

# Assessment of criteria used by veterinary practitioners to diagnose hypothyroidism in sighthounds and investigation of serum thyroid hormone concentrations in healthy Salukis

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**Objective**—To assess use of serum thyroid hormone concentrations by veterinarians to diagnose hypothyroidism in sighthounds and to evaluate serum thyroid hormone concentrations in healthy Salukis.

**Design**—Retrospective case series and cross-sectional study.

**Animals**—398 sighthounds of various breeds with a diagnosis of hypothyroidism and 283 healthy Salukis.

**Procedures**—Pretreatment thyroid hormone assay results from sighthounds subsequently classified as hypothyroid by practitioners were retrieved from a laboratory database. In healthy Salukis, serum concentrations of total thyroxine ( $T_4$ ), free  $T_4$ , total triiodothyronine ( $T_3$ ), free  $T_3$ , and thyroid-stimulating hormone (TSH) and antibodies against thyroglobulin and thyroid hormones were assayed.

**Results**—Records indicated hypothyroidism had been diagnosed in 303 (76.1%) sighthounds on the basis of low serum thyroid hormone concentrations alone and in 30 (7.5%) others despite all thyroid hormone indices being within reference limits. Only 65 (16.3%) dogs had a high TSH concentration or positive thyroglobulin autoantibody result to support the diagnosis. In healthy Salukis, median (reference limits) serum concentrations of total  $T_4$ , free  $T_4$ , total  $T_3$ , free  $T_3$ , and TSH were 13.0 nmol/L (2.8 to 40.0 nmol/L), 12.0 pmol/L (2.0 to 30.3 pmol/L), 1.0 nmol/L (0.4 to 2.1 nmol/L), 4.0 pmol/L (1.6 to 7.7 pmol/L), and 0.18 ng/mL (0 to 0.86 ng/mL), respectively.

**Conclusions and Clinical Relevance**—Diagnosis of hypothyroidism by practitioners was most often made without adequate supportive laboratory evidence. Thyroid hormone values in healthy Salukis differed markedly from standard reference limits for some, but not all, thyroid hormone indices. Breed-specific reference limits should be used when interpreting thyroid hormone profiles of sighthounds. (*J Am Vet Med Assoc* 2010;236:302–308)

Diagnosis of hypothyroidism is based on evidence of specific abnormalities in serum thyroid hormone concentrations in a dog with clinical and clinicopathologic changes consistent with the disease. The most commonly used diagnostic criteria are low total or free  $T_4$  concentration combined with a high TSH concentration in serum.<sup>1</sup> However, diagnosis is complicated by various factors that alter serum thyroid hormone concentrations in euthyroid dogs, including nonthyroidal illness, certain medications, age, sex, breed, and activity.<sup>2–16</sup>

The effect of breed is perhaps most pronounced with sighthounds. Low serum total  $T_4$  concentrations have

## ABBREVIATIONS

AKC	American Kennel Club
COO	Country of origin
$T_3$	Triiodothyronine
$T_4$	Thyroxine
TGAA	Thyroglobulin autoantibody
TSH	Thyroid-stimulating hormone

been reported in Greyhounds, Whippets, Scottish Deerhounds, Irish Wolfhounds, Basenjis, and Sloughis.<sup>5,8–16,a</sup> Low serum free  $T_4$  concentrations have been reported in Greyhounds but not Whippets or Sloughis.<sup>5,10–13</sup> Reports of total  $T_3$  concentration in healthy sighthounds are variable; relative to non-breed-specific reference intervals, values in Greyhounds can range from low to high,<sup>5,9,12,a</sup> whereas values in Irish Wolfhounds are similar to those in other dog breeds.<sup>16</sup> A minority of veterinary laboratories and dog-breed societies provide breed-specific reference limits for some sighthound breeds, but these are not widely reported and the manner in which some were derived is unclear.

