

# Primary Hyperparathyroidism

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## P Profile

- Primary hyperparathyroidism (PHPT) and primary hypoparathyroidism are the most common primary parathyroid gland diseases.
- Two external parathyroid glands lie outside the thyroid capsule, and two internal parathyroid glands are embedded within the thyroid parenchyma.<sup>1</sup>
- Parathyroid glands synthesize and secrete parathyroid hormone (PTH) from chief cells.<sup>2</sup>
  - PTH increases plasma calcium concentration by mobilizing calcium from bone, increasing renal calcium reabsorption, and promoting formation of calcitriol, which increases intestinal calcium absorption.
  - PTH promotes phosphaturia by decreasing renal phosphorus reabsorption.
- Parathyroid gland diseases are characterized by abnormalities in serum calcium and phosphorus concentrations.
  - Clinical signs are frequently secondary to serum calcium abnormalities.
- Parathyroid glands may also be affected secondary to other disease states (eg, renal secondary hyperparathyroidism).

### Definition & Pathophysiology<sup>3,4</sup>

- Excessive PTH production from autonomously functioning chief cells, usually in a single parathyroid adenoma
- Parathyroid carcinoma, hyperplasia, or multiple parathyroid adenomas are possible but rare.

### Systems

- Urinary, neuromuscular, and GI signs are possible.

### Incidence & Prevalence

- Accounts for ~13% of dogs with ionized hypercalcemia<sup>5</sup>
- PHPT is caused by adenoma of the parathyroid gland (75%–85% of cases), hyperplasia (5%–15% of cases), and carcinoma (5%–10% of cases).<sup>4,6,7</sup>
- Rarer in cats<sup>8</sup>
  - More common causes of hypercalcemia in cats include renal failure and idiopathic hypercalcemia (Table, next page).

### Signalment

#### Breed Predislection

- Autosomal dominant inheritance causes increased prevalence in keeshonds,<sup>9</sup> but PHPT should be considered as a differential for any dog or cat with hypercalcemia.

#### Age & Range

- Middle-aged to geriatric dogs

#### Sex Predislection

- No known predislection

### Clinical Signs<sup>3,6</sup>

- Mainly attributable to hypercalcemia, which may be found incidentally:
  - Up to 35% of patients show no clinical signs.



Parathyroid gland diseases are characterized by abnormalities in serum calcium and phosphorus concentrations.

For More



See the companion article **Primary Hypoparathyroidism** on page 15 of this issue.

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PHPT = primary hyperparathyroidism, PTH = parathyroid hormone

- ❑ Affected patients often appear healthier than those with other causes of hypercalcemia (eg, lymphoma).
- Causes(s) and approximate frequency of clinical signs:
  - ❑ Polyuria/polydipsia from decreased renal tubular response to antidiuretic hormone (50%–60%)
  - ❑ Hematuria, stranguria, pollakiuria, urinary tract infection, and urinary tract obstruction (50%)
    - Calcium phosphate or oxalate urolithiasis may result from calciuria and phosphaturia.

- Dilute urine-specific gravity predisposes patients to infection.
- ❑ Lethargy, muscle wasting, and stiffness from decreased neuromuscular tissue excitability (40%–45%)
- ❑ Inappetence (37%), vomiting (13%), and constipation (6%) caused by decreased excitability and motility of GI smooth muscle

**Physical Examination**

- Patients may appear lethargic or weak.
- A cervical mass may be palpated in cats.
- A palpable parathyroid mass is rare in dogs.

- ❑ A palpated mass could represent an alternative cause of hypercalcemia (eg, thyroid carcinoma).
- Examination should not identify any finding consistent with other causes of hypercalcemia (eg, lymphadenopathy).

**Dx Diagnosis**

**Definitive**

- Histologic examination of parathyroid gland mass(es) following successful surgical removal/ablation and resolution of hypercalcemia

