KEY POINTS

A. Thyroid Hormone

- T4 accounts for the majority of the thyroid hormone secreted by the thyroid gland
  - Small quantities of T3 released – primary hormone that induces physiologic effects
  - Minor amounts of rT3 released
- More than 99% of T4 is bound to plasma proteins
- <1% of T4 and T3 circulate in unbound 'free' state (fT4, fT3)
  - Biologically active, capable of entering cells throughout the body
  - fT4 Exerts negative feedback inhibition on pituitary TSH secretion
- Thyroid hormones entrance into cells is mediated by transporter proteins. Hormones bind to receptors in nuclei

B. Physiologic Function of Thyroid Hormones

- Stimulate calorigenesis
- Stimulate protein and enzyme synthesis
- Regulates every aspect of carbohydrate and lipid metabolism (synthesis, mobilization, degredation)
- *Have marked chronotropic and inotropic effects on the heart*
- *Increase the number and affinity of beta-adrenergic receptors*
- *Enhance the response to catecholamines*
- *Necessary for normal hypoxic and hypercapnic drive to the respiratory centers*
- *Stimulate erythropoiesis*
- *Stimulate bone turnover*

C. **Hypothyroidism in the Dog**

- Acquired primary hypothyroidism is most common cause (2 forms: lymphocytic thyroiditis, idiopathic atrophy)
- Common in middle age to older dogs. Golden Retrievers and Dobermans are most at risk

D. Clinical Signs of Canine Hypothyroidism

- 80% of the gland must be destroyed before clinical signs are evident
- **Most consistent clinical signs** are those due to **decreased cellular metabolism** and **dermatologic manifestations**
- Cardiovascular system
  - Can induce ECG and echo abnormalities. Rarely causes heart failure without preexisting heart condition
  - Hemodynamic effects caused by direct effect of thyroid hormone deficiency on myocardium
    - Decreased cardiac muscle myosin adenosine triphosphatase (ATPase) activity
    - Decreased sarcoplasmic reticulum calcium-ATPase activity
    - Decreased calcium channel activity
    - Decreased sodium-potassium ATPase activity
    - Reduced β-adrenergic receptors in the myocardium
- Neuromuscular system
  - Causal relationship between hypothyroidism, laryngeal paralysis, megaesophagus and myasthenia gravis has not been established
- Gastrointestinal and Reproductive system

E. Diagnosis and Treatment

- Recommendation for assessment of hypothyroidism in dogs: consider serum T4, fT4 and serum TSH
- Concurrent illness, drugs (especially glucocorticoids), and random fluctuations in thyroid hormone concentrations are most common factors resulting in lower baseline thyroid hormone concentrations in euthyroid dogs
- Initial treatment of choice is synthetic L-T4 sodium
- Severity of suppression of serum thyroid hormone concentrations can be used as a prognostic indicator
  - Lower serum thyroid hormone concentrations are associated with a higher mortality rate

Thyroid Gland and Regulation

- Functional unit of thyroid gland is the follicle, which contains a proteinaceous colloid called thyroglobulin (Tg)
    - Tg is a large glycoprotein dimer that serves as a reservoir for thyroid hormone
- Parafollicular cells (C cells) lie in the interstitium between the follicles
    - Synthesize and secrete calcitonin

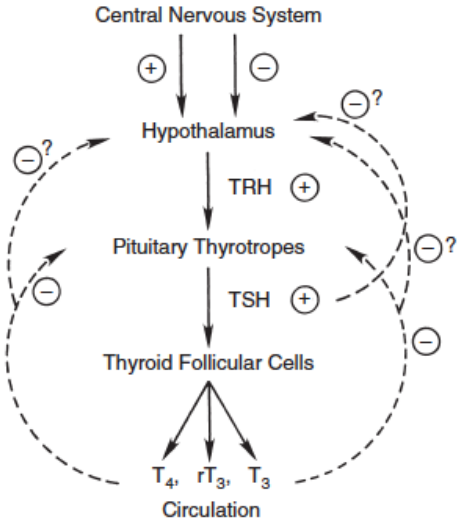

FIGURE 3-5 Regulation of thyroid hormone concentration by the hypothalamic-pituitary-thyroid axis. Thyroid hormone concentrations are controlled by the hypothalamic-pituitary-thyroid axis, which operates as a negative feedback loop. Thyrotropin *(TSH)* causes synthesis and release of thyroxine *(T_4)* and lesser amounts of 3,5,3′-triiodothyronine *(T_3)* from the thyroid gland. Intracellular T_3, derived from de-iodination of T_4 within the pituitary gland, causes decreased TSH synthesis and secretion and is the main determinant of TSH concentration. Thyrotropin-releasing hormone *(TRH)*, secreted by the hypothalamus, modulates TSH release from the pituitary gland. Increased thyroid hormone concentrations are also believed to decrease TRH synthesis and secretion. Hormones that inhibit TSH secretion include dopamine, somatostatin, serotonin, and glucocorticoids. TRH, prostaglandins, and alpha-adrenergic agonists increase TSH secretion. *rT_3*, Reverse 3,3′,5′-triiodothyronine; +, stimulation; –, inhibition.

