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HYPERTHYROIDISM

Rachel Korman

Hyperthyroidism is one of the most common endocrine diseases affecting older cats. Hyperthyroidism typically results from a functional thyroid adenoma (98%) or a carcinoma (1-2%). In the euthyroid cat the thyroid hormones are released from the thyroid gland in response to thyroid stimulating hormone (TSH). The hormones circulate as thyroxine (T4) and the biologically more active triiodothyronine (T3). Thyroxine (T4) acts as a circulating reservoir of thyroid hormone and is converted to T3 in response to concentrations of T3.

Functional neoplastic tissue breaks away from the negative feedback loop and overproduces thyroid hormones despite low concentrations of TSH.
The thyroid glands are bi-lobar and located on either side of the trachea, normally distal to the larynx. There are two associated parathyroid glands. One is extracapsular and situated adjacent to the thyroid capsule at the cranial pole while the other is surrounded by the thyroid tissue and is found at the caudal pole. Cranial pole of the capsule a branch of the carotid, the cranial thyroid artery, supplies each thyroid gland. Recurrent laryngeal nerves run close to the thyroid glands.

The epidemiology of hyperthyroidism in cats remains unclear and no single underlying cause has been identified. It is likely that diet and the environment play a role. In humans, hyperthyroidism is twice more likely to occur in humans with dietary iodine deficiency. However the pathophysiology of hyperthyroidism development in humans is different – humans develop autoantibodies against the TSH receptor, whereas this is not seen in cats. The second most common cause of human hyperthyroidism is toxic nodular goitre – one or more hyperfunctioning adenomas – similar to cats.
Several studies have demonstrated widely fluctuating levels of iodine in commercial cat foods (30 fold difference) and it has been speculated that cats fed dramatically different iodine levels throughout their lives could be at risk of developing thyroid abnormalities, however this remains unproven.
Risk factors that have been identified in multiple studies include an increased risk in cats consuming tinned food and a decreased risk in Siamese and Himalayan cats. Factors identified in some but not all studies include an increased risk in indoor, multi-cat households, cats receiving flea preparations and pesticides and the use of cat litter. Recent studies also identified higher concentrations of brominated flame retardants in the serum of hyperthyroid cats in comparison to euthyroid cats.
Increases in metabolic rate occur due to enhanced catecholamine activity and sympathetic drive.

Common presenting signs include:

- Weight loss
- PUPD
- Polyphagia
- Tachycardia
- Hyperactivity
- Diarrhoea
- Respiratory abnormalities
- Cardiac abnormalities
- Skin lesions
- Vomiting

A syndrome of apathetic hyperthyroidism has been described in 10 % patients. As regular routine health checks are becoming commonplace and Total T4 (TT4) levels are included in routine biochemistry panels, hyperthyroidism is being diagnosed earlier, with less advanced clinical signs. Typically, a history of gradual weight loss despite an increased appetite is common.

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Thyroid goitres are palpable in most cats with hyperthyroidism. False negatives may occur if the enlarged gland has descended into the thoracic inlet. A thyroid goitre may be present in euthyroid cats although enlargement may represent non-functional adenomas which may progress to cause hyperthyroidism in the future.

A recent study also identified a higher prevalence of severe hyperthyroidism, large thyroid tumours, multifocal disease, intrathoracic thyroid masses and suspected malignant disease (e.g. thyroid carcinoma) in hyperthyroid cats that received medical management over a longer period of time, compared with cats receiving radioactive iodine treatment earlier in the course of the disease.

Hyperthyroidism is diagnosed utilising thyroid hormone assays - circulating concentrations of serum total T4 (TT4) or free T4 (fT4). Care must be taken as thyroid hormone levels are also significantly affected by concurrent systemic disease, TT4 can be lowered into normal reference intervals by systemic illness. Additionally, fT4 levels can be increased in cats without hyperthyroidism. One study identified elevated fT4 in 10-15% of cats with other disease (i.e. not hyperthyroid).

Free T4 concentrations assayed by equilibrium dialysis closely correlate with TT4 concentrations but are more expensive to measure. Assessment of fT4 concentrations rarely offers a significant benefit over TT4 in obtaining a diagnosis. T3 can also be measured but it is more prone to producing false negative results.