**Table Differential Diagnoses for Hypercalcemia & Hypocalcemia**

<i>Differential</i>	<i>Hypercalcemia</i>	<i>Hypocalcemia</i>
<b>Anomalous</b>	Idiopathic hypercalcemia of cats*	
<b>Metabolic</b>	Acute kidney injury,* chronic kidney disease,* hypoadrenocorticism,* primary hyperparathyroidism secondary to adenomatous gland hyperplasia	Eclampsia,* intestinal malabsorption,* vitamin D deficiency, magnesium deficiency, acute kidney injury,* chronic kidney disease,* nutritional secondary hyperparathyroidism (eg, feeding a high-phosphorus, low-calcium diet), primary hypoparathyroidism secondary to another cervical disease
<b>Neoplastic</b>	Lymphoma,* anal sac adenocarcinoma,* primary hyperparathyroidism related to parathyroid adenoma* or carcinoma, multiple myeloma, leukemia, other carcinomas, thymoma, metastatic or primary bone tumors (eg, osteosarcoma)	Medullary thyroid carcinoma, tumor lysis syndrome, osteoblastic bone tumors
<b>Inflammatory Infectious Immune mediated Iatrogenic</b>	Granulomatous disease, canine angiostrongylosis (caused by <i>Angiostrongylus vasorum</i> infection), osteomyelitis	Sepsis,* trauma, pancreatitis,* primary hypoparathyroidism resulting from immune-mediated destruction or iatrogenic following PHPT surgery or sudden correction of hypercalcemia
<b>Toxic</b>	Vitamin D toxicity	Ethylene glycol toxicity
<b>Nonpathologic</b>	Immaturity, <sup>10</sup> lipemia, laboratory error, excessive calcium supplementation, thiazide treatment	Hypoalbuminemia,* laboratory error, phosphate-enema administration, transfusion with citrate-anticoagulated blood, EDTA sample contamination, sodium bicarbonate administration

\*Denotes common cause

- Plasma PTH can be measured to support diagnosis.

### Differentials

- Differential diagnoses for hypercalcemia can vary (Table).

### Laboratory Findings

- Chemistry panel: total hypercalcemia, decreased or borderline-low serum phosphorus concentration, possible azotemia
  - Ionized hypercalcemia in >90% of cases<sup>3</sup>
- Urinalysis: frequent hyposthenuria or isosthenuria
  - Crystalluria, bacteriuria, hematuria, and pyuria are possible.

### Imaging

- Ventral neck ultrasonography may identify parathyroid masses (Figure 1).
  - Most masses are small (4–9 mm in diameter).
  - Ultrasonography can be highly sensitive and is operator-dependent.
- Parathyroid scintigraphy with Technetium (99mTc) sestamibi, nuclear medicine imaging, can identify hyperfunctional parathyroid tissue

in patients with negative ultrasound findings but may show poor sensitivity and specificity in dogs.<sup>11</sup>

- Abdominal ultrasonography may reveal urinary tract calculi or other lesions causing hypercalcemia (eg, lymphoma).
- Plain radiography may reveal radio-opaque urinary calculi or intrathoracic lesions causing hypercalcemia (eg, anterior mediastinal mass).

### Other Diagnostics

- Plasma PTH concentration
  - Values that are increased or in the upper half of reference range are consistent with PHPT in hypercalcemic patients, which should have low PTH values.
- Serum PTH-related peptide concentration
  - Identifies most cases of hypercalcemia of malignancy

## Tx Treatment

- Definitive treatment requires removal or ablation of parathyroid mass(es).

### Medical

- No definitive medical cure
- Medical therapy can ameliorate severe hypercalcemia signs before definitive treatment or can be used to treat or prevent postoperative hypocalcemia following parathyroid nodule removal or ablation (see **Hypercalcemia: Treatment Basics and Prevention & Treatment of Hypocalcemia**, next page).

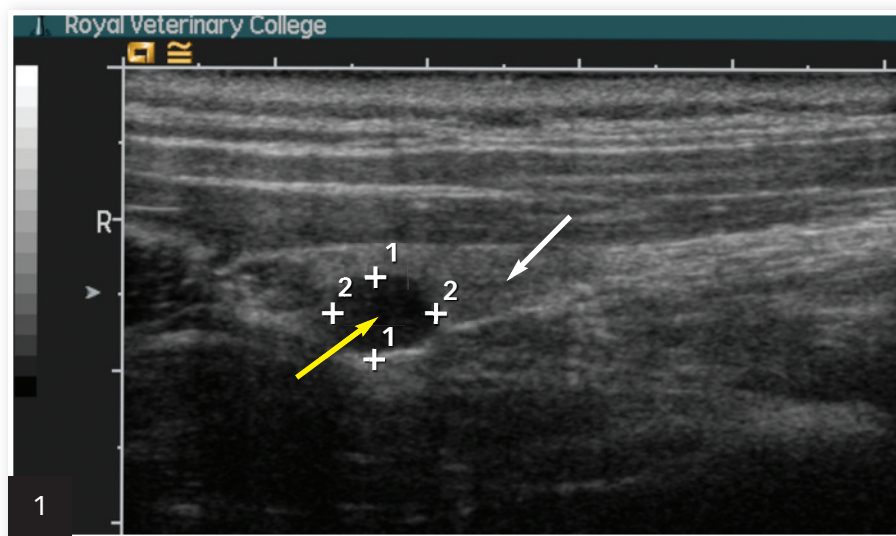
### Surgical & Interventional

- Three definitive treatments are described:
  - Surgical parathyroidectomy
    - Mass(es) should be located preoperatively using imaging.
    - Success rate, 89%–96%<sup>6,12</sup>
  - Percutaneous ultrasound-guided radiofrequency heat ablation
    - Nodule is destroyed by thermal necrosis from radiofrequency waves applied through IV catheter under ultrasound guidance.
    - Equipment is expensive.
    - Success rate, 81%–92%<sup>12,13</sup>
  - Percutaneous ultrasound-guided ethanol ablation
    - Ethanol is injected into the nodule with ultrasound guidance, causing coagulation necrosis.
    - Used less frequently because of lower success rates (~72%)<sup>12</sup>
- Parathyroidectomy is most commonly used by the authors, but preferred treatment method depends on local expertise and experience.

