

Canine Hypothyroidism: A Review and Recent Advances in Management

S. Yogeshpriya, M. Sivakumar and P. Selvaraj

Department of Veterinary Medicine¹, Teaching Veterinary Clinical Complex,
Veterinary College and Research Institute, Orathanadu – 614625, Tamilnadu, India

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Background

In dogs, hypothyroidism is usually primary, i.e., due to atrophy of the thyroid gland. In the majority of cases, this atrophy is associated with acquired autoimmune lymphocytic thyroiditis, similar to Hashimoto's thyroiditis in humans, as both are characterized by cellular lymphocytic, as well as humoral autoantibodies against thyroglobulin, T4 and T3 in the thyroid gland (Miller, 2015). The remainders of canine hypothyroid causes are non-inflammatory or of unknown etiology; congenital hypothyroidism is rare (Mooney, 2011).

Hypothyroidism is most often diagnosed in middle-aged dogs (approximately 7-8 years old) and is more likely in pure breeds. Graham et al. (2007) revealed that, there was no gender predisposition; however Golden Retrievers, Doberman Pinschers, Labradors and Cocker Spaniels are predisposed.

Clinical Signs

Miller et al (2015) suggested that the thyroxine is needed for normal cellular metabolic functions in all cells of the body, thus a deficiency in thyroxine affects almost all body systems. Clinical signs are therefore very varied and depend on the

disease stage and may also differ between breeds. He *et al.* (2011) observed that the most of the dogs with hypothyroidism have reduced activity and mental states, resulting in exercise intolerance and lethargy. Weight gain is seen in 48 per cent of cases as a result of up to a 15 per cent reduction in calorie expenditure. Their reduced metabolism makes hypothyroid dogs intolerant of cold temperatures (Mooney and Shiel, 2012). The vast majority of dogs with hypothyroidism have dermatological signs (>80 per cent of cases) that vary depending on the duration and the severity of the disease. Thyroid hormones are needed to initiate the anagen phase of hair growth, so their absence leads to persistence of telogen and, as a result, hairs are easy to epilate. Alopecia usually starts over areas of friction, such as the tail (resulting in the classic "rat tail" appearance) and neck, and progresses over time to bilaterally symmetrical truncal alopecia. This usually spares the head and limbs, and is usually non-pruritic. Dorsal nasal alopecia is seen in some breeds, especially Retrievers (Graham *et al.*, 2007).

Hyperpigmentation and comedones, with seborrhoea or dry, scaly skin, is commonly seen. Bacterial or *Malassezia* dermatitis is also common.

Mooney and Shiel (2012) stated that the breed-related differences are also noted, with Arctic breeds usually losing the primary hairs, leaving a coarse woolly appearance to the remaining hair. Increased hair coat (hypertrichosis) is sometimes seen in Boxers and Irish Setters. Delayed or poor wound healing is often reported.

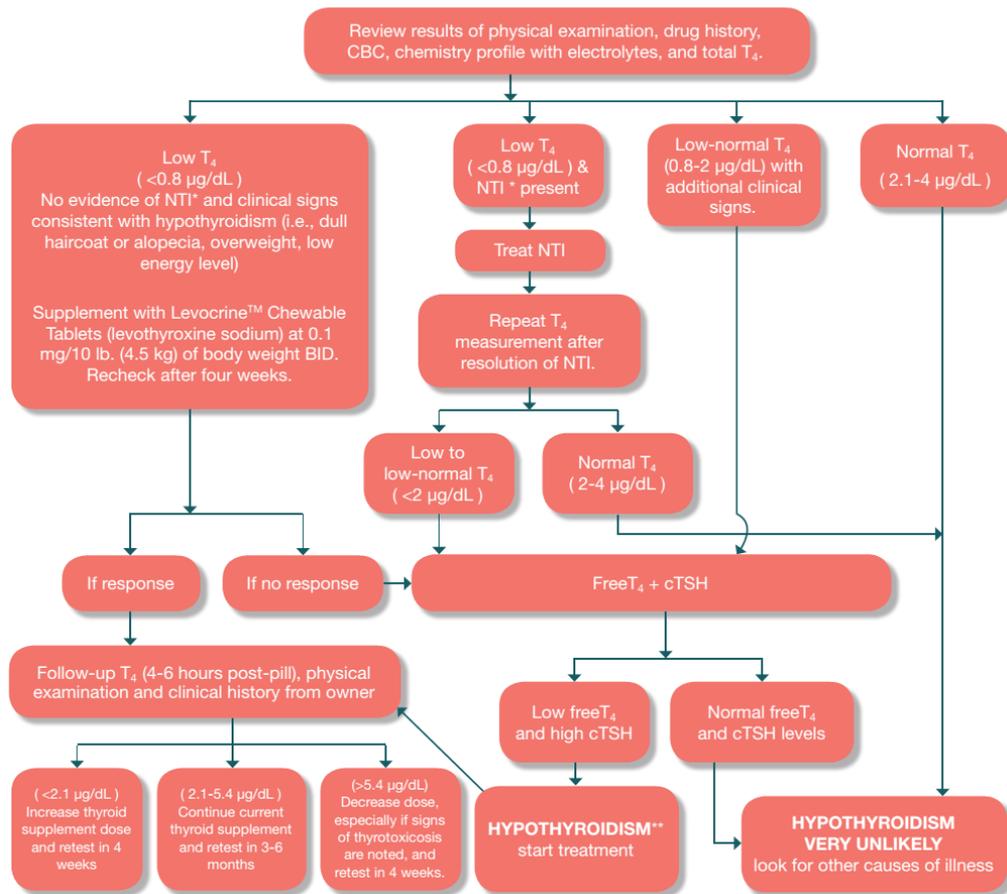
Neurological signs are commonly seen in association with hypothyroidism, through a variety of mechanisms; these include mucopolysaccharide accumulation around nerves, hyperlipidaemia and central atherosclerosis (He *et al.*, 2011). Generalised muscle weakness is common, leading to weakness, exercise intolerance and reduced reflexes. Abnormal

