بسم الله الرحمن الرحيم

Calcium Homeostasis

By

Amr S. Moustafa, M.D., Ph.D.

Ass. Prof. & Consultant
Clinical Biochemistry & Molecular Biology
College of Medicine and Obesity Research Center
King Saud University

Objectives:

- Physiological importance of calcium
- Distribution and forms of calcium
- Regulation of blood level of calcium
- Measurement of calcium level
- Clinical problems: Hypo- and hyper-calcemia

Calcium: Physiological importance

- Neuromuscular excitability
- Blood coagulation
- Mineralization of bones
- Release of hormones & neurotransmitters
- Intracellular actions of some hormones

Distribution and Forms of Calcium

- One Kg of calcium in human body
- 99% in bone (mainly, hydroxyapatite crystals)
- 1% in blood and ECF

  45% Free, ionized form

  40% Bound to protein (mostly albumin)

  15% Bound to HCO_3^-, PO_4^-, citrate, lactate

Distribution and Forms of Calcium

CONT'D

- **Effects of pH on forms of blood calcium**

  Acidosis favors ionized form & alkalosis enhances protein binding

  Numbness and tingling in hyperventilation

- **Avoid use of tourniquet for collection of blood samples for measurement of calcium**

- **Importance of direct measurement of ionized calcium Vs (calculated) or (total calcium) in acutely ill subjects**

Regulation of Blood Level of Calcium

- **Parathyroid hormone (PTH)**
- **Calcitriol: Active form of vitamin D**
- **? Calcitonin**

(1) Parathyroid Hormone (PTH)

- **Secreted by parathyroid glands**
- **Molecular mass: 9.5 kDa**
- **Full biologic activity: NT 1/3 (PTH_{1-34})**
- **Acts via membrane-bound receptor (G-protein stimulation and increase intracellular cAMP)**
- **Target organs: Bone, kidney, intestine**

Parathyroid Hormone (PTH)

CONT'D

- **Stimulus:** Decrease of ionized Ca^{2+}
- **Effects:**

Bone: ↑ **Bone resorption**
Activated osteoclasts break down bone and releases calcium into ECF

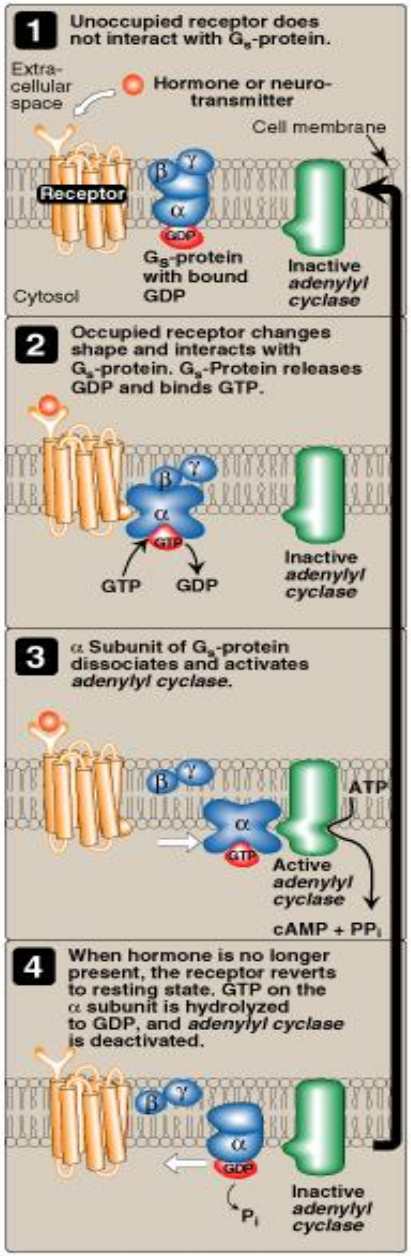
Kidneys: ↑ **Tubular reabsorption of calcium**
↑ **Renal production of active vitamin D**
↑ **Phosphate excretion (Phosphaturic effect)**

Intestine: ↑ **Intestinal absorption of calcium (Indirect)**

(Bone: Largest effect; Kidney: Rapid changes)

