

# **VETERINARY BULLETIN**

# **FAQs about HYPERTHYROIDISM IN CATS**



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#### Hyperthyroidism

Hyperthyroidism is a common condition, especially of older cats. Although many cases are straightforward to diagnose and treat, this is not always the case. This bulletin aims to inform and advise on some of the more common dilemmas.

Please note: Methimazole and thiamazole are the same active ingredient.

1. How common is hyperthyroidism – should I be routinely screening for this in all 'older' cats?

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Most published studies have indicated that around 10% of elderly cats suffer from hyperthyroidism. Since hyperthyroidism is a gradually progressive condition with an insidious onset, it can be difficult to spot until relatively advanced. This provides justification for proactive health screening in older cats. The author recommends that clinicians follow International Cat Care's Wellcat guidelines regarding the frequency and nature of check-ups of older cats (Table 1), for example, including an annual thyroid test (e.g. total thyroxine, T4) in cats aged 11 years and over. Owner education as to what clinical signs to look out for (Table 1) is also important so that prompt assessment and investigations can be performed if any of these develop.

2. Is there a 'gold standard' treatment for hyperthyroidism? How do I decide which treatment is best?

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There are four broad treatment options for hyperthyroidism, two curative options and two reversible options:

- Reversible options (lifelong treatment needed)
  - Antithyroid medication
  - Exclusive feeding of an iodine-restricted diet: Hill's y/d
- Potentially curative options
  - Surgical thyroidectomy
  - o Radioiodine

None of these options are perfect – all have both advantages and disadvantages (Table 2). The ideal treatment will therefore vary from patient to patient according to their individual circumstances. Where possible, curative treatment options should be pursued as these generally carry the best long-term prognosis.

3. What options exist for antithyroid medications in cats?

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A number of different preparations of antithyroid medications are available in the UK and include:

Methimazole (also known as thiamazole). This is a bitter tasting drug so oral preparations are presented in a sweetened suspension or as sugar coated tablets:

• Thyronorm (Norbrook), a liquid suspension containing 5 mg thiamazole per ml. It is



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recommended that the treatment is administered directly into the mouth but it can also be given with a small amount of tasty food (off-licence use). The liquid formulation offers infinite dose variations allowing the dose to be tailored to each individual cat.

- Felimazole (Dechra Veterinary Products), available in three tablet sizes: 1.25 mg, 2.5 mg and 5 mg of thiamazole.
- Thiafeline (Animalcare), available in two tablet sizes: 2.5 mg and 5mg of thiamazole.
- A methimazole gel is also available as a transdermal preparation (50 mg/ml, Summit Pharmaceuticals). This is not a licensed (veterinary authorised) medication but can be prescribed to cats under the Cascade regulations, providing both the licensed liquid and tablet preparations are deemed unsuitable for that animal.

Carbimazole is manufactured in the UK as the veterinary licensed product Vidalta by MSD Animal Health. Vidalta is a 'sustained release' preparation which means that the carbimazole is slowly released from the tablet and Vidalta therefore has a once daily or every other day dosing recommendation.

#### 4. Can I use thiamazole once a day or does it need to be given twice daily?

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Methimazole/thiamazole is generally more effective in inducing euthyroidism when administered twice daily but once euthyroid, many cats can be maintained on once daily treatment. For many owners, giving medication twice a day is not problematic although support – for example tuition on how to administer the medication – is important at the start of treatment. Some owners may find administration of a liquid medication easier than a tablet.

## 5. If I want to switch from a transdermal methimazole medication to an oral thiamazole medication, how should I do this?

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Please note: methimazole and thiamazole are the same active ingredient.

Poor compliance/difficulty dosing with oral medication is a common reason for prescribing a transdermal preparation of methimazole/thiamazole. However, transdermal medication is not always successful with some cats remaining difficult to dose, suffering from local adverse effects (e.g. inflammation of the inner pinna) or from other complications (e.g. other cats in the house grooming off the preparation). Some owners may find the oral liquid suspension of thiamazole (Thyronorm, Norbrook) a practical alternative to consider.

Cats receiving transdermal methimazole tend to need a higher dose of this compared to those receiving oral methimazole/thiamazole.

For example, the typical dose required to stabilise a hyperthyroid cat is 5 mg methimazole/thiamazole BID using the transdermal route versus 2.5 mg twice daily for the oral route. This and other factors should be considered before deciding a dose of oral methimazole/thiamazole.



