Learning Objectives

- **Feline Hyperthyroidism**
  - Describe common signs and symptoms of feline hyperthyroidism
  - Recognize major treatment options for feline hyperthyroidism
  - Identify common counseling points regarding veterinary methimazole prescriptions

- **Canine Hypothyroidism**
  - Recognize the causes, signs, symptoms, and pathogenic abnormalities of canine hypothyroidism
  - Describe the differences between T4 and T3 supplements
  - Describe thyroid hormone dosing and monitoring in dogs and contrast with human thyroid supplementation
  - Explain the important counseling points to tell a dog owner regarding thyroid supplements
Hyperthyroidism – Mostly in Cats

- Most common in aged cats: onset 12-13 yrs
- Rarely occurs in dogs
- Most common cause
  - Cat: functional thyroid adenoma
  - Dog: thyroid carcinoma
- Normal T4 levels
  - Dog: 0.8 – 4.0 ug/dL
  - Cat: 1.9 – 4.8 ug/dL
Hypothyroidism – Mostly in Dogs

- The most common endocrine disease in dogs
  - 0.2 – 0.8% prevalence
- Most common in dogs 4-10 years old
- Rarely affects cats
- Affects large-sized breeds >> toy and miniature breeds
  - Highest prevalence in golden retrievers and doberman pinschers
- Dysfunction anywhere in the HPT axis can cause hypothyroidism
- >95% of hypothyroidism in dogs results from thyroid gland destruction (primary hypothyroidism)
Feline Hyperthyroidism
Thyroid Hormones and Cats

- **What does the thyroid gland secrete?**
  - **Major:** Thyroxine (T4)
  - 3,5,3-triiodo-thyronine (T3)
  - Reverse T3 (rT3)
  - Other deiodinated metabolites

- **Most T3 is derived from its prohormone, T4**
  - Metabolized by iodothyronine deiodinase in peripheral tissues
  - T3 is 3-5 times more potent than T4

- In a healthy feline, >99% of circulating T4 is protein bound, and ~1% of circulating T3 is free.
  - Remember: Only **free, unbound** T4 and T3 are active.

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=feline%20hyperthyroidism&amp;alt=sh
Ettinger & Feldman, pp 1766
Thyroid Hormones

- $T_3$ (Thyronine)
- $T_4$ (Thyroxine)
- $r-T_3$
- $dT_4$ (Dextrothyroxine)
Hyperthyroidism – Mostly in Cats

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Hyperthyroidism Signs and Symptoms

**Common Signs**
- Weight gain / loss
- Increased / decreased appetite
- Hyperexcitability
- Polydipsia
- Polyuria
- Palpable thyroid gland enlargement
- Vomiting, diarrhea

**Cardiovascular Signs**
- Tachy- / Bradycardia
- Systolic murmurs
- Dyspnea & tachypnea
- Cardiomegaly
- CHF

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=feline%20hyperthyroidism&alt=sh
Ettinger & Feldman, p 1762-3
Diagnosis

- **Hallmark sign**: Elevated serum total thyroid hormone concentration
- Only 5-10% of cats have normal T4 values
- **Differential Diagnosis**:  
  - Mild or early hyperthyroidism  
  - Hyperthyroidism with a non-thyroidal illness causing suppression of T4 concentration to a normal value  
    - Elevated *free* T4 concentration  
    - Other clinical symptoms

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=feline%20hyperthyroidism&alt=sh
Treatment Options

Medical Management

- Anti-thyroid drugs

Cures

- Thyroid ablation using radioiodine therapy (treatment of choice)
- Surgical thyroidectomy

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=hyperthyroidism&alt=sh
Anti-thyroid Drugs: Methimazole

- Drug of choice: 2.5-10 mg/cat
- MOA: inhibits enzyme responsible for iodination during thyroid hormone synthesis
- Dosage forms
  - Compounded: Transdermal methimazole in PLO gel
  - Human-labeled: Methimazole tablets, Tapazole tablets
  - Veterinary-labeled: Felimazole tablets
- Recently approved in Europe: Carbimazole, controlled-release formula

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=hyperthyroidism&alt=sh
Ettinger & Feldman, pp 1772
Anti-thyroid Drugs:
Methimazole

- Counseling points
  - Transmissible via lactation; place offspring on milk replacer
  - Bitter taste
  - Effects are seen as early as 1 week, and as late as 4 weeks
  - Monitor serum T4 concentrations every 3-6 months
  - Wash hands and use finger cots when applying transdermal formulations

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=hyperthyroidism&alt=sh
### Methimazole Side Effects

