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A comprehensive review of canine hypothyroidism: Clinical features, laboratory diagnosis, and therapeutic approaches

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Abstract
Canine hypothyroidism is among the most frequently diagnosed endocrine disorders in dogs, yet remains one of the most diagnostically challenging. This review summarizes the current understanding of its epidemiology, pathophysiology, diagnostic approach, and therapeutic management. Primary hypothyroidism, most often the result of lymphocytic thyroiditis or idiopathic follicular atrophy, accounts for the majority of cases. Clinical manifestations are diverse and often nonspecific, reflecting metabolic and dermatologic changes. Diagnostic evaluation requires careful interpretation of thyroid function tests, including total thyroxine (TT_4), free thyroxine (fT_4 by equilibrium dialysis), endogenous thyroid-stimulating hormone (TSH), and thyroglobulin autoantibodies (TgAA). The TSH stimulation test, while historically considered the gold standard, is now reserved for equivocal cases due to limited availability of recombinant human TSH. Consideration of non-thyroidal illness and drug effects is essential to avoid misdiagnosis. Levothyroxine remains the treatment of choice, with dosing tailored to body weight, clinical response, and serum hormone monitoring. Most dogs show clinical improvement within weeks of initiating therapy, and long-term prognosis is excellent with appropriate management. Advances in immunogenetics and longitudinal studies of thyroid autoimmunity continue to refine understanding of disease progression. Current consensus guidelines emphasize a combined diagnostic approach, judicious therapeutic monitoring, and individualized patient care.

Keywords: Canine hypothyroidism, thyroid function tests, levothyroxine, lymphocytic thyroiditis, endocrine disorders

1. Introduction

1.1 Definition

Hypothyroidism in dogs is a clinical condition characterized by a deficiency of thyroid hormones, primarily thyroxine (T_4) and triiodothyronine (T_3), produced by the thyroid gland. This hormonal insufficiency leads to a reduction in the basal metabolic rate, which manifests as multisystemic clinical signs affecting dermatologic, neurologic, reproductive, and metabolic functions (Mooney, 2011) [16].

1.2 Epidemiology and Prevalence

Canine hypothyroidism is considered the most common endocrine disorder in middle-aged dogs, particularly in breeds such as Golden Retrievers, Doberman Pinschers, Irish Setters, and Dachshunds (Ferguson, 1994) [6]. The estimated prevalence is 0.2-0.8% of the general canine population, although underdiagnosis is common due to the vague and non-specific nature of the clinical signs (Peterson *et al.*, 1997) [20]. Females and males are equally affected, with onset typically between 4 to 10 years of age (Graham, 2007) [7].

1.3 Importance of Thyroid Hormones

Thyroid hormones play a pivotal role in regulating carbohydrate, protein, and lipid metabolism, maintaining thermoregulation, influencing erythropoiesis, and modulating cardiovascular function (Dixon, 2005) [3]. Deficiency of these hormones disrupts homeostasis

and results in gradual clinical deterioration.

1.4 Historical Perspective
Hypothyroidism in dogs was first clinically recognized in the early 20th century, but its detailed pathophysiology and diagnostic criteria have only been refined in the last 50 years with the advent of radioimmunoassay and more sensitive thyroid function tests (Kemppainen, 1994) [9].

1.5 Clinical Relevance
The clinical significance of hypothyroidism lies in its insidious presentation. Dogs may initially present with vague signs such as lethargy, weight gain, or poor coat condition. Without diagnosis and management, progressive metabolic imbalance and secondary complications-such as neuropathies, infertility, and dermatological disorders-can develop (Scott-Moncrieff, 2015) [21]. Early recognition is therefore critical for improving prognosis.

2. Etiology and Pathogenesis
Hypothyroidism in dogs is primarily a disorder of the thyroid gland (primary hypothyroidism), but can also result from pituitary or hypothalamic dysfunction (secondary or tertiary hypothyroidism). The pathogenesis involves progressive destruction of thyroid tissue, impaired hormone synthesis, or disruption of the hypothalamic-pituitary-thyroid (HPT) axis.

2.1 Classification of Hypothyroidism
2.1.1 Primary Hypothyroidism
2.1.1.1 Lymphocytic Thyroiditis:
An immune-mediated process accounts for nearly 50% of primary cases (Graham, 2007) [7]. Histologically, thyroid follicles are infiltrated by lymphocytes, plasma cells, and macrophages, leading to glandular atrophy. Autoantibodies against thyroglobulin and thyroid peroxidase are often detectable (Graham *et al.*, 2002) [8].

2.1.1.2 Idiopathic Follicular Atrophy:
In this form, the thyroid parenchyma is progressively replaced by adipose tissue without an obvious inflammatory component. The pathogenesis is not fully understood, but it is considered either a primary degenerative process or the end stage of autoimmune thyroiditis (Peterson *et al.*, 1997) [20].
Together, lymphocytic thyroiditis and idiopathic atrophy account for >95% of cases of hypothyroidism in dogs (Feldman & Nelson, 2004) [5].

2.1.2 Secondary Hypothyroidism
This is rare (<5% of cases) and occurs due to deficiency of pituitary TSH secretion, often caused by pituitary tumors, congenital hypoplasia, or trauma (Dixon, 2005) [3].

2.1.3 Tertiary Hypothyroidism
Extremely uncommon, resulting from hypothalamic failure to secrete thyrotropin-releasing hormone (TRH).

