Hyperthyroidism
Wendy Blount, DVM

Hyperthyroidism
- Grave’s Disease in people
- Aka thyrotoxicosis
- Excessive production of T3 and T4 by the thyroids
- In the feline, almost always caused by
  - Adenomatous hyperplasia or adenoma
  - Rarely caused by functional carcinoma (1-3%)
  - Nonfunctional thyroid tumors are rare in cats
- Feeding raw animal necks can rarely result in hyperthyroidism in small dogs and cats

Risk Factors
- Female (3) elderly (4) cats
- Siamese (2), Himalayans (1) and other purebreds (3) less likely to be hyperthyroid
- Diet – lack of iodine on label (1)
  - More than 50% canned food diet (5)
  - Pop top cans (1)
  - Fish flavored cat foods (1)
  - Baby food (1)
- Water
  - Drinking puddle water (1)
  - Well water (1)

Risk Factors
- Environmental conditions
  - Sleeping on the floor (1)
  - Increased carpet cleaning (1)
  - Exposure to gas fireplace (1)
- Toxin exposure
  - Flea (2) and fly control (1) products
  - Cat litter/indoor cats (3)
  - Chemical or Organic fertilizers (2)
- Lack of regular deworming (1)

Risk Factors
Summary
- Nutritional deficiencies or excesses
  - Iodine
  - Soy isoﬂavones
  - Selenium
- Exposure to goitrogens

Edinboro CH et al, *J Fel Med Surg* 2010

Risk Factors
Goitrogens (thyroid disrupters)
Chemically similar to T4, halogenated
- PCBs, dioxins, perfluorinated chemicals, phthalates, perchlorate, etc.
- Bisphenol A (BPA)
  - used to make plastics (that line cans)
  - Estrogenic activity disrupts the thyroid
- Flame retardants (PBDs)
  - polybrominated diphenyl ethers
  - interfere with thyroid function
Risk Factors

- Iodine
  - Iodine excess causes hyperT4 in people
  - Iodine deficiency causes hypoT4 in people, but may cause hyperT4 in cats
  - Fish are replete in iodine
- Soy isoflavones
  - Cats fed soy have increased TT4 and fT4
- Selenium
  - Thyroid contains more Se per gram than any other tissue
  - Se in the diet plays an unknown role

Clinical Presentation

- Age
  - Has been reported in young adults
  - <5% younger than 8 years
  - Median age 13 years
- Insidious onset over months to years
- Most common symptoms
  1. Weight loss (90%) despite increased appetite (81%)
  2. PU-PD (60%)
  3. Vomiting (55%) and diarrhea (30%)
- Many recommend including TT4 on all serology on cats >10 years of age

Clinical Presentation

- Other symptoms
  - Nervousness, hyperactivity, aggression
    - Yowling at night
  - Unkempt haircoat
  - Panting, respiratory distress
  - Inappetence, weakness, lethargy
  - Heat and stress intolerance

Physical Exam

- Palpable thyroid mass - goiter (90%)
  - Thyroid is palpable in 25% of euthyroid geriatric cats

Palpating the thyroid

- Extend the head and neck
- Palpate the jugular furrow from the larynx to the thoracic inlet
- Clipping can help
- Normal thyroid smaller than a lentil
- A Wolf – shake the cat with head down
**Physical Exam**

- Palpable thyroid mass - goiter (90%)

- Normal thyroid smaller than a lentil
- A Wolf – shake the cat with head down

**Cardiovascular Exam**

- Tachycardia
- Systolic murmur loudest at sternum
- Gallop murmur
- Hypertension (10-20%)
- CHF is very rare
- 50% have positive troponin I

**Ocular Lesions**

- Hypertensive retinopathy rare, even when hypertensive

**Thyroid Storm**

- Acute exacerbation of thyrotoxicosis
  - Fever, GI/hepatic upset
  - CNS agitation, cardiovascular effects
- Precipitated by:
  - Infection or other non-thyroid illness
  - Thyroid surgery or aspiration
  - Withdrawal of anti-thyroid drugs

**Diagnostics**

1. Confirm hyperthyroidism
2. Rule out concurrent illnesses that might influence treatment choices
- Especially chronic renal disease
  - hyperT4 increases cardiac output (CO)
  - The kidneys receive 25% of CO
  - Reverting to euthyroid can unmask kidney disease or failure by decreasing GFR
  - If CRF present, treatment will have to hit the “sweet spot” between euthyroidism and acceptable kidney function

