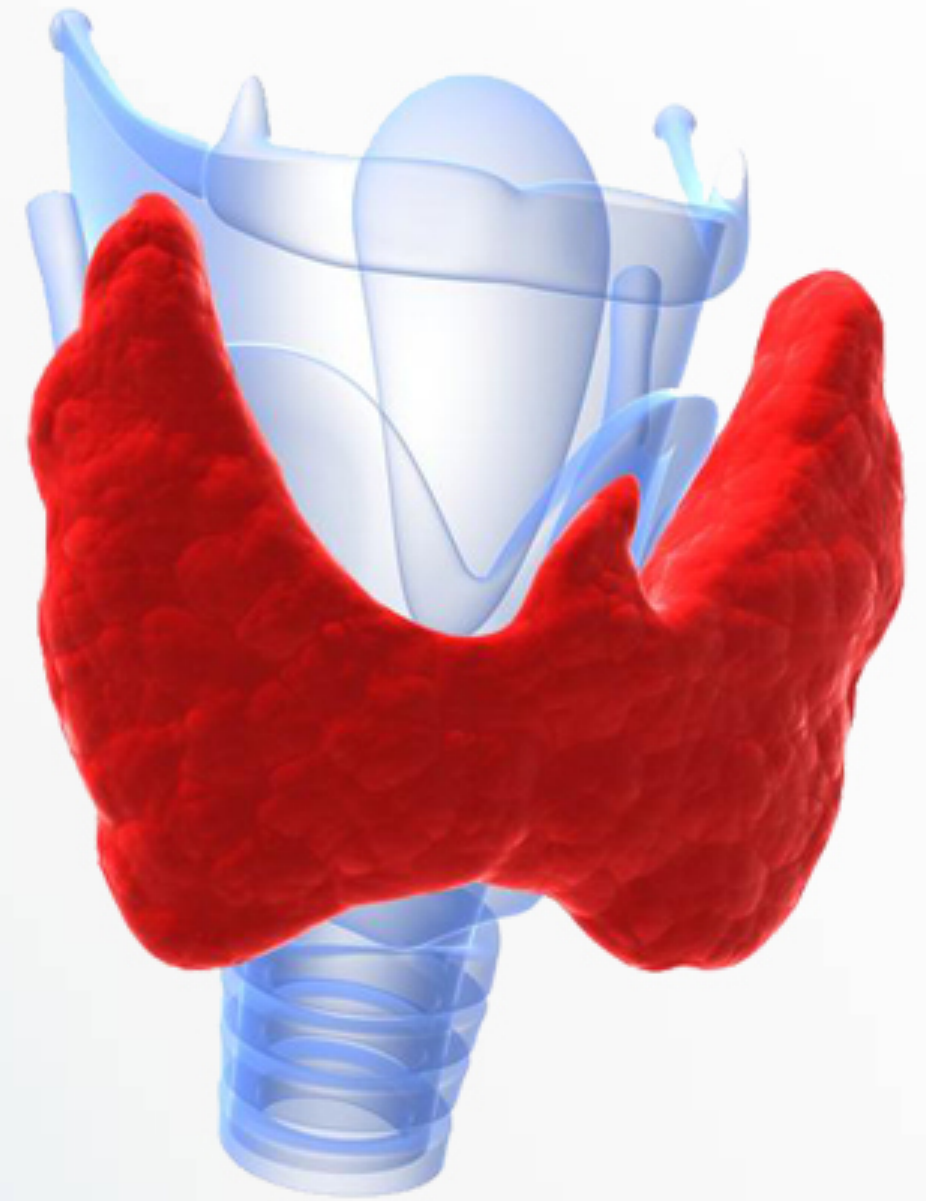




Physiology team



8 Calcium homeostasis



**Sources:
Female slides**

Objectives

- List the functions of calcium
- Describe calcium metabolism
- Describe physiology of bone
- Understand and explain hormonal regulation of calcium metabolism :
 - ✓ **Vitamin D3**

Ca⁺⁺ in Body

Distribution of Ca⁺⁺ in ECF

Total plasma calcium = **9-10.5 mg/dl** = **2.4 mEq/L**

- **41% Non Diffusible (Protein-bound calcium)**
- **59% Diffusible**
 - **9% Complexed to anions** (like phosphate)
 - **50% ionized (free)**

Protein-bound calcium

- ❖ **Most** of **Protein-bound** calcium is bound to **albumin** & much **smaller** fraction is bound to **globulin** .
- ❖ Binding of calcium to albumin is **pH-dependent** .
- ❖ Acute respiratory **alkalosis** **increases** calcium binding to protein thereby **decreases ionized** calcium level .



