Comparison of colloid, thyroid follicular epithelium, and thyroid hormone concentrations in healthy and severely sick dogs

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Objectives—To compare serum concentrations of total thyroxine (TT_4), free thyroxine (fT_4), and thyroid-stimulating hormone (TSH), as well as measures of thyroid follicular colloid and epithelium, between groups of healthy dogs and severely sick dogs.

Design—Cross-sectional study.

Animals—61 healthy dogs and 66 severely sick dogs.

Procedure—Serum samples were obtained before euthanasia, and both thyroid lobes were removed immediately after euthanasia. Morphometric analyses were performed on each lobe, and serum TT_4, fT_4, and TSH concentrations were measured.

Results—In the sick group, serum TT_4 and fT_4 concentrations were less than reference range values in 39 (59%) and 21 (32%) dogs, respectively; only 5 (8%) dogs had high TSH concentrations. Mean serum TT_4 and fT_4 concentrations were significantly lower in the sick group, compared with the healthy group. In the healthy group, a significant negative correlation was found between volume percentage of colloid and TT_4 or fT_4 concentrations, and a significant positive correlation was found between volume percentage of follicular epithelium and TT_4 or fT_4 concentrations. A significant negative correlation was observed between volume percentages of colloid and follicular epithelium in both groups.

Conclusions and Clinical Relevance—TT_4 and fT_4 concentrations are frequently less than reference range values in severely sick dogs. Therefore, thyroid status should not be evaluated during severe illness. The absence of any significant differences in mean volume percentages of follicular epithelium between healthy and severely sick dogs suggests that these 2 groups had similar potential for synthesizing and secreting thyroid hormones. (*J Am Vet Med Assoc* 2003;222:1079–1085)

Diagnosis of canine hypothyroidism is not straightforward because the clinical signs of the disease overlap with nonthyroidal disorders, and results of thyroid-related tests can be influenced by many factors not associated with thyroid function, such as severe illness and medications.[1-25,a] The need to find diagnostic tests that are not affected by these factors is clear. Recently, methods for measuring serum **thyroid-stimulating hormone (TSH)** and **free thyroxine (fT_4)** with equilibrium dialyses have become available for assessing the thyroid status of dogs. Results of a few studies[26,27] indicate that, as a single diagnostic test for hypothyroidism, measurement of fT_4 is more accurate than measurement of either **total thyroxine (TT_4)** or TSH. Conversely, results of other studies[26,28] indicate that although sole measurement of TSH is not a good diagnostic test for canine hypothyroidism, it can be a useful additional test if evaluated in combination with TT_4 values.

It has been stated that, before clinical signs of canine hypothyroidism become evident, more than 75% of both thyroid lobes must be destroyed.[29,30] To our knowledge, there have been no morphologic studies comparing the status of thyroid follicles in healthy, sick, and hypothyroid dogs. The purpose of the study reported here was to compare serum concentrations of TT_4, fT_4, and TSH, as well as measures of thyroid follicular colloid and epithelium, between groups of healthy dogs and severely sick dogs.

Materials and Methods

Study population—One hundred twenty-seven dogs were included in this study. Sixty-one dogs were clinically normal and had serum TT_4, fT_4, and TSH concentrations within the reference ranges established by our laboratory. These dogs were used in a 1-day terminal surgery laboratory and included 43 Beagles, 13 Coonhounds, and 5 mixed-breed dogs. Forty-eight dogs were intact females, 13 were sexually intact males, and ages ranged from 7 months to 10 years (mean, 6 years; median, 6 years). None of these clinically normal dogs had received any medication for at least 6 months prior to the study. Euthanasia was performed with pentobarbital sodium and phenytoin sodium[b] (0.22 mg/kg [0.1 mg/lb], IV). All dogs were obtained from the Research Animal Resources, and the study was approved and overseen by the Institutional Animal Care and Use Committee of the University of Minnesota.

