Evaluation of Thyroid-Stimulating Hormone, Total Thyroxine, and Free Thyroxine Concentrations in Hyperthyroid Cats Receiving Methimazole Treatment

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**Background:** Iatrogenic hypothyroidism (IH) after treatment of hyperthyroidism can impair renal function. No study compared the efficacy of measurement of serum free thyroxine by equilibrium dialysis (fT4ed) or thyroid-stimulating hormone (TSH) concentrations for monitoring cats receiving methimazole.

**Objectives:** To (1) compare the ability of total T4 and fT4ed concentrations in conjunction with TSH to define thyroid function in hyperthyroid cats receiving methimazole, (2) determine the prevalence of IH in cats receiving methimazole, and (3) examine the relationship between thyroid axis hormones and serum creatinine concentration.

**Animals:** One hundred and twenty-five serum samples from hyperthyroid cats receiving methimazole and total T4 concentrations ≤3.8 μg/dL.

**Methods:** Total T4, fT4ed, and TSH concentrations were measured to evaluate thyroid status and serum creatinine concentration was measured to assess renal function. A low total T4 or fT4ed concentration in combination with an increased TSH concentration defined IH.

**Results:** Forty-one cats (33%) had increased TSH concentrations. Of cats with total T4 and fT4ed concentrations below the reference range, 68% and 73%, respectively, had TSH concentrations above the reference range. Only 18% of cats with a normal TSH concentration had an increased serum creatinine concentrations as compared to 39% of those with increased TSH concentrations (P < .001).

**Conclusions:** Free T4ed does not identify more cats with potential IH as compared to total T4. The IH prevalence was approximately 20%. Measurement of TSH may be more helpful in indicating that azotemia, if present, is at least in part related to IH. Investigation is needed to define TSH assay utility in identifying possible subclinical IH.

**Key words:** Creatinine; Hypothyroidism; Subclinical.

The interplay between hyperthyroidism and renal function has been extensively studied in cats. Hyperthyroidism increases glomerular filtration rate (GFR), and its treatment results in a subsequent decrease in GFR. When underlying kidney disease is present, the decrease in GFR can contribute to development of azotemia and decreased survival time; iatrogenic hypothyroidism (IH) after treatment for hyperthyroidism may play a role. Approximately 15–17% of cats receiving methimazole and 33–49% of cats treated with radioactive iodine (131I) or bilateral thyroidectomy became azotemic within 6 months of treatment initiation. Pre-existing azotemia can decrease overall survival times in cats treated for hyperthyroidism. On the other hand, treatment of IH may improve renal function.

Despite the potential link between IH and azotemia, the best means of monitoring cats after treatment has not been determined. Iatrogenic hypothyroidism potentially could be defined best as the presence of a low serum thyroid hormone concentration in combination with the appropriate physiological response of an increased TSH concentration. Clinical hypothyroidism can be difficult to judge, because after resolution of hyperthyroidism, cats are expected to sleep more, eat less and gain weight, signs also consistent with hypothyroidism. To our knowledge, only a single study has measured total T4 and TSH concentrations in cats receiving medical treatment for hyperthyroidism. Surprisingly, 48% of cats had a combination of low total T4 and increased TSH concentrations, suggesting IH may be common. The prevalence of IH has not been confirmed in an independent study, to our knowledge.
Measurement of serum total thyroxine concentration (T4) is commonly used for therapeutic monitoring. Total T4 concentrations can be difficult to evaluate; however. Given that cats with hyperthyroidism are older and more likely to have other diseases, especially renal disease, total T4 concentration may be below the reference range even if IH is not present. Serum free thyroxine concentration as measured by equilibrium dialysis (fT4ed) may be a better marker of thyroid function than total T4 concentration. To our knowledge, fT4ed concentrations during treatment with methimazole have not been evaluated to determine if they are easier to interpret than total T4 concentrations. If fT4ed concentrations, as compared to total T4 concentrations, are more likely to be normal in cats with thyroid status in cats receiving methimazole treatment. Nonthyroidal illness (NTI) and age are not expected to increase TSH concentrations in the majority of patients. In dogs, for example, approximately only 10% of euthyroid patients with nonthyroidal disease have increased TSH concentrations. If high TSH concentrations are common in cats receiving methimazole treatment and the combination of a low total T4 or fT4ed concentration together with a high TSH concentration is associated with azotemia, veterinarians should routinely measure TSH concentrations in cats receiving methimazole, which is not the current practice.

