Parathyroid Gland & Calcium Balance

Advanced Medicine 2

4th Stage – Anesthesia Techniques

Lec: 1

2nd Course

Dr. Bashar Hadi Alaaraji

Parathyroid Gland & Calcium Metabolism

Calcium disorders are medical emergencies and common ward problems.

Calcium Distribution

Compartment	% Total Body Ca	Form
Bone	99%	Hydroxyapatite crystals
Extracellular fluid	1%	Ionized (50%), Protein-bound (40%), Complexed (10%)
Intracellular	<0.1%	Tightly regulated (~100 nM)

Critical Functions of Ionized Calcium (Ca^{2+})

1. ***Neuromuscular***: Membrane excitability, neurotransmitter release
2. ***Cardiac***: Myocardial contractility, conduction system stability
3. ***Coagulation***: Factor IV in clotting cascade
4. ***Cell signaling***: Second messenger for hormones
5. ***Bone mineralization***: Structural integrity

Calcium homeostasis: the triad

3 hormones maintain serum Ca^{2+} within narrow range (8.5–10.5 mg/dL) (ionized ~4.5–5.3 mg/dL)

Hormone	Stimulus for Secretion	Primary Target	Net Effect on Serum Ca^{2+}
PTH Rapid responder	↓ Ionized Ca^{2+} (via CaSR)	Bone, Kidney, Gut (indirect)	↑↑↑
Vitamin D ($1,25(OH)_2D$)	↑ PTH, ↓ PO_4	Gut, Bone, Kidney	↑↑
Calcitonin	↑ Ionized Ca^{2+}	Bone (osteoclasts)	↓ (minor role in humans)

Parathyroid Hormone (PTH):

The Rapid Responder

Secretion trigger: ↓ Ionized Ca^{2+} detected by (CaSR) Calcium-Sensing Receptor on chief cells.

CaSR is a **G-protein–coupled receptor** that detects the level of **calcium in the blood** and regulates **parathyroid hormone (PTH) secretion**.

- **Gain of function** (increased receptor sensitivity): The receptor senses calcium as high even when it is normal → **PTH secretion ↓ → hypocalcemia**.
- **Loss of function** (decreased receptor sensitivity): The receptor fails to sense high calcium → **PTH secretion ↑ → hypercalcemia**.

- Half-life: 2–4 minutes (rapid response system)

PTH Actions (Within Minutes-Hours)

Target Organ	Mechanism	Effect
Bone	**↑ RANKL →osteoclast activation** (Receptor Activator of Nuclear Factor *κ*B Ligand) protein essential for bone remodeling and immune function, primarily promoting differentiation and activation of osteoclasts	**Ca^{2+} & PO_4 release from bone**
Kidney	**↑ Ca^{2+} reabsorption (DCT)**	**↓ Urinary Ca^{2+} excretion**
	↓ PO_4 reabsorption (PCT)	**↑ Urinary PO_4 excretion**
	↑ 1α-hydroxylase activity	**↑ $1,25(OH)_2D$ (calcitriol)production → ↑ gut Ca^{2+} absorption**

Vitamin D Actions

1. **Intestine**: ↑ TRPV6 channels → ↑ Ca^{2+} absorption (duodenum)
2. **Bone**: Permissive for mineralization; ↑ osteoclast activity (with PTH)
3. **Kidney**: ↑ Ca^{2+} & PO_4 reabsorption
4. **Immune modulation**: Anti-inflammatory effects

TRPV6 (Transient Receptor Potential Vanilloid member 6) is a highly selective epithelial calcium channel critical for active calcium absorption in the intestine, kidney, and placenta.

- **Note:**

CKD Alert: Loss of renal 1α-hydroxylase → ↓ calcitriol → secondary hyperparathyroidism.

Clinical Disorders:

Hyperparathyroidism

1. Primary Hyperparathyroidism (PHPT)

- **Epidemiology**:
- Most common cause of hypercalcemia in outpatients;
- ♀:♂ = 3:1; peak 50–60 yrs
- **Etiology**:
  1. Solitary adenoma (85%)
  2. Hyperplasia (15%)
  3. Carcinoma (<1%)
- **Biochemical signature**: ↑ Ca^{2+} + ↑ or inappropriately normal PTH

Classic symptoms

(stones, bones, groans, moans)

1. Renal: Nephrolithiasis (calcium oxalate), nephrocalcinosis
2. Skeletal: Osteitis fibrosa cystica (rare now), osteoporosis
3. GI: Nausea, constipation, pancreatitis
4. Neuropsychic: Fatigue, depression, cognitive fog

Asymptomatic PHPT: Now >80% of cases (detected on routine labs)