An additional 66 dogs included in the study consisted of severely sick dogs that were euthanatized because of the severity of their illness at the Veterinary Teaching Hospital of the University of Minnesota. Their ages ranged from 7 weeks to 16 years (mean, 8 years; median, 9 years). Breeds

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included Golden Retriever (n = 6), Labrador Retriever (6), Dachshund (3), Bichon Frise (3), Cocker Spaniel (2), English Springer Spaniel (2), Greyhound (2), Siberian Husky (2), and Dalmatian (2). There were 17 mixed-breed dogs and 21 dogs representing 21 other breeds. Thirty-three dogs were male (11 sexually intact) and 33 were female (3 sexually intact). In most dogs, the diagnosed illness was confirmed or determined through a postmortem examination and categorized as neoplasia (n = 19), renal disorders (12), gastrointestinal disorders (9), infectious diseases (7), heart disorders (4), neurologic disorders (3), blood dyscrasias (3), motor vehicle trauma (3), toxicoses (2), respiratory disorders (1), and unknown (3). Duration of the illnesses ranged from 1 day to 270 days. Forty-three severely sick dogs were receiving a variety of medications at the time of euthanasia.

Determination of thyroid hormone and TSH concentrations—Blood samples for determination of baseline serum TT_4, fT_4, and TSH were collected from all dogs within 48 hours of euthanasia. Therefore, the time of day that the blood samples were collected could not be controlled in the group of severely sick dogs. Ninety-five percent of these sick dogs were receiving fluids IV at the time of euthanasia and had not received food PO for at least 24 hours before blood samples were collected. However, the feeding status of a small percentage of severely sick dogs was unknown. Blood samples were collected from dogs in the healthy group between 10:00 and 11:00 AM. Food was withheld from these dogs for at least 12 hours before blood samples were collected. All blood samples were centrifuged within 1 hour after collection, and serum was stored at 4°C until assayed.

All assays were previously validated for use in dogs in our laboratory, and assay procedures were performed according to the manufacturer's instructions. Serum TT_4 and TSH were analyzed by use of a chemiluminescent enzyme immunometric assay.[c] Serum fT_4 concentration was determined by use of equilibrium dialysis.[d] Measurement of dilutions of pooled canine sera that contained high concentrations of TT_4, fT_4, and TSH yielded curves that were parallel to the standard curves. Intra-assay coefficients of variation for TT_4, fT_4, and TSH concentrations were calculated by measuring 10 pools of canine sera that contained low and high hormone concentrations. Interassay coefficients of variation for TT_4, fT_4, and TSH concentrations were calculated by measuring controls provided by the manufacturer on 9 consecutive days for TSH, 12 consecutive days for TT_4, and 10 consecutive days for fT_4. Intra- and interassay coefficients of variation were < 10%. Assay sensitivities for TT_4, fT_4, and TSH concentrations were 3.2 nmol/L, 1.9 pmol/L, and 0.03 ng/mL, respectively. Reference ranges were established for each hormone by use of serum samples from 100 clinically normal dogs.

Morphometric colloid and follicular epithelium analyses—Both lobes of the thyroid gland were removed from each dog immediately after euthanasia. After fixation in neutral-buffered 10% formalin for at least 24 hours, one 5-µm-thick sagittal section through the middle of the gland was obtained from each thyroid lobe and stained with H&E. The decision to take only 1 longitudinal section/lobe was based on the results of a pilot study involving 9 dogs that had no significant difference among results of morphometric analyses of 3 longitudinal sections/lobe at 20-µm intervals.

The fraction of the parenchyma occupied by colloid, follicular epithelium, and interstitium was determined by use of a point count analysis. The area fraction measured by point counting is an unbiased estimate of the volume fraction of each tissue component, assuming representative sections through the gland. Four randomly chosen sampling sites per section were analyzed with a 6 × 6 reticule, resulting in 36 points counted/site and 144 points/section. The 4 sampling sites for each section were selected by tossing the glass slide containing the thyroid gland section onto a grid paper and marking sampling sites with a fine-point permanent marker where the grid lines intersected. The microscopic field to be counted was defined by moving the glass slide directly below the marked dot. Point-counting within the field was performed at 40× magnification. Follicular epithelium cells were counted at 200× to allow for better identification of these cells. For point-counting cells, 4 fields around each of the 4 marked dots were systematically examined. Thus, a total of 16 microscopic fields/section were examined for cell volume fraction determination.

Whenever an inflammatory infiltrate suggestive of lymphocytic thyroiditis was noticed, the mean percentage of inflammation in the sagittal sections of both thyroid lobes was qualitatively estimated at 40× magnification. In addition, the components of the infiltrate were characterized at 200× magnification.

Statistical analyses—Descriptive statistics were used to report the results of the mean volume percentage of colloid, mean volume percentage of follicular epithelium, mean percentage of inflammation, and hormone concentrations.

