Comparison of canine thyroid hormone values between laboratories
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Abstract
Blood was drawn from 10 dogs, serum harvested and frozen, and shipped to two laboratories, both of which measured total and free thyroxine (T4 and fT4), total and free triiodothyronine (T3 and fT3), thyroglobulin autoantibody (TgAA), and thyroid stimulating hormone (TSH). Information was collected about the dogs including past thyroid hormone testing, thyroid supplementation and other medications, chronic disease conditions including allergic dermatitis, and diet. Values differed between laboratories in four of six dogs with complete data (67%). One laboratory recommended thyroxine supplementation for four of the dogs; the author of the study did not recommend thyroxine supplementation for any of the dogs based on thyroid hormone results and clinical presentation.

Keywords: Canine, thyroid, hypothyroidism

Introduction
Thyroxine (T4) is the hormone secreted by the thyroid gland. It is broken down by type I iodothyronine deiodinase to form bioactive triiodothyronine (T3). Hypothyroidism may be due to inadequate stimulation of pituitary thyroid hormone secretion by thyroid stimulating hormone (TSH) from the hypothalamus, insufficient secretion of T4, or inadequate conversion of T4 to T3. Hypothyroidism is the most common endocrinopathy of dogs, with reported prevalence of 0.2 to 0.8%. Clinical manifestations include lethargy, weight gain, coat changes, intolerance for cold, unwillingness to exercise, variation in mentation, and neuropathies. Diagnosis is complicated by variation in circulating thyroid hormones in the absence of thyroid disease. Activity of iodothyronine deiodinase may be decreased in animals with severe illness, fasting or cachexia, or severe liver disease. Examples of other factors that may alter serum concentrations of T4 or T3 include breed, age, gender, reproductive status, concurrent use of drugs, and presence of non-thyroidal illness.

Hypothyroid dogs have less circulating T4, both free and bound, and due to lack of feedback from those hormones, have more circulating TSH. Accurate testing requires assay in serum of free (unbound) T4 (fT4) and TSH. The assay for fT4 has a sensitivity of 0.89 to 0.98, a specificity of 0.93, and an accuracy of 0.95 for assessment of hypothyroidism in dogs. The TSH assay is less sensitive, specific, and accurate, but if both assays are considered together, accuracy is 100%.

Several large testing laboratories provide thyroid panels to give veterinarians and their clients a more definitive idea of the animal’s thyroid hormone status. Most panels include assay for total T4, fT4, bound and free T3 (total T3 and fT3), and TSH. Some panels also include measurement of autoantibodies against thyroglobulin (TgAA) or against T3 and T4 (AAT3 and AAT4, respectively). Laboratories often provide interpretations with these assay results and differ greatly in the recommendations for treatment made.

The goal of this study was to compare values for concentration of total T4, fT4, total T3, fT3, TgAA, and TSH in serum between two different veterinary laboratories.

Materials and methods
Animals were enrolled from the population of dogs at the University of Minnesota College of Veterinary Medicine. Serum was harvested and frozen, and then shipped to two commercial laboratories for assessment. Information was collected regarding previous thyroid hormone testing, thyroid hormone supplementation or other medications received, chronic disease problems including allergic dermatitis, diet, and clinical signs of hypothyroidism including weight gain, lethargy, symmetrical alopecia, and heat-seeking behavior.
Results

Five spayed female and five castrated male dogs were enrolled in the study. Breeds represented were golden retriever (3), Labrador retriever, Siberian husky, Alaskan malamute, American Staffordshire terrier, English setter, Cavalier King Charles spaniel, and Olde English Bulldog. Age ranged from 1.9 to 10.4 years (6.3 ± 3.2 yrs [mean ± SD]).

Actual values from the two laboratories used are not reported. Concentrations were determined using different testing modalities and values were reported using different units and laboratory-specific reference ranges. Insufficient serum from four dogs was submitted, precluding analysis of those samples at one laboratory. Results were classified as normal or abnormal. Thyroid hormone results and specific information about each dog are listed in the Table.

Discussion

Dog breeders express concerns about evaluation of the thyroid status in their breeding bitches and stud dogs because of the many reports in the popular literature linking hypothyroidism to reproductive dysfunction in dogs.21 There are few reports substantiating such concerns and pathology in reproductive tissues secondary to hypothyroidism may be less likely because the uterus and testes do not rely on thyroid hormone for oxygen consumption as do most other tissues.3,22,23 Studies evaluating semen quality in male dogs with experimentally induced hypothyroidism failed to show any decline in libido or semen quality even in the presence of significant clinical manifestations of hypothyroidism.24 Similarly, a long-term study in bitches with experimentally induced hypothyroidism demonstrated decreased puppy birth weight and prolonged parturition but no change in estrous cyclicity, pregnancy rate, litter size, or gestation length.25,26 Despite this, and perhaps with valid concern that induced models of disease may not mimic spontaneous disease, many dog breeders ask their veterinarian to test their dogs for hypothyroidism in the absence of clinical manifestations of disease or treat their dog despite lack of evidence that the dog is hypothyroid.