## Follow-up

### Patient Monitoring

- Patients should be hospitalized with limited exercise for ≥5 days postoperatively to minimize risk and monitor for hypocalcemia.
- Total and ionized serum calcium concentrations should be measured q12–24h for ≥5 days postoperatively.



Cervical ultrasound of parathyroid mass (yellow arrow) within the parenchyma of a thyroid gland lobe (white arrow)

PHPT = primary hyperparathyroidism, PTH = parathyroid hormone

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- Slightly low serum calcium concentration (8–10 mg/dL) should be maintained to prevent iatrogenic hypercalcemia and promote return of parathyroid function.<sup>4</sup>
- If given, vitamin D and calcium therapy should be tapered and discontinued over 3–5 months, starting 14 days after treatment is initiated.
  - Serum calcium should be measured before each reduction.

**Complications<sup>4,7</sup>**

- Postoperative hypocalcemia can occur 4–7 days posttreatment in up to 30% of patients.
  - May develop after any treatment method
  - Causes signs in up to 10% of patients
  - Hypocalcemia risk may correlate with duration and magnitude of preoperative hypercalcemia, but currently there is no method for identifying which patients will be affected.<sup>14</sup>
- Horner syndrome and transient laryngeal paralysis have been reported following ultrasound-guided treatment.

**\* In General**

**Relative Cost**

- Definitive treatment can be expensive, especially if patient requires cystotomy or has clinical hypocalcemia after treatment: \$\$\$\$\$
- Surgical parathyroidectomy: \$\$\$\$\$
- Percutaneous ultrasound-guided radiofrequency heat ablation: \$\$\$\$
- Percutaneous ultrasound-guided ethanol ablation: \$\$\$\$

**Cost Key**

\$ = up to \$100  
 \$\$ = \$101–\$250  
 \$\$\$ = \$251–\$500  
 \$\$\$\$ = \$501–\$1000  
 \$\$\$\$\$ = more than \$1000

**Prognosis**

- Excellent with appropriate management
- Definitive treatment is curative in most cases.
- Approximately 10% of patients have recurrence.<sup>4,6</sup> ■ **cb**

**Prevention & Treatment of Hypocalcemia<sup>4</sup>**

**Prevention**

- PO calcium and vitamin D supplementation initiated 1–2 days preoperatively can decrease risk for postoperative hypocalcemia and may be appropriate in patients with marked preoperative hypercalcemia.
- Commonly used forms of vitamin D are calcitriol (0.03–0.06 µg/kg/day) or dihydrotachysterol (0.02–0.03 mg/kg/day).
  - Calcitriol tablets require compounding for smaller patients.
  - Dihydrotachysterol, not available in the U.S., has a longer half-life than calcitriol; both can cause hypercalcemia if oversupplementation occurs.

**Treating Postoperative Clinical Hypocalcemia**

- 10% calcium gluconate (5–15 mg/kg) IV can be administered over 10–30 minutes with ECG monitoring.
- This can be followed with continuous IV infusion of 10% calcium gluconate (60–90 mg/kg/day) to prevent signs while PO vitamin D is initiated.
- Intermittent boluses may be safer because of risk for tissue necrosis following extravasation.

**Treating Postoperative Hypocalcemia in Patients Without Clinical Signs**

- PO vitamin D and calcium therapy is suggested if serum total calcium concentration is <8.5 mg/dL or serum ionized calcium concentration is <0.8 mmol/L.

**Hypercalcemia: Treatment Basics**

The following can be used to treat patients with PHPT and preoperative clinical hypercalcemia<sup>2</sup>:

- 0.9% NaCl diuresis promotes urinary calcium excretion.
- Furosemide promotes urinary calcium loss.
- Calcitonin reduces osteoclast activity, but the effect is short-lived and the drug is expensive.
- Bisphosphonates decrease osteoclast activity and should only be given when subsequent surgery or mass ablation is not anticipated; otherwise postoperative hypocalcemia may be severe and protracted.
  - PO bisphosphonates should be used cautiously, as they may cause esophagitis and stricture.
  - IV bisphosphonates are more effective.
- Glucocorticoids are poorly effective in PHPT and should not be given if the cause of hypercalcemia is unknown, as they can interfere with the ability to diagnose lymphoma.

See Aids & Resources, back page, for references & suggested reading.