HYPOPARATHYROIDISM: GUIDELINES AND NEW TREATMENTS

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Disclosures

• Speaker (Honorarium): Shire Pharmaceuticals
PTH controls mineral metabolism

- Thyroid gland
- Parathyroid glands
- Bone
- Kidney
- Intestine

Low calcium sensed through calcium-sensing receptors (CaSR)

- Magnesium cofactor in PTH secretion
- 25(OH)D
- 1,25(OH)₂D (active vitamin D)

Regulates calcium release
Regulates reabsorption of calcium, magnesium and phosphate

Normal range of calcium, magnesium and phosphate

Impaired mineral homeostasis in hypoparathyroidism

Bone
- ↓bone turnover
- ↓calcium release

Kidney
- ↓calcium
- ↓magnesium
- ↑phosphate reabsorption

Intestine
- 25(OH)D
- 1,25(OH)2D
- Active vitamin D
- ↓calcium and ↓phosphate absorption

Hypocalcemia, Hypercalcuria, Hyperphosphatemia

Clinical symptoms of hypoparathyroidism

- Large spectrum of symptoms (mild to debilitating)
- Large inter-individual difference in threshold of calcium
- Highly variable descriptions of symptoms
- Most signs and symptoms due to hypocalcemia
  - Muscle cramps, twitching, tetany
  - Paresthesias

**Serious complications can occur with acute/severe hypocalcemia**
- Bronchospasm and laryngospasm
- Prolonged QTc/heart arrhythmias
- Seizures
Complications of chronic hypoparathyroidism

**Neurologic/psychiatric**
- Basal ganglia calcifications*
- Cataracts
- “Brain fog” and cognitive complaints
- Reduced quality of life*
- Anxiety/depression*
- Fatigue/irritability

**Kidney**
- Hypercalciuría
- Nephrocalcinosis*
- Kidney stones
- Renal failure*

**Skeletal**
- Very low bone metabolism
- Increased bone density
- Unclear effect on fractures
- Stunted growth in children

**Cardiac**
- Heart failure

**Other**
- Increased risk of infections*
- Dry, rough skin
- Brittle fingernails

Mendonça ML, et al. BMC Endocr Disord 2013; 13:1
Increased risk of chronic disease

- Mitchell et al. (Boston)
  - 120 patients, 52 ± 19 years (73% female)
  - 52% had basal ganglia calcifications (n=31 with imaging)
  - 31% had renal calcifications (n=54 with imaging)
  - Stage 3-5 chronic kidney disease 2- to 17-fold greater than age-appropriate normal values

- Underbjerg et al. (Denmark)
  - 688 patients, 49 years (88% female), age- and sex-matched 3:1
  - Risk of depression and bipolar disorders 2-fold higher in surgical hypoparathyroidism
  - Renal insufficiency 3-fold higher in postsurgical and 6-fold higher in nonsurgical hypoparathyroidism
  - Risk of hospitalization due to infection increased in postsurgical (HR, 1.42; 95% CI, 1.20-1.67) and nonsurgical disease (HR, 1.94; 95% CI, 1.55-2.44)

Quality of life (QoL) is reduced*

*Even when serum calcium levels are at goal with conventional therapy

- QoL is reduced compared to controls
  - Arlt et al. (Germany) (n=25) and controls (n=25)
  - Cho et al. (Harvard) (n=340) and controls (n=200); SF-36

- QoL is reduced compared to normative data
  - Cusano et al. (Columbia) (n=54); SF-36
  - Sikjaer et al. (Denmark) (n=62); SF-36

- Both physical and mental health domains are reduced
- No disease-specific questionnaire

Epidemiology of hypoparathyroidism

- Data from a large health plan claims database (77 million unique patients, 75 health plans across the US)
  - Number of diagnoses over 12 months and projected to the US population
  - Proportion of neck surgeries resulting in hypoparathyroidism

~77,000 patients in the US
- 75% postsurgical
- 75% female
- 75% 45 years or older

### Epidemiology, continued

<table>
<thead>
<tr>
<th></th>
<th>Hypoparathyroidism</th>
<th>Postsurgical</th>
<th>Nonsurgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>37/100,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td>29/100,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8/100,000&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>25/100,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>22/100,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.3/100,000&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Incidence</td>
<td>0.8/100,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mortality</td>
<td>-</td>
<td>HR 0.98&lt;sup&gt;c&lt;/sup&gt;</td>
<td>HR 1.25&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>95% CI, 0.76-1.26</td>
<td>95% CI, 0.90-1.73</td>
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</tbody>
</table>

