



# Al Mustaqbal University College of Medicine



# Calcium Homeostasis & Parathyroid, Calcitonin, & Vitamin.D Physiology

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**lec11**

## • Learning Objectives

- By the end of this lecture, students should be able to:
  1. Explain the importance of maintaining **calcium and phosphate balance** in the body.
  2. Describe **body calcium pools**, their turnover, and key organs regulating calcium movement.
  3. Outline **absorption and excretion** mechanisms of calcium and phosphate.
  4. Identify main **regulatory hormones** (vitamin D, PTH, calcitonin), their actions, and effects of dysfunction.
  5. Describe **bone-forming and resorbing cells** and disorders of bone homeostasis.

# • Calcium & Phosphorus Balance in The Body

## • Distribution of Calcium in the Body

- Total body calcium  $\approx$  **1.5% of body weight**

(about 1–1.2 kg).

- **99%** of calcium is in the **bones and teeth** as hydroxyapatite crystals.

- **1%** is in the extracellular and intracellular fluids.

- **Plasma calcium concentration: 9-10 mg/dL**

- 50% ionized (biologically active form)

- 40% protein-bound (mainly to albumin, non-diffusible)

- 10% complexes with citrate and phosphate

- Plasma  $\text{Ca}^{2+}$  is filtered in the kidneys, but **98–99%** of the filtered  $\text{Ca}^{2+}$  is reabsorbed.
- About **60%** of the reabsorption occurs in the proximal tubules and the remainder in the ascending limb of the loop of Henle and the distal tubule.
- Distal tubular reabsorption is regulated by PTH (increase  $\text{Ca}^{2+}$  reabsorption).

## • Physiological Functions of Calcium

1. Muscle contraction and nerve excitability
2. Neurotransmitter and hormone release
3. Enzyme activation and intracellular signaling
4. Blood coagulation (cofactor in clotting cascade)
5. Bone and teeth mineralization
6. Maintenance of cell membrane stability and permeability.

# • Phosphate Balance

- About 85–90% of body phosphate is in bone; plasma Pi is mostly inorganic.
- **Plasma phosphate:** 2.5–4.5 mg/dL.
- **Absorption:** occurs mainly in the small intestine by active and passive transport, enhanced by **1,25-dihydroxycholecalciferol (calcitriol)**.
- **Renal handling:** 85–90% reabsorbed in the **proximal tubule**; reabsorption is inhibited by **PTH**.
- Many stimuli that increase  $\text{Ca}^{2+}$  absorption from intestine, including 1,25-dihydroxycholecalciferol, also increase Pi absorption.

## • **Vitamin D (Calcitriol)**

- Fat-soluble vitamin acting as a **hormone**.
- Vitamin D produced by the action of ultraviolet light on certain provitamins.
- The normal plasma level of Vitamin D is about 30 ng/mL.

## • **Sources of Vit.D:**

### 1. Endogenous (Produced in the body):

- Skin synthesis: Ultraviolet B (UVB) rays from sunlight convert 7-dehydrocholesterol → vitamin D<sub>3</sub> (cholecalciferol) in the skin.

