1. **How common is feline hyperthyroidism?**
Feline hyperthyroidism is the most common feline geriatric endocrinopathy, even though the first cases were described in the late 1970’s. Hyperthyroidism is 3-4 times more prevalent than diabetes in cats.

2. **Describe the pathophysiology of feline hyperthyroidism (thyrotoxicosis):**
In 99% of cases, the cause is benign nodular adenoma(s). These nodules autonomously secrete the thyroid hormones T4 (thyroxine) and T3 (triiodothyronine) in excess, resulting in multisystemic disease. The excessive secretion has negative feedback to the pituitary, suppressing thyroid-stimulating hormone (TSH) secretion. Normal thyroid tissue atrophies because of lack of TSH from the pituitary gland and ceases secretion of T4 and T3. In the other rare 1% of cases, the cause is a mild to moderately malignant thyroid adenocarcinoma.

3. **What causes hyperthyroidism?**
What initiates the hyperplasia/tumor formation is unknown, but possible risk factors have been identified and are under study. Theories of the cause of feline hyperthyroidism suggest that dietary changes (canned foods), preservatives and food additives, environmental exposures (cat litter, toxins, and pollution), increased exposure to allergens, genetic mutation (altered TSH receptor gene and G protein), and abnormal immunologic responses may be involved. Recently fire retardant chemicals in carpets and furniture have been associated with hyperthyroidism in cats but a cause and effect relationship has not been established at this time.

4. **Describe the normal anatomy of the thyroid glands.**
Most of the normal thyroid tissue is located as a single gland that is divided into two lobes located ventral to the trachea in the mid-portion of the neck between the larynx and xiphoid process. One lobe is on either side of the trachea, with no connection between them. Small amounts of ectopic thyroid tissue may be scattered throughout the ventral neck and mediastinum. The thyroid gland cannot be palpated in normal cats. Enlarged thyroid tissue in the chest cannot be palpated and can be difficult to locate at exploratory surgery.

5. **What is the typical signalment of cats with hyperthyroidism?**
Hyperthyroidism is usually a geriatric disease, with a median age of 13 years. The reported age range is 2-28 years, however hyperthyroidism is extremely rare under the age of 7 years. There is no sex or breed predilection, but Siamese and Himalayan cats have a lower incidence.

6. **What historical and clinical findings are typically associated with feline hyperthyroidism?**
- Weight loss or emaciation (93%)
- Enlarged thyroid lobes (80-90%)
- Behavioral changes (80%)
- Polyphagia (49%)
- Tachycardia (42%)
- Vomiting (44%)
- Polydipsia/polyuria (36%)
- Increased activity (33%)
- Diarrhea (15%)
- Gallop rhythm (15%)
- Vocalization (10%)
- Poor Hair Coat (10%)

Other clinical signs seen in 5 – 10% of cases include dyspnea, panting, large fecal volumes, and the apathetic (sick) form of hyperthyroidism characterized by decreased activity, lethargy, anorexia, depression, and weakness.
7. **How does hyperthyroidism affect the body as a multisystemic disease?**

A human analogy for feline thyrotoxicosis is the “stressed out speed freak” or an “adrenaline junkie.”

**Systemic Effects of Feline Hyperthyroidism**

| Neuromuscular: | Behavioral changes, hyperactivity, muscle loss, weakness, aggression, |
| | Vocalization, pacing, restlessness |
| Gastrointestinal: | Changes in appetite, vomiting, diarrhea, maldigestion/malabsorption, |
| | Large fecal volumes, vitamin and nutritional deficiencies |
| Hepatic: | Elevated serum enzyme activities, hepatic lipidosis |
| Cardiac: | Systolic murmurs, tachycardia, gallop rhythm, cardiac hypertrophy, |
| | Hypertension, congestive heart failure |
| Respiratory: | Hyperventilation, dyspnea, pulmonary edema/congestive heart failure |
| Renal: | Hypertension-induced renal damage, polydipsia/polyuria |

8. **Can hyperthyroid cats be diagnosed on physical examination?**

Enlarged thyroid glands(s) can be palpated in 80-90% of cases. In published studies, approximately 25-30% of cases are unilateral, 70% are bilateral, and 3-5% are ectopic.

9. **What abnormalities can be detected on routine laboratory testing?**

On the complete blood count, increased packed cell volume and mean corpuscular volume are seen in approximately one-third to one-half of hyperthyroid cats. Increased activities of liver enzymes are common; approximately 90% of hyperthyroid cats have increased activity of alanine transaminase (ALT), alkaline phosphatase (ALP), and/or aspartate transaminase (AST). Increased ALP activity is the most common (approximately 80% of cases, but ALT and AST together increase in approximately 55%). Other less common biochemical abnormalities are elevated blood urea nitrogen (BUN) and creatinine (approximately 20%) and hyperglycemia (approximately 20%).