Hypothyroidism may be misdiagnosed or mistreated in several ways. Veterinarians may make the mistake of assaying only T4, and using a low result as evidence for hypothyroidism.27 Veterinarians and breeders may make the mistake of treating clinically normal dogs with “low normal” assay results, or treating empirically without any testing. A significant risk of hyperthyroidism exists if supplementation is provided unnecessarily: clinical manifestations of hyperthyroidism in dogs include agitation, tachypnea, tachycardia, atrial flutter, and syncope.28

None of the enrolled in this study was suspected of having hypothyroidism based on history or physical examination findings. Of the six dogs in this study with results from both laboratories, four (67%) had differing results for at least one parameter. Of the 10 dogs in the study, one laboratory recommended thyroid hormone supplement for four. Of these four dogs, three were recommended to be supplemented because of low thyroid hormone concentrations and normal TSH concentration. One of these dogs was on medications and had chronic disease that may have accounted for the change in thyroid hormone concentrations, although there are studies documenting that neither mild osteoarthritis nor use of non-steroidal anti-inflammatory drugs, including carprofen, are associated with changes in thyroid hormone concentration.29,30

The recommendation to supplement the fourth dog was based solely on presence of elevated TgAA concentrations. Some authors suggest that elevation in TgAA occurs early in disease, as an indication of presence of autoimmune destruction of the gland before there are other discernible changes in function.31 One study demonstrated elevated concentrations in TgAA in several breeds predisposed to hypothyroidism but did not show subsequent progression to a clinical hypothyroid state, as tracked by owner questionnaires.32 There is no evidence in the veterinary literature that supplementation in the presence of elevated TgAA only somehow alters trajectory of the disorder. In human medicine, among antibodies evaluated, TSH receptor blocking antibodies are considered likely to be associated with disease and TgAA is considered valuable only as diagnostic tool in childhood autoimmune thyroiditis.33 The author of this study recommends thyroid hormone supplementation only if T4 is decreased and TSH is elevated in the absence of other causes of thyroid hormone concentration change and if clinical
manifestations of hypothyroidism are present, and therefore, did not recommend thyroid hormone supplementation for any of these dogs.

Conclusion

Thyroid hormone concentrations in a given dog may differ depending on the laboratory used, and interpretations from some laboratories may differ from recommendations in the veterinary literature. Veterinarians are encouraged to develop a relationship with one laboratory whose testing regimen they trust, and to work with colleagues at that laboratory in considering test results to make joint decisions about patient care based not only laboratory findings but also on history and physical examination findings and assessment of clinical evidence of disease.

References

<table>
<thead>
<tr>
<th>BREED</th>
<th>DOG</th>
<th>AGE (YRS)</th>
<th>GENDER</th>
<th>LAB 1 T4</th>
<th>LAB 1 T3</th>
<th>LAB 1 TgAA</th>
<th>LAB 1 TSH</th>
<th>RECOMMENDATION</th>
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<td>1</td>
<td>1.9</td>
<td>F/S</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>H</td>
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<td>2</td>
<td>2.3</td>
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<td>N</td>
<td>N</td>
<td>N</td>
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<td>2.7</td>
<td>M/N</td>
<td>L</td>
<td>L</td>
<td>L</td>
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<tr>
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<td>4</td>
<td>5.0</td>
<td>F/S</td>
<td>M/N</td>
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<tr>
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<td>5.8</td>
<td>M/N</td>
<td>N</td>
<td>N</td>
<td>H</td>
<td>N</td>
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<td>6.9</td>
<td>F/S</td>
<td>N</td>
<td>N</td>
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<td>N</td>
<td>N</td>
<td>N</td>
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**Table:** Thyroid hormone results and demographic data for 10 dogs (N = normal, L = low, H = high).
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<tr>
<th>OTHER MEDICATIONS?</th>
<th>Heartgard Plus™</th>
<th>No</th>
<th>Interceptor™, Frontline™, diphenhydramine</th>
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<th>carprofen</th>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes (seasonal)</td>
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<td>Purina Large Breed</td>
<td>Purina Pro Plan</td>
<td>Purina Adult Performance</td>
<td>Purina Joint Mobility</td>
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<td>Purina OM or Weight Management</td>
<td>Purina JD</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Slow weight loss, some heat-seeking</td>
<td>No</td>
<td>No</td>
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