<sup>a</sup>Person-years
<sup>b</sup>US data
<sup>c</sup>Danish data

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**Classified as an orphan disease in the US and European Union**

Causes of hypoparathyroidism

• Postsurgical (~75%)
  • Inadvertent removal or irreversible damage to one or more of the parathyroid glands or their blood supply
• Risk factors in thyroid/parathyroid surgery include:
  • Reoperation
  • Extent of surgery (thyroid lobectomy vs. total, cancer)
  • Substernal goiter
  • Parathyroid localization studies, intraoperative PTH levels
  • High-volume surgeons on average have improved outcomes

7.6% of neck surgeries result in hypoparathyroidism
- 75% transient (<6 months)
- 25% chronic (≥6 months)

Chronic hypoparathyroidism: 1.9% of all neck surgeries
Causes of hypoparathyroidism

- Postsurgical (~75%)
- Medical (~25%)
  - Autoimmune [isolated or part of polyglandular syndrome type 1 (APS-1, also known as PGA-1 and PAS-1)]
  - Genetic (isolated or as part of complex disease)
    - \( PTH \) gene mutations
    - \( Calcium\ sensing\ receptor \) gene mutations
    - \( GCMB \) gene mutations
    - DiGeorge syndrome
    - Hypoparathyroidism-retardation-dysmorphism syndrome
    - Hypoparathyroidism-deafness-renal dysplasia syndrome
    - Mitochondrial mutations

Causes of hypoparathyroidism

- Postsurgical (~75%)
- Medical (~25%)
  - Autoimmune (isolated or part of polyglandular syndrome type 1)
  - Genetic (isolated or as part of complex disease)
  - Infiltration of parathyroid glands (copper, iron, tumor)
  - Radiation (rare)
  - Hypomagnesemia (the only reversible cause)
The burden of hypoparathyroidism

- The Patients’ Attitudes and Responses About Hypoparathyroidism Toleration Explored (PARADOX) study
- 374 hypoparathyroid adults (average age 49 years, average duration 13 years, 85% female)
- Key findings (no control group):
  - 56% felt “unprepared” to manage disease at diagnosis
  - 75% concerned about long-term complications of treatment
  - 72% experienced >10 symptoms in the last year
  - Symptoms experienced on average 13 hours/day
  - 79% of patients had hospital stays or emergency department visits in the last year

Case: Patient AL

- Ms. AL is a 23 year-old woman with a history of compressive goiter status post total thyroidectomy in April 2014 with postsurgical hypoparathyroidism
- She had a goiter for 2 years due to Hashimoto's thyroiditis which had been causing compressive symptoms, particularly dysphagia
- She is status post total thyroidectomy in April 2014
- The pathology report showed Hashimoto's disease with no cancer; one parathyroid gland was noted
History

• Her post-operative course was complicated by hypoparathyroidism, requiring hospitalization of almost 1 week
• She had persistent hypoparathyroidism and trouble with keeping her calcium level at goal, requiring approximately 5-6 emergency department visits since diagnosis
• She is compliant with her regimen
• Wakes up every day with perioral and extremity numbness/tingling; symptoms intermittent during the day
History, continued

• Medications:
  • Regimen for hypoparathyroidism:
    • Morning: calcium citrate 400 mg x 3, calcitriol 0.5 mcg x 2, yogurt
    • Mid-day: calcium citrate 400 mg x 3
    • Evening: calcium citrate 400 mg x 3, calcitriol 0.5 mcg x 2
      ➢ Total calcium: 3.9 g
      ➢ Total calcitriol: 2.0 mcg
      ➢ 13 pills daily
  • Vitamin D 6,000 IU daily from calcium citrate + 10,000 IU weekly
  • Levothyroxine 137 mcg daily
  • Generess Fe 0.8 daily
History, continued

• Social History/Habits
  • Occupation: Medical assistant, starting nursing school
  • Current/past tobacco: No
  • Alcohol: 2 drinks/week (beer, wine)
  • Exercise: Active, no formal exercise