Distribution of Ca⁺⁺ in Body

1300 g

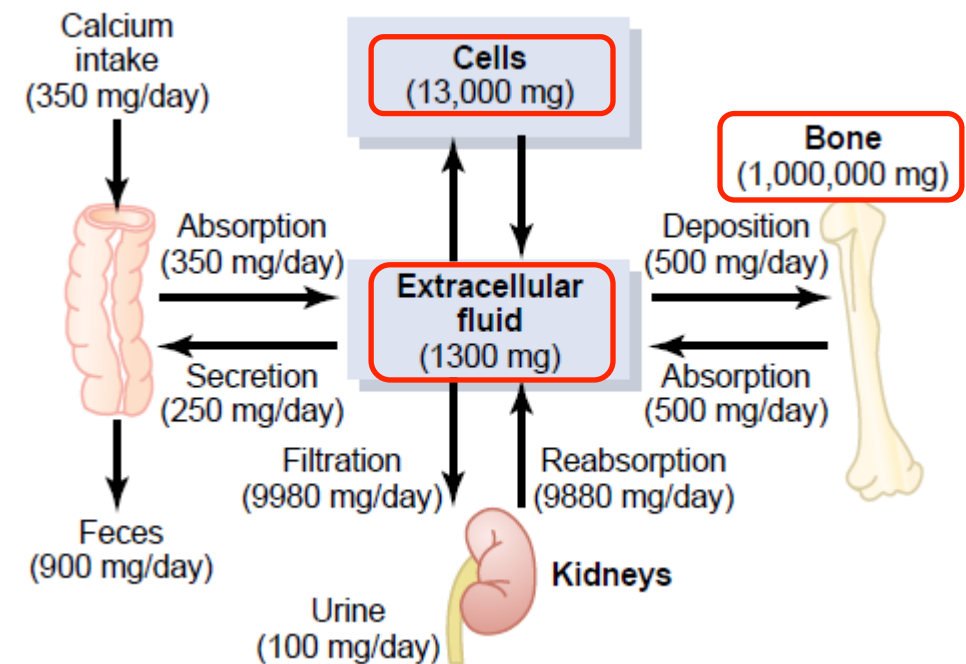
- ❖ **99%** in the **Skeleton & Teeth**
- ❖ **1%** in the **ICF "ER"**
- ❖ **0.1%** in the **ECF**

"ER" = endoplasmic reticulum

Physiological importance of Calcium

- ❖ Calcium salts in **bone** provide **structural** integrity of the skeleton .
- ❖ Calcium ions in **extracellular** and **cellular** fluids is essential to normal function for the **biochemical** processes :

- 1) **Neuromuscular excitability**
- 2) **Hormonal secretion**
- 3) **Enzymatic regulation**
- 4) **Blood coagulation**
- 5) **Second messenger.**



Source

- **Milk**
- **dairy products**
- **Fish**

Daily requirements

- ❖ **Infants & adults:**
12.5 -25 mmol/day
- ❖ **Pregnancy , Lactation and after menopause :**
25-35 mmol/day

Absorption

- ❖ **Duodenum:**
active transport
- ❖ **small intestine:**
concentration gradient
(facilitated diffusion)

Phosphate

Phosphate in body

- ❖ Phosphorous is an essential mineral necessary for ATP and cAMP second messenger systems .
- ❖ Phosphate plasma concentration is around 4 mg/dL.
- ✓ **Ionized (diffusible) = 50%**
- ✓ **un-ionized (non-diffusible) and protein- bound = 50%**
- ❖ **Calcium** is tightly regulated with Phosphorous in the body.

Bone

Bone cells

- ❖ **Osteoblasts** : bone forming cells .
- ❖ **Osteocytes** : osteoblasts surrounded by calcified matrix .
- ❖ **Osteoclasts** : bone eroding Cell “resorping” , originate from monocytes .

Physiology Of Bone

Bone composition

❖ Organic Matrix 30%

- Collagen Fibers 95%
- Ground Substance 5%
 - ECF and Proteoglycans

- give bone its **Tensile force** .

