Hypothyroidism
(sometimes a fat dog is just a fat dog)

- Normal physiology
- Canine adult hypothyroidism
  - Clinical Signs
  - Diagnosis
    - TSH Assay
    - Challenges in diagnosis
  - Therapy
- Congenital hypothyroidism

Thyroid Hormone Synthesis

- Functional unit is the FOLLICLE
- Wall of thyroid cells (cuboidal to columnar)
- Lumen of colloid
  - Contains thyroglobulin
    - Glycoprotein dimer
    - Iodotyrosines
    - Precursor for thyroid hormone synthesis

Thyroid Hormone Synthesis

- Iodide ingested in diet
- Iodide taken up from plasma by thyroid cells
  - Sodium-iodide symporter (NIS) – 1:2Na
  - Energy from Na-K ATPase pump
- Iodide trapping – controlled by TSH
- Can concentrate iodide 30-250 x blood level
Thyroid Hormone Synthesis

- Iodide transported out of cell into colloid
- Oxidised by thyroid peroxidase
  - Able to combine with tyrosine residues
- Oxidised Iodine incorporated into tyrosine residues on thyroglobulin (organification)
  - MIT = moniodotyrosine
  - DIT = diiodotyrosine

Thyroid Hormone Synthesis

- MIT + DIT forms T3 (triiodothyronine)
- 2 x DIT forms T4 (thyroxine)
- Deiodination of T4 forms reverse T3 (rT3)
- Several weeks supply of thyroid hormone stored in the follicles (thyroglobulin containing T4 and T3)
Thyroid Hormone Synthesis

- Thyroglobulin re-enters thyroid cells and undergoes proteolysis
- T4 (and much less T3) released into blood
  - 40-60% of T3 is produced in peripheral tissues by 5'-deiodination of T4
- Iodide also released (deiodination of MIT and DIT)
  - Recycled for more thyroid hormone
  - Leakage of intact thyroglobulin

- T3
  - Can be measured
  - Not clinically important (usually)

- T4 (thyroxine)
  - Can be measured
  - Clinically important

Thyroid Hormone Secretion

- Regulated by TSH (thyrotropin)
  - From pituitary
  - Negative feedback from locally produced T3 (from T4)
- TSH modulated by TRH from the hypothalamus
  - Negative feedback by T3 (produced from T4)
Thyroid Hormone Secretion

- Actions of TSH:
  - Increases thyroglobulin proteolysis
  - Increases activity of iodide pump
  - Increases iodination of tyrosine
  - Increases size and secretory activity of thyroid cells
  - Increases number of thyroid cells

Thyroid Hormone Secretion

- Autoregulation (intrathyroidal)
- Wolff-Chaikoff Block
  - Increased iodide intake decreases thyroid hormone synthesis
    - Iodinated radiographic contrast agents (hyperthyroidism therapy)
    - High iodine diet in puppies
    - Protective effect when Shearon Harris melts down

"In cases where you may be exposed to certain types of radioactive thy, the North Carolina Department of Health and Human Services may direct you to take KI tablets.”

Thyroid Hormones in Plasma

- Mostly protein-bound:
  - Thyroid hormone-binding globulin (TBG)
  - Thyroxine-binding prealbumin (TBPA)/Transthyretin
  - Albumin
  - Lipoproteins
- Protein-bound hormones act as a reservoir
- “Free” T4 and T3
  - Around 0.1% of total
  - Biologically active
  - Feedback on the pituitary
**Thyroid Hormones in Cells**
- T3 and T4 have high affinity for binding proteins in plasma
- Released to cells slowly
- Bind to intracellular proteins
- Used slowly, over days to weeks
- T4 converted to T3 in cells

**Thyroid Hormone Metabolism**
- Thyroxine (T4) is major secretory product
- Metabolised by deiodination
  - T4 to T3 = step-up
  - T4 to rT3 = step-down
- This regulates biological activity in the periphery
- Most T3 is produced by peripheral iodination in the tissues
  - Tissues concentrating most thyroid hormone:
    - Liver
    - Kidney
    - Muscle

**Cellular Effects**
- T3 (less T4) binds to thyroid hormone receptors
  - Close or attached to DNA
    - Thyroid hormone response element
- Receptor activation stimulates gene transcription
- Proteins produced
  - Actions of thyroid hormone
Actions of Thyroid Hormones
• Act on all tissues and organs
• Affect enzymes, other hormones, tissues responses to other hormones
• Increase cellular metabolic activity
• Increase number and activity of mitochondria
  • Increased energy production
• Increase active transport of ions across cell membranes

