Feline hyperthyroidism – an opinionated perspective

Feline hyperthyroidism is the most common endocrine disease of cats in Australia, and one of the most important diseases of the geriatric cat. Unlike many diseases of the older cat, it can be treated with complete success. Interestingly, the condition is thought to have occurred infrequently prior to about 1980, the time when commercially prepared cat food started to be fed more routinely to cats in the developed world. Thus, some current theories of causation implicate certain characteristics of commercially prepared rations, such as a high iodine content, or the chemicals involved in the preservation of canned foods. A logical inference, therefore, is that by feeding cats more natural food i.e. raw meaty bones, the disease is less likely to occur.

Whatever the cause, hyperthyroidism is commonly diagnosed in feline practice, and a veterinarian in a busy clinic seeing many cats will diagnose new cases on a weekly or monthly basis. In Sydney, one private clinical pathology laboratory routinely diagnoses more than 20 new cases each week.

In my opinion, most switched on vets working in practice are good at diagnosing hyperthyroidism. Thus, from my perspective, the controversial issues relate to how to best manage cases, and that will be the key focus of the present article. I should state at the outset that some of my views may not be shared by other colleagues.

Epidemiology

Hyperthyroidism is generally a disease of older cats, and in my experience most cats are greater than 10 years of age at the time of diagnosis. This is not to say that cats cannot develop this condition when they are seven or eight years old, however such cases are rare. From my experience, many diagnoses of hyperthyroidism in cats...
younger than 7 are made in the absence of compatible clinical signs and physical findings, and are likely attributable to laboratory error.

Hyperthyroidism occurs in both male and female cats with similar frequency, and my impression is that purebred cats are probably under-represented compared to moggies.

**Presenting complaints and physical findings**

In these enlightened times, most cats are diagnosed by an astute veterinarian during an annual health check, or as a result of screening before performing an elective procedure (e.g. dental scaling) in the geriatric patient. **Physical findings indicative of hyperthyroidism are detectable by a veterinarian some time before an owner recognises a health issue of their cat.** This is partly because clinical signs develop insidiously and are not associated with a reduction in appetite. Of signs likely to be noticed by owners, weight loss despite an excellent appetite is perhaps the most common, although occasionally owners will seek attention for polyuria/polydipsia, vomiting, change in temperament or signs referable to cardiorespiratory compromise. Physical findings suggestive of hyperthyroidism include:

- A loud, fast heart
- A systolic murmur, often loudest over the sternum
- A gallop rhythm or irregular cardiac rhythm
- A prominent cardiac impulse
- An easily palpable femoral pulse
- A palpable thyroid nodule or nodules

As some of these findings can also occur with primary cardiac disease, **the importance of thorough palpation of the ventral cervical region cannot be overemphasised.**

There is an art to thyroid palpation, and it must be acquired and polished by palpating cats of all ages. The technique involves supporting the patient’s head in a slightly elevated position with one hand, while running the thumb and index finger of the other hand gently down the jugular groove on either side of the trachea. Normally a “slipping sensation” or “pop” is felt as the nodule(s) run under the digits, rather than an actual goitre. This technique is easier in cats who have had hair clipped from the ventral cervical region, and the sensation is further exaggerated by smoothing down the skin with warm water prior to palpation (this is not necessary after you get the knack of thyroid palpation).

In a minority of longstanding cases the nodule(s) may have descended ventrally towards the thoracic inlet, and very rarely the hyperactive nodule is actually within the chest.

In summary, a tentative diagnosis of hyperthyroidism can be made by palpation of one or more thyroid nodules in a cat with a loud, fast heart; often in association with a history of weight loss despite good appetite.

