

# Canine Primary Hyperparathyroidism

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**Abstract:** Canine primary hyperparathyroidism (PHPT) is an endocrine disorder that results in hypercalcemia secondary to autonomous production of parathyroid hormone. Associated biochemical abnormalities also include hypophosphatemia and hyperphosphaturia. Clinical signs of PHPT are related to the effects of hypercalcemia on the renal, neuromuscular, and gastrointestinal systems. The diagnosis of PHPT relies on careful interpretation of laboratory data and imaging studies. Several modalities are available to treat PHPT, but the most important aspect of therapy is the postprocedure management of potential hypocalcemia.

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Canine primary hyperparathyroidism (PHPT) is characterized by abnormal parathyroid “chief” cells that function autonomously due to a parathyroid adenoma, a carcinoma, or adenomatous hyperplasia of one or more parathyroid glands. Other forms of hyperparathyroidism are usually due to non-endocrine disturbances in calcium and phosphorous homeostasis that indirectly affect the parathyroid glands, leading to diffuse hyperplasia. In these cases (renal or nutritional secondary hyperparathyroidism), the secretion of parathyroid hormone (PTH) is not autonomous but rather a secondary manifestation of disease.

## Hypercalcemia and Hyperparathyroidism

Hypercalcemia develops when the influx of calcium into the extracellular space overwhelms the mechanisms responsible for maintaining normocalcemia.<sup>1</sup> Hypercalcemia in dogs is most often caused by malignancy, followed by PHPT, hypoadrenocorticism, and chronic kidney disease.<sup>2,3</sup> Other possible causes, such as vitamin D toxicosis and granulomatous disease, have a lower overall prevalence<sup>3</sup> (TABLE 1).

In secondary disorders, serum calcium concentrations can range from low to increased, depending on the cause. In contrast, PHPT is always associated with hypercalcemia.<sup>2,4</sup> The autonomously secreted PTH in PHPT is not suppressible by the increased calcium concentration. Severe hypercalcemia arises from accelerated bone resorption. PTH and PTH-related peptide (PTHrp), common in hypercalcemia of malignancy, also directly inhibit renal calcium excretion. Thus, increased renal calcium loss—which combats severe hypercalcemia not mediated by PTH or PTHrp—does not occur in cases of PTH- or PTHrp-mediated hypercalcemia, eliminating the first line of defense. Furthermore, the hypercalcemic state interferes with renal mechanisms for resorption of sodium and water due to an acquired inability to respond to antidiuretic hormone.<sup>2</sup> Hypercalcemia in PHPT is also enhanced by increased production of vitamin D and the decreased amount of phosphorus that is available to form complexes with ionized calcium. All of these interactions result in the biochemical abnormalities classic for PHPT: hypercalcemia, hypophosphatemia, and hyperphosphaturia.<sup>2,4-6</sup>

## Pathology

Autonomously secreting parathyroid glands are classified into three histopathologic categories: carcinoma, adenoma (typically a solitary mass; **FIGURE 1**), and parathyroid hyperplasia (which commonly involves the simultaneous enlargement of more than one parathyroid gland). The exact percentage of each histopathologic diagnosis in canine PHPT is unknown. This may be partially due to the subjectivity involved in diagnosis and differences among

individual pathologists' readings as well as the lack of a large, single data set of dogs. In a data set collected for dogs that underwent surgery, 87% had a solitary adenoma, 8% had hyperplasia, and 5% had carcinoma.<sup>2</sup> Another study found a higher incidence of hyperplasia (approximately 20%).<sup>7</sup> Despite the presence of multiple criteria of malignancy in cases of parathyroid carcinoma, to our knowledge, distal metastases have not been reported in dogs.

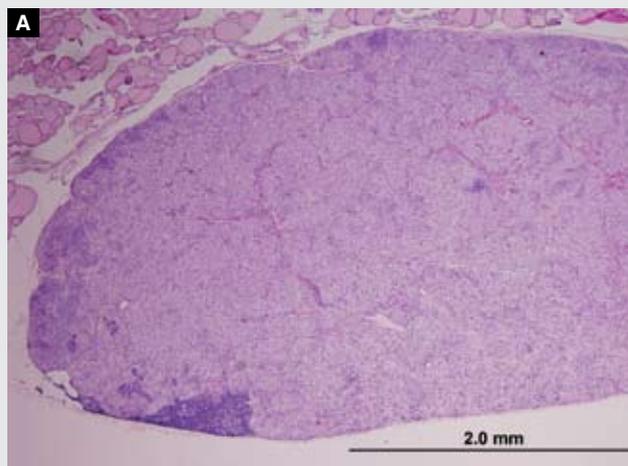
**TABLE 1** Differential Diagnosis of Hypercalcemia<sup>1,2,5,7,9</sup>