**Hypothalamic production and release of TRH is controlled by poorly understood neural pathways from higher brain centers.*

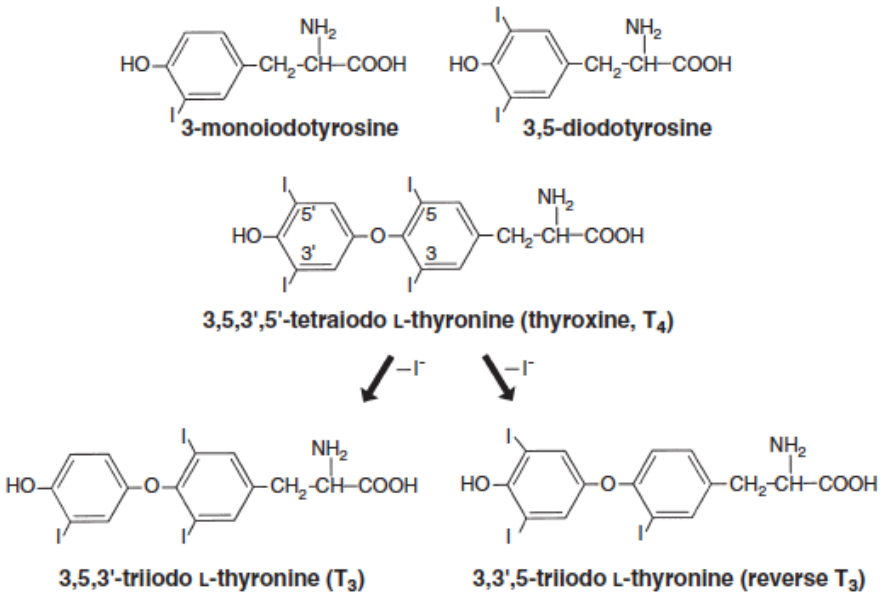

FIGURE 3-4 Structure of the thyroid hormones and their precursors.

- T4 is major secretory product of normal gland
- T4 accounts for the majority of the thyroid hormone secreted by the thyroid gland
    - Small quantities of T3 released – primary hormone that induces physiologic effects
    - Minor amounts of rT3 released
- More than 99% of T4 is bound to plasma proteins
- <1% of T4 and T3 circulate in unbound 'free' state (fT4, fT3)
    - Biologically active
    - Capable of entering cells throughout the body
    - fT4 Exerts negative feedback inhibition on pituitary TSH secretion

- Thyroid hormones entrance into cells is mediated by transporter proteins
    - Thyroid hormones bind to receptors in nuclei
- Within the cell, fT4 is de-iodinated to form either T3 or rT3, depending on the metabolic demands of the tissues
- T3 is primary hormone that induces physiologic effects
    - Enters cells more rapidly
    - Has more rapid onset of action
    - 3-5x more potent than T4 (greater biologic activity)
- T3 is preferentially produced during normal metabolic states
- rT3, which is biologically inactive, is produced during periods of illness, starvation, or excessive endogenous catabolism

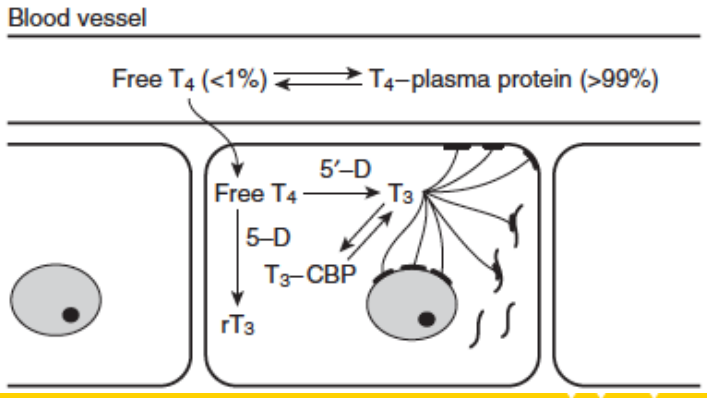

FIGURE 3-18 Schematic of intracellular metabolism of free T_4 (fT_4) to either triiodothyronine *(T_3)* or reverse T_3 *(rT_3)* by 5′- or 5-monodeiodinase, respectively. Intracellular T_3 formed from monodeiodination of fT_4 can interact with T_3 receptors on the cell membrane, mitochondria, or nucleus of the cell and stimulate the physiologic actions of thyroid hormone or bind to cytoplasmic binding proteins *(CBP)*. The latter forms an intracellular storage pool for T_3.

