Fast Facts:
Approximately 100,000 people develop primary hyperparathyroidism (PHPT) in the US each year, usually between the ages of 50-60 and three times more often in women than men. Also, the risk increases with age; 2 out of 1,000 women 60 years and over will develop hyperparathyroidism.\(^1,2\)

Overview
- **PHPT:** The most common clinical presentation in western populations is asymptomatic hypercalcemia detected by routine biochemical screening; 85% are caused by an adenoma.
- **Normocalcemic PHPT:** Increasingly, patients undergoing evaluation for low bone density or other conditions may have PTH levels drawn in the absence of hypercalcemia. An international panel of experts recognized a new phenotype of PHPT in which *PTH levels are elevated but serum calcium is normal.* In order to make this diagnosis, certain conditions must be met. In particular, *all secondary causes for hyperparathyroidism must be ruled out*, and ionized calcium levels should be normal. The most common explanation for the finding of an elevated PTH and normal serum calcium remains concomitant hypercalcemic PHPT and vitamin D deficiency.
- **Secondary hyperparathyroidism (SHPT):** Occurs when the parathyroid gland appropriately responds to a reduced level of extracellular calcium. PTH concentrations rise, and calcium is mobilized by increasing intestinal absorption (via increase in calcitriol) and by increasing bone resorption. Thus, it is *characterized biochemically by elevated PTH and normal or low serum calcium concentrations.*
- SHPT may occur in patients with *renal failure* and impaired calcitriol (1,25 dihydroxyvitamin D) production, as well as in individuals with inadequate calcium intake or absorption, as can occur with *vitamin D deficiency* or with *gastrointestinal diseases causing malabsorption.* Assessment of renal function (serum creatinine), vitamin D status (25-hydroxyvitamin D, 25OHD), and calcium sufficiency (urinary calcium excretion) may help differentiate normocalcemic primary and secondary hyperparathyroidism. Further assessment and work-up for specific gastrointestinal disorders is generally undertaken only when the clinical suspicion is high.\(^3\)
- **Tertiary hyperparathyroidism** may result from chronic SHPT, usually related to CKD or kidney transplant, causing irreversible abnormal production of PTH; PTH remains elevated even after serum calcium is normalized.\(^2\)
**Comparative Findings by Type**

<table>
<thead>
<tr>
<th>PHPT: Secondary</th>
<th>Normocalcemic PHPT</th>
<th>Secondary Renal:</th>
<th>Non-renal:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ↑iPTH</td>
<td>• ↑iPTH</td>
<td>• ↑iPTH</td>
<td>• ↑iPTH</td>
</tr>
<tr>
<td>• ↑Calcium*</td>
<td>• Normal calcium</td>
<td>• Normal/↓ calcium</td>
<td>• Normal/↓ calcium from non-renal cause</td>
</tr>
<tr>
<td>• Normal / ↑ 24hr Urine Calcium</td>
<td>• Normal 24hr Urine Calcium</td>
<td>• 24hr Urine Calcium↑</td>
<td>• ↓ 24hr Urine Calcium</td>
</tr>
<tr>
<td>• Normal / ↓ Vit D</td>
<td>• Normal Vit D Phosphorus†</td>
<td>• Normal / ↓ Vit D ↑Phosphorus</td>
<td>• ↓ Vit D Normal / ↓ Phosphorus</td>
</tr>
<tr>
<td>• Co-existing Vit D deficiency possible</td>
<td>• All secondary causes ruled-out</td>
<td>• Renal disease/CKD</td>
<td>• Vit D deficiency / intestinal malabsorption / lack of sunlight</td>
</tr>
</tbody>
</table>

*A single elevated serum calcium concentration should be repeated to confirm the presence of hypercalcemia. The total serum calcium concentration should be used for both the initial and the repeat serum calcium measurements.

† Unable to determine typical finding in currently available literature.

**Hyperparathyroid Disease**

- **Primary Hyperparathyroid**—The most common clinical presentation of primary hyperparathyroidism (PHPT) in western populations is asymptomatic hypercalcemia detected by routine biochemical screening.

- **Normocalcemic primary hyperparathyroidism** — increasingly, patients undergoing evaluation for low bone density or other conditions may have PTH levels drawn in the absence of hypercalcemia. An international panel of experts recognized a new phenotype of primary hyperparathyroidism in which PTH levels are elevated but serum calcium is normal. In order to make this diagnosis, certain conditions must be met. In particular, all secondary causes for hyperparathyroidism must be ruled out, and ionized calcium levels should be normal. The most common explanation for the finding of an elevated PTH and normal serum calcium remains concomitant hypercalcemic primary hyperparathyroidism and vitamin D deficiency.

- **Secondary hyperparathyroidism** — Secondary hyperparathyroidism occurs when the parathyroid gland appropriately responds to a reduced level of extracellular calcium. PTH concentrations rise, and calcium is mobilized by increasing intestinal absorption (via increase in calcitriol) and by increasing bone resorption. Thus, it is characterized biochemically by elevated PTH and normal or low serum calcium concentrations.

- **Secondary hyperparathyroidism** may occur in patients with renal failure and impaired calcitriol (1,25 dihydroxyvitamin D) production, as well as in individuals with inadequate calcium intake or absorption, as can occur with vitamin D deficiency or with gastrointestinal diseases causing malabsorption. Assessment of renal function (serum creatinine), vitamin D status (25-hydroxyvitamin D, 25OHD), and calcium sufficiency (urinary calcium excretion) may help differentiate normocalcemic primary and secondary hyperparathyroidism. Further assessment and work-up for specific gastrointestinal disorders is generally undertaken only when the clinical suspicion is high.
Signs/Symptoms 3, 4
Asymptomatic or mild:
• Fatigue/Need for sleep
• Muscle weakness
• Aches/pains in bones/joints
• Feeling depressed

Diagnostics
Labs:
• Serum iPTH
• Serum calcium
• 25-Vit D
• Serum phosphorus
• GFR
• Serum creatinine
• 24hr Urine Calcium
• UMA/creatinine ratio

Imaging:
• Bone mineral density (DEXA Scan)
• Parathyroid ultrasound/CT/sestamibi
• Renal ultrasound/CT

Treatment
Treatment will vary based on type & severity:
• Monitor (PHPT)
• Surgery (PHPT)
• Calcimimetics
• Correct calcium, Vit D, phosphorus levels
• Treat any underlying or co-existing conditions
• Referral to endocrinologist/nephrologist

Example Scenarios of SHPT Due to Renal Cause:

Scenario 1
• Elevated o PTH
• Normal o Calcium
• Normal o 25 Vit D
• Secondary hyperparathyroid, renal origin
• Follow-up 6 months

Scenario 2
• Elevated o PTH
• Elevated o Phosphorus
• Normal o Calcium
• Normal o 25 Vit D
• Secondary hyperparathyroid, renal origin
• Phosphorus restriction
• Refer to Nephrology
• Follow-up 6 months

Scenario 3
• Elevated o PTH
• Normal o Calcium
• Normal o 25 Vit D
• Secondary hyperparathyroid, renal origin
• Phosphorus restriction
• Refer to Nephrology
• Follow-up 6 months

Scenario 3a
• After recheck
• If calcium elevated,
• Primary Hyperparathyroid
• Refer to Endocrine

Scenario 3b
• After recheck
• If calcium normal,
• Hyperparathyroid NOS
• Monitor