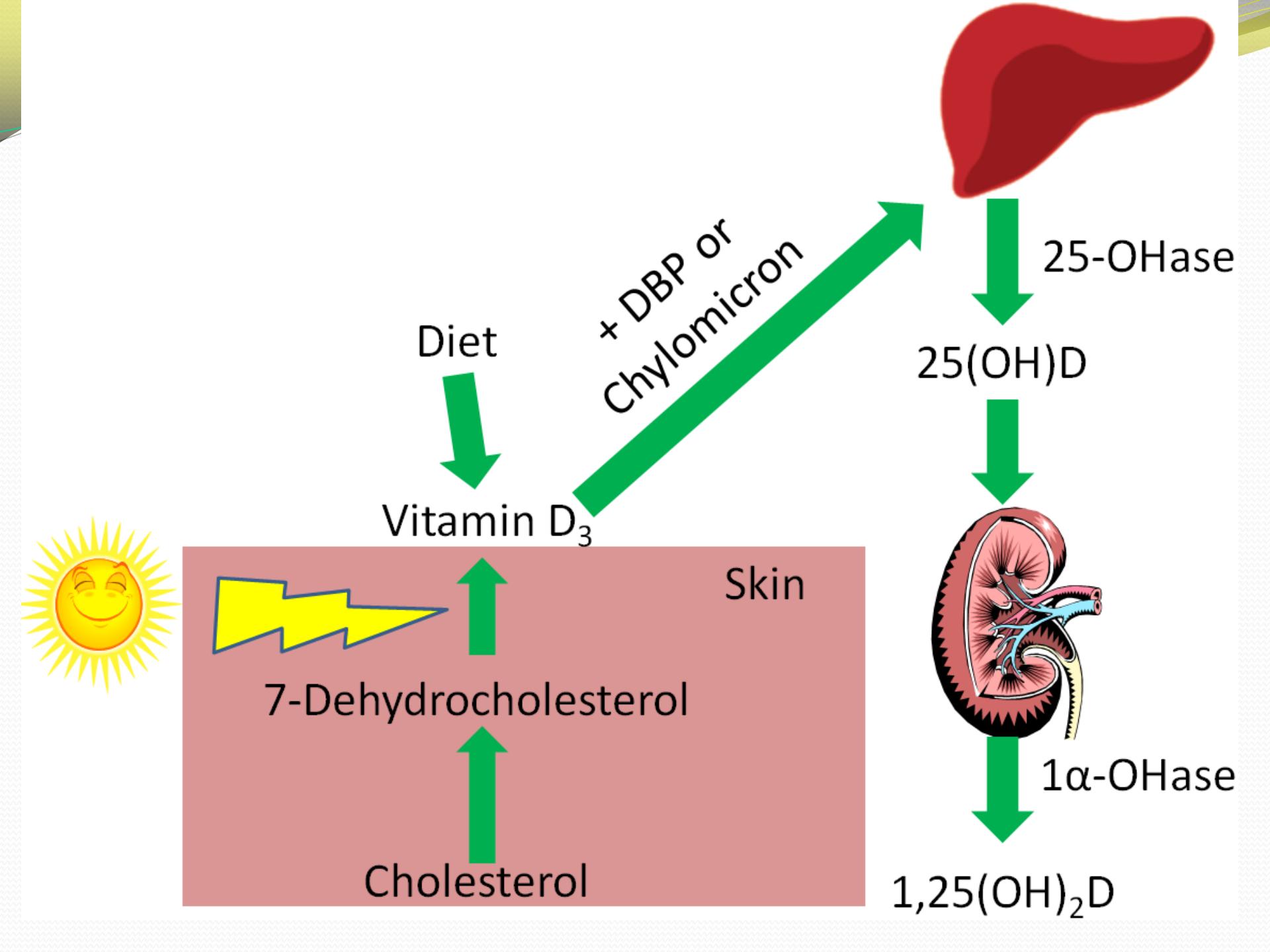
## 2. Dietary sources of Vitamin D:

- **Animal:** fish , liver, egg yolk, fortified milk.
- **Plant:** sun-exposed mushrooms, fortified cereals

### ➤ Activation Steps

**1. Liver:** cholecalciferol → 25-hydroxycholecalciferol  
(calcidiol)

**2. Kidney:** calcidiol → 1,25-dihydroxycholecalciferol  
(calcitriol) via **1- $\alpha$  hydroxylase** (stimulated by PTH).



## • Functions

1. ↑ Intestinal absorption of  $\text{Ca}^{2+}$  and phosphate.
2. ↑ Renal reabsorption of  $\text{Ca}^{2+}$ .
3. Promotes bone mineralization (normal level).

- **Deficiency**
- **Children:**
- **Rickets** → defective mineralization → bowed legs, growth retardation.
- **Adults:** osteomalacia → soft bones → fractures& muscle weakness.
- **Causes:** inadequate sunlight, malabsorption, renal or liver disease

