

Pretreatment clinical and laboratory findings in dogs with primary hyperparathyroidism: 210 cases (1987–2004)

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Objective—To evaluate pretreatment clinical and laboratory findings in dogs with naturally occurring primary hyperparathyroidism.

Design—Retrospective study.

Animals—210 dogs with primary hyperparathyroidism and 200 randomly selected, age-matched control dogs that did not have primary hyperparathyroidism.

Procedure—Medical records for dogs with primary hyperparathyroidism were reviewed for signalment; clinical features; and results of clinicopathologic testing, serum parathyroid hormone assays, and diagnostic imaging.

Results—Mean age of the dogs with primary hyperparathyroidism was 11.2 years (range, 6 to 17 years). The most common clinical signs were attributable to urolithiasis or urinary tract infection (ie, straining to urinate, increased frequency of urination, and hematuria). Most dogs (149 [71%]) did not have any observable abnormalities on physical examination. All dogs had hypercalcemia, and most (136 [65%]) had hypophosphatemia. Overall, 200 of the 210 (95%) dogs had BUN and serum creatinine concentrations within or less than the reference range, and serum parathyroid hormone concentration was within reference limits in 135 of 185 (73%) dogs in which it was measured. Urolithiasis was identified in 65 (31%) dogs, and urinary tract infection was diagnosed in 61 (29%). Mean serum total calcium concentration for the control dogs was significantly lower than mean concentration for the dogs with primary hyperparathyroidism, but mean BUN and serum creatinine concentrations for the control dogs were both significantly higher than concentrations for the dogs with primary hyperparathyroidism.

Conclusions and Clinical Relevance—Results suggest that urolithiasis and urinary tract infection may be associated with hypercalcemia in dogs with primary hyperparathyroidism, but that development of renal insufficiency is uncommon. (*J Am Vet Med Assoc* 2005;227:756–761)

In dogs with naturally occurring primary hyperparathyroidism, hypercalcemia develops secondary to autonomous production of parathyroid hormone (PTH).^{1,2} Most often, the condition is caused by a solitary parathyroid gland adenoma,^{3,4} but less commonly, it develops as a result of a parathyroid gland carcinoma or an autonomously functioning hyperplastic parathy-

roid gland or glands.⁵ A small percentage of affected dogs have been described as having 2 abnormal parathyroid glands simultaneously or sequentially.^{6,7}

Naturally occurring primary hyperparathyroidism is uncommon in dogs, and we are aware of fewer than 100 dogs with this disease having been described in the veterinary literature since 1988. Most previous reports of primary hyperparathyroidism in dogs have been small case series,^{3,4} descriptions of dogs with unusual forms of the disease (eg, dogs with primary parathyroid hyperplasia³), reports of new diagnostic tests (eg, assays for determining PTH concentration,^{8,9} methods for ultrasonography of the neck^{10,11} or scintigraphy of the parathyroid glands,^{12,13} and assays of blood samples from various venous locations¹⁴), or descriptions of novel therapeutic strategies (eg, ultrasound-guided chemical¹⁵ or heat¹⁶ ablation). As a result, a study involving a large number of dogs with primary hyperparathyroidism is needed to provide a more definitive description of the disease. The purpose of the study reported here, therefore, was to evaluate clinical and laboratory findings in a large group of dogs with naturally occurring primary hyperparathyroidism.

Criteria for Selection of Cases

Medical records of all dogs examined at the University of California Veterinary Medical Teaching Hospital between December 1987 and January 2004 in which a diagnosis of naturally occurring primary hyperparathyroidism had been made were reviewed. Dogs were included only if a diagnosis of primary hyperparathyroidism had been suspected on the basis of compatible history; clinical signs; and results of a physical examination, CBC, urinalysis, and serum biochemical analyses. Dogs in which primary hyperparathyroidism had been diagnosed were included only if serum total calcium concentration had been ≥ 12 mg/dL (reference range, 9.9 to 11.4 mg/dL) at least twice during a period of > 30 days prior to initiation of treatment and disorders other than chronic renal failure that can cause hypercalcemia had been excluded. In addition, dogs were included only if abdominal radiography or ultrasonography and thoracic radiography had been performed within 30 days prior to initiation of treatment and no evidence of neoplasia had been seen. Finally, dogs were included only if a solitary cervical parathyroid mass or 2 cervical parathyroid masses had been observed at surgery or by means of ultrasonography; the diagnosis had been confirmed on the basis of resolution of hypercalcemia within 5 days after initiation of specific treatment (ie, surgical removal of a parathyroid mass or masses or ultrasound-guided alcohol or heat ablation of a parathyroid mass or masses^{3,15,16}) for hyperparathyroidism; and, for dogs that underwent surgery, histologic changes in masses that

