they’ll begin to notice much improvement in their cat’s health. This process generally takes days to weeks, but may
occasionally take months. Some cats (3%) require a second treatment with I-131 to destroy all remaining hyperactive tissue, and therefore have an extended recovery period.

**Is it a Good Idea to Begin Methimazole Before or Resume it After I-131?**

If the cat hasn’t been on methimazole, we usually don’t recommend starting it if treatment with I-131 is soon. Unless significant renal failure is suspected, we no longer advise methimazole trials in the vast majority of cases. It’s usually best to simply treat with I-131 and eliminate the thyroid disease straight away, thereby avoiding potential side effects of the methimazole and delaying cure, as well as reducing cost and inconvenience for the owner.

The majority of candidates for I-131 are relatively stable, with slightly to moderately high T4 levels and no overt heart failure. If they’ve been on methimazole, they typically go off it 1 week prior to I-131, and never resume it.

Uncommon exceptions might be cats with severe heart disease or emaciation. The concern is that they’ll destabilize if off the methimazole. In these instances, we may discontinue the methimazole only a day or two before I-131 to enhance radioiodine uptake, and resume a day or two afterwards. By doing so we hope to protect the heart from undue thyrotoxicity and/or reduce cachexia while waiting for the thyroid disease to resolve. The methimazole would be discontinued about 3 weeks after I-131, or a week prior to the 1-month recheck.

**Other Considerations: Signs of Disease, Treatment Options**

**Mental Stress:**
Elevated thyroid hormone levels cause agitation and anxiety. At home these cats may haunt the halls with caterwauls, race around, and display aggression with the other animals in the household. They may be more clingy or irritable with their human companions, and don’t travel well.

**Ramping it down:**
We give anxiety-ridden cats alprazolam once daily while hospitalized, including the morning of their trip home. Ideally, this medication could be prescribed by the primary care veterinarian and started before they travel to us.

We do everything we can to create a stress-free environment at the FHTC, including cage drapes, no dogs, clean, soundproofed exam rooms and hospital wards, and we sometimes spray feline pheromones (Feliway®) into cages and carriers.

Occasionally we lightly anesthetize fractious cats in order to fully examine them and to administer the radioiodine. We want the cat to receive its entire dose, and need to avoid accidental exposure to our staff. If we receive an impression from the RDVM’s medical records or the owner that their cat has difficulty coping with veterinary visits, we try to prepare them in advance for the possible necessity of sedating their cat.

**Catabolism:**
Cats recovering from hyperthyroidism have typically been in a catabolic state with significant alterations in glucose metabolism. As carnivores, these patients need high amounts of meat-based proteins, found in canned and raw diets.
Protein-restricted renal failure diets should be reserved for those cats in advanced (stage 3,4) renal failure with severe azotemia, not our usual candidates for I-131.

**Cobalamin (B-12) Deficiency:**

Dr. Kenneth Simpson's (BVM. PhD, DACVIM, Cornell University) research relating to cobalamin deficiency in cats reveals that 40-47% of hyperthyroid cats are vitamin B-12 (cobalamin) deficient, and that percentage increases dramatically (60-70%) in those that are debilitated and/or have gastrointestinal disease. Low serum cobalamin is most likely a result from decreased ileal absorption of dietary cobalamin, rather than dietary deficiency.

Cobalamin deficiency isn't clinically recognizable, but depletions are linked with chronic wasting or failure to thrive, malaise, and gastrointestinal signs such as diarrhea. Hyperthyroid cats improve more rapidly after I-131 if concurrently treated with cobalamin; they gain weight more rapidly, feel better and have less diarrhea.

Although it's ideal to measure serum cobalamin, especially in cats with chronic gastrointestinal disease, we're not measuring concentrations in cats treated at FHTC. We err on the safe side and give 0.25 ml (250 µ) of 1000 µ/ml cyano-cobalamin SQ to the more debilitated patients. Cobalamin is inexpensive and harmless (any excess is readily disposed of by the body.) You may prescribe cobalamin to be given weekly (at home) until cobalamin levels are within your lab's normal range or, if treating empirically, about 6 weeks. It may be continued bi-weekly thereafter in cats with continued GI signs or longer-lasting thyroid disease.

**Dehydration:**

Hyperthyroid patients are predisposed to dehydration. They're typically older cats that often have some renal compromise and are unable to concentrate urine and conserve fluid as well, even if they're not yet in overt renal failure. The elevated thyroid hormone has a diuretic effect. And sick, stressed cats in the hospital don't always eat and drink enough.

We routinely give subcutaneous fluids to patients at risk for dehydration, and would recommend that you or your clients hydrate these cats before they arrive at our clinic, as well as after they go home. In cats with known chronic renal insufficiency, it may be ideal to continue SQ fluid administration daily or every other for 10 days after I-131.

Note: Both cats in CKD and those with HT4 are predisposed to hypertension. In either case, the BP should be established prior to fluid administration, and corrected if high.

**Hypertension:**

If the systolic blood pressure is higher than the normal ≤160 mm Hg, we start amlodipine (¼ of a 2.5 mg tablet orally Q 24 hours) to control the hypertension.

Uncontrolled hypertension in cats can cause retinal detachment, strokes, and worsens cardiac function. Because hypertension may worsen in hyperthyroid cats when off methimazole and hospitalized for treatment with I-131, we're more proactive about controlling it, not only while in the hospital, but for those first weeks at home as the thyroid disease resolves. We also advise treating hypertension prior to travel, especially if the BP is very high, the cat high-strung, and/or the travel prolonged or involving a flight.

