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Medicine

Diagnosis of Hypothyroidism in Dogs

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Although hypothyroidism is a relatively frequent hormonal disease in the dog, its diagnosis can pose a real challenge to the veterinarian. The factors affecting the difficulty of the diagnosis are the diversity of the clinical signs and the limitations of the diagnostic tests (especially in patients with other concurrent diseases or on treatment with other drugs).

The diagnosis of hypothyroidism should not be based only on the results of the tests of the thyroid panel but on the interpretation of the combination of the clinical examination and the results of the tests for thyroid function.

Clinical diagnosis

Hypothyroidism generally affects medium to large size dogs. The majority of hypothyroid dogs are middle-aged (4 – 10 years) and there is no sex predilection.

The thyroid hormones affect most of the tissues, therefore their deficiency will lead to multisystemic signs. The classic clinical symptoms are lethargy, weakness, exercise intolerance and weight gain. Some of these dogs tend to look for warm places. The severity of the symptoms is variable and some patients remain practically asymptomatic.



Image 1. Mixed-breed bitch of 7 years of age with apathy, lethargy, weight gain, ventral hyperpigmentation and alopecia in the tail.

The majority of hypothyroid dogs will have some dermatological clinical sign: dry and dull coat, seborrhea, trunk alopecia, "rat's tail", comedones, hyperpigmentation and pyoderma. They can suffer from myxoedema due to the accumulation of glycosaminoglycane in the dermis which gives causes a tragic facial expression in some hypothyroid dogs.

It is convenient that the clinician is familiar also with the less frequent signs of the disease. Amongst those are galactorrhea, which occurs as a consequence of the increased production of prolactin due to the stimulation of the hypothalamic-hypophysis axis in response to a deficiency of T4. Also less frequent are the clinical signs similar to acromegaly such as increase mandibule size and increased interdental space, due to an increase secretion of growth hormone (GH) also as a consequence of the alteration of the hypothalamic-hypophysis axis. Finally, we will also have to consider that some hypothyroid dogs can develop neurological signs such as peripheral vestibular syndrome, convulsions, lower motor neuron disease or laryngeal paralysis.

The haemogram, biochemistry and urinalysis will be helpful to support a clinical suspicion of hypothyroidism and will be necessary to rule out other concurrent diseases which can affect the results of thyroid tests. These tests should also be carried out before the hormonal tests for thyroid function. One third of hypothyroid dogs present mild, non-regenerative, normocytic, normochromic anaemia. In serum biochemistry, we can frequently find hypercholesteraemia and hypertriglyceridaemia, although we can also observe occasionally high levels of CK, LDH, AST, ALT and alkaline phosphatase.

Tests for Thyroid Function

There is a wide range of thyroid tests but none of them offer a 100% efficacy, which is why it is advisable to carry out more than one test.

Total thyroxine (T4). The plasma concentration of basal T4 is the addition of the fraction of hormone bound to proteins and the free circulating hormone in blood (0.1%). T4 test has a high sensitivity as approximately 90% of the hypothyroid dogs will show lower T4 concentrations than euthyroid dogs. It is unlikely for a hypothyroid dog to have T4 values in the middle of normal range, however some hypothyroid dogs will have low to normal T4 levels. There are various mechanisms that could explain normal T4 levels in hypothyroid dogs. One of them is the fluctuation of T4 plasma levels and another is the interference of antiT4 antibodies in the measurement of T4, leading to artificially high results of T4 (within normal range or above normal range).

The main limitation of T4 is its low specificity since 30% of ill dogs will automatically have low T4 concentrations, which is known as Sick Euthyroid Syndrome. The more severe the disease, the more likely it will be for a euthyroid dog to present low levels of T4 (60% of the dogs affected by non-thyroidal illnesses will have T4 levels below normal range). We should consider this on clinical practice and postpone the thyroid tests on animals with other diseases in order to avoid false positive cases of hypothyroidism. On the other hand, a large group of drugs can also decrease the T4 concentrations in euthyroid dogs: glucocorticoids, sulphonamides, anticonvulsant drugs and non-steroidal antiinflammatories.

Some breeds like the greyhound will frequently have concentrations of T4 below the canine reference range, which is why it has to be cautiously interpreted in this type of breeds.