**CBC**

- Often normal
- Mild polycythemia (increased HCT/PCV 40-50%)
- Macrocytosis (increased MCV 20%)
- Heinz bodies, but anemia is rare
- Enlarged platelets
Diagnostics

Serology – Liver Tests
- Increased ALT and SAP (75%)
- Increased ALT or SAP (>90%)
  - Usually less than 500-1000 U/L
- Increased fasting ammonia
- Normal bile acids and liver US
- These changes normalize after treatment for hyperT4

Serology – Other than Liver
- Stress hyperglycemia
- Azotemia (10%)
  - CRF is estimated to be present in 15% of cats older than 15 years
  - 25-50% of non-azotemic cats with hyperT4 will become azotemic after treatment
- Hypercortisolemia
- Low fructosamine

Urinalysis
- Decreased USG
- Proteinuria (75-80%)
- UTI (12% of cats without CRF and 22% of cats with CRF)
- Ketonuria (50%)
  - Ketonuria in an older non-diabetic cat should prompt checking TT4
- Urine cortisol:creatinine (UCC) normal

Imaging
- Chest x-rays and abdominal US evaluate for concurrent disease which might affect treatment and outcome
- Assess kidney size
- If no CHF, echocardiogram rarely produces information that changes outcome
- ECG can rule out arrhythmias that need to be treated until hyperT4 is treated
  - Atenolol for severe tachycardia

TT4
- Elevated TT4 (91%)
- Decreased TT4 usually indicates NTIS in cats
  - The lower, the worse the prognosis
- Recommend further diagnostics in geriatric cats with TT4 in upper half of normal, with signs of hyperT4
  - Or treat concurrent illness and recheck TT4

fT4
- $fT4ED$ – free T4 by equilibrium dialysis - sensitivity 98%, specificity 93% for hyperT4
- 6-12% of NTIS cats have elevated fT4 but TT4 not elevated
  - Recommend against fT4 alone in cats
  - Combine fT4 with TT4 in cats
- High fT4 + high TT4 = hyperT4
- High fT4 + high normal TT4 = Hypert4 likely
- High fT4 + low or low normal TT4 = NTIS likely
**Diagnostics**

**T3 Suppression Test**
- For cats with equivocal TT4 and fT4, suspected of hyperT4
- **Protocol**
  1. Baseline T3 and TT4
  2. Owners administer T3 (liothyronine, Cytomel®) beginning the next morning
     - 25 mcg PO TID x 2 days
     - Day 3 – 25 mcg T3 PO
  3. 2-4 hours post pill on day 3 – T3 and T4
     - Submit samples together
- **T3 assay confirms administration of T3**
  - If post pill T3 is not higher than baseline, test is invalid
- **Results**
  - **Normal** – post pill TT4 < 1.5 mcg/dl
  - **Equivocal** – post pill TT4 = 1.5 mcg/dl
  - **Hyperthyroid** – post pill TT4 > 1.5 mcg/dl

**TSH Stim/Response Test**
- Can distinguish euthyroid from hyperT4 cats with high TT4
  - **Protocol** in hypothyroid section
- **Cytomel® costs <$30, TSH costs hundreds to thousands**
- Hyperthyroid cats with normal TT4 have similar results to euthyroid cats
  - Adds little information to TT4 + fT4 results
- Rarely done to confirm hyperT4

**TRH Stim/Response Test**
- Hypersensitivity reactions to IV TRH are common
- Does not distinguish between euthyroid sick and hyperthyroid cats with normal TT4
  - Adds little information to TT4 + fT4 results
- Rarely done to confirm hyperT4

**Thyroid Nuclear Scan (Scintigraphy)**
- Distinguishes between NTIS cats and hyperthyroid cats with normal TT4
- Distinguishes between functional and non-functional thyroid nodules
- Establishes whether hyperT4 is unilateral or bilateral
- Identifies ectopic or metastatic hyperthyroid tissue
- Can help distinguish between benign and malignant tissues
- Determines dose for I^{131} treatment
**Diagnostics**

