



Physiology of Bone & calcium Metabolism

Parathyroid hormone& Vitamin D

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Physiology
MGM MC NM

Competency

PY. 8.1

Physiology of bone and calcium metabolism

PY. 8.2

Synthesis, secretion, transport, physiological actions, regulation and effects of altered (hypo and hyper) secretion of parathyroid gland

Learning objectives:

- Know the different types of bone cells and their functions
- Describe Calcium homeostasis
- Synthesis, secretion, transport, physiological actions, regulation of parathyroid hormone
- Functions of vit D

Physiology of bone

STRUCTURE OF BONE

- Connective tissue, hardened by mineralization
- Bone contains small number of cells entrenched in a matrix of collagen fibers with inorganic salt crystals to on the surface.
- These salt crystals form when calcium phosphate and calcium carbonate combine to create hydroxyapatite, with other inorganic salts like magnesium hydroxide, fluoride, and sulfate as it crystallizes, or calcifies, on the collagen fibers.
- The hydroxyapatite crystals give bones their hardness and strength, while the collagen fibers give them flexibility so that they are not brittle.

Chemicals:

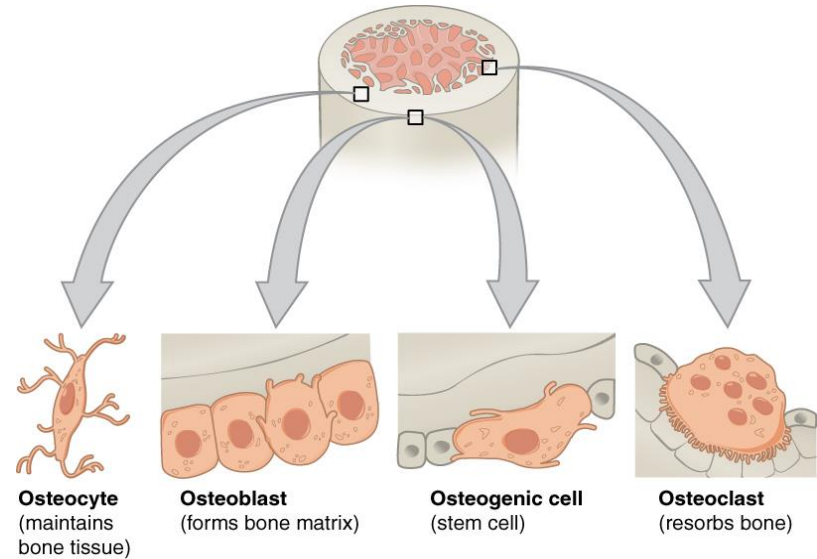
- 35% minerals; account for $\frac{1}{2}$ wt. of bone
 - ❖ 99% body Ca as hydroxypatite crystals
 - ❖ Provide '**compressional strength**'
- 20% organic matrix (95% collagen)
- 45% water

Cells: osteoblasts, osteocytes, osteogenic cells, and osteoclasts

Organic matrix:

- Bone fibers set in amorphous gel-like ground substance
- Bone fibres:
 - ❖ Fibrous protein — Collagen
 - ❖ Laid along tensile force, provide '**tensile strength**'
- Ground substance: Mucopolysaccharide
 - ❖ Proteoglycan, chondroitin-SO₄, hyaluronic acid
 - ❖ Ca-hydroxypatite crystals alongside the collagen fibers

