# Investigation and management of hyperthyroidism in dogs and cats

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**Rebecca Littler** discusses the diagnosis and treatment of a common condition, which includes radioactive iodine as an approach to thyroid carcinomas

**HYPERTHYROIDISM is one of the most commonly recognised feline endocrine disorders. However, despite the wealth and breadth of data available on its clinical signs, treatment and outcome, its cause – in most cases – remains obscure.**

In most cats, hyperthyroidism is due to a benign, predominantly bilateral, adenomatous hyperplasia of the thyroid gland. The hyperplastic glands are endocrinologically active, and clinical signs are caused by an overexposure to excess thyroid hormone. Approximately two per cent of cats have a thyroid carcinoma, which is often unilateral, but can present as bilateral disease or multiple cervical nodules. These tumours are similarly endocrinologically active, but are malignant and frequently highly metastatic.

Hyperthyroidism is infrequently diagnosed in the dog, but can result from an endocrinologically active thyroid carcinoma. However, such patients more frequently present with a palpable neck mass or signs associated with a mass, such as dysphagia.

Any canine neck mass warrants further investigation as the thyroid is not normally palpable and carcinomas tend to grow quickly. It has been reported that metastatic disease is present in 16-38 per cent of patients at diagnosis. Adenomas are frequently reported as a postmortem finding, but they tend to be small, non-palpable and non-secretory.

## Clinical signs and diagnosis

The clinical signs of feline hyperthyroidism are well known and frequently seen in older cats. The mean age of presentation is 13 years. Symptoms include polydipsia/polyurea (approximately 50 per cent) and polyphagia (approximately 90 per cent), with weight loss (approximately 50 per cent), diarrhoea and vomiting (approximately 40 per cent). Other symptoms include poor coat hair and irritability. Differentials for these clinical signs in older cats include diabetes mellitus, gastrointestinal disease and hyperadrenocorticism.

Other hyperthyroid cats will present with symptoms resultant from thyroid-induced cardiac disease, hyperdynamic function, hypertrophic cardiomyopathy, congestive heart failure (such as respiratory distress), tachycardia and thromboembolism. A systolic murmur or gallop sound may be auscultated.

Approximately 10-15 per cent of cats present with the apathetic form of the disease – where decreased appetite and lethargy are noted. A high level of clinical suspicion may be required to reach a diagnosis.

Clinical signs of hyperthyroidism in dogs include weight loss, polyphagia, polydipsia and weight loss, diarrhoea and vomiting. However, in contrast to feline patients – where owners rarely notice a goitre – canine patients' owners often describe neck masses and/or swellings, and signs associated with them, such as coughing and swallowing problems.

## Diagnostic investigations

Characteristic findings on haematology and biochemistry blood screens in cats include erythrocytosis (40 per cent), increased alanine aminotransferase and alkaline phosphatase. More than 90 per cent of hyperthyroid cats show a rise in one or other of these enzymes. Blood urea nitrogen and creatinine are frequently raised and, as discussed later, careful attention to renal function is required in recommending treatment options in hyperthyroid cats. Although urinalysis is often non-contributory in the diagnosis of hyperthyroidism, it is important in the assessment of renal function.

Hypertension (where persistent systolic blood pressure readings of 160-170mmHg or higher are noted) is well documented in older cats with renal disease, cardiac disease and hyperthyroidism. As persistent hypertension has the potential to cause end organ damage, such as retinal haemorrhage or complete detachment, it is important to include a measure of hypertension in older feline patients suspected of hyperthyroidism (Figure 1) and treat as indicated. Assessment of cardiac function, due to the high incidence of thyrotoxic cardiac disease, should include chest radiographs and, if possible, ECG and echocardiography.

Due to the high metastatic potential of thyroid carcinomas in cats, chest radiographs should be

carefully evaluated for metastatic disease, as should regional lymph nodes and, potentially, abdominal ultrasound scans where they are suspected. Ultrasonographic evaluation of the neck may be useful in distinguishing causes of feline hyperthyroidism (Figure 2). Referral for nuclear scintigraphy should be considered, especially where carcinoma is suspected.

Hyperthyroid dogs present more frequently due to their neck mass. Diagnostic findings in canine patients with thyroid hormone-producing tumours will include haematology and biochemistry findings similar to cats. Other diagnostic work up is aimed primarily at staging the neoplastic lesion and should, therefore, include ultrasound of the neck, checking and aspiration of regional nodes, thoracic radiographs, abdominal ultrasonography and, if possible, MRI or CT of the neck to examine invasion and margins of the mass. An important note to make is the size of the mass and whether it is freely movable. As with cats, referral for nuclear scintigraphy should be considered.