| Cause                                                                                                                                                                                                                                           | Comment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hypercalcemia of malignancy (lymphoma, carcinoma, multiple myeloma, melanoma)                                                                                                                                                                   | <ul style="list-style-type: none"> <li>▶ Mediated by PTHrp, which is released by tumor tissue</li> <li>▶ PTHrp increases osteoblastic bone resorption and renal tubular calcium resorption</li> <li>▶ ↑ total Ca, ↑ iCa, low-normal to ↓ PTH, normal to ↓ P</li> </ul>                                                                                                                                                                                                                                                                                                                                            |
| Hypoadrenocorticism                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>▶ Multifactorial pathogenesis</li> <li>▶ Hyperproteinemia from dehydration and hemoconcentration</li> <li>▶ Increased plasma protein-binding affinity for calcium</li> <li>▶ Increased concentration of calcium citrate complexes</li> <li>▶ Increased renal tubular resorption of calcium</li> <li>▶ ↑ total Ca, iCa in reference range</li> </ul>                                                                                                                                                                                                                        |
| Primary hyperparathyroidism                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>▶ Autonomous secretion of PTH from parathyroid chief cells</li> <li>▶ ↑ total Ca, ↑ iCa, normal to ↑ PTH, normal to ↓ P</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Chronic kidney disease                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>▶ Complex pathogenesis</li> <li>▶ Impedance of excretion of PTH and its metabolites</li> <li>▶ Decreased renal excretion of calcium due to reduction in GFR</li> <li>▶ Increased concentration of PTH due to excessive secretion and reduced renal tubular hormone degradation</li> <li>▶ Renal failure or PTH-induced increased concentration of organic cations and complexed calcium</li> <li>▶ Exaggerated response to vitamin D with increased intestinal absorption of calcium</li> <li>▶ ↓, normal, or ↑ total Ca; normal to ↓ iCa; normal to ↑ PTH; ↑ P</li> </ul> |
| Vitamin D toxicosis (cholecalciferol rodenticides, human psoriasis medications [calcipotriol, calcipotriene], overzealous dietary supplementation, plants [ <i>Cestrum diurnum</i> , <i>Solanum malacoxylon</i> , <i>Trisetum flavescens</i> ]) | <ul style="list-style-type: none"> <li>▶ ↑ total Ca, ↑ iCa, normal to ↑ P, normal to ↓ PTH</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Hemoconcentration (spurious)                                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>▶ Mild hypercalcemia</li> <li>▶ Fluid volume contraction and secondary hyperproteinemia</li> <li>▶ Resolves with fluid therapy</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Granulomatous disease                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>▶ Due to alteration of endogenous vitamin D metabolism</li> <li>▶ Activated macrophages can develop ability to convert 25-hydroxyvitamin D to calcitriol in an unregulated manner</li> <li>▶ ↑ total Ca, ↑ iCa, low-normal to ↓ PTH, normal to ↑ P</li> </ul>                                                                                                                                                                                                                                                                                                              |

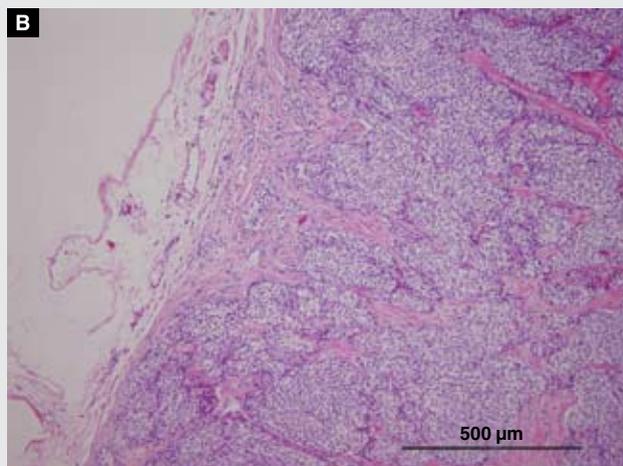
PTHrp = parathyroid hormone-related peptide; Ca = calcium; iCa = ionized calcium; PTH = parathyroid hormone; P = phosphorus; GFR = glomerular filtration rate.