Physiologic Function of Thyroid Hormones

1. Stimulate calorigenesis
2. Stimulate protein and enzyme synthesis
3. Regulates every aspect of carbohydrate and lipid metabolism (synthesis, mobilization, degredation)
4. Have marked chronotropic and inotropic effects on the heart
5. Increase the number and affinity of beta-adrenergic receptors
6. Enhance the response to catecholamines
7. Necessary for normal hypoxic and hypercapnic drive to the respiratory centers
8. Stimulate erythropoiesis
9. Stimulate bone turnover

CANINE HYPOTHYROIDISM

Classification

- Acquired primary hypothyroidism is most common cause is the dog
    - Two histologic forms recognized in dogs: lymphocytic thyroiditis and idiopathic atrophy
- Common in middle age to older dogs
- Golden Retrievers and Dobermans are most at risk

BOX 3-1 Potential Causes of Hypothyroidism in the Dog

Primary Hypothyroidism
Lymphocytic thyroiditis*
Idiopathic atrophy*
Neoplastic destruction*
Iodine deficiency*
Goitrogen ingestion
Iatrogenic*
  Surgical removal*
  Anti-thyroid medications/potentiated sulfonamides*
  Radioactive iodine treatment*

Congenital*
Thyroid gland dysgenesis*
Dyshormonogenesis*
Defective thyroid hormone transporters/receptors
Iodine deficiency
Maternal antibodies
Maternal medications

Secondary Hypothyroidism
Pituitary malformation*
Pituitary cyst
  Pituitary hypoplasia
Pituitary destruction*
  Neoplasia
Defective TSH molecule
Defective TSH-follicular cell receptor interaction
Iatrogenic*
  Drug therapy, most notably glucocorticoids
  Radiation therapy
  Hypophysectomy

Tertiary Hypothyroidism
Congenital hypothalamic malformation
Acquired destruction of hypothalamus
  Neoplasia*
  Hemorrhage
  Abscess
  Granuloma
  Inflammation
Deficient/defective TRH molecule
Defective TRH-thyrotroph receptor interaction

<u>Clinical Signs</u>

- 80% of the gland must be destroyed before clinical signs are evident
- Most consistent clinical signs are those due to **decreased cellular metabolism** and **dermatologic manifestations**
- Additional clinical signs can affect:
    - Cardiovascular system
    - Neuromuscular system
    - Gastrointestinal system
    - Reproductive system

BOX 3-2 Clinical Manifestations of Hypothyroidism in the Adult Dog

Metabolic
Lethargy*
Mental dullness
Inactivity*
Weight gain*
Cold intolerance

Dermatologic
Endocrine alopecia*
- Symmetric or asymmetrical
- Areas of friction and pressure
- "Rat tail"

Dry, brittle hair coat
Hyperpigmentation
Seborrhea
Pyoderma
Otitis externa
Myxedema

Reproductive
Prolonged parturition
Periparturient mortality
Low birth weight puppies
Female infertility
Inappropriate galactorrhea or gynecomastia

Neuromuscular
Polyneuropathy/myopathy
Vestibular signs (central or peripheral)
Facial/trigeminal nerve paralysis
Seizures
Disorientation/circling
Myxedema coma
Laryngeal paralysis (?)

Ocular
Corneal lipid deposits

Cardiovascular
Bradycardia
Cardiac arrhythmias

Gastrointestinal
Esophageal hypomotility (?)
Diarrhea
Constipation

Hematologic
Anemia*
Hyperlipidemia*

*Common.
?indicates that a causal relationship is not proven.

Dermatologic Signs

- Occur in 60-80% of hypothyroid dogs
- Most commonly observed abnormalities in dogs with hypothyroidism
- Bilaterally symmetric, nonpruritic truncal alopecia
    - Thyroid hormone is necessary to initiate and maintain the anagen phase (growing) of the hair cycle
    - With thyroid hormone deficiency hair follicles prematurely enter the telogen phase of the hair cycle
- Hyperpigmentation is common
- Myxedema or cutaneous mucinosis occurs in severe cases
    - Hyaluronic acid accumulates in the dermis, bind water, and results in increased thickness and non-pitting edema of the skin
    - Predominantly affects the forehead, eyelids, and lips (contributes to "tragic facial expression")
- Depletion of thyroid hormone suppresses humoral immune reactions, impairs T cell function, and reduces the number of circulating lymphocytes
    - Predisposes to adult demodecosis and otitis externa

Neurologic Signs

- Can affect both CNS and PNS
- Neurologic dysfunction may be multifocal, acute or chronic, and static or progressive
- Other physical examination findings consistent with hypothyroidism may be absent
- The reason for neurologic dysfunction is poorly understood and likely multifactorial
- Laryngeal paralysis, megaesophagus and myasthenia gravis may occur in association with hypothyroidism
    - Causal relationship has not been established
    - Treatment of hypothyroidism does not consistently result in improvement of clinical signs

Myxedema coma

- Extremely rare
- Characterized by profound weakness, hypothermia, bradycardia, and decreased consciousness (progress to stupor and then coma)