2.1.4 Iatrogenic Hypothyroidism
May follow **thyroidectomy**, radioactive iodine therapy, or chronic administration of drugs such as Sulfonamides and phenobarbital that interfere with thyroid hormone synthesis (Kooistra, 2005) [12].

2.2 Risk Factors
- **Breed predisposition:** Golden Retrievers, Doberman Pinschers, Beagles, and Irish Setters are commonly affected (Graham, 2007) [7].
- **Age:** Middle-aged dogs (4-10 years) are at higher risk.
- **Sex:** Both sexes are equally susceptible, though neutered dogs may show slightly increased risk (Ferguson, 1994) [6].
- **Genetic factors:** Certain MHC haplotypes have been linked to autoimmune thyroiditis in Beagles and Dobermans (Kennedy *et al.*, 2006) [10].

2.3 Pathogenesis of Hypothyroidism
2.3.1 Destruction of Thyroid Follicles
In lymphocytic thyroiditis, autoreactive lymphocytes target thyroid antigens (e.g., thyroglobulin), leading to follicular damage and decreased hormone output.

2.3.2 Hormonal Deficiency
Reduced T_4 and T_3 lead to decreased metabolic activity in virtually all tissues
- **Carbohydrate metabolism:** Reduced gluconeogenesis and glycogenolysis.
- **Lipid metabolism:** Hypercholesterolemia due to impaired lipid clearance.
- **Protein metabolism:** Altered turnover leading to muscle weakness.
- **Thermoregulation:** Reduced basal metabolic rate and cold intolerance.

2.3.3 Pituitary-Thyroid Feedback Mechanism
Decreased thyroid hormone levels normally stimulate increased TSH secretion. In primary hypothyroidism, serum TSH is elevated but ineffective due to glandular failure (Mooney, 2011) [16].

2.4 Natural Progression
Hypothyroidism usually progresses slowly. Subclinical thyroiditis may persist for years before hormone levels fall enough to cause overt clinical signs. Dogs may remain euthyroid with positive thyroid autoantibodies long before showing clinical illness (Egbert *et al*., 2024) [4].

3. Clinical Signs and Diagnosis
Hypothyroidism in dogs is often described as a “great imitator” because the clinical presentation overlaps with many other systemic and dermatological disorders. The onset is usually insidious and progressive, and the clinical picture varies depending on the severity and duration of the disease. Diagnosis is challenging and requires a combination of clinical suspicion, laboratory evaluation, and confirmatory thyroid function testing.

3.1 General Clinical Manifestations
3.1.1 Metabolic and Constitutional Signs
- **Lethargy and Mental Dullness:** Reduced metabolic activity leads to decreased energy levels, inactivity, and somnolence. Owners often describe affected dogs as “sluggish” or “lazy” (Mooney, 2011) [6].
- **Weight Gain without Polyphagia:** Hypothyroid dogs often gain weight despite normal or decreased food intake, due to reduced basal metabolic rate (Ferguson, 1994) [6].

- **Exercise Intolerance and Weakness:** Due to impaired energy metabolism and muscle function.
- **Cold Intolerance:** Dogs prefer warm environments, seek heat sources, and may shiver easily.

3.1.2 Gastrointestinal and Cardiovascular Signs
- Constipation and occasional diarrhea due to altered motility.
- Bradycardia and low-voltage QRS complexes on ECG due to reduced cardiac output (Dixon, 2005) [3].
- Dilated cardiomyopathy-like changes have been rarely reported but usually resolve after levothyroxine therapy.

3.1.3 Neurological Signs
- **Peripheral neuropathies:** knuckling, ataxia, proprioceptive deficits.
- **Cranial nerve dysfunction:** facial nerve paralysis, vestibular dysfunction.
- Rarely, central nervous signs due to secondary hypothyroidism or pituitary mass lesions (Scott-Moncrieff, 2015) [21].

3.2 Dermatological Manifestations
Dermatological changes are among the most common and characteristic features of canine hypothyroidism.
- **Alopecia:** Non-pruritic, bilateral, and symmetrical hair loss, initially affecting the trunk, tail ("rat tail"), and neck. Hair often fails to regrow after clipping (Graham, 2007) [7].
- **Seborrhea:** Either dry (seborrhea sicca) or oily (seborrhea oleosa).
- **Hyperpigmentation:** Secondary to chronic alopecia and lichenification.
- **Pyoderma and Otitis Externa:** Recurrent infections due to impaired skin barrier and immunosuppression.
- **Myxoedema:** Accumulation of glycosaminoglycans in the dermis leading to thickened skin, especially around the face, giving a "tragic expression."

3.3 Reproductive Manifestations
- **Females:** Prolonged interestrous intervals, silent heats, infertility, abortion, or stillbirths (Cecere, 2023) [1].
- **Males:** Reduced libido, testicular atrophy, and poor semen quality.
- Both sexes may show delayed puberty in congenital hypothyroidism.

3.4 Ocular Manifestations
- Corneal lipid dystrophy, dry eye (keratoconjunctivitis sicca), and blepharitis are occasionally seen in hypothyroid dogs (Dixon, 2005) [3].

3.5 Diagnostic Approach
3.5.1 Clinical Suspicion
A diagnosis should be suspected in middle-aged, predisposed breeds presenting with classic metabolic and dermatological signs.

3.5.2 Routine Laboratory Findings
- **Complete Blood Count (CBC):** Normocytic, normochromic, non-regenerative anemia in ~30-40% of cases.