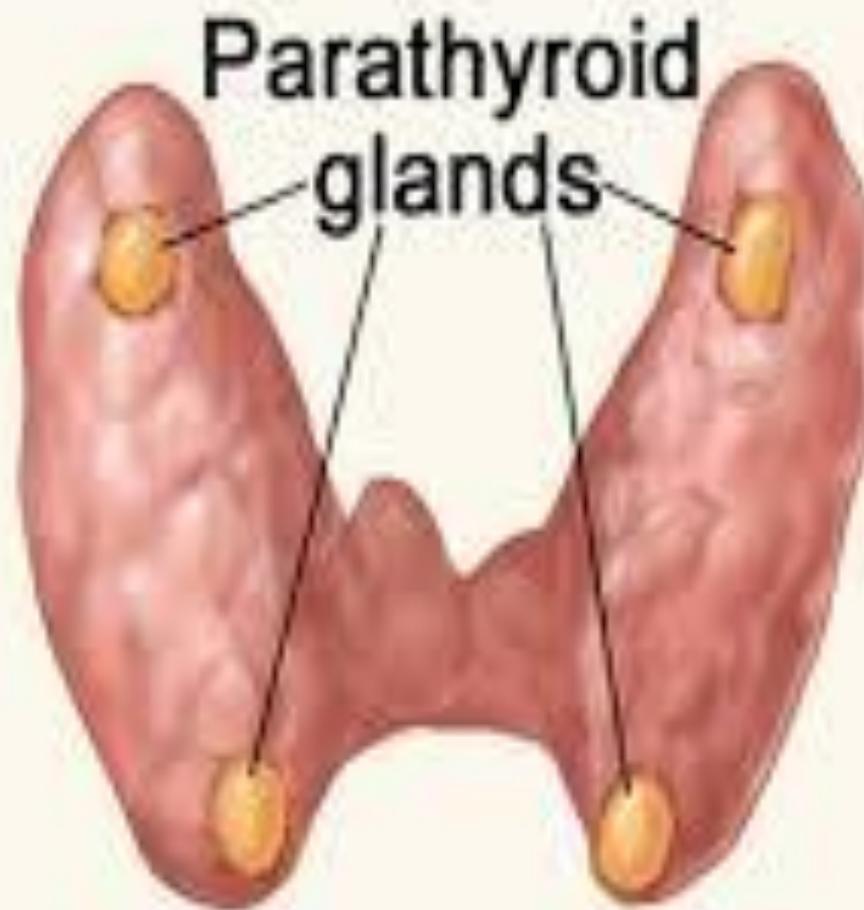
- **Parathyroid gland & Hormone (PTH)**
- **Anatomy and Structure**
  - Four small, yellowish glands located on the posterior surface of the thyroid gland.
  - The **parathyroid gland** is made up mainly of two cell types within a delicate connective tissue stroma rich in capillaries.

## 1. Chief (Principal) Cells

- Most abundant cell type secrete **parathyroid hormone (PTH)**,

2. **Oxyphil cells** Their function is not fully clear, but they are metabolically less active.

# Thyroid gland (back view)



Parathyroid  
glands

# ➤ Hormone & Regulation

- **Secreted by:** chief cells of parathyroid glands.
- **Stimulus:** ↓ plasma  $\text{Ca}^{2+}$  (hypocalcemia).
- **Inhibition:** ↑ plasma  $\text{Ca}^{2+}$  (negative feedback).
- **Nature:** peptide hormone synthesized as **pre-pro-PTH**
- The normal plasma level of intact PTH is 10–55 pg/mL

# ➤ Physiological Role of Parathyroid Hormone:

Target	Effect
Bone	Stimulates osteoclasts → ↑ bone resorption → ↑ $\text{Ca}^{2+}$ & phosphate release into the blood
Kidney	1. ↑ $\text{Ca}^{2+}$ reabsorption (distal tubule), 2. ↓ phosphate reabsorption (proximal tubule) 3. Stimulates 1- $\alpha$ hydroxylase → ↑ formation of active vitamin D (calcitriol)
Intestine	Indirectly ↑ $\text{Ca}^{2+}$ and phosphate absorption via activation of calcitriol

- **Calcitonin**
- **Calcitonin** is a **calcium-lowering hormone** secreted by the **parafollicular (C cells)** of the **thyroid gland**.
- **Stimulus:** High **plasma calcium** ( $>9.5$  mg/dL) directly increases calcitonin secretion..
- **Effect:** lowers plasma  $\text{Ca}^{2+}$  and phosphate.
- **Mechanism of Action**
- Calcitonin receptors are mainly found in bones and kidneys. The net results of the calcitonin are decreased  $\text{Ca}^{++}$  and phosphate plasma levels through the following mechanisms:

1. **Direct (immediate)** effect by inhibiting the activity of osteoclasts (inhibit bone resorption).
2. **Indirect (prolonged)** effect by reducing the formation of new osteoclasts.
3. **Increases** Ca++ and phosphate excretion in urine.