**Confirming a diagnosis of hyperthyroidism**

Usually, confirming a diagnosis of hyperthyroidism goes part and parcel with an overall health check in an older cat. Tests that should be run routinely include haematology, extensive serum biochemistries, urinalysis and a resting thyroxine (T4) determination. In my opinion, these tests are best sent off to a clinical pathology laboratory and done in concert; but some practices may instead prefer to do a packed cell volume (PCV) and total plasma protein (TPP) concentration using a microhaematocrit tube, an IDEXX, Vetscan or I-Stat biochemistry profile, in-house microscopic urinalysis and multi-reagent stick test, and most importantly a urine specific gravity determination. Many cats with hyperthyroidism have increased liver enzyme activities, especially alanine aminotransferase (ALT), and this observation in a cat which is eating well provides indirect support for a diagnosis of hyperthyroidism. The reason why liver enzyme activities rise in association with thyrotoxicosis is a mystery, as these cats have nothing wrong with their liver. Performing a full urinalysis is critical in any older cat as, viewed in concert with serum urea and creatinine concentrations, the PCV and TPP it provides some indication of a cat’s renal function and reserve.

Most cats with clinical signs of hyperthyroidism have an elevated resting thyroxine concentration in plasma. It is of key importance to use a laboratory in which you have great confidence concerning the accuracy of T4 determinations. **Some labs have assays that are far more reliable than others!** In-house assays that purport to accurately measure T4 levels are of questionable reliability. If the T4 value is above the reference range in a cat with one or more thyroid nodules and compatible physical findings, you have made a diagnosis of hyperthyroidism!

In some cases of hyperthyroidism the T4 level is “high normal” or within the normal range. In these tricky situations, repeating the T4 assay in a few weeks, or performing a T3 suppression test or a nuclear medicine thyroid scan (available at certain referral centres; see Table 1), will usually rule in or out a diagnosis of hyperthyroidism. A current textbook will provide further explanation and guidance in this scenario. It is rarely a significant problem in practice, as hyperthyroidism is generally a chronic disease, and so there is plenty of time to make a diagnosis in most “equivocal” cases in which suggestive clinical signs are detected early in the disease course.

Much is written concerning hyperthyroidism as a cause of hypertension, renal disease and cardiac dysfunction. It is difficult to critically review the published literature, as many cats with hyperthyroidism have concurrent renal and cardiac disease that may or may not have a causal relationship with their endocrinopathy. In my opinion, hyperthyroidism per se is rarely a cause of symptomatic hypertension; said another way, most cats with...
hypertension and hyperthyroidism have persistent hypertension after their thyroid disease is controlled. Cardiac disease is quite different, in that there is no doubt that hyperthyroidism induces a high cardiac output state, which in time can result in direct and indirect damage to the myocardium and eventually signs of congestive heart failure (CHF). Cats which develop CHF as a result of thyrotoxicosis have a characteristic echocardiographic picture, with features of both hypertrophic and dilatative cardiomyopathy. In other words, they have bialtrial dilatation, left ventricular hypertrophy, obvious ventricular chamber dilatation, and variable contractility (sometimes with a reduced fractional shortening).

**Table 1. Costs of treating a cat with carbimazole for 12 months**

<table>
<thead>
<tr>
<th>Cost Description</th>
<th>Cost ($</th>
</tr>
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<tbody>
<tr>
<td>Initial diagnostic investigation</td>
<td>$320</td>
</tr>
<tr>
<td>Including CBC, biochem panel, urinalysis, T4, BP check, fundoscopy</td>
<td></td>
</tr>
<tr>
<td>Re-check consultations at one month, then every 3 months</td>
<td>$160</td>
</tr>
<tr>
<td>CBC and T4 after starting carbimazole, then twice yearly</td>
<td>$242</td>
</tr>
<tr>
<td>One year supply of Neomercazole®, based on twice daily medication (7 bottles)</td>
<td>$357</td>
</tr>
<tr>
<td>Total</td>
<td>$1079</td>
</tr>
</tbody>
</table>

**The asymptomatic thyroid mass**

A cryptic problem for experienced clinicians is the detection of thyroid nodules in an asymptomatic cat. Gary Norsworthy and colleagues demonstrated that many elderly cats with normal thyroid status have a goitre, and certainly this is also my experience. Most of these cats have early thyroid hyperplasia, and in the fullness of time will develop symptomatic hyperthyroidism, if they live sufficiently long. If you are a good thyroid palpator, you will pick these cats 2-3 years before they develop clinical signs of hyperthyroidism.