Cardiac abnormalities

- Usually reversible with supplementation
- Hypothyroidism can induce echocardiographic changes BUT rarely causes heart failure without underlying condition
- ECG abnormalities:
    - Sinus bradycardia
    - Decreased amplitude of the P and R waves
    - Inversion of the T waves
    - First-degree and second-degree atrioventricular block
- Echo abnormalities:
    - Increased left ventricular end systolic diameter
    - Prolonged preejection period
    - Decreases in left ventricular posterior wall thickness during systole
    - Percentage change in left ventricular posterior wall from diastole to systole
    - Interventricular wall thickness during systole and diastole
    - Aortic diameter
    - Velocity of circumferential fiber shortening
    - Fractional shortening
- Hemodynamic effects attributable to direct effects of hypothyroidism on the myocardium
    - Decreased cardiac muscle myosin adenosine triphosphatase (ATPase) activity
    - Decreased sarcoplasmic reticulum calcium-ATPase activity
    - Decreased calcium channel activity
    - Decreased sodium-potassium ATPase activity
    - Reduced β-adrenergic receptors in the myocardium

Ocular signs

- Rare in hypothyroid dogs
- Most commonly are secondary to hyperlipidemia

Gastrointestinal Signs

- Not common
- Megaesophagus
    - No cause and effect relationship
    - Likely result of hypothyroid induced myopathy or neuropathy

Coagulopathy

- Humans:
    - Reduction in concentration of factors VIII and IX
    - Reduction in factor VIII–related antigen (von Willebrand factor)
    - Reduced platelet adhesiveness
    - Increased capillary fragility
- No evidence noted in dogs

<u>Diagnostics</u>

CBC

- Normocytic, normochromic, nonregenerative anemia (packed cell volume [PCV], 28% to 36%)
    - In 30% of dogs
    - Cause unknown

Biochemistry

- Fasting hypercholesterolemia (75% of hypothyroid dogs) AND Fasting hypertriglyceridemia
    - Synthesis and degradation of lipids are depressed in hypothyroidism (degradation >> synthesis)
- Mild to moderate increase in LDH, AST, ALT, ALP
    - Associated with hypothyroid myopathy

Nuclear Imaging

- 99m-TcO4 is concentrated but not organified by the thyroid gland
    - Most commonly used isotope used for thyroid scintigraphy in veterinary medicine
    - Parotid salivary glands concentrate isotope too
    - A 1:1 thyroid-to-salivary ratio is considered normal in the dog,

Serology

- Total serum T4 concentrations represent the sum of the protein-bound and free levels circulating in the blood
- fT4 concentration is a measure of the free hormone only
- Recommendation for assessment of hypothyroidism in dogs:
    - Serum T4
    - fT4
    - Serum TSH
- Serum T3 concentration is a poor gauge of thyroid gland function because of its predominant intracellular location and the minimal amount of T3 secreted by the thyroid gland compared with T4
- Baseline serum T4 is best to RULE OUT hypothyroidism
    - Nonthyroidal illness can suppress the baseline serum T4 concentration to < 0.5 µg/dL in a euthyroid dog
    - Hypothyroid dogs rarely have serum T4 concentrations > 1.5 µg/dL
- Baseline serum T3 is not useful when differentiating euthyroidism from hypothyroidism
- **Measurement of T3 may be justified in Greyhounds**
    - Tend to have low concentrations of T4 and fT4 but normal T3 concentrations

TABLE 3-7 INTERPRETATION OF BASELINE SERUM THYROXINE AND FREE THYROXINE CONCENTRATION IN DOGS WITH SUSPECTED HYPOTHYROIDISM

SERUM THYROXINE CONCENTRATION (µg/dL)	SERUM FREE THYROXINE CONCENTRATION (ng/dL)	PROBABILITY OF HYPOTHYROIDISM
> 2.0 µg/dL	> 2.0 ng/dL	Very unlikely
1.5 to 2.0 µg/dL	1.5 to 2.0 ng/dL	Unlikely
1.0 to 1.5 µg/dL	0.8 to 1.5 ng/dL	Unknown
0.5 to 1.0 µg/dL	0.5 to 0.8 ng/dL	Possible
< 0.5 µg/dL	< 0.5 ng/dL	Very likely*

TABLE 3-5 CANINE BREEDS WITH UNIQUE THYROID HORMONE REFERENCE RANGES

BREED	TOTAL THYROXINE (↓ OR N)	FREE THYROXINE (↓ OR N)	TOTAL TRIIODOTHYRONINE (↓ OR N)	THYROTROPIN (↑ OR N)	THYROXINE RESPONSE TO TSH
Greyhound	↓	↓	Usually N	N	Decreased
Whippet	↓	N	—	N	
Saluki	↓	↓	↓	N or ↑	
Sloughi	↓	↓ or ↑ (ED)	—	↑	Normal to slightly decreased
Basenji	↓	—	—	N	—
Irish Wolfhound	↓	—	—	—	
Conditioned Alaskan sled dogs	↓	↓	↓	Variable	