Actions of Thyroid Hormones
• Promote growth and development of fetal/postnatal brain
• General growth promoting effects
• Promote metamorphosis

Action of Thyroid Hormones
• Stimulate carbohydrate metabolism
  • Glycolysis
  • Glucose uptake
  • Gluconeogenesis
• Stimulate fat metabolism
  • Lipid mobilisation
• Decrease cholesterol, phospholipids, triglycerides
  • Increase cholesterol secretion in bile
Action of Thyroid Hormones

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Action of Thyroid Hormones

• Increased basal metabolic rate
• Decreased body weight
• Increased respiration
• Increased gastrointestinal motility
• CNS excitation

Action of Thyroid Hormones

• Cardiovascular
  • Increased blood flow
  • Increased cardiac output
  • Increased heart rate
  • Increased contractility
• Stimulate erythropoiesis
Canine Hypothyroidism

• Primary
  • Most common – 95% of cases
  • Disease in thyroid gland itself

• Tertiary
  • Deficient secretion of TRH
  • Extremely rare

Canine Hypothyroidism

• Secondary
  • Impaired secretion of TSH
  • Rare to uncommon
  • Pituitary dysfunction
    • Congenital malformation (uncommon)
    • Destruction by neoplasia (uncommon)
    • Trauma
    • Suppression by hormones or drugs (common)

Canine Primary Hypothyroidism

• Lymphocytic thyroiditis (=50%)
• Idiopathic atrophy (=50%)
• Neoplastic destruction
• Anti-thyroid medications
• Surgery, I-131
• Congenital
Canine Primary Hypothyroidism

- Lymphocytic thyroiditis = autoimmune thyroiditis
  - Immune-mediated
    - CMI and humoral (can measure antibodies in blood)
  - Lymphocytes, plasma cells, macrophages
  - Follicular destruction and fibrosis
  - Clinical signs when 75% of gland lost
  - Takes 1-3 years to develop
  - Highly heritable
  - Related to vaccination?
    - Probably not

Proposed Stages of Lymphocytic Thyroiditis
(Graham et al, VCNA, 2001, 2007)

<table>
<thead>
<tr>
<th>STAGE OF THYROIDITIS</th>
<th>CLINICAL SIGNS OF HYPOTHYROIDISM</th>
<th>SERUM T4 AND fT4</th>
<th>SERUM TSH</th>
<th>SERUM THYROGLOBULIN AUTOANTIBODY</th>
</tr>
</thead>
<tbody>
<tr>
<td>I - Subclinical thyroiditis</td>
<td>Not present</td>
<td>Normal</td>
<td>Normal</td>
<td>Positive</td>
</tr>
<tr>
<td>II - Subclinical hypothyroidism</td>
<td>Not present</td>
<td>Normal</td>
<td>Increased</td>
<td>Positive</td>
</tr>
<tr>
<td>III - Overt hypothyroidism</td>
<td>Present</td>
<td>Decreased</td>
<td>Increased</td>
<td>Positive</td>
</tr>
<tr>
<td>IV - Noninflammatory atrophic hypothyroidism</td>
<td>Present</td>
<td>Decreased</td>
<td>Increased</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Canine Primary Hypothyroidism

- Idiopathic atrophy
  - Loss of thyroid parenchyma
  - Replaced by fat
  - No inflammation
  - Thyroid antibodies negative in blood
  - Cause unknown
    - Primary degeneration?
    - End-stage of lymphocytic thyroiditis?
Canine Primary Hypothyroidism

• Signalment
  • Middle aged: mean age at diagnosis = 7 years
  • Rarely < 2 yr
  • Age of onset varies between breeds
  • Breeds at risk of thyroiditis present earlier
  • Disease progression varies between breeds
  • No gender predisposition
  • Breed: Any!
    • True breed prevalence difficult to assess
    • Geography?!!