A wash-out period (no medication) is suggested for 24-48 hours to ensure that any residual methimazole/thiamazole is metabolised and there is no potential for overdose.

Consideration should also be given to whether the patient was euthyroid and how compliant they were to the transdermal medication. For example, consider Sooty, a hypothetical patient that has been receiving 5 mg transdermal methimazole twice daily but where a switch to oral methimazole/thiamazole is desired:

- Was Sooty euthyroid on the 'old' (transdermal) regime?
  - Yes:
    - If compliance to the 'old' regime was <u>considered to be good</u>, then recommend starting at half of this dose: 2.5 mg Thyronorm twice daily
    - If compliance to the 'old' regime is <u>considered to be poor</u> then a dose reduction may be sensible to avoid potential overdose and iatrogenic hypothyroidism: 1.25 mg Thyronorm twice daily
    - Repeat T4 assessment is recommended 2-3 weeks after starting oral treatment with the dose titrated to maintain total T4 levels in the lower half of the reference range, where possible
  - No Sooty was still hyperthyroid:
    - If compliance to the 'old' regime was <u>considered to be good</u> then start dosing at the same dose used in the 'old' regime: 5 mg Thyronorm twice daily
    - If compliance to the 'old' regime was <u>considered to be poor</u> then start dosing at a standard oral dose, as you would for a newly diagnosed cat with hyperthyroidism, e.g. 2.5 mg Thyronorm twice daily
    - Repeat T4 assessment is recommended 2-3 weeks after starting oral treatment with the dose titrated to maintain total T4 levels in the lower half of the reference range, where possible

### 6. If I want to switch from a carbimazole medication to a thiamazole medication, how should I do this?

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If the patient is stable on their current treatment then the client should be advised against changing the medication. If wishing to switch medications to improve control or compliance, it is important to know that carbimazole is a pro-drug of methimazole and therefore dose rates will vary.

A 'wash out' period (a period free of antithyroid medication) of 48-72 hours is recommended to ensure that all carbimazole has been metabolized before commencing thiamazole medication.

Equivalent doses of carbimazole and thiamazole are 1: 0.6. Therefore 10 mg carbimazole is equivalent to 6 mg thiamazole. The table below (Table 2) contains suggested dose guidelines when switching from sustained release carbimazole (Vidalta, MSD Animal Health) to thiamazole. These



are just guidelines and the final dose required by the patient may differ.

Twice daily treatment of thiamazole is generally recommended since this tends to be more reliable in inducing euthyroidism and may be associated with fewer side effects.

Once stable, once daily dosage often maintains euthyroidism and may be more popular with the owner.

Total T4 levels should be assessed 2-3 weeks after making any treatment change with the dose amended if needed – the ideal being for total T4 levels to be in the lower half of the reference range.

Table 3 Suggested dose guidelines when switching from carbimazole to thiamazole

Vidalta dose and frequency	Suggested starting dose and frequency of methimazole/thiamazole (once daily dose)*
15 mg once daily	5 mg twice daily† (10 mg once daily)
15 mg every other day	2.5 mg twice daily† (5 mg once daily)
10 mg once daily	2.5 mg twice daily† (5 mg once daily)
10 mg every other day	1.25 mg twice daily† (2.5 mg once daily)

<sup>\*</sup> *Please note:* These recommendations assume that compliance to oral Vidalta was good and that the patient was euthyroid. If compliance was reported to be poor but the patient euthyroid, a reduction in dose may be safer to avoid iatrogenic hypothyroidism. Conversely, if compliance was good but the patient still hyperthyroid, a small dose increase may be appropriate.

## 7. What time of day should I collect blood samples for thyroid level monitoring in cats receiving oral or transdermal antithyroid medication?

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The aim of medical management of hyperthyroidism is for total T4 levels to be reduced to the lower half of the reference range. For cats receiving once or twice a day treatment with antithyroid medication (orally or transdermally) the timing of blood collection for T4 measurement relative to medication administration is unimportant ie it does not matter when you collect your blood sample. There is some evidence that methimazole/thiamazole concentrates in the thyroid tissue and this may be one reason why timing of blood sampling is unimportant.