The primary objectives of this study were: (1) to determine the prevalence of IH in an independent study with a large number of cats receiving methimazole treatment; (2) to compare the ability of total T4 and fT4ed concentrations in conjunction with TSH concentrations to define thyroid function status in hyperthyroid cats receiving methimazole, and (3) to examine the relationship between thyroid axis hormones and serum creatinine concentration. A secondary objective was to evaluate a possible association between the dose of methimazole and IH and azotemia. We hypothesized that serum fT4ed concentrations would be a better marker of thyroid function than total T4. Accordingly, fT4ed concentration would be below the reference range in more cats with an increased TSH concentration as compared to total T4 concentrations, thus identifying more cats with IH than identified by total T4. We further hypothesized that fT4ed concentrations would more closely correlate (negatively) with serum creatinine concentration as compared to total T4 or TSH.

Materials and Methods

Cats

A total of 125 serum samples from previously diagnosed hyperthyroid cats receiving methimazole treatment and with total T4 concentrations ≤3.9 µg/dL (ie, within or below the reference range) were included. Samples had been submitted consecutively to the diagnostic laboratories at Auburn University (n = 18) and Michigan State University (n = 107) between May 5 and October 25, 2012. Samples with sufficient volume for performance of all assays were used.

Experimental Protocol

All cats were receiving methimazole at the time of sample submission; doses ranged from 1.25 mg PO q24 h to 10 mg PO q12 h. Serum samples were submitted for routine evaluation of treatment and were frozen at −20°C until used for the study. For the study, all samples were reanalyzed at a single laboratory (see below). Age, breed, and sex of the cats and methimazole dose were obtained from the sample submission forms when provided. Reference ranges were 0.8–3.9 µg/dL, 0.8–3.9 ng/dL, and ≤0.3 ng/mL for total T4, fT4ed, and TSH concentrations, respectively. Lower reference ranges (ie, the lower half of the reference range) for total T4 and fT4ed were 0.8–1.9 µg/dL and 0.8–1.9 ng/dL, respectively. Higher reference ranges (ie, the higher half of the reference range) for total T4 and fT4ed were 2.0–3.9 µg/dL and 2.0–3.9 ng/dL. The reference range for serum creatinine concentration was ≤2.0 mg/dL.

Assay Procedures

Total T4 and fT4ed concentrations were measured by assays previously validated in cats. Circulating concentrations of TSH in feline serum were measured with a commercially available immunoradiometric assay for canine TSH that displays binding for feline TSH. Sample volumes and assay procedures were carried out according to the manufacturer’s protocol. Two pools of feline serum using clinical samples selected as having low or normal concentrations of thyroid hormones were made for validation studies. The “high-TSH” and “normal-TSH” pools had respective mean concentrations of 2.8 and 0.1 ng/mL across repeatability studies. When aliquots of the “high-TSH” pool were diluted with assay zero standard at rates of 1:2, 1:4, and 1:8, the percentages observed/expected results for the dilutions were 106%, 129%, and 133%, respectively. When aliquots of the “high-TSH” pool were mixed with the “normal-TSH” pool at rates of 1:2, 1:4, and 1:8, the percentages of observed/expected results were 114%, 105%, and 92%, respectively. The respective interassay coefficients of variation for 11 replicates of the “high-TSH” and “normal-TSH” pools were 1.3% and 14%. The respective interassay coefficients of variation for the “high-TSH” and “normal-TSH” pools were 2.9% and 9.7% across 8 assays.

To set the reference range, samples from 50 cats with were used. Twenty-one of the samples were from young adult, clinically healthy, neutered laboratory cats. Eight of the samples were from historically healthy cats; serum had been submitted for feline virus screening and viral tests were negative. The remaining 21 samples were clinical samples from cats with normal baseline thyroid hormone concentrations and normal response to a T3 suppression test (ie, suppression of the total T4 concentration to <1.6 µg/dL after administration of 20 µg liothyronine sodium [T3] 3 times daily for 2 days, then 20 µg liothyronine sodium on day 3; given 2–4 hours before sampling). The TSH concentrations from the clinical samples submitted for thyroid testing were compared with those of the other cats, and were not significantly different. Thus, they were combined to represent a group of cats with normal thyroid function. A reference range of 0.3–2.4 ng/mL was established using the 2.5–97.5 percentiles of the data set.