- **Metabolism**

- **Half-life:** Very short — **less than 10 minutes** in humans.
- Therefore, its **effects are brief and mainly serve as rapid protection** against sudden increases in blood calcium

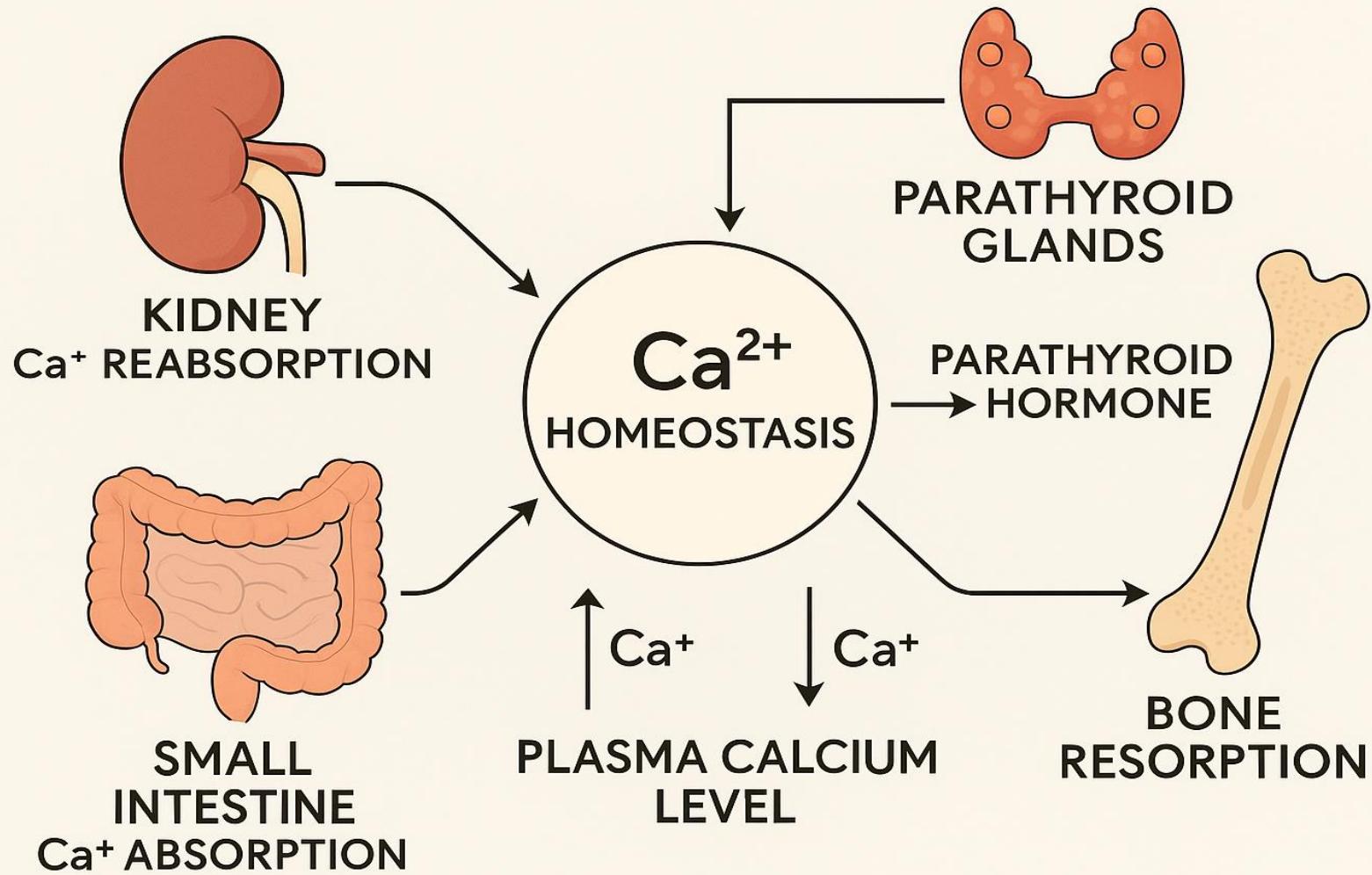
- **Clinical Notes**

- Used therapeutically in **osteoporosis**.
- Elevated levels may indicate **medullary thyroid carcinoma**

- **Calcium Homeostatic Mechanisms**
- Calcium homeostasis is maintained by coordinated actions of **three hormones**:
  - 1. Parathyroid hormone (PTH)** – mobilizes calcium from bone and increases renal phosphate excretion.
  - 2. 1,25-Dihydroxycholecalciferol (Vitamin D<sub>3</sub>)** – enhances intestinal calcium absorption.
  - 3. Calcitonin** – lowers plasma calcium by inhibiting bone resorption.