In some cases, optimal stabilisation of hyperthyroidism involves giving alternate day treatment (e.g. Vidalta – sustained release carbimazole – has a once a day or once every other day license). Alternatively, a different dose of methimazole/thiamazole may be needed on alternate days (e.g. 2.5 mg twice daily on one day, 2.5 mg once daily on the next, repeating).



<sup>†</sup> Twice daily dosing should be maintained at 12 hours apart and the medication administered in the same way each time i.e. if given in food, then consistently give the medication in food.

Where possible, the author prefers to avoid alternate day protocols since it can be difficult and confusing for owners to remember what medication their cat needs.

There is no published data regarding optimal timing of blood sampling relative to alternate day antithyroid medication administration. The author prefers to collect samples on the day 'off' treatment (or lower dose of treatment). If the cat is doing well clinically and total T4 is in the lower half of the reference range on this sample then it indicates that the hyperthyroidism is well controlled.

#### 8. Can antithyroid medication be added to food? Does this affect absorption of the product?

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The presence of food in the gastrointestinal tract at the time of administration has been shown to increase the bioavailability of thiamazole. In general, the author would advise that oral antithyroid medication can be given with or without food although the owner should try and be consistent in how they medicate their cat, including giving the medication at the same time/s of day.

For those cats that are difficult to medicate orally, hiding the treatment in a small amount of food can be helpful. If using pills ideally these should be hidden 'whole' as the sugar coating will help to encourage acceptance (thiamazole is a bitter tasting medication).

Although not ideal, occasionally crushing methimazole or carbimazole is sometimes necessary to achieve medication. Carers should be advised to wear gloves when crushing pills since some people can be sensitive to antithyroid medications. Pregnant women should not handle antithyroid medications since these are suspected to be teratogenic.

The crushed pill should be given in the smallest amount of food possible to try and ensure that the whole dose is eaten rather than being left in the food. Crushing medication constitutes 'off-licence' use of a veterinary authorised product and is not recommended unless this is the only way of successfully achieving medication.

If crushing Vidalta, users should be aware that this removes the sustained-release aspect of this medication therefore half of the crushed medication should be given twice daily. Alternatively a liquid preparation (Thyronorm; Norbrook) might be a preferable option to crushing the tablets.

#### 9. How is methimazole/thiamazole excreted?

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Thiamazole is hepatometabolised and renally excreted. Mild to moderate elevations of liver enzymes are commonly found in cats with hyperthyroidism and are not a barrier to use of antithyroid medication. However, if the elevation in liver enzymes is greater than expected, further investigation of liver disease is indicated to rule out primary hepatopathies.



## 10. If a cat has no clinical signs and a mild elevation in circulating total T4 concentration, does it necessarily require treatment?

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There are several situations in which this may occur:

- False positive test result: Occasionally mild false positive elevations in total T4 can be encountered. Sometimes these are a laboratory error and may be more common with inhouse T4 tests. In overweight cats there may be some thyroid resistance caused by the obesity and this has been hypothesised to potentially result in an increase in total T4.
- Early hyperthyroidism: in early disease the T4 may be elevated before clinical signs have been noted by the cat's owner.

If no goitre is present and/or there are no clinical signs of hyperthyroidism then a sensible plan would be to monitor the cat closely in the short-term, for example checking the patient history, bodyweight and physical examination once a month.

The owner should be educated regarding common clinical signs of hyperthyroidism and advised to return to you if concerned that any of these are developing. If clinical signs develop then repeating the total T4 test is indicated.

<u>Diagnosis of hyperthyroidism is not an emergency</u> since this is a disease which has an insidious onset and gradual progression. If in doubt over the validity of the T4 results received, consider sending serum to a reference laboratory for analysis.

#### 11. What should I do if I receive a normal total T4 in cat which I suspect to have hyperthyroidism?

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This usually occurs for one of three reasons:

- In cats with mild or early disease, T4 levels may vary from within the reference range to just above this due to fluctuating levels of thyroid hormones.
- Presence of concurrent illnesses (most commonly chronic kidney disease, CKD) can make diagnosis more difficult since total T4 levels can be suppressed into the reference range by the other illness what is referred to as the 'sick euthyroid' syndrome.
- Lastly, consider the possibility that your 'clinical hunch' is not correct and that
   hyperthyroidism is not responsible for your patient's clinical signs. For example, differential
   diagnoses for weight loss in spite of a good or increased appetite also include inflammatory
   bowel disease, diffuse alimentary lymphoma, diabetes mellitus and exocrine pancreatic
   insufficiency

If the total T4 result is in the lower half of the reference range, hyperthyroidism is unlikely. However, if the total T4 result is in the upper half of the reference range, hyperthyroidism remains a potential differential diagnosis. In these patients, a simple and often effective method of confirming the hyperthyroidism is to repeat the total T4 measurement after a few weeks. The author also



encourages clinicians to use a reference laboratory for confirmation of hyperthyroidism when borderline or confusing results are obtained.

