Parathyroid disorders are most often identified incidentally by abnormalities in serum calcium levels when screening for renal or bone disease or other conditions. Parathyroid hormone, which is released by the parathyroid glands primarily in response to low calcium levels, stimulates osteoclastic bone resorption and serum calcium elevation, reduces renal calcium clearance, and stimulates intestinal calcium absorption through synthesis of 1,25-dihydroxyvitamin D. Primary hyperparathyroidism, in which calcium levels are elevated without appropriate suppression of parathyroid hormone levels, is the most common cause of hypercalcemia and is often managed surgically. Indications for parathyroidectomy in primary hyperparathyroidism include presence of symptoms, age 50 years or younger, serum calcium level more than 1 mg per dL above the upper limit of normal, osteoporosis, creatinine clearance less than 60 mL per minute per 1.73 m², nephrolithiasis, nephrocalcinosis, and hypercalcuria. Secondary hyperparathyroidism is caused by alterations in calcium, phosphate, and vitamin D regulation that result in elevated parathyroid hormone levels. It most commonly occurs with chronic kidney disease and vitamin D deficiency, and less commonly with gastrointestinal conditions that impair calcium absorption. Secondary hyperparathyroidism can be managed with calcium and vitamin D replacement and reduction of high phosphate levels. There is limited evidence for the use of calcimimetics and vitamin D analogues for persistently elevated parathyroid hormone levels. Hypoparathyroidism, which is most commonly caused by iatrogenic surgical destruction of the parathyroid glands, is less common and results in hypocalcemia. Multiple endocrine neoplasia types 1 and 2A are rare familial syndromes that can result in primary hyperparathyroidism and warrant genetic testing of family members, whereas parathyroid cancer is a rare finding in patients with hyperparathyroidism. (Am Fam Physician. 2022;105(3):289-298. Copyright © 2022 American Academy of Family Physicians.)

The parathyroid glands typically lie adjacent to the thyroid gland, although they are occasionally located in the superior mediastinum. Parathyroid glands regulate serum calcium in response to abnormal levels. When the extracellular calcium-sensing receptor (CASR) on parathyroid cells detects low serum calcium levels, one or more of the parathyroid glands release parathyroid hormone (PTH), an 84-amino acid peptide. PTH stimulates osteoclasts to resorb bone and mobilize calcium into the blood, reduces renal calcium clearance, and stimulates intestinal calcium absorption through synthesis of 1,25-dihydroxyvitamin D (Figure 1). Conversely, high calcium levels drive PTH suppression, with hypermagnesemia and 1,25-dihydroxyvitamin D also inhibiting the production and release of PTH. Parathyroid disorders can be primary or secondary.

Initial Approach to Calcium Abnormalities

Parathyroid disorders are most often identified incidentally by abnormalities in serum calcium levels when screening for renal or bone disease or other conditions. Once a calcium abnormality has been identified, the evaluation should include a systematic search for signs and symptoms associated with abnormal calcium levels (Table 1). A history should include dietary intake of calcium and phosphorus, medications that increase
serum calcium levels (Table 2), supplements that contain calcium, and family history of endocrine disorders. A patient history of conditions such as fractures, pancreatitis, and nephrolithiasis may indicate or contribute to abnormal calcium levels.

Initial laboratory testing (Figure 2 and Figure 3) can be used to identify potential etiologies of parathyroid disorders that affect calcium levels. Primary hyperparathyroidism and malignancy are the most common causes of hypercalcemia. Additional causes are listed in Table 2. Humoral hypercalcemia of malignancy, a paraneoplastic syndrome mediated by PTH-related peptide, should be considered in patients with low PTH levels, rapid onset of symptoms, and other signs and symptoms of malignancy (e.g., weight loss, fatigue, loss of appetite, night sweats). It is most often associated with squamous cell carcinoma and solid tumors of the lung, breast, esophagus, skin, cervix, and kidney.

