

Perspective 88

Management of hyperthyroidism and hyperparathyroidism in cats



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General considerations

Hyperthyroidism is the most common endocrinopathy of domestic cats. It is usually the result of thyroid adenoma(s) or multiple hyperplastic nodules which may be unilateral or bilateral. Not all nodules are palpable. Functional thyroid tissue may elaborate increased amounts of thyroxine (T4) and T3, producing clinical signs including (i) a loud and fast heart, (ii) a prominent precordial impulse, (iii) a strong pulse and (iv) weight loss with good appetite. Heat intolerance, behavioural changes and polydipsia/polyuria can also be evident. Left untreated, hyperthyroidism damages a variety of end organs, particularly the heart and kidneys. The resulting catabolic state likely foreshortens life expectancy.

Hyperparathyroidism is reported to be rare in geriatric cats but, in my opinion, it is likely under-diagnosed. A functional parathyroid tumour secretes parathyroid hormone (PTH), causing hypercalcaemia, which results in azotaemia, polyuria, incessant polydipsia, sporadic vomiting, twitching and reduced appetite. These signs also occur with chronic renal insufficiency which can confuse the issue, as many elderly cats have some degree of kidney dysfunction. To confuse matters further, some cats have concurrent thyroid and parathyroid lesions.

Experienced veterinarians with sensitive palpation skills can detect ventral cervical nodule(s) in many old cats – some are thyroid in origin, others are parathyroid. Some are functional; some are non-functional or 'pre-functional'. Indeed, the presence of an incidental mass in the cervical/(para) thyroid area is an enigma in feline medicine because the only unequivocal way to distinguish thyroid from parathyroid masses is excisional biopsy. This may not be justified if lesions are non-functional, which is often the case early in the clinical course, because at this stage spot T4 and calcium determinations are in the reference interval.

The presence of a palpable thyroid nodule is one of the cornerstones in securing a diagnosis of hyperthyroidism, but a functional hyperthyroid state must be confirmed on the basis of other characteristic physical findings, specifically tachycardia, an enlarged cardiac impulse, a systolic heart murmur or gallop rhythm, and documented weight loss (in the face of a normal to increased appetite). A firm presumptive diagnosis is often made on the basis of these findings.

Diagnosis

It is usually straightforward to confirm the diagnosis using simple laboratory studies, such as a serum biochemistry panel and T4 determinations. In-house thyroid testing is notoriously unreliable and cannot be recommended. It is prudent to do a

urinalysis as well to assess urine concentrating ability, using a feline specific refractometer (or a human refractometer and a conversion scale). Many cats with hyperthyroidism have increased activities of alkaline phosphatase and alanine aminotransferase. Diabetes mellitus should be ruled out in cats with weight loss in the face of good appetite. If calcium concentration in the biochemical panel is high, or even high normal, consider an ionised calcium determination and/or measuring the serum PTH concentration. Both of these tests are a bit tricky, but with an I-Stat unit or blood gas analyser you can achieve the former, while to achieve the latter you need to freeze the serum specimen quickly and make sure it remains on ice on the way to a reputable endocrine laboratory. Diagnosis of hyperparathyroidism is not that common but these cases can be very gratifying to treat.

Often a single T4 determination is sufficient to diagnose hyperthyroidism. Sometimes a second T4 determination will be required, and in a small number of troublesome cases one has to resort to free T4 determination using equilibrium dialysis or (better) a T3 suppression test. Scintigraphy can also be useful, although this requires referral and is more expensive. If the cervical mass is large, ultrasound the lesion with the highest frequency transducer available. Large lesions are often cystic. If they have an anechoic centre it is worth aspirating the fluid. **Thyroid masses tend to contain bloody fluid, whereas parathyroid masses tend to contain clear fluid.** You can also determine T4 and PTH levels in the fluid, if you get enough, and this can be helpful in determining the nature of the nodule. Be wary of diagnosing hyperthyroidism on the basis of a T4 determination in the absence of supportive clinical findings. Laboratory procedures are rarely perfect, and a falsely elevated T4 concentration is not unheard of in a euthyroid cat. Fortunately, most sick cats tend to have low T4 levels (i.e. euthyroid sick syndrome).

An important part in the evaluation of geriatric cats is the detection of co-morbidities, especially chronic renal insufficiency. This is critical because cats with a marginal glomerular filtration due to renal disease may be reliant on the augmented cardiac output of the thyrotoxic state to maintain their urea and creatinine concentrations within normal limits.