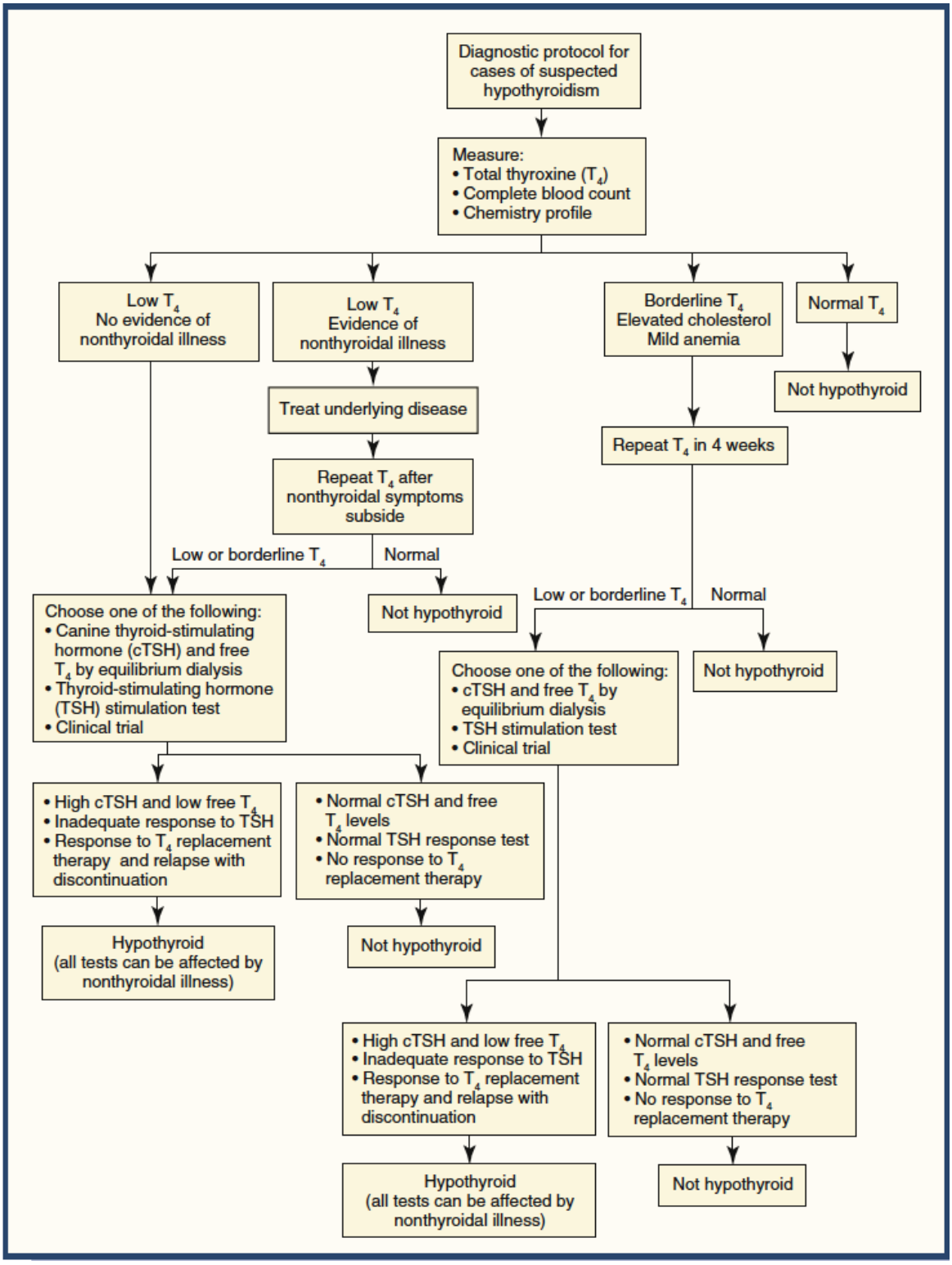

FIGURE 3-20 Algorithm for diagnosis of canine hypothyroidism.

Factors Affecting Thyroid Gland Function Tests

- Factors that affect baseline thyroid hormone and endogenous TSH concentrations
  - Age
  - Breed
  - Body size
  - Diurinal fluctuations

- **Random fluctuations**
- Athletic training
- Reproductive status
- **Concurrent illness**
- **Drug therapy**

- Most common factors that result in lower baseline thyroid hormone concentrations in euthyroid dogs are concurrent illness, use of drugs (especially glucocorticoids), and random fluctuations in thyroid hormone concentrations.