Vitamin D deficiency is the most common cause of hypocalcemia. Severe symptomatic hypercalcemia (serum calcium level greater than 14 mg per dL [3.50 mmol per L]) should be managed acutely with intravenous fluids, bisphosphonates, calcitonin, denosumab, or dialysis. Severe symptomatic hypocalcemia, which can present acutely with carpopedal spasm, tetany, seizures, and a prolonged QT interval, should be managed with intravenous calcium gluconate while the cause is being determined.

Hyperparathyroidism

Primary hyperparathyroidism is a common condition and the most common cause of hyperparathyroidism and mild hypercalcemia. In primary hyperparathyroidism, calcium levels are usually elevated without appropriate suppression of PTH levels, which can be normal or high. However, in normocalcemic cases, calcium levels can be normal with elevated PTH levels, which may be encountered incidentally when screening for bone and renal disorders. In nations with readily accessible laboratory services, primary hyperparathyroidism is most often identified in asymptomatic individuals as an incidental finding of hypercalcemia on routine laboratory testing.

Risk factors for primary hyperparathyroidism include neck radiation, lithium use, and multiple
PARATHYROID DISORDERS

endocrine neoplasia (MEN). Most causes result from a single adenoma, with less than one-third of cases due to multiglandular disease.

Comprehensive evaluation of hypercalcemia (Figure 2) to identify primary hyperparathyroidism should begin with symptom assessment and laboratory testing, including measurements of serum total or ionized calcium, albumin (for calcium correction), PTH, serum creatinine, 25-hydroxyvitamin D, and 24-hour urinary calcium and creatinine levels (to distinguish from hypocalciuric hypercalcemia). Dual-energy x-ray absorptiometry is also recommended.

Para-thyroid imaging is not needed to diagnose primary hyperparathyroidism but may be helpful for perioperative management.

Familial hypocalciuric hypercalcemia is a rare, autosomal dominant disorder that presents with abnormally high levels of calcium in the blood, low urinary calcium excretion, and normal or slightly elevated PTH levels. Familial hypocalciuric hypercalcemia generally does not require treatment, including surgery. Genetic counseling to identify the approximately 10% of patients with a CASR gene mutation is recommended for patients with primary hyperparathyroidism who are younger than 40 years or have a suspected familial cause (familial hypocalciuric hypercalcemia), clinical findings suspicious for MEN1, or multiglandular disease.

**TABLE 1**

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Hypercalcemia</th>
<th>Hypocalcemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Arrhythmias, bradycardia, hypertension, palpitations, prolonged PR interval, shortened QT interval</td>
<td>Arrhythmias, dyspnea, heart failure, hypotension, palpitations, prolonged QT interval, syncope, torsades de pointes</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Abdominal pain, anorexia, constipation, dyspepsia, epigastric pain, nausea, pancreatitis, vomiting</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Arthralgias, bone pain, fractures, myalgias</td>
<td>Muscle spasms</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Confusion, delirium, headache, impaired concentration, impaired vision, lethargy, memory loss, sleep disturbance</td>
<td>Acute: Chvostek sign,* circumoral numbness, headache, impaired vision, seizures, tetany, Trousseau sign† Chronic: dementia, parkinsonism</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Anxiety, depression, emotional instability</td>
<td>Anxiety, depression</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>—</td>
<td>Bronchospasm, laryngospasm, wheezing</td>
</tr>
<tr>
<td>Renal</td>
<td>Polydipsia, polyuria, renal colic, renal failure</td>
<td>—</td>
</tr>
</tbody>
</table>

*—Chvostek sign is twitching of the facial muscles after tapping the facial nerve.
†—Trousseau sign is carpopedal spasm after inflation of a sphygmomanometer cuff.

Information from references 1, 2, and 4-6.