Serum thyroid hormone concentrations that differ considerably from those of the general canine popula-

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tion can lead to an inappropriate diagnosis of hypothyroidism in sighthounds. Although the frequency of such misdiagnoses is unknown, a recent Web-based study<sup>17</sup> revealed that hypothyroidism had been diagnosed in 11% of retired racing Greyhounds in the United States, suggesting that such errors are common. This is supported by the relatively low prevalence of positive test results for TGAA in Greyhounds (3.6%),<sup>15</sup> which is similar to the prevalence of 5% in euthyroid dogs.<sup>18,19</sup>

To the authors' knowledge, there has been only 1 other study<sup>20</sup> in which serum thyroid hormone concentrations were evaluated in Salukis. Although low total  $T_4$  concentrations were identified, no other indices were assessed, and the study included only 2 dogs. In addition, in the United States, the Saluki breed can be subclassified into AKC-registered and COO dogs. This classification is largely based on origin: AKC dogs are bred within the United States with emphasis on adherence to the AKC conformation standard, whereas COO dogs are imported from the Middle East and mainly bred for performance. The effect of selective breeding on thyroid hormone concentrations within these 2 groups has not been evaluated.

The purpose of the study reported here was to retrospectively analyze results of thyroid hormone profiles in untreated sighthounds in which hypothyroidism was subsequently diagnosed, with the aim of assessing the criteria used to make the diagnosis in clinical practice. A second objective was to perform a cross-sectional study to assess serum thyroid hormone concentrations in healthy Salukis; calculate breed-specific reference limits for each of these indices; determine any effects of sex, age, body weight, activity (participating in competition vs nonperforming or pet dogs), and origin (AKC-registered or COO) on these indicators; and estimate the prevalence of serum antibodies against thyroglobulin and thyroid hormones ( $T_4$  and  $T_3$ ) within the breed.

## Materials and Methods

**Animals**—This study involved 2 parts. In part 1, test results were retrieved for thyroid hormone concentrations in serum from various sighthound breeds (Greyhound, Borzoi, Saluki, Irish Wolfhound, and Scottish Deerhound) performed by the Diagnostic Center for Population and Animal Health between January 2001 and August 2005. Dogs that received levothyroxine replacement treatment were identified, and the database was searched to determine whether pretreatment diagnostic thyroid hormone testing had been performed at the laboratory. Review of pretreatment results allowed determination of the laboratory criteria used by the sample-submitting veterinarian to support a diagnosis of hypothyroidism. For dogs for which multiple blood samples had been submitted, only the results of the last pretreatment sample were included.

In part 2 of the study, blood samples were collected via cephalic or jugular venipuncture from healthy Salukis  $\geq 12$  months of age at various national and regional specialty conformation shows, kennels, and coursing events in the United States. Owner consent was obtained prior to sample collection. Information collected on individual dogs included reproductive

status, body weight, recent and current medications, health status, activity, and origin. Blood samples from dogs with nonthyroidal illness, as determined by means of owner interview and clinical examination at the time of sample collection, were excluded. For the purposes of this study, NSAIDs, anticonvulsants, corticosteroids, trimethoprim-potentiated sulfonamides, and thyroid hormone replacement medications were considered capable of affecting thyroid function. Dogs that had received any of these drugs within the preceding 6 weeks were excluded. Collected blood samples were placed in evacuated plain glass tubes, allowed to clot, centrifuged ( $2,500 \times g$ ), and separated within 2 hours after collection. After separation, serum samples were frozen, transported cold to one of the author's (MDS) veterinary clinic, and stored at  $-20^\circ\text{C}$  until thyroid hormone assays were performed. The study protocol complied with Michigan State University guidelines for research on animals.

**Thyroid hormone assays**—All serum assays were performed at the Diagnostic Center for Population and Animal Health; each has been validated for use in dogs. Total  $T_4$  concentration was measured by use of a commercially available radioimmunoassay kit.<sup>21,b</sup> Free  $T_4$  concentrations were determined by use of equilibrium dialysis.<sup>22,c</sup> Serum total  $T_3$  concentrations were measured with an in-house charcoal-separation radioimmunoassay.<sup>23</sup> Free  $T_3$  concentrations were measured with a commercial analogue-based radioimmunoassay.<sup>24,d</sup> Thyroid-stimulating hormone concentrations were measured with an immunoradiometric assay.<sup>25,e</sup> Thyroglobulin autoantibody concentrations were determined by use of an ELISA.<sup>26,f</sup> The presence of autoantibodies against  $T_3$  and  $T_4$  was determined via radiometric assays as described elsewhere.<sup>27</sup> Not all measurements were performed on each sample because of insufficient volume in some samples. Because of the potential for autoantibodies to interfere with thyroid hormone assays and yield artifactually high or low results, data regarding total  $T_4$  and total and free  $T_3$  values were removed from the statistical analyses for dogs with positive  $T_4$  and  $T_3$  autoantibody results, respectively.