Assumption of normality for volume percentage of colloid and volume percentage of follicular epithelium was checked (Wilk-Shapiro method), and the normal distribution was improved by use of arcsine transformation. Statistical analyses for these 2 variables were carried out with arcsine transformed data, although the means, SD, and ranges reported here are not transformed.

A nonpaired *t*-test was used to compare mean hormone concentrations between the healthy and severely sick groups. The nonpaired *t*-test was repeated without data from 19 severely sick dogs that were receiving medications that could potentially affect thyroid function.

The group of severely sick dogs was further divided into 2 subgroups on the basis of hormone concentration values. One-way ANOVA was performed to compare mean volume percentage of colloid and mean volume percentage of follicular epithelium among the group of healthy dogs and the 2 subgroups of severely sick dogs.

The correlation between volume percentage of colloid and volume percentage of follicular epithelium and between each of these variables and the measured hormones was performed by use of the nonparametric Spearman rank correlation coefficient method.

Statistical analyses were performed with computer software.[e] For all statistical analyses, values of $P < 0.05$ were considered significant.

Results

Forty-three (65%) sick dogs had 1 or more serum hormone concentrations that were not within reference ranges. Of these dogs, 17 (40%) had only low serum TT_4 concentrations, 2 (5%) had only low serum fT_4 concentrations, and 2 (5%) had only high TSH serum concentrations. Nineteen of the 43 (44%) dogs had serum TT_4 and fT_4 concentrations less than the reference ranges, and 3 (7%) had low TT_4 and high TSH concentrations. None of the dogs in this group had low fT_4 and high TSH concentra-

tions together. Thus, 39 (59%) sick dogs had TT_4 concentrations less than the reference range, 21 (32%) dogs had fT_4 concentrations less than the reference range, and 5 (8%) had high TSH concentrations. Twenty-three of the 66 (35%) sick dogs had serum concentrations of TT_4, fT_4, and TSH in the reference ranges.

Mean serum TT_4 and fT_4 concentrations were significantly lower in the sick group, compared with the healthy group (**Table 1**). However, mean serum fT_4 concentrations in the sick group were still within the reference range. No significant differences in mean serum TSH concentrations were found between the healthy and sick groups.

When the sick group was reanalyzed after removing 19 dogs that had received medications that could affect thyroid function, mean serum TT_4 and fT_4 concentrations were still significantly lower, compared with the healthy group. No significant differences in mean serum TSH concentrations were found between the healthy group and this group of severely sick dogs (Table 1).

In 19 dogs in the sick group that had at least 1 hormone value greater or less than reference range values, medications known to affect thyroid hormones and TSH concentrations included prednisone (n = 10 dogs), dexamethasone sodium phosphate (1), methylprednisolone sodium succinate (2), furosemide (2), phenobarbital (1), phenobarbital and dexamethasone sodium phosphate (1), phenobarbital and prednisone (1), and sulfadimethoxine-ormetoprim and prednisone (1).

The sick group was further divided into 2 groups for purposes of statistical analyses. Forty-three dogs in the sick group with 1 or more serum hormone concentration outside the reference ranges were designated the sick abnormal group. Twenty-three dogs with serum hormone concentrations within the reference ranges were designated the sick normal group. Mean volume percentages of colloid and follicular epithelium were not significantly different among the healthy, sick abnormal, and sick normal groups (**Table 2**). No significant differences were found in mean duration of the diseases between the 2 subgroups of severely sick dogs.

A significant negative correlation was found between volume percentage of colloid and TT_4 and volume percentage of colloid and fT_4 in the healthy group (**Fig 1 and 2**). A significant positive correlation was found between volume percentage of follicular epithelium and TT_4 and volume percentage of follicular epithelium and fT_4 in this group (**Fig 3 and 4**). In contrast, no significant correlation was found between volume percentage of colloid and volume percentage of follicular epithelium and TSH in the healthy group. No significant correlation was observed between volume percentage of colloid and volume percentage of follicular epithelium and TT_4, fT_4, or TSH in the sick group. A significant negative correlation was observed between volume percentage of colloid and volume percentage of follicular epithelium in the healthy group ($r = -0.63$; $r^2 = 0.40$; $P = 0.001$) and the sick group ($r = -0.78$; $r^2 = 0.60$; $P = 0.001$).

