WHAT YOU SHOULD KNOW ABOUT HYPERTHYROIDISM IN CATS

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Hyperthyroidism is the most common endocrine disorder in the cat. Since being first recognized in 1977, the incidence has increased steadily. This is no doubt partly due to greater awareness and early screening, but certainly also to a real increase in occurrence of this disease. The etiology and pathogenesis are not certain, but epidemiological surveys have shown that an increased incidence of this disease is seen in cats:

* fed a majority of canned food in their diet;
* living strictly indoors, using litter;
* having a reported exposure to lawn herbicides, fertilizers, and pesticides;
* having been regularly treated with flea sprays or powders;
* who are NOT Siamese (one study only, breed predilection has not confirmed in any other study); and
* have been exposed to flame retardants.

The disease has been reported in North America, Europe, Australia, and New Zealand, but less frequently, or not at all, in other parts of the world. These risk factors implicate environmental, nutritional, and genetic factors. It is also logical to assume, however, that cats who are well cared for and thus live longer, will be exposed to litter and canned foods.

Some of the goitrogens that are being studied include iodine and phthalates (common in cat foods), resorcinol, polyphenols, and PCBs, all of which may also be in diets, especially those containing fish, or in the environment. These hydrocarbons need to be metabolized in the liver, by glucuronidation, a process compromised in the cat, making this species more prone to toxicities. Goitrogen exposure may be sporadic, rather than ongoing, as sporadic exposure has been shown to induce thyroid hyperplasia in experimental models. Other theories consider that nodular goiter development may be a normal age-related condition.

Regardless of the cause(s), the condition of hyperthyroidism is a multi-systemic disorder caused by excessive concentrations of circulating thyroglobulins, T4 and T3, produced most commonly by benign, hyperplastic adenomatous glands, but rarely by malignant, adenocarcinomatous glands. 97–99% of hyperplastic glands are benign and adenomatous. Approximately 70% of cases have bilateral disease, a fact that is critical when considering surgical therapy, and favors presurgery technetium scanning.

Most recently, attention has been directed toward brominated-flame retardants. Dr. Janice Dye presented an abstract at ACVIM 2007 in which she states: “Coincident with global introduction of BFRs into household consumer products nearly 30 years ago, hyperthyroidism in cats has increased considerably. The etiopathogenesis of feline hyperthyroidism remains unknown. We hypothesized that increasing exposure of pet cats to BFRs such as the polybrominated diphenyl ethers (PBDEs) has, in some manner, contributed to the abrupt increase in and now common occurrence of feline hyperthyroidism. . . . Our finding that pet cats in the U.S. have high PBDE serum levels is in good accord with the most consistently identified risk factor for development of FH, namely indoor living. We further propose that house cats—because of their meticulous grooming behavior—only come in direct contact with these consumer products, they readily ingest any volatilized PBDE-like material or PBDE-laden dust that deposits on their fur. Future studies are needed to elucidate if and how PBDE bioaccumulation of this magnitude in cats can disrupt maintenance of their thyroid-endocrine-axis.”

Signalment: While hyperthyroidism is a disease of middle aged to old cats (4–22 years old), it has been reported in cats aging from 8 months–22 years of age. There is no breed or sex predilection.

History: The frequency and severity of clinical signs has decreased since the condition was originally reported. This is likely due to screening, as clients often aren’t aware that the cat is ill early in this disease. In fact, because the thyroid hormones are generally anabolic and stimulatory, the client usually feels that the cat is in good health, with a good to excellent appetite, and is lively (in fact hyperactive) relative to its age. The only sign may be defecating outside of the litter box and/or large, voluminous stools.

In a study comparing findings in hyperthyroid cats in 1983 and 1993, weight loss was the most common historical finding in both studies, but its prevalence was much higher in 1983 (98% vs. 87% in 1993). Other clinical signs also
have significantly decreased prevalence in 1993 (all following statistics given as 1983 vs. 1993): polyphagia (81% vs. 49%), hyperactivity (76% vs. 31%), polyuria/polydipsia (60% vs. 36%), diarrhea (33% vs. 15%), muscle weakness (25% vs. 12%), panting (25% vs. 9%), large fecal volume (31% vs. 8%), and anorexia (25% vs. 7%). Vomiting is still prevalent in approximately 50%.

Exam findings: Generally thin, active, bounding, rapid heart with a cardiac murmur (b-lub-dub), palpably enlarged thyroid gland, +/- agitated, unkempt coat. Apathetic hyperthyroidism is a less common presentation (~5%) in which the cats are depressed, weak, and may be anorectic. Be aware that obesity may also be present in some hyperthyroid cats.

