

CANINE HYPOTHYROIDISM: FACT OR FICTION

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Authors almost always refer to hypothyroidism as a common (if not the most common) endocrine disease in dogs, but there is little evidence to support this claim. In fact, canine hypothyroidism may be one of the most over-diagnosed diseases in small animal medicine. Just about any medical disorder can be associated with decreases in circulating concentrations of thyroid hormone, causing hypothyroidism to be over-diagnosed. In addition, it is common practice for veterinarians to treat hypothyroidism empirically following a presumptive diagnosis. This practice is not recommended for several reasons. First of all, it is not scientifically sound medical practice. Secondly, it may allow another disorder to progress undiagnosed. Thirdly, unnecessary supplementation With thyroid hormone disrupts the normal regulation of TRH, TSH, and thyroid hormone production, the consequences of which are not understood.

Clinical signs of hypothyroidism result from generalized decreases in metabolic functions supported by thyroid hormone action. The clinical signs of hypothyroidism are multi-systemic and varied. Their onset is gradual. The classic presentation of a hypothyroid dog includes obesity, inactivity, mental dullness, decreased appetite, dermatological abnormalities, and intolerance to exercise and cold. These signs may or may not be present in all dogs with hypothyroidism.

Dermatologic abnormalities are the most common presenting complaints of owners of dogs with hypothyroidism². Approximately 85% of hypothyroid dogs are reported to have skin lesions. Care should be taken in interpreting the reports of the prevalence of dermatologic signs in canine hypothyroidism because many of the reports have been written by dermatologists. Whatever the true incidence of these signs, they include alopecia (arrest of hair growth cycle in the telogen phase), dryness, scaling, dull hair which is easily epilated, seborrhea, slow hair re-growth, various degrees of hyperpigmentation, poor wound healing. In extreme cases, mucopolysaccharides accumulate in the skin causing it to thicken, especially in the face. This condition is called myxedema. Dogs with myxedema are classically referred to as having "tragic" facial expressions. The typical skin problem of canine hypothyroidism is usually not itchy, although secondary bacterial infections are possible, and could cause a degree of itchiness. Hypothyroidism is also commonly mentioned as an underlying cause of chronic ear infection. There is little or no scientific support for this claim.

FACT OR FICTION: HYPOTHYROIDISM IS A CAUSE OF OTITIS

Hypothyroidism is commonly cited as a cause of bacterial pyoderma which can occur locally, manifesting as otitis externa (infection of the outer ear). A recent paper stated, "Recurrent bacterial and yeast infections of the skin and ears often occur secondary to hypothyroidism and may be the only presenting signs," although the statement is not supported by any reference to a published study.⁴ The paper goes on to explain that hypothyroidism can cause decreased function of lymphoid cells, decreased T cell function, decreased humoral immunity, and decreased barrier function of the skin, making reference to the leading textbook on veterinary dermatology. Statements to this effect are made in the 6th edition of the textbook, referencing the 5th edition.⁵ The 5th edition cites the 4th edition.⁶ The 4th edition cites the 3rd edition.⁷ In the 3rd edition,⁸ the effects of hypothyroidism on the function of the immune system are

referenced by the author's unpublished data from 1982, and a research paper in mice published in 1980.' Examination of the reference reveals that it is not a study of hypothyroidism at all, but rather a study of the effects of thyroid hormone excess on the immunologic response to administration of sheep red blood cells in mice. The effects were minimal. Athyreotic human patients have been shown to have similar white blood cell function when compared to normal controls." Still, there is no credible evidence to suggest that otitis externa, especially as the sole clinical sign, is a feature of hypothyroidism in dogs.

FACT OR FICTION: HYPOTHYROIDISM IS A CAUSE OF NEUROLOGIC DISEASE

Many neurological signs have been blamed on hypothyroidism in dogs. Bichsel et al reported 4 dogs with neurological diseases associated with low concentrations of serum total T4 and inadequate responses to exogenous TSH administration. "Three of the dogs had no non-neurological clinical signs of hypothyroidism. One was a 7-year-old Boxer with facial paralysis that was also treated with sulfamethoxazole, a drug known to cause severe hypothyroidism." Another was an 11-year-old Old English Sheep Dog with a head tilt that did not resolve on thyroxine therapy. Another was a 10-year-old Cocker Spaniel with circling and a head tilt that did not respond to thyroxine therapy, and the other was a 10-year-old mixed breed dog with vestibular signs (head tilt, abnormal eye movements, loss of balance) that resolved. Idiopathic vestibular disease, which is clinically the same, is common in older dogs, and resolves spontaneously as well. In another paper by Jaggy et al.¹³, 29 dogs with hypothyroidism (diagnosed by TSH stimulation testing) and neurologic signs were studied retrospectively. Eight of nine dogs with vestibular disease recovered. Four dogs with megaesophagus (dilated, flaccid esophagus leading to the inability to swallow) did not recover despite thyroxine therapy. Of the 29 dogs studied, only 10 had increased concentrations of serum cholesterol. This common biochemical finding is usually present in more than 75% of dogs with hypothyroidism. It is doubtful that many of the dogs in the study actually had hypothyroidism.

