

# Borderline Thyroid Disease: Testing Updates

## *T4 via RIA is No Longer The Gold Standard*

We can all agree on the diagnosis for the “classic” hyperthyroid cat. However, many cats have physical and laboratory findings that are not black and white. Signs can be vague and overlap with co-existing conditions. Like making a diagnosis of FIP, we build a case based on multiple factors rather than any one test or sign. We assimilate history, labs, and physical findings to form a picture that “looks like” hyperthyroidism (HT4).

Let’s start by reviewing the diagnostic tests we might use. Some diagnostic tests and physical exam findings have higher value than others.

The most valuable indicators of hyperthyroidism are an elevation in total T4 values and the presence of thyroid nodules. However, in borderline cases, the T4 level may be equivocal and the nodules may be small and difficult to palpate. And even “the best” T4 tests have variable results. Comparing simultaneous thyroid test results, such as T4 and canine thyroid-stimulating hormone (cTSH), markedly improves overall diagnostic accuracy. Therefore, veterinarians should consider combining more than one test method for cats with equivocal disease.

## Thyroid Function Test Updates

### Total T4 Test

Know the upper limit of normal for the geriatric cat:

- We feel that the “normal” T4 ranges posted by most diagnostic laboratories are too high for geriatric cats.
- T4 values should be  $\leq 2.5$   $\mu\text{g}/\text{dl}$  in most older cats.
- The older the cat is, the lower the upper limit of normal will be. For example, a value of  $3.0$   $\mu\text{g}/\text{dl}$  may be normal in a 9-year-old, but is too high for many 15-year-olds.

### Method Matters for T4 Testing

1. The RIA method has been the “gold standard” for T4 tests for years.

However, regulations regarding radioactivity and recent disparity in RIA results have resulted in a search for alternative methods.

*Dr. Faye Sturtevant, DVM, PhD, and Director of Phoenix Central Laboratories (PCL) explains: “Manufacturers have changed and quality of materials is not consistent. Changes can be made to the kit components without communication from the manufacturer. These changes have little to no effect for human testing but may greatly affect veterinary results.”*

2. Chemiluminescent enzyme immunoassays, CEIA, (Immulite®) use the same type of antibody testing as RIA except instead of measuring radioisotope activity, a photomultiplier tube is used to count light emissions. Used by professional labs.
3. DRI® thyroxine assay: an enzyme immunoassay method is used by professional labs and in some analyzers designed for veterinary clinic use.
4. ELISA in-house assays, used in test kits designed for veterinary clinic use.

Unfortunately, we have seen far more inaccurate T4 levels with the in-house scans, so we depend more upon T4’s run by the professional diagnostic labs.

## Thyroid-Stimulating Hormone (TSH) Test

In humans, measurement of serum thyroid-stimulating hormone (TSH) concentration is commonly used as a first-line discriminatory test of thyroid function. Recent reports indicate that cTSH assays can be used to measure feline TSH and results can help diagnose or exclude hyperthyroidism.

*As Mark Peterson, DVM, ACVIM, Animal Endocrine Center, NYC suggests, “...finding undetectable serum TSH concentration with either a high T4 or high ft4 concentration markedly improves the overall diagnostic accuracy in this subset of hyperthyroid cats. Conversely, finding a measurable serum TSH concentration, even*

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*with high-normal T4 or fT4 concentrations, makes hyperthyroidism extremely unlikely. Thus, clinicians should consider combinatorial testing in cats with equivocal disease.”*

He adds, “Serum TSH concentrations are suppressed in 98% of hyperthyroid cats”, but concentrations are measurable in a few cats with mild-to-moderate hyperthyroidism. Measurement of serum TSH represents a highly sensitive but poorly specific test for diagnosis of hyperthyroidism and is best measured in combination with T4 and fT4.

Indeed, some investigators have suggested that a measurable TSH concentration effectively rules out hyperthyroidism in equivocal cases, especially in sick euthyroid cats.“

Note: “Undetectable cTSH” is defined as <0.03 ng/ml

## A Winning Combination: T4 and cTSH

*Combining results of cTSH and T4 tests improves the ability to correctly differentiate hyperthyroid cats with occult or mild disease from euthyroid cats* suspected of having thyroid disease, especially when serum concentrations of T4, T3, or fT4 are within the upper limits of their reference interval or are only marginally increased.

## Second Tier Tests

### Free-T4 via Equilibrium Dialysis (fT4(ED))

This test simply isn’t as accurate as we once thought: False positives are problematic.

- FT4 tests are not as specific as we used to believe. This means that non-thyroidal illness (NTI) affects this test. Approximately 20% of sick euthyroid cats have false positive fT4 results.
- Overweight cats often have falsely high fT4 levels. Fat cats have high fatty acid levels, which displace T4 from serum binding proteins.
- The fT4 ED assay presently in use simply isn’t as accurate as the original Nichols Diagnostics® assay used several years ago before the company sold the distribution rights. The false-positive rate is higher now, up to 25%.

### T3 Test

This test lacks sensitivity; about 25-30% of HT4 cats will have normal T3 values, so this test isn’t useful by itself.

## Methimazole Trials

We believe these have limited application for diagnosing hyperthyroidism.

Giving methimazole to normal cats will decrease thyroid hormone levels which may cause weight gain. In a debilitated cat, a methimazole intolerance could make the cat sicker and a trial might delay the search for the real cause of the cat’s condition. Driving the T4 lower can cause anemia and exacerbate azotemia, even if the cat has no thyroid disease.