To make matters even more complex, a small proportion of these cervical masses are actually parathyroid in origin, and these too may eventually evolve into functional parathyroid tumours. By performing a T4 determination and serum biochemical panel (which typically includes a whole calcium concentration), you are doing a good job in screening for EARLY hyperthyroidism and EARLY hyperparathyroidism. In cases where the total calcium is elevated, ionised calcium and PTH determinations are indicated to further pursue the diagnosis of primary hyperparathyroidism. These latter two assays are difficult to arrange, and your clinical pathology laboratory should be consulted re sample collection and handling.

**Therapy for hyperthyroidism**

Before embarking on therapy for hyperthyroidism, baseline haematology, biochemistry and urinalysis data must be reviewed. This is because concurrent disease may need to be addressed in addition to management of the overproduction of T4. It is particularly important to assess renal function, by consideration of blood urea, creatinine and phosphate determinations in association with the urine specific gravity. It is well known that renal function is “proped up” by increased renal blood flow in hyperthyroid cats, hence urea and creatinine may rise following effective therapy. In a small number of cases this is just enough to tip a cat from compensated to decompensated renal insufficiency, despite correction of the myriad of adverse sequellae of thyrotoxicosis.

Thus, it is VITAL to ensure absence of azotaemia and adequate renal concentrating ability (urine sg >1.030 as a rule of thumb) before embarking on irreversible anti-thyroid therapy.

There are four ways to treat a cat with hyperthyroidism:

1. medical therapy with carbimazole
2. thyroidectomy
3. radio-iodine therapy with 131I
4. “benign clinical neglect” i.e. palliative therapy with atenolol and treatment of concurrent disease conditions

This is where this review becomes very subjective. I have a strong bias AGAINST the use of carbimazole, and instead will focus on other treatment options. I mention in passing that ethanol ablation of thyroid nodules using ultrasound guidance seems to have fallen completely into disrepute because of a higher prevalence of side effects than seen with simple surgical thyroidectomy.

**Carbimazole therapy**

Why am I so against the use of Neomercazole®? I guess it is because for many years I would encounter referral cases where it had not done what it was supposed to have done. Such cats would have endured poorly controlled hyperthyroidism, with lots of home medication and trips to the vet for monitoring, but ultimately required radio-iodine therapy. However, by the time they were referred for this the thyroid nodule was often very large, and the cat’s physiology had been irretrievably affected by poorly controlled hyperthyroidism. Why do vets like carbimazole? The answer is obvious. They can treat the patient themselves, without resorting to referral. Furthermore, cats do not need to be hospitalised for therapy, which is a big advantage for many owners. There is also a general perception that this is a cheaper option than surgery or 131I.

Let me tackle these issues one at a time. If you do the mathematics, the cost of treating a cat for one year using carbimazole, including regular re-checks and appropriate monitoring – which includes serial thyroxine
A critical additional consideration is that carbimazole must be given on a regular basis, usually twice daily, for the rest of the patient’s life (which is typically in excess of two years), and if we are honest with ourselves we will admit that this is beyond the ability of the vast majority of owners. Some people may have a different opinion, but the number of repeat T4 determinations submitted to private clinical pathology laboratories in Sydney to monitor carbimazole therapy would suggest that a substantial proportion of hyperthyroid cats treated in this manner are not well controlled. So what starts out with the best of intentions as ideal therapy, frequently lapses into a treatment regimen which is marginally effective or not effective at all, and which does not come cheap!

There are two situations when carbimazole has an important role. Firstly, in cats with a unilateral nodule awaiting surgery, preliminary medical therapy with carbimazole can establish euthyroidism and thus reduce the patient’s anaesthetic risk. Secondly, for cats with marginal renal reserve (mild azotaemia and/or urine specific gravity between 1.018 and 1.030), trial therapy with carbimazole can be helpful in determining whether establishment of a euthyroid state will induce decompensated renal insufficiency.