• Family History:
  • Father: Hypothyroidism

• Exam
  • Unremarkable, other than: negative Chovstek’s sign, well-healed neck incision with no palpable thyroid tissue
Laboratories

- Calcium 8.4 mg/dL (nl: 8.7-10.2; 2.10 mmol/L)
- PTH 5 pg/mL (nl: 15-65; 5 ng/L)
- 25-hydroxyvitamin D 34.0 ng/mL (nl: >30 ng/mL; 85 nmol/L)
- BUN/creatinine 13/0.5 mg/dL (eGFR 154 mL/min)
- Phosphorus 4.8 mg/dL (nl: 2.5-4.5; 1.55 mmol/L)
- Calcium-phosphate 40 mg²/dL² (nl: <55; 3.25 mmol²/L²)
- Magnesium 1.6 mg/dL (nl: 1.6-2.6; 0.80 mmol/L)
- 24-hour urine calcium 407 mg (nl: 100-250; 10.2 mmol)
Guidelines

European Society of Endocrinology Clinical Guideline: Treatment of chronic hypoparathyroidism in adults

Jens Bollerslev¹,²,*, Lars Rejnmark³,*, Claudio Marcocci⁴, Dolores M Shoback⁵, Antonio Sitges-Serra⁶, Wim van Biesen⁷ and Olaf M Dekkers⁸,⁹,¹⁰

European Journal of Endocrinology
(2015) 173, G1–G20

Management of Hypoparathyroidism: Summary Statement and Guidelines

Maria Luisa Brandi, John P. Bilezikian, Dolores Shoback, Roger Bouillon, Bart L. Clarke, Rajesh V. Thakker, Aliya A. Khan, and John T. Potts, Jr

J Clin Endocrinol Metab, June 2016, 101(6):2273–2283
ESE guidelines: Management goals *(Suggest)*

- Target treatment to serum calcium in lower part or slightly below normal range – keeping patients free of symptoms or signs of hypocalcemia
- Maintain 24-hour urine calcium within sex-specific reference ranges
  - Women: <250 mg (<6.25 mmol); Men: <300 mg (<7.5 mmol)
- Serum phosphate and magnesium in normal range
- Calcium x Phosphate <55 mg²/dL² (4.4 mmol²/L)
- Aim for “adequate vitamin D status”
- *Recommend* – Personalized treatment focusing on quality of life and well-being
1st International Workshop: Management goals

1. Prevent signs and symptoms of hypocalcemia
2. Maintain the serum calcium concentration slightly below normal (i.e., no more than 0.5 mg/dL below normal) or in the low normal range
3. Maintain the calcium-phosphate product <55 mg\(^2\)/dL\(^2\) (4.4 mmol\(^2\)/L\(^2\))
4. Avoid hypercalciuria
5. Avoid hypercalcemia
6. Avoid renal (nephrocalcinosis/nephrolithiasis) and other extraskeletal calcifications
## ESE guidelines: Routine care

### Monitoring guidelines on conventional therapy

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Calcium, phosphate, magnesium, BUN/creatinine</td>
<td>every 3 to 6 months; weekly or every other week after change in therapy</td>
</tr>
<tr>
<td>24-hour urine calcium and creatinine</td>
<td>yearly or every other year</td>
</tr>
<tr>
<td>Monitor annually for comorbidities</td>
<td></td>
</tr>
<tr>
<td>Renal imaging if stones or creatinine</td>
<td>increases</td>
</tr>
<tr>
<td>Advise against routine monitoring of bone mineral density</td>
<td></td>
</tr>
</tbody>
</table>
### Monitoring guidelines on conventional therapy

**Calcium, phosphate, magnesium, BUN/creatinine and eGFR annually or more frequently if the clinical situation is appropriate**

**24-hour urine calcium and creatinine annually**

**As clinically indicated:**
- Renal imaging for nephrolithiasis or nephrocalcinosis at baseline and every 5 years
- Ophthalmologic examination for cataracts
- Central nervous system imaging for calcification
- Bone density per International Society of Clinical Densitometry guidelines
Patient AL: Routine care