The limits of quantification for the total  $T_4$ , free  $T_4$ , total  $T_3$ , free  $T_3$ , and TSH assays were 2.1 nmol/L, 1.8 pmol/L, 0.28 nmol/L, 0.3 pmol/L, and 0.03 ng/mL, respectively. Hormone results less than the limit of quantification of the assay were assigned a value equal to the limit of quantification. Standard reference limits were based on values obtained from the sera of healthy dogs of various breeds owned by staff, students, and faculty of the College of Veterinary Medicine, Michigan State University, and were those used by the endocrine laboratory at the time the study was performed.

**Statistical analysis**—Statistical analysis was performed with commercially available software.<sup>8</sup> Continuous data were tested for normality by use of the Kolmogorov-Smirnov method. Because this method revealed a nonparametric data distribution, the median and associated reference limit based on 2.5th to 97.5th percentiles were reported for each thyroid hormone variable. A  $\chi^2$  analysis was performed to ensure equal distribution of each categorical variable between groups

(AKC vs COO; performing vs nonperforming). Mann-Whitney *U* testing was used to compare results between groups. The Holm-Bonferroni correction method was applied when multiple comparisons were performed. Spearman rank correlation testing was used to determine the effect of age and body weight on each variable. Values of  $P < 0.05$  were considered significant.

## Results

**Animals**—In part 1 of the study, 4,309 serum samples from sighthounds were submitted for assessment during the investigation period; 803 samples were from dogs that were receiving  $T_4$  supplementation at the time of sample collection. Pretreatment thyroid hormone results were available for 398 dogs, comprising results for 347 Greyhounds, 22 Borzois, 11 Salukis, 14 Irish Wolfhounds, and 4 Scottish Deerhounds.

For part 2 of the study, blood samples were collected from 335 Salukis. Samples from 52 Salukis failed to meet inclusion criteria, leaving results from 283 dogs for interpretation. Of the 283 dogs, 154 (54.4%) were female (15 neutered) and 129 (45.6%) were male (6 neutered), with ages ranging from 12 to 167 months (median, 61 months). The median body weight was 22.7 kg (49.9 lb; range, 13.6 to 34.2 kg [29.9 to 75.2 lb]). Two hundred thirty-one were AKC-registered dogs, and 52 were COO dogs. Forty-nine (17.3%) were actively competing in coursing events, and 234 (82.7%) were pet or nonperforming dogs.

**Diagnosis of hypothyroidism in sighthounds**—Examination of the pretreatment diagnostic profiles revealed that practitioners who had submitted blood samples for thyroid hormone testing had also diagnosed hypothyroidism in 286 of 398 (71.9%) sighthounds on the basis of low serum concentrations of total  $T_4$  or total  $T_3$ . Seventeen (4.3%) sighthounds also had low free  $T_4$  or free  $T_3$  concentrations, and 30 (7.5%) sighthounds received a diagnosis of hypothyroidism despite all measured thyroid hormone concentrations being within their respective reference limits. Only 65 (16.3%) sighthounds had additional abnormalities suggestive of hypothyroidism (high serum TSH concentration or positive TGAA result in addition to a low iodothyronine concentration). When individual breeds were assessed separately, 305 (87.9%) Greyhounds, 9 (40.9%) Borzois, 7 (63.6%) Salukis, 8 (57.1%) Irish Wolfhounds, and 4 (100%) Scottish Deerhounds received a diagnosis of hypothyroidism on the basis of low serum iodothyronine concentration alone.

**Serum thyroid hormone concentrations in Salukis**—Results of thyroid hormone assays were summarized (Table 1; Figures 1–5). When compared with standard (non-breed-specific) reference limits, 154 of 282 (54.6%) Salukis had total  $T_4$  values and 67 of 216 (31.0%) Salukis had free  $T_4$  values that were lower than respective lower reference limits. Less than 1% of values were higher than respective upper reference limits. One hundred twenty of 281 (42.7%) Salukis had total  $T_3$  concentrations less than and 2 Salukis (0.7%) had values greater than the lower and upper reference limit, respectively. Fifty-one of 271 (18.8%) Salukis had free

Table 1—Median serum concentrations of total and free  $T_4$ , total and free  $T_3$ , and TSH in healthy Salukis  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States.