**Thyroidectomy**

In my experience, there are five different types of thyroids you can encounter when palpating a cat with symptomatic hyperthyroidism. The most common finding is two nodules, often one larger than the other; on either side of the trachea i.e. a left thyroid nodule and a right thyroid nodule. In a smaller number of cases, a single (unilateral) large thyroid nodule is palpable. In still other cats, there are several small thyroid nodules, of different sizes, palpable in the ventral cervical area. Cats with thyroid carcinomas usually have a single large firm thyroid nodule. Finally, some cats have cystic thyroids or parathyroids, which can become considerable in size (Figure 1A). This latter diagnosis is made using ultrasonography, or by doing a FNA (Figure 1B), which typically yields a large volume of fluid. Fluid retrieved by needle aspiration should be stored frozen, as in some cases it is helpful to measure the T4 and PTH levels within this fluid to determine whether the cystic mass is thyroid or parathyroid in origin (Figure 2).

Cats with a single thyroid nodule are excellent candidates for surgical thyroidectomy using an extra-capsular technique. This is an EASY surgery. Experienced surgeons describe it as cervical spay! The dissection on the ventral midline is anatomically simple, and although there are some scary structures like the carotid artery and vagosympathetic trunk, these are easily avoided with good technique and adequate lighting. As with all surgeries, it is ideal to practice first on a cadaver if you have never done this operation previously.

Determinations during induction therapy, at the lower doses of Neomercazole® used for ongoing therapy, and also monitoring for adverse hematological sequelae (in particular thrombocytopenia) – is comparable to surgical or radio-iodine therapies, and the overall cost of therapy over the course of the cat’s life is substantially higher.

**Figure 1A.** Photograph of a hyperthyroid cat with a very large goitre. Ultrasound demonstrated presence of a cystic thyroid mass.

**Figure 1B.** Drainage of the cystic fluid using a 23 gauge butterfly needle. Thyroid cysts often contain sanguineous fluid, whereas parathyroid cysts often contain clear fluid. T4 and PTH determinations of the fluid are required for more definitive differentiation, however in this case the elevated T4 concentration in serum further suggested the mass was thyroid in origin.
Radio-iodine therapy

There is really no argument that $^{131}$I therapy is the treatment of choice for cats with hyperthyroidism, and if all had the facilities, we wouldn’t use anything else 90% of the time! The treatment involves the administration of a small dose of a radiopharmaceutical, which is taken up selectively by the overactive thyroid tissue, and subsequently emits a high-energy $\alpha$-particle which destroys this tissue. The $^{131}$I can be given as a capsule or as an injection (IV or SCI). Both methods work equally well, although oral dosing is less stressful. Cats should be fasted for at least 6 hours before being given a radioactive iodine capsule, and a small amount of water should be dribbled into the cat’s mouth immediately after dosing to ensure that the capsule passes through the oesophagus and into the stomach rapidly, from where it is absorbed in a matter of minutes. Usually injections are reserved for fractious cats in which administration of a capsule may be problematic.

Although some authorities disagree, I believe it is prudent to STOP carbimazole for at least one week before dosing with $^{131}$I, as sometimes this drug prevents the uptake of radioiodine by hyperplastic thyroid tissue.

The cat is then isolated in an appropriately shielded environment (Figure 4A) for several days, until the dose of radiation emitted from the cat is sufficiently low that it can be sent home safely. Generally, cats treated on a Monday can be sent home on the Friday or Saturday, although the occasional cat with renal insufficiency needs to stay in for a few extra days.

The destruction of hyperplastic cells by the I-$^{131}$I can be appreciated by palpating the nodules 5 to 7 days after therapy, as they feel somewhat ‘mushy’. This renders the cat temporarily hypothyroid. Subsequently, elevated levels of TSH are released from the anterior pituitary, and the residual (previously quiescent) normal thyroid tissue becomes functional again. Thus, over several weeks, the cat becomes euthyroid.