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were removed were consistent with parathyroid adenoma, parathyroid carcinoma, or parathyroid hyperplasia. Dogs that had received glucocorticoids in the 30 days prior to or following diagnosis of primary hyperparathyroidism and initiation of treatment were excluded.

Medical records of all dogs examined at the University of California Veterinary Medical Teaching Hospital between December 1987 and January 2004 were reviewed, and 200 dogs were randomly selected as a control population. Dogs were eligible for inclusion in the control group if they were ≥ 6 years old and results of serum biochemical analyses performed at the time of the hospital visit were available for review. Dogs in which primary hyperparathyroidism had been diagnosed were excluded from the control group.

Procedures

Medical records for dogs with primary hyperparathyroidism were reviewed for signalment; clinical features; and results of clinicopathologic testing, serum parathyroid hormone assays, and diagnostic imaging. Routine methods were used to perform serum biochemical analyses, CBCs, and urinalyses. Serum total calcium concentration was determined by means of colorimetric evaluation.^a Serum ionized calcium concentration was determined by means of ion-selective electrode analysis.^b Serum PTH concentration was determined by use of a validated 2-site immunoradiometric method that recognizes the amino- and carboxy-terminal ends of the intact molecule.^{8,9} All assays were performed in the clinical chemistry laboratory of the Veterinary Medical Teaching Hospital. Ultrasonography of the neck (ie, cervical ultrasonography), when performed, was performed with a 10-MHz, linear, phased-array transducer and a standard ultrasonography machine.^c

Statistical analyses—Data are reported as mean \pm SD. Two-tailed *t* tests were used to compare serum biochemical test results between dogs with primary hyperparathyroidism and control dogs. All analyses were performed with standard statistical software^d; values of *P* < 0.05 were considered significant.

Results

Signalment—Two hundred ten dogs in which primary hyperparathyroidism had been diagnosed met the criteria for inclusion in the study. Mean age of the dogs with primary hyperparathyroidism (11.2 years; range, 6 to 17 years) was not significantly different from mean age of the 200 control dogs (10.9 years; range, 6 to 16 years).

Mean body weight of the dogs with primary hyperparathyroidism was 22.2 kg (48.8 lb; range, 2.6 to 58.8 kg [5.7 to 129.4 lb]). There were 114 males (54%) and 96 females (46%); 106 of the males (93%) and 93 of the females (97%) were neutered. Forty-one (20%) of the dogs were Keeshonds; 29 (14%) were of mixed breeding; 18 (9%) were Labrador Retrievers; 13 (6%) each were German Shepherd Dogs or Golden Retrievers; 9 (4%) each were Poodles, Shih Tzu, or Springer Spaniels; 7 (3%) each were Australian Shepherds or Cocker Spaniels; 5 (2%) were Rhodesian Ridgebacks; and 4 (2%) each were Doberman Pinschers or Lhasa Apsos. The remaining 42 dogs comprised 31 other breeds.

Clinical features—Owners of 88 of the 210 (42%) dogs with primary hyperparathyroidism had sought veterinary care for reasons that appeared to be unrelated to any problems likely associated with hypercalcemia or primary hyperparathyroidism. The most common reasons given by these owners for having laboratory testing done were that it was part of routine screening of their geriatric dog or that it was done as part of the routine preanesthetic evaluation prior to a dentistry procedure. When questioned after hypercalcemia had been identified and information on problems typically associated with hypercalcemia had been provided, 19 owners reported that their dog had had abnormalities potentially caused by hypercalcemia (eg, polyuria and polydipsia), but that these clinical abnormalities had not been considered worrisome or bothersome enough to mention initially. Owners of 69 dogs reported that they had not observed any clinical problems in their pet even after hypercalcemia had been identified and explained.