Physical examination findings in the 1993 paper: Number of cats (% of 202 cats): Large thyroid gland: 167 (83%), Thin: 132 (65%), Heart murmur: 109 (54%), Tachycardia: 85 (42%), Gallop rhythm: 30 (15%), Hyperkinesis: 30 (15%), Aggressiveness: 20 (10%), Unkempt hair coat: 19 (9%), Increased nail growth: 13 (6%), Alopecia: 6 (3%), Congestive heart failure: 4 (2%), Ventral neck flexion: 2 (1%).

Thyroid hormones regulate metabolic processes in virtually every tissue. Thus, increased appetite, weight loss, polydipsia, polyuria, vomiting, diarrhea, tachycardia, heat intolerance, hyperexcitability/nervousness, behavioural changes, tremor, and tachycardia are classic findings in the hyperthyroid cat. However, as the signs are gradual in onset and range from mild to severe, a client may not be aware of any abnormalities.

Preliminary testing: baseline CBC, chemistry screen, urinalysis, T4

Results: Elevations of the liver enzymes alanine aminotransferase (ALT) and serum alkaline phosphatase (SAP) are common findings in > 90% of hyperthyroid cats, although the cause for this is not clear. Histologic evaluation of the liver of these cats shows mild, nonspecific changes. SAP has been hypothesized to increase due to increased metabolism of bone. Increases in ALT are harder to explain, as ALT is an intra-hepatocellular enzyme, yet there is no increased hepatocellular membrane damage. Thyroid hormones may have direct toxic effects on the liver, and hypoxia, CHF, infection, and malnutrition may all play a role, but the exact cause for increases in ALT and SAP are not known. These enzyme values return to normal when euthyroidism is achieved.

Concurrent renal dysfunction is also fairly common in untreated hyperthyroid cats, allowing for low urine specific gravity (usg), +/- elevations of blood urea nitrogen (BUN) and serum creatinine (SC). However, the beneficial effect of the excessive thyroid hormone on cardiac output, causing an increase in renal blood flow, can also act to mask underlying renal disease. Therefore, it is essential to continue to monitor these renal parameters during therapy. Numerous studies have shown that amelioration of the hyperthyroid state by any method (i.e., medical therapy, 131I treatment, or surgery) can lead to decreased GFR, elevations in BUN and creatinine, and, in some cases, overt azotemia.

The question that remains is how to assess cats prior to definitive therapy (131I or surgery) and which cats need to be evaluated. One study found that none of the cats with a GFR above 2.25 ml/kg/min prior to 131I administration developed renal failure as the hyperthyroidism resolved. While this GFR value may represent a cut-off for deciding if renal failure/insufficiency is a possibility, measurement of GFR is not easily obtained, and another study could not substantiate this finding. Another option is to treat cats transiently with methimazole until the serum T4 is adequately controlled. When the serum T4 is maintained within the normal range, the effect of definitive therapy can be assessed. If renal failure does become overt after definitive correction of hyperthyroidism, exogenous thyroid hormone can be supplemented to support the kidneys. A balance must then be struck between creating iatrogenic hyperthyroidism and maintaining renal function.

Thyroid function tests: The total T4 is the first test used to assess thyroid function. Total T4 values may fall within normal reference range a) early in the course of disease; b) because of normal fluctuations of this hormone; and c) when there is concurrent, nonthyroidal illness present (“euthyroid sick syndrome”). When one is suspicious of hyperthyroidism but T4 values are normal, one can use one of the alternative testing methods or repeat the T4 measurement at a later date. In-house testing has been shown to be inaccurate for measurement of T4 in cats (and dogs).

Free T4 can be helpful in confirming a diagnosis of hyperthyroidism in a patient with high normal total T4 along with clinical signs suggestive of hyperthyroidism. It must be noted that nonthyroidal illness can, in <1.0% of cats,
cause artificial elevations, resulting in an incorrect diagnosis. Thus, its use should be restricted to cases where confirmation is needed rather than as a screening test. Equilibrium dialysis is the methodology that has been shown to be the most reliable for measurement of this hormone.3

**Thyrotropin Releasing Hormone (TRH) Stimulation Test:** This test is easily performed. Collect a serum sample prior to administration of Relefact TRH (0.1 mg/kg IV, max 1 vial/cat), then collect a second serum sample 4 hours later requesting a T4 measurement. A fresh baseline value must be taken at time zero. Common side effects include panting, vomiting, salivation, and defecation. This can be minimized or prevented by administration of dolasetron (Anzemet) beforehand.

*Recall:* Hypothalamus (TRH) -> Pituitary (TSH) -> Thyroid (T4 --> T3) -> negative feedback loop. Hyperthyroid cats, because of the autonomy of their thyroid gland function, experience less, if any, elevation in their post TRH serum T4 values.