electromyogram (EMG) changes are seen but clinical signs usually improve within three months of treatment. Peripheral vestibular syndrome and facial paralysis are rare complications of hypothyroidism. The relationship between laryngeal paralysis and hypothyroidism is controversial, however treatment generally does not improve laryngeal function. As of yet no causal relationship has been proven (Diaz *et al.*, 2007).

The clinical signs of canine hypothyroidism typically develop gradually, affect a number of different organ systems, and range from mild to severe. Clinical signs are summarized below by body system.

General Appearance / Behavior	Skin / Hair	Cardiovascular System	Eyes
• <i>Weight gain</i>	• <i>Excessive scale and dry hair coat</i>	• <i>Slow heartbeat</i>	• <i>Corneal lipid deposits</i>
• <i>Lethargy, dullness</i>	• <i>Excessive shedding</i>	• <i>Weak pulses</i>	• <i>Chronic uveitis</i>
• <i>Cold intolerance, heat-seeking</i>	• <i>Hair loss, usually symmetrical</i>	• <i>Arrhythmias (rare)</i>	
• <i>Exercise intolerance</i>	• <i>Increased pigmentation of the skin</i>	Nervous System / Muscle	Reproductive System
	• <i>Recurrent skin/ear infections</i>	Peripheral neuropathy	Anestrous, infertility,
	• <i>Thickening of the skin</i>	Megaesophagus (rare)	And abortion

Diagnostic and monitoring algorithm of canine hypothyroidism



Advantages and disadvantages of the most commonly used tests to evaluate thyroid function in dogs

Test	Advantages	Disadvantages
TT4	Easy	Decreased with SNTD (Systemic non-thyroid disease)
	Not expensive	Decreased after administration of certain drugs
	Readily available	A decreased T4 alone does not allow a reliable diagnosis of hypothyroidism (low specificity)
	Normal values allow 'exclusion' of hypothyroidism TSH	
TSH	Easy	1/4 of hypothyroid dogs have TSH values within the reference range (low sensitivity)
	Not expensive	Always use in combination with T4
	Available	
FT4	Is less influenced by SNTD or through drug administration than TT4	The only reliable method includes equilibrium dialysis
		Not readily available in all countries

Therapeutics

Drugs

Levothyroxine is the only hormone that appears necessary for treatment of hypothyroidism (Jonklass and Talbert, 2014). The frequency of levothyroxine dosing is controversial, and the only study to closely evaluate the response to treatment showed that once daily treatment is adequate. However, in clinical practice some dogs seem to respond better to twice-daily treatment. The initial starting dose is 0.02 mg/kg PO q 24 h. In general you will never have to exceed 0.8 mg as an initial daily dosage even in very large dogs. If the dog has significant cardiovascular disease, diabetes mellitus, or hypoadrenocorticism, treatment should be instituted at 25% of the standard dose, with the dosage increased by 25% every 2 weeks based on clinical response and post-pill testing. Most dogs show improvement within the first 1-2 weeks, with increased activity, improved attitude, and partial or complete resolution of neurologic signs.

The cutaneous manifestations of hypothyroidism may take several weeks to months to resolve. Post treatment monitoring may be carried out but clinical response is the most important monitoring tool. Peak T4 concentrations generally occur 4-6 hours after administration of levothyroxine and should be in the high normal to slightly above normal range (40-70 nmol/L). However, the bioavailability of thyroxine ranges from 13 to 87% in the same dog from day to day bringing into the question the utility of random post pill monitoring of TT4. It is likely more meaningful (though more expensive) to

measure TSH (especially if the TSH concentration was elevated pre-treatment) or fT4 concentrations after replacement therapy has been started, especially in animals that show a poor clinical response to therapy. Serum TSH concentrations should be in the normal range or undetectable and fT4 concentrations should be in the normal range (Diaz et al.,2007). Serum concentrations of TSH and fT4 should not be performed until the patient has been on supplementation for at least 2 weeks. If the patient was initially started on twice daily therapy, treatment can be reduced to once daily treatment when a good clinical response has been obtained. Hyperthyroidism is the most common complication of treatment with levothyroxine, but it is rare in dogs. Clinical signs are similar to those of hyperthyroidism in cats and the diagnosis is confirmed by documenting a substantial elevation of serum T4. Treatment consists of stopping levothyroxine treatment for 2-3 days, then instituting treatment at a lower dose.

Expected course and prognosis

Response to therapy should be observed in the first 4- 8 weeks post treatment. Improvements in mentation and physical activity may be noted within the first week though some abnormalities, especially dermatologic signs, may take several months to resolve. An absent or incomplete response to therapy may be due to an incorrect diagnosis, poor owner compliance, inadequate dosing, or poor absorption.

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