Owners of the remaining 122 dogs with primary hyperparathyroidism reported having observed abnormalities that may have been associated with that condition or with hypercalcemia. Signs most consistent with urolithiasis or urinary tract infection (ie, straining to urinate, increased frequency of urination, and hematuria) reportedly had been observed for days to months in 106 dogs (50%). In 42 of these 106 dogs, urolithiasis had been diagnosed in the preceding 6 months and cystic calculi had been removed surgically, and in 27 of the 42, cystic calculi had recurred, prompting referral to the veterinary teaching hospital. In an additional 41 dogs, cystic calculi had not been identified, but results of bacterial culture of a urine sample collected by means of cystocentesis had been positive and antimicrobials had been administered. In the remaining 23 dogs, cystic calculi, urinary tract infection, or both were diagnosed for the first time following referral to the veterinary teaching hospital.

Other abnormalities reported by owners of the 210 dogs with primary hyperparathyroidism included polyuria and polydipsia (*n* = 102 [48%]), weakness (97 [46%]), decreased activity (90 [43%]), decreased appetite (77 [37%]), weight loss or muscle wasting (37 [18%]), vomiting (28 [13%]), and shivering or trembling (20 [10%]). The interval between the onset of clinical signs and the diagnosis of primary hyperparathyroidism ranged from 0 days (ie, dogs without clinical signs) to 2.5 years (mean, 5 months).

Few abnormalities were detected on physical examination, and for 149 of the 210 (71%) dogs with primary hyperparathyroidism, the medical record contained a notation that no obvious abnormalities were seen on physical examination. Abnormalities that were recorded included muscle wasting, slow to rise or apparent weakness, obesity, and thin body condition. Each of these abnormalities was identified in < 20 dogs (< 10%).

Most (189/210 [90%]) of the dogs with primary hyperparathyroidism had been referred to the veterinary teaching hospital for evaluation and treatment. The most common reason for referral (118/189 [62%]) was hypercalcemia, with the added concern that any

delay in resolving the hypercalcemia could result in renal failure. For 37 dogs (20%), the stated reason for referral was hypercalcemia, but neither the owner nor the referring veterinarian mentioned impending renal failure as a concern. Twenty-seven (15%) dogs were referred because of recurrence of cystic calculi, and 7 (4%) were referred because of weight loss, decreased activity, or polyuria and polydipsia.

In 151 of the 189 (80%) dogs referred to the veterinary teaching hospital, serum PTH concentration was measured prior to referral. In 99 of the 151, serum PTH concentration was within reference limits, and the dogs were referred, in part, because it was thought that this finding negated a diagnosis of primary hyperparathyroidism. In the remaining 52 dogs, serum PTH concentration was high, and this finding was thought to have confirmed the diagnosis of primary hyperparathyroidism.

Clinicopathologic abnormalities—Analysis of results of CBCs performed at the time primary hyperparathyroidism was diagnosed did not reveal any consistent abnormalities in the 210 dogs. Six dogs (3%) had mild anemia, but in all 6, Hct was $\geq 30\%$. Four dogs (2%) had slightly high total WBC counts, but none had a WBC count $> 25,000$ cells/mL. No dog had leukocytopenia.

Hypercalcemia (ie, serum total calcium concentration > 12 mg/dL) was identified in all 210 dogs with primary hyperparathyroidism (Table 1). Mean \pm SD serum total calcium concentration was 14.5 ± 1.8 mg/dL (range, 12.1 to 23.4 mg/dL). Most dogs ($n = 109$ [52%]) had moderate hypercalcemia, arbitrarily defined as a serum total calcium concentration > 12 but ≤ 14 mg/dL; 64 dogs (30%) had concentrations between 14 and 16 mg/dL; 25 dogs (12%) had concentrations between 16 and 18 mg/dL, and 12 dogs (6%) had concentrations > 18 mg/dL. Mean serum total calcium concentration for the control dogs (10.0 ± 0.8 mg/dL; range, 7.1 to 11.8 mg/dL) was significantly lower than mean concentration for the dogs with primary hyperparathyroidism.