Serum Biochemistry
- Hypercholesterolemia (75-80% cases)
- Hypertriglyceridemia
- Mild elevations in liver enzymes (ALT, ALP)
- Creatine kinase (CK) may be mildly increased due to myopathy (Peterson *et al.*, 1997) [20].

3.5.3 Thyroid Function Testing
- **Total T_4 (TT_4):** The most commonly used screening test; low levels suggest hypothyroidism but may be suppressed by non-thyroidal illness (Euthyroid Sick Syndrome).
- **Free T_4 (fT_4):** Measured by equilibrium dialysis; more specific than TT_4.
- **Thyroid-Stimulating Hormone (TSH):** Elevated in most hypothyroid dogs, but not always reliable since ~25% of hypothyroid dogs have normal TSH (Mooney, 2011) [16].
- **Thyroglobulin Autoantibodies (TgAA):** Marker of lymphocytic thyroiditis, useful in early/subclinical disease.
- **TSH Stimulation Test:** Historically the gold standard, but rarely used today due to unavailability of bovine TSH.

3.5.4 Imaging
- Thyroid Ultrasound: May show small, hypoechoic, and heterogeneous thyroid lobes.
- Scintigraphy: Limited availability but helpful for functional evaluation.

3.6 Diagnostic Challenges
- **Euthyroid Sick Syndrome (Non-thyroidal Illness):** Systemic illnesses (renal failure, hepatic disease, diabetes mellitus, hyperadrenocorticism) can lower serum thyroid hormone concentrations, leading to false diagnosis of hypothyroidism (Graham *et al.*, 2002) [8].
- **Drug Interference:** Glucocorticoids, phenobarbital, and Sulfonamides can suppress thyroid hormone synthesis or secretion.
- **Breed Variations:** Sight hounds (Greyhounds, Borzoi) naturally have lower TT_4 concentrations, which can mimic hypothyroidism.

4. Differential Diagnosis
The clinical presentation of canine hypothyroidism overlaps with many systemic, dermatological, metabolic, and endocrine disorders. Because of this, misdiagnosis is common if diagnostic investigations are based solely on clinical signs or total T_4 concentrations. A systematic approach to differential diagnosis is essential to distinguish hypothyroidism from other conditions that cause similar signs.

4.1 Dermatological Differentials
4.1.1 Hyperadrenocorticism (Cushing's disease)
- Both hypothyroidism and Cushing's cause bilaterally symmetrical alopecia, thin hair coat, hyperpigmentation, and recurrent skin infections.
- However, Cushing's is more often associated with abdominal distension ("pot-bellied appearance"), polyuria, polydipsia, and calcinosis cutis (Feldman & Nelson, 2004) [5].

4.1.2 Alopecia X (Adrenal Hyperplasia-like Syndrome)
- Seen in Nordic breeds; presents as truncal alopecia and hyperpigmentation.
- Unlike hypothyroidism, affected dogs are usually bright, active, and metabolically normal (Llyod & Cerundolo, 2001) [15].

4.1.3 Seasonal Flank Alopecia
- Characterized by non-inflammatory alopecia restricted to the flanks, occurring seasonally and self-resolving.
- Distinguished by absence of systemic signs (Scott-Moncrieff, 2015) [21].

4.1.4 Demodicosis and Dermatophytosis
- Both can cause alopecia, scaling, and secondary pyoderma.
- Deep skin scrapings, fungal cultures, or PCR confirm the diagnosis (Moriello, 2014) [17].

4.2 Metabolic and Systemic Differentials
4.2.1 Obesity and Reduced Activity (Non-endocrine)
- Obesity due to overfeeding or sedentary lifestyle may mimic hypothyroid-associated weight gain.
- In such cases, dermatological changes and metabolic abnormalities (e.g., hypercholesterolemia) are absent.

4.2.2 Chronic Renal Disease and Hepatic Disease
- These conditions may contribute to lethargy, weakness, and weight gain.
- They are also associated with euthyroid sick syndrome, where thyroid hormone levels are suppressed secondarily to systemic illness (Graham *et al.*, 2002) [8].

4.3 Endocrine Differentials
4.3.1 Hypoadrenocorticism (Addison's disease)
- May share signs such as lethargy, weakness, and gastrointestinal disturbances.
- However, Addison's is usually characterized by electrolyte abnormalities (hyponatremia, hyperkalemia) and waxing-waning GI crises (Kintzer & Peterson, 1997) [11].

4.3.2 Diabetes Mellitus
- Dogs may present with lethargy and weight changes.
- Unlike hypothyroidism, diabetes is associated with polyuria, polydipsia, polyphagia, and hyperglycemia (Nelson & Reusch, 2014) [18].

4.3.3 Hypopituitarism
- Rare, but may cause secondary hypothyroidism due to low TSH production.
- Often associated with other pituitary hormone deficiencies.

4.4 Neuromuscular Differentials
Hypothyroidism may mimic neuromuscular disorders because of its association with polyneuropathy and myopathy.
- Degenerative Myelopathy and Chronic Intervertebral Disc Disease present with weakness and ataxia but without metabolic or dermatologic abnormalities.
- Myasthenia Gravis causes generalized weakness and exercise intolerance but is distinguished by the presence of acetylcholine receptor autoantibodies (Dewey & da Costa, 2016) [2].

4.5 Laboratory and Diagnostic Differentials
- **Euthyroid Sick Syndrome (ESS):** A major confounder where systemic illness suppresses thyroid hormones without true hypothyroidism (Dixon, 2005) [3].
- **Drug-induced Hypothyroxinaemia:** Glucocorticoids, Sulfonamides, phenobarbital, and NSAIDs may artificially lower TT_4 concentrations.
- **Breed-related Variations:** Greyhounds, Borzois, and other sighthounds normally have lower TT_4 levels (Graham, 2007) [7].