Cells



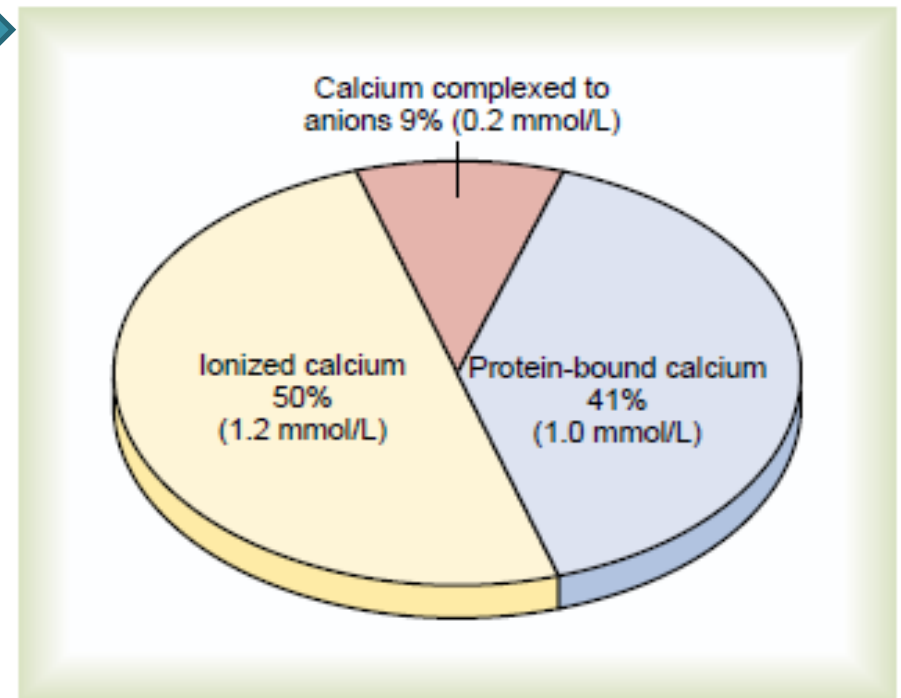
- The **osteoblast** is the bone cell responsible for forming new bone and is found in the growing portions of bone, including the periosteum and endosteum.
- As the secreted matrix surrounding the osteoblast calcifies, the osteoblast becomes trapped within it; as a result, it changes in structure and becomes an **osteocyte**, the primary cell of mature bone and the most common type of bone cell.
- The **osteogenic cells** are undifferentiated cells with high mitotic activity and they are the only bone cells that divide and are found in the deep layers of the periosteum and the marrow.
- The cell responsible for bone resorption, or breakdown, is the **osteoclast**. They are found on bone surfaces, are multinucleated, and originate from monocytes and macrophages, not from osteogenic cells.

Calcium Homeostasis

- Total Calcium – 1000gm in 70 kg adult
- 99% - in the bones
- 0.1 % - extracellular fluid,
- 1 % is in the cells,
- and the rest is stored in bones

Inorganic Phosphate in the Extracellular Fluids

- 85 % stored in bones,
- 14 to 15 % is in the cells,
- and less than 1 % is in the ECF
- Ca in Plasma →



CALCIUM METABOLISM

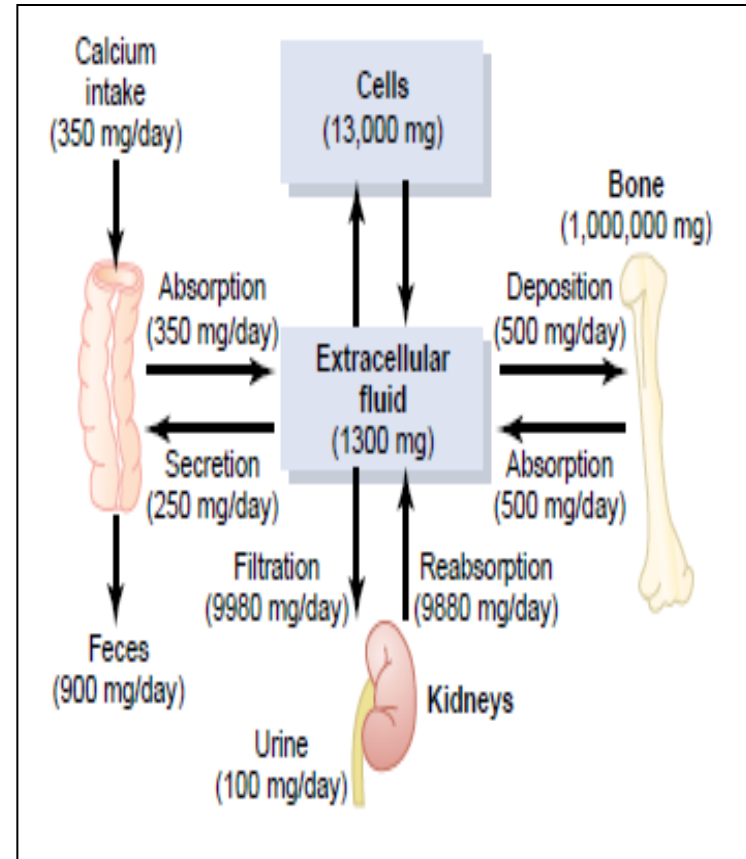
- **Calcium Equilibrium:**
 - Intake = losses

