



Canine Euthyroid Sick Syndrome (CESS): a Clinical Overview

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Abstract:

Canine Euthyroid Sick Syndrome (CESS), also known as Low T3 Syndrome or Non-Thyroidal Illness Syndrome (NTIS), occurs due to extra-thyroidal pathway disturbances that cause a decrease in Thyroid Stimulating Hormone (TSH), thyroid hormones, and their tissue concentrations, along with an increase in reverse Triiodothyronine (rT3 - an inactive metabolite). These changes result from alterations in the Hypothalamic-Pituitary-Thyroid (HPT) axis and thyroid hormone metabolism. Rather than being considered a disease, this syndrome can be regarded as a coping mechanism by the body to reduce catabolism and metabolic rate through decreased circulating thyroid hormone concentrations. It is commonly observed in extra-thyroidal pathologies such as organ insufficiency or dysfunction (heart, kidney, liver, pancreas), tumours, chronic infections and inflammation, drug administration (phenobarbital, corticosteroids), hormonal imbalances, metabolic disorders such as diabetes mellitus, as well as during severe stress and starvation. Regardless of the cause, there is decreased peripheral conversion of thyroxine (T4) to triiodothyronine (T3) and reduced degradation of inactive rT3.

Cytokines, glucocorticoids, and more recently, leptin (a 16-kDa protein) are recognized as important mediators in the pathogenesis of NTIS (S.M. Reed *et al.*, 2004). In human endocrinology, euthyroid sick syndrome is believed to arise from the influence of pro-inflammatory cytokines, including interleukin-1, interleukin-6, tumour necrosis factor-alpha, and interferon-beta, which interfere with hypothalamic-pituitary regulation. These

mediators suppress the release of TSH and TRH, and inhibit the synthesis of thyroglobulin (TG), triiodothyronine (T3), and thyroid-binding globulin (TBG) (Ganesan K *et al.*, 2025). When the serum thyroid profile of affected dogs is evaluated, it typically shows decreased T3, while thyroxine (T4) levels may vary being low, normal, or occasionally high. TSH levels are usually within normal limits or only mildly decreased, contrasting with primary hypothyroidism, in

which TSH is markedly elevated. This condition is well established and reported in dogs, followed by cats, though horses may also be affected. Since canine hypothyroidism is one of the most over diagnosed metabolic disorders in dogs, understanding and ruling out CESS is crucial. CESS does not require levothyroxine therapy, as there will be no clinical improvement unless the animal is concurrently suffering from true hypothyroidism. Instead, treatment focuses on identifying and resolving the underlying cause of the decreased serum hormone levels.

The TSH stimulation test is considered the gold standard for diagnosing canine hypothyroidism; however, its clinical use is limited due to cost and availability. It can, however, help in differentiating CESS, as post-

exogenous TSH administration, there is a mild increase in thyroxine (T4), which is not observed in true hypothyroidism. Because of the physiological reduction in hormone conversion, the clinical signs may mimic hypothyroidism, leading to potential misdiagnosis. With normal thyroid gland function, thyroid ultrasonography can assist in assessing gland size, echogenicity, and volume. A thorough health evaluation, including detailed illness history, past and current medications, thyroid profile, thyroglobulin antibody testing, and serum cholesterol estimation can provide valuable insights for clinicians in approaching diagnosis and treatment. The prognosis of this condition depends on the root cause of illness, timely intervention, and early diagnosis.

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