#### Most frequent (Occur within 3 months)

<table>
<thead>
<tr>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Anorexia</td>
</tr>
<tr>
<td>Depression / Lethargy</td>
</tr>
</tbody>
</table>

**Transient**

<table>
<thead>
<tr>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophilia</td>
</tr>
<tr>
<td>Leukopenia</td>
</tr>
<tr>
<td>Lymphocytosis</td>
</tr>
</tbody>
</table>

#### Rare, but serious

<table>
<thead>
<tr>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-induced excoriations</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Hepatopathy</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Agranulocytosis</td>
</tr>
<tr>
<td>Positive direct antiglobulin test</td>
</tr>
<tr>
<td>Acquired myasthenia gravis</td>
</tr>
</tbody>
</table>

**Biggest reasons for therapy discontinuation**

- Hepatic toxicity
- Self-induced excoriation on the face
- Hematological abnormalities (severe leukopenia)

Symptomatic Treatment of Hyperthyroidism: β-blockers

- **Propranolol** and **atenolol**

- Have no effect on circulating T4 concentration*

  - Used for symptomatic control of hyperthyroidism:
    - Tachycardia
    - Tachypnea
    - Hypertension
    - Hyperexcitability

*Evidence suggests that propranolol might inhibit one of the peripheral enzyme responsible for the conversion of T4 to T3

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html
http://www.pharmacologyweekly.com/articles/propranolol-preferred-thyroid-storm-thyrotoxicosis
Prescription Diet

- Hill’s y/d Thyroid Health diet
  - Controlled iodine deficiency to prevent excess synthesis of thyroid hormone
  - Intended for cases of moderate elevations in T4
  - Excluded to cats that are not candidates for radioiodine therapy or thyroidectomy

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html
Hillspet.hk
Radioiodine Therapy

- **Curative**
- **Simple, safe, and effective**

Radioiodine concentrates in the thyroid tumor

Selectively irradiates and destroys the hyperfunctioning thyroid tissue

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=hyperthyroidism&alt=sh
Thyroidectomy

- **Curative**
  - For unilateral thyroid tumors:
    - A hemithyroidectomy will correct the hyperthyroidism
    - Thyroxine supplementation is usually not necessary.
  - For bilateral thyroid tumors:
    - A complete thyroidectomy is indicated
    - Parathyroid function must be preserved to avoid post-op hypocalcemia.
    - Start thyroxine supplementation 1-2 days after complete thyroidectomy.
    - If iatrogenic hypoparathyroidism develops, supplement both calcium and vitamin D.

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hyperthyroidism.html?qt=hyperthyroidism&alt=sh
Hyperthyroidism in dogs is usually caused by a tumor (likely a carcinoma).

Treatment is determined by:
- Size of the primary tumor
- Extent of local tissue invasion
- Presence of detectable metastasis
- Available treatment options

Treatment options:
- Surgery
- Chemotherapy
- Radioiodine
- Radioactive iodine therapy (alone or in combination)

Methimazole can be used for daily control, but will not prevent tumor growth or metastasis.

The long term prognosis in these dogs is poor to grave 😞
Canine Hypothyroidism
Hypothyroidism – Mostly in Dogs

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- Rarely affects cats
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- >95% of hypothyroidism in dogs results from thyroid gland destruction (primary hypothyroidism)
Types of Hypothyroidism

- **Common types**
  - Adult-onset primary hypothyroidism causes:
    - Lymphocytic thyroiditis (probably immune-mediated)
    - Idiopathic atrophy of the thyroid gland
  - Secondary hypothyroidism is caused by tumors that destroy the pituitary thyrotrophs
    - Deficiency of TSH

- **Rare types**
  - Congenital (juvenile-onset) primary hypothyroidism
  - Congenital secondary hypothyroidism
  - In cats: iatrogenic hypothyroidism from hyperthyroidism treatment/surgery (extremely rare)

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html
Signs and Symptoms

- Hypothyroidism affects the function of most organ systems, which means the symptoms are non-specific.

- Directly related to slowed metabolism:
  - Mental dullness
  - Lethargy
  - Exercise intolerance
  - Weight gain without appetite increase
  - Body temperature regulation problems (‘heat seekers’)

- Skin and coat changes
  - Bilateral and symmetric
  - Dryness
  - Excessive shedding
  - Hair thinning / alopecia (observed in 2/3 of dogs)
  - Recurrent bacterial infections of the skin

- Reproductive disturbances

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html
Diagnosis

- Canine hypothyroidism is one of the most over-diagnosed diseases.