FIGURE 1

Histopathologic sections of parathyroid masses from two dogs with primary hyperparathyroidism (PHPT).



**Parathyroid adenoma; note the expansive but non-infiltrative nature.** The darker cells represent the remnant of the normal parathyroid gland tissue. (Hematoxylin–eosin stain; magnification: 40×)



**Parathyroid carcinoma; note the capsular invasion and marked cellular atypia.** (Hematoxylin–eosin stain; magnification: 100×)

## QuickNotes

**In many cases of canine primary hyperparathyroidism, clinical signs attributable solely to hypercalcemia are mild or absent.**

### Signalment

#### Age and Gender

PHPT is usually diagnosed in older dogs (mean age: 11.2 years; range: 6 to 17 years).<sup>1,2,6</sup> There is no apparent sex predisposition. In a retrospective study of 210 dogs, 54% were male and 46% were female.<sup>8</sup>

#### Breed and Heredity

There is a single report of a familial form of neonatal hyperparathyroidism in a litter of German shepherd puppies in which an autosomal-recessive mode of inheritance was suspected.<sup>2,4</sup> However, a 10-year review of cases<sup>3,7</sup> revealed that keeshonden are most likely to be affected by PHPT, with 214 positive samples and an average American Kennel Club registration of 4375, yielding the highest breed-associated odds ratio (OR) of 50.7. Other breeds with more than 100 positive samples were dachshunds (OR: 2.0) and golden retrievers (OR: 1.6). Keeshonden represented 26% of dogs and approximately 40% of dogs in two other studies, respectively.<sup>6,7</sup>

#### Primary Hyperparathyroidism in Keeshonden

A recent study<sup>7</sup> investigating the inheritance, mode of inheritance, and candidate genes for

PHPT in keeshonden identified a heritable, autosomal-dominant form of PHPT in this breed. In keeshonden, the condition is due to a single gene mutation that is transmitted via simple Mendelian genetics with a high degree of penetrance. Genes known to cause human familial isolated hyperparathyroidism have been excluded as the cause of PHPT in dogs.<sup>7</sup> A test for a gene that has been found to be highly associated with PHPT in keeshonden is available for owners and breeders.<sup>9</sup> Genetic testing of young keeshonden for this disease should facilitate a decrease in the incidence of PHPT in this breed, as well as promote identification of older keeshonden with the genetic predisposition so that they can undergo frequent monitoring of calcium concentration.

### Clinical Signs

In many cases of PHPT, clinical signs attributable solely to hypercalcemia are mild or absent. Most cases are identified as a result of routine screening tests. In the retrospective study of 210 dogs with PHPT,<sup>8</sup> the owners of 42% of the dogs had sought veterinary care for reasons apparently unrelated to hypercalcemia or PHPT.

The most common clinical signs of PHPT-induced hypercalcemia involve the renal, neu-

romuscular, and gastrointestinal systems.<sup>2,4,8</sup> Polyuria, polydipsia, and urinary incontinence are the most common clinical signs.<sup>2,4,5,8</sup> These signs develop because of an impaired renal tubular response to antidiuretic hormone and impaired renal tubular resorption of sodium and chloride. This results in a significant increase in urine volume. Compensatory polydipsia develops to maintain a normovolemic state.<sup>2,4</sup> Lower urinary tract signs of pollakiuria, stranguria, and hematuria are also common. As many as 32% of dogs with PHPT have urolithiasis, and 24% have urinary tract infections.<sup>2,8</sup> Clinical signs related to the neuromuscular system (e.g., listlessness, depression, decreased activity) are thought to be due to the effects of calcium on the central and peripheral nervous tissue, suppressing the excitability of central and peripheral nerves by decreasing cell membrane permeability. Shivering, muscle twitching, and seizure activity have also been observed, but the underlying mechanisms for these problems are not well understood.<sup>2,4</sup> Gastrointestinal signs such as vomiting and constipation are thought to be due to a hypercalcemia-induced decrease in excitability of gastrointestinal smooth muscle. Inappetence may also be due to direct calceinic effects on the CNS. The less common clinical signs of fractures, lameness, and stiff gait may be due to excessive osteoclastic resorption of bone induced by chronic hyperparathyroidism leading to replacement of bone matrix with fibrous tissue, as well as thinning and weakening of cortical bone. Metastatic calcification of tendons and joint capsules may also contribute to stiffness and lameness.<sup>2,4</sup>