**TABLE 2**

**Differential Diagnosis of Hypercalcemia**

**PTH dependent**

Genetic disorders: familial hyperparathyroidism, familial hypocalciuric hypercalcemia, hyperparathyroidism—jaw tumor syndrome, multiple endocrine neoplasia

Medications: lithium

Primary hyperparathyroidism

Tertiary hyperparathyroidism*

**PTH independent**

Cancer: humoral hypercalcemia of malignancy (mediated by PTH-related peptide), osteolytic metastases (e.g., multiple myeloma)

Excess vitamin D

Endogenous sources: Williams syndrome, granulomatous diseases such as sarcoidosis, tuberculosis, histoplasmosis, or coccidioidomycosis

Exogenous sources: vitamin D supplements or analogues

Medications: thiazides, theophylline, vitamin A, synthetic PTH (teriparatide [Forteo], abaloparatide [Tymlos]), calcium (milk-alkali syndrome)

Other endocrine disorders: thyrotoxicosis, adrenal insufficiency, pheochromocytoma

Renal failure (acute or chronic)

PTH = parathyroid hormone.

*—Excessive secretion of PTH after long-standing secondary hyperparathyroidism, usually in patients with end-stage renal disease or after kidney transplantation.

Information from references 1, 2, and 4-6.
Hypercalcemia confirmed with corrected* and/or ionized calcium level

Hypercalcemia is severe (> 14 mg per dL [3.50 mmol per L]) or accompanied by severe symptoms?

Yes

Treat hypercalcemia immediately and assess for malignant causes

No

Perform history and physical examination

Review diet and medications

Measure PTH

PTH low

PTH-independent hypercalcemia:

Measure PTH-related peptide, 1,25-dihydroxyvitamin D, 25-hydroxyvitamin D

PTH-related peptide level elevated?

Yes

Humoral hypercalcemia of malignancy likely; reassess for evidence of malignancy

No

1,25-dihydroxyvitamin D elevated?

Yes

Granulomatous diseases or lymphoma likely; order chest radiography and computed tomography

No

25-hydroxyvitamin D level elevated?

Yes

Vitamin D toxicity likely; reassess medications

No

Measure serum and urine protein electrophoresis, thyroid-stimulating hormone, vitamin A, or cortisol to rule out other potential causes

PTH-dependent hypercalcemia:

Measure serum creatinine, 25-hydroxyvitamin D, 24-hour urinary calcium and creatinine, and bone density

Urinary calcium to creatinine clearance ratio < 0.01?

Yes

Familial hypocalciuric hypercalcemia

No

Primary hyperparathyroidism; risk factors for MEN‡?

Yes

Patient is symptomatic or meets criteria for surgery (Table 3)?

No

No

Yes

Refer for parathyroidectomy

Initiate medical management of primary hyperparathyroidism (Table 4), with continued assessment

MEN = multiple endocrine neoplasia; PTH = parathyroid hormone.

*—Corrected calcium = measured serum calcium + 0.8(4 – measured serum albumin).

†—Calcium to creatinine clearance ratio = (24-hour urinary calcium x serum creatinine) ÷ (serum calcium x 24-hour urinary creatinine).

‡—Risk factors for MEN include familial hyperparathyroidism, hyperparathyroidism before 40 years of age, multiglandular primary hyperparathyroidism, characteristic neuroendocrine tumors, and relatives with known MEN mutations.27

Algorithm for the evaluation of hypercalcemia.

Information from references 1, 2, and 4-6.
Indications for parathyroidectomy in patients with primary hyperparathyroidism include the presence of symptoms, age 50 years or younger, serum calcium level more than 1 mg per dL (0.25 mmol per L) above the upper limit of normal, osteoporosis, creatinine clearance less than 60 mL per minute per 1.73 m² (1.00 mL per second per m²), nephrolithiasis, nephrocalcinosis, and hypercalcemia. Patients who desire surgery and do not have contraindications may also be considered for parathyroidectomy. Increasing evidence regarding the benefits and risks of operative management has expanded the number of asymptomatic patients who are recommended for surgery.