Canine Primary Hypothyroidism

• High prevalence of TgAA
  • English Setter
  • Old English Sheepdog
  • Boxers
  • Giant Schnauzer
  • American Pit Bull Terrier
  • Beagle
  • Dalmatian
  • German WH Pointer

• Hypothyroidism often associated with TgAA
  • English Setter
  • Chesapeake Bay Retriever
  • Golden Retriever
  • Rhodesian Ridgeback
  • Boxer
  • Siberian Husky
  • Irish Setter
  • Cocker Spaniel

K9 HypoT4: Clinical Signs

• Thyroid hormone affects all cells and tissues
• Slow onset and progression of signs
• Signs can be very variable
  • Depends on age
  • Depends on breed
  • Depends on type of coat
### K9 HypoT4: Clinical Signs
Panciera, VCNA, 2001: 162 Dogs

#### Derm signs (88%)
- Alopecia (40%)
- Seborrhea (22%)
- Pyoderma (14%)
- Dry/poor coat (9%)
- Otitis externa (5%)
- Obesity (49%)
- Lethargy (48%)
- Weakness (12%)

#### Neurologic signs
- Facial nerve paralysis (4%)
- Periph vert dz (3%)
- Polyneuropathy (2%)
- Megaesophagus (3%)
- Lar paralysis (4%)
- Cervical spondylomyelopathy (5%)

#### Reproductive signs
- Male (<1%)
- Female (1%)

#### Cardiovascular signs
- Bradycardia (10%)
- Low-voltage R (58% of 19 dogs)
- Anemia (36%)

#### Ophthalmic
- KCS (1%)
- Conjunctivitis (<1%)

#### Gastrointestinal
- Diarrhea (3%)
- Vomiting (2%)

### Common Signs
- Lethargy
- Weight gain
- Alopecia
- Pyoderma
- Seborrhea
Uncommon Signs
• Neuromuscular
• Female infertility
• Myxedema
• Ocular disorders
• Cretinism

Unknown Signs
• Male infertility
• Coagulopathy
• Dilated cardiomyopathy
• Gastrointestinal disorders
• Behavioral disorders

K9 HypoT4: Dermatologic Signs
• Most common signs observed
• Variable and depend on breed
  • Bilaterally symmetrical non-pruritic truncal alopecia
  • Hair easily epilated
  • Failure to shed normally
  • Failure of hair regrowth after clipping
K9 HypoT4: Dermatologic Signs

- Hair loss on pressure or wear-points
- “Rat-tail”

K9 HypoT4: Dermatologic Signs

- Hyperpigmentation
- Seborrhea
- Bacterial infections
- Poor wound healing

K9 HypoT4: Dermatologic Signs

- Myxedema
  - Increased skin thickness due to accumulation of mucopolysaccharide and hyaluronic acid
  - Bind water in the skin
  - Puffiness of face and extremities
  - “tragic” expression
K9 HypoT4: Clinical Signs

- Dull, lethargic, exercise intolerance
- Weight gain without increased intake

K9 HypoT4: Neuromuscular Signs

- CNS or PNS
- Mechanisms:
  - Demyelination
  - Axonopathy
  - Mucopolysaccharide accumulation
  - Atherosclerosis
  - Hyperlipidemia
- Myopathy
  - Type II fiber loss
  - Decreased fiber size
  - Nemaline rods

K9 HypoT4: Neuromuscular Signs

- CNS Signs
  - Rare
  - Seizures, ataxia, circling
- Cranial Nerve Signs
  - Vestibular disease
  - Facial paralysis
- PNS Signs
  - Polyneuropathy
  - Rapid response to therapy
- Myopathy
- Myasthenia gravis?
K9 HypoT4: Neuromuscular Signs

- Questionable Neurologic Disease:
  - Megaeosophagus
    - Evidence very weak
  - Laryngeal paralysis
    - Controversial
  - Behavioural problems
    - Cause and effect not established

K9 HypoT4: Cardiovascular Signs

- Hypothyroidism rarely causes heart failure
- Dogs in heart failure may be euthyroid sick
- Subtle effects
  - Bradycardia
  - EKG changes:
    - Low voltage P and R waves
    - First- and second-degree AV block
  - Echo changes:
    - Decreased contractility
    - Increased LV end-systolic diameter
    - Decreased LV posterior wall thickness in systole
    - Decreased IV septal thickness in systole and diastole

K9 HypoT4: Ocular Signs

- Rare
- Probably secondary to hyperlipidemia
  - Corneal lipid deposits
  - Corneal ulceration
  - Uveitis
  - Lipid effusion in aqueous
  - Glaucoma
  - KCS
  - Horner’s
  - Eyelid edema
K9 HypoT4: Other Signs

- Coagulopathy
  - Reported in humans
  - Bleeding very rare
  - In dogs:
    - von Willebrand disease?
      - Probably not
      - Subclinical vWd may be become clinical in hypothyroid dogs
    - No significant effects on primary hemostasis