**Free T4** measured by equilibrium dialysis can be another useful diagnostic tool. This test is highly sensitive in diagnosing hyperthyroidism although a small number of false positive results can occur, meaning that the <u>free T4 test should not be used as a screening test</u> for diagnosis of hyperthyroidism.

An elevated free T4 (> 40 pmol/l) in addition to total T4 in the upper half of the reference range (> 30 nmol/l) is consistent with a diagnosis of hyperthyroidism in cats showing clinical signs compatible with this condition.

If finances limit the extent of repeat blood tests then clinicians should consider monitoring the patient's clinical status for example with monthly check-ups: weight loss and more noticeable clinical signs of hyperthyroidism (Table 1) are expected to develop in patients genuinely suffering from this condition. If noted, repeat total T4 measurement is recommended to confirm hyperthyroidism.

#### 12. What is the ideal pre-operative stabilisation if wishing to perform a surgical thyroidectomy?

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Medical stabilisation of the hyperthyroidism and any associated complications such as systemic hypertension are recommended prior to anaesthesia and surgical thyroidectomy. These measures reduce the possibility of anaesthetic complications associated with hyperthyroidism. Medical stabilisation can be achieved through use of antithyroid medication or exclusive feeding of an iodine-restricted food. Antithyroid medications tend to be more rapid and efficient at achieving euthyroidism with total T4 levels typically falling into the reference range within 3-4 weeks of initiating therapy.

### 13. If I diagnose concurrent diabetes mellitus and hyperthyroidism in a patient, how does this affect my treatment plan?

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In most cases where both of these diseases are present concurrently, one condition develops before the other and therefore should be stabilized first.

If a cat develops hyperthyroidism first then in most situations it will be stabilized before the cat subsequently develops diabetes mellitus. Management of the hyperthyroidism does not need to be changed and the clinician should focus on treatment of the diabetes mellitus in these cats.

Although many antithyroid medications contain sugar, the author does not consider this to be a significant contra-indication to their use in cats suffering from concurrent diabetes mellitus.

If a well-controlled diabetic cat develops hyperthyroidism then typically their diabetic control will deteriorate leading to a return of clinical signs such as polydipsia/polyuria and weight loss. A higher dose of insulin is typically needed to maintain diabetic control.

Assessment of fructosamine levels is less helpful as an indicator of diabetic control in cats with uncontrolled hyperthyroidism since accelerated protein turnover leads to a reduction in levels of



fructosamine – in other words the fructosamine levels of a cat with concurrent diabetes mellitus and hyperthyroidism are often lower than expected (and may be within the reference range).

Following treatment of the hyperthyroidism, the insulin dose may need to be decreased so care should be taken to monitor patients for evidence of hypoglycaemia. Presence of diabetes does not have any impact on medications used for hyperthyroidism so these can be used at their standard doses.

### 14. If I diagnose concurrent chronic kidney disease (CKD) and hyperthyroidism in a patient, how does this affect my treatment plan?

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All treatments for hyperthyroidism have the potential to worsen kidney function. This is because the hyperthyroid condition increases renal blood flow and glomerular filtration rate (GFR). When the hyperthyroidism is treated, the increased blood flow to the kidneys decreases and GFR may fall by up to 50%.

In spite of these concerns, for most patients, optimal management of concurrent hyperthyroidism and CKD is still possible. Optimal management of hyperthyroidism is highly desirable since hyperthyroidism causes renal damage, worsening the CKD.

In a cat known to have CKD, treatment for hyperthyroidism may worsen renal function although typically, it is only cats with very serious CKD (e.g. IRIS Stage 4, creatinine > 440  $\mu$ mol/I) where optimal management of hyperthyroidism proves difficult/impossible without inducing a clinical and laboratory deterioration in renal function. For this reason, medical treatment of hyperthyroidism is often recommended initially since this is a reversible treatment which can be reduced or stopped if problems are seen.