Five of the 43 (11.6%) Beagles included in the healthy group had some degree of inflammation in both thyroid lobes. One dog had 1% of both parenchyma occupied by inflammatory cells, 2 dogs had 8%, 1 dog had 10%, and 1 dog had 20%. The inflammatory infiltrate was focal, did not invade the thyroid follicles, and was composed of lymphocytes, plasma cells, and macrophages.

Table 1—Serum total thyroxine (TT_4), free thyroxine (fT_4), and thyroid-stimulating hormone (TSH) concentrations in groups of healthy and severely sick dogs

	TT_4* (nmol/L)			fT_4† (pmol/L)			TSH‡ (ng/mL)		
Group	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Healthy (n = 61)	29.6[a]	10.3	12.9–54.1	25.7[a]	7.7	10.2–32.1	0.2[a]	0.1	0.03–0.6
Sick (66)	11.6[b]	7.7	3.9–41.2	12.8[b]	7.7	2.5–32.1	0.2[a]	0.3	0.03–1.5
Sick§(47)	13.9[b]	8.5	3.9–41.2	15.0[b]	6.6	2.5–32.1	0.3[a]	0.3	0.03–1.5

*Reference range, 12.9 to 51.5 nmol/L. †Reference range, 10.2 to 29.6 pmol/L. ‡Reference range, 0.03 to 0.7 ng/mL. §Sick group without 19 dogs receiving medications that can affect thyroid function.
[a,b]In each column, values with different superscript letters are significantly ($P < 0.05$) different.

Table 2—Measurements of colloid and thyroid follicular epithelium in groups of healthy and severely sick dogs

	Colloid (%)*			Follicular epithelium (%)*		
Group	**Mean**	**SD**	**Range**	**Mean**	**SD**	**Range**
Healthy (n = 61)	49.2	11.7	20.9–73.2	34.2	6.7	20.7–59.6
Sick (66)	53.5	10.4	30.6–75.2	34.3	7.6	17.7–56.7
Sick abnormal (43)	53.7	10.6	30.6–75.2	33.7	7.4	17.7–50.8
Sick normal (23)	54.6	10.2	33.5–72.3	35.6	8.0	22.4–56.7

*No significant ($P < 0.05$) differences among groups.
Sick abnormal = Sick dogs with 1 or more hormone concentrations outside reference ranges. Sick normal = Sick dogs with serum hormone concentrations within reference ranges.

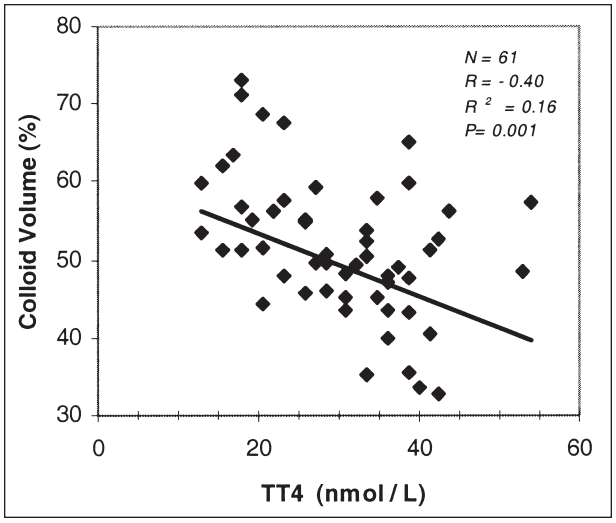

Figure 1—Scattergram of mean thyroid colloid volume versus serum total thyroxine (TT_4) concentration in healthy dogs.

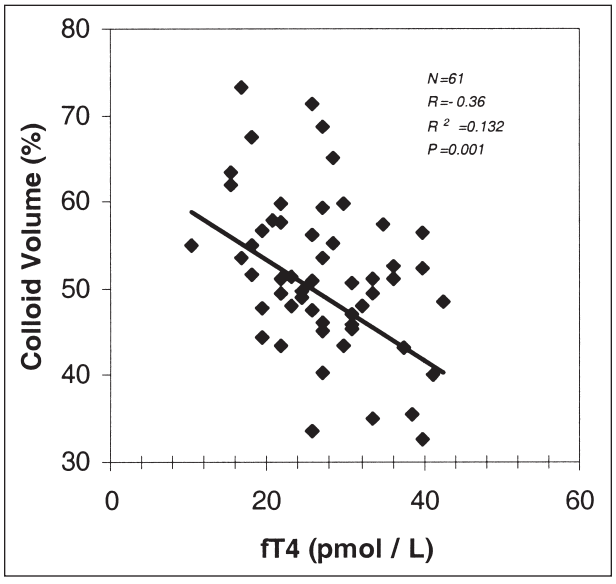

Figure 2—Scattergram of mean thyroid colloid volume versus serum free thyroxine (fT_4) concentration in healthy dogs.