- Gastrointestinal Signs
  - Uncommon
  - Relationship unclear
    - Constipation
    - Diarrhea
    - Vomiting
    - Risk factor for pancreatitis?
      - Hyperlipidemia

K9 HypoT4: Other Signs

- Myxedema Coma
  - Rare
  - Severe hypothyroidism:
    - Weakness, lethargy, dullness
    - Hypothermia, bradycardia
    - Hypotension, hypoventilation
    - Non-pitting edema
  - Biochemistry change
    - Usual findings
      - ↓ Na
      - ↓ BG
  - Therapy:
    - Supportive care
    - IV levothyroxine (5 µg/kg IV BID)

K9 HypoT4: Laboratory Tests

- CBC
  - Anemia (<50% cases)
    - Normocytic
    - Normochronic
    - Non-regenerative
  - WBC
    - Variable
  - Platelets
    - Normal to high

- Biochemistry
  - Increased cholesterol
  - Increased fasting TGs
  - ↓ hepatic LDL receptor
  - ↓ lipoprotein lipase
  - ↓ hepatic lipase
  - Mildly increased LEs
    - ALT
    - AST
Canine Hypothyroidism: Diagnosis

- Remember this is a *clinical* disorder
  - Should have clinical signs
  - Biochemical changes
  - CBC changes

- If considering trial therapy, need something to monitor

Canine Hypothyroidism: Diagnosis

- “Premium” Thyroid Panel at MSU
  - Includes free T4 by ED, TSH, and autoantibodies
  - Total T3:
    - Very little secreted by thyroid gland
    - Cannot distinguish normal from hypothyroid from euthyroid sick
    - Of minimal value
  - Free T3:
    - Diagnostic value unknown
    - May be low in very advanced hypothyroidism

Total T3

- Total T4 (and free T4) reference ranges are normally lower in greyhounds - but T3 is not
  - Probably in other sight hounds too

- Could T3 be useful in these breeds?
8 yr MN Mix, Alopecia, Pyoderma

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<th>Result</th>
<th>Normal</th>
<th>Units</th>
</tr>
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<tbody>
<tr>
<td>Total T4</td>
<td>22</td>
<td>15-67</td>
<td>nmol/l</td>
</tr>
<tr>
<td>Total T3</td>
<td>0.7</td>
<td>1.0-2.5</td>
<td>nmol/l</td>
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<tr>
<td>Free T4 by ED</td>
<td>20</td>
<td>6-42</td>
<td>pmol/l</td>
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<tr>
<td>Free T3</td>
<td>3.8</td>
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<td>pmol/l</td>
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<tr>
<td>T4 Autoantibody</td>
<td>1</td>
<td>&lt;20</td>
<td></td>
</tr>
<tr>
<td>T3 Autoantibody</td>
<td>2</td>
<td>&lt;10</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>18</td>
<td>0-37</td>
<td>mU/l</td>
</tr>
<tr>
<td>Thyroglobulin Autoantibody</td>
<td>162</td>
<td>&lt;200</td>
<td>%</td>
</tr>
</tbody>
</table>

**Total T4**

- Can be normal (low normal) in a small % of hypothyroid dogs
- Sensitivity for diagnosing hypothyroidism: 89-100%
- Could miss around 10% of cases
- Depends on lower limit of reference range
- May be affected by T4 autoantibodies
- If signs suggest hypothyroidism (i.e., you want to rule it IN)
  - Run another test if TT4 is within the normal range

- Specificity for diagnosing hypothyroidism is poor
- TT4 can be low in the presence of other illnesses (NTI) or medications
- If total T4 is low or below normal, evaluate for non-thyroidal factors (drugs, other illnesses)
  - If present, run another test
  - Or retest after resolving NTI or removing medications
Total T4

- When do I run this?
  - Patient otherwise healthy
  - Patient not on any other medications
  - I am trying to RULE OUT hypothyroidism
- Example:
  - Working up an otherwise normal dog that has elevated cholesterol

Interpretation of T4 (n:1.5-4.3 μg/dl)

<table>
<thead>
<tr>
<th>Serum Total T4 (μg/dl)</th>
<th>Probability of Hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2.0</td>
<td>Very unlikely</td>
</tr>
<tr>
<td>1.5 - 2.0</td>
<td>Unlikely</td>
</tr>
<tr>
<td>1.0 - 1.5</td>
<td>Unknown</td>
</tr>
<tr>
<td>0.5-1.0</td>
<td>Possible</td>
</tr>
<tr>
<td>&lt; 0.5</td>
<td>Very likely (assuming no severe systemic illness)</td>
</tr>
</tbody>
</table>