10. **How is hyperthyroidism diagnosed?**

Clinical signs (the first and most reliable sign is weight loss) give a clue to the diagnosis, and if enlarged thyroid nodules are palpated, hyperthyroidism is likely. Palpation may be the earliest and most reliable way to detect the disease, but the presence of enlarged nodules does not necessarily mean that the cat is hyperthyroid. Definitive diagnosis requires thyroid testing. The total T4 (TT4) concentration should be the first screening test. If the TT4 is above normal, there is a 98-100% chance that the cat is hyperthyroid. Cats with enlarged thyroid glands but normal TT4 concentrations should be considered thyroid suspects and monitored closely for hyperthyroidism.

11. **Is it possible for a hyperthyroid cat to have a TT4 in the normal range?**

In some hyperthyroid cats, the TT4 is in the upper half of the normal range. Total T4 concentrations fluctuate between normal and elevated levels in many mildly hyperthyroid patients. Non-thyroidal disease also may suppress TT4 into the normal range in hyperthyroid cats (i.e., sick euthyroid syndrome). If the TT4 is in the upper half of the normal range in a cat suspected of hyperthyroidism, a free T4 (fT4) level should be measured by equilibrium dialysis. Alternatively, a T3 suppression test can be done, but it is more difficult to run and time-consuming. If done well a T3 suppression test is very accurate.

12. **How is the T3 suppression test used to aid in the diagnosis of hyperthyroidism?**

In borderline cases of hyperthyroidism with clinical signs but normal TT4 levels, the T3 suppression test can be used to define the condition more accurately. The test uses administration of T3 to suppress production of thyroid hormones through negative feedback. To perform the test, a baseline blood sample is taken, and seven 25-mg doses of T3 are administered orally every 8 hours, starting on the morning of day 1. Two to
four hours after the seventh dose is administered (day 3), a blood sample is drawn. T3 should be measured before administration of dose #1 and after dose #7 and the T3 concentration should increase to ensure administration of the drug. Hyperthyroid cats have a post-test TT4 that does not suppress; the values are >1.5µg/dl (20 nmol/L). In normal cats or cats ill from other causes, the TT4 is suppressed below this level.

13. Does an elevated fT4 necessarily mean that the cat is hyperthyroid?
Free T4 can be elevated in up to 12% of sick, euthyroid cats. Free T4 ED should be measured in combination with TT4. If the fT4 is high and TT4 is in the upper half of the normal range or above, the cat is probably hyperthyroid. If the fT4 is high and TT4 is in the lower half of the normal range, the cat is probably not hyperthyroid.

14. How can a pertechnetate scan help in the diagnosis of hyperthyroidism?
In a pertechnetate or technetium (99mTc) scintigraphy scan, radiolabeled pertechnetate is injected intravenously and is concentrated by the thyroid gland. 99mTc has a half-life of 6.01 hours, meaning that about 94% of it decays in 24 hours. Specialized equipment (gamma camera) is required to perform the scan and therefore this study is typically reserved for academic and referral institutions. In normal euthyroid cats, technetium uptake is roughly equal in thyroid tissue and salivary glands. In hyperthyroid cats, thyroid uptake is greater than salivary uptake. The scan can help to confirm a diagnosis of hyperthyroidism and locate all abnormal tissue (even intrathoracic), although it is not currently part of routine hyperthyroidism diagnosis. The uptake pattern may also raise suspicion for malignant disease, however definitive diagnosis of malignancy is biopsy and histopathology.

15. What are the three most important factors to assess in hyperthyroid patients?
Hyperthyroidism, if left untreated, eventually kills the patient. The two major organ systems most affected are the heart and kidneys. Another factor to assess, which has been underappreciated in thyrotoxicosis, is systemic hypertension.

16. How does hyperthyroidism affect the heart?
In cats with mild hyperthyroidism, the heart may be normal or have a slightly increased rate. As the disease progresses, tachycardia, gallop rhythms, myocardial hypertrophy, or, in rare cases, dilation develops. Congestive heart failure may be seen in some cats. Echocardiography cannot differentiate between hypertrophic changes due to hyperthyroidism and primary hypertrophic cardiomyopathy. Hyperthyroidism-induced hypertrophic changes revert to normal in the majority of treated patients within 6 months.