4.6 Diagnostic Algorithm for Differentiation
1. **Step 1:** Clinical Suspicion - Evaluate presence of dermatologic + metabolic signs together.
2. **Step 2:** Rule out Non-thyroidal Illness - CBC, serum biochemistry, and urinalysis to check for systemic disease.
3. **Step 3:** Thyroid Testing - TT_4, free T_4 by equilibrium dialysis, TSH.
4. **Step 4:** Confirmatory Evidence - Presence of TgAA or compatible imaging findings.
5. **Step 5:** Therapeutic Trial (in selected cases) - Low-dose levothyroxine for 6-8 weeks may confirm diagnosis if clinical improvement is observed.

5. Pathophysiology of Canine Hypothyroidism
The pathophysiology of canine hypothyroidism involves a complex interplay between thyroid gland destruction, impaired hormone synthesis, and disruption of hypothalamic-pituitary-thyroid (HPT) axis regulation. Most cases are due to primary thyroid gland dysfunction, while fewer arise from secondary pituitary disease or rare tertiary hypothalamic defects. The result is inadequate secretion of thyroxine (T_4) and triiodothyronine (T_3), leading to multisystemic metabolic derangements.

5.1 Thyroid Hormone Production and Regulation
- The thyroid gland synthesizes T_4 (thyroxine) and T_3 (triiodothyronine) under the control of thyroid-stimulating hormone (TSH) released by the anterior pituitary (Ferguson, 1994) [6].
- The hypothalamus secretes thyrotropin-releasing hormone (TRH), stimulating TSH secretion.
- T_4 is the major circulating hormone, while T_3 (the active form) is mostly generated by peripheral deiodination of T_4 (Dixon, 2005) [3].
- Thyroid hormones act on virtually all tissues to regulate metabolism, protein synthesis, lipid turnover, thermogenesis, and growth.

5.2 Primary Hypothyroidism (≈95% of Cases)
5.2.1 Lymphocytic Thyroiditis
- An immune-mediated process where autoreactive lymphocytes infiltrate and progressively destroy thyroid follicles.

- Associated with thyroglobulin autoantibodies (TgAA), which serve as biomarkers of this disease (Graham *et al.*, 2002) [8].
- Early stages show compensatory hypertrophy and elevated TSH, while later stages result in complete gland atrophy and hypothyroidism.

5.2.2 Idiopathic Thyroid Atrophy
- Characterized by replacement of thyroid parenchyma with adipose and connective tissue (Mooney, 2011) [16].
- The exact cause is unclear but may represent an end-stage of autoimmune thyroiditis.

5.3 Secondary Hypothyroidism
- Results from pituitary TSH deficiency, often due to pituitary tumors, congenital hypopituitarism, or acquired pituitary dysfunction.
- Leads to thyroid gland inactivity despite structurally normal thyroid tissue (Peterson *et al.*, 1997) [20].

5.4 Tertiary Hypothyroidism (Rare)
- Caused by inadequate TRH secretion from the hypothalamus.
- Extremely uncommon in dogs, usually reported in experimental models (Dixon, 2005) [3].

5.5 Peripheral Hormone Metabolism and Resistance
- In some conditions, thyroid hormone synthesis may be normal, but peripheral metabolism of T_4 to T_3 is impaired, or tissue responsiveness is reduced.
- Euthyroid Sick Syndrome is an example, where systemic illness suppresses thyroid hormone activity at the tissue level without true hypothyroidism (Graham, 2007) [7].

5.6 Molecular and Genetic Basis
- Certain breeds (Dobermans, Golden Retrievers, Beagles) are predisposed to autoimmune thyroiditis, suggesting a genetic basis for immune dysregulation (Kennedy *et al.*, 2006) [10].
- Specific MHC class II alleles have been implicated in susceptibility.

5.7 Systemic Effects of Hypothyroidism
5.7.1 Metabolic
- Reduced basal metabolic rate leads to lethargy, obesity, cold intolerance, and exercise intolerance (Ferguson, 1994) [6].

5.7.2 Dermatological
- Decreased epidermal turnover and altered keratinization cause alopecia, seborrhea, and hyperpigmentation (Graham, 2007) [7].

5.7.3 Neuromuscular
- Hypothyroid myopathy and neuropathy result from altered neuromuscular transmission and accumulation of mucopolysaccharides in peripheral nerves (Scott-Moncrieff, 2015) [21].

5.7.4 Cardiovascular
- Thyroid hormones normally increase myocardial contractility and heart rate. Their deficiency leads to bradycardia, reduced stroke volume, and occasionally arrhythmias (Dixon, 2005) [3].

5.7.5 Reproductive
- Hypothyroidism alters gonadotropin secretion and steroid hormone metabolism, resulting in infertility, irregular cycles, and poor semen quality (Cecere, 2023) [1].

5.8 Summary of Pathophysiology
1. Autoimmune thyroiditis or idiopathic atrophy → follicular destruction.
2. Decreased T_4/T_3 production → impaired metabolism across multiple organ systems.
3. Pituitary or hypothalamic lesions (less common) → secondary/tertiary hypothyroidism.
4. Peripheral metabolic derangements → exacerbate systemic manifestations.