Treatment

Radio-iodine is the treatment of choice for cats with hyperthyroidism. The following specific considerations apply to I-131 therapy: - ►

1. It is reliable and highly effective when a dose of between 140 and 250 MBq is given (depending on the size and number of thyroid nodules, and the extent of the T4 elevation; in my experience, most cats need 150 to 200 MBq). In Australia we seem to err on the side of giving too much, rather than not enough.
2. From the point of view of the cat, I-131 is safe and not stressful to administer as either a capsule or a subcutaneous injection. Most centres prefer the capsules (less expensive), but the injections are superior for feisty cats that may be hard to pill. Australian regulatory authorities require cats to be hospitalised for about 5-10 days.
3. There is no requirement for anaesthesia or surgery, and no risk of post-operative hypocalcaemia, laryngeal paralysis etc.
4. It fixes the primary problem, generally permanently, at the first attempt and without side-effects.
5. In most facilities, in Australia at least, I-131 therapy will 'cost out' cheaper than bilateral staged thyroid surgery.
6. A variety of therapy centres exist in NSW, Victoria, South Australia, Brisbane and the ACT. The development of commercially available purpose-built cages makes radio-iodine therapy possible in any practice with a start-up cost of less than \$10,000 AUD, including training and licensing.



Figure 1. Purpose built lead-lined radio-iodine therapy cages used by many centres in Australia. The photo above shows the outside appearance, while the opened cage showing accommodation for the feline patient is shown below. These photographs were taken at Double Bay Veterinary Clinic.

7. There is insufficient evidence in the peer reviewed literature to recommend the additional cost of routine thyroid scans prior to I-131 therapy, although this is done routinely at Gladesville Veterinary Hospital and selectively at the University of Melbourne. Simple tables that take into consideration the size of the thyroid lesion(s) and the extent of the T4 elevation seem adequate to determine the radioiodine dose.

Score	Severity of clinical signs	Total T4 (nmol/L)	Size of goitre	Total score	Dose I-131 (MBq)
1	Mild	< 80	Barely palpable		
2	Mild – moderate	< 100	1.0 X 0.5 cm	3 – 9	< 120
3	Moderate	100 – 150	1.5 X 0.5 cm	9 – 12	120 - 150
4	Moderate – severe	150 – 400	>1.5 X 0.5 cm	>12	160 or more
5	Severe	> 400	Visible to naked eye		

Estimating the dose of radioactive iodine from clinical signs, total thyroxine (T4) and size of goitre as estimated by palpation. Adapted from Mooney CT. Radioactive iodine therapy for feline hyperthyroidism: efficacy and administration routes. *J Small Anim Pract* 1994, 35:239.

Table 1 – A simple chart for estimating the dose of I-131 for treatment of hyperthyroidism. In Australia we tend to use larger doses of I-131 compared to the ones used in the UK, from where this table was developed. Perhaps this is because we give I-131 orally rather than subcutaneously.

8. From a pathophysiological point-of-view, radio-iodine fixes the underlying problem, i.e. the abnormal thyroid tissue is ablated. (With anti-thyroid drug therapy – the underlying problem continues, the goitre gets larger, often necessitating higher doses of medication as time goes on). Other non-specific effects of the thyroid lesion e.g. paraneoplastic substances, mass effects are avoided.



Figure 2. Marked thyroid gland enlargement in a cat given long term carbimazole therapy. Ultrasound showed the thyroid to be cystic. Such large masses require surgical excision or large doses of radio-iodine.

9. There is no requirement for twice daily medication and regular trips to the veterinary clinic to maintain a euthyroid state (the new once daily controlled-release carbimazole formulation Vidalta® is currently not available in Australia). In contrast, cats treated with carbimazole or methimazole typically require frequent and careful monitoring. The dose of medication may change as the primary lesion gets larger.
10. The presence of concurrent parathyroid lesions becomes easier, as abnormal thyroid tissue is ablated by the I-131. Thus, the detection of concurrent parathyroid lesions – either functional or nonfunctional – is facilitated.
11. Under-dosing with radio-iodine requires that the cat be given a 2nd dose at some point in time, typically after waiting 3-6 months for delayed effects of treatment.
12. Over-dosage with radio-iodine can result in permanent hypothyroidism, although this is rare. Transient hypothyroidism occurs in most patients, and is the stimulus for increased TSH levels to 'kick start' normal thyroid tissue that was previously quiescent. Signs of permanent hypothyroidism include lethargy, a poor coat and myxoedema of the head, resulting in thickened facial features and mild stridor referable to the upper airways. Hypothyroidism is easily treated with replacement therapy, typically 100 µg of thyroxine once daily, and given indefinitely. It is noteworthy that many human patients with Graves' disease are treated with ablative radio-iodine, and subsequently given life-long replacement therapy. Because thyroxine is a natural substance, it is well tolerated.
13. Much is made of the risk of 'unmasking' renal insufficiency following treatment of hyperthyroidism. However, if cats have urea and creatinine concentrations within the reference range, and a urine s.g. > 1.025 (>1.035 is even better!), it is rare for them to develop clinically significant azotaemia immediately after therapy with I-131.