A presumptive diagnosis of thyroid neoplasia can be made on these investigations. However, biopsy remains the gold standard. Excisional biopsies have the advantage of being potentially curative and diagnostic in smaller thyroid masses. In larger or non-mobile masses, fine-needle aspirate of needle-core biopsies should be considered. As thyroid carcinomas can be highly vascular, ultrasound guidance, if available, is also recommended.

## Definitive diagnosis and measuring thyroid function

The basal total T4 concentration is greater than the reference range in most hyperthyroid cats, with the majority being below 100nmol/ml. Serum total T4 concentration may also be within the middle to high end of the reference range (more than 30nmol/L) in approximately 10 per cent of hyperthyroid cats, possibly because of earlier diagnosis or the fluctuation of thyroid hormones. If basal thyroid hormone concentrations are only mildly elevated, the degree of fluctuation can result in reference range values.

In cats with markedly elevated serum thyroid hormone concentrations, the degree of fluctuation is of little diagnostic significance. In cases with reference T4, measurement of T4 – three to four weeks after initial measurement – will often result in an elevated reading being recorded. The presence of concurrent non-thyroidal illness can also affect the circulating total T4 concentration in hyperthyroid cats. Low total T4 concentrations are only expected in cats with severe non-thyroidal illness. In patients with clinical signs suspicious of hyperthyroidism, measurement of free T4 is recommended, as serum-free T4 concentration remains elevated in hyperthyroid patients with non-thyroidal illnesses when the total T4 concentration is suppressed into the reference range.

Dynamic thyroid function tests are described in feline clinical literature (thyroid-stimulating hormone [TSH] stimulation test, thyrotropin-releasing hormone [TRH] stimulation test). However, using free T4, or repeating total T4 measurement at intervals until the patient becomes demonstrably hyperthyroid, is usually sufficient to make the diagnosis.

Thyroid hormone measurements may be made in dogs with cervical masses and suggestive clinical signs. However, the majority of canine patients with thyroid masses do not have raised total T4 or free T4 measurements. Occasionally, canine patients suspected of having hypothyroidism will have elevated total T4 measurements. These patients are not hyperthyroid; the presence of thyroid hormone auto-antibodies can artificially increase concentrations of T4 measured by radioimmunoassay.

Free T4 measurements are not affected if a membrane dialysis technique is used, as the antibodies cannot pass through the membrane. Therefore, if a spuriously high T4 measurement is returned in a dog with signs of hypothyroidism-free T4 and thyroid antibody, measurements should be made.

## Considerations prior to treatment

**• Cats**

The most importan t consideration prior to treatment recommendation in feline patients is renal function. Chronic kidney disease can be masked in cats – due to significantly increased glomerular filtration rates attributable to the haemodynamic effects of hyperthyroidism. Therefore, careful assessment of renal function is warranted.

It is possible that azotaemia may result post-treatment, due to unmasking of renal disease. Development of azotaemia after treatment for hyperthyroidism can be predicted from pre-treatment glomerular measurements. However, these cannot usually be performed in general practice. Attempts have been made to predict azotaemia development from factors in the history, physical examination, biochemistry and urinalysis.

It has been suggested that azotaemia is more likely to develop in older patients and in those with small or irregular kidneys. Potentially, those with higher creatinine concentrations (even high normals within laboratory reference range), lower urine septic gravity and very high pre-treatment total T4 concentrations have an increased risk of being azotaemic after treatment for hyperthyroidism.

No single parameter has been shown to be consistently useful in this prediction. In recognition of this, medical management of patients prior to any other treatment is often recommended, so, renal functional deterioration can be assessed.

Cardiac disease, resultant from thyrotoxicosis, is common in a cat’s assessment, and the treatment of symptoms of congestive failure are warranted. In general, however, treatment considerations are centred on control of the underlying hyperthyroid state, as well as addressing its cardiovascular consequences. Provided that antithyroidal drugs are well tolerated, it is sensible to stabilise the condition of hyperthyroid patients before general anaesthesia for other treatment

options, because a high occurrence of catecholamine-induced arrhythmias has been reported.