Intake (Diet + Juices) =
 $1000 + 500 = 1500 \text{ mg/d}$

Losses (U + F) =
 $1300 + 200 = 1500 \text{ mg/d}$

 - @ Equilibrium state: No accumulation or loss of 'Ca' in body
 - Children → +ve Balance;
Osteoporosis → (-)ve balance
- **Serum Calcium Levels:**
 - 9-11 mg/dl (almost entire blood content in serum)

A) **Active forms:**
Free (ionised) form = 50%
Complexed – 5% (citrate, PO_4^- , etc.)
Ultrafiltrable (diffusible) B)
Protein-bound = 45%,
Blood pH decides of ratio of bound-to-diffusible forms.
- $\text{ECF-Ca} > \text{ICF-Ca}$
 - Gradient = 10,000:1
- *Mitochondrial Ca > cytosolic- Ca*



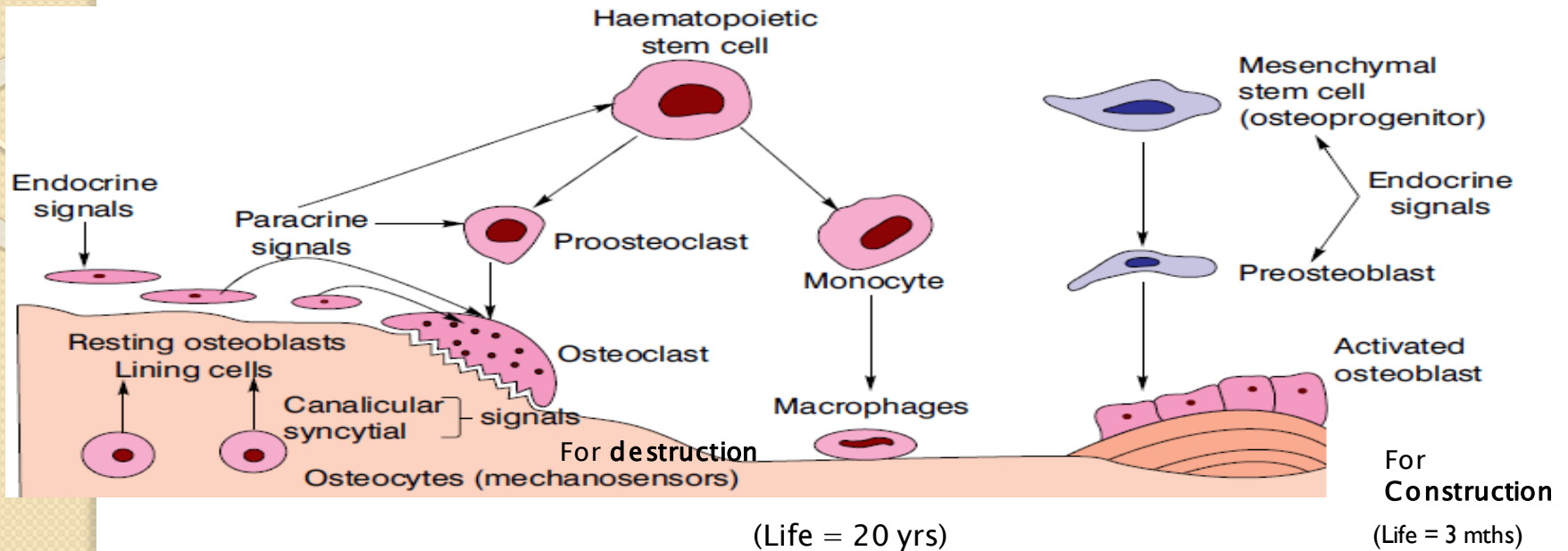
PHOSPHORUS

- Total body-content:
 - 500–600 gm as phosphate
 - 85% skeletal & rest in body fluids (ICF > ECF)
 - Plasma level = 3–5 mg/dl
 - ❖ ↑ in children
 - ❖ Fluctuation $\pm$ 50%
 - ❖ Forms: inorganic > organic HPO_4^- : H_2PO_4^- (80:20)
- Closely related to Ca^{2+} metabolism
 - *Inverse relation to serum Ca (exception: Rickets)*
 - *Serum Ca $\times$ serum $\text{PO}_4 = \text{constant}$*
- Regulated by D_3 & PTH
- Forms of 'P' in body:
 - Organic $\rightarrow$ majority of non-osseous 'P' (e.g., ATP, nucleotides, phospholipids, G-6- PO_4 , etc.)
 - Osseous: Inorganic hydroxypatites
- Functions of P_i :