It should be emphasised that urea and creatinine concentrations in cats with hyperthyroidism generally do rise to some extent following re-establishment of euthyroidism. Unfortunately, some cats develop the uraemic syndrome following therapy (particularly very old cats). The only definitive way to determine whether this will occur is with a carbimazole trial, which adds greatly to the cost and complexity of therapy.

The latest work from Hattie Syme's group at the Royal Veterinary College in London suggests that the abrupt transient hypothyroidism that follows radio-iodine therapy or surgical ablation adversely impacts on kidney function. In cases where kidney function is of concern, it is therefore prudent to start replacement therapy with thyroxine routinely for the first 4-6 weeks after definitive therapy. This prevents a sudden transition from hyperthyroidism to hypothyroidism, and the adverse impacts of transient hypothyroidism on the kidneys are therefore prevented. (Conceptually, this is similar to giving an animal cortisol replacement therapy after removing a functional cortisol-producing adrenal tumour). This replacement therapy can eventually be tapered, once the cat is stable and ideally having started kidney prescription diets etc.

Renal insufficiency following I-131 therapy can still be managed using prescription diets, phosphate binders, and attention to hydration; it is prudent to also treat them with

supra-physiological doses of thyroxine to re-establish a slightly hyperthyroid state and thereby increase renal blood flow.

14. It may be prudent not to treat cats with clinical or biochemical evidence of **advanced** renal insufficiency – even though some of these cats will actually benefit from correction of their thyrotoxicosis. A good way forward in this situation is a trial with carbimazole – although sometimes adverse effects from this drug trial can be problematic. Another strategy is to manage the cardiac signs of thyrotoxicosis with atenolol, treat hypertension with amlodopine and forgo any attempt to treat the underlying problem specifically.
15. The current cost of therapy (~\$900-\$1,500 AUD) is acceptable and less expensive in the long term than ongoing medical management for 6-12 months. See Table 1.

It is well worth ringing around for the 'best quote' as some centres are far less expensive than others (see Table 2 and Table 3). ▶



Figure 3. Marcus Gunew from The Cat Clinic Brisbane, dosing a cat with radio-iodine. Regulations about protective clothing etc vary from state to state.

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Table 2. List of Australian practices offering this service and details of treatment and associated costs.

