Hypothyroidism in Dogs

David Bruyette, DVM, DACVIM
VCA West Los Angeles Animal Hospital
Los Angeles, CA

1. Introduction

A. Due to deficiency of thyroid hormones (T3/T4). T4 is the predominate hormone secreted by the thyroid. T4 is converted in the periphery to the biologically active hormone T3.
B. Thyroid hormone regulates the metabolic rate of most organ systems so clinical signs are extremely variable, vague, and rarely pathognomonic.
C. Diagnosis depends on a combination of clinical signs, biochemical abnormalities, and thyroid function tests.

2. Etiology

A. Primary hypothyroidism
    1. Accounts for over 90% of cases.
    2. May be due to lymphocytic thyroiditis, idiopathic atrophy, or neoplastic destruction.
        a. Lymphocytic thyroiditis (50% of cases)
            1) Immune-mediated destruction of the thyroid.
            2) Antithyroglobulin antibodies present.
            3) Genetic predisposition (borzoi, beagle, great dane and cocker spaniel).
            4) Most common form.
        b. Idiopathic atrophy (40 – 45% of cases)
            1) Degenerative disorder of thyroid follicular cells.
            2) No inflammatory infiltrate.
            3) Cause unknown.
            4) May be the end stage of lymphocytic thyroiditis.
        c. Neoplastic destruction
            1) Canine thyroid tumors usually hormonally inactive.
            2) Hypothyroidism follows total destruction of the gland by tumor invasion, surgery or radiation.
B. Secondary hypothyroidism
    1. Impaired TSH secretion.
    2. Congenital malformation (German Shepherd dog), pituitary destruction, medications (glucocorticoids).
    3. Less than 5% of cases.
C. Tertiary hypothyroidism
    1. Hypothalamic disorder resulting in decreased TRH secretion.
        a. Congenital defects, mass lesions, destructive lesions
        b. Suspected in a line of giant schnauzers
    2. Abnormal TRH molecule.
    3. Abnormal TRH binding in pituitary.
D. Miscellaneous causes
    1. Congenital defects
        a. Thyroid dysgenesis
        b. Dyshormonogenesis
    2. Iodine deficiency
        a. Unlikely if eating commercial cat and dog food.
    3. Defect in conversion of T4 to T3
        a. Not documented to occur in man or animals.
        b. Low T3 with normal T4 usually due to concurrent illness (Sick Euthyroid Syndrome) or medications.
E. Feline hypothyroidism
    1. Extremely rare with only a few documented cases of naturally occurring disease.
    2. Pet owners may consider lethargic, obese cats to be normal.
    3. May occur secondary to therapy for hyperthyroidism (surgery, I-131, antithyroid medication). See Feline Hyperthyroidism

3. Signalment

A. Breed predisposition: Boxer, Dachshund, Doberman, Golden Retriever, Great Dane, Irish Setter, Miniature Schnauzer, Poodle.
B. No sex predilection.

4. Clinical signs

A. Adult dogs
   1. Onset of signs 4-6 years
      a. High risk, large, and giant breeds develop signs at an earlier age.
   2. General signs
      a. Lethargic
      b. Exercise intolerant
      c. Increased weight without polyphagia. Morbidly obese animals are rarely hypothyroid.
   3. Dermatologic
      a. Bilaterally symmetric endocrine truncal alopecia. Head and extremities spared.
      b. Non-pruritic unless secondary infection.
      c. Alopecia may be focal; "Rat tail".
      d. Dull, dry hair coat.
      e. Hyperkeratosis and hyperpigmentation.
      f. Increased skin thickness (myxedema).
      g. Secondary pyoderma.
   4. Reproductive
      a. Female
         1) Irregular estrus intervals.
         2) Gynecomastia, galactorrhea.
      b. Male
         1) Recent evidence indicated no reproductive abnormalities in intact males dogs with experimentally induced hypothyroidism.
   5. Cardiovascular
      a. Bradycardia
      b. Arrhythmias
      c. Atherosclerosis
      d. Most effects secondary to decreased metabolic rate.
   6. Ocular
      a. Corneal lipid deposits.
      b. KCS
      c. Corneal ulceration.
   7. Neuromuscular
      a. Weakness
      b. Peripheral polyneuropathy (LMN disease)
      c. Facial nerve paralysis.

B. Congenital (Cretinism)
   1. Dwarfism
   2. Inappetence
   3. Lethargy
   4. Delayed dental eruption.
   5. Alopecia or juvenile hair coat.
   6. Epiphyseal dysplasia.