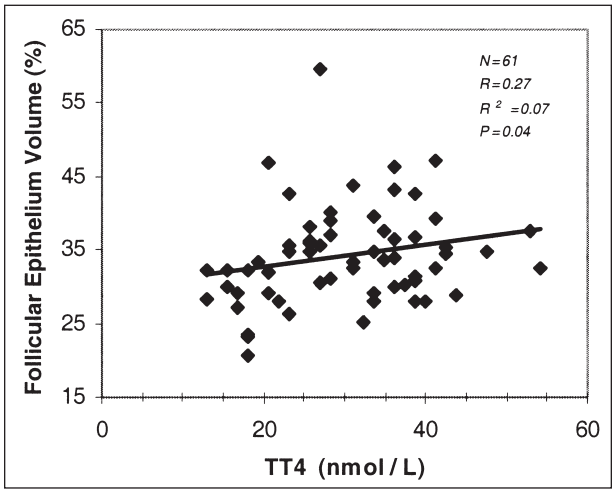

Figure 3—Scattergram of mean thyroid follicular epithelium volume versus serum TT_4 concentration in healthy dogs.

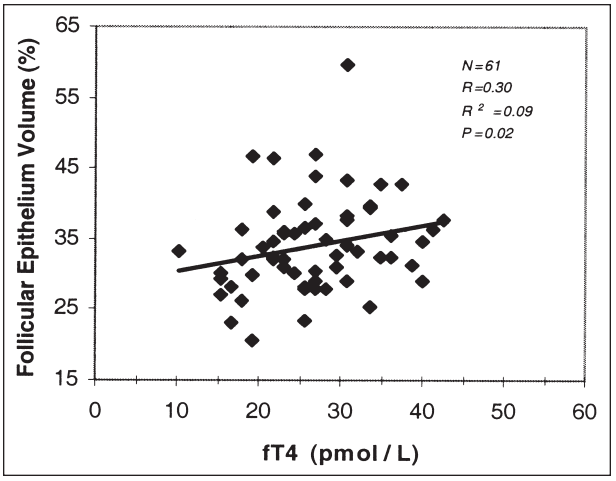

Figure 4—Scattergram of mean thyroid follicular epithelium volume versus fT_4 concentration in healthy dogs.

Discussion

The hormone profile frequently observed in severely sick dogs in this study and in a recent report[25] (TT_4 and fT_4 less than reference range values and TSH concentration within or less than reference range) was similar to findings in humans with severe nonthyroidal illness.[31,32] The reason for this hormone pattern is probably multifactorial and, therefore, may be different among individuals. Factors reported to affect serum concentrations of TT_4 and fT_4 in humans with nonthyroidal illness are transient central hypothyroidism, inhibitors of hormone binding, drugs, metabolites, and free fatty acids in the serum.[31-37] To our knowledge, factors that cause hormone alterations in nonthyroidal illness have not been extensively investigated in dogs; however, it is likely that they are similar to those reported in humans.

The results of our study corroborate results of a recent investigation[25] into the effects of nonthyroidal illness on serum thyroid hormones and TSH concentrations in dogs. In contrast to that study of dogs with mild, moderate, and severe illnesses, we included only dogs with severe diseases in our study. The criterion we used to classify dogs as severely sick was based on the poor prognoses of their illnesses, determined by the attending veterinarian, which resulted ultimately in euthanasia. It is possible that this criterion allowed inclusion of moderately sick dogs, because in some situations and for various reasons, clients may force a premature decision to have their pets euthanatized when their pets would not have died of their illnesses. However, the percentages of sick dogs in our study with low concentrations of TT_4 and fT_4 and high concentrations of TSH were almost identical to the percentages observed in the group of severely sick dogs of the previous report,[25] indicating that, despite the different selection criteria used for classification of the dogs, the populations of severely sick dogs in both studies were similar.