A single batch was run for each hormone when possible. The sensitivities of the assays were 0.5 µg/dL and 0.4 ng/dL for total T4 and fT4ed, respectively. For statistical purposes, concentrations below the sensitivity of the assays were set at 0.25 µg/dL for total T4 and 0.2 ng/dL for fT4ed. For TSH, results were not
extrapolated below the concentration of the lowest standard and were reported as 0.1 ng/mL; concentrations above the highest standard (12.3 ng/mL) were reported as 13 ng/mL. Serum creatinine concentration was measured by an automated analyzer.

### Statistical Analyses

The Shapiro-Wilk test was used to evaluate normality of data, and the data were determined to be nonparametric. The Mann-Whitney test was used to compare total T4 and fT4ed concentrations as well as methimazole dose between cats with a TSH concentration within or above the reference range. Nonparametric correlation was tested using a Spearman Rank Order test. The correlations were qualified using the following scale: $r = 0 - 0.10$ was no correlation, $r = 0.11 - 0.30$ was a weak correlation, $r = 0.31 - 0.70$ was a moderate correlation, and $r > 0.71$ was a strong correlation. Frequencies were compared among groups using a Chi-squared test. Data are expressed as median (range). Significance for all tests was set at the $P < .05$ level.

### Results

#### Patient Population

Cats included 59 spayed females, 1 intact female, 59 castrated males, and 1 intact male; sex was not specified for 5. The breeds represented included 87 domestic short hair, 19 domestic long hair, 7 domestic medium hair, 4 Siamese, 2 Siamese crosses, 2 Himalayans, 1 Burmese and 3 unknown. Ages ranged from 6 to 20 years (median, 14.5; mean, 14.3) for 123 cats and were not provided for the remaining 2.

#### Relationship between Total T4, fT4ed, and TSH

The median total T4 concentration for all cats was 1.2 (range, 0.2–3.7) µg/dL. Of 38 cats with total T4 concentrations below the reference range, 26 (68%) had TSH concentrations above the reference range. For cats with TSH concentrations above and within the reference range, the median total T4 concentrations were 0.5 (range, 0.2–3.1) µg/dL and 1.7 (range 0.2–3.7) µg/dL, respectively, which were significantly different ($P < .001$; Fig 1). The median fT4ed concentration for all cats was 1.4 (range, 0.2–6.0) ng/dL. Of 30 cats with low fT4ed concentrations, 22 (73%) had increased TSH concentrations. For cats with TSH concentrations above and within the reference range, the median fT4ed concentrations were 0.6 (range, 0.2–2.7) ng/dL and 1.9 (range, 0.2–6.0) ng/dL, respectively, which were significantly different ($P < .001$; Fig 1). The TSH concentrations were within reference limits for 84 cats (0.1 [range, 0.1–0.3] ng/mL) and above reference range for 41 (1.6 [range, 0.4–13] ng/mL). Fifteen cats (12%) and 19 cats (15%) had an increased TSH concentration and a total T4 and fT4ed concentration, respectively, within the reference range. Thirteen cats (10%) had increased TSH concentrations and both total T4 and fT4ed were within the reference range. If defining IH by a combination of a low total T4 concentration or low fT4ed concentration with increased TSH concentration, the prevalence of IH in this study was 20.8% or 17.6%, respectively.

### Relationship between Thyroid Hormones and Creatinine Concentration

The serum creatinine concentration in cats with a total T4 concentration below the reference range (1.7 [range, 0.6–3.5] mg/dL) was not significantly different ($P = .063$) than the serum creatinine concentration in cats with a total T4 concentration within the reference range (1.6 [range, 0.4–3.6] mg/dL; Fig 2). The serum
creatinine concentration in cats with a fT4ed concentration below the reference range (1.7 [range, 0.6–3.5] mg/dL) was significantly different than the serum creatinine concentration in cats with a fT4ed concentration within the reference range (1.5 [range, 0.4–3.6] mg/dL; \( P = 0.033 \)). The serum creatinine concentration in cats with a TSH concentration above the reference range (2.0 [range, 0.7–3.5] mg/dL) was significantly different than the serum creatinine concentration in cats with a TSH concentration within the reference range (1.6 [range, 0.4–3.6]) mg/dL; \( P < 0.001 \)).