17. How does hyperthyroidism affect the kidneys?
The kidneys are a common site of geriatric disease in general, and a “normal” progressive loss of renal reserve occurs as the cat ages. Hypertension secondary to hyperthyroidism speeds the loss of nephrons. In the early stages of hyperthyroidism, increased cardiac output from hyperdynamic cardiac function increases glomerular blood flow and glomerular filtration rate (GFR). This improved function can mask low-grade renal insufficiency, and azotemia may not be detected until the cat is euthyroid. Renal disease in the aged patient can be insidious and difficult to detect accurately by laboratory testing and hyperthyroidism can mask renal disease. Many cats with hyperthyroidism present with normal kidney laboratory values but are bordering on kidney compromise. Hyperthyroidism can mask renal disease by increasing cardiac output and systemic blood pressure, thus abnormally increasing renal perfusion and GFR. If a cat treated for hyperthyroidism (medically, surgically, or with radioiodine) has “masked” kidney disease, renal compromise may result when blood pressure and renal blood flow return to normal – this can be life-threatening.

18. How can underlying renal disease be detected?
A methimazole challenge (administration of therapeutic doses of methimazole for 30 days) may be a reversible way to assess cats with suspected renal disease (see questions about treatment). Masked laboratory blood testing results from the effects of hypertension and thyrotoxicosis. Some authorities
believe that a urine specific gravity < 1.035 before treatment may be predictive of renal compromise. Also, if a senior cat has better than expected values for BUN, Creatinine, and Phosphorus suspect that hypertension is causing improved GFR and that the true blood values are much higher. The hyperthyroid condition needs to be addressed and potential heart and kidney disease must be given equal importance in the therapeutic plan. If surgery or radioiodine therapy un_masks renal disease and failure occurs, low levels of L-thyroxine supplementation (0.05-0.1mg/cat orally q24h) can be used to increase renal perfusion and GFR to a safer, higher level. Other kidney support measures also should be part of the overall treatment including: benazepril, kidney friendly diets, SQ fluids, monthly B vitamins, etc.

19. How common is hypertension in hyperthyroidism?
Systemic hypertension is detected in up to 94% of hyperthyroid cats and may be one of the most significant pathophysiologic factors in hyperthyroidism. Use of new blood pressure detection systems may better define the importance of high blood pressure in cats as clinicians obtain both diastolic and systolic pressures in a more reliable and convenient manner (see Chapter 63). This manifestation appears to be caused by a combination of a hyperdynamic cardiac state, sodium retention, glomerular capillary and arteriolar scarring, low levels of renal vasodilators, loss of the autoregulation of glomerular blood pressure, and activation of the renin-angiotensin system. Isolated intra-renal hypertension should be suspected even with a normal systemic blood pressure reading in senior cats. The American Kidney Society has stated that hypertension is the number one cause of kidney failure in humans. Managing hypertension in hyperthyroid and recovered hyperthyroid patients is very important especially in follow-up care.

20. How is hyperthyroidism treated?
Radioiodine, surgery, and medical management are options. A high level of systemic geriatric medicine is important to consider when designing a treatment protocol for hyperthyroidism. Hyperthyroid cats are commonly over 13 years old, which makes treatment of the whole cat as a senior patient a priority. 131I and surgery are best for long term treatment/cure and methimazole is good for short term treatment/suppression.

21. How does radioiodine work? How successful is it?
Radioiodine (131I) is highly selective in killing adenomatous tumor tissue wherever it is located, and response rates are high (>95%). The abnormal tissue concentrates the radioiodine and is killed by the radioactivity, whereas normal, atrophied tissue does not take up the radioiodine and is spared. Normal thyroid function returns in most patients within 30-90 days, but up to 6 months may be required. A second treatment is needed in only about 1% of patients. Even compromised patients, when given supportive care to address concurrent disease, respond favorably to 131I. The half life of 131I is 8.02 days. Hospitalization of treated patients is regulated by individual states and ranges from 2-30 days. The length of stay for radioiodine therapy in Colorado is 3 days. [Cat Specialist Nuclear spent 4 ½ years petitioning the State of Colorado to lower the length of hospitalization (from 7-14 days to 3 days) and was successful in 2005.] The shortest stay is 2 days in Florida. The average stay is 7-10 days in most states. The cost for the procedure ranges from $950-$1,800+, depending on the length of stay and what is included in the treatment protocol. 131I treatment only or treating the whole cat is where the cost differential results. Follow-up care and diagnostic testing every 6 months or sooner are very important in these senior patients.