❖ Bone Salts 70%

- Salts of Ca^{++} & PO_4^- 99%
 - in form of **Hydroxyapatite crystals** .

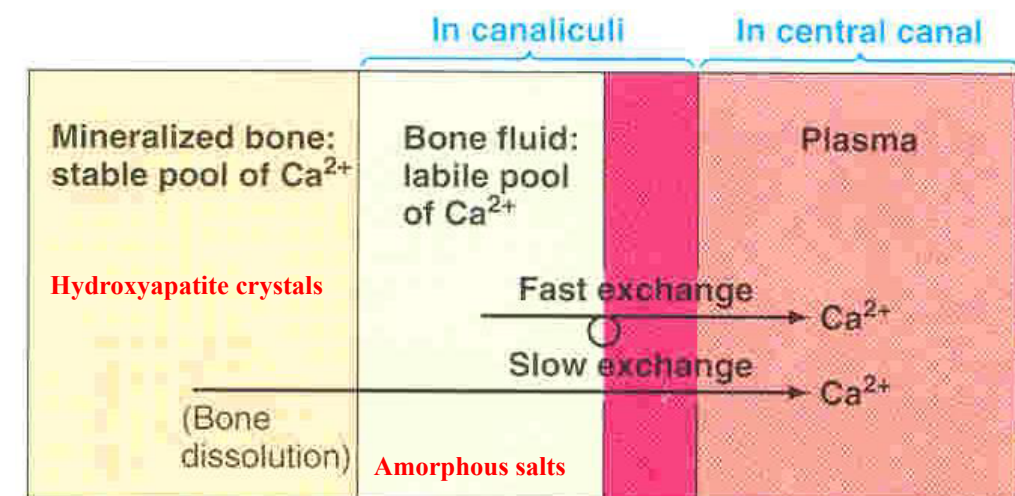
- Mg, Na, K, Carbonate ions .

- Amorphous salts 1%

- A type of **exchangeable** calcium
- Play role in **rapid** regulation of ionized Ca^{++} level in ECF
- always in **equilibrium** with Ca^{++} in ECF

- give bone its **Compressional force** .

total body content Present in bone	
Calcium	99%
Phosphate	86%
Carbonate	80%
Magnesium	50%
Sodium	35%
Water	9%



Regulation of Calcium level

Regulation of Plasma Ca and Po_4^{-3} Concentrations

1) Non-hormonal Mechanisms :

Can **Rapidly** Buffer **Small** Changes in Plasma Concentrations of **Free Calcium** (first line of defense against changes in calcium levels) .

2) Hormonal Mechanisms :

Provide **High-Capacity** and **Long-Term Regulation** of Plasma **Calcium** and **Phosphate** Concentrations .

Less than 9 mg/dl Ca in plasma → Tetany

More than 10.5 mg/dl Ca in plasma → Renal stone

Hormonal Control

I. Parathyroid hormone

II. Calcitonin

III. Vitamin D “ 1,25 Dihydroxycholecalciferol ”

Vitamin D

Functions of Vitamin D

❖ Intestinal tract :

- Increase calcium & phosphate absorption by increasing calcium binding protein .

❖ Renal :