<table>
<thead>
<tr>
<th>Monitoring guidelines on conventional therapy</th>
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</thead>
<tbody>
<tr>
<td>✓ Calcium, phosphate, magnesium, BUN/creatinine and eGFR annually or more frequently; weekly with therapy changes</td>
</tr>
<tr>
<td>✓ 24-hour urine calcium and creatinine annually</td>
</tr>
<tr>
<td>As clinically indicated:</td>
</tr>
<tr>
<td>✓ Renal imaging for nephrolithiasis or nephrocalcinosis <em>(NEGATIVE)</em></td>
</tr>
<tr>
<td>✓ Ophthalmologic examination for cataracts <em>(NEGATIVE)</em></td>
</tr>
<tr>
<td>Central nervous system imaging for calcification <em>(NOT INDICATED)</em></td>
</tr>
<tr>
<td>Bone density <em>(NOT INDICATED)</em></td>
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</table>
Conventional therapy of hypoparathyroidism

- Calcium, calcium, calcium (diet + supplements)
- IV calcium in the acute setting (lasts only a few hours)
- Typically 500-1000 mg (elemental) 3-4 times/day by mouth for chronic management
- Not unusual to require very high doses
- Most commonly used formulations are carbonate and citrate
- “Natural” formulations (i.e. oyster shell) can contain lead

# Common calcium brands

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcium carbonate</strong></td>
<td>40% elemental calcium</td>
</tr>
</tbody>
</table>
| Os-Cal (GlaxoSmithKline) | 1.25 g tablet (500 mg elemental)  
1.5 g tablet (600 mg elemental)  |
| Tums (GlaxoSmithKline)  | Regular 500 mg tablet (200 mg elemental)  
E-X 750 mg tablet (300 mg elemental)  
Ultra 1000 mg tablet (400 mg elemental)  |
| Caltrate (Wyeth) | 1.5 g tablet (600 mg elemental) |
| **Calcium citrate** | 21% elemental calcium                                                  |
| Citracal (Bayer Healthcare) | 950 mg tablet (200 mg elemental)  
1.2 g tablet (250 mg elemental)  
1.5 g tablet (315 mg elemental)  |

Points to consider with calcium

- Dietary calcium can be helpful but must be consistent
- Calcium carbonate must be taken with food for best absorption
- Consider calcium citrate if the patient is taking an acid reducing medication
- Consider additional calcium supplementation with exercise or with menses
- Calcium should be separated by levothyroxine by at least 1 hour

Conventional therapy of hypoparathyroidism

- Calcium, calcium, calcium
  - Typically 500-1000 mg 3-4 times/day
- Active vitamin D analogues

<table>
<thead>
<tr>
<th>Medication</th>
<th>Typical dose</th>
<th>Time to onset of action (days)</th>
<th>Time to offset of action (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcitriol 1,25(OH)$_2$D$_3$</td>
<td>0.25-2.0 mcg, once or twice daily</td>
<td>1-2</td>
<td>2-3</td>
</tr>
<tr>
<td>Alfacalcidol 1α(OH)D$_3^*$</td>
<td>0.5-4 mcg once daily</td>
<td>1-2</td>
<td>5-7</td>
</tr>
<tr>
<td>Dihydrotachysterol*</td>
<td>0.3-1.0 mg once daily</td>
<td>4-7</td>
<td>7-21</td>
</tr>
</tbody>
</table>

*Not available in the US; rapidly activated in the liver to 1,25(OH)$_2$D$_3$ and 25(OH) dihydrotachysterol, respectively

Conventional therapy of hypoparathyroidism

- Calcium, calcium, calcium
  - Typically 500-1000 mg 3-4 times/day
- Active vitamin D analogues
  - Calcitriol, typically 0.25-2.0 μg/day, divided doses
- Parent vitamin D₂ or D₃
  - Over-the-counter or prescription for goal 25-hydroxyvitamin D >30 ng/mL
Conventional therapy, continued

- Thiazide diuretics
  - Can decrease urine calcium
  - Hydrochlorothiazide, chlorthalidone
  - Used in conjunction with a low salt diet
- Replete magnesium if low
- In some patients, a low phosphate diet or phosphate binders can be considered
Therapeutic challenges

• Blood calcium levels vary during the day

• Calcium must be taken throughout the day to keep levels stable

• Difficult to control symptoms completely

• Vomiting/diarrhea, menstruation, excessive exercise, anxiety/stress can all change requirements

• Drug interactions: Thyroid hormone, acid reducing medications (proton pump inhibitors, H₂ blockers)
Is AL meeting goals of therapy?