For the dogs with primary hyperparathyroidism, mean \pm SD plasma ionized calcium concentration was 1.71 ± 0.19 mg/dL (range, 1.22 to 2.41 mg/dL; reference range, 1.12 to 1.41 mg/dL). Nineteen dogs (9%) had a plasma ionized calcium concentration within reference limits, 57 dogs (27%) had a concentration between 1.42 and 1.65 mg/dL; 101 dogs (48%) had a concentration between 1.66 and 1.90 mg/dL, and 33 dogs (16%) had a concentration > 1.9 mg/dL. Plasma

ionized calcium concentration was measured in only 7 of the 200 control dogs.

For the 210 dogs with primary hyperparathyroidism, mean \pm SD BUN concentration was 16.9 ± 1.8 mg/dL (range, 5 to 92 mg/dL; reference range, 18 to 30 mg/dL). Six dogs (3%) had a BUN concentration < 10 mg/dL, 126 dogs (60%) had a concentration between 10 and 17 mg/dL, 48 dogs (23%) had a concentration between 18 and 22 mg/dL, 21 dogs (10%) had a concentration between 23 and 28 mg/dL, and 9 dogs (4%) had a concentration > 30 mg/dL (range for these 9 dogs, 31 to 92 mg/dL). Serum total calcium concentrations for the 9 dogs with high BUN concentration were not substantially different from concentrations for the group as a whole (mean, 14.9 mg/dL; range, 12.7 to 18.9 mg/dL). Four of the 9 dogs with high BUN concentrations at the time primary hyperparathyroidism was diagnosed had had high BUN concentrations 3 months to 1 year earlier, when serum calcium concentration was within reference limits.

Mean \pm SD serum creatinine concentration for the 210 dogs with primary hyperparathyroidism was 0.8 ± 0.6 mg/dL (range, 0.4 to 4.1 mg/dL; reference range, 0.5 to 1.5 mg/dL). One hundred twenty-six dogs (60%) had a serum creatinine concentration ≤ 1.0 mg/dL, 77 dogs (37%) had a concentration > 1 but ≤ 1.5 mg/dL, 4 dogs (2%) had a concentration ≥ 1.6 but ≤ 2.0 mg/dL, and 3 dogs (1%) had a concentration ≥ 2.1 but ≤ 4.1 mg/dL. Six of the 7 dogs with high serum creatinine concentrations also had high BUN concentrations. The remaining dog with a high serum creatinine concentration (1.7 mg/dL) had a BUN concentration within reference limits (26 mg/dL).

For the 200 control dogs, mean BUN concentration (24 ± 25 mg/dL) and mean serum creatinine concentration (1.2 ± 1.3 mg/dL) were both significantly higher than concentrations for the dogs with primary hyperparathyroidism. Forty control dogs (20%) had a high BUN concentration, high serum creatinine concentration, or both. Thirty-five control dogs had both a high BUN concentration and a high serum creatinine concentration, 3 had a high BUN concentration but a serum creatinine concentration within reference limits, and 2 had a high serum creatinine concentration but a BUN concentration within reference limits. Thirty-two of the control dogs (16%) had chronic renal failure, compared with 9 of the dogs (4%) with primary hyperparathyroidism. However, at least 4 of these 9 dogs with primary hyperparathyroidism had had evidence of chronic renal disease prior to development of hypercalcemia.

Mean \pm SD serum inorganic phosphorus concentration for the 210 dogs with primary hyperparathy-

Table 1—Results of clinical laboratory testing in dogs with primary hyperparathyroidism.

Variable	No. tested	Mean \pm SD	Range	No. (%) with high values	No. (%) with low values	Reference range
Calcium (mg/dL)	210	14.5 \pm 1.8	12.1–23.4	210 (100)	0 (0)	9.9–11.4
Ionized calcium (mg/dL)	210	1.71 \pm 0.19	1.22–2.41	191 (91)	0 (0)	1.12–1.41
BUN (mg/dL)	210	16.9 \pm 1.8	5–92	9 (4)	132 (63)	18–28
Creatinine (mg/dL)	210	0.8 \pm 0.6	0.4–4.1	7 (3)	9 (4)	0.5–1.5
Inorganic phosphorus (mg/dL)	210	2.8 \pm 0.8	1.3–6.1	0 (0)	136 (65)	3.0–6.2
Alkaline phosphatase (U/L)	210	241 \pm 280	12–4,431	85 (40)	0 (0)	5–92
Parathormone (pmol/L)	185	11.3 \pm 7.1	2.3–121	50 (27)	0 (0)	2–13
Urine specific gravity	210	1.012 \pm 0.006	1.004–1.037	NA	NA	NA