PRACTICE	PRICE	WHAT'S COVERED	APPROX NO. OF CATS TREATED PER YEAR	AVERAGE WAITING TIME FOR THERAPY
NSW				
Double Bay Vet Clinic (02) 9363 4045	\$1,100	Use 160-210 MBq depending on the cat. Use ORAL capsule for most cats, injectable if they are FRACTIOUS. Includes free pick-up and delivery to the referring vet.	40 per year	7-10 days; typically 5-7 days
Gladesville Vet Hospital (02) 9817 5758	\$1,500 to \$1,600	Includes a charge for thyroid scintigraphy used to initially confirm the diagnosis and then help us calculate the appropriate treatment dose of an injectable form of I-131. Doses vary from 150MBq-300MBq for benign disease and up to 800MBq for confirmed malignancy. Do not use iodine capsules in our treatment protocol.	200	1-2 weeks
Valentine Charlton Cat Centre, University of Sydney (02) 9351 3437	\$1,500 to \$1,700	Includes: Specialist consultation, blood pressure (admission and discharge), fundoscopy, urine testing (culture, protein: creatinine ratio, sediment exam), maropitant pre-treatment, oral radioiodine, hospitalisation). Dose individualised, average 180MBq, cure rate > 95% (Wong <i>et al</i> Proc ACVSc Gold Coast, July 2010.) Veterinarians and their clients can discuss cases with a feline medicine specialist on (02) 9351-3437.	Not supplied Have the facilities to treat 3 cats at any one time.	1-3 days
North Nowra Vet Hospital (02) 4423 1688	\$977	Use 150 to 180 MBq depending on the cat. Use capsule unless the cat is impossible to dose. Same price regardless of time in hospital.	25	1 week
VIC				
University of Melbourne, Werribee (03) 9731 2000	\$1,100	A standard dose of 138 MBq radio-iodine is administered by capsule. Includes the initial consultation to examine the cat and discuss the treatment options with the owner, sedation for administration of radio-iodine and hospitalisation.	90 (i.e. 2 per week). Don't treat over Christmas and Easter.	2-4 weeks.
	\$1,600	Includes thyroid scintigraphy and a dose of radio-iodine between 180 and 350 MBq.		
	\$2,300	Minimum cost for investigation and treatment of neoplasia (carcinoma). Exact cost will depend on length of stay and includes thyroid scintigraphy.		
Mount Evelyn Veterinary Clinic (03) 9736 3088	\$1,085	Treatment is via a 150 or 200MBq capsule depending on the cat's T4 level. Includes sedation and oral administration of I-131 capsule followed by one week stay in our radiation ward.	50	1-4 weeks
Seaford Veterinary Clinic (03) 9785 2611	\$855 for 150MBq capsule \$885 for 200MBq capsule	Actual dosage is approximately 135 MBq for cats with TT4 90-200 and 180 MBq for cats with TT4>200 administered by oral capsule. A follow up T4 is required to be done at the referring clinic 2 months post treatment. Cats are hospitalised for 8 days & sedation (valium/ketamine) is required in approximately half the cats.	50	1-3 weeks
QLD				
The Cat Clinic Mt Gravatt: (03) 3349 0811 Paddington: (03) 3367 0011 Clayfield: (03) 3357 9902	\$1,200	Use oral dosing typically, with doses ranging from 150 to 200MBq. Includes the initial consultation, treatment, 1 week stay in the radiation ward and discharge.	85	2 weeks
Greencross Chermiside Veterinary Hospital (07) 3350 1333	\$1,200	Use capsules rather than injectable. Typically use 150-200 MBq but have the capability to treat thyroid carcinoma with higher doses if required. Includes one week of hospitalisation, quick GA and administration of I-131 capsule and care within the radiation ward. It assumes that the referring vet has completed the relevant blood tests prior to referral. All this information is faxed to the referring vet when we are first contacted to enable them to perform these tests before referral.	42 to 50	1-2 weeks average.

Table 2. List of Australian practices offering this service and details of treatment and associated costs (continued)

SA				
Adelaide Vet Specialist Centre (08) 8132 0533	~\$1,700	Oral dose of 170-250 MBq I-131 (dependent on pre-treatment assessment). Includes sedation and maropitant pre-medication followed by 1 week hospitalisation in isolation ward. Does not include initial consultation. Temporary treatment with carbimazole/methimazole may be recommended prior to I131 if renal function is questionable.	9	1-2 weeks.
Hills Veterinary Centre (08) 8278 4147	\$1,350	Oral dose of 150MBq orally, administered under ultrashort propofol anaesthesia. Includes 8 days hospitalisation, anaesthesia, and the I-131 capsule.	10	2 weeks
ACT				
Canberra Vet Hospital (02) 6241 3333	\$1,069	Method = Capsule. Dose = approx 180 MBq. Charge \$1,069 regardless of how long they need to be hospitalised.	30	1-2 weeks
Kippax Vet Hospital (02) 6255 1242	\$1,009	Use I-131 capsules at a dose of between 150 and 190 MBq. Can treat a thyroid carcinoma with higher doses if required. Fee includes capsule, premedication of an antiemetic and hospitalisation. Before therapy commences, we recommend a minimum data base to the referring vets but are happy to complete the investigation here prior to therapy for such things as a blood pressure reading.	20	1-2 weeks at most

Author's Note: Grateful thanks to the above participating practices for sharing this information with CVE members/readers. To the best of our knowledge the information collected is correct at the time of publication.

Table 3. List of UK practices offering this service and details of treatment and associated costs.