- Free of symptoms of hypocalcemia ✗
- Serum calcium in the low normal range ✓ (but using very high doses of calcium/calcitriol)
- Avoid hypercalciuria ✗
- Serum phosphate in the normal/high-normal range ✓
- Calcium-phosphate product < 55 mg²/dL² (4.4 mmol²/L) ✓
- Avoid calcium deposition in tissues ✓
PTH therapy in hypoparathyroidism

• Dr. Fuller Albright first experimented with parathyroid extract in hypoparathyroid subjects in 1929
• This research was abandoned until more recently
• Potential advantages of PTH in the management of hypoparathyroidism:
  • A reduction in the amounts of calcium and vitamin D requirements
  • Reduction in urinary calcium
  • Improvement in quality of life
  • Reduction in ectopic soft tissue calcification
  • Improvement in abnormal bone dynamics
Parathyroid hormone

PTH(1-84)

H₂N—Ser Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Val Arg Glu Met Ser Asn Leu His Lys Trp Leu Arg Lys Lys Leu Gln Asp Val His Asn Phe Val Ala Asp Arg Pro Ala Leu Pro Ala Gly Leu Ala Gly Ser Gln Arg Pro Arg Lys Lys Glu Asp Asn Val Leu Ala Glu Gly Leu Ser Lys Glu His Ser Glu Val Asp Lys Ala Asp Val Asp Val Leu Thr Lys Ala Lys Ser Gln

PTH(1-34)

—COOH
PTH formulations studied in hypoparathyroidism

- **PTH(1-34)**
  - The dose of PTH was titrated by investigators to achieve independence from active vitamin D therapy
  - Requires multiple injections per day

- **PTH(1-84)**
  - PTH was used as an add-on to standard therapy
  - Once daily injections
Evidence for PTH(1-34)

• In research studies:
  • PTH(1-34) has been shown to decrease requirements for active vitamin D\(^1-4\)
  • When administered continuously by pump, PTH(1-34) decreases urinary calcium\(^4\)
  • PTH(1-34) has been shown to improve low bone remodeling\(^1-3\)
• Clinical use of PTH(1-34) in hypoparathyroidism would be off-label

\(^1\)Winer KK, et al. J Clin Endocrinol Metab 2003; 88:4214-20
Until 2015, hypoparathyroidism was the only classic endocrine deficiency disease for which there was not an approved hormone replacement treatment.

**PTH(1-84) [Natpara] was approved by the US Food and Drug Administration on January 23, 2015 for treatment of patients with difficult to control disease.**
The REPLACE Trial

- 134 subjects, 18-85 years of age
- Multicenter, randomized, double-blind, placebo-controlled trial
- PTH(1-84) 50 μg daily versus placebo for 24 weeks
  - Dose of PTH was titrated up by investigators as needed to 75 or 100 μg daily
- The primary outcome was the proportion of patients at week 24 who achieved:
  - ≥ 50% reduction in both oral calcium and active vitamin D
  +
  - Serum calcium maintained ≥ baseline and ≤ the upper limit of normal

REPLACE Trial: Primary outcome


Statistically significant (p<0.0001)

Responders Rate, %

rhPTH(1-84) n=90
Placebo n=44

Week
REPLACE Trial: Supplementation requirements

- 36/84 (43%) of subjects receiving PTH(1-84) were able to stop taking active vitamin D and were taking ≤ 500 mg calcium/day compared to 2/37 (5%) of subjects taking placebo.
- Subjects in the PTH(1-84) group had an average decrease in calcium requirements of -52% and a decrease in vitamin D requirements of -78%.

REPLACE Trial: Serum and urine calcium

REPLACE Trial: Serum and urine calcium

In the PTH(1-84) group:
- Serum calcium unchanged (despite ↓ calcium/vitamin D requirements)
- Urine calcium unchanged

REPLACE Trial: Other results

• Average serum phosphate concentration decreased significantly in the PTH group by 0.15 mg/dL (0.05 mmol/L)

• Average calcium-phosphate product decreased significantly from 39.7 to 34.7 mg^2/dL^2 (3.2 to 2.8 mmol^2/L^2)

