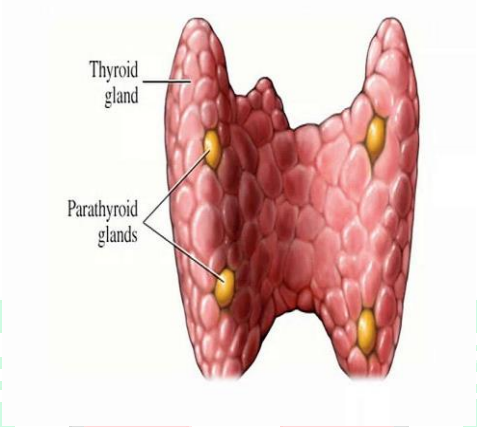
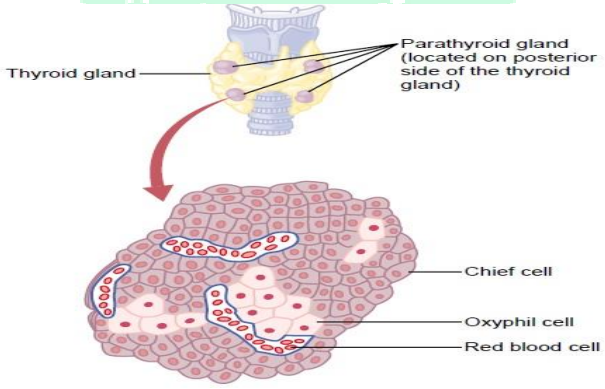
UNIT-4 PARATHYROID GLAND



- Human beings have **four parathyroid glands**, which are situated on the posterior surface of upper and lower poles of thyroid gland.
- Parathyroid glands are very small in size, measuring about 6 mm long, 3 mm wide and 2 mm thick, with dark brown color.

HISTOLOGY:

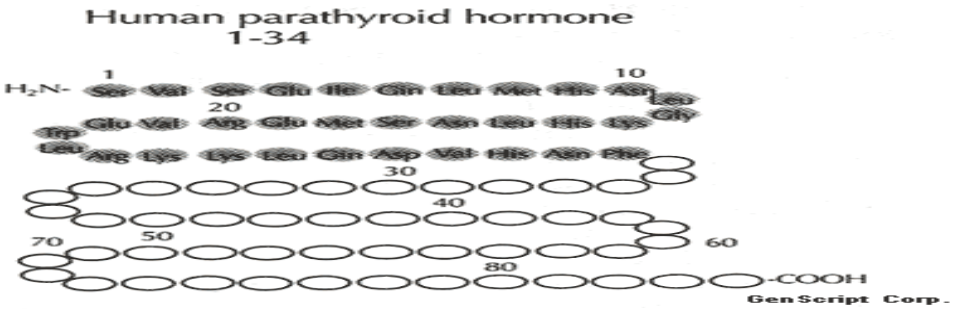


- Each parathyroid gland is made up of **chief cells** and **oxyphil cells.**
- Chief cells secrete **parathormone.**

- Oxyphil cells are the degenerated chief cells and their function is unknown. However, these cells may secrete parathormone during pathological condition called **parathyroid adenoma.**

- The number of oxyphil cells increases after puberty.

PARATHORMONE



- Parathormone secreted by parathyroid gland is essential for the **maintenance of blood calcium level** within a very narrow critical level.

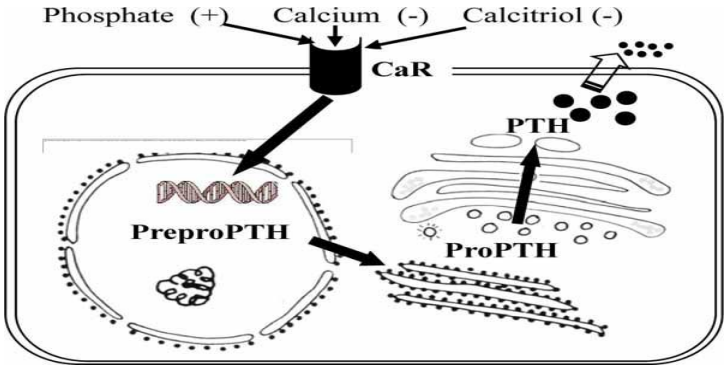
- Parathormone is **protein in nature**, having 84 amino acids.