 - Provide skeletal rigidity
 - Role in pH regulation
 - Synthesis of nucleic acids, PL, phospho-proteins & ATP etc.

Bone Metabolism & Remodeling

- **Growth & Replacement:** Continuous activity throughout life, with rate changes
 - In growing age: Chondrocytes influenced by hormones (GH) elongate & build bone-mass
 - **Closure of epiphyses**→ Chondrocytes get entombed in the matrix
 - Migrated osteoblasts maintain bone health
 - New bone formation: In concentric circles (**osteon**)
 - 10% of total bone mass undergoes renewal/yr→ called '*Bone Remodeling*'
- **Advantages of Remodelling:**
 - Matching the bone strength to bone-stress, reshaping in accordance to mechanical forces and replacing aged & brittle bone
- **Bone Mineral Homeostasis:**
 - Under hormonal control
 - Mainly Parathyroid, Calcitonin, Vit D3
 - Secondly under GH, thyroid, steroids (cortisol & gonadal), insulin etc.

MECHANISM OF BONE REMODELLING



- Under cell-control:
 - Osteoblast (& osteocyte) → construction
 - Osteoclast → destruction
 - Both are in equilibrium

PARATHYROID HORMONE

Essential hormone to life

Absence → ASPHYXIAL Death

Two cell-types:

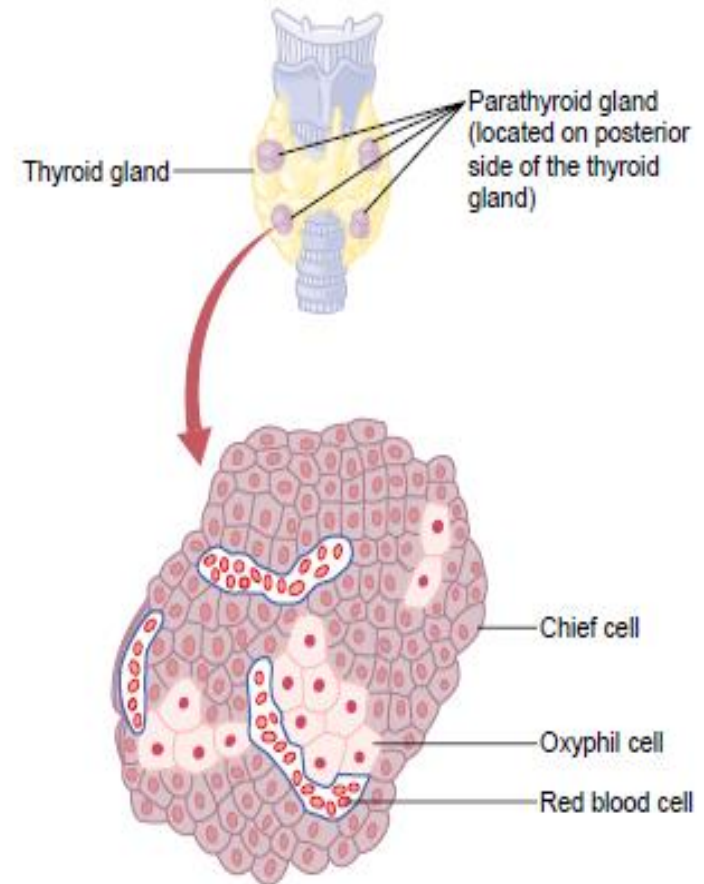
- ❑ **Chief cells:** ↑'ER', Golgi apparatus, eosinophilic → PTH
- ❑ **Oxyphilic cells**