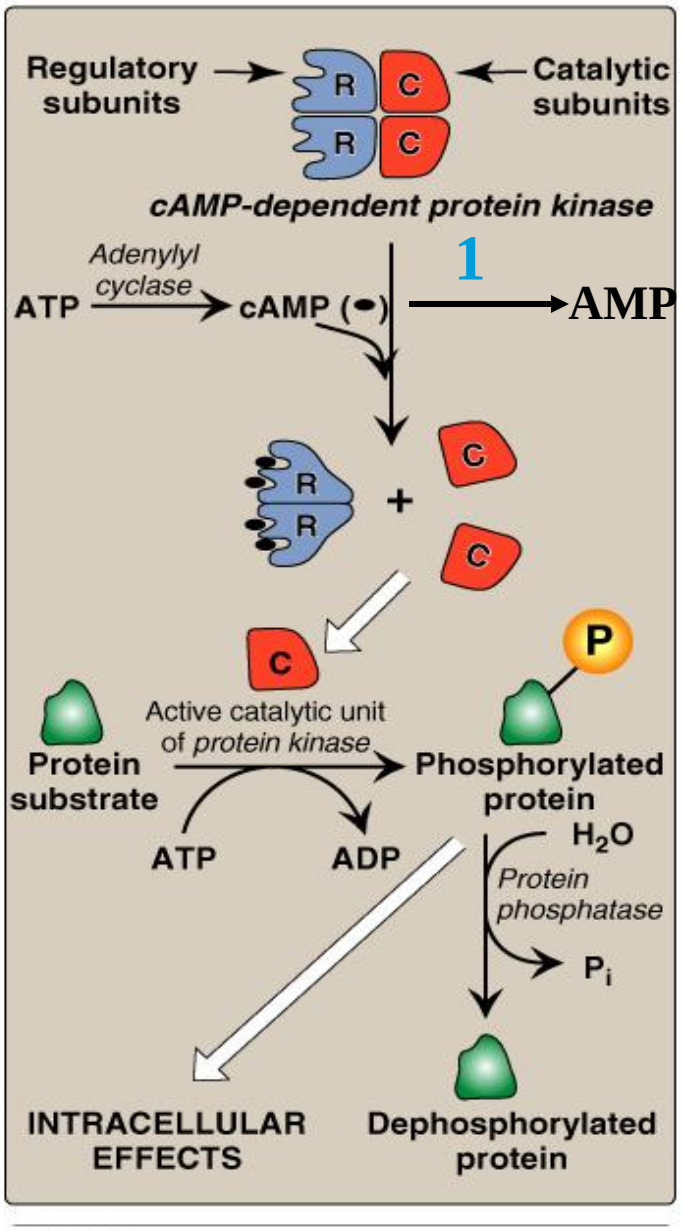
Parathyroid Hormone (PTH) CONT'D

Signal Transduction: G-protein Coupled Membrane Receptor



Actions of cAMP

[1]Phosphodiesterase

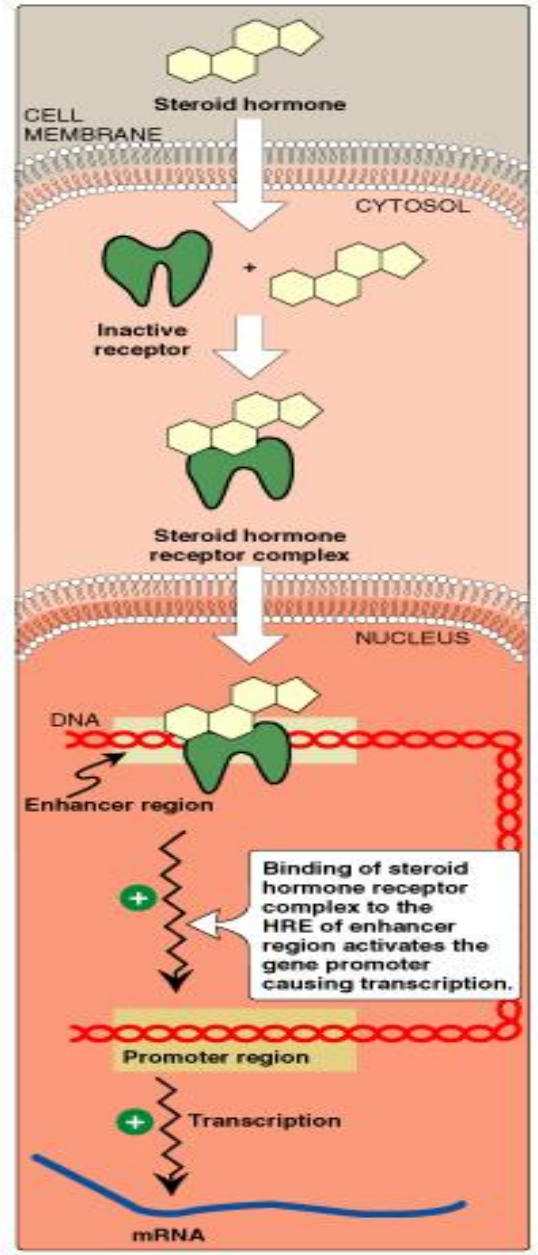


(2) Calcitriol

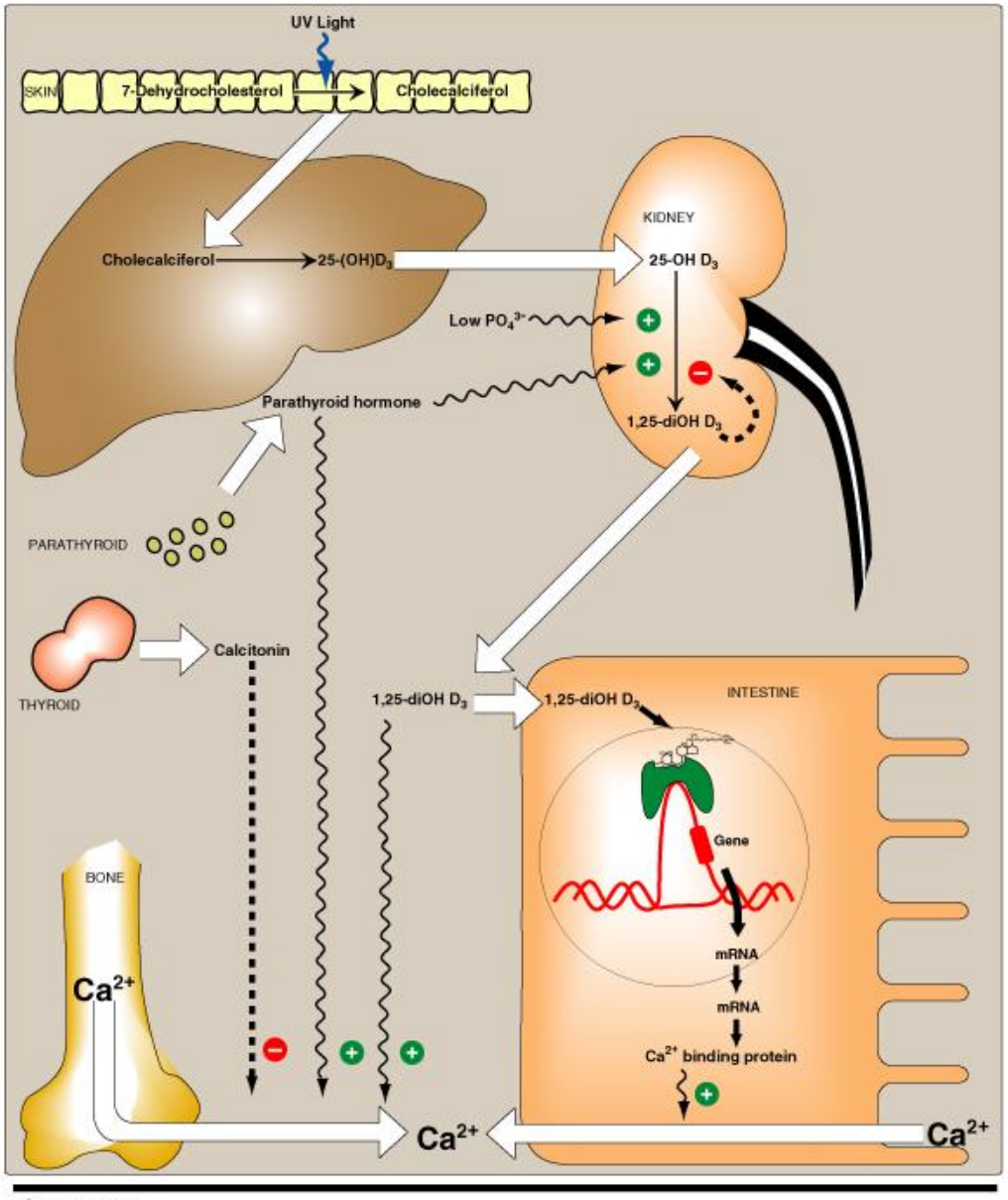
- ↑ Intestinal absorption of calcium (& phosphate)
- Enhances the effects of **PTH** on bone and kidney to ↑ blood calcium level
- Acts via intracellular receptors of steroid/thyroid superfamily
- Hormone/receptor complex binds to HRE of DNA & gene ↑ expression of important proteins for calcium homeostasis, e.g., CBP