PHPT-associated renal failure is relatively uncommon in North American dogs. The retrospective study of 210 dogs revealed that increases in serum calcium and PTH concentrations were rarely associated with renal failure.<sup>8</sup> In contrast, a British case series of 29 dogs with PHPT concluded that renal failure was more likely in dogs with a high total calcium level, with at least seven of the 29 dogs developing renal failure.<sup>10</sup> It is difficult to say why these two studies differed so markedly regarding the prevalence of kidney disease in dogs with PHPT. In addition to the much smaller sample size of the British study, it is also possible that the dogs in the US study were identified and treated at an earlier stage

of the disease, possibly because many of the dogs in this study were diagnosed via routine screening before developing obvious clinical signs of hypercalcemia.

Hyperparathyroidism in dogs with hyperadrenocorticism is also under investigation. A recent study<sup>11</sup> revealed a high prevalence of increased PTH levels in dogs with hyperadrenocorticism. The mechanism for increased PTH in these animals is not known. In these dogs, PTH and phosphorus values were increased, but calcium concentrations were unaffected.<sup>11</sup>

### Physical Examination

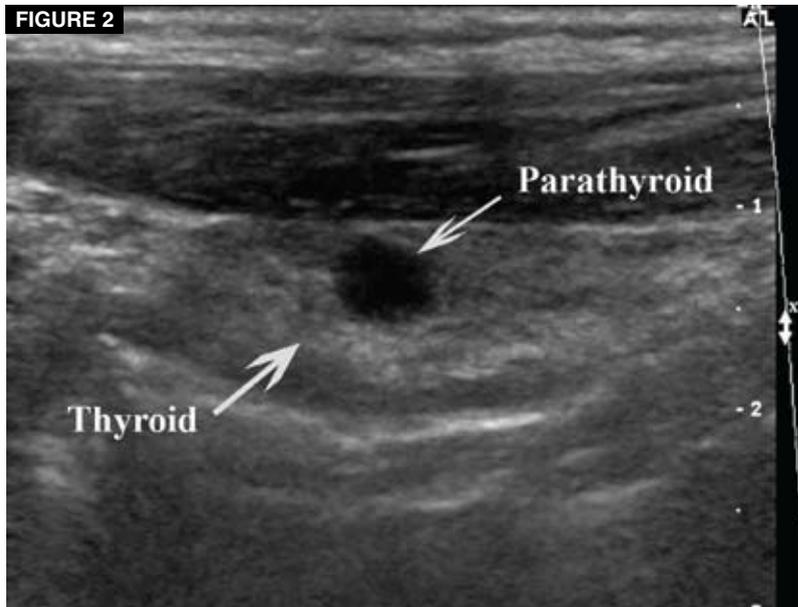
Dogs with PHPT often have unremarkable physical findings. The most commonly associated abnormalities are usually caused by the presence of uroliths.<sup>2,4,8,12</sup> Other, more subtle physical findings may include thin body condition, generalized muscle atrophy, and variable degrees of weakness. Bone deformities involving the mandible and maxilla and long bone fractures are uncommon.<sup>2,4</sup>

### Diagnosis

A complete database, including physical examination, complete blood cell count, serum chemistry profile with ionized calcium, and PTH and PTHrp assays, is indicated when PHPT is suspected. The diagnosis is established based on ionized hypercalcemia, a low or low-normal serum phosphorus level, an inappropriately high PTH level, and exclusion of other causes of hypercalcemia (**TABLE 1**). The key to diagnosing PHPT using PTH assay results is the recognition of an inappropriate PTH concentration in the presence of hypercalcemia. If the serum ionized calcium concentration is increased, the PTH level should be very low.<sup>2,4,8</sup> Therefore, a serum PTH value that falls in the reported reference range should not be considered normal in a dog with hypercalcemia.<sup>6</sup> In the retrospective study,<sup>8</sup> 73% of the dogs with PHPT had serum PTH levels within the reference range at the time of diagnosis. Several commercial veterinary laboratories accept plasma (in EDTA) or serum for PTH measurement; PTHrp measurement requires plasma exclusively. The samples for PTH or PTHrp should be centrifuged and the plasma or serum separated from the cells and stored and shipped frozen to the laboratory. A human two-site (“sandwich”) assay, which includes