If medical treatment with methimazole or carbimazole is inefficient at controlling cardiac manifestations associated with hyperthyroidism, betablockers are usually successful in treating many of the cardiovascular effects. Congestive failure should obviously be treated in the standard way, with the introduction of diuretics.

• **Dogs**

The most important consideration in hyperthyroid dogs is the determination of metastatic disease and its extent. Therefore, an attempt at tumour, node, metastases (TNM) staging should be made. The most common site of metastasis in canine thyroid carcinoma is the lungs.

Metastasis to local lymph nodes is also seen. In addition, the type of tumour and likelihood of achieving clean surgical margins should be addressed. If metastatic disease is present, a partial thyroidectomy and referral for chemotherapy can be considered. A poor surgical candidate, or one in which margins will be difficult, can also be offered referral, with the possibility of surgery and adjunctive radiotherapy and chemotherapy.

## Treatment options for feline patients

Three main treatment options exist for cats with hyperthyroidism caused by benign adenomatous hyperplasia:

• medical management with thioureylenes (methimazole or carbimazole);

• surgery; and

• radioactive iodine therapy.

Those suspected of having carcinoma should be given radioactive iodine as a preferential treatment. Feline patients with any suspicion of renal disease should be offered medical therapy in the first instance, with renal parameters carefully assessed during treatment. Significant worsening of renal disease would be a reason not to recommend surgery or radioactive iodine treatment and may prompt alteration in drug dosages.

Medical treatment can also be used to control clinical signs prior to surgery (making anaesthesia safer) or prior to radioactive iodine treatment (to assess the response of renal function). Preparations of both methimazole and, more recently, a longacting once-daily preparation of carbimazole (Vidalta: Intervet) are licensed for the treatment of feline hyperthyroidism. The bio-availability of the controlledrelease preparation is similar to that of the conventional methimazole preparation – both have greater absorption if they are given with food.

Medical management controls thyroid hormone production, but does not treat the underlying cause. In addition, administering tablets to cats long term can prove challenging. If renal parameters do not worsen during initial management of the feline hyperthyroid patient, surgery, or radioactive iodine therapy, should be discussed. It should be noted that few studies have been carried out that offer a direct comparison of medical, surgical or radiation management. However, if indicated in a patient and available, radioactive iodine is probably superior in efficacy, safety and compliance.

The thyroid cells concentrate radioactive iodine, and a combination of ? and ? destroys abnormally functioning thyroid tissue. Most damage is caused by ? particles. Doses of radioactive iodine are administered subcutaneously after a scoring system – to take into account the size of goitre and severity of clinical signs – has been used to calculate dosages. Approximately 95 per cent of cats only require a single dose to acquire euthyroidism – a small percentage need a second treatment. Extremely high doses are required to treat feline thyroid carcinoma and, at present, to the author's knowledge, these are only offered at Langford Veterinary Services (University of Bristol). Referral to a centre with the special facilities for housing the radioactive iodine-treated cats is essential, and isolation periods of between two and four weeks are required. This extended isolation period makes any concurrent disease a relative contraindication to radioactive iodine therapy. However, the majority of hyperthyroid cats can be treated successfully.

Although there is debate as to the effect on radioactive iodine therapy of prior methimazole or carbimazole treatment, concurrent administration is not recommended, as the half life of the radioactive iodine is shortened. Therapy should be withdrawn approximately seven days prior to the commencement of radiation treatment.

Where referral for radioactive iodine is not accessible, thyroidectomy is recommended as a curative treatment in suitable feline patients. The techniques are described fully in the standard surgical texts. It is preferable to stabilise patients prior to general anaesthesia and, due to the close anatomical association of parathyroid and thyroid glands, a short postoperative period of hospitalisation is recommended with careful monitoring of serum calcium. An algorithm (based on Feldman and Nelson, 2004) is suggested for decision making in the treatment of feline hyperthyroid patients (Figure 3).

## Treating canine patients

Surgical treatment is required on canine thyroid tumours that result in hyperthyroidism. Oral anti-thyroid medications are not recommended, as they are not cytotoxic. However, the use of carbimazole or methimazole prior to surgery to stabilise the patient is described. In a patient without metastatic disease, where clean margins can be achieved, thyroidectomy is recommended, with close postoperative assessment of the surgical site and lymph nodes. Where margins are not achieved, or the mass is poorly mobile, referral for radiotherapy should be offered. Patients in which metastatic disease is present, or with poor surgical margins, should be considered for chemotherapy.