NA = Not applicable.

roidism was 2.8 ± 0.8 mg/dL (range, 1.3 to 6.1 mg/dL; reference range, 3.0 to 6.2 mg/dL). Twenty-seven dogs (13%) had a serum inorganic phosphorus concentration < 2.0 mg/dL, 109 dogs (52%) had a concentration between 2.0 and 2.9 mg/dL, 59 dogs (28%) had a concentration between 3.0 and 3.9 mg/dL, 11 dogs (5%) had a concentration between 4.0 and 4.9 mg/dL, and 4 dogs (2%) had a concentration > 4.9 mg/dL. All 4 dogs with serum inorganic phosphorus concentrations > 4.9 mg/dL had high BUN and serum creatinine concentrations, and 3 of these dogs were among the 6 dogs with mild anemia. Mean serum inorganic phosphorus concentration for the control dogs (4.6 ± 1.9 mg/dL) was significantly higher than mean concentration for the dogs with primary hyperparathyroidism.

A urinalysis was performed in all 210 dogs with primary hyperparathyroidism. Urine was obtained free-catch by the owners the morning of their appointment or by means of cystocentesis within 6 hours after the dogs were hospitalized. An additional urine sample was obtained later for bacterial culture by means of cystocentesis if the initial sample had been collected free-catch.

Mean \pm SD urine specific gravity was 1.012 ± 0.006 (range, 1.004 to 1.037). Fifty dogs (24%) had a urine specific gravity < 1.008 , 75 dogs (36%) had a specific gravity between 1.008 and 1.012, 70 dogs (33%) had a specific gravity between 1.013 and 1.020, 8 dogs (4%) had a specific gravity between 1.021 and 1.030, and 7 dogs (3%) had a specific gravity > 1.030 . A urinalysis was performed in 141 of the control dogs. Mean urine specific gravity (1.025 ± 0.013 ; range, 1.004 to 1.052) for the control dogs was significantly higher than mean specific gravity for the dogs with primary hyperparathyroidism.

For all 210 dogs with primary hyperparathyroidism, a urine sample was submitted for bacterial culture, and results were positive for 61 (29%). Twenty of these 61 dogs were confirmed to have cystic calculi at the time urinary tract infection was documented.

Forty-two of the 210 (20%) dogs with primary hyperparathyroidism had had cystic calculi surgically removed within the 6 months prior to referral. Fifty dogs (24%) had cystic calculi at the time of referral to the veterinary teaching hospital, but 27 of these were among the 42 dogs that had recently had cystic calculi removed. Therefore, 65 of the 210 (31%) dogs with primary hyperparathyroidism were found to have cystic calculi at about the time that hypercalcemia was identified. All calculi were either calcium phosphate or calcium oxalate.

Serum PTH concentration was measured in randomly obtained serum samples from 185 of the 210 dogs with primary hyperparathyroidism. Mean \pm SD serum PTH concentration was 11.3 ± 7.1 pmol/L (range, 2.3 to 121 pmol/L; reference range, 2 to 13 pmol/L). For 135 of the 185 (73%) dogs, serum PTH concentration was within reference limits. Eighty-three dogs (45%) had a concentration between 2.3 and 7.9 pmol/L, 52 dogs (28%) had a concentration between 8.0 and 13.0 pmol/L, 20 dogs (11%) had a concentration between 13 and 20 pmol/L, and 30 dogs (16%) had a concentration > 20 pmol/L.

Diagnostic imaging findings—Cervical ultrasonography was performed in 130 of the 210 dogs with primary hyperparathyroidism. For 116 of these 130 dogs, the final report indicated that a solitary parathyroid mass had been identified, and for 13, the report indicated that 2 parathyroid masses had been identified. In the remaining dog, a parathyroid mass was not seen ultrasonographically, but a 5-mm right-sided parathyroid adenoma was removed surgically. Thus, a total of 142 parathyroid masses were seen ultrasonographically.