We cannot conclude that the observed altered hormone values were solely attributable to a dog's severe illness, because 19 of the 43 (44%) dogs with 1 or more hormone values outside the reference ranges were

receiving at least 1 medication known to affect serum thyroid hormones and TSH concentrations.[6,10,11,18,20-24,38-44] However, considering the medication history of these dogs, only 9 were receiving drugs for the duration and at the dosage reported to affect thyroid function in dogs. These included 7 dogs receiving immunosuppressive dosages of prednisone and 2 dogs treated long term with phenobarbital.[6,20,21-24]

Thyroid function of the other dogs was not likely affected by the medications they were receiving. Five dogs were receiving anti-inflammatory dosages of prednisone, which does not significantly alter TT_4 and fT_4 concentrations.[9,12] Two dogs were treated with a single injection of dexamethasone sodium phosphate. The effect of injectable dexamethasone on thyroid function of dogs has not been investigated to our knowledge, although a single orally administered dose of dexamethasone had no effect on serum T4 concentrations.[3] One injection of methylprednisolone sodium succinate was administered to 2 dogs. The effect of this glucocorticoid on thyroid function of dogs has not been investigated to our knowledge; however, a single injection of prednisone does not significantly reduce TT_4 concentrations in dogs.[1] Phenobarbital was administered to 1 dog for only 19 days, and a recent study[20] revealed that phenobarbital given for 3 weeks has no effect on TT_4, fT_4, and TSH concentrations in dogs. One of the 7 dogs receiving immunosuppressive dosages of prednisone was also treated with 1 dose of sulfadimethoxine-ormetoprim. Results of 4 studies[10,11,14,18] indicate that long-term treatment with potentiated sulfonamides is necessary before the suppressive effect of these drugs on thyroid function develops. Therefore, it is most likely that any suppressive effect of medications on serum hormones in this dog was a result of prednisone administration. Two dogs in our study received a single therapeutic dose of furosemide. The effects of this drug on the thyroid function of dogs have not been investigated. In vitro studies[40-42] reveal that furosemide competes with TT_4 for plasma binding proteins, resulting in reduced TT_4 concentrations and increased fT_4 fraction. These effects have been detected in vivo only when high doses of furosemide were administered.[43,44] Therefore, it is not likely that therapeutic doses of furosemide administered to 2 dogs in our study had any effect on their thyroid function.

When all 19 dogs that were receiving medications that could potentially interfere with thyroid function were excluded from analysis, the mean serum concentrations of TT_4 and fT_4 of the other 43 severely sick dogs were still significantly lower than the mean hormone concentrations of the healthy dogs.

Hypothyroidism had not been diagnosed in the severely sick dogs with at least 1 hormone value outside the reference ranges; however, no information indicating that their thyroid status had been evaluated by the referring veterinarian was found in these dogs' records, most likely because they were referred for disorders other than hypothyroidism. Therefore, we cannot completely eliminate the possibility that some of these severely sick dogs also had hypothyroidism.

Thirty-five percent of the severely sick dogs investigated here had serum concentrations of TT_4, fT_4, and TSH within reference ranges. It is difficult to explain these findings, because the categories of diseases affecting these dogs and the dogs with hormone values outside the reference ranges were similar. Fifty-seven percent of the sick dogs with hormone values within reference ranges were not receiving any medication at the time of euthanasia, compared with 23% of the sick dogs with hormone values outside the reference ranges. In addition, only 1 severely sick dog with hormone concentrations within reference ranges was receiving a medication (phenobarbital) known to affect hormone values in dogs.[20,21-24] These findings may indicate that medication, more than illness, may have an effect on thyroid hormone and TSH concentrations. However, results of a recent study[25] indicate that severe illnesses resulted in a high frequency of low TT_4 and fT_4 concentrations in groups of dogs that did not receive any medications known to affect hormone values. Disease duration could potentially be a factor, but no significant differences were found in mean duration of the diseases between these 2 subgroups of severely sick dogs. Therefore, it is likely that individual responses to stress associated with illness have a more important effect on the test results.

Regarding the morphometric analysis, our goal was to determine the volume percentage (volume fraction) of the parenchyma occupied by colloid and follicular epithelium in the study groups. We applied the point-counting method because it is efficient and provides an unbiased estimate of the volume fraction, given representative sections of the gland. Based on histologic examination of the thyroid gland, we are confident that our sections were representative, and we randomly sampled measurement fields within each section.