Typically cats with hyperthyroidism and concurrent systemic disease will still have Total T4 (TT4) levels within the top end of the normal reference interval and repeat testing in 4-6 weeks is likely to identify an elevated result. Cats with early or mild disease can have inherent fluctuations in TT4. Cats with suggestive clinical signs, a TT4 within the top end of the normal range and an elevated fT4 are very likely to have hyperthyroidism.

Dynamic thyroid testing can be performed but is rarely clinically necessary. Hyperthyroid cats have very low concentrations of endogenous TSH due to the negative feedback loop. A TSH test is not required for diagnosis in cats with raised Total T4 concentrations but may be helpful in borderline cases. Unfortunately access to TSH as an assay or for dynamic testing is limited. T4 suppression testing is reported with euthyroid cats demonstrating reduced concentrations of T4 following oral administration of T3. Hyperthyroid cats with abnormal functioning tissue continue producing T4 in the despite high T3 concentrations.

Assessment of renal and hepatic parameters is indicated in all hyperthyroid cats. Raised concentrations of liver enzymes are common in hyperthyroid cats. Increases tend to be mild.
Approximately 20 % of hyperthyroid cats have elevated urea and creatinine concentrations due to either pre-renal failure associated with advanced hypertrophic cardiomyopathy or primary renal failure.

Glomerular filtration rate (GFR) can fall following return to a euthyroid state – unmasking occult renal dysfunction. Hyperfiltration in the hyperthyroid cat may contribute to renal compromise in which case early treatment may be beneficial. Predicting the development of reduced kidney function following definitive treatment of hyperthyroidism remains difficult, however it is important to avoid inducing iatrogenic hypothyroidism.

Cardiac ultrasound, radiography and electrocardiography (ECG) should be considered prior to anaesthesia due to the high incidence of tachydysrhythmias and hypertrophic cardiomyopathy.
These changes occur secondary to increased sympathetic drive, the effect of thyroid hormone on cardiac tissue and altered peripheral tissue function.

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Thoracic radiographs may also provide useful screening for thyroid carcinoma metastatic disease, although this is unusual.

Thyroid carcinomas are seen with higher frequency in patients treated long term with non-definitive treatments such as medical therapy compared with radioactive iodine or throidectomy

Systolic blood pressure (SBP) should be measured in all hyperthyroid cats. Mild increases in SBP may be present, however severe hypertension is unlikely unless concurrent renal dysfunction is present.

Scintigraphy can be performed using short acting radioactive isotopes (e.g. technetium) and images of the thyroid tissue can be obtained. Studies have identified that approximately 70% of cats have bilateral disease. Scintigraphy is also useful for identifying ectopic thyroid tissue (negating the possibility of surgical treatment). Unfortunately access to scintigraphy is limited in Australia.

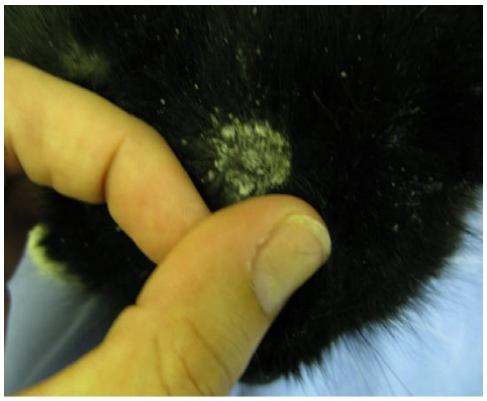
Treatment of hyperthyroidism involves:

- Anti-thyroid drug therapy
- Dietary therapy
- Radioactive iodine or
- Surgical thyroidectomy.

Antithyroidal medication accumulates in the thyroid and inhibits synthesis and release of thyroid hormone (by blocking iodine incorporation and coupling of iodotyrosines). Euthyroidism can be obtained in 90 % of cats within two weeks, however some cats require significant titration of medication to avoid hypothyroidism and close monitoring maybe required. If treatment is stopped, a return to pre-treatment thyroid hormone concentrations occurs within 48 hours.