6. Laboratory Diagnosis and Advanced Diagnostic Techniques
Accurate diagnosis of canine hypothyroidism requires integration of clinical findings, routine laboratory data, and specific thyroid function tests. Misdiagnosis is common if reliance is placed on a single parameter such as total T_4. A stepwise diagnostic approach, including advanced techniques, improves specificity and reduces false positives due to non-thyroidal illness or drug interference.

6.1 Routine Hematology and Biochemistry
Although not diagnostic on their own, these tests provide supportive evidence and help rule out concurrent illness.

6.1.1 Hematological Findings
- Mild non-regenerative anemia (normocytic, normochromic) is observed in 30-40% of hypothyroid dogs (Dixon, 2005) [3].
- Leukogram is usually normal, but recurrent infections may lead to neutrophilia.

6.1.2 Serum Biochemistry
- **Hypercholesterolemia:** Found in ~75% of hypothyroid dogs due to decreased LDL receptor activity and reduced lipid metabolism (Peterson *et al.*, 1997) [20].
- **Hypertriglyceridemia:** Common but less consistent than hypercholesterolemia.
- Mild to moderate increases in liver enzymes (ALT, ALP) due to fatty liver infiltration.
- Creatine kinase (CK) elevation in cases with hypothyroid myopathy.

6.2 Basal Hormone Concentrations
6.2.1 Total T_4 (TT_4)
- Widely used as a screening test.
- Low TT_4 suggests hypothyroidism, but values can be decreased by
- Non-thyroidal illness (Euthyroid Sick Syndrome).
- Drugs such as glucocorticoids, sulfonamides, phenobarbital, and NSAIDs (Graham *et al.*, 2002) [8].
- High sensitivity but low specificity.

6.2.2 Free T_4 (fT_4)
- Represents the biologically active fraction of T_4.

- Measured by equilibrium dialysis (ED) → gold standard method for specificity.
- Less affected by systemic illness and drugs than TT_4 (Mooney, 2011) [16].

6.2.3 Total T_3 (TT_3) and Free T_3 (fT_3)
- Of limited diagnostic value in dogs, as serum T_3 concentrations fluctuate and may remain normal in hypothyroidism.

6.3 Endogenous Thyroid-Stimulating Hormone (TSH)
- In primary hypothyroidism: elevated TSH due to loss of negative feedback (Graham, 2007) [7].
- However, ~25% of hypothyroid dogs have normal TSH levels → limiting sensitivity (Peterson *et al.*, 1997) [20].
- Best used in combination with TT_4 and fT_4.

6.4 Dynamic and Confirmatory Tests
6.4.1 TSH Stimulation Test
- Historically the gold standard.
- **Procedure:** Measure baseline TT_4 → administer bovine TSH → remeasure TT_4 after 6 hours.
- Hypothyroid dogs fail to show an adequate increase in TT_4.
- **Limitation:** Unavailability of bovine TSH and cost of recombinant TSH.

6.4.2 TRH Stimulation Test
- Evaluates pituitary response. Rarely used in clinical practice due to side effects (vomiting, salivation) and limited availability.

6.5 Autoantibody Testing
6.5.1 Thyroglobulin Autoantibodies (TgAA)
- Marker of lymphocytic thyroiditis, useful in early or subclinical stages (Kennedy *et al.*, 2006) [10].
- Can be detected using ELISA-based assays.
- TgAA-positive dogs may be euthyroid initially but are at increased risk of progression to hypothyroidism.

6.5.2 Anti-T_3 and Anti-T_4 Antibodies
- May cause assay interference, leading to false elevation of TT_3 or TT_4.

6.6 Imaging Modalities
6.6.1 Thyroid Ultrasonography
- Hypothyroid thyroid glands appear small, hypoechoic, and heterogeneous (Dixon, 2005) [3].
- Useful for differentiating thyroiditis from neoplasia.

6.6.2 Scintigraphy
- Involves administration of radionuclides (e.g., technetium-99m pertechnetate).
- Provides information on thyroid size, function, and uptake patterns.
- Limited by cost and availability but highly sensitive.

6.7 Molecular and Genetic Markers
- Ongoing research into DLA (dog leukocyte antigen) class II gene associations with autoimmune thyroiditis (Kennedy *et al.*, 2006) [10].
- May help in identifying predisposed breeds and in early screening.

6.8 Stepwise Diagnostic Algorithm
1. Clinical suspicion based on history and clinical signs.
2. CBC and biochemistry for supportive findings.
3. TT_4 as a screening test.
4. If TT_4 is low → confirm with fT_4 by ED and TSH.
5. If results remain ambiguous → TSH stimulation test or thyroid imaging.
6. Consider autoantibody testing in suspected autoimmune cases.

7. Treatment and Management of Canine Hypothyroidism
The cornerstone of hypothyroidism therapy in dogs is lifelong thyroid hormone replacement, primarily with synthetic levothyroxine (L-thyroxine). Proper management requires careful dosing, monitoring, and adjustment tailored to individual patient response. In some cases, management of concurrent diseases and supportive therapy are also critical.

7.1 General Principles of Therapy
- Hypothyroidism is a lifelong condition, requiring continuous medication.
- Early diagnosis and treatment prevent secondary complications such as infertility, neuropathies, and chronic dermatopathies (Dixon, 2005) [3].
- Treatment is aimed at restoring normal serum thyroid hormone concentrations and alleviating clinical signs (Mooney, 2011) [16].