## Conclusions

Feline hyperthyroidism is a common disease that is usually caused by benign endocrinologically active bilateral thyroid adenomas. Various treatments are available and consideration should be given to radioactive iodine where possible. Before any treatment is considered, careful patient evaluation with reference to renal and cardiac function should be made. The possibility of a malignant thyroid carcinoma should be borne in mind in diagnostic evaluation.

In contrast, canine hyperthyroidism is rare. Signs are usually attributable to a significantly sized thyroid mass. These tumours are often malignant and surgery offers the best chance of cure, with consideration of adjunctive radiotherapy and chemotherapy.

• References are available on request to the editor.

*Figure 1 (left). Blood pressure monitoring is essential in small animal hyperthyroid patients.*

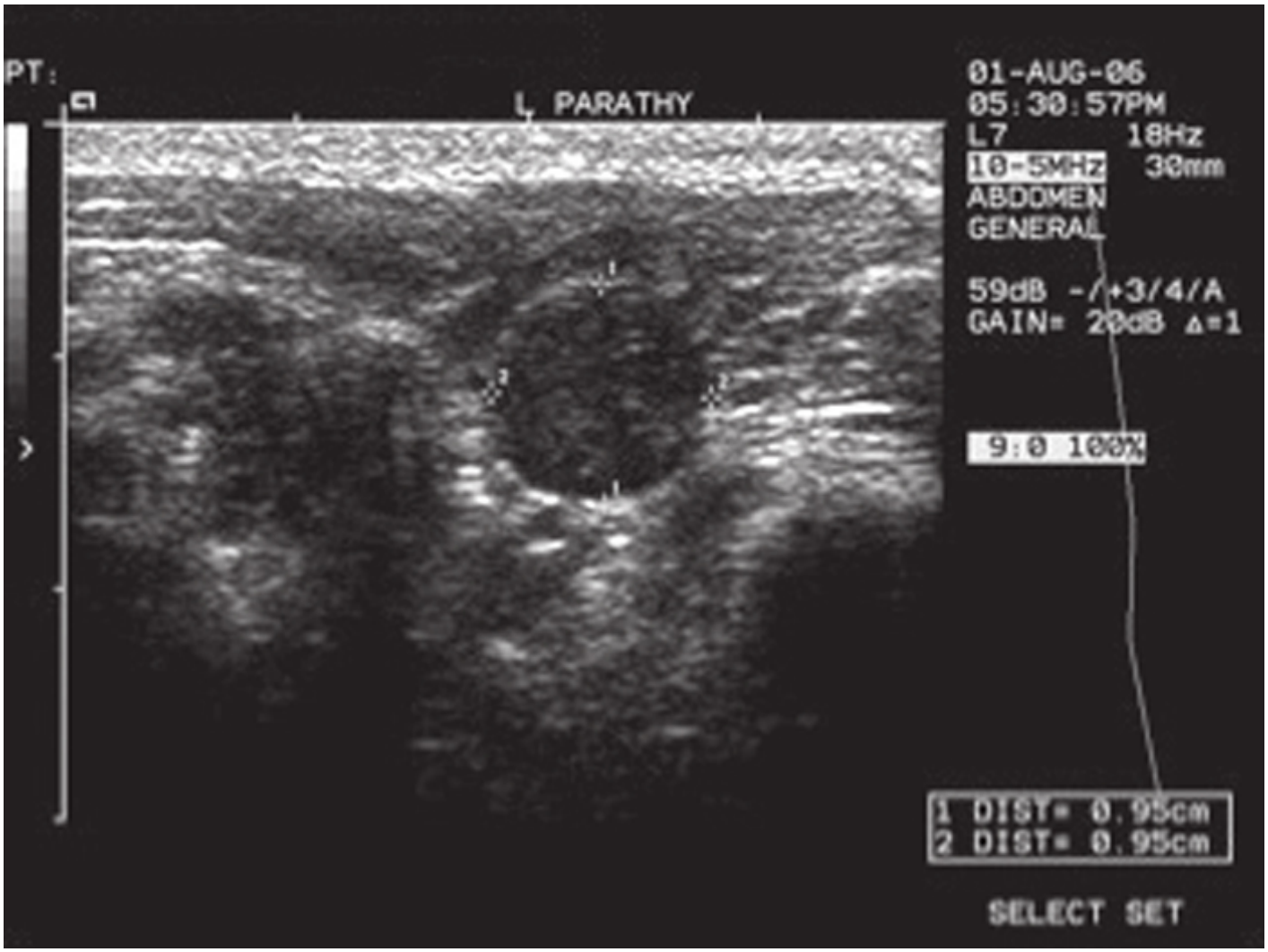


*Figure 2 (below). Neck ultrasound may be helpful in the diagnosis of causes of hyperthyroidism in both cats and dogs.*