Methimazole is available in a transdermal formulation, however its efficacy is unpredictable. Methimazole dosage is 5-10 mg per cat twice daily. Carbimazole has a recommended starting dose of 5 mg per cat two to three times daily.

Anorexia, vomiting and lethargy is identified in approximately 10-20% of cats receiving methimazole. It is typically mild and temporary and may resolve with reducing the medication dosage and giving with food. Methimazole has been linked to more severe adverse effects such as hepatopathies, agranulocytosis and thrombocytopaenia. This occurs in approximately 3% of cats and typically occurs within 3 months. If identified treatment should be stopped immediately and alternative treatments considered. Carbimazole is metabolised to methimazole, but appears to be better tolerated in many cats.



A patient with an adverse drug reaction to methimazole

Effect of return to euthyroid status on renal function should be monitored by assessing creatinine and urine specific gravity (USG).

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Treatment should be tailored to maintain a serum TT4 in the lower half of normal range after 2-3 weeks. Starting with a lower treatment dose and titrating every 2-3 weeks may help to prevent side effects. It is important to remember that the thyroid adenoma will progress with time and become larger and produce more thyroid hormone, thus treatment dose will also change with time and monitoring and dose adjustment is required for life.
Dietary therapy is also available in some countries (Hills y/d). This diet has a 10x lower iodine content. Cats must eat solely this diet and dietary supplements may negate the effects. Clinical signs of hyperthyroidism may not always resolve. For cats that cannot receive medication or if radioactive iodine or surgery is not an option, this may be a suitable treatment.

The gold standard treatment for hyperthyroidism in cats remains radioactive iodine (I^{131}) administration. This is performed using either oral capsules or via subcutaneous injection. I^{131} selectively destroys hyperfunctioning adenomatous thyroid tissue. B particles penetrate to 2mm, thus it is safe for adjacent tissues.

Cats must remain isolated during this treatment and all waste (e.g. urine, faeces) stored for a defined period of time until no longer deemed a radioactive risk. The time period required for isolation of cats and waste differs depending on local legislation. Single dose treatment achieves success in 93-97% of cats. Early treatment is likely to prove more economical than life long treatment with anti-thyroidal medications or iodine restricted diets.

Surgical thyroidectomy can be curative in patients without ectopic thyroid tissue. It is important to stabilize patients prior to surgery. Achieving euthyroid status significantly reduced anaesthesia risks in hyperthyroid cats.

In cats who have had severe reactions to anti-thyroidal medications, propranolol may be used 3-5 days prior to surgery to reduce anaesthetic risk associated with cardiac changes and high sympathetic drive, but should be used with extreme caution in cats with congestive heart failure due to its negative inotrophic effects.

Anaesthetic agents should be chosen based on their lack of dysrhythmogenic potential. Avoid ketamine as it might sensitise the heart to catecholamine induced dysrhythmias. Halothane should be avoided. Acepromazine included in the premedication may reduce autonomic tone and potential for arrhythmias. Stress free induction with propofol or alfaxalone to effect and maintainence with isofluorane is suggested. Intraoperative ECG and fluid therapy to maintain circulating volume and renal function is recommended.
Risks of surgery include hypoparathyroidism (severe hypocalcemia), Horner's syndrome and laryngeal paralysis. Recurrence of disease can occur due to lack of removal of adenomatous tissue, bilateral disease (70% of cats), ectopic thyroid tissue or recurrence of adenomatous change. A staged bilateral procedure affords greater safety from hypocalcamia whilst reducing the duration of surgery and period of hospitalisation. The prevalence of bilateral disease and the potential for temporary restoration of euthyroid status for several months in bilaterally affected cats following unilateral thyroidectomy must be considered for these cases.

FACTOR	DIET	MEDICAL	SURGERY	I^{131}
Curative	No	No	Maybe	Yes
Side effects	Not yet identified	+++	++	+
Hypothyroidism	+	No	+	+
Recurrence	+++	+++	++	+
Hospitalisation	No	No	+	+
Availability	+++	+++	++	++
Cost upfront	+	+	+++	+++