### QuickNotes

**Diagnosis of primary hyperparathyroidism based on parathyroid hormone (PTH) assay results relies on the recognition of inappropriate PTH levels in the presence of hypercalcemia.**



**FIGURE 2**  
Longitudinal ultrasonographic view of the cervical region of a dog with PHPT. Note the oblong-shaped thyroid gland with a round, hypochoic parathyroid nodule in its center.

the binding of antibodies to two separate sites on the PTH molecule, can be used successfully to measure canine PTH.<sup>2</sup>

Once the clinical pathologic diagnosis of PHPT is established, many centers perform cervical ultrasonography. Although this modality requires somewhat specialized ultrasonographic equipment and expertise, the parathyroid glands are now routinely visualized with ultrasonography in dogs.<sup>2,4</sup> Experienced veterinary radiologists can successfully identify 90% to 95% of parathyroid adenomas.<sup>4</sup> Most adenomas are 4 to 9 mm in diameter and are fairly easy to visualize (FIGURE 2).<sup>4</sup> However, not all parathyroid nodules are obvious, and the subjectivity of ultrasonography as a diagnostic tool must be taken into account.

In humans, radionuclide scanning with technetium-99m sestamibi has been used to localize parathyroid adenomas. To date, parathyroid scintigraphy in dogs has lacked sufficient sensitivity and specificity to be recommended as a diagnostic tool.<sup>4,13</sup> Selective venous sampling for serum PTH from the jugular veins to localize functioning parathyroid masses has also not been shown to be useful in identifying the side of the affected gland.<sup>4,14</sup>

### Treatment

#### Management of Hypercalcemia

Identifying and treating the underlying cause

takes priority over management of hypercalcemia. However, given the deleterious effects of hypercalcemia on renal function (impaired renal tubular concentrating ability, reduced renal flow, decreased glomerular filtration rate), interim treatment to reduce the serum calcium level may be indicated.<sup>5</sup> Animals with azotemia or an increase in calcium-phosphorus product (calcium  $\times$  phosphorus  $>70$ ) are more likely to warrant therapy. The severity of hypercalcemia alone is not considered sufficient reason for immediate therapy.<sup>5</sup> In dogs with PHPT, hypercalcemia is not typically viewed as an acute problem, and these animals rarely have a calcium-phosphorus product greater than 60 to 80 because of concurrent hypophosphatemia.<sup>4</sup>

If immediate treatment for hypercalcemia is deemed necessary (chronic kidney disease, vitamin D toxicosis, clinical signs of hypercalcemia), fluid therapy is the ideal initial method for lowering serum calcium and preserving renal perfusion.<sup>5</sup> Saline diuresis (0.9% saline) at a rate of 120 to 180 mL/kg/day can promote calcium excretion. This therapy is often combined with the loop diuretic furosemide (given IV q8h or as a constant-rate infusion) to potentiate calciuresis. Supplementation with potassium chloride may be necessary to prevent the development of hypokalemia. If this treatment does not decrease the serum calcium concentration sufficiently, additional medications may be needed. Glucocorticoids have been shown to effectively decrease serum calcium concentrations by increasing calciuresis, reducing intestinal absorption of calcium, and inhibiting calcium resorption from bone. Glucocorticoids are most effective for hypercalcemia of malignancy (lymphoma). It is crucial to withhold glucocorticoid treatment until neoplasia has been ruled out so as not to interfere with diagnosis.

Hypercalcemia refractory to these therapies may respond to bisphosphonates (pamidronate, clodronate), plicamycin (mithramycin), or calcitonin therapy.<sup>5</sup> These medications are costly and may have severe adverse effects as well as benefit; therefore, they are not typically used to treat canine PHPT. Bisphosphonates act primarily by inhibiting osteoclast activity and bone resorption. Their use in veterinary medicine has increased in recent years, especially in cases of hypercalcemia of malignancy.