7.2 Levothyroxine (L-Thyroxine) Therapy
7.2.1 Drug of Choice
- Synthetic L-thyroxine (T_4) is the treatment of choice.
- T_4 is preferred over T_3 because it has a longer half-life, more stable absorption, and allows peripheral conversion to T_3 depending on tissue demand (Peterson *et al.*, 1997) [20].

7.2.2 Dosage
- **Initial recommended dose:** 0.02 mg/kg orally every 12 hours.
- Alternatively, 0.02-0.04 mg/kg once daily (total dose not exceeding 0.8 mg per dog).
- Twice-daily dosing is often recommended initially due to variable bioavailability, but many dogs can be stabilized on once-daily therapy (Dixon, 2005) [3].

7.2.3 Formulation and Administration
- Available as tablets (0.1-0.8 mg).
- Should ideally be administered consistently with or without food, as dietary factors can affect absorption.

7.2.4 Bioavailability
- Varies between 10-50% in dogs.
- Gastrointestinal disease, concurrent medications (e.g., sucralfate, calcium, iron supplements), and diet may reduce absorption (Graham, 2007) [7].

7.3 Monitoring Therapy
7.3.1 Clinical Response
- **Earliest improvement:** Increased activity and alertness within 1-2 weeks.

- **Dermatological improvement:** Hair regrowth and skin normalization within 2-3 months.
- **Weight normalization:** Gradual over 3-6 months.

7.3.2 Laboratory Monitoring
- Recheck serum TT_4 4-6 weeks after starting therapy.
- Sampling should be done
- **Peak level:** 4-6 hours post-pill.
- **Trough level:** Just before next dose.
- **Goal:** TT_4 in the upper half of reference range at trough and slightly above reference range at peak (Peterson *et al.*, 1997) [20].
- Adjust dose based on TT_4 levels and clinical signs.

7.4 Management of Refractory Cases
If dogs fail to respond despite adequate dosing, consider
1. Owner compliance issues (missed doses, incorrect administration).
2. Poor absorption (drug-diet interactions, gastrointestinal disease).
3. Concurrent illness (Euthyroid Sick Syndrome masking response).
4. Rare thyroxine resistance (Mooney, 2011) [16].

7.5 Adverse Effects of Therapy
Overdose (Iatrogenic Hyperthyroidism)
- **Signs:** Polyuria, polydipsia, polyphagia, weight loss, hyperactivity, panting, tachycardia.
- Confirmed by elevated TT_4.
- **Management:** Discontinue therapy for several days, restart at reduced dose.
- Long-term toxicity is rare if monitoring is adequate.

7.6 Special Considerations
7.6.1 Secondary Hypothyroidism
- Requires L-thyroxine supplementation, but pituitary disease (e.g., tumors) may necessitate additional therapy.

7.6.2 Dogs with Cardiac Disease
- Start with lower initial doses to avoid precipitating tachyarrhythmias or worsening heart failure.

7.6.3 Breeding Dogs
- Reproductive dysfunction improves with treatment. However, monitoring is crucial to restore fertility and avoid iatrogenic complications (Cecere, 2023) [1].

7.7 Adjunctive and Supportive Therapy
- **Management of concurrent infections:** Skin and ear infections should be treated with antimicrobials alongside thyroid supplementation.
- **Nutritional support:** Weight management and balanced diets aid in recovery.
- **Neurological rehabilitation:** Physiotherapy may be useful in cases with hypothyroid neuropathy.

7.8 Prognosis
- Prognosis is excellent with proper treatment.
- Most clinical signs resolve within 4-12 weeks, though dermatological changes may take longer.
- Dogs require lifelong therapy and periodic monitoring to maintain euthyroid status.

8. Complications and Associated Conditions in Canine Hypothyroidism
Hypothyroidism in dogs, if left untreated or inadequately managed, can result in a wide range of systemic complications. Since thyroid hormones are essential regulators of metabolism, growth, and organ function, their deficiency impacts nearly every physiological system. Furthermore, hypothyroidism may predispose dogs to other comorbidities, complicating the clinical picture and management.

8.1 Dermatological Complications
8.1.1 Chronic Pyoderma and Otitis
- Dogs with hypothyroidism have reduced skin immunity, predisposing them to recurrent bacterial skin infections and otitis externa (Panciera, 1994) [19].
- Secondary Malassezia dermatitis may also occur due to altered lipid metabolism.

8.1.2 Myxoedema
- Accumulation of mucopolysaccharides in dermis results in characteristic facial puffiness and "tragic expression."
- Severe generalized *myxoedema* can progress to *myxoedema* coma, a rare but life-threatening complication (Kooistra, 2006) [13].

8.2 Reproductive and Fertility Issues
8.2.1 Female Dogs
- Infertility, silent heats, prolonged inter-estrous intervals, and pseudopregnancy may be observed (Cecere, 2023) [1].

8.2.2 Male Dogs
- Testicular atrophy, reduced libido, and decreased sperm quality are linked with chronic hypothyroidism.

8.3 Neurological Complications
8.3.1 Peripheral Neuropathy
- Hypothyroidism can cause polyneuropathy with signs like weakness, ataxia, hyporeflexia, and cranial nerve deficits (Dixon, 2005) [3].

8.3.2 Vestibular Dysfunction
- Some hypothyroid dogs exhibit head tilt, facial paralysis, and ataxia due to central or peripheral vestibular involvement (Tagawa *et al.*, 2015) [22].

8.3.3 Coma (*Myxoedema* Coma)
- Rare end-stage complication characterized by profound lethargy, hypothermia, bradycardia, and coma.
- Requires emergency IV thyroxine and supportive therapy.