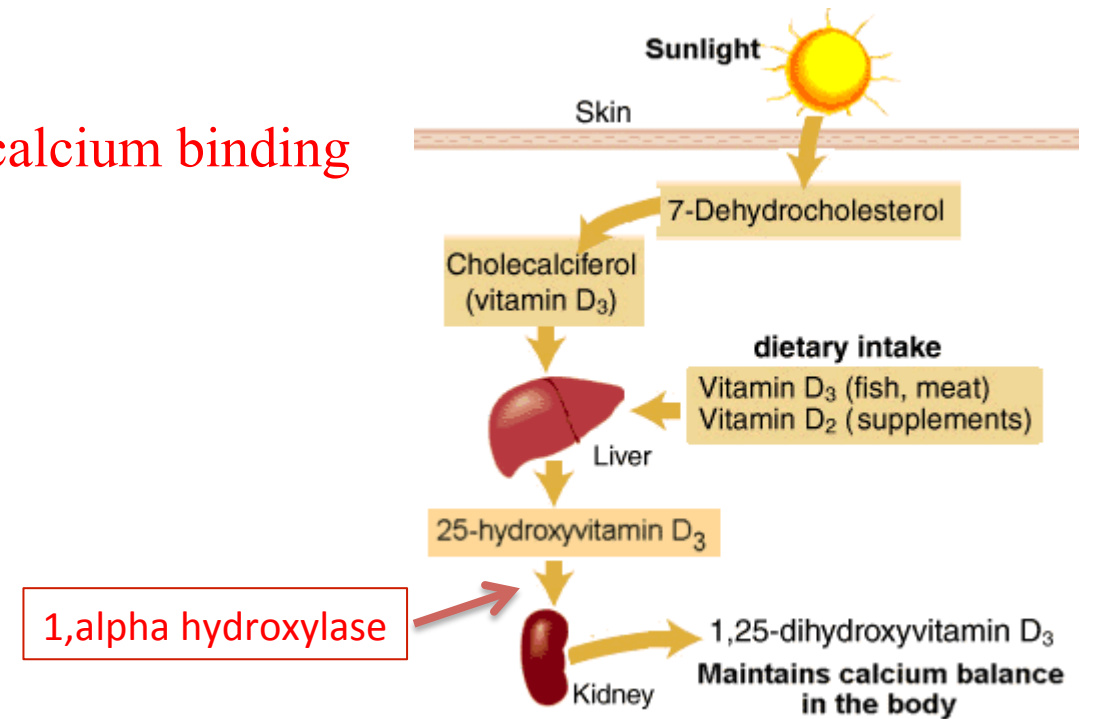
- Increases Renal calcium and Phosphate reabsorption .

❖ Bone :

- Stimulates osteoclasts “Minor role“ .

➤ Immune system :

- stimulates differentiation of immune cells. “has nothing to do with Ca”



Vitamin D in **smaller** quantities

promotes bone **calcification**

by **increase** calcium and phosphate **absorption** from the intestine and enhances the **mineralization** of bone .

Vitamin D in **extreme** quantities

causes **absorption** of bone

by **facilitating** PTH action on bones and by **increase** number & activity of **osteoclasts**.