Thyroid hormone	No. of dogs tested	Median	Saluki reference limits	General canine reference limits
Total $T_4$ (nmol/L)	282	13.0	2.8–40.0	15.0–50.0
Free $T_4$ (pmol/L)	216	12.0	2.0–30.3	9.0–40.0
Total $T_3$ (nmol/L)	281	1.0	0.4–2.1	1.0–2.5
Free $T_3$ (pmol/L)	271	4.0	1.6–7.7	2.8–6.5
TSH (ng/mL)	282	0.18	0–0.86	0–0.48

The Saluki reference interval was calculated on the basis of 2.5th and 97.5th percentile values. The non-breed-specific (general canine) reference limit represents that of the testing laboratory at the time the study was performed.

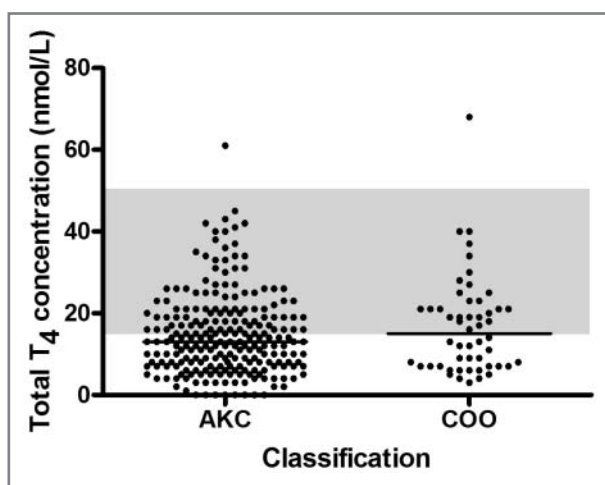


Figure 1—Dot plots summarizing serum total  $T_4$  concentrations in healthy Salukis ( $n = 282$ )  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States. Data are grouped by dog origin (AKC or COO). The shaded region indicates the non-breed-specific laboratory reference limits for each variable at the time the study was performed, and the horizontal bars indicate the median value within each group.

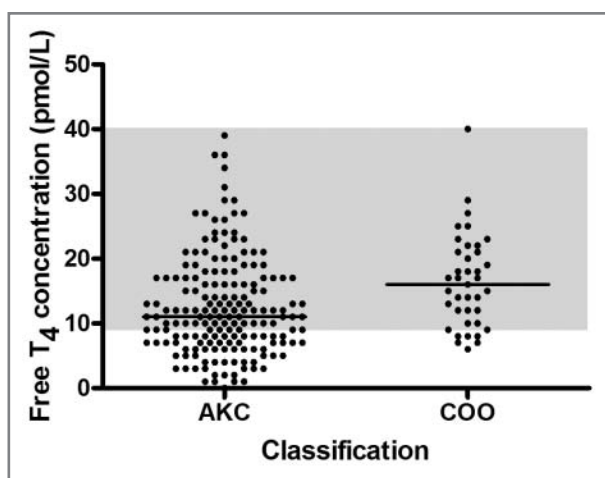


Figure 2—Dot plots summarizing serum free  $T_4$  concentrations in healthy Salukis ( $n = 216$ )  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States. See Figure 1 for remainder of key.

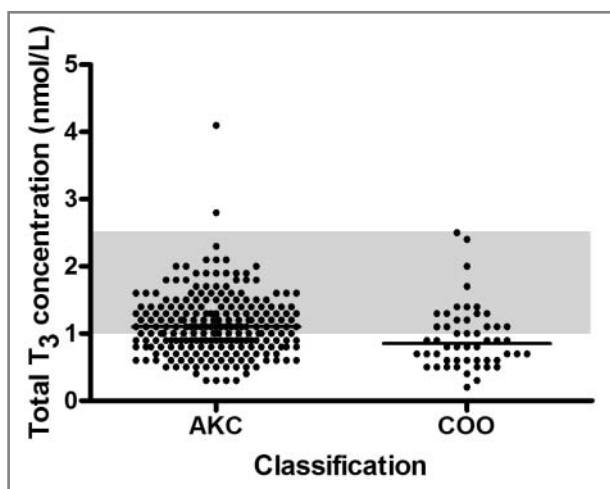


Figure 3—Dot plots summarizing serum total  $T_3$  concentrations in healthy Salukis ( $n = 281$ )  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States. See Figure 1 for remainder of key.