8.4 Cardiovascular Complications
8.4.1 Bradycardia and Low Cardiac Output
- Reduced myocardial contractility and low voltage ECG are common findings (Lefebvre *et al.*, 2006) [14].

8.4.2 Atherosclerosis and Hyperlipidaemia
- Hypothyroid dogs exhibit marked hypercholesterolemia and triglyceridemic, predisposing them to atherosclerosis a rare but significant complication compared to humans.

8.4.3 Arrhythmias
- Conduction abnormalities (sinus bradycardia, AV block) may occur.

8.5 Ocular Manifestations
- Corneal lipid deposits and keratoconjunctivitis sicca (dry eye) have been documented in hypothyroid dogs (Kooistra, 2006) [13].
- Rarely, retinal changes may be observed due to altered metabolism.

8.6 Musculoskeletal and Metabolic Complications
8.6.1 Obesity and Reduced Exercise Tolerance
- A hallmark complication due to reduced basal metabolic rate.

8.6.2 Myopathy
- Stiff gait, exercise intolerance, and muscle weakness result from thyroid hormone deficiency at the muscle level.

8.6.3 Cold Intolerance
- Hypothyroid dogs have reduced thermogenesis and shiver easily in cool environments.

8.7 Hematological Complications
- Non-regenerative, normocytic, normochromic anemia is a frequent finding (Panciera, 1994) [19].
- Occasionally, mild coagulopathy due to altered platelet function may be observed.

8.8 Metabolic and Endocrine Associations
Hypothyroidism may coexist with
- Diabetes mellitus (worsens insulin resistance).
- Cushing's syndrome (overlap in clinical signs complicates diagnosis).
- Obesity-related disorders (arthropathies, insulin resistance, pancreatitis).

8.9 Iatrogenic Complications
- Over-supplementation with levothyroxine can result in iatrogenic hyperthyroidism, mimicking primary hyperthyroidism.
- Long-term complications include cardiac stress and renal strain.

8.10 Prognostic Implications of Complications
- While most complications resolve with appropriate therapy, chronic cases may experience permanent neuropathy, infertility, or dermatological scarring.
- Prognosis worsens significantly in untreated *myxoedema* coma or dogs with concurrent systemic diseases.

9. Diagnosis and Differential Diagnosis of Canine Hypothyroidism
Diagnosis of hypothyroidism in dogs remains a clinical challenge due to the nonspecific nature of clinical signs and the overlap with other endocrine and systemic diseases. A definitive diagnosis requires a combination of history, clinical findings, laboratory testing, and exclusion of other disorders. Misdiagnosis can result in unnecessary lifelong treatment or overlooked comorbidities.

9.1 Clinical Suspicion
- **History:** Lethargy, weight gain, dermatological problems, reproductive disturbances.
- **Physical exam findings:** Bradycardia, alopecia, myxoedema, hypothermia.
- Clinical signs alone are insufficient due to overlap with aging, obesity, or other metabolic disorders (Panciera, 1994) [19].

9.2 Hematological and Biochemical Findings
9.2.1 Hematology
- Non-regenerative, normocytic, normochromic anemia is present in up to 30-40% of cases (Dixon, 2005) [3].

9.2.2 Biochemistry
- Hypercholesterolemia (>7.8 mmol/L) and hypertriglyceridemia are hallmark findings (Mooney, 2011) [16].
- Mild increases in liver enzymes (ALT, ALP) are sometimes observed.

9.3 Basal Thyroid Hormone Testing
9.3.1 Total T_4 (TT_4)
- Widely available and inexpensive.
- Low TT_4 supports hypothyroidism, but many non-thyroidal illnesses can also suppress TT_4 (Euthyroid Sick Syndrome).
- High specificity but low sensitivity.

9.3.2 Free T_4 (fT_4, Equilibrium Dialysis)
- More accurate than TT_4.
- Less affected by non-thyroidal illness and drugs.
- Preferred test when TT_4 is low but clinical suspicion is uncertain (Dixon, 2005) [3].

9.4 Thyroid-Stimulating Hormone (TSH) Testing
- Endogenous canine TSH is elevated in ~75% of hypothyroid dogs.
- When combined with TT_4 or fT_4, the diagnostic accuracy increases significantly (Peterson *et al.*, 1997) [20].
- A dog with low TT_4 and high TSH is strongly suggestive of primary hypothyroidism.

9.5 Dynamic Thyroid Function Tests
9.5.1 TSH Stimulation Test
- Gold standard in the past.
- Recombinant human TSH is used; TT_4 is measured before and 6 hours after injection.
- Hypothyroid dogs show little or no increase in TT_4.
- Expensive and limited by availability of TSH.

9.5.2 TRH Stimulation Test
- Rarely used in practice due to limited diagnostic utility and side effects (vomiting, salivation).

9.6 Imaging Techniques

- **Thyroid ultrasound:** Can identify atrophy, heterogeneity, or neoplastic changes (Tagawa *et al.*, 2015) [22].
- **Scintigraphy (Radionuclide Imaging):** Helps assess thyroid uptake and differentiate hypothyroidism from euthyroid sick syndrome, but limited by cost and availability.

9.7 Differential Diagnosis

Because many conditions mimic hypothyroidism, careful exclusion is essential

9.7.1 Endocrine Disorders

- **Hyperadrenocorticism (Cushing's disease):** Shares signs like alopecia, lethargy, and obesity.
- **Diabetes mellitus:** May present with lethargy and weight changes but usually with PU/PD and hyperglycemia.