Age

- Progressive decline in T4 with age
- Serum T4 highest in puppies
- Older dogs have higher mean TSH concentration than younger dogs
- Reasons for decline with age not fully understood. Proposed mechanisms:
  - Effect of concurrent illness
  - Change in responsiveness of the thyroid gland to TSH
  - Subclinical thyroid pathology (fibrosis, atrophy, degenerative changes)
  - Decreased biologic activity of TSH with age

Body size

- Mean serum T4 greater in small than in medium-sized and large dogs

Breed

- Sighthounds (see table3-5)

Concurrent illness (Non-Thyroidal Illness Syndrome)

- Mechanisms:
  - Decreased TSH secretion
  - Decreased synthesis of T4
  - Decreased concentration or binding affinity of circulating binding proteins
  - Presence of serum protein binding inhibitors
  - Inhibition of the de-iodination of T4 to T3
  - Any combination of these factors
- Disorders that are frequently associated include:
  - Neoplasia
  - Renal disease
  - Hepatic disease
  - Cardiac failure
  - Neurologic disease
  - Inflammatory disorders
  - Diabetic ketoacidosis
  - Diabetes Mellitus
  - Addison's
- Severity of suppression of serum thyroid hormone concentrations can be used as a prognostic indicator
  - Lower serum thyroid hormone concentrations are associated with a higher mortality rate
- Supplementation not recommended in NTIS as it is suspected to be a protective mechanism to reduce cellular metabolic demands

Drugs

- Glucocorticoids are the most commonly used drugs that influence serum thyroid hormone concentrations
  - Decreases serum T4, fT4, and T3 (often into the hypothyroid range)
- Sulfonamide antibiotics, anticonvulsants and NSAIDs can also affect thyroid hormone concentrations

TABLE 3-12 MECHANISMS BY WHICH DRUGS INFLUENCE THYROID FUNCTION IN HUMANS

MECHANISM	EXAMPLE
Decrease TSH secretion	Glucocorticoids
Change thyroid hormone secretion	Amiodarone
Decrease gastrointestinal absorption	Sucralfate
Alter serum binding	Phenylbutazone
Change hepatic metabolism	Phenobarbital
Inhibit TPO	Sulfonamides

TPO, Thyroid peroxidase; *TSH*, thyroid-stimulating hormone (also known as thyrotropin).

TABLE 3-13 DRUGS THAT HAVE BEEN DEMONSTRATED TO INFLUENCE THYROID FUNCTION IN DOGS

DRUG	TOTAL THYROXINE (↓ OR N)	FREE THYROXINE (↓ OR N)	THYROTROPIN (↑ OR N)	CLINICAL SIGNS OF HYPOTHYROIDISM? (Y/N)	NOTES
Glucocorticoids	↓	(↓ or N)	N	N	Effect dose and duration dependent
Phenobarbital	↓	↓	Slight ↑	N	TSH not increased outside reference range
Trimethoprim/sulfonamides	↓	↓	↑	Y	Effect dose and duration dependent
Nonsteroidal anti-inflammatory drugs					Effect varies depending on specific drug used
Aspirin	↓	N or ↓	N	N	
Deracoxib	N	N	N	N	
Ketoprofen	N	N	N	N	
Meloxicam	N	N	N	N	
Carprofen	N	N	N	N	
Etodolac	N or ↓	N	N or ↑	N	
Clomipramine	↓	↓	N	N	

TSH, Thyroid-stimulating hormone (also known as thyrotropin).

BOX 3-5 Proposed Alterations in Thyroid Hormone Physiology Caused by Glucocorticoids

Decreased 5′-monodeiodination enzyme activity
Decreased binding affinity of plasma proteins for T_4, T_3
Decreased cellular binding of T_4, T_3
Increased metabolic clearance rate of T_4
Decreased metabolic clearance rate of T_3, rT_3
Inhibition of TSH secretion (secondary hypothyroidism)
Inhibition of TRH secretion

T_3, Triiodothyronine; T_4, thyroxine; *TRH*, thyrotropin-releasing hormone; *TSH*, thyroid-stimulating hormone (also known as thyrotropin).

BOX 3-6 Some Drugs and Diagnostic Agents that can Alter Basal Serum Thyroid Hormone Concentrations in Humans and Possibly Dogs

Decrease T_4 and/or T_3
Amiodarone (T_3)
Androgens
Cholecystographic agents
Diazepam
Dopamine
Flunixin
Furosemide
Glucocorticoids
Heparin
Imidazole
Iodide
Methimazole
Mitotane
Nitroprusside
Penicillin
Phenobarbital
Phenothiazines
Phenylbutazone
Phenytoin
Primidone
Propranolol
Propylthiouracil
Radiopaque dyes (ipodate) (T_3)
Salicylates
Sulfonamides (sulfamethoxazole)
Sulfonylureas

Increase T_4 and/or T_3
Amiodarone (T_4)
Estrogens
5-Fluorouracil
Halothane
Insulin
Narcotic analgesics
Radiopaque dyes (e.g., ipodate) (T_4)
Thiazides

- NSAIDs may decrease serum T4, fT4, T3, and TSH concentrations. Proposed mechanisms include:
    - Displacement of thyroid hormone binding to plasma proteins
    - Decreased thyroid hormone de-iodination
    - Inhibition of binding of thyroid hormone to receptors in the plasma membrane, cytoplasm, and nucleus

Treatment

- Initial treatment of choice is synthetic L-T4 sodium
- The dose in dogs is 10x higher than the dose used in humans
    - Because of poorer gastrointestinal absorption and a shorter serum half-life of T4 in dogs