Parathyroidectomy has been shown to normalize PTH and calcium levels, decrease nephrolithiasis, reduce renal function deterioration, and improve bone mineral density. Postoperative hypoparathyroidism is a rare complication (0% to 3.6%). Risks of untreated primary hyperparathyroidism include increased mortality, cardiovascular disease, cerebrovascular disease, renal failure, nephrolithiasis, and reduced bone mineral density. The effects of nontreatment on neurocognitive symptoms are less clear.

### TABLE 3

**Indications for Parathyroidectomy in Primary Hyperparathyroidism**

Asymptomatic primary hyperparathyroidism and any of the following:

- 50 years or younger at diagnosis
- Serum calcium level > 1 mg per dL (0.25 mmol per L) above the upper limit of normal
- Osteoporosis (T-score < −2.5), fragility fracture, or evidence of vertebral compression fracture on spinal imaging
- Creatinine clearance < 60 mL per minute per 1.73 m² (1.00 mL per second per m²) or other renal involvement, including silent nephrolithiasis on imaging, nephrocalcinosis, or hypercalcemia (24-hour urinary calcium level > 400 mg per dL)

Patients who desire surgery and have no medical contraindications

Symptomatic hypercalcemia

Information from references 13 and 15-17.
Asymptomatic patients who are not surgical candidates should be monitored to identify those who may benefit from risk reduction and medical management of the complications of untreated primary hyperparathyroidism. This surveillance includes serum calcium, creatinine, and estimated glomerular filtration rate measurements annually and bone density evaluation every one to two years. Annual renal imaging and 24-hour urine collection are also indicated in patients with a history of renal calculi.

All patients should be encouraged to maintain adequate hydration to reduce the risk of nephrolithiasis, maintain adequate physical activity to minimize bone resorption, and avoid medications that increase hypercalcemia (e.g., thiazides, lithium). Maintaining adequate dietary calcium intake (1,000 mg per day) and vitamin D intake (400 to 800 IU per day) to keep 25-hydroxyvitamin D levels at 20 or 30 ng per mL (49.92 or 74.88 nmol per L) or higher helps avoid further increases in PTH level.

### TABLE 4

**Medical Management of Primary Hyperparathyroidism**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Primary indication</th>
<th>Bone mineral density</th>
<th>Calcium</th>
<th>PTH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bisphosphonates</strong>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate (Fosamax)</td>
<td>Increase bone mineral density</td>
<td>Increased, no fracture data</td>
<td>Serum: unchanged</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Pamidronate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risedronate (Actonel)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoledronic acid (intravenous; Reclast)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Calcimimetics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cinacalcet (Sensipar)</td>
<td>Reduce serum calcium</td>
<td>Unchanged</td>
<td>Serum: decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Etelcalcetide (Parsabiv)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evocalcet (not available in the United States)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hormone therapy (postmenopause)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td>Reduce menopausal symptoms</td>
<td>Increased, no fracture data</td>
<td>Serum: decreased</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Selective estrogen receptor modulators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Monoclonal antibodies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denosumab</td>
<td>Increase bone mineral density</td>
<td>Increased</td>
<td>Serum: decreased</td>
<td>Unchanged or increased</td>
</tr>
<tr>
<td><strong>Thiazide diuretics†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>Reduction of urinary calcium can reduce risk of nephrolithias</td>
<td>Increased</td>
<td>Serum: increased or unchanged</td>
<td>Decreased</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td></td>
<td></td>
<td>Urine: decreased</td>
<td></td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholecalciferol (D_{3})</td>
<td>Increase vitamin D</td>
<td>Increased</td>
<td>Serum and urine: increased or unchanged</td>
<td>Decreased</td>
</tr>
<tr>
<td>Ergocalciferol (D_{2})</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PTH = parathyroid hormone.

*—Pamidronate, risedronate, and zoledronic acid are not as well studied as alendronate and may be less effective.
†—Thiazides are typically avoided in patients with primary hyperparathyroidism because of the further increase in hypercalcemia, and they are contraindicated in severe hypercalcemia. They can be considered in patients at risk of calcium stone disease.