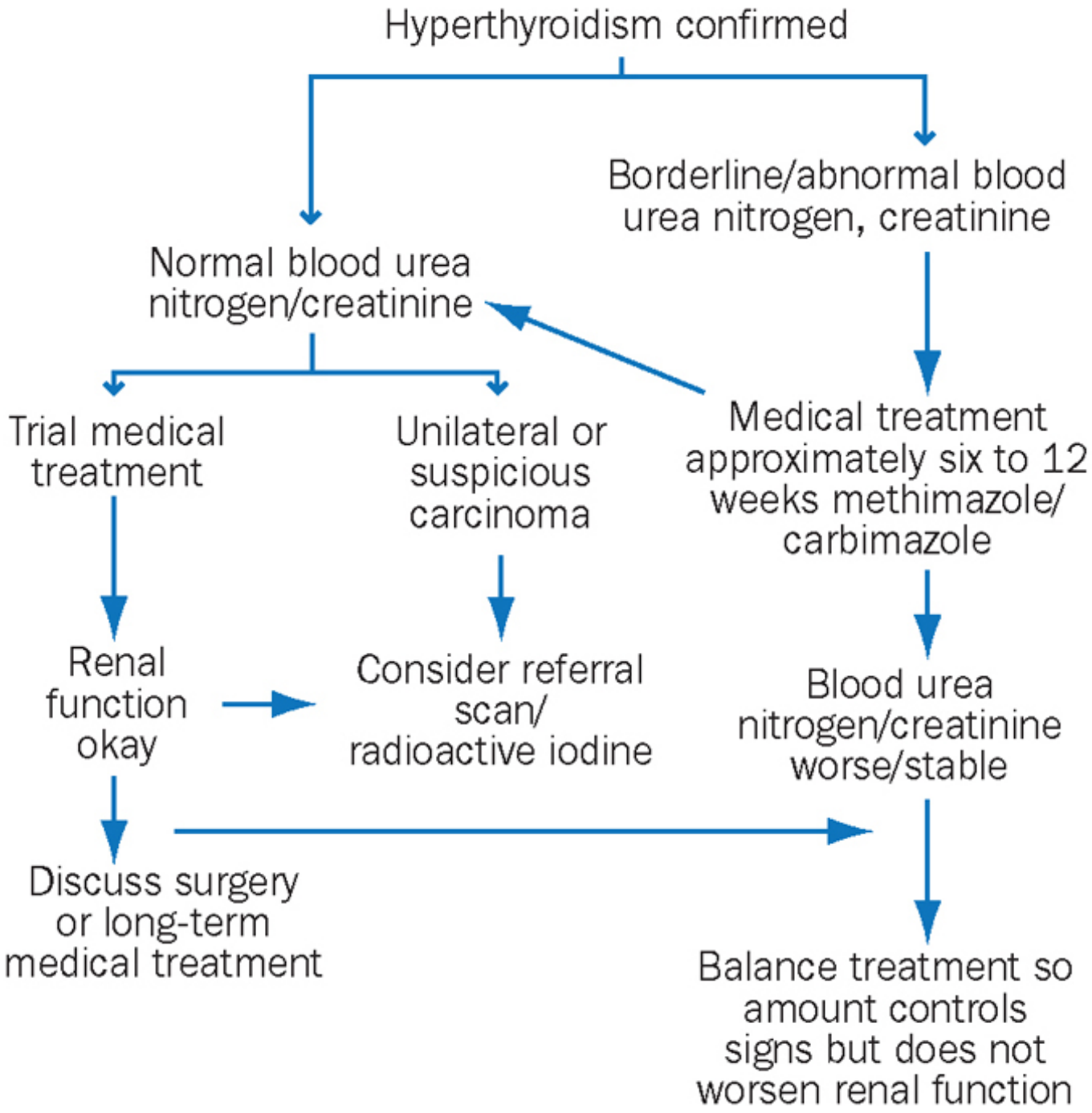


*Figure 3. Suggestions for the treatment of hyperthyroidism in cats.*