Hyperthyroidism: Diagnostic and Therapeutic Options

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1) Diagnosis
   a) Age: 10+ years with few exceptions
   b) Clinical signs
      i) T4 controls metabolic rate
      ii) Increased metabolic rate results in
          (1) Weight loss
          (2) Polyphagia
          (3) Tachycardia
          (4) Hypertension
          (5) Hyperactivity
          (6) Unkempt hair coat
          (7) Increased renal perfusion
          (8) Left ventricular hypertrophy
             (a) Results in Thyrotoxic Cardiomyopathy, not Hypertrophic Cardiomyopathy
          (9) Increased liver enzymes, most notably the ALT
   c) Thyroid palpation
      i) Over 90% have palpable thyroid enlargement
      ii) Exceptions
          (1) Technique
          (2) Intrathoracic disease
      iii) Sensitive thyroid palpation: J Fel Med Surg; June 2000
          (1) Palpate one side at a time.
          (2) Cat is standing.
          (3) Turn the head 45° away from the side to be palpated.
          (4) Place your index finger in the groove between the trachea and the adjacent muscle.
          (5) Begin at the level of the larynx and slide down the trachea to the thoracic inlet.
          (6) Change hands and palpate the other side.
          (7) Repeat both sides.
          (8) Size on a 0-6 scale
             (a) 0: normal
             (b) 1-3: pre-clinical enlargement; a functional adenoma is not present; do not treat unless the TT4 is elevated.
                i) 1 = Split Green Pea; 0.5 cm (Sizing courtesy of Dr. Jim Olson)
                ii) 2 = Lentil; 0.75 cm
                iii) 3 = Black Eye Pea; 1.0 cm
             (c) 4-6: clinical hyperthyroidism; should have elevated TT4; should be treated.
                i) 4 = Kidney Bean; 1.5 cm
                ii) 5 = Fava Bean; 2.0 cm
                iii) 6 = Peanut; 2.5+ cm
   d) Total T4
      i) A very sensitive and specific test.
      ii) The most inexpensive test.
      iii) Use it first.
   e) Free T4
      i) Reported to be more sensitive than the TT4.
      ii) But, it may be too sensitive: JAVMA June 15, 1996
      iii) May be elevated in non-thyroidal illness when the TT4 is normal or even decreased.
         (1) Euthyroid sick syndrome.
      iv) Be VERY careful when relying on this test if the clinical signs are not right and if thyroid palpation is negative.
   f) T3 Suppression Test
      i) Indication
         (1) Correct age and clinical signs for hyperthyroidism
         (2) Palpation for thyroid enlargement is positive
         (3) TT4 is normal
      ii) Protocol
         (1) T3 is given orally
In a normal cat, it should induce negative feedback to the pituitary gland that stops TSH production. The thyroid is no longer stimulated to make T4. The T4 level decreases to less than 50% of the pre-test level.

iii) The non-hyperthyroid cat
   (1) T3 increases, TT4 decreased by 50% or more

iv) The hyperthyroid cat
   (1) T3 increases, TT4 does not decrease by 50% or more because the tumor is making T4 independent of TSH.

v) Why is T3 given?
   (1) To validate the test. If it does not increase significantly, the tablets were not given, swallowed, or absorbed.

Technetium Scan
i) A radioisotope is given.
ii) The radioisotope concentrates in the thyroid and salivary glands
iii) A scan for it shows where it is located and the relative amount.

Indications
(1) Diagnosis or confirmation of diagnosis
(2) Adenoma vs. Adenocarcinoma
   (a) Multiple nodules
   (b) Not a histologic test so confirmation is not sure.
(3) To determine the dose of I\textsuperscript{131}.
(4) Note that all of these can be done other ways.

