THE HYPERTHYROID CAT WITH CHRONIC KIDNEY DISEASE

Dennis J. Chew, DVM, Diplomate ACVIM
*Scott Brown, DVM, PhD, Diplomate ACVIM
The Ohio State University College of Veterinary Internal Medicine, Columbus, OH
*University of Georgia College of Veterinary Medicine Athens, GA

Chronic kidney disease (CKD) and hyperthyroidism are relatively common conditions of older cats. Hyperthyroidism is the most common endocrinopathy of older cats and CKD is diagnosed commonly in older cats, especially those older than 10 years of age. End-stage CKD is estimated to be the number two cause of death in domestic cats of the USA (Morris Animal Foundation Survey). It can be difficult to accurately diagnose cats with CKD, hyperthyroidism, or both conditions as there are many overlapping clinical signs (weight loss, polydipsia, polyuria, dilute urine). It is likely that hyperthyroidism is underdiagnosed in cats with CKD since nearly half of cats with both conditions will have a normal T4 level on a single measurement. In cats with a palpable thyroid nodule and CKD, definitive diagnosis of hyperthyroidism may require thyroid scintigraphy or T3-suppression testing.

The possibility that hyperthyroidism develops as a consequence of CKD has not been explored. The possibility that hyperthyroidism causes or exacerbates CKD in some cats has received little attention. Hyperthyroidism potentially could induce renal failure through effects of systemic hypertension, intraglomerular hypertension, excessive renal hypertrophy, atypical hyperparathyroidism, and hypercalciuria.

EFFECTS OF THYROID HORMONE ON THE KIDNEY

Thyroid hormones exert major effects on renal structure and functions. Normal cats undergo increased RBF and GFR (decreased BUN and serum creatinine) following administration of exogenous thyroxine administration for 30 days (Adams 1997). They also undergo a dramatic increase in kidney size (Brown 1995 – unpublished observations). Groups of cats with hyperthyroidism often have increased GFR compared to normal cats. Plasma iohexol clearance in 12 hyperthyroid cats was 3.83±1.82 ml/min/kg (N = 13) compared to normal cats at 1.83 ± 0.56 ml/min/kg (n = 10) (Becker 2000). Similar results were found when GFR was determined using DTPA clearance nuclear medicine (2.51±0.69 ml/min/kg in 13 hyperthyroid cats vs. 2.02 ± 0.27 ml/min/kg in 11 normal cats) (Graves 1994).

Hyperthyroidism is known to result in dilute urine and polyuria with polydipsia. This effect is likely due to increased RBF and medullary solute washout, though a direct effect on the collecting ducts and/or ADH receptor interaction cannot be excluded. Psychogenic mechanisms also cannot be excluded. Hyperthyroidism is known to result in hypercalciuria in other species due to enhanced bone calcium mobilization; this effect may have some role in the development of polyuria as well as a possible role in creating chronic renal damage by excessive exposure of renal tissue to calcium. Many cats with hyperthyroidism also have increased systemic blood pressure, which could injure renal tissue. Hyperparathyroidism was noted in 77% of 30 cats with untreated hyperthyroidism; the magnitude of increased PTH levels was very large in some instances (Barber 1996). The reversibility of hyperparathyroidism following correction of hyperthyroidism has not been reported. Though serum creatinine (and calcium) was lower in this population of hyperthyroid and hyperparathyroid cats, the possibility of renal secondary hyperparathyroidism cannot be excluded (renal disease may still exist and not be detected).

Although there are dramatic effects of thyroid hormone on the kidney, most of the attention on the relation between these 2 conditions has focused on the simultaneous occurrence of CKD and hyperthyroidism in those cats under consideration for treatment of hyperthyroidism. It has been observed that some hyperthyroid cats develop azotemia or display a worsening of azotemia following therapy that induces euthyroidism.

EFFECTS OF TREATMENT OF HYPERTHYROIDISM ON KIDNEY FUNCTION

A major concern is the possibility that correction of the hyperthyroid state will lower renal function. Hyperthyroid cats (n = 12) decreased GFR (iohexol clearance) from 3.83±1.82 to 2.02 ± 0.81 four to six weeks following treatment with methimazole (Becker 2000). Two of these 12 cats developed overt azotemia following treatment in this same study though as a group increases in BUN or serum creatinine did not achieve statistical significance. Twenty-two hyperthyroid cats treated with radioiodine experienced no change in GFR, BUN, or creatinine 6 days following treatment (T4 was decreased), but BUN and creatinine were significantly increased at 30 days (T4 was also further lowered) (Adams 1997). No cats with a GFR > 2.25 ml/min/kg developed post treatment renal failure in this same study. Thirteen of 15 cats with GFR < 2.25 ml/min/kg were in renal failure 30 days following radioiodine treatment (2/15 that failed to suppress T4 did not develop azotemia); 9 of these 15 were azotemic prior to treatment; the others had normal parameters initially (Adams 1997). GFR (DTPA nuclear clearance) decreased from 2.51±0.69 ml/min/kg to 1.40±0.41 ml/min/kg 30 days following bilateral thyroidectomy in 13 cats (Graves 1994) while creatinine increased from 1.26±0.34 to 2.05±0.60 and BUN increased from 26.62±8.3 to 34.92±8.95.