Chemistry:

- ❖ Single polypeptide chain of 84 AA, MW = 9500

Synthesis, storage and metabolism:

- Synthesized as Prepro 'H' → Pro 'H' → **PTH** (granular storage)
- Active circulating forms with MW = 7000 & 4500
- Plasma levels = 10–55 pg/l; Half-life = 20 min. Degraded @ liver (fragments show low activity)



ACTIONS OF PARATHARMONE

Three target tissue-Bone ,Kidney, Intestine

PTH Increases Calcium and

Phosphate Absorption from the Bone

Rapid Phase of Calcium and Phosphate Absorption—
Osteolysis.

Slow Phase of Bone Absorption and Calcium

Phosphate Release—Activation of the Osteoclasts

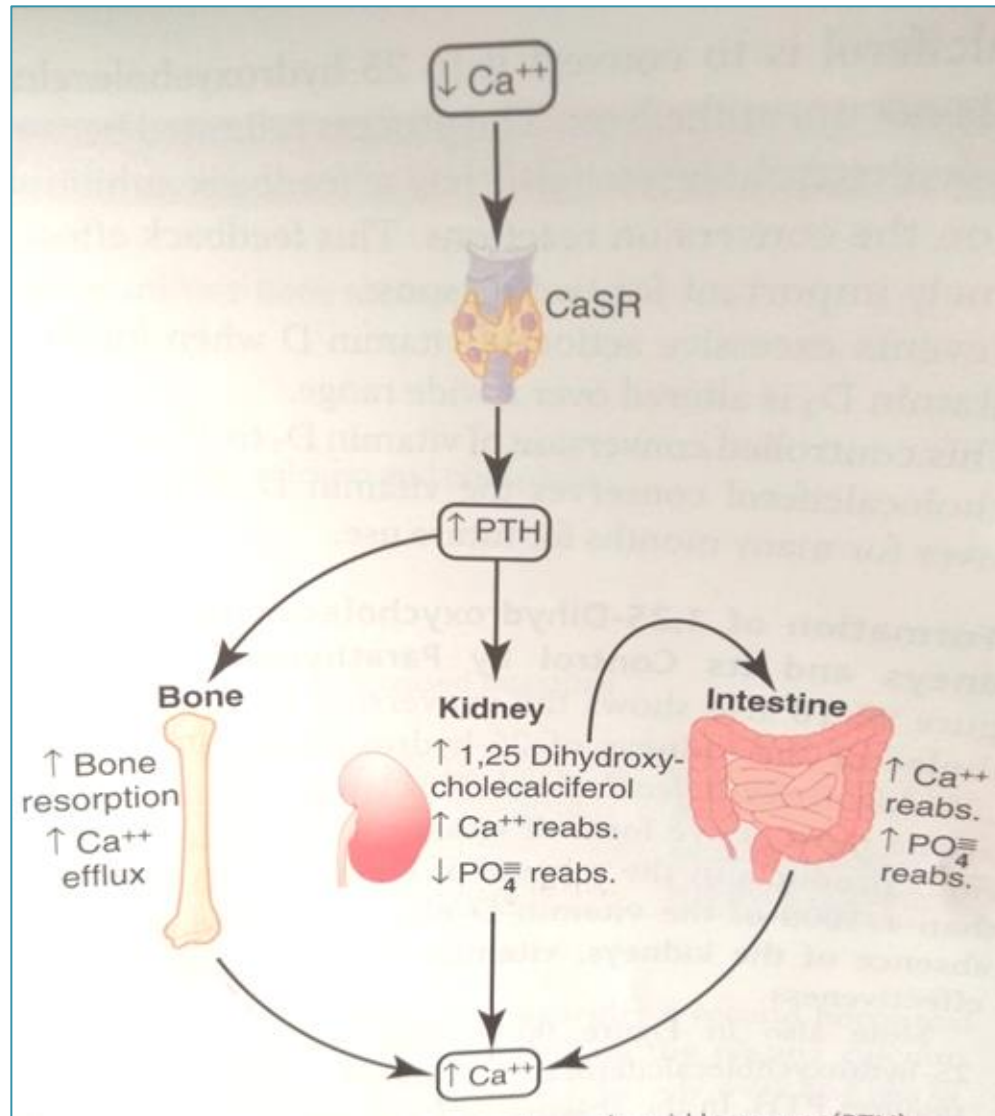
Parathyroid Hormone Decreases Calcium

Excretion and Increases Phosphate Excretion by
the Kidneys

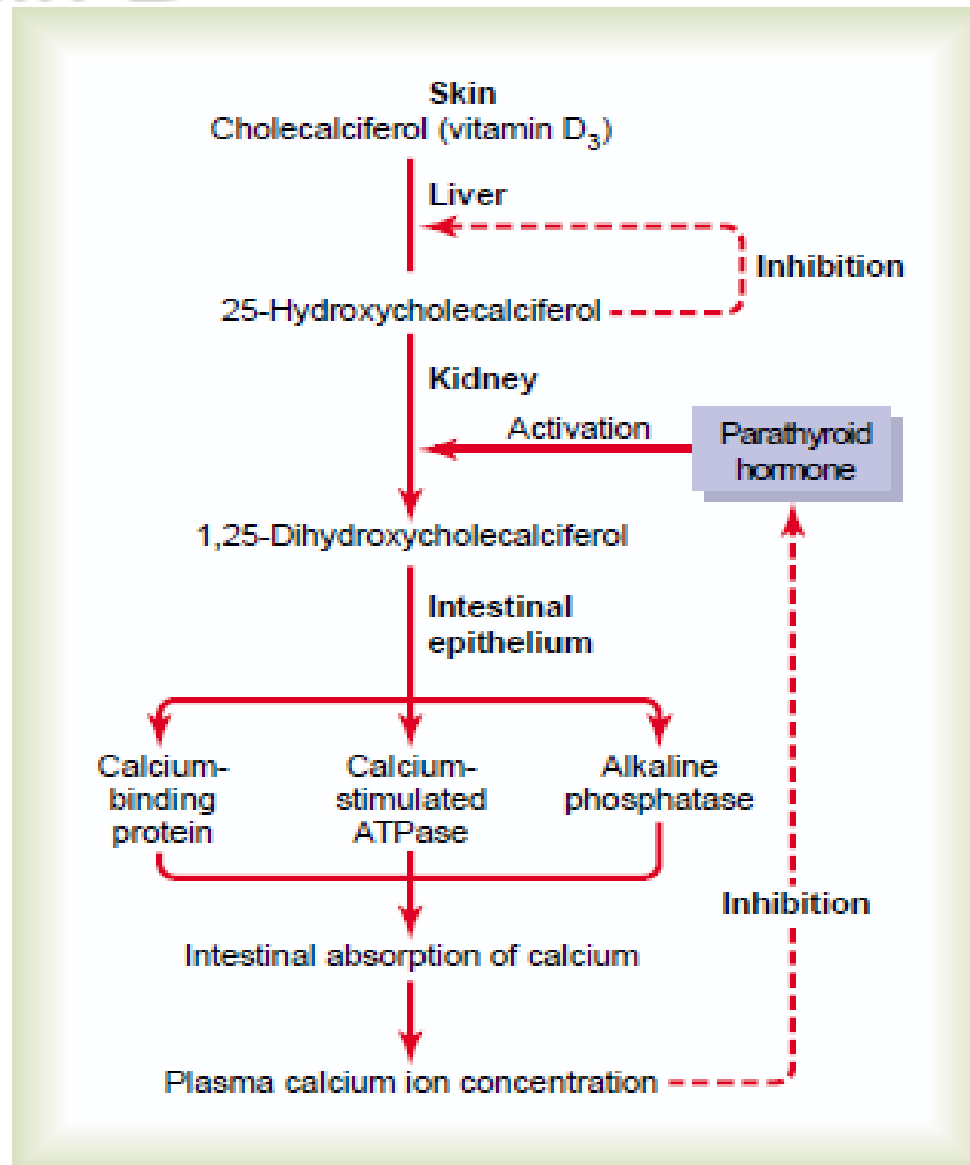
Parathyroid Hormone Increases Intestinal

