

Diagnosis and management of feline iatrogenic hypothyroidism

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Categories : [Companion animal](#), [Feline](#), [Vets](#)

Date : July 13, 2015

ABSTRACT

Iatrogenic hypothyroidism (IH) is an acknowledged potential complication following treatment of hyperthyroidism. Although previously considered rare, IH is now thought to be more common than previously appreciated. Cats affected by IH are more likely to suffer renal complications and shortened survival times. All cats undergoing treatment for hyperthyroidism should be monitored closely for this complication. Permanent IH is managed by supplementing with thyroid hormone. Where identified in cats receiving reversible treatments for their hyperthyroidism, IH can be managed by titrating their dose of medication.

Hyperthyroidism is a common diagnosis of older cats. Four treatment options are available.

Reversible treatments:

- antithyroid medication
- exclusively feeding an iodine-restricted food (Hill's y/d)

Curative treatments:

- surgical thyroidectomy
- radioiodine

Iatrogenic hypothyroidism (IH) is possible with all the hyperthyroidism treatments. Published data suggests IH is most common following treatment with radioiodine.

Importance



Weight gain can be a feature of iatrogenic hypothyroidism, although many owners will interpret this as a good outcome following treatment for hyperthyroidism.

A study has shown development of IH is associated with a significantly worse prognosis. A significantly higher proportion of cats with post-treatment hypothyroidism suffered from azotaemia compared to those cats that were euthyroid following treatment of their hyperthyroidism. In addition, those hypothyroid cats that did develop azotaemia post-treatment suffered significantly shorter survival times than those that remained non-azotaemic (Williams et al, 2010).

Hypothyroidism reduces renal blood flow and glomerular filtration rates, and this is likely to be an important mechanism for negatively impacting on renal function in these cats. Restoring euthyroidism is of benefit in improving renal function in those cats suffering from IH (Williams et al, 2014).

Given this information, it is now important for all clinicians to consider IH in their patients, irrespective of which treatment modality is used.

How is IH diagnosed?

Diagnosis of IH is based on clinical signs, physical examination, and results of screening and specific laboratory tests. Clinical signs include lethargy, weight gain, hypothermia, seborrhoea sicca, alopecia (especially affecting the pinnae) and myxoedema.

Recognition of IH can be difficult, since many owners interpret lethargy and weight gain as a normal finding in an elderly cat, and also representative of a good response to treatment for hyperthyroidism. Routine laboratory profiles may reveal hypercholesterolaemia and a mild non-regenerative anaemia.

Overt clinical signs are not common with IH. A diagnosis of IH cannot be made solely on the basis of subnormal total T4 values, although a normal total T4 result generally rules out IH. Serum-free T4 levels are generally low in cats with IH and this test may be more sensitive than the total T4 for identification of IH, although false-high results have also been reported with this test. Serum T3 levels are generally low to subnormal in cats with hypothyroidism.

Presence of intercurrent disease can suppress levels of T3, T4 and free T4 (euthyroid sick syndrome) meaning a basal T4, free T4 or T3 measurement alone is not sufficient to confirm a diagnosis of IH.

As always, attention should be paid to assessing the individual cat and ensuring test results “make sense”. With the wide array of different T4 tests, both at commercial labs and in-house, if the results do not fit the cat, consideration should be given to repeating the test at a suitable reference laboratory. For T4 and free T4 measurement, laboratories using radioimmunoassay or chemiluminescent enzyme immunoassay are considered most reliable (Peterson, 2013).

The diagnosis of IH can be confirmed by performing one of the following tests.

- Measuring endogenous thyroid stimulating hormone levels using the canine assay (cTSH). Levels of cTSH are high in cats suffering from IH (generally > 1.0ng/ml).
- Performing a recombinant human TSH stimulation test: cats with IH have low basal T4 levels and little, if any, increase in T4 levels following administration of recombinant human TSH. Samples are collected before and six hours after administration of 25 micrograms of recombinant human TSH (Thyrogen: Genzyme) given by intravenous injection. In normal cats and those with non-thyroidal illness, the T4 concentrations generally increase by at least two fold.
- Imaging the thyroid tissue by scintigraphy: uptake of radioactive technetium by the thyroid is proportional to thyroid function. In cats with IH there is little or no uptake of radioactive technetium by the thyroid tissue.

If total T4 is low, but free T4 and TSH levels are normal, then suppression of T4 by intercurrent disease, most commonly chronic kidney disease, is likely.