There are various methods for the measurement of the concentration of T4 in the dog (RIA, chemoluminescence and ELISA) and all of them are reliable, although the reference ranges can vary significantly between different methods.

However, if there is a strong suspicion of hypothyroidism and our aim is to confirm the diagnosis of hypothyroidism, it is convenient to measure also other hormones (TSH) to minimise the risk of a false positive result.

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Total triiodothyronine (T3). The serum concentration of T3 remains normal in many hypothyroid dogs, which is why it is not usually recommended to test this hormone for the diagnosis of canine hypothyroidism.

TS stimulation test. This test has been considered the test of choice for the diagnosis of canine hypothyroidism for years. However, its limited availability, cost and potential anaphylactic reactions have made its use very limited nowadays.

Free thyroxine (FT4). The concentration of FT4 reflects the amount of T4 circulating freely (not bound to proteins) and available to enter the cells. There are three methods to measure the levels of free T4: equilibrium dialysis, RIA and chemolumuniscence. Equilibrium dialysis is the reference treatment for the determination of FT4.

The sensibility of FT4 to detect hypothyroidism is high (98%) and particularly effective in hypothyroid dogs with anti-T4 antibodies, as the antibodies will not affect the measurement of FT4 by equilibrium dialysis.

The concentration of FT4 will decrease in concurrent diseases in a lesser degree to the concentration of T4. Even so, 20% of euthyroid sick dogs will present low FT4 concentrations.

Endogenous TSH. The majority (>95%) of hypothyroid dogs will suffer from primary hypothyroidism (of thyroid origin), whereas in less than 5% of the cases the origin will be secondary (hypophysial) or tertiary (hypothalamic). Due to the fact that the large majority have primary origin, we could expect that the large majority of hypothyroid dogs will have a high TSH level. However, the concentration of TSH remains normal in 20-40% of the cases of hypothyroidism in dogs (Image 2). It is likely that all dogs suffering from primary hypothyroidism will have a high TSH concentration initially and with time, the hypophysis loses the ability to respond to a low T4 concentration and therefore the concentraion of TSH stabilises. Due to a low sensitivity (60-80%) of TSH, a normal value of TSH in a dog presenting clinical signs compatible with hypothyroidism will not rule out the disease.

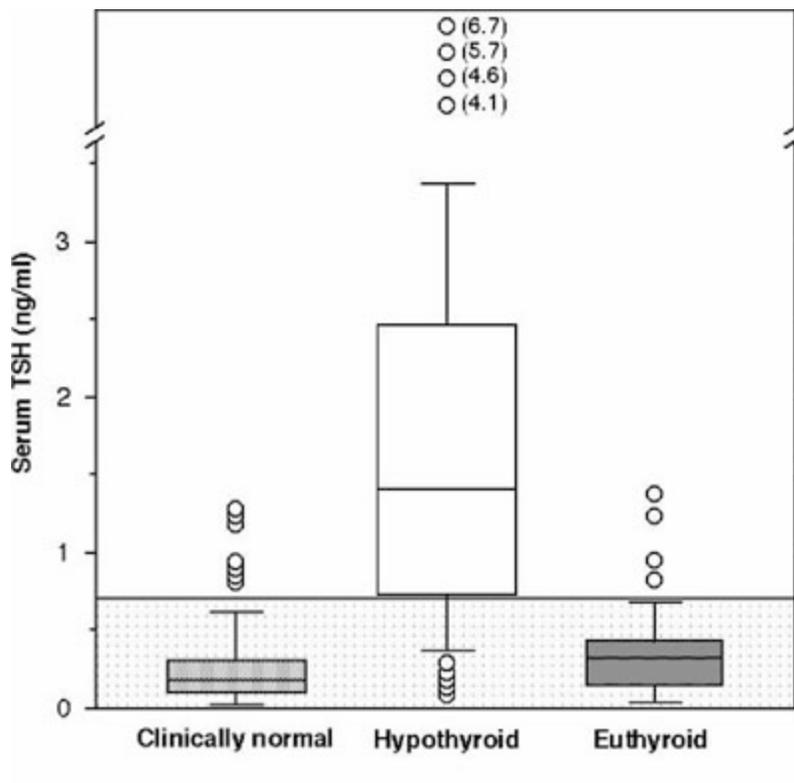


Imagen 2. concentration of TSH in healthy, hypothyroid and euthyroid animals. Although the sensitivity of TSH for the diagnosis of hypothyroidism is around 70%, it is still a useful test because it provides specificity, minimizing false positive results. (Peterson ME, Melián C and Nichols CE. Measurement of serum total thyroxine, triiodothyroxine, free thyroxine, and thyrotropin concentrations for diagnosis of hypothyroidism in dogs. J. Am. Vet. Med. Assoc. 1997; 211: 1396-1402)