CENTRE	LOCATION	COST	WHAT'S INCLUDED?	NORMAL TIME IN HOSPITAL	WAITING LIST
Barton Lodge	Canterbury (SE England)	£1,000	Just the treatment, referring vet has to have completed a thorough work up including blood, urine, chest X-rays, virology	4 weeks	2 weeks
Barton Lodge	Canterbury (SE England)	£1,460	Assessment and treatment	4 weeks	2 weeks
University of Edinburgh	Edinburgh (Scotland)	£2,000	Really thorough assessment, treatment including follow up check at 3-6 months	11 days (3 days in hot room, 7 in ward); Must stay indoors at home for first 2 weeks	2-4 weeks
University of Glasgow	Glasgow (Scotland)	£1,300	Assessment and treatment	3 weeks	?
University of Bristol	SW England	£2,000 to £2,500	Thorough assessment and treatment	3 weeks (indoors for 2 weeks at home afterwards)	10 weeks
RVC, London	London	£1,300	Assessment and treatment	2 weeks	12 weeks
Bishopton Vet Group	NE England	£1,250 to £1,500	Just the treatment, referring vet has to have done a work up including blood and urine tests	2 weeks (inside at home for 2-4 weeks after this)	up to 6 weeks

Thyroidectomy

Surgical management of hyperthyroidism – either using a staged bilateral approach, or one side at a time – has most of the advantages of radioiodine. Risks associated with anaesthesia are less than in the 1980/90s because of earlier diagnosis and the widespread use of modern induction regimens, isoflurane or sevoflurane for maintenance, intra-operative fluid support and good intra- and post-operative analgesia. For these reasons, risks are extremely small (as has recently been shown in a European study), especially if cats are rendered euthyroid with carbimazole therapy prior to surgery.

Surgery is especially attractive in the following circumstances:-

1. When the owner will not travel to a referral centre, or send the cat via an animal courier.
2. When there is an easily accessible large unilateral nodule.
3. When a thyroid mass is present and growing – without clear cut signs of either hyperthyroidism or hyperparathyroidism. Indeed, it could well be that early surgical intervention is more appropriate than we currently realise, removing thyroid and parathyroid lesions before the adverse effects of endocrine hyperfunction develop, and while the mass is small. ▶

4. When the clinician is prepared to accept less than 'the going rate' for surgery because of a desire to help the patient and/or the client. In experienced hands, this is an easy and quick surgery that generally goes well as long as only removal of unilateral lesions is attempted. There is the additional benefit that histopathology provides a definitive diagnosis. There are, however, dangers of inexperienced surgeons attempting bilateral thyroidectomy, and the risk of post-operative hypocalcaemia is sufficiently high that this technique cannot (in my opinion) be recommended as a single procedure. Gary Norsworthy's idea of doing one side at a time, with transplantation of normal parathyroid to the strap muscles is clever, safe and easy. An instructional video of this technique is available (Contact CVE.)



Figure 4. Surgical thyroidectomy in the cat. This is straightforward surgery for an experienced surgeon, especially if only unilateral disease is being treated.

Long term carbimazole or methimazole therapy

My negative view of carbimazole comes from having been referred many cases where it has either failed to produce the expected euthyroid state, or produced unacceptable side effects. The latter are NOT TRIVIAL in a geriatric cat with several concurrent problems, and I have seen many cats euthanased because of the development of carbimazole-induced problems, which have resulted in the owners losing a positive attitude towards ongoing case management. Clients can lose confidence in the veterinary team if it takes some time for the cat to become outwardly normal, or if the cat requires what the owner perceives as an excessive number of veterinary consultations. For owners who want the problem fixed quickly at the first attempt, radioiodine or surgery is more appropriate than drug therapy.

From my perspective, the principal issues with these drugs are:-

1. The underlying problem is never fixed.
2. Concurrent hyperparathyroidism may be missed until the serum calcium concentration has been elevated for quite some time.
3. The requirement for the drug is variable and many cats need frequent dose alterations.
4. There are compliance issues for many owners although new once-daily formulations and transdermal preparations can get around this.

5. There are ongoing bills and the need for regular veterinary consultations.
6. Specific drug-related adverse effects that have been recorded include gastrointestinal side effects (anorexia, vomiting, diarrhoea), symptomatic thrombocytopenia, neutropenia and liver dysfunction.

Parathyroidectomy

Hyperparathyroidism is usually caused by benign parathyroid tumours – either unilateral or bilateral. Treatment involves surgical removal of the affected parathyroid glands. As many cats will be hypercalcaemic at the time of surgery, they should receive intravenous saline preoperatively and during the surgery, with careful attention to anaesthesia including monitoring of blood pressure and avoidance of NSAIDs following surgery. Usually the serum calcium will drop into the reference range following surgery, and rarely there can be problems with transient hypocalcaemia. Vets should have intravenous calcium gluconate and calcitriol on hand should hypocalcaemia become problematic.

BOOK

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