Although a reference range for parathyroid gland size has not been established for dogs, previous reports^{6,7} have suggested that in healthy dogs, the parathyroid glands are typically ≤ 3 mm in greatest diameter when visualized ultrasonographically. For the 142 parathyroid masses identified ultrasonographically in the present study, median greatest diameter was 6 mm (range, 3 to 23 mm). Eighty-five masses were 4 to 6 mm in greatest diameter, 34 were 7 to 10 mm in greatest diameter, 14 were 11 to 15 mm in greatest diameter, and 9 were 16 to 23 mm in greatest diameter. The only consistent abnormality identified during abdominal radiography and ultrasonography was cystic calculi in the 50 dogs previously discussed.

Discussion

In the present study, primary hyperparathyroidism was diagnosed in both male and female dogs, with the numbers of males and females being almost equal. Most of the dogs were ≥ 8 years old, and although numerous breeds were represented, the Keeshond was the most common breed, although Keeshonds are not commonly seen at this hospital. Forty-two percent (88/210) of the affected dogs reportedly did not have any clinical signs at the time hypercalcemia was identified, and even after hypercalcemia was identified and problems typically associated with hypercalcemia were explained, owners of 69 dogs still indicated that their dogs did not have any clinical abnormalities.

Dogs were included in the present study only if they had a persistent increase in total serum calcium concentration. Nevertheless, 19 of the 210 (9%) dogs with primary hyperparathyroidism had serum ionized calcium concentrations within reference limits. It is possible that if we had selected dogs for inclusion on the basis of a high serum ionized calcium concentration, we might have identified some dogs with total serum calcium concentration within reference limits. Furthermore, although serum ionized calcium concentration was determined for all dogs by a single laboratory, it is possible that the collection method or the time between collection and assay may have varied. Accurate determination of serum ionized calcium concentration requires that samples be collected and processed anaerobically to ensure that no increase in pH occurs because of loss of CO_2 .¹⁷ All samples for determination of serum ionized calcium concentration were collected anaerobically and immediately placed on ice for transport to the laboratory, where assays were to have been performed within minutes of sample receipt. Nevertheless, serum ionized calcium determination is more likely to be altered by such variables than is serum total calcium concentration. Thus, for a small percentage of samples,

serum ionized calcium concentrations may have changed during or after collection despite attempts to use proper sample-handling techniques.

Veterinary clinicians are encouraged to evaluate serum inorganic phosphorus concentration when the serum calcium concentration is abnormal. Differential diagnoses that should be considered when both values are high (eg, renal failure and vitamin D toxicosis) generally are different from those that should be considered when serum total calcium concentration is high but serum inorganic phosphorus concentration is within reference limits or low. Two hundred six of the 210 dogs with primary hyperparathyroidism in the present study had serum inorganic phosphorus concentrations less than the lower reference limit or in the lower half of the reference range. Furthermore, 132 of the 210 dogs had BUN concentrations less than the lower reference limit, and 201 of the 210 (96%) dogs had BUN concentrations that were low or within reference limits. Two hundred three of the 210 (97%) dogs with primary hyperparathyroidism had serum creatinine concentrations that were low or within reference limits, and only 10 dogs had a high BUN concentration, high serum creatinine concentration, or both. Nine dogs had a high BUN concentration when primary hyperparathyroidism was diagnosed, but at least 4 of these dogs had had a high BUN concentration prior to developing hypercalcemia. Thus, abnormal renal parameters developed after the onset of hypercalcemia in no more than 6 of the 210 (3%) dogs with primary hyperparathyroidism. In addition, because it was not known whether BUN or serum creatinine concentration was high prior to the onset of hypercalcemia in these dogs, whether renal failure will develop as a result of hypercalcemia or high serum PTH concentrations in dogs with primary hyperparathyroidism is still speculative. Thus, although our results suggest that urolithiasis and urinary tract infection may be associated with hypercalcemia in dogs with primary hyperparathyroidism, they also indicate that development of renal insufficiency is uncommon. Further, it is possible and perhaps likely that in some of the dogs in which abnormal renal parameters were documented after the onset of hypercalcemia, renal insufficiency was a result of obstruction of renal, ureteral, or urethral urine flow by uroliths and not a direct effect of the primary hyperparathyroidism.