### QuickNotes

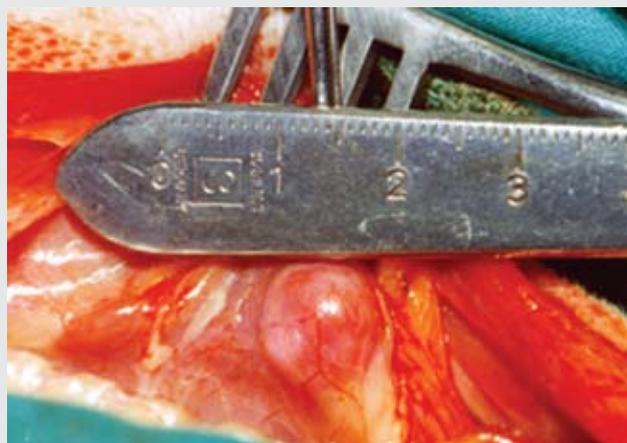
**Successful treatment of primary hyperparathyroidism depends on appropriate procedure selection and postoperative care and monitoring.**

FIGURE 3

Images taken at the time of parathyroidectomy in a dog with PHPT.



Note the enlarged, darkened parathyroid mass.



The typical appearance of a 1-cm parathyroid mass at surgery.

In a review of seven hypercalcemic dogs (four with neoplasia, none with PHPT), the bisphosphonate pamidronate disodium was shown to be safe and relatively efficacious when given as a single infusion of 1.05 to 1.7 mg/kg.<sup>15</sup> Calcitonin decreases osteoclast activity as well as formation of new osteoclasts. It has been used in dogs, especially in cases of vitamin D toxicosis (5 U/kg IM or SC q8h), although large studies regarding its efficacy and safety are lacking.<sup>2</sup>

### Treatment of PHPT

Three treatment modalities are available for PHPT in dogs: surgery, percutaneous ultrasonography-guided ethanol ablation (with 96% ethanol), and percutaneous ultrasonography-guided radiofrequency heat ablation.<sup>2,4,5</sup> If surgical treatment is sought, complete cervical exploratory surgery of the thyroid area is recommended. An effort should be made to evaluate both sides of the neck and the ventral and dorsal surfaces of the thyroid glands.<sup>5</sup> In most dogs with PHPT, the abnormal parathyroid tissue (adenoma) is a solitary nodule that is darker and larger than normal parathyroid tissue. It is typically easily recognized and removed by an experienced surgeon (FIGURE 3).<sup>5</sup> If possible, only the abnormal tissue is removed, but it is sometimes necessary to remove part or all of a thyroid lobe along with abnormal parathyroid tissue. If no abnormal parathyroid tissue is seen at the time of sur-

gery and the diagnosis of PHPT is thought to be correct, then one thyroid lobe–parathyroid complex can be removed and submitted for histopathologic analysis. If two or three abnormal parathyroid glands are found, all should be removed. If all four parathyroid glands appear to be abnormal, one gland is often left in situ to maintain calcium homeostasis and prevent permanent hypocalcemia.<sup>2,5</sup> The presence of two, three, or four abnormal glands is atypical and suggests hyperplasia rather than an adenoma.<sup>5</sup>

Ethanol and heat ablation require visualization of a parathyroid nodule using cervical ultrasonography (FIGURE 2).<sup>16–19</sup> The nodule must also be large enough (>3 mm) for accurate needle placement.<sup>2</sup> Ethanol ablation causes coagulation necrosis and vascular thrombosis in the parenchyma of the exposed tissue.<sup>2,16</sup> The injection procedure requires a high-resolution transducer (i.e., frequency of 10 MHz or greater) to visualize the superficial tissues of the neck, and the animal must be under general anesthesia.<sup>2,16</sup> Considerable experience with ultrasonography-guided needle placement is necessary because parathyroid nodules are small and close to the carotid artery and vagosympathetic trunk. Complete certainty about needle location is crucial in this procedure. The goal of the procedure is to inject enough ethanol to allow complete diffusion throughout the mass. This procedure is considered to be an effective alternative to surgery.<sup>16</sup> Over the past

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**Surgery, ethanol ablation, and heat ablation can be used to treat primary hyperparathyroidism.**

7 years, this procedure has been performed on more than 30 dogs at our institution with a success rate of >90%, defined as a decrease in serum calcium sufficient to achieve a sustained (at least 1 year) normocalcemic state. No recurrence in a successfully injected gland has been reported in these cases. Adverse effects associated with the procedure are minimal, but a local reaction to the ethanol involving transient internal swelling in the laryngeal region is possible. For this reason, bilateral injections are not recommended in cases of bilateral parathyroid nodules. Compared with surgical excision, ethanol ablation is a faster, less invasive procedure with a faster recovery time. However, it does require advanced ultrasonography equipment and expertise, with a success rate of approximately 90% versus almost 100% for surgery. Injections should be performed a few months apart in cases of bilateral parathyroid nodules.