Most cats with hyperthyroidism require between 160 and 220 MBq of $^{131}$I to restore a normal thyroid status in the long term, so a standard dose of 200 MBq is used for most patients. Cases with smaller nodules, lower T4 values and milder clinical signs can be successfully managed with a dose towards the lower end of this range, whereas cats with large thyroid nodules or massively elevated T4 levels are generally given higher doses. Most centres determine a dose based on their clinical experience, findings of physical examination (especially thyroid size) and the degree of T4 elevation. One centre in Sydney arrives at a dose on the basis of a preliminary scintigraphy scan.
Following radio-iodine therapy, cats should avoid prolonged close contact with their owners for approximately two weeks after they are discharged from the treatment facility i.e. they should not sleep with them or sit on their laps for a protracted period. In most cases euthyroidism is quickly established (indeed transient asymptomatic hypothyroidism is not uncommon). In a small proportion of cases the T4 level takes several months to normalise, and some cases require 6 months to determine whether the treatment has been successful. Perhaps 90% of cases are treated successfully from the outset. Of the remainder, some may be mildly hypothyroid and require thyroxine supplementation, while others will require a second dose of radioiodine. It is therefore prudent to re-assess the cat by clinical examination and follow-up T4 determination approximately two months after radio-iodine therapy.

There are a few specific points about the actual hospitalization for radio-iodine therapy. Cats with hyperthyroidism are often geriatric cats with significant comorbidities, typically degenerative joint disease and some degree of renal insufficiency. Even though the actual treatment is pain free, hospitalization can be stressful. It is therefore to be recommended that owners bring in a selection of the cat’s favourite foods (fresh meat, favourite canned flavours, dry food) to be fed during the period of hospitalization, and an item of clothing of the owner or a favourite towel or blanket (Figure 4B) to provide some reassurance to the patient. Clothing items may not be returnable for many weeks, because they become contaminated during the period of hospitalization.

An important consideration is which facility to use for radio-iodine therapy. After all, the main disadvantage of this therapeutic approach is its cost. The bottom line cost to the owner is of some moment, as is the service, geographic proximity and waiting list of the referral facility. As well as cost, some centres offer additional features such as free pick up and drop off of cases from the referring veterinarian. All these considerations are germane when considering whether to pursue surgical or medical therapy, and in choosing which facility to utilize. In order to demonstrate the range of costs involved and services provided, the author has conducted a ‘ring around’ of facilities offering this service around the country, and this information is assembled in Table 1.

Again, I would like to emphasise that although 131I treatment represents a substantial one-off cost, in the vast majority of cases the patient is “cured” and requires no further ongoing drug therapy or monitoring.

Heart failure due to hyperthyroidism

Nowadays it is unusual to diagnose hyperthyroidism in cats that present with CHF, either with pleural effusion or pulmonary oedema. This is because thyrotoxic cardiomyopathy resulting in CHF is typically a late manifestation of hyperthyroidism, and most cases are diagnosed during annual health checks well before this stage is reached. It is only when owners forgo regular veterinary attention that cats are thyrotoxic for sufficiently long to develop overt CHF.

Cats with CHF in the setting of hyperthyroidism are very tricky to manage. The first priority is to improve respiratory function by draining pleural effusion by thoracocentesis (using a 23 gauge butterfly needle, ideally inserted using ultrasonographic guidance) and diuretic therapy (4 mg/kg frusemide SC). The next priority is to quickly re-establish a euthyroid status. Surgery is probably an unacceptable risk for these patients, so the choice is between 131I and carbimazole. Personally, I prefer 131I because it reliably and rapidly establishes euthyroidism (Figure 5 and 6 A,B,C), but the problem with this option is that you then have to manage a radioactive patient that has the propensity
to develop recurrent pleural effusion. For this reason, many colleagues prefer to first stabilise these patients with carbimazole, while simultaneously managing the CHF with frusemide, and possibly an ACE inhibitor such as benazepril. It is vital to NOT give this cohort of cats a β blocker such as atenolol or propranolol while they are in congestive failure, as this often causes marked decompensation and sometimes death.