C. Secondary and tertiary hypothyroidism
   1. Congenital forms similar to cretinism.
   2. In the acquired form signs related to etiology and degree of involvement of the pituitary and/or hypothalamus. May also see:
      a. Hypoadrenocorticism (glucocorticoid insufficiency)
      b. Hyperadrenocorticism
      c. Diabetes insipidus
      d. Reproductive failure
      e. CNS abnormalities

5. Laboratory abnormalities

A. Hematology
   1. Mild normocytic, normochromic, nonregenerative anemia.

B. Biochemistry profile
   1. Elevated serum cholesterol.

6. Diagnosis of hypothyroidism

A. Basal T4 concentration
   1. As for all endocrine testing, check with the laboratory for normal values and to see if a given assay is validated for the species you are evaluating.
   2. In general, normal basal T4 levels support euthyroidism, but low levels do not confirm hypothyroidism as many factors affect basal T4 levels.
   3. A low T4 indicates the need for further testing (see below).

B. Basal T3 concentrations
   1. Basal levels of little use in discriminating normal from hypothyroid as:
      a. Vast majority of T3 is intracellular.
      b. The majority of T3 produced by peripheral deiodination of T4.

C. Factors causing low T4 and T3 in euthyroid animals
   1. Hourly fluctuations
   2. Fasting over 48 hours
   3. Concurrent illness
   4. Hyperadrenocorticism
   5. Medications: Glucocorticoids, valium, anticonvulsants, propranolol, many others.
   6. Aging

D. Factors causing increased T4 and T3 in euthyroid animals
   1. Obesity
   2. Hourly fluctuations
   3. Estrus, pregnancy
   4. Medications: Estrogen, progesterone
   5. Antithyroid antibodies
      a. TSH stimulation test
         1) Designed to eliminate variables affecting basal T3 or T4.
         2) Protocol depends on laboratory used. Check first.
         3) A common protocol is 0.1 IU TSH/kg IV, serum T4 at time 0 and 6 hours post-TSH.
         4) Exogenous thyroid supplementation should be stopped 4 weeks prior to testing.
         5) Post-TSH T4 should be within or above normal post-TSH range for laboratory used.
         6) Serum T3 response is more variable than T4 and less diagnostic.
         7) Human recombinant TSH can be used in the dog although the cost may be prohibitive and the use of assays for free T4 by equilibrium dialysis has limited the use of TSH stimulation testing in dogs.
      b. Interpretation of TSH Stimulation Test
         1) With primary hypothyroidism
            a) Pre and post-TSH T4 should remain below normal basal T4 range.
         2) With secondary and tertiary hypothyroidism
            a) Results depend on degree of thyroid atrophy; can resemble normal, sick euthyroid or hypothyroid. May need to treat with TSH for several days to assess the degree of thyroid atrophy.
         3) Sick euthyroid
            a) Animals with non-thyroidal disease or drug-induced lowering of T4 and T3 will have a blunted response to TSH administration when compared to normal. Differentiating between the sick euthyroid syndrome and hypothyroidism can be difficult and depends on clinical signs, presence of concurrent illness or drug administration, and owners recollection of the onset of signs.
      c. TRH stimulation test
         1) To differentiate secondary from tertiary hypothyroidism. Measurement of cTSH concentrations is also recommended.
         2) Evaluates release of TSH in response to stimulation by TRH.
         3) TSH stimulation test should be performed first to document thyroid responsiveness.
         4) Lack of post-TRH T4 increase implies primary or secondary hypothyroidism. If the animal has a normal response to TSH administration, then secondary hypothyroidism is diagnosed.
         5) Follow protocol recommended by your lab.
         6) Primarily used in evaluating patients with suspected or known abnormalities involving one or multiple pituitary hormones; I.e. pituitary dwarfs or animals with CNS lesions.

d. Free T4
   1) Recently, determination of free T4 (fT4) by equilibrium dialysis, has been shown to correlate very well with results of TSH stimulation testing in the diagnosis of canine hypothyroidism. Evaluation of fT4 allows us to assess the biologically active fraction of thyroid hormone and has been shown to be much less affected by non-thyroidal factors (medications, concurrent illness, binding abnormalities, etc). The term "sick euthyroidism" is often used to describe the effect of these various non-thyroidal factors on decreasing TT4 concentrations in the face of normal thyroid function. Although a number of fT4 assays are commercially available, only those that employ a dialysis step are valid in the dog. We have derived the following chart to assist in the diagnosis of canine hypothyroidism utilizing either the TSH stimulation test or evaluation of a resting TT4 and fT4.