2) Treatment
a) Thyroid tumors
   i) “98% are adenomas”
   ii) However, adenocarcinomas begin as adenomas and transition over time
      (1) If diagnosed in the early stages, all will be adenomas.
      (2) If diagnosed 4 years later, up to 20% will be adenocarcinomas.
   iii) Control with methimazole or y/d does not prevent this transition.

b) Two categories of treatment options
   i) Control the clinical signs
      (1) Methimazole
      (2) y/d
   ii) Cure the cat
      (1) Thyroidectomy (remove the tumor)
      (2) I\textsuperscript{131} (destroy the tumor)

c) Methimazole
   i) Action: prohibits the thyroid from making T4 so the clinical signs are controlled.
   ii) Must be given long term
   iii) Does not destroy the adenoma.
   iv) Does not prevent an adenoma from enlarging or transitioning to an adenocarcinoma.
   v) Pros
      (1) The least expensive option in the short-term
      (2) Usually first choice for very old cats.
      (3) No anesthesia.
      (4) Non-invasive.
      (5) No hospitalization.
      (6) No radiation.
      (7) Good for intrathoracic disease.
      (8) Reversible if renal failure occurs during treatment.
   vi) Cons
      (1) Long-term daily treatment; may result in owner avoidance.
      (2) Possible pill issues.
      (3) The transdermal form is much more expensive.
      (4) Recheck needed every 4-6 months to adjust the dose because the tumor continues to grow.
      (5) Becomes a more expensive option after 1-2 years.
      (6) Not curative – only control.
      (7) Does not prevent the transition from adenoma to adenocarcinoma.
      (8) Side-effects possible.
         (a) Gastric irritation
             (i) Causes anorexia and/or vomiting: up to 20% of cats.
             (ii) Felimazole (enteric coated; more expensive) or the transdermal form reduces this.
         (b) Hepatotoxicity
(c) Facial pruritus/excoriation
(d) Peripheral lymph node enlargement (rare)
(e) Transdermal: may cause pinnal dermatitis; may soil the owner’s furniture.

d) y/d (Hill’s)
   i) Pros
      (1) No pilling.
      (2) The cat has to eat anyway so not a change in lifestyle.
   ii) Cons
      (1) Must be fed exclusively without exceptions.
      (2) Not all cats will eat it and eat it long-term
      (3) More expensive than other therapeutic diets.

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Prices as of January 2017

(4) Multicat households
   (a) Separate feedings OR
   (b) All cats eat y/d

(5) Long-term effects on the hyperthyroid cat and the non-hyperthyroid cat have not been determined.
(6) Does not work in all cats.

e) Thyroidectomy
   i) Pros
      (1) Cures the disease.
      (2) Only one night in the hospital.
      (3) Safe and effective when performed properly.
      (4) No radiation.
   ii) Cons
      (1) Availability of a surgeon qualified to perform this surgery.
      (2) Anesthesia required.
      (3) Only 1 night of hospitalization needed.
      (4) Hypocalcemia may occur due to damage to the parathyroid gland.
      (5) If bilateral, two surgeries are required (if I do the surgery)
         (a) Two surgeries are more expensive than treating with I$^{131}$.
      (6) More expensive than methimazole in the short-term.
      (7) Intrathoracic disease
         (a) Tumors here are not palpable so they may go undetected.
         (b) If a technetium scan is performed before surgery, it is likely to be more expensive than I$^{131}$ without a technetium scan.
         (c) Not surgically approachable.
   iii) Radioiodine Therapy (I$^{131}$)
      (1) Pros
         (a) Cures the disease.
         (b) No tablets to administer
         (c) No anesthesia (with exceptions; the cat must be cooperative during the injection.)
         (d) Highly effective when doses properly (98+ %)
         (e) No side effects; the radioisotope concentration in the thyroid tumor (rapidly dividing cells with an affinity for iodine) is up to 20 times higher than in other body tissues.
         (f) Good for intrathoracic disease.
         (g) No cat alienation by the owner.
      (2) Cons
         (a) Hospitalized for 3-10 days (as determined by the state in which treatment occurs)
         (b) Limited availability: state license required
         (c) Involves radiation
(d) The most expensive treatment in the short-term.
(e) The cat must be off methimazole for 5+ days or y/d for 2+ weeks prior to treatment.
(f) Incorrect dosing results in:
   (i) Underdosing: the tumor is still present and needs to be retreated.
   (ii) Overdosing: results in long-term hypothyroidism and the need for daily thyroxine.