- Its molecular weight is 9,500.

- Parathormone has a **half-life of 10 minutes**.

- Normal plasma level of PTH is about **1.5 to 5.5 ng/dL**.

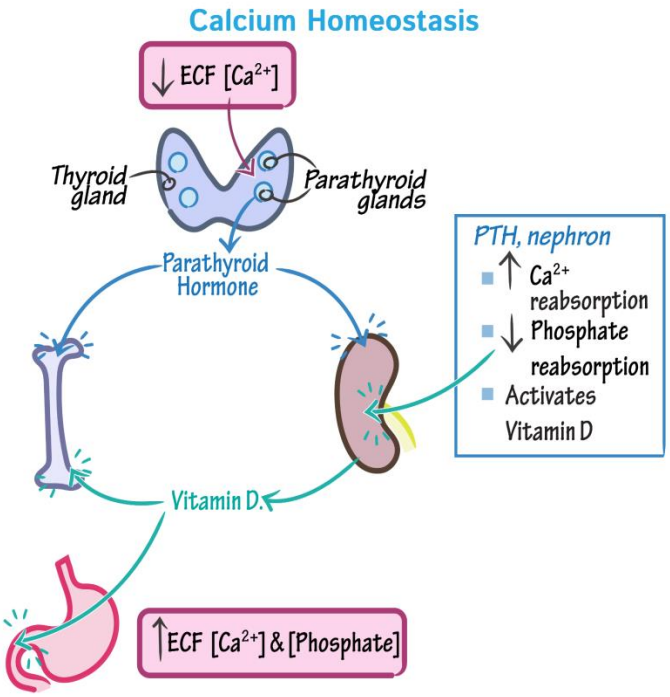
SYNTHESIS



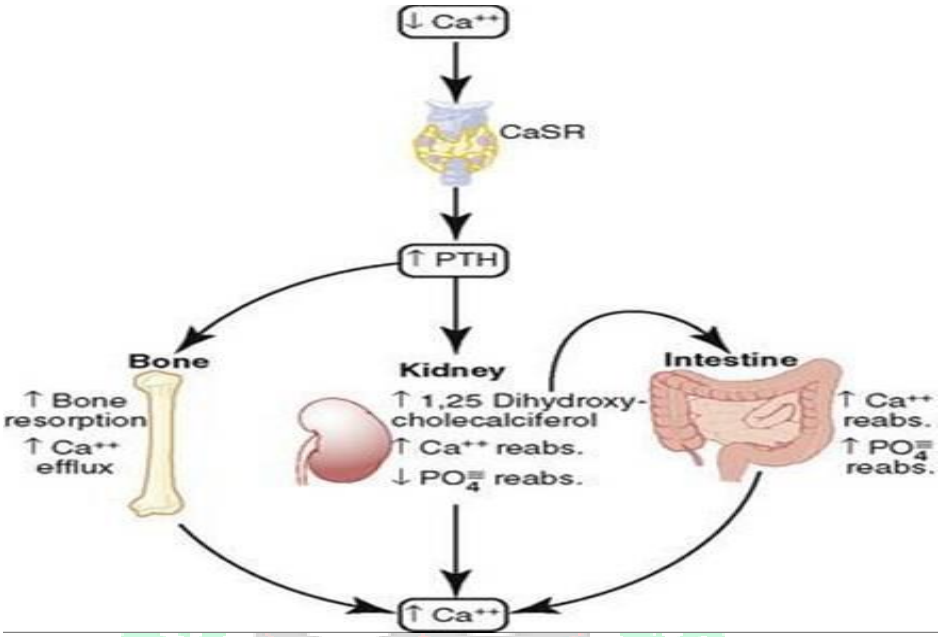
- Parathormone is synthesized from the precursor called **prepro-PTH** containing 115 amino acids.
- First, the prepro-PTH enters the endoplasmic reticulum of chief cells of parathyroid glands.
- There it is converted into a prohormone called **pro-PTH,** which contains 96 amino acids.
- Pro-PTH enters the Golgi apparatus, where it is converted into PTH.

METABOLISM

- Sixty to seventy percent of PTH is degraded by **Kupffer cells** of liver, by means of proteolysis.
- Degradation of about 20% to 30% PTH occurs in kidneys and to a lesser extent in other organs.