e. Thyroid Function Testing: Interpretation (Refer to your laboratories reference ranges)
   1) TSH Stimulation Testing

      TT4 Resting range: 0.6 - 3.7 ug/dl
      TT4 post-TSH: 2.5 - 7.3 ug/dl

      a) Values less than 2.5 ug/dl are diagnostic of hypothyroidism.

f. Canine TSH Assay
   1) Recently, an advance in the diagnostic approach to hypothyroidism was achieved with the advent of a reliable assay for canine TSH (cTSH). A kit for cTSH (Diagnostic Products Corporation; DPC Inc) is now available and should help in our approach to the patient with suspected hypothyroidism. A cTSH together with a free T4 by dialysis should provide the most relevant information with respect to thyroid function. A patient with hypothyroidism should have an elevated cTSH in conjunction with a decreased fT4. However, with the current cTSH assay, up to 25% of patients with confirmed hypothyroidism have a cTSH concentration within the normal range.
   2) Thyroid Panel (fT4 and cTSH)
      a) cTSH Reference Range : 0.0 - 0.45 ng/ml
      b) fT4ED Reference Range: 11 - 43 pmol/L
   3) Antithyroglobulin and anti-T3 and anti-T3 autoantibody testing:
      a) The presence of antithyroglobulin antibodies indicates the presence of lymphocytic thyroiditis. Occasionally, these animals may also have anti-T3 and anti-T4 (rare) autoantibodies. The presence of thyroiditis does not equal a diagnosis of hypothyroidism. Animals with thyroiditis likely will become hypothyroid in the future but the decision on whether to supplement with thyroid hormone should be based on the presence of clinical signs and abnormal function tests (low TT4, low fT4ED and an elevated cTSH level). Animals with thyroiditis should not be used for breeding and this test in now included as part of the OFA thyroid registry. The OFA thyroid panel consists of a TT4, fT4ED, cTSH and antithyroglobulin antibody. To receive a registry number animals must be at least 1 year of age and have normal test results.

E. Trial therapy with thyroxine
   1. Has been advocated as a diagnostic aid for hypothyroidism
   2. Response to therapy is nonspecific however and normal animals may show some clinical effect due to the anabolic effects of thyroxine.
   3. Indiscriminate therapy with thyroxine, while it may not be harmful, is not cost-effective and may lead to a delay in obtaining a correct diagnosis and instituting proper therapy. Supplementing a sick, euthyroid animal may be detrimental.
      a. As can be seen from the preceding discussion the diagnosis of hypothyroidism depends on a combination of clinical signs, results of routine laboratory tests, and tests of thyroid function. Measurement of fT4 by equlibrium dialysis together with a cTSH provides the most accurate information regarding thyroid function.

7. Treatment of hypothyroidism

A. Sodium levothyroxine (T4)
   1. Dose
      a. Dog:
         1) 0.22mg/m2 SID. Not to exceed 0.8 mg or
         2) 0.10 mg/10# SID.
      b. Cat:
         1) 0.05 to 0.10 mg once daily.
      c. Decrease initial starting dose by 75% if concurrent heart disease, hypoadrenocorticism, or diabetes mellitus is present.
   2. Response to therapy
      a. Attitude, activity, and appetite generally improve within 1 – 2 weeks.
      b. Dermatologic abnormalities improve 4 - 8 weeks.

3. Failure to respond to therapy
    a. Wrong diagnosis.
    b. Inappropriate dosage or frequency of administration.
    c. Poor absorption of T4.
    d. Use of dessicated thyroid is discouraged.
4. Monitoring therapy
    a. Not routinely needed unless there is a poor response to therapy or signs of thyrotoxicosis (PU/PD, restlessness, polyphagia, weight loss) are present.
        1) Monitoring Therapy
            i. Wait one month after starting therapy or changing dosage.
            ii. Inquire about owner compliance and expiration date of medication.
            iii. Measure serum T4 immediately prior to next dose (trough).
            iv. Normalization of serum cTSH levels may be the best way to monitor therapy but this requires that an elevated cTSH existed prior to therapy. Samples for cTSH may be obtained 2 – 3 weeks after starting supplementation and concentrations are not dependent on the time the sample is obtained relative to the dosing of thyroxine.