(3) Post-Treatment Renal Function Prediction
(a) The “methimazole test”
   1. A look at what kidney function is likely to be after treatment because we are making the cat euthyroid with methimazole then performing renal tests.
   2. However, even if it is abnormal, treatment is still needed because hyperthyroidism will be fatal.
   3. I recommend it very infrequently – primarily to give comfort to the owner or referring DVM.
(ii) Other tests
   1. SDMA (IDEXX): Equivalent to the GFR at the time of the test. It has no predictive value for post-treatment kidney function.
   2. Technetium (DTPA) scan of the kidneys: same as SDMA
   3. There is no reliable test to predict post-treatment renal function other than the methimazole test (and it is not perfect).

(4) Dosing
(a) In the UK in the past, all cats were given the same dose
   (i) Results in underdosing of some and overdosing of others.
(b) The dose is based on the size of the tumor, not the size of the cat.
(c) Determination: No absolutely precise protocol.
   (i) Based on the results of thyroid palpation and the TT4 (without the influence of methimazole or y/d) at the time of treatment.
   (ii) Adenocarcinomas are treated with 3-10 times the dose for an adenoma.
   (iii) The technetium scan
      1. Concentration of the isotope reflects the size of the tumor.
      2. It cannot conclusively differentiate adenoma from adenocarcinoma unless multiple nodules are present.

(5) The I$^{131}$ Referral
(a) The cat needs to be free of the influence of methimazole (5+ days) or y/d (estimated to be at least 2 weeks; withdrawal time not well established)
(b) The dose is based on the size of the tumor (not the size of the cat). Therefore, the treating veterinarian needs to know:
   (i) The TT4 level at the time of treatment (without methimazole or y/d)
   (ii) The size of the thyroid lobes based on palpation.
(c) The TT4 level needs to be determined before the cat is referred because: (per Texas law)
   (i) All cats in a batch must be treated on the same day.
   (ii) More cats cannot be treated until all of the first batch is discharged.
   (iii) The isotope cannot be ordered and stored ahead of time.
   (iv) Each dose that is ordered and delivered must be given at a precise time.
   (v) Therefore, the order is placed on the day of treatment AFTER the cat is admitted.
(d) Fortunately, the dose does not have to be absolutely precise (UK experience: all cats got same dose)
(e) But, an actual TT4 number is needed.
   (i) The IDEXX SNAP tests reports “normal” or “>6”
   (ii) The Abaxis VetScan chemistry machine reports “>8” or “>10”
      1. If abnormal but < 8, a precise number is given.
      2. “>8” means between 8 and 10. That is precise enough.
      3. “>10” requires that blood be submitted to a commercial laboratory for an actual number.
(f) Common Scenarios
   (i) HT is diagnosed (with a precise number), no treatment is given, I$^{131}$ is given within 1 month of diagnosis.
      1. This is the ideal scenario.
   (ii) HT is diagnosed, the cat is treated up to 4 months with methimazole or y/d, treatment is stopped (5+ days or 2+ weeks, respectively), I$^{131}$ is given.
      1. This is acceptable because the size of the tumor will not change significantly in 4 months.
      2. An absolutely precise dose is not needed (UK experience).
   (iii) HT is diagnosed, the cat is treated for > 4 months, the cat is referred for I$^{131}$.
      1. There has been enough time for the original TT4 level to no longer be accurate.
      2. TT4 testing is needed again – with the cat off methimazole (5+ days) or y/d (2+weeks).
3. TT4 testing cannot be done the same day as I131 treatment because it must be sent out to a commercial lab (unless it is < 10 and the Abaxis VetScan chemistry machine is used).

(g) Post-treatment testing
   (i) At one month post-treatment check
      1. TT4
      2. Creatinine/BUN
   (ii) If …
      1. the TT4 is below normal, recheck in another 4-6 weeks.
         a. This is common because the normal thyroid tissue has been suppressed by high TT4 levels caused by the thyroid tumor. Sometimes they need longer than 4 weeks to resume function.
         b. It is very uncommon if there is not a return to euthyroidism and true iatrogenic hypothyroidism is created.
      2. the renal tests are abnormal, begin treatment for chronic renal disease.