Radiofrequency heat ablation destroys tissue by causing thermal necrosis at the needle tip. The advantage of heat ablation over ethanol is that there is no potential for leakage because the radiofrequency damage is restricted to a discrete amount of tissue surrounding the uninsulated portion of the needle, and regional vasculature is unaffected.<sup>2</sup> Heat ablation has been reported to be a safe, effective treatment.<sup>1,17</sup> However, to our knowledge, the heat ablation unit needed to perform this procedure is only available at the University of California, Davis.

### Management of Posttreatment Potential Hypocalcemia

Successful treatment of PHPT must include appropriate postprocedure care and monitoring, which are similar regardless of the therapeutic modality. It is essential to remember that normal parathyroid glands atrophy if their function is suppressed for a prolonged period of time. The surgical removal or ablation of the autonomous source of PTH results in a rapid decline in circulating PTH and serum calcium. We recommend hospitalization for 7 to 10 days after treatment, regardless of the presurgical calcium level. Clinically significant hypocalcemia typically develops 3 to 7 days after treatment.<sup>16</sup> Additionally, hospitalization restricts the dog's activity, decreasing the risk of clinical tetany due to hypocalce-

mia.<sup>2</sup> Carefully allowing serum calcium levels to decline after PHPT therapy enables the remaining glands to return to function, avoiding unnecessary prolonged calcium and vitamin D supplementation.

Treatment of hypocalcemia is recommended if the serum calcium level falls below 8.5 mg/dL (assuming a lower reference limit of 9 to 10 mg/dL), the ionized calcium value falls below 0.8 to 0.9 mmol/L (assuming a lower reference limit of 1.12 mmol/L), or clinical signs of hypocalcemia are noted (e.g., facial rubbing, focal seizures, muscle stiffness, twitching).<sup>2</sup> Initiating treatment with vitamin D may also be indicated if there is concern about the rate of decrease in the calcium concentration. Prophylactic vitamin D therapy, given either on the morning of surgery or immediately after recovery from anesthesia, has been recommended in dogs with a serum calcium concentration chronically greater than 14 mg/dL to prevent the development of profound hypocalcemia. Due to the known delay in the onset of action of vitamin D in some cases (severe hypercalcemia exceeding 18 mg/dL), treatment has been initiated 24 to 36 hours before surgery.<sup>2</sup>

Short-term treatment of hypocalcemia is required for dogs exhibiting clinical signs or that have severe hypocalcemia without clinical signs. Calcium gluconate in a 10% solution is the calcium salt of choice; it is given at a recommended dose of 0.5 to 1.5 mL/kg (5 to 15 mg/kg of elemental calcium) IV slowly over 10 to 30 minutes to effect.<sup>6</sup> Ultimately, patient response should be the determining factor for the volume administered. During IV administration of calcium gluconate, the patient's heart rate should be monitored (ideally along with electrocardiography) to prevent calcium-induced cardiotoxicity (bradycardia, sudden elevation in ST segment, shortening of QT interval, premature ventricular complexes).<sup>6</sup> The effect of IV calcium therapy has a limited duration (1 to 12 hours), so oral maintenance therapy must be initiated concurrently. Because oral vitamin D and calcium may take 24 to 96 hours to achieve maximum effect, support with parenteral calcium is needed during this period.<sup>6</sup> This could include repeated IV or subcutaneous calcium gluconate administration dosed as noted previously every 6 to 8 hours or, ideally, as a constant-rate infusion at

## QuickNotes

**Short-term treatment of hypocalcemia is required for dogs exhibiting clinical signs or that have severe hypocalcemia without clinical signs.**

60 to 90 mg/kg/day for approximately 24 to 48 hours, followed by weaning while monitoring serum calcium levels. Sterile abscess formation and skin sloughing can occur with subcutaneous calcium therapy, especially when calcium salts other than calcium gluconate are used.<sup>2</sup>

Maintenance therapy includes oral calcium supplementation and vitamin D analogues. The vitamin D compound of choice is 1,25-dihydroxycholecalciferol (calcitriol) due to its rapid onset of action (1 to 4 days for maximal effect) and short biologic half-life (2 to 4 days).<sup>6</sup> A loading dose of 0.02 to 0.03 µg/kg/day PO divided twice daily for 3 to 4 days is recommended, followed by 0.005 to 0.015 µg/kg/day, divided twice daily. Calcium carbonate is the oral calcium supplement of choice because of its high percentage of calcium (40%), low cost, and wide availability. When used in conjunction with vitamin D, the recommended dose of oral elemental calcium is 25 mg/kg q8–12h as needed based on the individual patient's serum calcium levels.<sup>6</sup> Normal dietary intake of commercial pet food provides an adequate calcium level in the presence of vitamin D metabolite treatment for most patients.