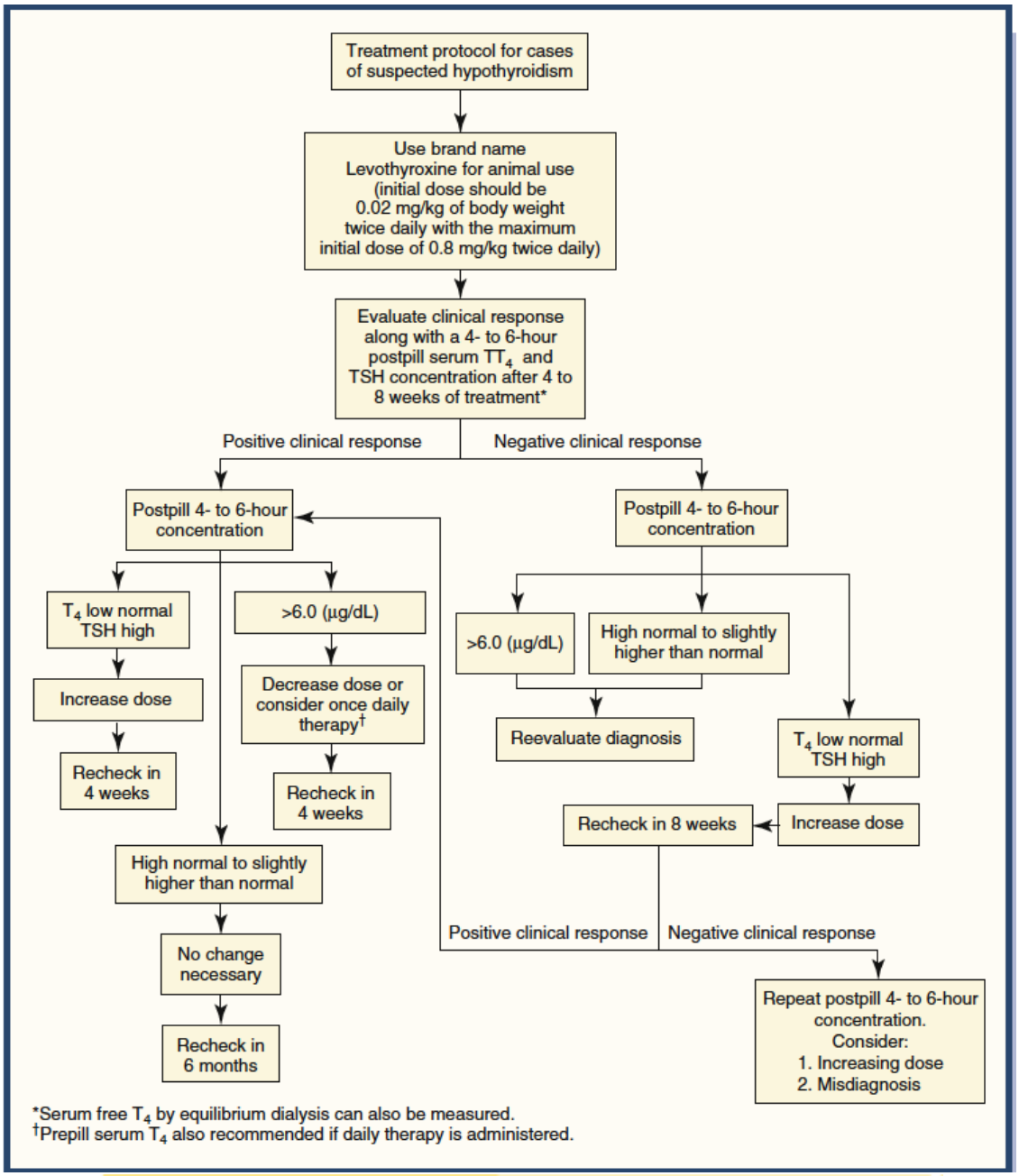

FIGURE 3-33 Algorithm for treatment of canine hypothyroidism.

TABLE 3-14 **ANTICIPATED TIME OF CLINICAL RESPONSE TO SODIUM LEVOTHYROXINE TREATMENT IN DOGS WITH HYPOTHYROIDISM**

AREA OF IMPROVEMENT	TIME TO IMPROVEMENT
Mentation and activity	2 to 7 days
Lipemia and clinical pathology	2 to 4 weeks
Dermatologic abnormalities	2 to 4 months
Neurologic abnormalities	1 to 3 months
Cardiac abnormalities	1 to 2 months
Reproductive abnormalities	3 to 10 months

BOX 3-8 Potential Reasons for Poor Clinical Response to Treatment with Levothyroxine Sodium (Synthetic Thyroxine)

Owner compliance problems
Use of inactivated or outdated product
Use of some generic levothyroxine ($L\text{-}T_4$) sodium preparations
Inappropriate $L\text{-}T_4$ sodium dose
Inappropriate frequency of administration
Use of thyroid extracts or combination thyroxine/triiodothyronine products
Poor bioavailability (e.g., poor gastrointestinal absorption)
Inadequate time for clinical response to occur
Incorrect diagnosis of hypothyroidism
Concurrent disease causing clinical signs (e.g., allergic dermatitis)