On the other side, the majority (90%) of euthyroid sick dogs will have normal TSH concentrations and this is of great value to improve the specificity of the tests of thyroid function in the dog. A low T4 with high concentration of TSH confirms the diagnosis of hypothyroidism, whereas the probability of finding this combination in euthyroid sick dogs is less than 2%.

Antithyroid Antibodies. Approximately half to the dogs suffering from hypothyroidism undergo idiopathic thyroid atrophy, whereas the other half will present immune-mediated thyroiditis. The presence of antithyroid antibodies in a hypothyroid dog will suggest that the aetiology of hypothyroidism in that patient is lymphocytic thyroiditis. It is a hereditary disease, which is why breeding from these animals is not recommended. However, the clinical management for both types of canine hypothyroidism (thyroiditis and idiopathic atrophy) is the same.

The clinical purpose of a high concentration of antithyroid antibodies (antithyroidglobulin: TGAA, antiT4: T4AA or antiT3: T3AA) for the diagnosis of hypothyroidism is uncertain. These antibodies indicate thyroiditis but not all dogs with thyroiditis are hypothyroid and not all progress towards hypothyroidism, although they will be predisposed. After monitoring for a year those euthyroid dogs with high levels of antithyroid antibodies, we find that approximately 20% of these cases develop hypothyroidism, 60% will remain euthyroid and TGAA positive and 20% remain euthyroid and TGAA negative.

Diagnostic Imaging

Thyroid Echography. It has been recently proved that the echographic evaluation of the thyroid gland can be useful to differentiate between hypothyroid and euthyroid dogs (both healthy and ill). Euthyroid

dogs present a homogeneous thyroid parenchima which appears isoechoic or hyperechoic with respect to the surrounding tissue. However, hypothyroid dogs present more heterogeneous and hypoechoic parenchima, with a significantly smaller size and a more irregular thyroid capsule. The thyroid volume will continue to decrease during the treatment with levothyroxine

Thyroid Gammagraphy. The use of nuclear medicine (particularly per technetium-99m or ^{99m}Tc O₄) behaves in a similar way to iodine and will accumulate selectively in thyroid and salivary glands. It has been used during decades in human medicine for the detection of hyperfunctional thyroid nodules. Its use has been recently reported for the diagnosis of canine hypothyroidism, resulting specially useful to differentiate between hypothyroid and euthyroid sick animals. Its main disadvantage is its limited availability.

Response to Treatment with Levothyroxine.

The response to treatment has been suggested as a valid diagnostic method in dogs where hypothyroidism is suspected, although is only recommended when the results of the thyroid tests do not confirm diagnosis. The cost of the diagnostic tests can be an obstacle to the owner but the cost is still inferior to a life-long thyroid therapy and we will then avoid giving life-long treatment to animals which are actually not hypothyroid. Another inconvenient of the treatment as a diagnostic test is that it will cause long-term suppression of the secretion of endogenous TSH, which can affect the results of the thyroid tests. Therefore, the confirmation of the diagnosis after thyroid supplementation can quite difficult and we should wait between 6 and 8 weeks after the ceasing the treatment.

Even so, if we need to use the response to treatment as a diagnostic tool, we will do it defining clearly the criteria to follow to assess the response to treatment. The response should be complete after a period of 2-3 months, resolving all the clinical signs initially present (apathy, lethargy, obesity, alopecia, anaemia and hypercholesterolemia). This is important because, due to the anabolic nature, thyroid supplementation can generate partial response in dogs without thyroid disease, specially in respect to hair regrowth. If after this period of 2-3 months we have not observed the expected improvement, we should interrupt treatment and reconsider the diagnosis.

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