## 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

- (2) In a normal cat, it should induce negative feedback to the pituitary gland that stops TSH production.
- (3) The thyroid is no longer stimulated to make T4.
- (4) 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.

#### g) 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.
- iv) 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  $I^{131}$ .
  - (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)  $I^{131}$  (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 pilling 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.

		Wholesale	MSRP
Canned k/d	\$33.79/24	\$1.40 each	\$2.04 each
Canned i/d	\$31.72/24	\$1.32 each	\$1.92 each
Canned w/d	\$30.34/24	\$1.26 each	\$1.83 each
Canned y/d	\$38.96/24	\$1.62 each	\$2.35 each
Dry k/d	\$32.06/8.5#	\$3.77/#	\$5.47/#
Dry i/d	\$26.20/8.5#	\$3.08/#	\$4.47/#
Dry w/d	\$48.27/17.6#	\$2.74/#	\$3.98/#
Dry y/d	\$36.89/8.5#	\$4.34/#	\$6.29/#

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<sup>131</sup> without a technetium scan.
      - (c) Not surgically approachable.
  - iii) Radioiodine Therapy (I<sup>131</sup>)
    - (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<sup>+</sup>%)
      - (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.
  - 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<sup>131</sup> 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<sup>131</sup> 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<sup>131</sup> 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.