The distribution of cats with an increased serum creatinine concentration did not change significantly with the total T4 and fT4ed concentration (Table 2). However, the distribution did change significantly with TSH concentration (\( P = 0.019 \)); 18% (15/84) and 39% (16/41) of cats with a TSH concentration within and above the reference range, respectively, had a serum creatinine concentration above the reference range.

Total T4 and fT4ed concentrations each were significantly but weakly negatively correlated with serum creatinine concentration (\( P = 0.037 \) and 0.001, respectively; \( r = -0.187 \) and -0.290, respectively; data not shown). Serum creatinine and TSH concentrations had a significant positive, but weak correlation with each other (\( P = 0.009 \); \( r = 0.294 \); data not shown).

### Relationship between Methimazole Dose and Thyroid Function

Dose information was available for 113 cats. The dose ranged from 2.5 mg total/cat/day to 20 mg total/cat/day with a median of 5 mg/cat/day. Fifteen different dosing regimens were reported with doses being given 1 (13 cats, 12%), 2 (99 cats, 88%), and 3 (1 cat <1%) times daily. The median doses for cats with a total T4 concentration below the reference range and within the reference range were 7.5 mg/cat/day (range, 5–15) and 5 mg/cat/day (range, 2.5–20), respectively. Cats with a low total T4 concentration received a significantly higher dose of methimazole (\( P = 0.018 \)) than cats with a total T4 concentration within the reference range, but dose was not significantly different when comparing cats with a TSH concentration in the reference range to those with an increased TSH concentration. A significant correlation between dose and serum creatinine concentration was not detected.

### Discussion

In this study, we determined that approximately 20% of cats had IH if defined as a combination of a low thyroid hormone concentration and an increased TSH concentration.

### Table 2. Percentage of cats with serum creatinine concentrations above or within the reference range as categorized by total T4 and fT4ed concentration.

| Concentration Range | Serum Creatinine Concentration Categorized by Total T4 Concentration | Serum Creatinine Concentration Categorized by fT4ed Concentration |
|---------------------|--------------------------|--------------------------|
|                     | % Within the Reference Range (n = 94) | % Above the Reference Range (n = 31) | % Within the Reference Range (n = 90) | % Above the Reference Range (n = 30) |
| Below the reference range | 66 (n = 25) | 34 (n = 13) | 67 (n = 20) | 33 (n = 10) |
| Lower half of the reference range | 82 (n = 40) | 18 (n = 9) | 74 (n = 40) | 26 (n = 14) |
| Upper half of the reference range | 76 (n = 29) | 24 (n = 9) | 83 (n = 30) | 17 (n = 6) |
Serum creatinine concentrations in hyperthyroid cats receiving methimazole. RR = reference range. See Figure 1 for explanation of plot.

Fig 2. Serum creatinine concentrations in hyperthyroid cats receiving methimazole. RR = reference range. See Figure 1 for explanation of plot.
of thyroid hormone concentrations within the reference range in combination with a TSH concentration above the reference range results in a diagnosis of subclinical hypothyroidism (SH), and SH is linked to renal insufficiency and an increase in all-cause mortality. In our study, the percentage of cats with increased TSH concentrations was significantly higher in those with total T4 and fT4ed concentrations in the lower half of or below the reference range compared to those with concentrations in the upper half of the reference range. Thus, a low normal total T4 or fT4ed concentration in combination with an increased TSH concentration also may represent SH in cats, but further study is required for confirmation.

In the meantime, given the association of SH and mortality in humans, if a cat has a total T4 concentration within the reference range compared to those with concentrations in the lower half of or below the reference range, the percentage of cats with serum creatinine concentrations above the reference range (i.e., secondary to NTI) and the TSH concentration returns to the reference range after recovery and discharge from the hospital. A small percentage of dogs with NTI can have TSH concentrations above the reference range. Because TSH concentrations did not normalize in some cats suspected of IH after supplementation with a T4 concentration in the upper half of the reference range, other possible causes for increased TSH concentrations in cats with total T4 concentrations within the reference range are artifactual errors or the presence of NTI. Hypertension can cause TSH concentrations above the reference range as a result of NTI, and the TSH concentration returns to the reference range after recovery and discharge from the hospital. A small percentage of dogs with NTI can have TSH concentrations above the reference range.