Once the T4 is determined to be normal, at the post I-131 rechecks, you may opt to discontinue the amlodipine for 3-5 days.
and recheck the BP to see if this medication is still needed. If the BP remains elevated after the thyroid disease is resolved we assume other etiologies, such as CKD or heart disease, play a role and that the amlodipine (or benazepril) should be resumed and continued indefinitely.

Tachycardia:
Tachycardia is expected in most hyperthyroid patients. If the HR ≤ 220, we don’t intervene, without information about the heart function from a cardiologist’s assessment and echocardiography.

However, if a new patient’s heart rate is extremely high, e.g., 240-300 BPM, and remains so after an anxiolytic medication and rest in a quiet room with a cage drape, we may start a beta blocker, such as atenolol or propranolol, for rate control. We advise continuing the medication until the thyroid hormone decreases and the RDVM reevaluates at the post-I-131 recheck (s).

We also check the blood pressure in every cat with extremely high HR’s (240-300.) The β-blocker alone may or may not control the hypertension as well as lower the HR, in which case amlodipine is added.

A consultation with a cardiologist is advisable for cats with tachycardia (or bradycardia), heart murmurs, and/or arrhythmias, that persist after the thyroid hormone normalizes.

Hypokalemia:
Causes of hypokalemia, such as muscle wasting, vomiting, and urinary loss are common in hyperthyroid cats. Many of these older cats have renal insufficiency and pre-diabetes that cause potassium wasting. Those on diuretics for CHF are often hypokalemic as well. Chronic hypokalemia in turn may cause hypokalemic nephropathy, leading to even more loss.

Potassium is essential for nerve impulse transmission; smooth, skeletal and cardiac muscle contraction; and maintenance of normal renal function. Potassium is also needed for carbohydrate utilization and protein synthesis.

Severe hypokalemia targets neuromuscular and cardiac cells primarily. Classic signs may include ventroflexion of the head and neck, stiff gait, plantigrade stance, and cardiac arrhythmia.

Cats with mild to moderate hypokalemia don’t show clinical signs, so we depend upon laboratory evaluation to know when to begin supplementation. However, there are no universal reference ranges for potassium. Potassium levels are method dependent, and methods vary lab from lab. So, we can’t make a blanket statement that “K+’s below 4 mEq/L should be treated”. It’s best to establish that individual’s normal based on prior lab work, and to refer to your own lab’s reference range.

Keeping in mind that >90% of the K+ is intracellular and IC levels have to be depleted before the loss is evident in serum, it’s better to begin supplementation when the levels are even borderline-low for any cat, any lab.

For mild, chronic hypokalemia, we recommend oral potassium gluconate (Tumil K®, Renakare®) 2 mEq Q 12 hours.

Urinary Tract Infections:
In older cats, most urinary tract infections involve the kidneys. Inadequately treated pyelonephritis can cause the kidneys to degenerate more quickly.
We advise treating UTI's more aggressively in these patients, so that they don't exhaust scanty reserves of nephrons. Along with a UA, C/S testing is ideal, but if WBCs and/or bacteria are seen, we treat with longer term antibiotics even if the culture reveals 'no growth'. The expense to renal tissue of missing an infection is far greater than the risk of antibiotic treatment. The ease of an injection of Convenia® is appealing, but cephalosporins are less likely to be effective against cocci (often Enterococci) than rods (usually E. coli) and would best be reserved for use with those more susceptible bacteria with less resistance from repeated use.

**Anorexia:**

Not all hyperthyroid cats are polyphagic, especially if they have non-thyroidal disease(s) as well. Appetite stimulants, such as mirtazapine, can help. However, higher doses may amplify the agitation already present in many hyperthyroid cats. Also, mirtazapine clearance is delayed in cats with renal insufficiency. Therefore, the conservative dose of 1 mg Q 3 days is the recommended dose for these cats.

**Gastrointestinal Signs:**

*Regardless of underlying cause, vomiting and diarrhea should be controlled while waiting for the hyperthyroidism to resolve.*

- **Vomiting:** Nauseous cats not only eat less, but they are more likely to ‘lose’ what they do ingest. If undue vomiting is a presenting sign, we suggest dispensing a 4-tablet blister pack of Cerenia® (maropitant) 16 mg tablets, and giving 1/3 to ½ tablet per cat e.o.d. during the recovery interim.

- **Diarrhea:** If IBD or LSA are suspected/proven, initiating appropriate management with prednisolone, chlorambucil, hypoaalergenic diets, probiotics, and cobalamin may aid recovery. Because corticosteroids may worsen hypertension, it is wise to check the blood pressure prior to their use in hyperthyroid cats.

**What Should We Be Telling Our Clients?**

The time before I-131 treatment until the thyroid disease resolves can be the most difficult for hyperthyroid cats. Treating various signs of illness regardless of cause helps hyperthyroid cats recover more quickly. We encourage plans to stabilize these cats before travel to our facility, to manage their signs of both hyperthyroidism and NTI’s during their hospitalization, and for continued supportive care after their return home with the owner.

As always, feel free to contact us with any questions or concerns.

Best Wishes,

Faythe Vaughan and Dennis Wackerbarth