Pharmacodynamics of PTH(1-84): Urine calcium effects over 24 hours

Clarke BL, et al., Clin Ther 2014; 36:722-36
Potential benefits of PTH therapy

✓ Control of serum calcium

+/- Urinary calcium

Quality of life

Extra-skeletal calcifications

Skeletal changes
PTH(1-84) effects on quality of life

- Cusano et al.\(^1\): Open-label PTH(1-84) titrated to serum calcium associated with beneficial effects through 5 years of therapy
  - Most subjects maintained serum calcium values of \(\geq 8.0\) mg/dL, although less had values within the normal range (8.6-10.2 mg/dL)
  - Hypercalcemia was rare (2.1% of values)
- Sikjaer et al.\(^2\): Randomized placebo-controlled trial of PTH(1-84) 100 μg daily showed no between-group differences at 6 months
  - 71% of subjects had hypercalcemia during the study
  - Large fluctuations in serum calcium might have negated any potential advantage of the PTH therapy

**PTH therapy: Skeletal effects**

**Baseline**
Few tetracycline labels

**PTH therapy for 1 year**
- Increased single and double labels
- Dramatically increased bone formation rate

Summary: Potential benefits of PTH therapy

- Control of serum calcium
+/- Urinary calcium
+/- Quality of life
? Extra-skeletal calcifications
✓ Skeletal changes
Safety

- No difference in adverse or serious adverse events between PTH(1-84) and placebo in the REPLACE trial\(^1\)
- Hypercalcemia can occur, usually within the first few months of therapy, and is easily corrected\(^1\)\(^-\)\(^4\)
- We have data for safety through 6 years of use of PTH(1-84)\(^3\)\(^,\)\(^4\)

\(^2\)Sikjaer T, et al. J Bone Miner Res 2011; 26:2358-70
Safety, continued

- Osteosarcoma is a bone cancer that has been seen in rats given very high doses of PTH(1-34) or PTH(1-84) for long periods of time\(^1\)
- No increased risk of osteosarcoma in humans since teriparatide was approved in 2002\(^2\)
- No signals from the use of PTH(1-84)\(^3\)
- Worldwide human exposure: >1.5 million\(^2,3\)
- Post-marketing surveillance is important

Indications for PTH(1-84) therapy

- **FDA insert:** “patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone”
- Which patients are considered difficult to control?
- Guidance from the 1st International Workshop on Hypoparathyroidism
- **ESE guidelines:** Recommend against routine use of replacement therapy with PTH or PTH analogues
Indications for PTH(1-84) therapy

- Inadequate control of the serum calcium concentration
- Calcium requirements >2.5 g and/or active vitamin D >1.5 g daily
- Hypercalciuria, renal stones, nephrocalcinosis, stone risk, or reduced creatinine clearance or eGFR (<60 mL/min)
- Hyperphosphatemia and/or calcium-phosphate product >55 mg²/dL² (4.4 mmol²/L²)
- A gastrointestinal tract disorder associated with malabsorption
- Reduced quality of life
Patient AL: Indications for PTH(1-84) therapy

- Multiple ER visits for hypocalcemia
- Oral calcium requirements >2.5 g and active vitamin D >1.5 g daily
- Hypercalciuria
Case, continued: Plan

- Discussed treatment with PTH(1-84)
- Enrolled in the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program
  - All patients monitored for incidence of osteosarcoma
- Started PTH(1-84) 50 mcg SC daily into thigh
  - A representative went to her home and showed her how to mix the medication and administer
Plan, continued

- Titrated PTH(1-84) up to 75 mcg and then 100 mcg daily
- She no longer has hypocalcemic symptoms in the morning
- She is now off all calcium/calcitriol supplementation (!)
  - Previously taking calcium 3900 mg and calcitriol 2 mcg (13 pills)
- Her urine calcium did not significantly improve with PTH therapy and started hydrochlorothiazide, up to 50 mg daily
  - Repeat 24-hour urine calcium excretion 206 mg
Summary

• Hypoparathyroidism is a rare, complex endocrine disorder characterized by absent or inappropriately low levels of PTH, hypocalcemia, and hyperphosphatemia.
• Conventional management includes using large doses of calcium and active vitamin D.
• PTH(1-84) has been approved for treatment of hypoparathyroidism that is difficult to control with calcium and vitamin D.
• Therapy for hypoparathyroidism is a balance between symptom management and long-term complications.
QUESTIONS OR COMMENTS?