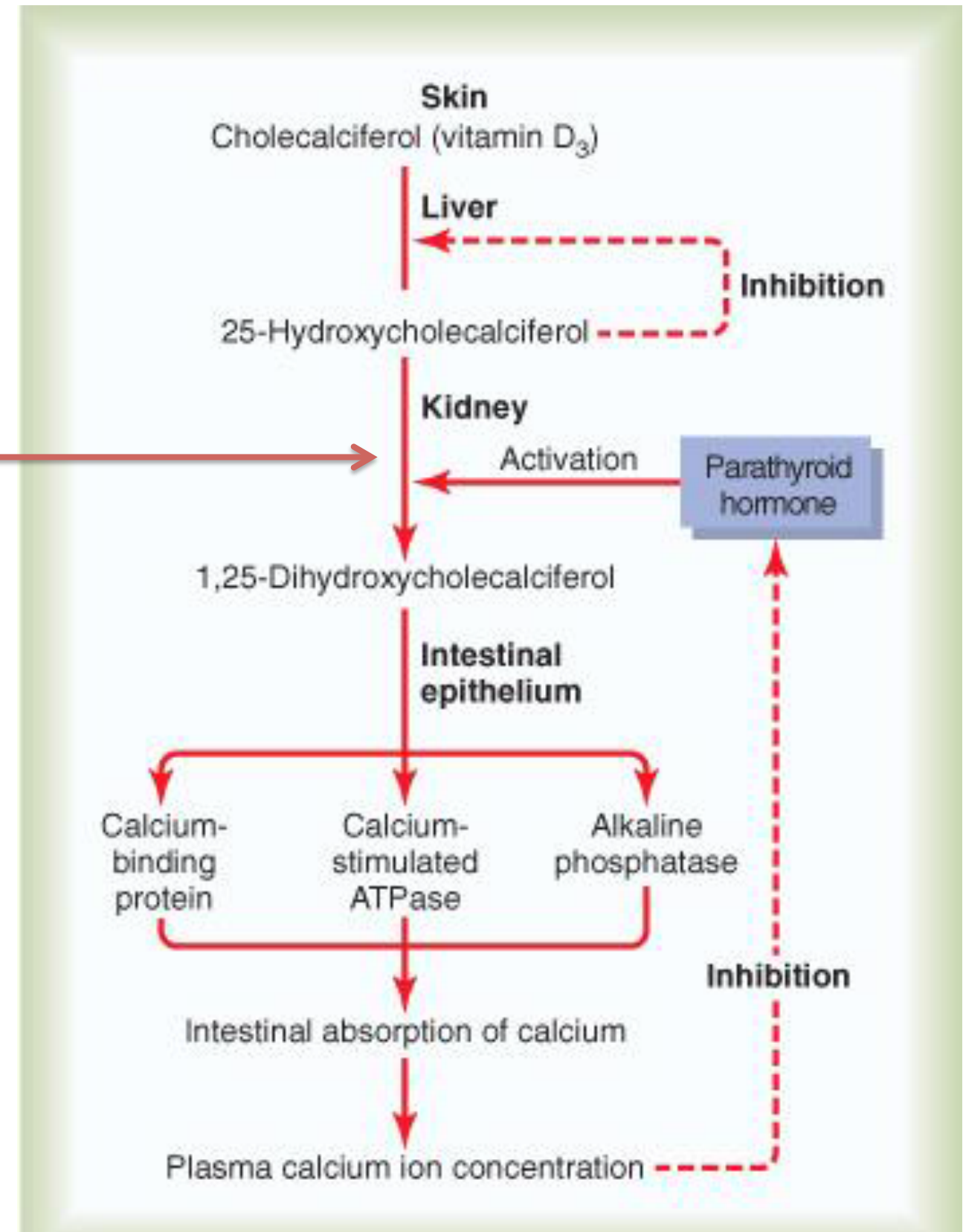
Control of Vitamin D

✓ **low Ca^{++} ions**

✓ **Prolactin** (for production of milk)

✓ **PTH**

❖ All **stimulate** renal **1,α hydroxylase**.