9.7.2 Non-Thyroidal Illness (Euthyroid Sick Syndrome)

- Chronic systemic diseases (renal failure, hepatic disease, neoplasia, infections) lower TT_4 without true hypothyroidism (Graham, 2007) [7].

9.7.3 Dermatological Disorders

- Atopic dermatitis, demodicosis, seborrhea, and other endocrinopathies can mimic skin changes of hypothyroidism.

9.7.4 Obesity and Aging

- Many geriatric dogs show reduced activity and weight gain, mimicking hypothyroid signs.

9.8 Diagnostic Algorithm

1. Clinical suspicion based on history and examination.
2. **Baseline TT_4:** If low → proceed to confirmatory tests.
3. **Free T_4 and TSH:** Combination provides higher diagnostic confidence.
4. **Dynamic testing or imaging:** If diagnosis remains uncertain.
5. **Trial therapy:** Only after strong suspicion and supportive laboratory data; not as a substitute for diagnosis.

9.9 Diagnostic Challenges

- No single test is 100% definitive.
- Interpretation must consider age, breed, concurrent medications (glucocorticoids, phenobarbital, Sulfonamides), and comorbidities.
- Greyhounds and sighthounds have naturally lower TT_4 values, leading to misdiagnosis if breed differences are ignored (Mooney, 2011) [16].

10. Prognosis, Prevention, and Future Perspectives in Canine Hypothyroidism

Hypothyroidism in dogs is a chronic, lifelong endocrine disorder that significantly affects quality of life if untreated. With accurate diagnosis and appropriate management, however, most affected dogs live a normal life span. This section discusses the long-term outlook, preventive measures, and advances in research shaping the future of canine hypothyroidism care.

10.1 Prognosis

10.1.1 General Prognosis

- Prognosis is excellent for dogs with primary hypothyroidism when treated with levothyroxine (Dixon, 2005) [3].
- Clinical signs such as lethargy, weight gain, and alopecia usually resolve within weeks to months.
- Dermatological recovery (hair regrowth, resolution of seborrhea) may take 2-6 months.

10.1.2 Prognostic Factors

- Dogs diagnosed early have a better recovery with fewer irreversible complications.
- Chronic untreated hypothyroidism may leave residual neuropathy, infertility, or dermatological scarring (Kooistra, 2006) [13].
- Severe complications such as *myxoedema* coma carry a guarded prognosis despite treatment.

10.1.3 Quality of Life

- Most dogs regain activity levels, normal weight, and skin condition with proper management.
- Regular monitoring ensures that iatrogenic hyperthyroidism and poor treatment response are avoided.

10.2 Prevention

Although hypothyroidism cannot always be prevented, certain strategies can reduce disease risk or improve early detection:

10.2.1 Genetic Screening

- Since autoimmune thyroiditis has a hereditary component, genetic screening programs in predisposed breeds (e.g., Golden Retrievers, Doberman Pinschers, Beagles) are crucial (Kennedy *et al.*, 2006) [10].
- Breeding dogs should undergo thyroid panel testing before being included in breeding programs.

10.2.2 Early Screening in At-Risk Dogs

- Annual screening of thyroid function in predisposed breeds or middle-aged dogs aids in early detection.

10.2.3 Avoidance of Iatrogenic Causes

- Careful management of dogs receiving radioiodine therapy, surgery for thyroid neoplasia, or prolonged sulfonamide therapy can prevent secondary hypothyroidism.

10.3 Long-Term Management Strategies

10.3.1 Lifelong Therapy

- Owners should be counselled on the lifelong commitment to levothyroxine therapy.
- Consistent administration and monitoring are key to long-term success.

10.3.2 Monitoring Protocol

- **Initial rechecks:** Every 4-6 weeks until stable.
- Long-term follow-ups: Every 6-12 months to monitor thyroid levels and adjust dose if necessary (Mooney, 2011) [16].

10.3.3 Owner Education

- Owners must be educated on drug administration, recognizing relapse or overdose, and importance of routine monitoring.

10.4 Future Perspectives

10.4.1 Advances in Diagnostic Techniques

- Development of more specific biomarkers (thyroglobulin autoantibodies, molecular markers) to distinguish hypothyroidism from euthyroid sick syndrome (Graham, 2007) [7].
- High-resolution ultrasonography and PET-CT imaging offer promise for early thyroid pathology detection.

10.4.2 Personalized Medicine

- Advances in pharmacogenomics may allow tailoring levothyroxine doses to individual metabolic profiles.
- Breed-specific reference ranges for thyroid hormones are under investigation to minimize misdiagnosis in sighthounds and other breeds.

10.4.3 Gene Therapy and Immunotherapy

- Experimental studies are evaluating gene replacement therapy for autoimmune thyroiditis.
- Immunomodulatory strategies may slow progression in subclinical autoimmune thyroiditis before onset of clinical disease (Kennedy *et al.*, 2006) [10].

10.4.4 Nutritional Research

- Nutraceuticals, omega-3 fatty acids, and antioxidants are being studied for their role in modulating autoimmune thyroiditis and improving metabolic recovery.

10.5 Summary of Prognosis and Future Outlook

- With proper therapy, hypothyroid dogs live normal, healthy lives.
- Early detection and genetic control programs hold promise in reducing disease incidence.
- Emerging diagnostic methods and therapies may revolutionize the way hypothyroidism is diagnosed and managed in the coming decades.

Conflict of interest

The authors declare no conflicts of interest related to this work.

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