ACTIONS OF PARATHORMONE ON BLOOD CALCIUM LEVEL



- Primary action of PTH is to **maintain the blood calcium level** within the critical range of **9 to 11 mg/dL.**
- PTH maintains blood calcium level by acting on:

1. Bones
2. Kidney
3. Gastrointestinal tract.

On Bone

- Parathormone enhances the resorption of calcium from the bones **(osteoclastic activity)** by acting on **osteoblasts** and **osteoclasts** of the bone.
- Resorption of calcium from bones occurs in two phases:

i. Rapid phase

ii. Slow phase.

Rapid phase

- Immediately after reaching the bone, PTH gets attached with the receptors on the cell membrane of osteoblasts and osteocytes.
- The hormone-receptor complex increases the permeability of membranes of these cells for calcium ions.
- It accelerates move out of these bone cells and enter the blood at a faster rate.

Slow phase

- Slow phase of calcium resorption from bone is due to the **activation of osteoclasts** by PTH.
- When osteoclasts are activated, some substances such as proteolytic enzymes, citric acid and lactic acid are released from lysosomes of these cells.
- All these substances **digest or dissolve the organic matrix of the bone**, releasing the calcium ions.
- The calcium ions slowly enter the blood.
- PTH increases calcium resorption from bone by stimulating the proliferation of osteoclasts also.

On Kidney

- PTH increases the reabsorption of calcium from the renal tubules along with magnesium ions and hydrogen ions.
- It increases calcium reabsorption mainly from distal convoluted tubule and proximal part of collecting duct.
- PTH also increases the formation of **1,25- dihydroxycholecalciferol** (activated form of vitamin D) from 25-hydroxycholecalciferol in kidneys.

On Gastrointestinal Tract

- PTH increases the absorption of calcium ions from the GI tract indirectly. It increases the formation of 1,25- dihydroxycholecalciferol in the kidneys. This vitamin, in turn increases the absorption of calcium from GI tract.
- Thus, the activated vitamin D is very essential for the absorption of calcium from the GI tract. And PTH is essential for the formation of activated vitamin D.

ROLE OF PTH IN THE ACTIVATION OF VITAMIN D

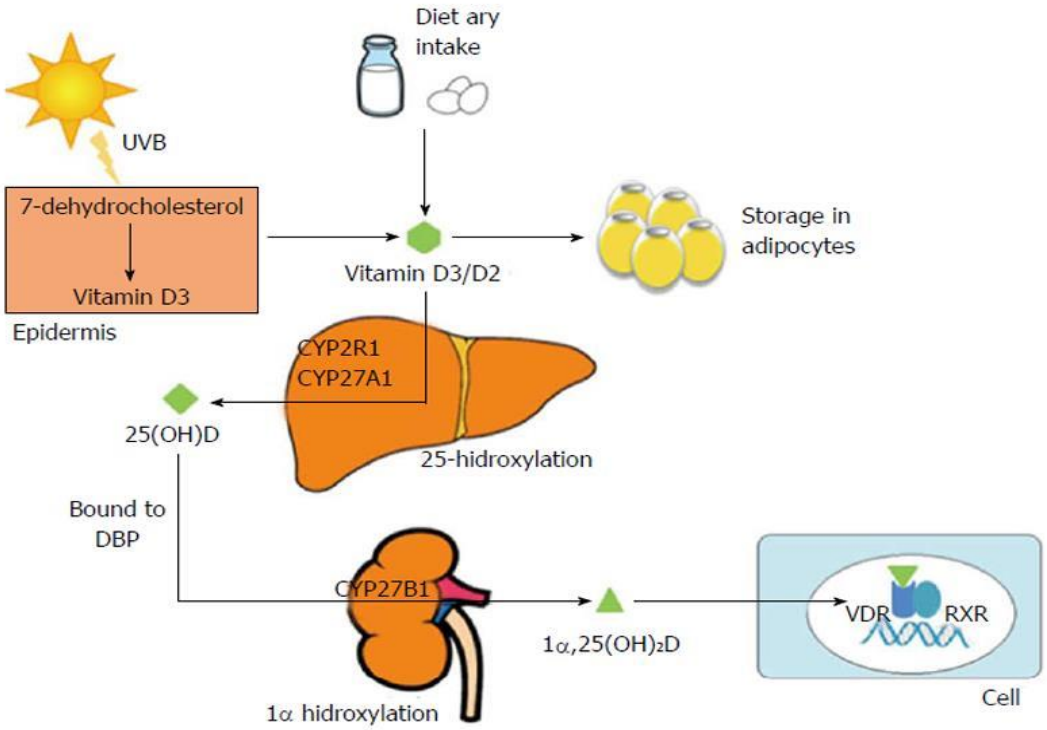
- There are various forms of vitamin D. But, the most important one is vitamin D3 (cholecalciferol).
- Vitamin D3 is synthesized in the skin from 7-dehydrocholesterol, by the action of **ultraviolet rays** from the **sunlight.** It is also obtained from dietary sources.
- The activation of vitamin D3 occurs in two steps