But what about the TSH stimulation test results in the dogs with reported hypothyroidism and neurological disease? The TSH stimulation test is not perfect, and even though it is considered a gold standard test for hypothyroidism, it can be difficult to interpret. Even its position as a gold standard is in question. A recent study of dogs with low T4 and thyroid biopsy results, showed that the TSH stimulation test is often false positive.¹⁴ This report also supported earlier reports showing the overlap between total T4, free T4, and endogenous TSH concentrations in sick vs hypothyroid dogs."

FACT OR FICTION: HYPOTHYROIDISM IS A CAUSE OF INFERTILITY

Hypothyroidism has been implicated as a cause of infertility in both male and female dogs. It should be noted that the most common reason for infertility in dogs is mistiming of breeding. Still, bitches failing to conceive are often treated empirically with thyroid hormone supplementation. Early investigators reported sperm abnormalities in dogs with hypothyroidism. More recent studies have shown no effect of experimentally induced hypothyroidism on testicular size, sperm count, motility, or morphology, although actual fertility studies have not been done."

FACT OR FICTION: HYPOTHYROIDISM IS A CAUSE OF AGGRESSION

Recently, hypothyroidism has been implicated as a cause of aggression in dogs.^{15, 19} Only a handful of cases appear in the literature. In all cases, physical examination findings and results of CBC and biochemistry profiles were normal. All dogs had low serum T4 and high TSH concentrations. All

but one were intact males. One dog responded to thyroid supplementation, but was also castrated and subjected to behavioral modification therapy.

FACT OR FICTION: VACCINES CAUSE HYPOTHYROIDISM

Hypothyroidism is an immune-mediated disease, and attempts have been made to blame the presence of canine immune-mediated diseases on over-vaccination. In one study, dogs were vaccinated repeatedly at 8, 10, 12, 16, 20, 26, and 52 weeks of age and antibodies against thyroglobulin were studied.²⁰ Thyroglobulin is a key protein involved in thyroid hormone production, and antibodies against this protein are routinely measured as a test for the presence of an immune-mediated process attacking the thyroid gland. In the study, antibodies were higher in excessively vaccinated dogs than in control dogs. In a subsequent study by the same authors,²¹ however, the thyroid glands of over-vaccinated dogs were not different from unvaccinated dogs. If anti-thyroglobulin antibodies truly do indicate the presence of lymphocytic thyroiditis (the most commonly cited type of immune-mediated thyroid disease causing hypothyroidism), there should have been more inflammation found in the over-vaccinated dogs. There are lots of possibilities for why antibody tests could be positive when there is no underlying immune-mediated thyroid disease, but it cannot be explained in the context of hypothyroidism.

HOW IS HYPOTHYROIDISM DIAGNOSED?

The measurement of both total T3 (TT3) and total T4 (TT4) are commonly performed in canine practice. There is some value to the determination of TT4, because a finding of a normal TT4 excludes a diagnosis of hypothyroidism. The finding of a low basal TT4, however, is of little diagnostic value, because TT4 concentrations are falsely lowered by just about any concurrent illness, and by a large number of drugs, including benzodiazepines, phenobarbital, glucocorticoids, imidazoles, penicillins, sulfonyleureas, salicylates, and phenothiazines. Unfortunately, many dogs are diagnosed with hypothyroidism based only on findings of low TT4 concentrations. Measurement of serum TT3 is without value in the diagnosis of thyroid disorders in dogs.²²

Most thyroid hormone circulates bound to plasma protein. Approximately 1 percent of TT4 is not protein-bound and is referred to as free T4 (FT4). In true hypothyroidism, basal FT4 concentrations should be low, and most of these measurements in hypothyroid dogs are low. There is, however, a degree of overlap with normal dogs and dogs with non-thyroidal illness, so this test alone does not confirm a diagnosis of hypothyroidism.

The combination of FT4 and serum TSH measurement is considered nearly 100 percent diagnostic for hypothyroidism in people. Unfortunately, the results of serum TSH measurement are not nearly as clear cut in canine hypothyroidism. Most dogs with primary hypothyroidism, as expected, have high concentrations of TSH in the serum. Serum TSH concentrations, however, are normal in some dogs with hypothyroidism, making this test less reliable in this species.

Thyroid autoantibodies - Antibodies against thyroglobulin, T4 and T3 are considered by some to be a marker for lymphocytic thyroiditis. Probably the most consistent, although by no means absolute, antibody found in dogs with hypothyroidism is anti-thyroglobulin antibody. This test may be of some use, when combined with other findings, in the diagnosis of hypothyroidism. False positives and false negatives occur.