Treatment of myxedema coma

- IV thyroid hormone as absorption of therapeutic agents from the gut or from SQ/IM sites is unpredictable
    - Because of the sluggish circulation and severe hypometabolism
    - Recommended initial dosage for injectable L-T4 sodium: 4 to 5 µg/kg q 12 hours
- Correct electrolyte abnormalities and supplement with dextrose

Thyrotoxicosis

- Rare
- May develop in dogs receiving excessive amounts of L-T4 sodium (Iatrogenic hyperthyroidism)
- May develop in dogs with impaired metabolism of L-T4 sodium (e.g., concurrent renal or hepatic insufficiency)
- Clinical signs of thyrotoxicosis:
    - Panting
    - Nervousness
    - Anxiety
    - Tachycardia
    - Aggressive behavior
    - Polyuria
    - Polydipsia
    - Polyphagia
    - Weight loss
    - Sinus tachycardia, atrial flutter, syncope (Iatrogenic hyperhthyroidism dogs with concurrent cardiac disease)
- Supplementation may have to be discontinued for a few days if the clinical signs are severe
    - Signs of thyrotoxicosis should resolve within 1 to 3 days if iatrogenic

FELINE HYPOTHYROIDISM

- Rare naturally occurring disease in the cat
- Iatrogenic hypothyroidism is common

<u>Questions</u>

1. What % of the thyroid gland must be destroyed before clinical signs of hypothyroidism are evident?
    a. 60%
    b. 50%
    c. 70%
    d. 80%

2. Clinical signs related to which organ system is most common in dogs affected by hypothyroidism
    a. Neurologic system
    b. Dermatologic system
    c. Cardiovascular system
    d. Gastrointestinal system

3. True or False. Treatment of hypothyroidism can result in improvement in signs of of laryngeal paralysis, megaesophagus and myasthenia gravis.

4. Name 4 clinical signs or physical exam abnormalities identified in dogs with myxedema coma.

5. Why is serum T3 concentration NOT recommended for assessment of thyroid gland function? (Provide 2 reasons)

6. Which combination represents the most common factors that cause lower baseline thyroid hormone concentrations in euthyroid dogs?
    a. Concurrent illness, drugs, random fluctuations
    b. Diurinal fluctuations, concurrent illness, age
    c. Age, drugs, random fluctuations
    d. Age, breed, gender

7. True or False. Severity of suppression of serum thyroid hormone concentrations can be used as a prognostic indicator.

8. Name 2 direct effects of hypothyroidism on the myocardium that can cause altered hemodynamic effects.

9. Bonus. Why is the dosage of L-T4 sodium in dogs so much higher than that used for treatment of human hypothyroidism?

Answers

1. What % of the thyroid gland must be destroyed before clinical signs of hypothyroidism are evident?
    a. 60%
    b. 50%
    c. 70%
    d. 80%

2. Clinical signs related to which organ system is most common in dogs affected by hypothyroidism
    a. Neurologic system
    b. Dermatologic system
    c. Cardiovascular system
    d. Gastrointestinal system

3. True or False. Treatment of hypothyroidism can result in improvement of laryngeal paralysis, megaesophagus and myasthenia gravis.
    False. Causal relationship has not been established
    Treatment of hypothyroidism does not consistently result in improvement of clinical signs

4. Name 4 clinical signs or physical exam abnormalities identified in dogs with myxedema coma.

Characterized by profound weakness, hypothermia, bradycardia, and decreased consciousness (progress to stupor and then coma)

5. Why is serum T3 concentration NOT recommended for assessment of thyroid gland function? (Give 2 reasons)
    a. **Because of its predominant intracellular location**
    b. **Due to minimal amount of T3 secreted by the thyroid gland compared with T4**

6. Which combination represents the most common factors that cause lower baseline thyroid hormone concentrations in euthyroid dogs?
    a. **Concurrent illness, drugs, random fluctuations**
    b. Diurinal fluctuations, concurrent illness, age
    c. Age, drugs, random fluctuations
    d. Age, breed, gender

7. True or False. Severity of suppression of serum thyroid hormone concentrations can be used as a prognostic indicator.
    True. Lower serum thyroid hormone concentrations are associated with a higher mortality rate

8. Name 2 direct effects of hypothyroidism on the myocardium that can cause altered hemodynamic effects.
    Hemodynamic effects caused by direct effect of thyroid hormone deficiency on myocardium
    a. **Decreased cardiac muscle myosin adenosine triphosphatase (ATPase) activity**
    b. **Decreased sarcoplasmic reticulum calcium-ATPase activity**
    c. **Decreased calcium channel activity**
    d. **Decreased sodium-potassium ATPase activity**
    e. **Reduced β-adrenergic receptors in the myocardium**

9. Bonus. Why is the dosage of L-T4 sodium in dogs so much higher than that used for treatment of human hypothyroidism?
    Because of poorer gastrointestinal absorption and a shorter serum half-life of T4 in dogs