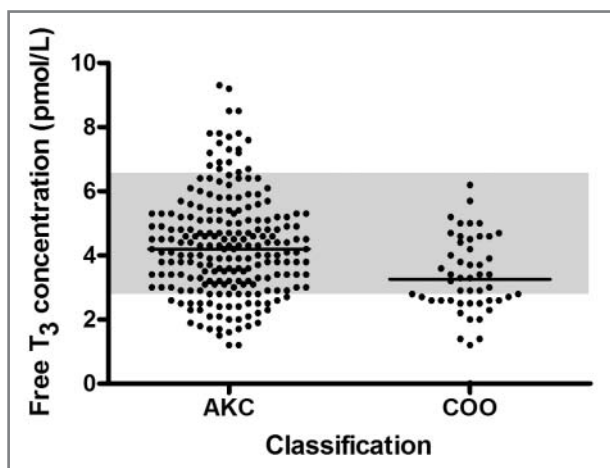


Figure 4—Dot plots summarizing serum free  $T_3$  concentrations in healthy Salukis ( $n = 271$ )  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States. See Figure 1 for remainder of key.

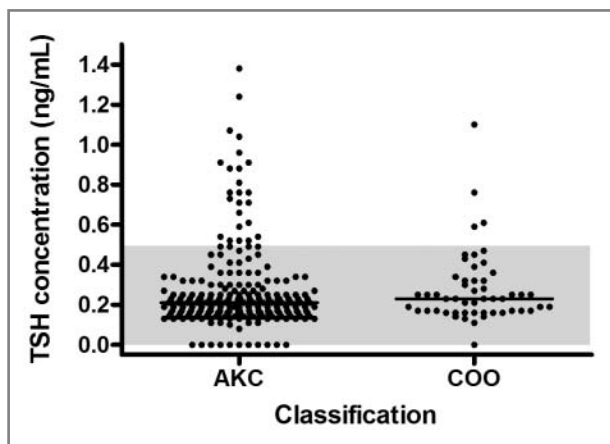


Figure 5—Dot plots summarizing serum TSH concentrations in healthy Salukis ( $n = 282$ )  $\geq 12$  months of age from which blood samples were obtained at various events and locations in the United States. See Figure 1 for remainder of key.

$T_3$  concentrations less than the lower reference limit, and 20 (7.4%) had values greater than the upper reference limit.

Two hundred fifty-seven of 282 (91.1%) TSH values were within reference limits, and 25 (8.9%) values exceeded the upper reference limit. Twelve of these 25 Salukis had total  $T_4$ , 5 of 19 had free  $T_4$ , 8 of 25 had total  $T_3$ , and 2 of 24 had free  $T_3$  concentrations that were less than the lower limit of their respective standard reference limits. Four of the 25 Salukis with TSH values exceeding the upper reference limit had positive results of TGAA testing, and none had positive results for  $T_4$  or  $T_3$  autoantibodies. No significant differences were detected between dogs with high and within-reference-interval TSH concentrations when iodothyronine concentrations or body weights were compared.

Thyroxine and  $T_3$  autoantibodies were detected in the serum of 1 (0.4%) and 2 (0.8%) Salukis, respectively. Thyroglobulin autoantibodies were detected in the serum of 13 (4.6%) Salukis. Among the Salukis with positive TGAA results, 7 of 13 had total  $T_4$ , 2 of 8 had free  $T_4$ , 5 of 13 had total  $T_3$ , and 0 of 12 had free  $T_3$  concentrations in serum less than the lower limit of their respective standard reference limits. Five of 13 Salukis had an increased serum TSH concentration. Serum total  $T_4$ , free  $T_4$ , total  $T_3$ , free  $T_3$ , and TSH concentrations and body weight were not significantly different when values from TGAA-positive and TGAA-negative Salukis were compared.