**Triiodothyronine (T3) Suppression Test:** The protocol for this test is slightly more involved, but still very simple. Draw a serum sample to determine baseline T3 and T4, separate the serum by centrifugation, then refrigerate or freeze the serum. Clients are instructed to administer T3 (Cytomel: 25 mcg) PO q8h for 2 days; on the morning of the third day, a seventh dose of T3 is administered, and serum is collected within 2–4 hours for T3 and T4 determinations. Both the basal (day 1) and post T3 serum samples should be submitted to the laboratory together to eliminate inter-assay variation. Again, as a hyperthyroid gland is autonomous from superior control, we expect to see no suppression of the T4 value. The T3 assays must be run to ascertain that the client was successful in administering the Cytomel to the cat. Although Cytomel is much less expensive than Relefact, this test is prone to inconclusive results.

**Technetium Scanning:** Thyroid imaging is a safe, easy, and reliable adjunct in diagnosing hyperthyroidism in cats. It has the advantage of determining the extent of involvement, namely whether both lobes are involved and whether metastasis is present, as well as being a good predictor of thyroid metabolic status.7

**Thyroid Stimulating Hormone (TSH) Response Test:** This test is currently unavailable and not validated in cats.

**Therapeutic Options**

**Medical**

1) Methimazole (Tapazole) acts by inhibiting synthesis of thyroid hormones. Initially dose at 2.5 mg/cat PO BID, recheck T4 after 10–14 days and adjust dose accordingly. Side effects to be aware of include an acute facial pruritus, with red wheals on the ears (uncommon). Gastrointestinal upset (anorexia, vomiting) and lethargy are more common (up to 15%), but these are transient and resolve when the drug is stopped and then started again at a lower dose. Hepatotoxicity may arise and is a serious side effect if it occurs. Severe thrombocytopenia and leukopenia (agranulocytosis) or development of ANA titers may occur and will require cessation of the drug. Because of these potential effects, as well as the renal precautions discussed above, and the possible growth of the tumor, regular monitoring of CBC, T4, BUN, SC, and a urine specific gravity should be done at 3–4 month intervals. Transdermal methimazole has been shown to be absorbed, but it may take 4 weeks of use to get therapeutic serum levels.8, 9

2) Propothiouracil

3) Ipodate (Orografin) or iopanoic acid (Telepaque)

The major disadvantage of medical therapy is that it must be continued (along with monitoring) *lifelong*.

**Surgery**

Thyroidectomy is an easy procedure. Ideally, a techniciun scan should be performed ahead of time to determine whether unilateral or bilateral disease is present as well as to detect whether an extrathyroidal tumor is present. Thoracic radiographs and an echocardiographic evaluation of cardiac function are recommended precautions prior to anesthesia. It is important to achieve preoperative euthyroidism and cardiac stability by treating with methimazole and atenolol for 4–6 weeks prior to surgery. These cats are *major* anesthetic risks, and the choice of anesthetic regimes needs to be considered carefully. Avoid xylazine and atropine; be aware of the hyperthyroid predisposition to catecholamine-induced arrhythmias and choose agents accordingly. Ketamine may be contraindicated because of its propensity toward creating hypertension.
Postoperative measurement of serum calcium at 48 and 72 hours postoperative is necessary if bilateral surgery is done. A cat who is hypocalcemic will present with facial twitching (early), muscle weakness and spasms, and even full-blown seizures and death.

Therapy for Hypocalcemia:
1. DHT (Dihydrotachysterol) 0.03 mg/kg daily
2. Ca gluconate tablets (1–3/day)
3. For acute hypocalcemic tetany
   a. 2-5 cc calcium gluconate (10%) IV SLOWLY!
   b. EKG monitoring advisable
   c. Do not use calcium chloride

Other possible post-op complications include paralysis of the laryngeal nerve, or Horner’s syndrome. Levothyroxine supplementation is advised in cats who have had bilateral thyroidectomy performed, starting (0.1–0.2 mg/day PO) 24–48 hours post-op for several weeks or months. Monitor T4 levels, to determine when this supplementation can be ceased.

Radioiodine Therapy: “The Gold Standard”
Other treatments that have recently been evaluated are ethanol injection of the thyroid and percutaneous heat ablation of the thyroid. The former cannot be recommended because of serious adverse effects, and the latter is not a permanent solution.

Monitoring
Regardless of form of therapy, the T4 should be checked every 4–6 months, as the condition may recur either due to incomplete surgical removal, an inadequate 131I dose, or growth of the tumor, necessitating a higher dose of methimazole. Following 131I, 1-month and 3-month evaluations of BUN and creatinine are advisable.

References