ENDOCRINE
PHARMACOLOGY

04

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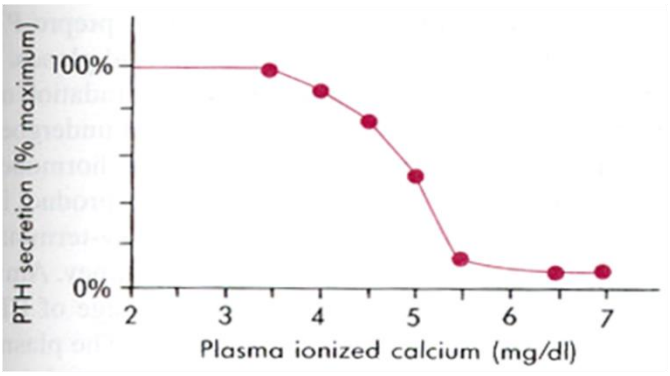
- ❖ **3 factors PTH, Vitamin D, Calcitonin.**
- ❖ **3 tissues Bone, Intestine, Kidneys.**

PARATHYROID HORMONE (PTH)

- ❖ **84 A.A peptide translated as a pre-prohormone (**Originated from larger precursor (pre-proparathyroid hormone) that Cleaved in rough endoplasmic reticulum into pro-parathyroid hormone then in Golgi apparatus to parathyroid hormone)
- ❖ **Regulation of synthesis & release:**
- ❖ **↓ [Ca++] → ↑ PTH; ↑ [Ca++] → ↓ PTH.**
- ❖ **Little if any regulation by (PO4--).**

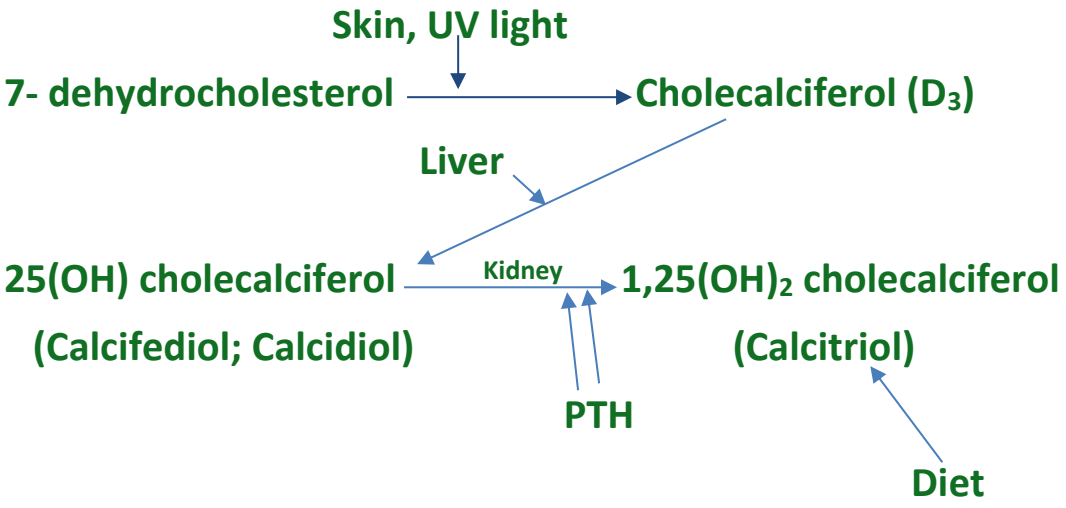
- **Maximum secretion of PTH occurs at plasma Ca++ below 3.5 mg/dl.**
- **At Ca++ above 5.5 mg/dl, PTH secretion is maximally inhibited.**



- ➢ **On bone (1º target tissue):**
- ▪ **PTH ↑ resorption of Ca^{++}& PO_4^{--}**
- ▪ **(cAMP) mediated effect.**
- ➢ **-On intestine:**
- ▪ **↑ absorption of Ca^{++}& PO_4^{--}**
- ▪ **An indirect effect through ↑ vitamin D synthesis**
- ➢ **-On kidneys:**
- ▪ **↑ reabsorption of Ca^{++}, ↑↑↑ excretion of PO_4^{--}**
- ▪ **(cAMP mediated effect).**

The effect of PTH on kidney result in increasing the release of phosphate (exceeding the absorption of it under the effect of vit D & resorption from bone)

SYNTHESIS OF VITAMIN D



According to the above pathway first step in vit D synthesis occurs In skin, and first step in activation occurs in liver, the last step of synthesis occurs in the kidneys.

VITAMIN D (Normal daily requirement 400 IU/day)

- On intestine (1º target tissue): ↑ absorption of Ca++& PO4--
- On bone: ↑ bone resorption
- On kidney: ↑ reabsorption of Ca++& PO4 --

CALCITONIN (32 A.A peptide)

Synthesized and released from parafollicular cells of the thyroid.