22. Does previous medical treatment interfere with 131I therapy?
Effective uptake of radioiodine by the abnormal thyroid tissue determines the efficacy of the treatment. Because hyperthyroid medication may interfere, it should be stopped 5 days before radioiodine treatment. If the patient will be compromised by discontinuance of antithyroid medication, stopping 1-2 days before radioiodine treatment is prudent. After methimazole is discontinued, thyroid hormone levels return to high concentrations in 24-72 hours.

23. What adverse effects and complications may be seen with 131I therapy?
Side effects of treatment are few, rare and transient; dysphagia and voice change have been documented in less than 10 cases. Clinical hypothyroidism may occur in <1% of 131I-treated cases.
24. **Can surgery be used for treatment of hyperthyroidism?**
If radioiodine is not available, surgery is the only other option for definitive/cure therapy in stable patients. Success depends on the competence of the surgeon, the stability of the patient, and a proven surgical protocol. If surgery misses ectopic hyperthyroid tissue, then the only recourse is to treat either medically or cure with radioiodine. Because ectopic tissue is relatively uncommon, surgery leads to remission in approximately 85% of cases. The recurrence rate after surgery is approximately 10-15%, depending on the technique used.

25. **What risks are associated with surgery?**
Surgery and anesthesia in a compromised hyperthyroid patient have inherent risks and may cause iatrogenic injury to vital local tissues (e.g. damage to the recurrent laryngeal nerves(s), leading to laryngeal paralysis, or removal of all parathyroid tissue, leading to hypocalcemia). With experienced surgeons, the rate of side effects is low (<10%). Ideally, patients should be treated medically to resolve the hyperthyroidism before surgery to make the patient a better anesthetic and surgical candidate. A thorough physical examination, diagnostic testing and evaluation of cardiac/kidney status are paramount. Do not use atropine in the anesthetic protocol! If the heart rate is dramatically elevated, medications such as propanolol (2.5-5 mg/cat every 8-12 hr to effect) or atenolol (6.25 mg/cat every 12-24 hr to effect) may be needed to prevent arrhythmias and help control heart rate and hypertension.

26. **Does a low serum TT4 after radioiodine therapy or surgery necessarily mean that the cat is hypothyroid?**
The diagnosis of clinical hypothyroidism must be made by a combination of thyroid testing and clinical signs such as lethargy, obesity, nonpruritic seborrhea sicca, poor hair coat, hypothermia, and bradycardia. Only if these clinical signs are seen in combination with a low TT4 and fT4 ED should thyroid supplementation (L-thyroxine, 0.1 mg orally q24h) be initiated. The normal lab ranges on the low end of T4 and fT4 ED do not seem to diagnose hypothyroidism in the cat. Naturally occurring hypothyroidism is a rare clinical finding in felines.

27. **Can hyperthyroidism be treated medically?**
In general, antithyroid medications are used in three scenarios:
- As short term therapy when $^{131}$I treatment and surgery are not possible in a terminal patient.
- As short term therapy preoperatively or before $^{131}$I treatment to make the patient a better candidate for surgery or hospitalization. Because anesthesia can worsen hyperthyroidism-induced cardiac abnormalities, cats should be rendered euthyroid before surgery, if possible.
- As long term therapy with close supervision of TT4 values. Medical therapy better fits short term therapy because it does nothing to the tumor that continues to grow and secrete thyroid hormone. Studies have shown life expectancy is less than half of $^{131}$I or surgery. At best, medical treatment is a crude approximation of dose to effect medicine because methimazole levels vary significantly, and it is notoriously difficult to administer chronic oral medications to most cats.

28. **How effective is medical therapy?**
Methimazole, which lowers circulating thyroid hormone concentrations by blocking T3 and T4 synthesis, is used most frequently. Medical therapy with methimazole is successful if the patient is stable, the client is compliant, the clinician is vigilant in performing routine blood testing (CBC, blood chemistry, and TT4 levels) to make medication adjustments, and the patient tolerates the medication. Unfortunately, if any of the above criteria are not met, treatment may not be ideal. Methimazole is effective in approximately 75% of cats. Giving pills to feline patients and lack of follow-up testing seem to be the biggest challenges to this life-long therapy. Short-term therapy is relatively inexpensive, but long-term therapy and lab tests performed for the life of the patient can be quite expensive.
29. **What methimazole treatment regimen should be used?**

For mild hyperthyroidism (cats that have mild clinical signs and normal or mildly elevated TT4 values), administer 2.5-5 mg orally q24h for 7-10 days. TT4 concentration, liver enzyme activities, and CBC are rechecked at that time. Timing of the post-pill TT4 determination does not matter. Ideally, the TT4 value should be in the lower half of the normal range. An increase to twice-daily dosing may be needed. During the initial 3 months, CBC, liver enzymes, and TT4 should be monitored every 2-3 weeks to assess control and monitor for serious hematologic side effects. For severe hyperthyroidism (cats with severe clinical signs and elevated TT4 usually twice the high-normal value), administer methimazole at 5 mg orally every 12 hr for 7-10 days. The first recheck should be at that time, with subsequent rechecks every 2-3 weeks as for mild disease. Increasing the dose and frequency to every 8 hrs depends on the reduction of the TT4 value and clinical signs. As the tumor grows and more thyroid hormone is made the dose of methimazole may need to be adjusted. For moderate to severe hyperthyroid patients a cure with $^{131}$I or surgery is preferred.