Usually, as the vitamin D dose and serum calcium concentration reach a steady level, the dose

of oral calcium can be tapered gradually and discontinued over a period of 2 to 4 months.<sup>6</sup> As the atrophied parathyroid glands regain control of calcium homeostasis, vitamin D supplementation and oral calcium supplementation can be tapered gradually.<sup>2</sup> The serum calcium level should be checked before each adjustment in dosing interval. The entire withdrawal process generally takes 3 to 6 months, but individual response to therapy varies considerably.<sup>2</sup>

### Prognosis

The prognosis for dogs with PHPT is excellent with appropriate treatment and monitoring,<sup>2</sup> and successful treatment is considered curative in dogs with solitary parathyroid adenomas. Dogs with parathyroid hyperplasia are likely to experience recurrences in the remaining parathyroid glands.

### Conclusion

Although it is more prevalent in older dogs, PHPT can be treated successfully with little risk to the patient, provided the procedure is done by an experienced surgeon. Postprocedure calcium supplementation is an essential part of treatment but is generally required for only a few months. **C**

## QuickNotes

**The prognosis for dogs with PHPT is excellent with early diagnosis and appropriate treatment and monitoring.**

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**CE TEST 2**

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- 1. Which of the following serum values is not consistent with a diagnosis of PHPT?**
  - a. increased ionized calcium
  - b. increased phosphorus
  - c. increased total calcium
  - d. normal to increased PTH
- 2. Which statement is true?**
  - a. Hyperadrenocorticism commonly causes marked hypercalcemia.
  - b. Hypercalcemia of malignancy is uncommon in dogs.
  - c. PHPT is a very likely diagnosis in an older, hypercalcemic keeshond.
  - d. Vitamin D toxicosis commonly causes markedly increased serum calcium and markedly decreased serum phosphorus concentrations in dogs.
- 3. Which statement is true regarding PTH?**
  - a. PTH secretion causes an increase in serum calcium.
  - b. PTH is secreted from the thyroid gland.
  - c. PTH is not usually increased in renal secondary hyperparathyroidism.
  - d. PTH is always increased out of the reference range in canine PHPT.
- 4. Which of the following can cause PHPT?**
  - a. solitary adenoma
  - b. adenoma of multiple glands
  - c. adenomatous hyperplasia of one or more glands
  - d. all of the above
- 5. Which statement is true regarding hypercalcemia of malignancy and PHPT?**
  - a. Both conditions can be associated with marked hypercalcemia.
  - b. Accelerated bone resorption and decreased renal excretion of calcium contribute to the hypercalcemia seen in these conditions.
  - c. PTH secretion is not suppressed by hypercalcemia in a normal fashion in dogs with PHPT.
  - d. all of the above
- 6. Which mode of inheritance has been identified in PHPT in keeshonden?**
  - a. autosomal recessive
  - b. autosomal dominant
  - c. X-linked recessive
  - d. mitochondrial
- 7. Treatment modalities for PHPT include**
  - a. surgery.
  - b. percutaneous ultrasonography-guided ethanol ablation.
  - c. percutaneous ultrasonography-guided radiofrequency heat ablation.
  - d. all of the above
- 8. Immediate therapy for hypercalcemia is warranted in the presence of**
  - a. azotemia.
  - b. a calcium–phosphorus product >70.
  - c. a calcium–phosphorus product <70.
  - d. a and b
- 9. Immediate therapy for hypercalcemia may include**
  - a. saline diuresis (0.9% saline).
  - b. furosemide.
  - c. glucocorticoids.
  - d. all of the above
- 10. Which statement regarding posttreatment management of dogs with PHPT is true?**
  - a. Almost all dogs require posttreatment calcium supplementation.
  - b. The typical time frame for the development of clinically significant hypocalcemia is 3 to 7 days posttreatment.
  - c. Preemptive treatment with calcium supplementation is recommended in all cases.
  - d. If the serum calcium concentration before surgery or ablation chronically exceeds 15 mg/dL, the incidence of posttreatment hypocalcemia is decreased.