Hypothyroidism occurs due to decreased secretion of T3 and T4 from the thyroid gland. As spontaneous hypothyroidism is rare in cats, iatrogenic hypothyroidism is the most common form, and occurs after treatment with antithyroidal drugs, radioiodine therapy, and thyroidectomy. Prevalence is approximately 10% (range 1-30%) in cats after radioiodine therapy, 15-20% in cat treated with antithyroidal drugs, and 37% in cats treated antithyroidal drugs +/- thyroidectomy. In those studies, the majority of cats were diagnosed 3-6 mo. after treatment and did not display overt signs of hypothyroidism. It has been previously thought that if cats did not develop clinical signs that treatment is unnecessary, but the clinical significance of hypothyroidism has become more apparent as hypothyroid cats are more likely to develop azotemia and have a shorter life expectancy. Given the effects on renal function and survival, it is now recommended that cats with permanent hypothyroidism be treated (if possible) with thyroid supplementation even if they lack overt clinical signs.

**Diagnosis**

As most cats develop the iatrogenic form of hypothyroidism, diagnosis starts with identifying a history of treatment for hyperthyroidism whether that be radioiodine, methimazole, etc. Relying on clinical signs is not usually helpful as clinical signs will overlap with resolution of hyperthyroidism and most cats do not develop overt signs until years later. Nonetheless, clinical signs typically include lethargy, decreased appetite, and weight gain. In addition, cats may experience dermatologic changes (seborrhea sicca, hair thinning, unkempt hair coat). In most instances, diagnosis of hypothyroidism occurs while monitoring effects of treatment for hyperthyroidism.

The screening test of choice for hypothyroidism is total thyroxine (tT4); however, finding a tT4 below the reference interval does not definitively diagnose hypothyroidism. The presence of nonthyroidal illness (such as CKD, neoplasia, diabetes, hepatic disease) can confound the diagnosis. Such illnesses lower serum tT4 concentration in euthyroid cats and it is frequently below the reference interval. This is particularly true of cats with CKD where serum tT4 is low in approximately 50% of cases. Analysis of other thyroid hormones are necessary to
support a diagnosis of hypothyroidism and include free thyroxine (fT4) and thyrotropin (TSH) concentrations. Unfortunately, these tests are also susceptible to nonthyroidal illness making the diagnosis problematic. Free T4 is affected by nonthyroidal illness (NTI) to a lesser degree than tT4, but up to 17% of ill cats, and as many as 34% of cats with severe illness have a serum fT4 concentration below the reference interval.\textsuperscript{10} Importantly, NTI can result in an elevation of fT4 in some cases, confounding interpretation of thyroid function even more.\textsuperscript{10,12,13} While limited information is available regarding the effects of NTI on serum TSH concentrations, there appears to be little to no effect. TSH concentrations were not significantly different between euthyroid cats with NTI and normal cats,\textsuperscript{11,14} although cats with severe NTI had significantly lower TSH concentrations compared to cats with mild NTI.\textsuperscript{10} Conversely, TSH can occasionally be above the reference interval in cats with NTI\textsuperscript{14} as well as healthy cats.\textsuperscript{15} Currently, the combination of low tT4 and high TSH concentration are used for the diagnosis of iatrogenic hypothyroidism, but further studies are still necessary to evaluate the diagnostic utility of TSH in hypothyroid cats.

The majority of cats undergoing radioiodine therapy develop transient hypothyroidism that resolves in 1-3 months. Thus, in cats treated with radioiodine therapy, it is recommended to wait at least 3 months before evaluating a patient for permanent iatrogenic hypothyroidism unless overt clinical signs of hypothyroidism or marked worsening of azotemia occurs.\textsuperscript{9} Some cats have a low-normal T4 and high TSH indicating the possibility of subclinical hypothyroidism. It is also unclear if these cats have subclinical hypothyroidism and if thyroid hormone supplementation is warranted. These cats are generally monitored unless progressive or severe azotemia occurs in which thyroid hormone supplementation should be considered.

**Treatment**

In cats with permanent hypothyroidism, treatment generally consists of administrating levothyroxine to normalize T4 and TSH. Treatment may also improve GFR thus improving azotemia. Starting doses of levothyroxine range from 0.05 to 0.15 mg/day\textsuperscript{9,16} (I typically start no lower than 0.1 mg/day) and can be given once daily or split q 12 hr. It has been suggested that starting with 0.075 mg by mouth twice daily may combat issues with poor absorption and short plasma half-life of T4.\textsuperscript{9} Food can decrease GI absorption of levothyroxine, so it should be given on an empty stomach (1hr before or 3 hours after a meal). If necessary, a very small amount of food may be given to enhance compliance.

Monitoring therapy includes assessing serum tT4 and TSH concentrations. Goals are to have tT4 within the reference range and avoid development of hyperthyroidism, and TSH should
be decreasing and become within reference range. Ideal post-pill T4 concentrations depend upon on whether peak (4 hours post pill) or trough (12-24 hrs post pill) samples are measured. Peak T4 concentrations should be within at least the upper half of the reference range (e.g. 2.5 - 3.5 ug/dL if RR is 0.8-4.0 ug/dL). Although, ideal post treatment tT4 concentrations may be achieved, some cat fail to achieve normalization of serum TSH concentrations.

In cats receiving antithyroidal drugs, doses should be decreased by 25-50% in cats with low T4. Dose adjustments may also be necessary in cats with low normal T4 but progressive or worsening azotemia. The goal would be to keep tT4 within midrange of the reference interval. Restoration of euthyroidism may improve kidney function in hypothyroid azotemic cats as has been shown to occur with dose adjustments in antithyroidal drugs. This may also occur in cats treated with levothyroxine for hypothyroidism but further studies are necessary.

Further research is necessary to gain information on effects of levothyroxine supplementation on renal function in hypothyroid cats, clinical significance of subclinical hypothyroidism, ideal treatment protocols for iatrogenic hypothyroid cats, as well as diagnostic utility of TSH in hypothyroid cats.

References