- Regulation of synthesis & release: ↑ [Ca++] → ↑ calcitonin; ↓ [Ca++] → ↓ calcitonin.
- Effects: On bone: ↓ bone resorption (↓Ca++&PO4 --movement) On kidneys: ↑ Ca++& PO4 -- excretion? On intestine: ↓ Ca++& PO4 – absorption.
- May be more important in regulating bone remodeling than in Ca++ homeostasis: Evidence: Chronic excess of calcitonin does not produce hypocalcemia and removal of parafollicular cells does not cause hypercalcemia.

-PTH and Vitamin D3 regulation dominate.

-	PTH	Vit. D	Calcitonin
[Ca++]	↑	↑	↓
[PO4 --]	↓	↑	↓

-Disorders affecting the parathyroids:

HYPOSECRETION(HYPOPARATHYROIDISM):

-Causes:

- Thyroidectomy (most common cause)

- Idiopathic

- ↓ sensitivity of target tissues to PTH (pseudohypoparathyroidism)→ PTH level is normal here.

- ❖ Pay attention to the way of treatment of these cases, PTH administration is not effective.

SYMPTOMS OF HYPOPARATHYROIDISM:

Are those of hypocalcemia:

- ➢ **Parasthesia, tingling lips, fingers, and toes, carpopedal spasm, muscle cramps, tetanic contractions, convulsions (seizures)**

Paresthesia refers to a burning or prickling sensation that is usually felt in the hands, arms, legs, or feet, but can also occur in other parts of the body.

- ➢ **Bronchospasm**
- ➢ **Depression, anxiety, abdominal pain**
- ➢ **Cataract...**

LAB. TESTS (HYPOPARATHYROIDISM):

↓ blood [Ca++]

↑ blood [PO4 --]

↓ urinary [cAMP]

↓ urinary [PTH]

↓ urinary [Ca++]

↓ urinary [PO4 --]

RX OF HYPOPARATHYROIDISM:

- Vitamin D Calcifediol, Calcitriol, Ergocalciferol, α-Calcidol, Dihydrotachysterol…(the doctor said he usually don't focus on them)

- **Drug of choice for chronic cases**

- Ca++ supplement
- Ca++ rich diet
- Ca++ salts (carbonate, gluconate, chloride...)

Drug of choice in acute cases

- Thiazide diuretics could help, they inhibit excretion of Ca++
- Teriparatide (synthetic rPTH in small doses)-recently approved in the management of osteoporosis; given SC.

HYPERSECRETION (HYPERPARATHYROIDISM):

Causes: - 1º hyperparathyroidism (adenomas)

- 2º hyperparathyroidism

2º to any cause of hypocalcemia

e.g., malabsorption syndrome, renal disease…

- 3º hyperparathyroidism

Results from hyperplasia of the parathyroid glands and a loss of response to serum calcium levels; this disorder is most often seen in patients with chronic renal failure.

SYMPTOMS OF HYPERPARATHYROIDISM:

-Are those of hypercalcemia:

- Generalized weakness and fatigue depression, bone pain, muscle pain (myalgias), decreased appetite, feelings of nausea and vomiting, constipation, polyuria, polydipsia, cognitive impairment, kidney stones and osteoporosis…

LAB. TESTS (HYPERPARATHYROIDISM):

↑ blood [Ca++]

↓ blood [PO4 --]

↑ urinary [cAMP]

↑ urinary [PTH]

↑ urinary [Ca++]

↑ urinary [PO4 --]

Bone x-ray → bone decalcification

RX OF HYPERPARATHYROIDISM:

- **Low Ca++ diet**
- **Na+ phosphate** (Constituent of bone & teeth)
- **Steroids e.g. Prednisolone... ↓ Ca++ absorption**
- **Calcitonin - Surgery (best Rx)**
- **Cinacalcet (calcimimetic) (oral tab) is used to treat secondary hyperparathyroidism in patients with end-stage renal disease who are on dialysis & also used to treat patients with 1º hyperparathyroidism & cancer of parathyroid gland.**

OTHER DRUGS EFFECTIVE IN THE MANAGEMENT OF HYPERCALCEMIA:

- **Diuretics e.g., Furosemide (↑ Ca++ excretion)**
- **Plicamycin inhibits bone resorption.**

  Biophosphonates Etidronate, Pamidronate… ↑ bone formation and ↓ bone resorption

PAGET'S DISEASE:

- **Rare bone disorder characterized by demineralization of bone, disorganized bone formation, ↑ bone resorption, fractures, spinal cord injuries, deafness…**

➢ **Rx:**

- **Salmon calcitonin (was considered drug of choice) whether extracted from salmon fish or synthetic, S.C, I.M. Also effective in the management of osteoporosis in postmenopausal women**
- **Biophosphonates** (To treat osteoporosis)

Etidronate, zoledronate, alendronate, residronate, pamidronate… (most preferred drugs in the management of Paget's disease). Such drugs are known as antiresorptive agents (Inhibit bone resorption)

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