Information from references 16, 17, and 21-23.
PARATHYROID DISORDERS

Medical management of primary hyperparathyroidism (Table 4) can be considered to improve bone mineral density and/or reduce calcium in patients who are not candidates for surgery.16,17,21-23

SECONDARY

Secondary hyperparathyroidism is a result of alterations in calcium, phosphate, and vitamin D regulation from nonparathyroid causes that lead to elevated PTH levels. It most commonly occurs with chronic kidney disease (CKD) and vitamin D deficiency and less commonly with gastrointestinal conditions that impair calcium absorption.7 Laboratory testing to evaluate for potential causes and management should include measurement of serum PTH, creatinine, calcium, phosphate, albumin, alkaline phosphatase, and 25-hydroxyvitamin D.8 Management of secondary hyperparathyroidism is important for prevention of bone and cardiovascular diseases.8

Family physicians commonly care for patients with renal impairment who are not undergoing dialysis and play an important role in laboratory monitoring (eTable A) and initial management of CKD–bone mineral disorder (BMD), which is a disorder of mineral and bone metabolism as a result of renal disease. In patients with CKD stage 3a to 5, bone density measurement can predict fracture risk.8 Initial treatment of secondary hyperparathyroidism (Table 5) is focused on treating underlying causes and can include calcium replacement, vitamin D replacement, and reduction of high phosphate levels, with the goal of avoiding severe hyperphosphatemia and hypercalcemia, which have been associated with increased mortality.8

Limited evidence shows that dietary interventions to increase calcium intake and reduce phosphorus and protein intake can improve CKD-BMD.9 The Endocrine Society recommends supplementation with 50,000 IU of vitamin D2 or D3 once per week for eight weeks or its equivalent of 6,000 IU per day of vitamin D2 or D3 to achieve a 25-hydroxyvitamin D level above 30 ng per mL, followed by maintenance therapy of 1,500 to 2,000 IU per day.9

### TABLE 5

<table>
<thead>
<tr>
<th>Medication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcimimetics</strong></td>
<td></td>
</tr>
<tr>
<td>Cinacalcet (Sensipar)</td>
<td>Decrease PTH</td>
</tr>
<tr>
<td>Etelcalcetide (Parsabiv)</td>
<td>Adverse effects: hypocalcemia, nausea</td>
</tr>
<tr>
<td>Evocalcet (not available in the United States)</td>
<td>May reduce need for parathyroidectomy in adults undergoing dialysis</td>
</tr>
<tr>
<td></td>
<td>No effect on cardiovascular events, fractures, mortality</td>
</tr>
<tr>
<td><strong>Calcium supplements</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>Increase serum calcium</td>
</tr>
<tr>
<td>Calcium citrate</td>
<td></td>
</tr>
<tr>
<td>Calcium gluconate</td>
<td></td>
</tr>
<tr>
<td><strong>Phosphate binders</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium based</td>
<td>Decrease serum phosphorus, PTH</td>
</tr>
<tr>
<td>Calcium acetate (21% elemental calcium)</td>
<td>Adverse effects: hypercalcemia (calcium-based medications), kidney stones (calcium-based medications), gastrointestinal upset (lanthanum, sevelamer), constipation (sevelamer), metabolic acidosis (sevelamer hydrochloride)</td>
</tr>
<tr>
<td>Calcium carbonate (40% elemental calcium)</td>
<td>No effect on cardiovascular events, stroke, fracture, mortality</td>
</tr>
<tr>
<td>Non–calcium based</td>
<td></td>
</tr>
<tr>
<td>Lanthanum (Fosrenol)</td>
<td>Higher cost (non–calcium-based medications)</td>
</tr>
<tr>
<td>Sevelamer</td>
<td></td>
</tr>
<tr>
<td><strong>Vitamin D analogues</strong></td>
<td></td>
</tr>
<tr>
<td>Calciifiediol (25-hydroxycholecalciferol)</td>
<td>Increase serum calcium and phosphorus</td>
</tr>
<tr>
<td>Calcitriol (1,25-dihydroxycholecalciferol; Rocaltrol)</td>
<td>Decrease PTH and bone resorption</td>
</tr>
<tr>
<td>Doxercalciferol (1alpha-hydroxyergocalciferol; Hectorol)</td>
<td>Not shown to cause hypercalcemia</td>
</tr>
<tr>
<td>Paricalcitol (1alpha-hydroxyergocalciferol; Zemplar)</td>
<td></td>
</tr>
<tr>
<td><strong>Vitamin D supplements</strong></td>
<td></td>
</tr>
<tr>
<td>Cholecalciferol (D2)</td>
<td>Increase 25-hydroxyvitamin D and serum calcium</td>
</tr>
<tr>
<td>Ergocalciferol (D3)</td>
<td></td>
</tr>
</tbody>
</table>