Although total T4, fT4ed, and TSH concentrations correlated significantly with serum creatinine concentrations, the correlation was weak. Serum creatinine concentrations were significantly different between cats with a T4 concentration within or below the reference range and those with a TSH concentration within or above the reference range. Although populations overlapped, the amount of overlap was less when cats were classified by TSH concentration. In addition, although the percentage of cats with a serum creatinine concentration above the reference range was not significantly different between cats grouped by total T4 or fT4ed concentrations, the percentage of cats with serum creatinine concentrations above the reference range was significantly lower in cats with normal TSH concentrations (18%) as compared to those with increased concentrations (39%). Thus, TSH concentration may be a better indicator in cats receiving methimazole that treatment is causing IH and potentially contributing to azotemia. Alternatively, TSH has been shown to be increased in 20% of people with chronic renal failure and may be the result instead of the cause of the changes in serum creatinine concentration (i.e., secondary to NTI). Further study is needed to determine if decreasing the dose of methimazole lowers the TSH concentration and decreases azotemia.

The median methimazole dose for cats with a total T4 concentration within the reference range was 5 mg/cat/day (range, 2.5–20). Cats with low serum total T4 concentrations received significantly higher doses of methimazole ($P = .015$) than cats with total T4 concentrations within the reference range but dose was not significantly different when comparing cats with TSH concentrations in the reference range to those with increased TSH concentrations. In an early publication on treatment of hyperthyroid cats with methimazole, the median dose required was 10 mg/cat/day (range, 2.5–20). Thus, the doses required may have decreased over time, perhaps because of earlier diagnosis and treatment (i.e., lower doses required with milder disease). Accordingly, veterinarians should be conservative with the initial prescribed dose of methimazole.

This study had several limitations. As discussed above, the TSH assay is not species-specific, likely underestimating the incidence of IH. The retrospective nature of the study as well as the lack of data on clinical signs of hypothyroidism, other medications administered, and presence of NTI may make it more difficult to determine if the findings more difficult. In addition, information regarding duration of methimazole treatment was lacking. The possibility for persistent pituitary thyrotroph atrophy also may have led to an underestimation of the percentage of cats with IH.

In conclusion, our findings suggest that IH may be common in cats receiving methimazole treatment for treatment of hyperthyroidism, especially in those with total T4 or fT4ed concentrations below the reference range. Measurement of fT4ed concentration does not identify more cats with increased TSH and possible IH as compared to total T4 concentration. Measurement of TSH may be more helpful in identifying that azotemia, if present, is at least in part related to IH. Given the limitations of TSH measurement, a total T4 concentration, fT4ed concentration or both always must be measured together with the TSH concentration, and all hormone concentrations interpreted together. Because some cats had TSH concentrations above the reference range despite having total T4 or fT4ed concentrations within the reference range, further investigation is warranted in defining the clinical utility of the TSH assay in identifying SH and its possible role in morbidity and mortality associated with treatment of hyperthyroidism. In the meantime, in cats receiving methimazole treatment that have increased TSH concentrations and normal T4 or fT4ed concentrations in the lower half of the reference range or below, consideration should be given to lowering the methimazole dose. Last, methimazole doses used currently are lower than those reported in earlier literature, and consideration should be given to starting methimazole at a low dose.

Footnotes

a Coat-A-Count T4 assay, Siemens Medical Solution Diagnostics, Los Angeles, CA.
The study was funded in part by the Scott-Ritchey Research Center of Auburn University. The data were presented in part as a poster at the 2013 ACVIM Forum, Seattle, WA.