Steroid/Thyroid Superfamily:

- Steroid Hormones
- Thyroid Hormones
- Calcitriol (Vitamin D)
- Retinoic acid (Vitamin A)

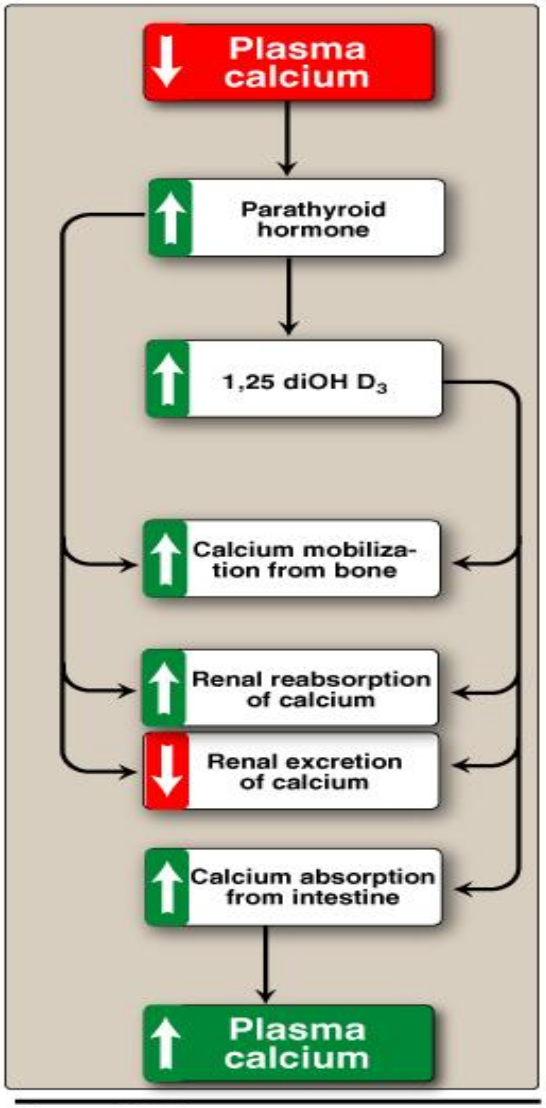


Calcitriol and Calcium Homeostasis



Calcium Homeostasis: PTH & Calcitriol

Response to low blood calcium



(3) Calcitonin

- **Secretion:** Medullary cells of thyroid gland
  Peptide hormone (32 amino acids)

- **Stimulus:** Increase of blood level of ionized Ca^{2+}

- **Effects:** Inhibits the actions of both PTH & calcitriol in hypercalcemic state

- **Physiological role in adult humans:** Uncertain

Measurement of Calcium

Types:

- Total calcium
- Ionized Ca^{2+}: direct *(ISE) and ? calculated
- Corrected calcium (adjusted to albumin)

Specimen:

- Avoid use of tourniquet
- Serum or Lithium-heparin plasma
- Urine: Acidified with HCl (1 ml/100 ml urine)

*ISE: Ion selective electrode

Reference Ranges:

Serum total calcium:

Child (< 12 years):	**2.20 – 2.7 mmol/L**
Adult:	**2.15 – 2.5**

Serum ionized calcium:

Child (< 12 years):	**1.20 – 1.38 mmol/L**
Adult:	**1.16 – 1.32**

Thank You