In sum, our findings suggest that reducing the risks of urolithiasis and urinary tract infection is a valid reason for recommending treatment of primary hyperparathyroidism, but that treatment should not be advocated simply to avoid development of renal failure, because results of renal function tests indicate that increases in serum calcium and PTH concentrations are uncommonly associated with renal failure. Another reason to recommend treatment for dogs with primary hyperparathyroidism would be to improve clinical abnormalities induced by hypercalcemia, such as polydipsia, polyuria, decreased appetite, and muscle weakness, some of which may not be appreciated by the owners. This same reasoning has been promoted for treating people with asymptomatic primary hyperparathyroidism. That is, some human patients will not

recognize that they had clinical signs until after resolution of the condition.^{18,19}

Results of thoracic radiography were unremarkable in the dogs with primary hyperparathyroidism in the present study. Because lymphosarcoma is one of the most common causes of hypercalcemia, evaluation of thoracic radiographs is indicated in any dog with hypercalcemia. In particular, the cranial aspect of the mediastinum should be examined for evidence of a mass effect, and the visible bones (ie, the vertebrae, ribs, and scapulae) should be examined for lytic lesions suggestive of neoplastic conditions, such as multiple myeloma. Finally, the lungs should be examined for any abnormalities that could explain the hypercalcemia and to identify any possible concurrent conditions.

Abdominal radiography and ultrasonography identified cystic calculi in 50 of the 210 dogs examined at the veterinary teaching hospital and in 65 dogs total. However, results of abdominal imaging were otherwise unremarkable in dogs with primary hyperparathyroidism. Abdominal imaging is recommended in any dog with hypercalcemia to check for evidence of urolithiasis, unsuspected concurrent conditions, and any condition that might explain the hypercalcemia.

Cervical ultrasonography has become a routine method for evaluating dogs with hypercalcemia. However, although results appeared to be excellent in the present study, with masses identified ultrasonographically in 129 of 130 dogs, the subjective nature of ultrasonography must be appreciated. Data recorded only in the final ultrasonography report in each dog's medical record were used in the present study, and it must be pointed out that many of these dogs were evaluated by several radiologists, either at the time that primary hyperparathyroidism was first identified or during a subsequent examination. As has been suggested previously,¹⁴ results of ultrasonography are subjective, and operator skill and experience vary widely. Some of these dogs might have had negative cervical ultrasonography results before a positive result was obtained by a more experienced ultrasonographer. In healthy dogs, the parathyroid glands are typically ≤ 3 mm in greatest diameter. In dogs with hyperparathyroidism in the present study, typically only 1 gland could be imaged, and that gland was ≥ 4 mm in greatest diameter. Parathyroid masses varied in size and location, but most of the 142 parathyroid masses were between 4 and 6 mm in greatest diameter, suggesting that most dogs had a rather subtle increase in parathyroid gland size. No large case study has evaluated the ultrasonographic appearance of the parathyroid glands in healthy dogs, but it can be assumed, given the subjective nature of ultrasonography and individual variation among dogs, that some percentage of healthy dogs would have parathyroid glands measuring > 3 mm in greatest diameter. Thus, it is unlikely that sensitivity or specificity of cervical ultrasonography would be perfect in identifying dogs with primary hyperparathyroidism.

An area of potential confusion regarding the diagnosis of primary hyperparathyroidism involves the interpretation of randomly obtained serum PTH concentrations. The root of this confusion, perhaps, can be traced to the use of the term normal range when interpreting test results, rather than the preferred term reference range. It

seems counterintuitive to suggest that a dog could have a condition caused by autonomous, excessive secretion of PTH and, at the same time, have a serum PTH concentration considered normal. Physiologically, however, as serum calcium concentration increases, serum PTH concentration should decrease. If serum calcium concentration is high, serum PTH concentrations should be low. Thus, a serum PTH concentration within reference limits should not be considered normal in a dog with hypercalcemia. Results of the present study support this concept, in that mean serum PTH concentration was within reference limits and 135 of 185 (73%) dogs had a serum PTH concentration within reference limits.

- a. Hitachi 717, Roche Laboratories, Indianapolis, Ind.
- b. 634 Ca/pH Analyzer, Bayer/Ciba-Corning Diagnostics Corp, East Walpole, Mass.
- c. HDI 5000, ATL Ultrasound, Philips Medical Systems Co Inc, Bothell, Wash.
- d. SPSS for Windows, version 12.0, SPSS Inc, Chicago, Ill.

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