**Thyroid Scintigraphy**
- 30% of hyperT4 cats are unilateral
  - Surgery a good option
- 70% bilateral
- 12% have ectopic functional tissue
  - Neck, thoracic inlet and thorax
- Carcinoma suspected in cats with
  - large masses, especially when fixed
  - Uptake with irregular margins or linear multifocal extension
  - Multiple uptake foci in the thorax

**Drug Interference - Thyroid Scintigraphy**
- Withdraw methimazole for 2 weeks prior to thyroid scan

**GFR Scintigraphy prior to treatment**
- Assesses safety of I\(^{131}\) treatment
- Iohexol clearance can be done in practice

**Normal Thyroid scan**
Thyroids = salivary glands

**Unilateral Hyperthyroid scan**
hyper thyroid enhanced
normal thyroid suppressed

**Bilateral Asymmetric Hyperthyroid scan**
one thyroid enhanced
more than the other

**Bilateral Symmetric Hyperthyroid scan**
both thyroids enhanced
**Diagnostics**
Carcinoma Hyperthyroid scans

**Diagnostics**
Thyroid Carcinoma
Before and 60 days after treatment

**Iohexol Clearance - GFR**

**Michigan State U:**
1. 12 hour fast from food (not water)
2. Make sure patient is well hydrated
3. Iohexol 300 mgIE/kg
4. Samples taken 2, 3 and 4 hours post
   - Clot tube or SST – decant serum
   - Label samples to the nearest minute
5. Submit to lab - include patient weight and iohexol dose (form)
6. Results provided as ml/min/kg clearance and comparison to normal

**DDx Weight Loss + Polyphagia**
Felines:
1. Hyperthyroidism
2. Inflammatory bowel disease
   - (Triaditis - Exocrine pancreatic insufficiency - EPI)
3. Diabetes mellitus
   - (Hyperadrenocorticism)
   - (Acromegaly)

**Treatment**
1. Anti-thyroid hormone drugs
2. Iodine restricted diet
3. Surgery – thyroidectomy
4. Radioactive Iodine ($^{131}$I, $^{123}$I)

**Treatment**
Hyperthyroidism and Renal Disease
- It is rare but possible for a cat with no apparent kidney disease to go into acute renal failure and die after treatment for hyperthyroidism
  - USG 1.035+ makes CRF less likely
- 15% of non-azotemic cats will develop azotemia within 8 months of treatment for hyperthyroidism
  - However, post-treatment azotemia did not decrease survival time
- GFR is the best predictor of CRF in hyperthyroid cats
Hyperthyroidism and Renal Disease

- Ability to concentrate urine is lost when 66% of nephrons are lost
- 75% of nephrons must be lost before changes in GFR and azotemia become apparent
- GFR decreases within 4 weeks of treatment, but does not decrease thereafter
- One study - Cats with GFR > 2.25 ml/kg/min are unlikely to develop renal failure after treatment for hyperT4
  - Not confirmed by other studies
- Consider a methimazole trial for 4 weeks or until euthyroid, prior to permanent hyperT4 treatment

Thioureylenes

- All inhibit synthesis of thyroid hormones
  1. methimazole
  2. Carbimazole
  3. Propylthiouracil (PTU)
    - Unacceptable adverse side effects
    - GI effects, IMHA-ITP, lethargy

Methimazole

- Trial therapy
  1. To assess kidney tolerance of euthyroid condition
    - Effect on GFR is reversible
  2. To reduce clinical signs of hyperT4 prior to permanent treatment
    - Safer anesthesia and hospitalization
- Long term therapy for hyperthyroidism
- PO or topical – veterinary sugar coated
- Side effects: first 2-3 months
  - Lethargy, anorexia, vomiting, hepatopathy
  - Cytopenias, facial pruritus (2-3%)
  - IMHA-ITP, myasthenia gravis

- Methimazole
  1. Starting dose 1.25-2.5 mg PO BID
  - Lower dose for more debilitated cats
  2. Check every 2-3 weeks, and titrate up as needed
    - TT4, CBC, kidney panel
    - Target TT4 in lower half of normal range
    - Most require 2.5-5 mg PO BID
    - Up to 20 mg PO BID may be required for cats with large goiters
  3. Check 4-6 weeks after ideal TT4
  4. Then check 1-2x yearly