Serum total and free  $T_4$  concentrations were significantly ( $P < 0.001$ ) lower in male versus female Salukis. There was no significant sex difference in any other measured variable, nor was there a significant difference between sexually intact and neutered Salukis when males and females were grouped or between sexually intact and spayed females. Sample sizes were too small to allow comparison of sexually intact male and castrated dogs.

Serum total  $T_4$ , free  $T_4$ , and TSH concentrations were correlated with age ( $r = -0.12$ ,  $P = 0.036$ ;  $r = -0.22$ ,  $P < 0.001$ ; and  $r = 0.35$ ,  $P < 0.001$ , respectively) and body weight ( $r = -0.17$ ,  $P = 0.006$ ;  $r = -0.27$ ,  $P < 0.001$ ; and  $r = 0.14$ ,  $P = 0.020$ , respectively). Multicollinearity confounded interpretation of these results; the correlation identified between age and body weight ( $r = 0.19$ ;  $P = 0.001$ ) precluded the use of multiple regression analysis to assess the individual effect of each factor on serum concentrations of each type of thyroid hormone.

Salukis registered with the AKC had significantly higher total  $T_3$  ( $P = 0.001$ ) and free  $T_3$  ( $P < 0.001$ ) and significantly ( $P = 0.001$ ) lower free  $T_4$  concentrations in serum than did COO Salukis. When values for performing and nonperforming Salukis were compared, no significant differences were detected.

Male Salukis were significantly ( $P < 0.001$ ) heavier than female Salukis (median weight, 25.0 and 20.5 kg [55.0 and 45.1 lb]), respectively. There was no significant difference in median age and median body weight or activity and sex distribution between the AKC and COO dogs. The low number of TGAA-positive Salukis within each group precluded comparison of the prevalence of positive TGAA results between groups.



## Discussion

Part 1 of the present study involving various sighthound breeds revealed that low iodothyronine concentration was the most common criterion used by veterinarians who submitted serum samples for thyroid hormone testing to support a diagnosis of hypothyroidism. Although low iodothyronine concentrations in several breeds of healthy sighthounds have been reported,<sup>5,8-16,a</sup> a diagnosis of hypothyroidism was made on the basis of this abnormality alone in > 80% of dogs in our study.

There are some limitations to this form of analysis. First, it can be argued that some of the sighthounds in the present study were truly hypothyroid, given that 49% of hypothyroid dogs have negative TGAA results, and TSH concentrations are reportedly within reference limits in 13% to 42.3% of affected dogs.<sup>1,18,28</sup> Second, individual test results should be considered in conjunction with clinical and routine clinicopathologic findings, but this information was not available in our study. Third, because the interval between collection and testing of pretreatment blood samples and commencement of treatment for hypothyroidism was variable, a small proportion of dogs may have developed hypothyroidism in the intervening period. However, the results suggested that when hypothyroidism was diagnosed within these breeds by practitioners, that diagnosis was most commonly based upon apparently low iodothyronine concentrations when compared with non-breed-specific reference limits. Given the low values previously reported for healthy sighthounds,<sup>5,8-16,a</sup> low iodothyronine concentrations cannot be used reliably to confirm a diagnosis of hypothyroidism. In addition, the diagnosis of hypothyroidism in 7.5% of dogs despite all thyroid hormone concentrations being within reference limits was inappropriate given the high sensitivity of indices such as serum total and free  $T_4$  concentrations for detecting hypothyroidism.<sup>1</sup>

The median serum total  $T_4$  concentration (13 nmol/L) identified in healthy Salukis in part 2 of the present study was comparable to the mean total serum  $T_4$  concentrations of 4.9 to 18.8 nmol/L reported elsewhere for Greyhounds.<sup>5,8-10,12,15,a</sup> Similarly, low total  $T_4$  values have been detected in Whippets<sup>11</sup> (mean, 20.7 nmol/L) and Irish Wolfhounds<sup>16</sup> (median, 21.0 to 25.0 nmol/L). The median serum free  $T_4$  concentration (12.0 pmol/L) was also comparable to mean values of 11.6 to 29.6 pmol/L reported for Greyhounds.<sup>5,10,12</sup> This finding was in contrast to that of a report involving Whippets in which mean serum free  $T_4$  concentration (20.4 pmol/L) was not significantly different from that of a control group, and only 2% of dogs had values less than the lower standard reference limit.<sup>11</sup> Although an early report<sup>b</sup> involving Greyhounds suggested that low serum  $T_4$  concentration is associated with clinical signs of hypothyroidism, it is now generally accepted that the low concentration reflects physiologic variation rather than a pathological state. Given the comparable results in the healthy Salukis in our study, the same is likely true within that breed.