These hormones act on **bone, kidney, and intestine** to maintain constant calcium and phosphate levels

# Calcium Homeostatic Mechanisms



# • **Bone Structure and Remodeling**

- Bone is a specialized connective tissue made of collagen fibers (organic matrix for flexibility), calcium and phosphate salts, mainly hydroxyapatite crystals.
- **Bone growth** is the process by which bones increase in length and thickness.

## • **Bone Growth Patterns**

### 1. **Longitudinal (Linear) Growth**

1. Occurs at **epiphyseal plates**.
2. **Chondrocytes proliferate** on the epiphyseal side, **osteoblasts replace cartilage** with bone on the diaphyseal side.
3. Responsible for **increase in bone length** (height)

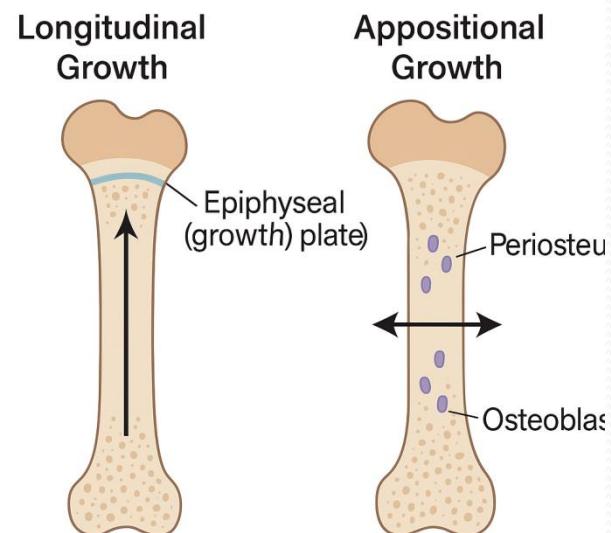
## 2. Appositional Growth

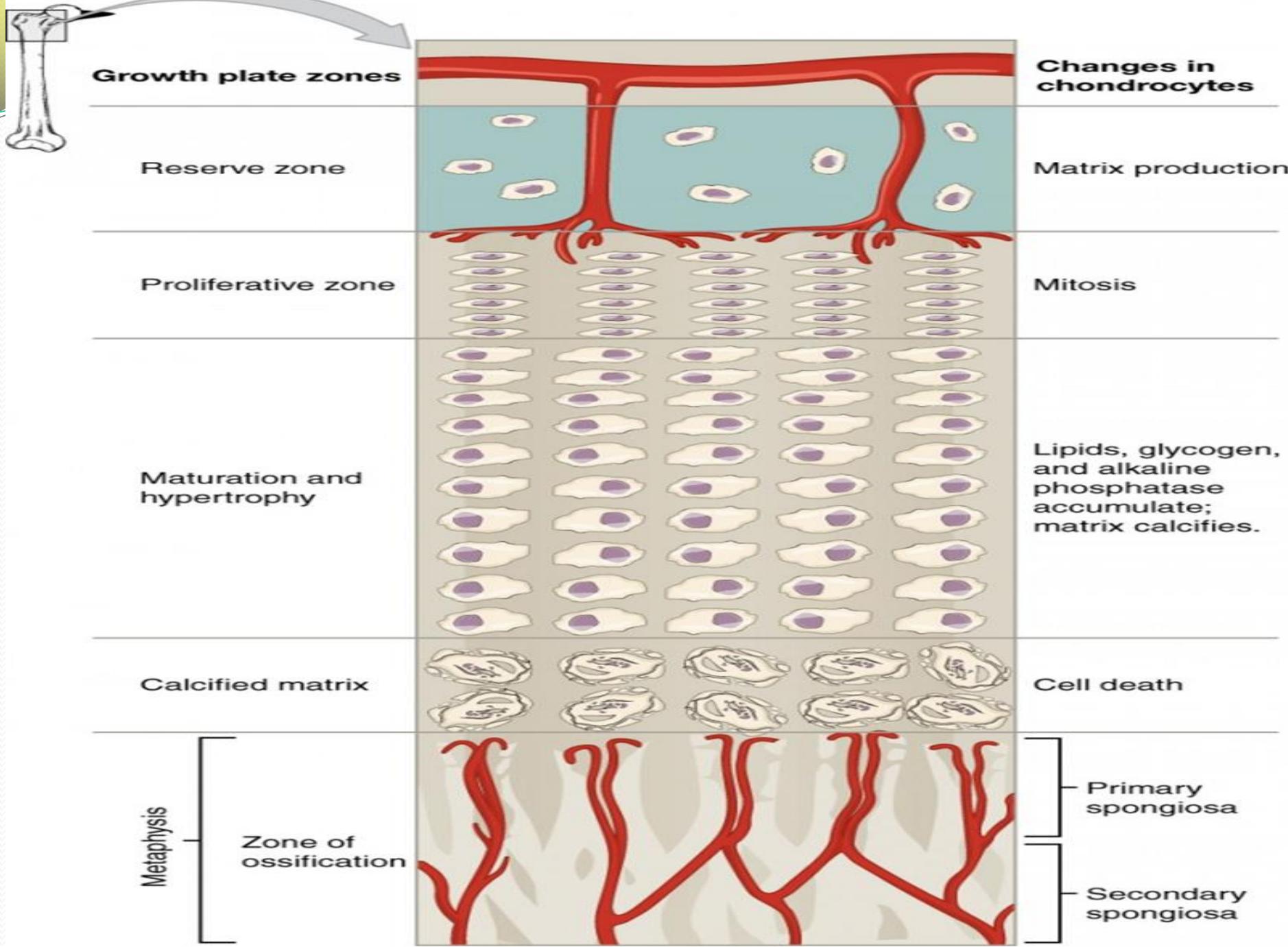
- Occurs at the outer surface (periosteum). Osteoblasts add new bone to the outer layer, osteoclasts resorb bone from the inner surface . Responsible for increase in bone thickness or diameter