An iodine-restricted food is not recommended as the management option for cats with significant renal disease (IRIS Stage 3 or 4, creatinine > 250 umol/l) since a renal diet is indicated for these patients. When using antithyroid medication, it is prudent to start at a low dose – for example 1.25 – 2.5 mg methimazole/thiamazole per day. If tolerated but insufficient to control the hyperthyroidism, the dose can be increased as needed.

### 15. I know that renal complications are possible following treatment for hyperthyroidism — is there any way I can predict which cases are likely to suffer from these?

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Unfortunately there is no proven way of predicting which cats will suffer a clinically significant deterioration in renal function following treatment of their thyroid disease. The deterioration seen may worsen pre-existing renal disease or reveal ('unmask') renal disease that was not previously known about. Published studies have shown that assessment of pre-treatment creatinine, urine specific gravity, proteinuria and other laboratory parameters is not reliable in predicting which patients will develop renal complications. GFR assessment may offer some advantages but this is an expensive test to perform.

The fall in GFR following achievement of euthyroidism is typically stable within 4 weeks.



### 16. If my patient develops renal complications whilst receiving antithyroid medication, what should I do?

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If possible the hyperthyroidism should be treated optimally (i.e. reducing total T4 to the lower half of the reference range if using antithyroid medication). However, if a clinical and laboratory deterioration in renal function is experienced then the dose of antithyroid medication should be reduced, for example reducing the dose of methimazole/thiamazole by 2.5 mg per day initially.

Where renal disease is diagnosed, other treatments for this such as feeding a specially formulated renal diet are also important to ensure the best long-term outcome for the patient.

17. I have heard that iatrogenic hypothyroidism is a potential complication of treatment for hyperthyroidism – is this something I should worry about?

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Yes, new data suggests that iatrogenic hypothyroidism (IH) is more common than previously thought and that, when present, it is associated with a worse prognosis due to increased likelihood of renal complications. Clinical signs of IH are not always obvious but include lethargy, weight gain, seborrhoea sicca and alopecia. Routine lab profiles may reveal hypercholesterolaemia, mild non-regenerative anaemia and azotaemia.

18. How is iatrogenic hypothyroidism diagnosed and managed in cats receiving antithyroid medication or an iodine-restricted food?

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In cats receiving reversible treatment for their hyperthyroidism (e.g. antithyroid medication, iodine-restricted food), the aim should be for total T4 levels to be in the lower half of the reference range. The dose of antithyroid medication should be adjusted to achieve this aim. If T4 results are below this level, clinicians should consider reducing the dose of antithyroid medication or withdrawing the iodine-restricted food. It is important to remember that concurrent disease can suppress T4 levels so a low total T4 is not diagnostic for IH. If in doubt, IH can be confirmed either by measuring endogenous TSH levels (elevated in a cat with IH) or performing a TSH or TRH stimulation test (cats with IH fail to respond adequately to TSH or TRH).

19. How is iatrogenic hypothyroidism diagnosed and managed in cats that have had radioiodine or surgical thyroidectomy?

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In cats that have received curative treatments for their hyperthyroidism, IH may develop as a transient or permanent complication. The total T4 should be checked at 1, 3 and 6 months following treatment. If T4 levels are low and especially if azotaemia is present, then confirmation of IH is recommended by measuring endogenous TSH levels (elevated in a cat with IH) or performing a TSH or TRH stimulation test (cats with IH fail to respond adequately to TSH or TRH). If IH is confirmed



and especially if azotaemia is present, then supplementation with L-thyroxine is recommended, as discussed below.

If T4 levels are low but no azotaemia is present then the patient can be monitored initially to see if the IH is transient.

Thyroid hormone supplementation (L-thyroxine at an initial dose of 0.1 mg 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 (4 hours post pill) and endogenous TSH levels.

#### 20. If my patient is receiving treatment for other conditions can I still use antithyroid medication?

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In most situations, antithyroid medications such as methimazole/thiamazole and carbimazole can be used safely in combination with other medications. For example, there are no reported drug interactions between the mentioned antithyroid medications and non steroidal anti-inflammatory treatments (e.g. meloxicam), anti-hypertensive treatments (e.g. amlodipine), ACE inhibitors (e.g. benazepril) and ARBs (e.g. telmisartan).