Methimazole

- PLO gel – pluronic lecithen organogel
  - Disrupts the stratum corneum
  - Regulation with PO is more likely in the first 2 weeks
  - By 4 weeks, PLO is as effective as PO
  - Fewer GI side effects
  - IMHA-ITP and facial pruritus are the same
  - Dosing similar for PO and PLO
  - Take care that children are not exposed to PLO

Carbimazole

- Converted to methimazole
- Starting dose 5 mg PO BID-TID
- There is a sustained release form
  - Starting dose 10-15 mg PO SID
- Lower rate of adverse effects than methimazole
- Not available in the USA at this time
**Thyroidectomy**

**Pre-surgical Management**
- Control symptoms that might increase anesthetic risk
  - Methimazole until euthyroid
  - Atenolol for tachycardia or SVT if methimazole not tolerated

**Anesthesia**
- Judicious IV fluids
  - Protect the kidneys
  - Do not overburden the heart
- Avoid adrenergics and ketamine
- Premedicate with butorphanol + 0.025 mg/kg acepromazine
- Induce propofol
- Intubate and maintain on gas
- Buprenorphine 0.02 mg/kg q6-8 hrs

**General Guidelines**
- Normal thyroid is pale tan to pink
- Hyperthyroid tissue is brick red
- The caudal thyroid artery looks teeny tiny (<1mm)
  - Tie it off or cauterize it anyway
- External parathyroids:
  - At the cranial pole of the thyroid
  - Much smaller than the thyroids
  - Pale and round

**Unilateral vs. Bilateral**
- 70% have bilateral disease
  - Pre-op scintigraphy is ideal, but often not possible
- Staging bilateral in 2 surgeries 2-4 week apart makes post-op hypoparathyroidism unlikely
  - Check TT4 prior to 2nd surgery
- If one thyroid is bigger, I remove that one first
Thyroidectomy

Intracapsular vs. Extracapsular

- **Intracapsular**
  - Thyroid gland is “teased out” of its capsule with sterile cotton tip applicator
  - Less likely to disturb the external parathyroid
  - Increased rate of recurrence

- **Extracapsular**
  - Entire thyroid with parathyroids removed, and the external parathyroid reattached to revascularize

Iatrogenic Hypoparathyroidism

- Post-op hypocalcemia is usually mild and transient
  - Especially if right and left thyroidectomies are staged
  - Rarely needs to be treated unless it falls below 7 mg/dl
  - Or ionized calcium <0.8 mmol/L
- Treatment usually corrects in 3-6 days
  - Vitamin D
  - Calcium

Post-op Management

- Hospitalize for 2-3 days post-op
  - Longer if complications
- Check calcium once daily for 4-7 days
- Inform clients of signs of hypocalcemia
  - Facial twitching
- Treat mildly symptomatic and asymptomatic hypocalcemia PO
- If significant clinical signs, give 1cc calcium gluconate IV PRN
- May need calcium & vitamin D for a few days, weeks or months
- Lifelong calcium therapy needed only if all parathyroid tissue is damaged
Thyroidectomy

**Vitamin D Therapy**
- Calcitriol – VitD$_3$ (Rocaltrol$^\text{®}$)
  - 0.02-0.03 mcg/kg/day x 2-4 days
  - Then tapered to effective dose
- Ergocalciferol - VitD$_2$
  - not recommended
  - Takes 5-21 days to take effect
- Dihydrotachysterol (DHT)
  - Synthetic vitamin D
  - 0.03 mg/kg PO SID x 1-7 days

Thyroidectomy

**Calcium Therapy**
- Calcium gluconate 1:1 with PSS SC
  - 2-5cc (4-10 cc 1:1) BID-QID
- NEVER give calcium chloride SC
  - Causes tissue slough
- Calcium carbonate (TUMS$^\text{®}$)
  - 0.5-1g PO SID
- Calcium chloride gel (CalSorb$^\text{®}$)
  - 1cc PO SID-TID

Thyroidectomy

**Prognosis**
- Persistent hyperthyroidism
  - Rare – consider scintigraphy looking for ectopic functional thyroid tissue
- **Eventual recurrence is likely**
  - In years, more likely in young cats
  - Higher complication rate if surgery repeated after recurrence
  - Consider $^{131}$I for re-ops
- Hypoparathyroidism
  - Less likely if one side done at a time