13 yr FS mix breed, weight gain

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<td>Total T4</td>
<td>18</td>
<td>15-67</td>
<td>nmol/l</td>
</tr>
<tr>
<td>Total T3</td>
<td>0.9</td>
<td>1.0-2.5</td>
<td>nmol/l</td>
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<tr>
<td>Free T4 by ED</td>
<td>6</td>
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<td>Free T3</td>
<td>QNS</td>
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<tr>
<td>T4 Autoantibody</td>
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<td>T3 Autoantibody</td>
<td>1</td>
<td>&lt;10</td>
<td></td>
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<tr>
<td>TSH</td>
<td>14</td>
<td>0-37</td>
<td>mU/l</td>
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<tr>
<td>Thyroglobulin Autoantibody</td>
<td>40</td>
<td>&lt;200</td>
<td>%</td>
</tr>
</tbody>
</table>
Free T4

- Should be measured by equilibrium dialysis (ED)
- Other methods no better than total T4
- Single best test
  - Best combination of sensitivity, specificity, and accuracy
  - Correlates best with thyroid status of the dog

Free T4

- Not perfect!
- Can be low with:
  - Chronic glucocorticoids
  - Hyperadrenocorticism
  - Phenobarbital
  - TMS
  - Carprofen
  - Clomipramine
  - Other illnesses
- Look at the patient!

2 yr F Doberman, no clinical signs

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<td>1.0-2.5</td>
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<td>Free T4 by ED</td>
<td>9</td>
<td>6-42</td>
<td>pmol/l</td>
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<tr>
<td>Free T3</td>
<td>10.3</td>
<td>4.5-12.0</td>
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<tr>
<td>T4 Autoantibody</td>
<td>15</td>
<td>&lt;20</td>
<td></td>
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<tr>
<td>T3 Autoantibody</td>
<td>30</td>
<td>&lt;10</td>
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<tr>
<td>TSH</td>
<td>44</td>
<td>0-37</td>
<td>mU/l</td>
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<tr>
<td>Thyroglobulin Autoantibody</td>
<td>1211</td>
<td>&lt;200</td>
<td>%</td>
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TSH

• Expected to be elevated in dogs with hypothyroidism
• In reality:
  • Up to 25% of hypothyroid dogs have a normal TSH
  • Up to 8% of normal dogs have a high TSH
• TSH high as autoimmune thyroiditis develops - maintains thyroid hormone secretion from remaining thyroidal cells

TSH

• Highly sensitive for hypothyroidism in humans
• Used to monitor therapy in humans
• Why is it less accurate in dogs?
  • Sensitivity 0.76/0.87
  • Not a good screening test for dogs
  • Specificity 0.93/0.82
  • Accuracy 0.84

Canine TSH Assay

• Canine species-specific immunoassay for TSH (made by DPC)
• Three types of assay:
  • Chemiluminescent (Immulite)
  • Immunoradiometric
  • ELISA
• Same basic assay – different detection methods
• Standard is highly purified pituitary extract
  • Cross-reactivity with other pituitary glycoproteins?
Canine TSH Assay

- Poor sensitivity?
  - Pulsatile release of TSH in hypothyroid dogs
  - Pituitary “exhaustion” with prolonged disease
- Glycosylation pattern
  - Heterogeneity in carbohydrate constituents
  - Affects immunoreactivity
  - Create recombinant glycosylation independent assay standards?

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2 yr F Doberman, no clinical signs

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Autoantibodies

- Suggest presence of autoimmune thyroiditis
- Do not predict current thyroid status
- Could be a marker for future hypothyroidism
  - Monitor panel q 3-6m
  - About 20% may become hypothyroid within 1 year
4 yr MN Lab, lethargy, mild anemia

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2 yr FS Chesapeake Bay retr, weight gain

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<td>Total T4</td>
<td>&gt;156</td>
<td>15-67</td>
<td>nmol/l</td>
</tr>
<tr>
<td>Total T3</td>
<td>0.2</td>
<td>1.0-2.5</td>
<td>nmol/l</td>
</tr>
<tr>
<td>Free T4 by ED</td>
<td>1</td>
<td>6-42</td>
<td>pmol/l</td>
</tr>
<tr>
<td>Free T3</td>
<td>8.6</td>
<td>4.5-12.0</td>
<td>pmol/l</td>
</tr>
<tr>
<td>T4 Autoantibody</td>
<td>29</td>
<td>&lt;20</td>
<td></td>
</tr>
<tr>
<td>T3 Autoantibody</td>
<td>9</td>
<td>&lt;10</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>136</td>
<td>0-37</td>
<td>mU/l</td>
</tr>
<tr>
<td>Thyroglobulin Autoantibody</td>
<td>1912</td>
<td>&lt;200</td>
<td>%</td>
</tr>
</tbody>
</table>