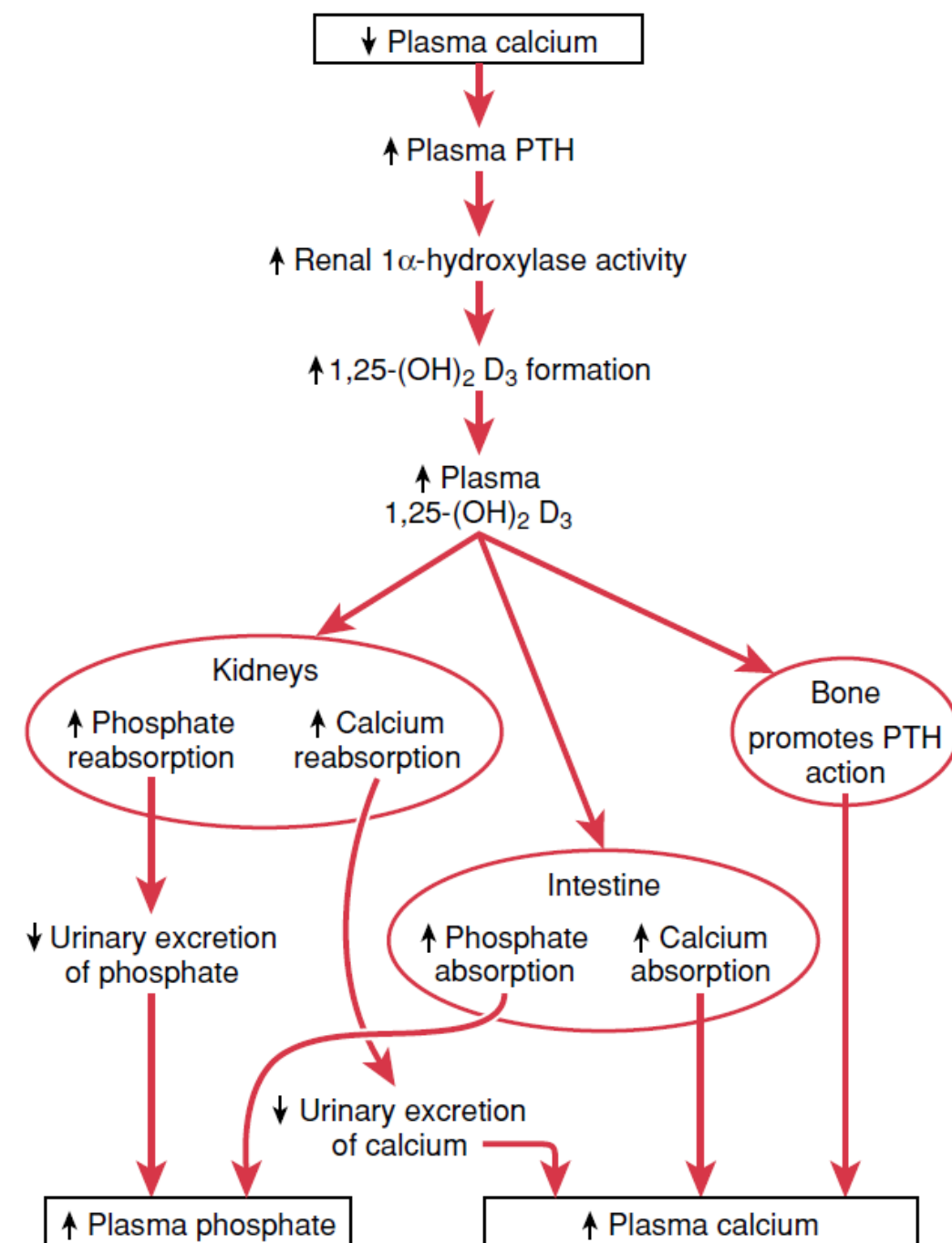
Summery

Overall Ca²⁺ homeostasis (Figure 7-13)

- 40% of the total Ca²⁺ in blood is **bound to plasma proteins**.
- 60% of the total Ca²⁺ in blood is not bound to proteins and is ultrafilterable. **Ultrafilterable Ca²⁺** includes Ca²⁺ that is complexed to anions such as phosphate and free, ionized Ca²⁺.
- Free, ionized Ca²⁺ is biologically active.**
- Serum [Ca²⁺] is determined by the interplay of intestinal absorption, renal excretion, and bone remodeling (bone resorption and formation). Each component is hormonally regulated.
- To maintain Ca²⁺ balance, net intestinal absorption must be balanced by urinary excretion.

	PTH	Vitamin D	Calcitonin
Stimulus for secretion	↓ Serum [Ca ²⁺]	↓ Serum [Ca ²⁺] ↑ PTH ↓ Serum [phosphate]	↑ Serum [Ca ²⁺]
Action on:			
Bone	↑ Resorption	↑ Resorption	↓ Resorption
Kidney	↓ P reabsorption (↑ urinary cAMP)	↑ P reabsorption	
Intestine	↑ Ca ²⁺ reabsorption ↑ Ca ²⁺ absorption (via activation of vitamin D)	↑ Ca ²⁺ reabsorption ↑ Ca ²⁺ absorption (calbindin D-28K) ↑ P absorption	
Overall effect on:			
Serum [Ca ²⁺]	↑	↑	↓
Serum [phosphate]	↓	↑	

cAMP = cyclic adenosine monophosphate. See Table 7-1 for other abbreviation.



Summery

Vitamin D

- provides Ca^{2+} and phosphate to ECF for bone mineralization.
- In children, vitamin D deficiency causes **rickets**.
- In adults, vitamin D deficiency causes **osteomalacia**.

1. Vitamin D metabolism (Figure 7-14)

- Cholecalciferol, 25-hydroxycholecalciferol, and 24,25-dihydroxycholecalciferol are inactive.
- The active form of vitamin D is **1,25-dihydroxycholecalciferol**.
- The production of 1,25-dihydroxycholecalciferol in the kidney is catalyzed by the enzyme 1α -hydroxylase.
- **1α -hydroxylase activity is increased** by the following:
 - a. ↓ serum $[\text{Ca}^{2+}]$
 - b. ↑ PTH levels
 - c. ↓ serum [phosphate]

2. Actions of 1,25-dihydroxycholecalciferol

- are coordinated to **increase both $[\text{Ca}^{2+}]$ and [phosphate]** in ECF to **mineralize new bone**.
- a. **Increases intestinal Ca^{2+} absorption.** Vitamin D–dependent Ca^{2+} -binding protein (**calbindin D-28K**) is induced by 1,25-dihydroxycholecalciferol.
 - PTH increases intestinal Ca^{2+} absorption indirectly by stimulating 1α -hydroxylase and increasing production of the active form of vitamin D.
- b. **Increases intestinal phosphate absorption.**
- c. **Increases renal reabsorption of Ca^{2+} and phosphate**, analogous to its actions on the intestine.
- d. **Increases bone resorption**, which provides Ca^{2+} and phosphate from “old” bone to mineralize “new” bone.