First step

- Cholecalciferol (vitamin D3) is converted into 25- hydroxycholecalciferol in the liver. This process is limited and is inhibited by 25-hydroxycholecalciferol itself by feedback mechanism.
- If vitamin D3 is converted into 25-hydroxycholecalciferol, it remains in the body only for 2 to 5 days. But vitamin D3 is stored in liver for several months.

Second step

- 25-hydroxycholecalciferol is converted into 1,25- dihydroxycholecalciferol **(calcitriol)** in kidney.
- It is the active form of vitamin D3.
- This step needs the presence of PTH.



ACTIONS OF PARATHORMONE ON BLOOD PHOSPHATE LEVEL

PTH decreases blood level of phosphate by increasing its urinary excretion. It also acts on bone and GI tract.

1. On Bone

Along with calcium resorption, PTH also increases phosphate absorption from the bones.

2. On Kidney

Phosphaturic action

It is the effect of PTH by which phosphate is excreted through urine. PTH increases phosphate excretion by inhibiting reabsorption of phosphate from renal tubules. It acts mainly on proximal convoluted tubule.

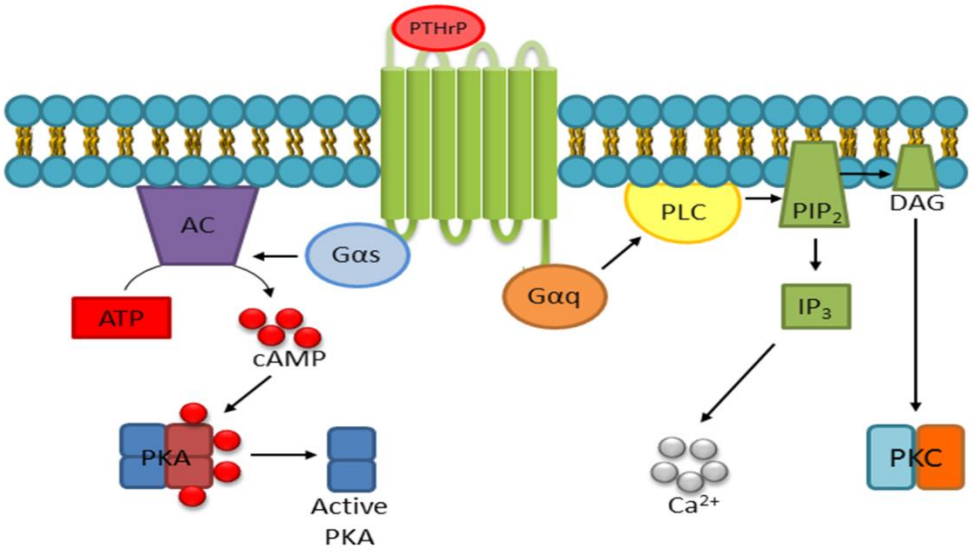
3. On Gastrointestinal Tract

Parathormone increases the absorption of phosphate from GI tract through calcitriol.

MODE OF ACTION OF PARATHORMONE

Parathormone Receptors

- Parathormone receptors (PTH receptors) are of three types, PTHR1, PTHR2 and PTHR3, which are G protein coupled receptors.
- PTHR1 is physiologically more important than the other two types. PTHR1 mediates the actions of PTH and **PTH-related protein.**
- Role of PTHR2 and PTHR3 is not known clearly.
- On the target cells, PTH binds with PTHR1 which is coupled to G protein and forms hormone-receptor complex. Hormone-receptor complex causes formation of cAMP, which acts as a second messenger for the hormone.



REGULATION OF PARATHORMONE SECRETION