- **Controlled by:**

- Growth hormone,
- Thyroid hormones,
- Sex hormones,
- Vitamin D.

- **Bone thickens under load and thins during immobilization**





## • Clinical Correlations

- **Primary Hyperparathyroidism**
- Usually due to parathyroid adenoma.
- $\uparrow$  PTH  $\rightarrow$  hypercalcemia, hypophosphatemia, bone demineralization, renal stones.
- **Secondary Hyperparathyroidism**
- In disease of kidney and in rickets, chronic low Ca++ level exert a feedback stimulation on PTH.
- **Hypoparathyroidism**
- Commonly post-thyroidectomy.
- $\downarrow$  PTH  $\rightarrow$   $\downarrow$  plasma  $\text{Ca}^{2+}$   $\rightarrow$  neuromuscular hyperexcitability, tetany, laryngospasm

- **Disorders of Calcium Metabolism**

- **Hypocalcemia**

- ↓ plasma  $\text{Ca}^{2+}$  ( $< 8.5 \text{ mg/dL}$ ).
- **Causes:** hypoparathyroidism, vitamin D deficiency, renal failure.
- **Effects:** neuromuscular hyperexcitability, **tetany**, **carpopedal spasm**, **laryngeal spasm**, **prolonged QT interval**.
- Note: Normally, extracellular  $\text{Ca}^{2+}$  stabilizes the neuronal membrane by reducing  $\text{Na}^+$  channel excitability. When  $\text{Ca}^{2+}$  decreases,  $\text{Na}^+$  channels open more easily → increased  $\text{Na}^+$  entry → spontaneous depolarization → neuromuscular hyperexcitability.

## • **Hypercalcemia**

- ↑ plasma  $\text{Ca}^{2+}$  ( $> 10.5 \text{ mg/dL}$ ).
- **Causes:** hyperparathyroidism, excessive vitamin D.
- **Effects:** depressed CNS activity, **muscle weakness, constipation, shortened QT interval, renal stones.**

# Bone Diseases

Disease	Main Cause	Pathophysiology	Features
1. Rickets / Osteomalacia	Vitamin D deficiency	Poor bone mineralization	Bone deformity, fractures
2. Osteoporosis	Aging, menopause, inactivity	Decreased bone matrix & minerals	Fragile bones, vertebral & hip fractures
3. Renal Osteodystrophy	Chronic kidney disease	Secondary hyperparathyroidism	Bone pain, deformity, growth retardation

## • **Summary**

- PTH: increases plasma  $\text{Ca}^{2+}$ , decreases phosphate.
- **Calcitonin**: decreases plasma  $\text{Ca}^{2+}$  and phosphate.
- **Vitamin D**: increases both  $\text{Ca}^{2+}$  and phosphate absorption.
- Calcium balance depends on coordinated action on **bone, kidney, and intestine**