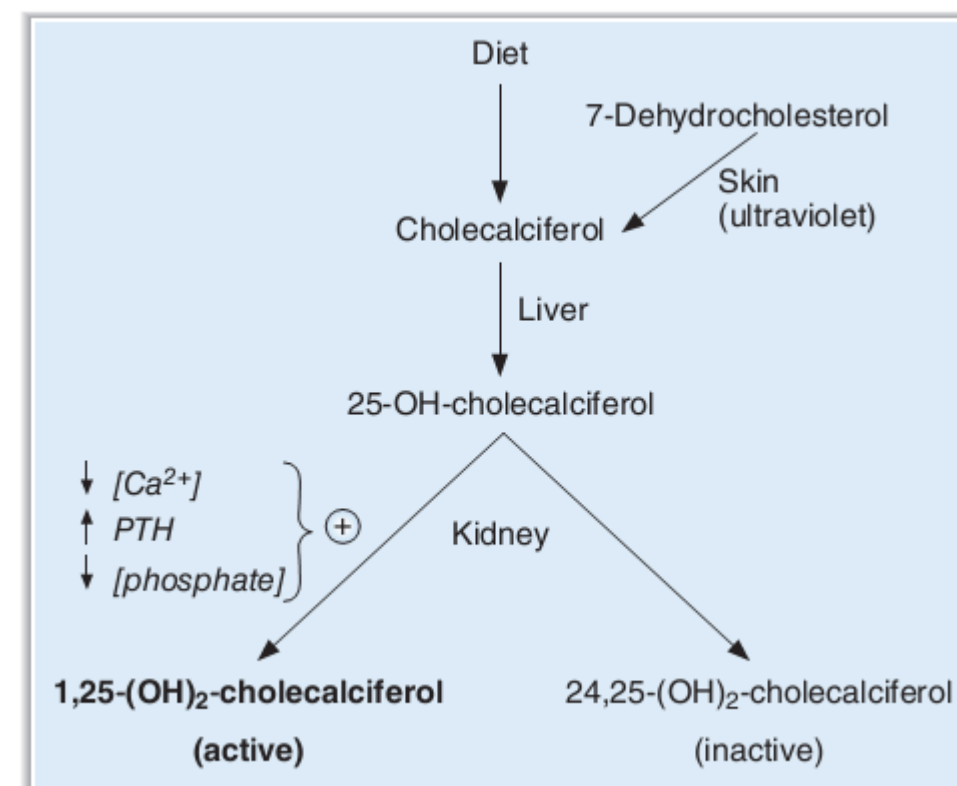


FIGURE 7-14 Steps and regulation in the synthesis of 1,25-dihydroxycholecalciferol. PTH = parathyroid hormone.

MCQs

1- Total plasma calcium is equal to :

- A-6.4 mEq/L
- B-2.4 mEq/L
- C-10.4 mEq/L
- D-12.4 mEq/L

2- Binding of calcium to albumin is :

- A-Heat-dependent
- B-Neural-dependent
- C-pH-dependent
- D-Water-dependent

3- Which of the following is a bone eroding Cell ?

- A-Osteoclasts
- B-Osteoblasts
- C-Osteocytes
- D-Monocytes

4- The majority of bone salts are in form of :

- A-ionized Ca^{++}
- B-Hydroxyapatite crystals
- C-Carbonate ions
- D-Proteoglycans

5- the first line of defense against changes in calcium levels is :

- A-Non-hormonal Mechanisms
- B-Hormonal Mechanisms
- C-Vitamin D
- D-A&B

6- Vitamin D in extreme quantities cause :

- A-bone calcification
- B-PTH secretion
- C- Tetany
- D-absorption of bone

7-PTH control vitamin D through :

- A-25 Transferases
- B-1,25 dehydrogenase
- C-1, alpha hydroxylase
- D-beta Lipase

1- B 2- C 3- A 4- B 5- A 6- D 7- C



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Endocrine Block