The following drug interactions have been reported or are considered possible when using methimazole/thiamazole or carbimazole with:

- Benzimidazole antiparasitics: Methimazole/thiamazole can reduce hepatic oxidation of benzimidazoles and increase blood levels.
- Beta-Blockers: Veterinary label states: A reduction in dose may be needed when the patient becomes euthyroid.
- Phenobarbital: Veterinary label states: Concurrent use of phenobarbital may reduce the clinical effectiveness.
- Theophylline: Veterinary label states: A reduction in dose may be needed when the patient becomes euthyroid.

Although many preparations of methimazole/thiamazole contain sugar, the author does not consider this to be a significant contra-indication to its use in cats suffering from concurrent diabetes mellitus.

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Table 1
International Cat Care's Wellcat guidelines for lifestage appropriate health screening of cats

Age of cat	Screening recommended	Possible indications of hyperthyroidism	
0 – 6 years  7 – 10 years – 'Mature' lifestage	<ul> <li>12 monthly health check including history, physical examination, weight check</li> <li>12 monthly health check including history, physical examination, weight check</li> <li>12 monthly blood pressure assessment</li> <li>12 monthly urinalysis</li> </ul>	Common clinical signs associated with hyperthyroidism (in order of decreasing frequency):  • Weight loss  • Polyphagia  • Vomiting  • Polyuria/Polydipsia  • Increased activity	
11 – 14 years - 'Senior' lifestage	<ul> <li>(specific gravity, dipstick)</li> <li>6-12 monthly health check including history, physical examination, weight check</li> <li>6-12 monthly blood pressure assessment</li> <li>6-12 monthly urinalysis (specific gravity, dipstick)</li> <li>12 monthly blood profile (ideally haematology, serum biochemistry, total T4)</li> </ul>	<ul> <li>Diarrhoea</li> <li>Common physical examination findings associated with hyperthyroidism (in order of decreasing frequency):</li> <li>Goitre</li> <li>Weight loss</li> <li>Heart murmur</li> <li>Tachycardia</li> </ul>	
15 years and over – 'Geriatric' lifestage	<ul> <li>3-6 monthly health check including history, physical examination, weight check</li> <li>6 monthly blood pressure assessment</li> <li>6 monthly urinalysis (specific gravity, dipstick)</li> <li>12 monthly blood profile (ideally haematology, serum biochemistry, total T4)</li> </ul>	<ul> <li>Gallop rhythm</li> <li>Hyperactivity</li> <li>Systemic hypertension</li> <li>Aggressiveness</li> <li>Poor coat</li> <li>Common laboratory findings associated with hyperthyroidism:</li> <li>Elevated total T4</li> <li>Raised liver enzymes</li> <li>Erythrocytosis</li> <li>Eosinopaenia</li> <li>Leucocytosis</li> <li>Reduced urine specific gravity</li> </ul>	

Table 2

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Treatment considerations for each of the management options

Factor	Medical management: thioureylenes (Methimazole, Carbimazole)	Nutritional management: Hill's Prescription diet <sup>TM</sup> y/d <sup>TM</sup>	Surgical thyroidectomy	Radioiodine
Is it possible to cure the condition with this treatment?	No	No	Yes	Yes
Other than the potential for reduced kidney function which can occur with all treatments for hyperthyroidism, are side-effects possible?	Yes	None reported	Yes	Yes
How common and how serious are the side effects?	< 20% of cats have mild and transient side- effects  < 5% of cats have serious side effects	None reported	Typically < 10% of cats suffer side- effects but these can be very serious	< 5% of cats suffer side- effects and these are usually treatable
Is there a risk of permanent hypothyroidism?	No - the dose of treatment can be reduced to resolve this	No – if hypothyroidism is seen the food can be withdrawn	Very rare (< 5%)	Very rare (< 5%)
Is there a risk of recurrence?	Yes	Yes, if the cat eats other foods	Yes	Yes (much less common)
Will the cat need to stay in hospital?	Not usually	No	Yes, usually < 3-5 days	Yes, usually at least 1 week
Will the treatment be available in my location?	Yes	Available in most countries	Yes	Less common

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