In the present study, median serum total and free  $T_3$  concentrations were 1.0 nmol/L and 4.0 pmol/L, respectively, in healthy Salukis. Reports of serum total  $T_3$

concentrations in Greyhounds have indicated conflicting results, with studies revealing similar,<sup>5</sup> relatively high,<sup>9,12</sup> or relatively low<sup>a</sup> serum total  $T_3$  concentrations in comparison with concentrations in other dog breeds. Irish Wolfhounds have values comparable to those of other breeds.<sup>16</sup> Although > 40% of the total  $T_3$  values in the present study were less than the lower standard reference limit, most dogs had free  $T_3$  concentrations within reference limits. Because  $T_3$  is more metabolically active than  $T_4$ , and free hormone concentration correlates with tissue uptake,<sup>29</sup> this could explain how metabolic function is maintained in these dogs despite marked decreases in total and free  $T_4$  and total  $T_3$  concentrations.

The TSH concentration exceeded the upper standard reference limit in 25 (8.9%) serum samples from healthy Salukis in the present study. Subclinical hypothyroidism cannot be excluded in these dogs; however, iodothyronine concentrations in those samples were not significantly different from those of the other Salukis, only 4 had positive results of TGAA testing, and none had detectable  $T_4$  or  $T_3$  autoantibodies. Most Salukis had TSH values within the standard reference limits, which has been reported for other sighthound breeds.<sup>5,10-13</sup>

The prevalences of antibodies against thyroglobulin and thyroid hormones were comparable to values of < 5% in other reports<sup>18,19</sup> of dogs with healthy thyroid function and to values of 3.6% and 2.0% in healthy Greyhounds<sup>15</sup> and Whippets,<sup>11</sup> respectively. However, because most studies regarding the prevalence of autoantibodies in individual breeds are biased by inclusion of samples from dogs in which there is already a clinical suspicion of hypothyroidism, breed-specific prevalences cannot be easily compared with the results of the present study.

Serum total and free  $T_4$  concentrations were significantly lower in male versus female Salukis in our study. Results of studies in which the effect of sex on thyroid gland function in dogs was evaluated are conflicting. Although lower mean 24-hour serum total  $T_4$  concentrations in male versus female crossbreed dogs were detected in 1 study,<sup>30</sup> other studies failed to reveal a significant difference between the sexes.<sup>4</sup> Results of the present and previous studies may have been confounded by the effect of diestrus in the female dogs; an increase in serum total  $T_4$  concentration can develop during this phase of the reproductive cycle.<sup>31</sup> Information on stage of reproductive cycle was not collected in the present study. Our results also could have been affected by the significantly higher body weight of male versus female dogs; increasing body weight was associated with a decrease in total and free  $T_4$  concentrations.

Significant differences between AKC-registered and COO Salukis were detected in serum total and free  $T_3$  and free  $T_4$  concentrations. The AKC first recognized and registered the Saluki as a pure breed in 1929,<sup>32</sup> and these dogs have generally been selectively bred for adherence to conformation standards rather than athletic ability since that time. By contrast, COO dogs are imported from the Middle East and can be registered with the Society for the Perpetuation of the Desert Bred Saluki. The COO dogs have been selectively bred in their

native habitat largely for hunting performance rather than adherence to AKC breed conformation standards. There is some overlap between classifications because the third generation of these dogs bred to AKC Salukis can be registered and can compete in AKC events. Although significant differences between AKC and COO Salukis were identified in our study, there was no difference between those groups in the proportion of dogs with low thyroid hormone concentrations. This suggested that the observed deviations from the standard reference limits reflected a physiologic difference in thyroid hormones within the breed, similar to that reported for other sighthound breeds,<sup>4,5,8-16</sup> rather than an effect of selective breeding within the AKC-registered Salukis.