We now use methimazole trials to define candidacy of cats in advanced (st 3) CKD for I-131, rather than as a test method to diagnose hyperthyroidism.

## Does The Cat Match The Lab Work?

Not every cat manifests every sign, as we all know. But most hyperthyroid cats show more than one sign of thyroid disease.

Look for supporting history:

- Polyphagia
- Polyuria, polydipsia
- Changes in behavior due to agitation caused by high thyroid hormone levels. Owners describe HT4 cats as “playful, restless, clingy, aggressive, and/or more vocal.” Some cats groom excessively; they may barber large areas or snatch tufts from their coats.
- Vomiting and diarrhea: These signs aren’t statistically correlated to HT4, meaning there’s an equal chance they’re caused by something else. But gastroenteritis of any etiology may be exacerbated by HT4.

Identify typical physical and laboratory findings:

- Unexplained weight loss
- Muscle wasting: thinning over the spine and hips despite ample fat in abdomen.
- Tachycardia and/or new heart murmur
- Thyroid nodule(s)
- Elevated ALT
- High-normal hematocrit (often 40-50% unless concurrent non-thyroidal disease)
- Creatines that are lower than expected with high BUN and low urine S.G.

- Hypokalemia
- Tachypnea: hyperventilation, especially during car rides or veterinary visits

## Correlate The Level of Illness: Does It Make Sense?

Borderline thyroid disease isn't typically responsible for severe illness. If a cat has severe illness with only mild T4 elevation, look for other possible etiologies.

If the T4 value doesn't make sense, or the result surprises you, always re-run a T4 in combination with a cTSH.

In cats that we're having difficulty clearly diagnosing as hyperthyroid, we tell the owners that thyroid disease may be emerging. On the other hand, borderline T4 values may be normal for this individual. Either way, I131 therapy is not generally warranted at such time.

## More Tests?

If a cat has pressing issues, such as cardiac disease or diabetes mellitus, which can be impacted by even low-level thyrotoxicity, we attempt to diagnose and eliminate the thyroid disease sooner than later.

## Dynamic Tests

### T3 Suppression Test

Normal thyroid glands suppress T4 production by at least 50% when an outside source of T3 is supplied. Hyperthyroid cats do not suppress.

The caveat: if the starting T4 is only slightly elevated to begin with, then a positive or negative response may be harder to identify.

Also, this test is cumbersome for the owner (7 tablets administered exactly every 8 hours, with a blood draw pre-administration and one 4 hours post). We are no longer advising it.

### Thyrotropin-releasing Hormone (TRH) Stimulation Test: Not Useful in Practice

In theory, giving TRH should boost T4; in hyperthyroid cats, the T4 doesn't rise.

Unfortunately, sick cats with NTI don't respond much to TRH either, so it doesn't help us tell them apart. We don't use this test.

## Technetium-99M (Pertechnetate) or I-123 Scans: Useful But Expensive

- Scintigraphy uses radioactive isotopes that don't harm thyroid cells and do identify thyroid tissue regardless of its location. This information is especially useful to identify ectopic thoracic thyroid masses in cats facing surgery for large neck tumors.
- Scans may identify abnormal iodine uptake in hyperthyroid cats even before blood test abnormalities or clinical signs appear.
- Scans are reasonable in cost (about \$260 at WSU). However, the exam, a couple of days' hospitalization, and travel multiply the cost.

Because most hyperthyroid cats with borderline T4 values and little signs of clinical disease probably don't have to be identified immediately, we seldom suggest that clients go to this trouble and overall expense.

## FNA of Thyroid Nodules

- May distinguish adenomatous hyperplastic from normal thyroid tissue, if the nodules are large enough to localize and aspirate. This is rare in the borderline cat.
- Large thyroid nodules should be aspirated, regardless of T4 level. Nodules, thyroid cancers, or non-thyroid cancers may or may not be associated with increased T4.

If a tiny nodule(s) is palpated, but the TT4 levels are normal and the cat has no signs of hyperthyroidism, it may be wiser to monitor rather than treat for hyperthyroidism prematurely.

## Can It Be Right To Do Fewer Tests?

If the cat has no significant symptoms and continues to be stable, simply waiting 3-6 months and retesting with a combination of T4 and cTSH tests is often the best and least expensive way to explore this.

*Good News: Phoenix Central Laboratories (PCL) now offers feline profiles which include cTSH.*



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## **INSIDE - Borderline Thyroid Disease: Testing Updates** *T4 via RIA is No Longer The Gold Standard*

### **Consultation Appointments**

We are here to help you with complicated or border-line cases. Consultation appointments (\$95.00) can help clarify the diagnosis, identify coexisting conditions, or shed light on non-thyroidal illness. We can assist in developing diagnostic and treatment plans, including I131 if indicated. Rest assured that we recommend treatment with I131 only when the diagnosis is clear and the patient meets treatment criteria. For consultation referrals, please provide all pertinent medical records.

*We'd like to thank Dr. Lora Schuldt, of Cats Exclusive Veterinary Center, for initiating the most recent investigation of disparate RIA test results. She recruited blood samples from 60 cats, and Dr. Faye Sturtevant tested each with 3 different T4 assays in order to compare and identify discordancy.*

*Dr. Sturtevant has continued to dedicate her time and PCL's additional testing, at no cost to the DVMs, to make certain we all receive the most accurate results possible.*

*Thank you both!*

As always, please feel free to contact us if you have any questions.

**Faythe Vaughan, DVM**

**Dennis Wackerbarth, DVM**

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