The volume percentages of colloid and follicular epithelium in the parenchyma of both thyroid lobes of healthy dogs and severely sick dogs were compared. No significant differences were observed in mean volume percentages of colloid and follicular epithelium between these 2 groups of dogs. Colloid and follicular epithelium represent the functional structure of the thyroid gland. It has been stated that a dog with ≥ 25% of normal thyroid parenchyma does not have clinical signs of hypothyroidism.[29,30] The mean proportion of the thyroid parenchyma occupied by the colloid and follicular epithelium each was at least 30% in the 2 study groups. These results may indicate that the severely sick dogs in this study were euthyroid. Although the thyroid glands of these dogs appeared to have sufficient functional parenchyma to maintain a euthyroid state, we can state only that they seem to have had the potential to synthesize and secrete adequate amounts of hormone. We cannot state for certain that the dogs were euthyroid at the time blood and tissue samples were collected for the study.

Our study revealed a significant negative correlation between volume percentage of colloid and TT_4 and fT_4 concentrations and a significant positive correlation between volume percentage of follicular epithelium and TT_4 and fT_4 concentrations in the group of healthy dogs. These results indicate that when the follicles are actively synthesizing and secreting thyroid hormones,

the follicular epithelium will be taller, and less colloid will be present inside the follicle lumen.[45] However, despite the fact that the observed correlation between these variables was significant, it is probably not clinically useful because the association was not strong. For the relationship between volume percentage of colloid and thyroid hormones, only 16% of the variation in 1 variable could be accounted for by the other (Fig 1 and 2). Considering the correlation between volume percentage of follicular epithelium and thyroid hormones, only 9% or less of the variation in 1 variable could be accounted for by the other (Fig 3 and 4).

No significant correlation was observed between volume percentage of colloid and volume percentage of follicular epithelium and TT_4 or fT_4 concentrations in the group of severely sick dogs. The lack of association between these variables can be explained by the effect of severe illness, medications, or both on the serum hormone concentrations, which was identified in large numbers of the severely sick dogs. This effect most likely disrupted the physiologic relationship between the thyroid follicles and serum thyroid hormone concentrations.

As expected, a significant negative correlation was observed between volume percentages of colloid and follicular epithelium in the groups of healthy dogs and severely sick dogs. As the follicular epithelium actively synthesizes and secretes thyroid hormones into the circulation, it becomes hypertrophied (taller) and hyperplastic, and colloid is absorbed from the lumina of the follicles. Therefore, larger volume fraction of follicular epithelium and less volume fraction of colloid will be present.

Forty-three of the 61 (70%) dogs included in the healthy group were laboratory Beagles, which are known to be genetically predisposed to develop lymphocytic thyroiditis.[46] However, only 5 (11.6%) of these dogs had focal inflammatory infiltrates characteristic of lymphocytic thyroiditis in their thyroid parenchyma. A semiquantitative estimate of the degree of inflammation revealed that only 1 to 20% of the parenchyma was occupied by inflammatory cells, and the infiltrate was not invading and destroying the thyroid follicles of the dogs. Lymphocytic thyroiditis in laboratory Beagles is usually focal and rarely associated with hypothyroidism, and findings of our 5 dogs corroborate those of previous reports.[46-49]

The major limitation of our study was the fact that a subset of severely sick dogs was receiving medications that can potentially affect the thyroid function. This is a situation that many clinicians will encounter in practice and reflects the real difficulty in assessing thyroid status during severe illness. When this subset of dogs was not included in analyses, mean thyroid hormone concentrations were still significantly lower, compared with the healthy dogs. On the basis of this observation, we conclude that severe illness affected the thyroid function of the dogs in this study.

Our results suggest that severely sick dogs frequently have TT_4 and fT_4 concentrations that are less than reference range values; therefore, we recommend evaluating the thyroid status of such dogs only after resolution of their illnesses.

[a]Ferguson DC, Moore GE, Hoenig M. Carprofen lowers total T4 and TSH, but not free T4 concentrations in dogs (abstr), in *Proceedings*. 17th Annu Meet Am Coll Vet Intern Med 1999;709.
[b]Beuthanasia-D Special, Schering-Plough Corp, Union, NJ.
[c]Immulite, Diagnostic Products Corp, Los Angeles, Calif.
[d]Free T4 by equilibrium dialyses, Nichols Institute Diagnostics, San Juan Capistrano, Calif.
[e]SAS Institute Inc, Cary, NC.

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