In the study reported here, serum total and free  $T_4$  concentrations were negatively correlated and serum TSH concentrations were positively correlated with age. Results of most prior studies suggest a similar inverse correlation between total  $T_4$  and free  $T_4$  concentrations and age<sup>4,13,33</sup> as well as a high TSH concentration in older dogs.<sup>34</sup> Although lower mean total  $T_3$  concentrations have been detected in older versus younger dogs,<sup>4</sup> age had no effect on total or free  $T_3$  concentrations in our study. The reason for the difference between our findings and those of the other studies is unclear.

Serum total and free  $T_4$  concentrations were also negatively correlated, and TSH concentrations were positively correlated, with body weight. Large- and medium-sized dog breeds reportedly have lower total  $T_4$  concentrations than do small-sized breeds (25.0, 26.1, and 31.5 nmol/L, respectively), and medium-sized breeds have a higher mean serum total  $T_3$  concentration than do small- or large-sized breeds.<sup>4</sup> By contrast, obese dogs have a 51.6% to 71.6% higher serum total  $T_4$  concentration than do healthy dogs in good body condition.<sup>35,36</sup> Higher total  $T_3$  concentrations have also been detected in obese versus nonobese dogs, but free  $T_4$  and TSH concentrations do not appear to differ between the 2 groups.<sup>36</sup> In the present study, it is likely that weight differences were attributable to variation in body size and body condition. Because no information on body condition was obtained, comparisons between our results and those of other studies are difficult. Hypothyroidism can be associated with weight gain; however, none of the Salukis in our study had any additional clinical signs of hypothyroidism, and the presence of a small number of hypothyroid obese dogs in our study would be unlikely to alter the results to a considerable degree. The correlation between age and body weight precluded use of additional statistical analyses to determine the relative effect of either factor on serum total  $T_4$ , free  $T_4$ , or TSH concentration. Although statistically significant, the effects of age and body weight were unlikely to be clinically important because of the small magnitude of change.

The cause of the differences between serum thyroid hormone concentrations in sighthound and other dog breeds is unknown. A decrease in the function or affinity of thyroid hormone-binding protein could affect circulating thyroid hormone concentrations. Differences in  $T_4$  and  $T_3$  metabolism, thyroid hormone receptor function, or pituitary sensitivity to thyroid

hormone feedback could also contribute. Research into the physiologic actions and effects of thyroid hormones in sighthound breeds is needed.

The diagnosis of hypothyroidism in Salukis and other sighthounds poses a considerable challenge for practitioners. Existence of multiple low serum iodothyronine concentrations in healthy sighthounds decreases the ability to distinguish between euthyroid and hypothyroid dogs; however, maintenance of thyroid hormone concentrations within non-breed-specific reference limits may be useful to exclude hypothyroidism. In nonsighthound breeds, serum total and free  $T_4$  concentrations are sensitive indicators for diagnosis of hypothyroidism, with reported sensitivities ranging from 88% to 100% and 80% to 97%, respectively.<sup>1,37,38</sup> Therefore, dogs from both sighthound and nonsighthound breeds with values within the standard reference limits are unlikely to be hypothyroid. The reported sensitivity (52%) of serum total  $T_3$  measurement is lower than the value for  $T_4$  measurement; thus, maintenance within reference limits cannot exclude hypothyroidism.<sup>37</sup> In Salukis, most serum free  $T_3$  concentrations are within the standard reference limits; however, the value of free  $T_3$  measurement to distinguish between hypothyroid and euthyroid dogs is largely unknown. Serum TSH concentrations in sighthounds are similar to those reported for other breeds, and results of most studies<sup>1,28,39-41</sup> indicate the specificity of this test for the diagnosis of hypothyroidism is high, ranging from 69% to 100%. Measurement of serum TSH concentration may be particularly useful for the diagnosis of hypothyroidism in sighthound breeds in which the specificities of  $T_4$  and  $T_3$  measurements are low; however, the poor sensitivity of serum TSH measurement limits its value as a routine screening test.<sup>1,28,39-41</sup> Although ultrasonography and scintigraphy of the thyroid gland have promise in distinguishing between hypothyroid and euthyroid dogs,<sup>42-44</sup> diagnostic laboratory-based tests would be ideal in a clinical setting. Additional studies are necessary to determine which thyroid hormone measurements are useful to distinguish between hypothyroid and euthyroid sighthounds and to define optimal cutoff values for the confirmation or exclusion of hypothyroidism in these breeds.

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