BMD = bone mineral disorder; CKD = chronic kidney disease; PTH = parathyroid hormone.

*—Consider for adults not undergoing dialysis who have CKD stage 4 or 5 with severe, progressive hyperparathyroidism. Consider a PTH goal of 2 to 9 times the upper limit of normal in patients undergoing dialysis.

Information from reference 8.
2,000 IU per day.\textsuperscript{10} Phosphate levels can be reduced through dietary restriction and phosphate binders, which include calcium-based and non–calcium-based agents. However, phosphate binders have not demonstrated clinically relevant effects on bone disease, cardiovascular disease, or mortality in patients with CKD who are not undergoing dialysis.\textsuperscript{24}

After management of calcium, vitamin D, and phosphate levels, calcimimetic agents (which reduce secretion of PTH by binding to the CASR) and vitamin D analogues may be considered for reduction of persistently elevated PTH levels in adults with stage 4 or 5 CKD and severe, progressive hyperparathyroidism.\textsuperscript{8} However, the optimal PTH level is unknown. Although calcimimetics have been shown to effectively lower PTH levels, they may cause hypocalcemia and have not been shown to reduce fractures, cardiovascular disease, or mortality.\textsuperscript{25,26}

In patients with secondary hyperparathyroidism who are undergoing dialysis, parathyroidectomy improves
hypercalcemia, hyperphosphatemia, bone mineral density, and health-related quality of life and is associated with 15% to 57% greater survival.\(^2\)

**Hypoparathyroidism**

Hypoparathyroidism is rare and usually caused by iatrogenic destruction of the parathyroid glands during anterior neck surgery (75% of cases).\(^2\) Other, less common etiologies include autoimmune, genetic, metabolic, and malignant causes. Hypoparathyroidism is due to inadequate PTH secretion or an activating mutation of the \(\text{CASR}\) gene, either of which results in renal calcium loss, decreased osteoclast activity, and decreased production of 1,25-dihydroxyvitamin D.\(^1,2\) This typically leads to signs and symptoms consistent with hypocalcemia (Table 1, Table 2). Figure 3 is an algorithm for evaluating symptomatic or incidental hypocalcemia,\(^7\) and Table 6 lists common laboratory findings based on etiology.\(^2\) Hypoparathyroidism is diagnosed by a low or normal intact PTH level with concomitant low serum corrected calcium level and normal serum magnesium level.\(^1,11,28,30\)

In chronic hypoparathyroidism, goals of treatment are preventing symptoms of hypocalcemia, maintaining serum calcium concentration at the low end of the normal range while also avoiding hypercalcemia, and limiting hypercalciuria.\(^1,2,28\) Oral calcium (1.5 to 3 g of elemental calcium per day) and vitamin D analogues, such as calcitriol (1,25-dihydroxycholecalciferol; Rocaltrol), are the mainstays of therapy.\(^1,2\) In the absence of adequate PTH, these supplements may lead to hypercalciumia and subsequent complications of nephrocalcinosis and nephrolithiasis. Thiazide diuretics can mitigate these effects by decreasing hypercalciuria.\(^2\)