Thyroidectomy

**Prognosis**
- Hypothyroidism – rarely clinically significant
  - Treat only if persistent for 3-6 months after surgery
  - or if azotemic
- Neurologic damage
  - Horner’s Syndrome
    - Damage to sympathetic chain
  - Laryngeal paralysis
    - Damage to recurrent laryngeal nerve

Radioactive Iodine

$^{131}$I
- Thyroid cells concentrate iodine
- $^{131}$I is 95% effective
- SC injection - Dose proportional to pertechnitate uptake in thyroid scan
- Post-treatment hypothyroidism is very rare
- Discontinue Y/D and methimazole for 14 days prior to treatment
  - May need atenolol 6.25-12.5 mg PO SID-BID for tachycardia
- **The treatment of choice (for decades) for feline hyperthyroidism in cats whose kidneys tolerate euthyroidism**

Radioactive Iodine

$^{131}$I
- Hospitalization 5-10 days
- Confinement to the home for 2 weeks
- Rechecks – 1, 3, 6, 12 months
  - Weight, TT4, kidney panel
- Treat low TT4 only if symptomatic
  - Some treat if persistent for > 6 months
  - Some will take 6 months for TT4 to fall to normal
  - If still high after 6 months, retreat
  - 20% have or develop thyroid carcinoma
- 3% recurrence (median 3 years)
Low Iodine Diet

- Y/D like G/D but < 0.2 mg/kg iodine
- Iodine in commercial diets varies by 30 fold
  - Hyperthyroidism may be fostered by both extremes
- Hill’s Y/D study showed 33 hyperthyroid cats became euthyroid within 4-8 weeks of eating Y/D
- None of the cats became azotemic

Client owned cat study
- 71% euthyroid in 60 days
- 96% euthyroid in 180 days
- On average, the cats did not gain weight
- Some cats do not find Y/D palatable
- Not suitable for cats that go outdoors
- Not suitable for euthyroid cats
- Even small amounts of iodine can make Y/D ineffective
- Should not be used concurrently with methimazole

Transitioning from methimazole to Y/D
1. Wean off methimazole over 1-2 weeks
   - Increased hunger may increase acceptance of Y/D
2. Transition from current diet to Y/D over several days

When Y/D is indicated
- Renal disease that precludes surgery or radioactive iodine therapy
  - Y/D not a protein restricted diet, but BUN and creat improve because ingredients are kidney friendly
- Methimazole is not tolerated
  - Side effects
  - Can’t pill the cat
  - Ears irritated by PLO gel

Feeding Y/D in mult-cat households
- All cats can eat Y/D
- Supplement euthyroid cats with 1 tablespoon of life stage appropriate dry or canned food daily.
- Some think that after 6 months, euthyroid cats can adapt to low iodine diet and do fine
- Time will tell whether Y/D predisposes to thyroid carcinoma

Thyroid Carcinoma
- Thyroid mass may be larger and is more likely to be fixed
- Voice change has been reported
- Hypercalcemia occasionally present
- Mediastinal mass or pulmonary metastasis may be seen on chest rads
- Many have history of thyroidectomy
- Brighter pertechnitate uptake
  - May be irregular, ectopic or extending into cranial mediastinum
  - Bronchogenic adenocarcinoma has similar uptake
### Thyroid Carcinoma

- Can treat with higher dose of I\(^{131}\)
  - Longer hospitalization needed
  - 10-21 days
- Or surgery + I\(^{131}\) (high dose)
  - Complete excision can be curative
  - But many will recur within weeks to months
  - Parathyroid preservation can be more difficult if invasive
  - Pertechnitate scan 8 weeks post-op will indicate need for I\(^{131}\)
  - Re-scan post-I\(^{131}\) at 3 months, 6 months, and 12 months, then as indicated

### Prognosis

- Median survival longer for I\(^{131}\) than other treatments
- Unknown survival for low iodine diet
- 30-40% of 10 year old cats survived 5 years
- 4% of 16 year old cats survive 5 years
- 41% die of renal failure
- 16% die of cancer

### Summary

- **PowerPoint Handout** goes behind the blue tab
- **Laboratory Forms**
  - MSU Toxicology Submission Form – for Iohexol GFR
  - MSU Iohexol GFR Test Information
- **Client Handouts**
  - Feline Hyperthyroidism

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