Conflict of Interest Declaration: Authors disclose no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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References

1. Adams WH, Daniel GB, Legendre AM. Investigation of the effects of hyperthyroidism on renal function in the cat. Can J Vet Res 1997;61:53–56.
2. Adams WH, Daniel GB, Legendre AM, et al. Changes in renal function in cats following treatment of hyperthyroidism using 131I. Vet Radiol Ultrasound 1997;38:231–238.
3. Boag AK, Neiger R, Slater L, et al. Changes in the glomerular filtration rate of 27 cats with hyperthyroidism after treatment with radioactive iodine. Vet Rec 2007;161:711–715.
4. Graves TK, Olivier NB, Nachreiner RF. Changes in renal function with treatment of hyperthyroidism in cats. Am J Vet Res 1994;55:1745–1749.
5. Williams TL, Elliot J, Syme HM. Association of iatrogenic hypothyroidism with azotemia and reduced survival time in cats treated for hyperthyroidism. J Vet Int Med 2010;24:1086–1092.
6. Becker TJ, Graves TK, Kruger JM, et al. Effects of methimazole on renal function in cats with hyperthyroidism. J Am Anim Hosp Assoc 2000;36:215–223.
7. Williams TL, Peak KJ, Brodbelt D, et al. Survival and the development of azotemia after treatment of hyperthyroid cats. J Vet Int Med 2010;24:863–869.
8. Milner RJ, Channell CD, Levy J, Shaer M. Survival time for cats with hyperthyroidism treated with iodine 131, methimazole, or both: 167 cases (1996–2003). J Am Vet Med Assoc 2006;228:559–563.
9. Williams TL, Elliott J, Syme HM. Effect on renal function of restoration of euthyroidism in hyperthyroid cats with iatrogenic hypothyroidism. J Vet Intern Med 2014;28:1251–1258.
10. Wakeling J, Moore K, Elliot J, Syme HM. Diagnosis of hyperthyroidism in cats with mild chronic kidney disease. J Small Anim Pract 2008;49:287–294.
11. Peterson ME, Melian C, Nichols CE. Measurement of serum concentrations of free thyroxine, total thyroxine, and total triiodothyronine in cats with hyperthyroidism and cats with non-thyroidal disease. J Am Vet Med Assoc 2001;218:529–536.
12. Peterson ME, Gamble DA. Effect of nonthyroidal illness on serum thyroxine concentrations in cats: 494 cases (1988). J Am Vet Med Assoc 1990;197:1203–1208.
13. Skinner ND. Thyroid hormone levels in cats: Colony average and the decrease with age. J Nutr 1998;128:2636S–2638S.
14. 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;219:765–769.
15. Peterson ME, Broussard JD, Gamble DA. Use of the thyrotropin-releasing hormone stimulation test to diagnose mild hyperthyroidism in cats. J Vet Int Med 1994;8:279–286.
16. Rutland BE, Nachreiner RF, Kruger JM. Optimal testing for thyroid hormone concentration after treatment with methimazole in healthy and hyperthyroid cats. J Vet Intern Med 2009;23:1025–1030.
17. Peterson ME, Becker DV. Radioiodine treatment of 524 cats. J Am Vet Med Assoc 1995;207:1422–1428.
18. Ferguson DC, Caffall Z, Hoenig M. Obesity increases free thyroxine proportionally to nonesterified fatty acid concentrations in adult neutered female cats. J Endocrinol 2007;194:267–273.
19. Wakeling J, Elliott J, Syme H. Evaluation of predictors for the diagnosis of hyperthyroidism in cats. J Vet Intern Med 2011;25:1057–1065.
20. Lo JC, Chertow GM, Go AS, Hsu C-Y. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. Kidney Int 2005;67:1047–1052.
21. Haentjens P, Van Meerhaeghe A, Poppe K, Velkeniers B. Subclinical thyroid dysfunction and mortality: An estimate of relative and absolute excess all-cause mortality based on time-to-event data from cohort studies. Eur J Endocrinol 2008;159:329–341.
22. Spencer C, Eigen A, Shen D, et al. Specificity of sensitive assays of thyrotropin (TSH) used to screen for thyroid disease in hospitalized patients. J Clin Chem 1987;33:1391–1396.
23. Peterson ME. Diagnostic testing for feline thyroid disease: Hypothyroidism. Compend Conti Educ Vet 2013;35:E4–E9.
24. Peterson ME, Kintzer PP, Hurvitz AI. Methimazole treatment of 262 cats with hyperthyroidism. J Vet Intern Med 1988;2:150–157.