Absorption of Calcium and Phosphate

Summary of PTH action



Vitamin D



Actions of Vit D3

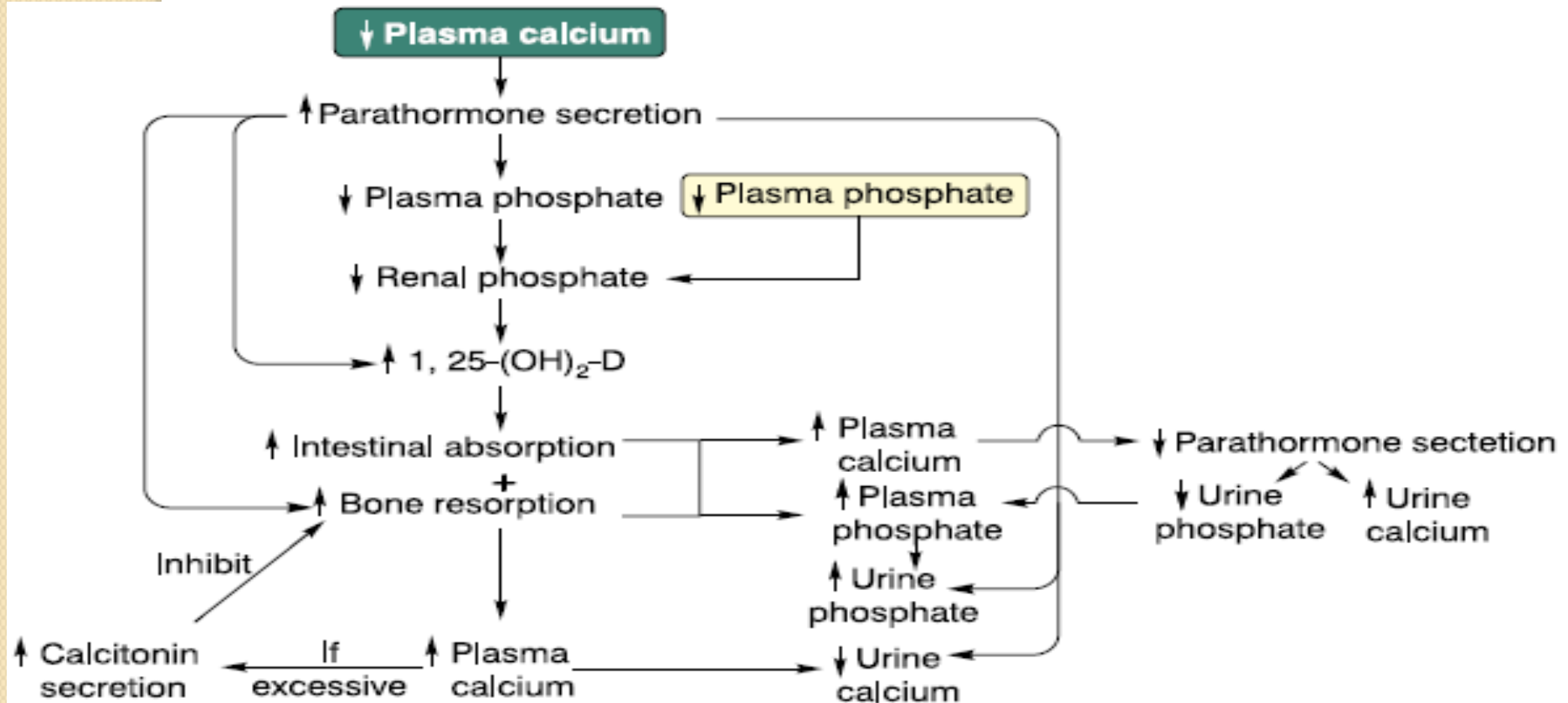
1. Hormonal Effect of Vitamin D to Promote Intestinal Calcium Absorption.
2. Vitamin D Promotes Phosphate Absorption by the Intestines.
3. Vitamin D Decreases Renal Calcium and Phosphate Excretion.
4. Effect of Vitamin D on Bone and Its Relation to Parathyroid Hormone Activity.