In the past, the most reliable test for canine hypothyroidism was the TSH stimulation test. Exogenous TSH administered to a normal dog causes a consistent rise in the serum concentration of TT4, whereas dogs with hypothyroidism exhibit little or no response to TSH. While there were plenty of gray

areas in interpreting this test, it was considered a very useful diagnostic tool. Recent work has called the validity of the test into question and has suggested that quantitative scintigraphy may be the most accurate test¹⁴

My personal opinion is that in order to have a diagnosis of hypothyroidism, a dog should have appropriate clinical signs and a low FT₄, as well as at least two of the three following results: high TSH, positive anti-thyroglobulin antibodies, hypercholesterolemia. Other clinicians have less stringent diagnostic criteria. Thyroid biopsy would probably be the best test, but it is invasive and not practical.

REFERENCES

1. Chastain CB, Ganjam VK. Clinical Endocrinology of Companion Animals, Lea & Febiger, Philadelphia, 1986, p.135.
2. Beale KM, Dermatologic manifestations of hypothyroidism. In: Hypothyroidism: diagnosis and clinical manifestations. Daniels Pharmaceuticals, St. Petersburg, FL 1993, p 16.
3. Scott DW, Miller WH, Griffin CE. Endocrine and metabolic diseases. Muller and Kirk's Small Animal Dermatology, 5th edition, W.B. Saunders, Philadelphia, 2001
4. Frank LA. Comparative dermatology--canine endocrine dermatoses. Clin Dermatol. 2006;24:317-25.
5. Scott DW, Miller WH, Griffin CE. Endocrine and metabolic diseases. Muller and Kirk's Small Animal Dermatology, 5th edition, W.E. Saunders, Philadelphia, 1995., p.784
6. Scott DW, Miller WH, Griffin CE. Endocrine and metabolic diseases. Muller and Kirk's Small Animal Dermatology, 5th edition, W.E. Saunders, Philadelphia, 2001. p.63 1. •
7. Muller GH, Kirk RW, Scott DS. Small Animal Dermatology, 4th edition, W.B. Saunders, Philadelphia, 1989
8. Muller GH, Kirk RW, Scott DS. Small Animal Dermatology, 3th edition, W.E. Saunders, Philadelphia, 1983, p.531.
9. Chen Y. Effects of thyroxine on the immune responses of mice in vivo and in vitro. Immunol Commun. 1980;9:269.
10. Marino F, Guasti L, Cosentino M, De Piazza D, et al. Thyroid hormone regulation of cell migration and oxidative metabolism in polymorphonuclear leukocytes: Clinical evidence in thyroidectomized subjects on thyroxine replacement therapy. Life Sciences 2006;78: 1071-1077.
11. Bichsel P, Jacobs G, Oliver JE Jr. Neurologic manifestations associated with hypothyroidism in four dogs. J Am Vet Med Assoc. 1988;192:1745-7.
12. Frank LA, Hnilica KA, May ER, Sargent SJ, Davis JA. Effects of sulfamethoxazole-trimethoprim on thyroid function in dogs. Am J Vet Res. 2005 Feb;66(2):256-9.
13. Jaggy A, Oliver JE, Ferguson DC, Mahaffey EA, Glaus T Jr. Neurological manifestations of hypothyroidism: a retrospective study of 29 dogs. J Vet Intern Med. 1994;8:328-36.



14. Diaz Espineira MM, Mol JA, Peeters ME, Pollak YW, Iversen L, van Dijk JE, Rijnberk A, Kooistra HS. Assessment of thyroid function in dogs with low plasma thyroxine concentration. *J Vet Intern Med.* 2007;21 :25-32.

15. Kantrowitz LB, Peterson ME, Melian C, Nichols R.. Serum total thyroxine, total triiodothyronine, free thyroxine, and thyrotropin concentrations in dogs with nonthyroidal disease. *J Am Vet Med Assoc.* 2001;21:765-9.

16. Johnson C, Olivier NB, Nachreiner R, Mullaney 1. Effect of I3II-induced hypothyroidism on indices of reproductive function in adult male dogs. *J Vet Intern Med.* 1999; 13:104-10.

17. Beaver BV, Haug LI. Canine behaviors associated with hypothyroidism. *JAm Anim Hosp Assoc.* 2003;39:431-4.

18. Fatjo J, Stub C, Manteca X. Four cases of aggression and hypothyroidism in dogs. *Vet Rec.* 2002;151:547-8

19. Fatjo J, Amat M, Manteca X. Animal behavior case of the month. Aggression in dogs. *J Am Vet Med Assoc.* 2003;223:623-6.

20. Scott:Moncrief JC, Azcona-Olivera J, Glickman NW, Glickman LT, HogenEsch H. Evaluation of antithyroglobulin antibodies after routine vaccination in pet and research dogs. *J AM Vet Med Assoc* 2002;221 :515-521.

21. Scott-Moncrief JC, Glickman NW, Glickman LT, HogenEsch H. Lack of association between repeated vaccination and thyroiditis in laboratory beagles. *J Vet Intern Med* 2006;20:818-821.

22. Peterson ME, Melian C, Nichols R. Measurement of serum total thyroxine, triiodothyronine, free thyroxine, and thyrotropin concentrations for diagnosis of hypothyroidism in dogs. *JAm VetMedAssoc.* 1997;211:1396-402.