Autoantibodies

- TgAA (thyroglobulin autoantibody)
  - 50-60% of hypothyroid dogs
  - 234 dogs followed for 1 year:
    - About 20% become hypothyroid within 1 year
    - 15% became AA negative
    - 57% stayed positive and euthyroid
    - 8% went from positive to borderline
Autoantibodies

- **T3AA**
  - 33% of hypothyroid dogs
  - May explain lack of value of TT3
- **T4AA**
  - 15% of hypothyroid dogs
  - 5% no effect on TT4
  - 9% kept TT4 in normal range
  - 1% TT4 elevated
  - FT4 (ED) not affected by T4AA

What's The Best Test?

- Best sensitivity
  - TT4 + FT4 (ED) + TSH
- Best specificity
  - FT4 (ED) + TSH

- Drugs or non-thyroidal illness
  - FT4 (ED) + TSH + TgAA (autoantibodies)

Thyroid Test Comparisons
(Ferguson, VCNA July 2007)

<table>
<thead>
<tr>
<th>TEST</th>
<th>Low TT4</th>
<th>Low TT3</th>
<th>Low FT4D</th>
<th>High TSH</th>
<th>Low TT4/ High TSH</th>
<th>Low FT4D/High TSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.89/1</td>
<td>0.1</td>
<td>0.98/0.8</td>
<td>0.76/0.87</td>
<td>0.67/0.87</td>
<td>0.74/0.8</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.82/0.75</td>
<td>0.92</td>
<td>0.93/0.94</td>
<td>0.93/0.82</td>
<td>0.98/0.92</td>
<td>0.98/0.97</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.85</td>
<td>0.55</td>
<td>0.95</td>
<td>0.84</td>
<td>0.82</td>
<td>0.86</td>
</tr>
</tbody>
</table>
Other Diagnostic Tests

- TSH stimulation
- TRH stimulation
- Scintigraphy
- Thyroid ultrasonography
- Trial therapy
  - Only if there is something to monitor

Therapy for Hypothyroidism

- Levothyroxine (T4)
  - Many products available
  - Start with brand name?
    - Controversial
    - Soloxine®, Thyrotabs®
  - Liquid product now available
    - Leventa® - Intervet

- Therapy for Hypothyroidism

  - Levothyroxine (T4)
    - 20 μg/kg (0.02 mg/kg) (0.8 mg max to start)
      - Large dogs: 0.5 mg/m

  - Once or twice daily?
    - Usually start twice daily
    - Decrease to once daily if doing well

  - T3 not used therapeutically
Therapy for Hypothyroidism

• Individual variation in bioavailability
• Half-life is 12-15 hours
• Monitoring is important

• Dogs are not humans!
  • Dogs need much higher doses of levothyroxine
  • TSH primarily monitored in humans

Therapy for Hypothyroidism

• Therapeutic Drug Monitoring
  • Monitor T4 levels
  • 4-6 hr post-pill
    • Aiming for high-normal/slightly above normal
  • Trough (pre-pill) value?
    • May be useful with once daily therapy

Therapy for Hypothyroidism

• When to monitor?
  • 5 half-lives for drug levels (about 3 days)
  • Biological effects take much longer
    • Energy levels improve in 2-4 weeks
    • Skin changes take up to 3 months
  • First recheck typically at 14 days
Feline Hypothyroidism

- Acquired
  - Rarely spontaneous
  - Iatrogenic
    - Surgery
    - Anti-thyroid medications
    - I-131
- Congenital

Congenital Hypothyroidism

- Cretinism
- Disproportionate dwarf
- Short, broad skull
- Shortened mandible
- Enlarged cranium
- Shortened limbs
- Kyphosis
- Gait abnormalities

Congenital Hypothyroidism

- Mentally dull/lethargic
- Inappetant
- Constipation
- Delayed tooth eruption
- Alopecia
- Dry or "puppy" coat
- Thick skin
- Delayed epiphyseal appearance
- Retarded epiphyseal growth