**Other Parathyroid Disorders**

MEN is a rare, diverse group of familial disorders characterized by benign and malignant tumor formation of various endocrine glands. MEN1 encompasses a variety of tumors commonly involving the parathyroid gland, pituitary gland, and pancreas.\(^31\) MEN2A includes medullary thyroid carcinoma, pheochromocytoma, and hyperparathyroidism.\(^31\)

Given the autosomal dominant inheritance pattern of MEN syndromes, family physicians may need to discuss screening for family members. Genetic screening and laboratory monitoring are recommended for all first-degree relatives of patients with known MEN1 or MEN2 mutations.\(^31-33\) Subtotal parathyroidectomy is typically indicated for all patients with MEN syndromes who are surgical candidates. The approach depends on the location, pathology, and extent of tumor involvement.\(^31,33\)

Although rare, parathyroid cancer can affect 0.5% to 5% of people with primary hyperparathyroidism and may present with marked hypercalcemia, a palpable cervical mass, or laryngeal nerve palsy.\(^34\) Diagnosis of parathyroid cancer is difficult because of the lack of unique biomarkers and imaging characteristics and is often made postoperatively. Treatment involves surgical resection and mitigating hypercalcemia, which can lead to significant morbidity and mortality.\(^34\)

This article updates a previous article on this topic by Michels and Kelly.\(^2\)

**Data Sources:** A PubMed search was completed in Clinical Queries using the key terms hypocalcemia, hypercalcemia, hyperparathyroidism, and hypoparathyroidism. Also searched were Essential Evidence Plus, the Cochrane database, and reference lists of retrieved articles. Search dates: February to October 2021.

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SARAH RAMIREZ, MD, is an assistant professor in the Department of Family and Community Medicine at Penn State Health Hershey Medical Center.

---

**TABLE 6**

<table>
<thead>
<tr>
<th>Hypocalcemia: Laboratory Findings Based on Etiology</th>
<th>Level</th>
<th>PTH</th>
<th>Phosphorus</th>
<th>25-hydroxyvitamin D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium-sensing receptor mutation</td>
<td>Normal or low</td>
<td>Elevated</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Elevated</td>
<td>Elevated</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Hypoparathyroidism</td>
<td>Low</td>
<td>Elevated</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>PTH resistance (pseudo-hypoparathyroidism)</td>
<td>Elevated</td>
<td>Elevated</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>Elevated</td>
<td>Normal or low</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** See Figure 3 for an algorithm on the evaluation of hypocalcemia.

PTH = parathyroid hormone.

MICHAEL PARTIN, MD, is an assistant professor in the Department of Family and Community Medicine at Penn State Health Hershey Medical Center. At the time this article was written, he was a resident at Penn State Health Hershey Medical Center.

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References

# Laboratory Monitoring Recommendations for Patients With CKD-BMD

<table>
<thead>
<tr>
<th>CKD stage</th>
<th>eGFR (mL per minute)</th>
<th>Serum laboratory tests</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a or 3b</td>
<td>30 to 59</td>
<td>Calcium, phosphorus PTH</td>
<td>At baseline and then every 6 to 12 months At baseline and then repeat based on baseline level and CKD progression</td>
</tr>
<tr>
<td>4</td>
<td>15 to 29</td>
<td>Calcium, phosphorus PTH, Alkaline phosphatase</td>
<td>Every 3 to 6 months Every 6 to 12 months Every 12 months, or more often based on baseline level</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15</td>
<td>Calcium, phosphorus PTH, Alkaline phosphatase</td>
<td>Every 1 to 3 months Every 3 to 6 months Every 12 months</td>
</tr>
</tbody>
</table>

BMD = bone mineral disorder; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; PTH = parathyroid hormone.