30. **After the initial 2-3 months, how should methimazole therapy be monitored?**

After the initial period, a TT4 and fT4 ED should be measured every 3-6 months to assess control and adjust methimazole dosage as needed. Methimazole has the capacity to cause adverse effects in the short and long term so the need for blood panels every 3-6 months is necessary with methimazole therapy. The health of senior patients can change quickly so physical exams, blood panels, blood pressure and urinalysis are needed every 6 months or sooner.

31. **What clinical adverse effects are seen with methimazole? How common are they?**

Clinical side effects occur in approximately 18% of cats overall and include anorexia (11%), vomiting (11%), lethargy (9%), excoriation of the face and neck (2%), hemorrhage (2%), and icterus (1.5%). Anorexia, vomiting, and lethargy typically occur during the first month and tend to resolve despite continuing drug administration. Treatment with methimazole should be permanently stopped in cats that develop hepatopathy or bleeding tendency or excoriate their face or neck. Myasthenia gravis has been reported after methimazole treatment in 10 cats so there appears a linked immune drug reaction associated with the drug. The drug has a very bitter taste to cats which may cause drooling, vomiting and aversion to being pilled.

32. **What kind of hematologic adverse effects may be seen? How common are they?**

Eosinophilia (11% of cats), lymphocytosis (7%), leucopenia (5%), thrombocytopenia (3%), and agranulocytosis (2%) may occur. The milder adverse effects—eosinophilia, lymphocytosis, and leucopenia—are usually noted within 1-2 months of initiation of treatment and are transient despite continued therapy. The more serious complications (thrombocytopenia, agranulocytosis) typically occur within the first 3 months of therapy and require discontinuation of methimazole.

33. **What immunologic adverse effects may occur? How significant are they?**

Immunologic effects, including positive antinuclear antibodies (ANA) and positive direct antiglobulin test (Coombs’ test), cold agglutinin like disorder, and acquired myasthenia gravis have been noted. Up to 50% of cats receiving methimazole chronically (>6 months) will develop a positive ANA, which requires dosage reduction (Plumb).

34. **What other medical therapies are available?**

Calcium ipodate, a radiopaque organic iodine agent, was used with some success but is no longer available. Carbimazole is metabolized to methimazole. When used at the same doses described for methimazole in question 29, carbimazole is sometimes tolerated by cats showing gastrointestinal signs when treated with methimazole. Cats that have immunologic reactions to methimazole probably will react also to carbimazole. The drug must be formulated for use. The beta-adrenergic blockers (atenolol or propranolol) and ACE inhibitors (benazepril) have no effect on thyroid hormone concentration but decrease the neuromuscular and cardiovascular effects (myocardial hyperexcitability, hypertension, and cardiac hypertrophy. These beta blocker and ACE inhibitors can be used in combination with an antithyroid drug or alone if a patient cannot
tolerate antithyroid medications. They can be helpful in preparing a patient for thyroidectomy or radioactive iodine by making the cat a better candidate for surgery or hospitalization.

35. **What is the prognosis of treated hyperthyroidism?**

With any type of treatment for hyperthyroid disease, the patient must be assessed thoroughly. Geriatric-related disease must be evaluated and treated along with hyperthyroidism. Hyperthyroidism is a fatal disease and must be treated.

**Prognosis:**

- **Medical treatment:** guarded to good, depending on medication regulation and drug side effects. Even with treatment the tumor continues to grow and the need to adjust the medication is always present.
- **Surgical treatment:** guarded to very good, depending on surgical protocol, competency of the surgeon, and follow-up care. There is a 10-15% recurrence rate which is resolved by \( ^{131}\text{I} \) treatment.
- **Radioiodine:** excellent with a few exceptions. The quality of the \( ^{131}\text{I} \) protocol and hospitalized patient support is important. A single treatment yields a >96% success rate. Recurrence is \( \leq 1\% \). Radio-iodine therapy is the gold standard in human and veterinary medicine and it is used to treat and cure both the benign adenoma and adenocarcinoma tumors.

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