Table 2. Centres offering radiiodine therapy for feline hyperthyroidism

<table>
<thead>
<tr>
<th>Facility</th>
<th>Special features</th>
<th>Cost</th>
<th>Phone number</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New South Wales</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double Bay Veterinary Clinic</td>
<td>Free pickup and drop off of patients from referring veterinarian</td>
<td>$875 (includes pick-up and drop-off)</td>
<td>02 9363 4045</td>
</tr>
<tr>
<td>Gladesville Veterinary Hospital</td>
<td>Cats are given a thyroid scan prior to therapy</td>
<td>$900-$1100 (includes scintigraphy)</td>
<td>02 9817 5758</td>
</tr>
<tr>
<td>University Veterinary Centre Sydney</td>
<td></td>
<td>$990 (includes referral consult and blood pressure check)</td>
<td>02 9351 3437</td>
</tr>
<tr>
<td><strong>Victoria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Melbourne, Werribee</td>
<td></td>
<td>$879</td>
<td>03 9731 2000</td>
</tr>
<tr>
<td>Mt Evelyn Veterinary Clinic</td>
<td>$771.50-$784.50 depending on dose</td>
<td>03 9736 3088</td>
<td></td>
</tr>
<tr>
<td>Seaford Veterinary Clinic</td>
<td>$755-$785 depending on dose</td>
<td>03 9785 2611</td>
<td></td>
</tr>
<tr>
<td><strong>Queensland</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chermside Veterinary Hospital</td>
<td>$880-$920 depending on dose</td>
<td>07 3350 1333</td>
<td></td>
</tr>
<tr>
<td><strong>South Australia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adelaide Veterinary Specialist Centre</td>
<td></td>
<td>$1052.70 plus the cost of a preliminary consultation</td>
<td>08 8132 0533</td>
</tr>
<tr>
<td><strong>Australian Capital Territory</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canberra Veterinary Hospital</td>
<td></td>
<td>$803.00</td>
<td>02 6241 3333</td>
</tr>
</tbody>
</table>

*NB This is a old article and the prices are incorrect now.*

Figure 5. Lateral thoracic radiographs of a cat with high output congestive heart failure due to long-standing thyrotoxicosis. Note the resolution of the severe pleural effusion.
Figure 6 – A,B,C
Echocardiograms from the cat in Figure 3 before and after radio-iodine therapy. The right parasternal short access view (top) shows endomyocardial fibrosis, left ventricular hypertrophy and pericardial effusion. The M-mode traces in the middle image shows tachycardia, left ventricular hypertrophy, volume overload and suboptimal myocardial contractility. The lower image is some weeks after radio-iodine therapy; note the absence of volume overload and lower heart rate.

What to do with the old cat with early hyperthyroidism and renal insufficiency?

The “jury is out” on what to do with this subgroup of cats. Some cats with renal insufficiency and hyperthyroidism improve after definitive therapy, putting on condition without deterioration in renal status and having a good quality of life. However other cats, and it can be difficult to predict exactly which ones, decompensate after radiiodine therapy or thyroidectomy, and develop overt signs of decompensated renal insufficiency. I suspect this latter group were not going to do well in the long term in any case, however it looks really bad (in the eyes of the owner) to recommend an expensive treatment, and to then find the treatment has precipitated decompensated renal failure.

Therefore, in cats with substantial loss of renal concentrating ability and/or azotaemia, it may be prudent to determine the effect of establishing a euthyroid state by using carbimazole, before deciding whether to proceed to more definitive therapy. This is an unnecessary step in patients without azotaemia and with good urine concentrating ability.

An alternate approach is to treat the renal insufficiency with appropriate dietary therapy (your favourite prescription diet(s)), phosphate binders, blood pressure control (if indicated) etc., while administering atenolol (1/4 25 mg tablet once daily) to protect the cat’s heart from some of the effects of uncontrolled hyperthyroidism. I guess this is really benign clinical neglect, but in some patients, and for some owners, it represents an acceptable option.

Further reading