Cats that have had curative treatment

Although one publication suggested as many as 30% of radioiodine-treated hyperthyroid cats suffered from hypothyroidism (Nykamp et al, 2005), most publications have suggested less than

10% of cats treated with radioiodine suffer from permanent hypothyroidism (Meric and Rubin, 1990; Jones et al, 1991; Slater et al, 1994; Peterson and Becker, 1995, Slater et al, 2001).



Iatrogenic hypothyroidism following treatment with radioiodine. Pinnal alopecia and seborrhoea sicca is present.

Hypothyroidism is more likely to develop in cats with bilateral disease (Nykamp et al, 2005) and in those with thyroid carcinomas in which a higher dose of radioiodine is administered (Guptill et al, 1995). In many cases, the hypothyroidism that develops is transient (Mooney, 1994) and euthyroidism returns within three to six months.

Total T4 monitoring is recommended post-treatment in all cats receiving curative treatments. An appropriate protocol would include measurement at one, three, six and 12 months post-treatment with six-monthly monitoring thereafter.

In those cats where total T4 levels are persistently low (low at three or six months post-treatment) cTSH measurement is indicated to confirm IH. Attention should also be paid to looking for concurrent illnesses that could be responsible for suppression of T4 levels. A normal total T4 generally rules out IH.

Thyroid hormone supplementation (L-thyroxine at an initial dose of 0.1mg orally once or twice daily) is recommended in confirmed cases of IH, especially in those cats that are azotaemic or showing clinical signs of hypothyroidism. The dose is adjusted according to clinical response, total T4 (four

hours post-pill) and cTSH levels. Most treated cats will show improvements in their renal parameters as the IH is successfully treated. Absorption of thyroxine may be better on an empty stomach, as is the case in people and dogs.

A few clinicians advocate routine supplementation of cats following curative treatments such as radioiodine, at least for a short period (for example, 0.05mg to 0.1mg L-thyroxine per cat per day for the first six weeks post-treatment) to cover the transient IH that may develop.

Azotaemic cats are most likely to benefit from this intervention. A study of 195 cats with pre-existing CKD showed those supplemented with 0.1mg of L-thyroxine post-radioiodine had significantly smaller increases in their renal parameters following radioiodine compared to those cats where no supplement was routinely given, suggesting supplementation may reduce progression of azotaemia through preventing hypothyroidism (Broome and Peterson, 2013).

Following this study, it is now standard for Mark Peterson's clinic to provide short-term L-thyroxine supplementation as part of the protocol for treating hyperthyroid cats with renal disease. Supplementation can be stopped after two to three months and the cat's thyroid and renal status reassessed a few weeks later to determine whether IH is still present – and thus whether ongoing L-thyroxine treatment will be required.

Cats receiving reversible treatments

A study reported approximately 20% of methimazole-treated hyperthyroid cats were found to have IH, based on a low total T4 and raised cTSH (Aldridge et al, 2015). Medical treatment should be titrated to maintain euthyroidism – the aim being to suppress total T4 levels to the lower half of the reference range in treated cats. In general, the dose of anti-thyroid medication should be reduced if total T4 levels fall below the reference range. Presence of intercurrent disease can also suppress total T4 levels so diagnosis of IH is not always straightforward. Additional tests that can be of value include free T4 and cTSH levels as discussed previously.

In patients where total T4 levels are measurable, but below the laboratory reference range, it is not always easy to make treatment decisions. If the cat is clinically doing very well it may be preferable to continue with the current treatment regime rather than risk “rocking the boat” by reducing the dose. Micro-management of antithyroid medication doses can be challenging and any change in dosage necessitates repeat blood testing, which can become expensive for the carers. TSH measurement can be helpful in some of these borderline patients – if levels are normal then hypothyroidism is ruled out.

To the author's knowledge, hypothyroidism has not been definitively confirmed in any cats receiving sole management of their hyperthyroidism using an iodine-restricted food, although one cat was

reported to have a transiently subnormal T4 (van der Kooij et al, 2013). If hypothyroidism is encountered, the iodine-restricted food should be withdrawn.

Conclusion

IH is an acknowledged potential complication of treatment for hyperthyroidism. Vigilance for this possibility is recommended, especially in azotaemic cats, since the treatment outcome is significantly worse in these patients.

- Please note Thyrogen is not licensed for veterinary use and is prescribed under the cascade.

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