2. Secondary Hyperparathyroidism

- **Cause:** Compensatory ↑ PTH due to chronic hypocalcemia
  1. CKD (↓ renal 1α-hydroxylase → ↓ calcitriol → ↓ gut Ca^{2+} absorption)
  2. Vitamin D deficiency
  3. Malabsorption
- **Biochemical signature:** ↓ Ca^{2+} + ↑ PTH (appropriate response)

3. Tertiary Hyperparathyroidism

- ✓ **Cause:** Autonomous PTH secretion after long-standing secondary HPT (e.g., post-renal transplant)
- ✓ **Biochemical signature**: ↑ Ca^{2+} + ↑ PTH (like PHPT but history of CKD)

Hyperparathyroidism – Clinical Pearls

Type	Cause	Biochemical Signature	Key Features
Primary	Adenoma (85%), hyperplasia (15%)	↑ Ca^{2+} + ↑/normal PTH	"Stones, bones, groans, moans • Nephrolithiasis/nephrocalcinosis • Osteoporosis (osteitis fibrosa rare now) • >80% asymptomatic (routine labs)
Secondary	CKD, Vit D deficiency, malabsorption	↓ Ca^{2+} + ↑ PTH (appropriate)	Compensatory response to chronic hypocalcemia
Tertiary	Long-standing secondary → autonomy	↑ Ca^{2+} + ↑ PTH (post-renal transplant)	History of CKD required for diagnosis

Clinical Disorders: Hypoparathyroidism

- **Causes:**

1. ***Postsurgical*** (75%): Thyroidectomy/parathyroidectomy (most common cause).
2. ***Autoimmune***: Isolated or part of polyglandular syndromes.
3. ***Genetic***: DiGeorge syndrome.
4. ***Infiltrative***: Hemochromatosis, Wilson disease

Clinical Presentation:

- **Acute hypocalcemia (<7 mg/dL):**
  1. ***Neuromuscular***: Paresthesia's, carpopedal spasm, Chvostek's sign (facial nerve tap → twitch), Trousseau's sign (BP cuff → hand spasm)
  2. ***Cardiac***: Prolonged QT interval → ventricular arrhythmias
  3. ***Seizures, laryngospasm*** (life-threatening)
- **Chronic hypocalcemia:**
  1. Basal ganglia calcification → parkinsonism
  2. Cataracts
  3. Dental enamel hypoplasia
  4. Dry skin, brittle nails

Clinical Presentation:

Acute (<7 mg/dL)	Chronic
1. Paresthesias, carpopedal spasm 2. Chvostek's sign (facial tap → twitch) 3. Trousseau's sign (BP cuff → hand spasm) 4. Prolonged QT → arrhythmias 5. Seizures, laryngospasm (life- threatening)	1. Basal ganglia calcification → parkinsonism 2. Cataracts 3. Dental enamel hypoplasia 4. Dry skin, brittle nails

- **Diagnosis:**

1. ↓ Ionized Ca^{2+} + ↓ PTH (inappropriately low/undetectable)
2. ↑ Phosphate (loss of PTH phosphaturic effect)

- **Management:**

- **Acute**: IV calcium gluconate (10–20 mL of 10% solution over 10–20 min)
- **Chronic**:
  - ✓ First-line: Calcium carbonate/citrate + active vitamin D (calcitriol 0.25–1.0 μg/day)

Diagnostic Approach to Calcium Disorders

Step 1: Confirm abnormal calcium

1. Repeat ionized calcium (gold standard) or albumin-corrected total Ca+)
2. Check magnesium (hypomagnesemia → functional hypoparathyroidism)

Step 2: Measure PTH

(PTHrP) Parathyroid hormone-related protein is a hormone acting in autocrine, paracrine, and endocrine fashions to regulate bone development, calcium transport in the placenta, and cell proliferation/differentiation. It is often produced by tumors (e.g., lung, breast), causing hypercalcemia of malignancy.

Ca^{2+}	PTH	Diagnosis
↑	↑ or inappropriately normal	Primary HPT
↑	↓	Malignancy (PTHrP), granulomatous disease
↓	↑	Secondary HPT (CKD, Vit D def)
↓	↓ or inappropriately normal	Hypoparathyroidism

Diagnostic Approach to Calcium Disorders

- **Step 3: Additional tests**

✓ PHPT(primaryHPT) workup:

24-hr urine Ca+, creatinine clearance.

- Hypocalcemia workup:

Mg^{2+}, PO_4, 25(OH)D, renal function

Practical Teaching Tips

1. **Always check ionized ca+ in hypoalbuminemia, critical illness**
2. **Hypomagnesemia must be corrected first before treating hypocalcemia (Mg required for PTH secretion)**
3. **In hypercalcemia:**

- **PTH ↑/normal = primary HPT;**
- **PTH ↓ = think malignancy (PTHrP)**

- **Asymptomatic primary HPT now >80% of cases – screen with routine labs**

- **CKD patients: Monitor for secondary HPT due to ↓ calcitriol production**


Thank You!