Azotemia prior to treatment of hyperthyroidism was detected in as many as 41% of cats and in 59% of cats 30 days post treatment in one study (Adams 1997). Twenty-three percent developed azotemia for the first time following treatment in the same study. Mean serum creatinine and BUN increased at 30 and 90 days post-treatment in 58 cats treated by surgery, methimazole, or radioiodine; there were no differences in the magnitude of the problem by treatment group (Dibartola 1996). Nine of these 58 cats had increased serum creatinine concentration prior to treatment. Two of 12 (Becker 2000) and 2 of 13 (Graves 1994) cats developed overt azotemia following treatment with methimazole or bilateral thyroidectomy respectively.

Based on results of these three studies, it appears that an estimate for the development of de novo azotemia following treatment for hyperthyroidism in cats is from 15-23%. Some increase in serum creatinine concentration is expected following the development of euthyroidism due to increased muscle mass (origin of creatinine), though decreased GFR certainly contributes to increased serum creatinine concentration. It is likely that lessening the degree of hyperthyroidism results in decreased RBF and GFR that unmasks azotemia in cats with marginal renal function prior to therapy.
SERUM CREATININE – DOES IT ACCURATELY REFLECT GFR IN AFFECTED CATS?

Another important caveat marks this complex relationship is that serum creatinine concentration in cats with reduced lean muscle mass may seriously underestimate any degree of excretory renal dysfunction since less creatinine will be generated from these atrophied muscles. Reduced muscle mass is common in advanced hyperthyroidism and in those with CKD. In these instances, serum creatinine will be lower than it would be if muscle mass were greater. The use of BUN to evaluate GFR is actually fraught with even more limitations as a cat’s appetite (and protein intake) will often be altered by treatment of hyperthyroidism, presence of coexistent CKD, and/or institution of special low-protein diets. It is best to rely on serum creatinine but wise to ask the question “What would the serum creatinine likely be if muscle mass were normal?” It is possible that cats with upper range “normal” serum creatinine concentration and poor muscle condition have underlying renal disease. It is especially important in these situations to critically evaluate the results of urinalysis. If the urinary specific gravity is less than 1.040, then increased suspicion for primary renal disease is warranted. Measurement of GFR using nuclear medicine clearance methods or iohexol clearance is recommended in cats whose renal function is uncertain prior to permanently inducing a euthyroid from hyperthyroid state. Those cats with lower values for GFR are at risk to develop overt azotemia and possibly clinical signs of CKD following conversion to euthyroidism. Rarely, some cats without pre-existing azotemia and with urinary specific gravity greater than 1.040 prior to treatment develop CKD within 6 months of treatment for hyperthyroidism — whether this is a consequence of the conversion to euthyroidism in unclear.

DECIDING WHICH CATS TO TREAT

Should cats with overt azotemia and hyperthyroidism be treated for hyperthyroidism? Some endocrinologists and nuclear medicine specialists advocate so. It is likely that many of these cats will increase their level of azotemia following treatments that result in euthyroidism or hypothyroidism. In some cats this increase in creatinine will be mild, while other cats will experience large increases in serum creatinine. If clinical signs related to hyperthyroidism are severe, attempted treatment is warranted. We recommend screening cats for azotemia and initially treating those suspected of having CKD with a methimazole challenge test in all cats with hyperthyroidism. Methimazole treatment provides a reversible means of inducing euthyroidism and observing what happens to the level of renal function. An initial dose of 2.5 mg BID is given for 2 weeks and then serum biochemistry is repeated to evaluate renal function and T4 levels. If renal function is stable, the dose is gradually increased every two weeks as needed until T4 levels have entered the normal range if renal function remains stable. The dose can be increased to 2.5 mg TID, then 5 mg BID, and 5 mg TID if needed. Methimazole is discontinued if renal function deteriorates during the methimazole challenge. If renal function remains stable, then long-term methimazole can be considered for therapy or more-definitive treatment of hyperthyroidism provided by I-131 treatment or surgery. The definition of “stable” renal function is arbitrary but could be taken as a serum creatinine increase of less than 2.0 mg/dl (180 micromol/L) in those cats without initial azotemia and less than 1.0 mg/dl (90 micromol/L) in those with azotemia.

SUPPLEMENTATION WITH THYROID HORMONE

Supplementation with thyroxine should be considered for those cats with worsening azotemia that become hypothyroid following bilateral thyroidectomy or radiiodine treatment. About 9% of cats develop low T-4 values post I-131 treatment. Anecdotal evidence suggests that excretory renal function can be supported in some post-treatment hyperthyroid cats when supplemental thyroxine is supplied. We usually recommended a starting oral dosage of 0.1 mg levothyroxine in this setting. As a compromise, it may be desirable to titrate the dose of methimazole in cats with marginal renal function in such a way as to partially control the hyperthyroidism without decreasing GFR too much. Other treatments to control cardiac effects of uncontrolled hyperthyroidism may be warranted (beta blockers such as atenolol).

REFERENCES