- Confirmative tests
  - Total T4 serum concentration
    - Most common
    - ~90% diagnostic sensitivity
  - Free T4
  - TSH
  - Thyroid function tests (ex: TSH stimulation test)
  - Thyroid gland imaging
  - Response to thyroid hormone supplementation

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html
Pathologic Abnormalities Associated with Hypothyroidism

The presence of these ‘other disease states’ supports the hypothyroidism diagnosis

- Classic hematologic finding: 40-50% of cases
  - Normocytic, normochromic, nonregenerative anemia
- Classic serum biochemical abnormality: ~80% cases
  - Hypercholesterolemia
- Others: high triglycerides, alkaline phosphatase, and creatine kinase

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html
Myxedema Coma

- Rare syndrome
- Severe hypothyroidism
- Treated with IV levothyroxine
  - 4 to 5 mcg/kg

### Hypothyroidism
- Normal signs PLUS
- Hypoventilation
- Hypotension
- Bradycardia
- Profound hypothermia

## Hypothyroidism Signs

1. **Lethargy**
2. **Stupor**
3. **Coma**

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http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html

## Treatment

- Dogs/Cats: High doses relative to human
- Common in dogs/rare in cats

<table>
<thead>
<tr>
<th></th>
<th>Levothyroxine Sodium</th>
<th>Liothyronine Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is it?</strong></td>
<td>Thyroxine (T4)</td>
<td>Active T3</td>
</tr>
<tr>
<td><strong>Treatment Option</strong></td>
<td>Drug of choice</td>
<td>Used in animals unresponsive to T4</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>Minimal to none</td>
<td>Minimal to none</td>
</tr>
<tr>
<td><strong>Products Available</strong></td>
<td>Human and veterinary</td>
<td>Just human (Cytomel, Triostat)</td>
</tr>
<tr>
<td><strong>Pharmacokinetics</strong></td>
<td>Half-life: 12 – 16 hours [Peak]: 4 – 12 hours</td>
<td>Half-life: 5 – 6 hours [Peak]: 2 – 5 hours</td>
</tr>
<tr>
<td><strong>Which species?</strong></td>
<td>Vet-labeled are approved in dogs only Can give human-labeled to cat or dog</td>
<td>Can give human-labeled to cat or dog</td>
</tr>
<tr>
<td><strong>Dog Dose</strong></td>
<td>20mcg/kg PO BID Max: 800mcg BID</td>
<td>4-6mcg/kg PO Q8H</td>
</tr>
<tr>
<td><strong>Cat Dose</strong></td>
<td>50mcg-1000mcg PO QD</td>
<td>4.4mcg/kg PO BID to TID</td>
</tr>
<tr>
<td><strong>Human Dose</strong></td>
<td>Max dose: ~2mcg/kg PO QD</td>
<td>25 - 75mcg/day</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Much larger doses than human</td>
<td>Shorter half-life, possible TID dosing, iatrogenic hyperthyroidism</td>
</tr>
</tbody>
</table>

[http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html](http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html)


Micromedex.
Monitoring

- **Initial monitoring of serum T4 concentrations**
  - 4-8 weeks after starting therapy
  - Then every 6-12 months

- **Time frame of improvements:**
  - Activity level: 1-2 weeks
  - Weight loss: 8 weeks
  - Normal hair coat: several months and may worsen before it improves

[http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html](http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html)

If no clinical improvement:

- Inadequate dose or frequency
- Non-compliance (Counseling is big!)
- The dog is not absorbing the product well
- The product is outdated
  - Short shelf-life
- The diagnosis is incorrect

http://www.merckmanuals.com/vet/endocrine_system/the_thyroid_gland/hypothyroidism.html
Counseling Points

- Take *without* food
- Take on an empty stomach (30 minutes before OR 2 hours after food)
- Don’t give with calcium-containing products
- May take several weeks to see improvement
- *Not all generic brands are equivalent*
  - Dose adjustments may be necessary if switching brands
Veterinary-Labeled Levothyroxine Sodium Products

- **Tablets**
  - Levothyroxine sodium
  - Soloxine
    - Ex: Available in 0.1-1.0 mg tabs
  - Levosyn
  - Thyro-Tabs
  - Thyrosyn
  - Thyroxine-L
  - Thyrozine
  - Thyrokare

- **Chewable tablets**
  - Canine Thyroid
  - Nutrived T-4
  - Heska Thyromed

- **Oral solution**
  - Leventa (1 mg/mL in 30 mL bottles)

- **Various powder products**
  (labeled for use in horses)
Human-Labeled Levothyroxine Sodium Products

- Tablets
  - Levothyroxine sodium
  - Synthroid
    - Ex: Available in 0.025-0.3 mg tabs
  - Levothroid
  - Levoxyl
  - Thyro-Tabs
  - Unithroid
- Powder for injection
  - Generic only
  - Used for myxedema coma