Calcitonin

- Secreted by parafollicular cells of thyroid gland
- Increased Plasma Calcium Concentration Stimulates Calcitonin Secretion
- Calcitonin Decreases Plasma Calcium Concentration.

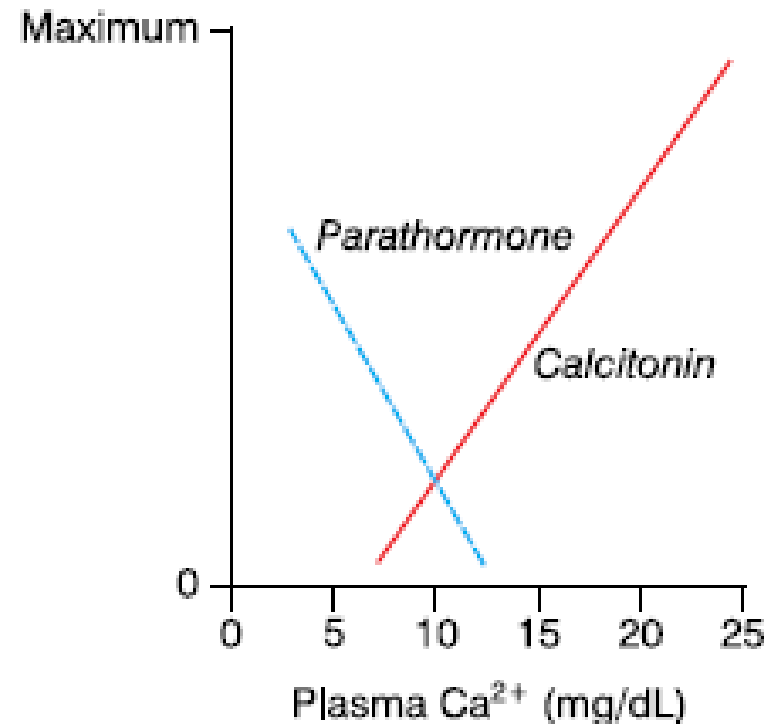
Summary of Ca Homeostasis

- Buffer Function of the Exchangeable Calcium in Bones—the First Line of Defense.
- Hormonal Control of Calcium Ion Concentration—the Second Line of Defense.



CONTROL OF 'PTH' SECRETION

- Primarily Substrate Regulation
 - PTH & Ca (ionised) form negative feedback pair (relation is inverse)
1. Signal: Ca levels in perfusing fluids of gland
 - $\downarrow \text{Ca} \rightarrow \uparrow \text{PTH}$
 2. Vit. D deficient (show hypersecretion of PTH),
 - On intake of 'D' show decrease in PTH secretion
 3. Conclusion: 1,25 DHCC changes set point around which Ca-levels control PTH



Assignment

SAQ

1. Functions of Parathyroid hormone
2. Functions of Vit D3