



ENDOCRINE

PHARMACOLOGY

Modified 4



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Parathyroid Gland & Calcium Metabolism



3 factors PTH, Vitamin D, Calcitonin

3 tissues Bone, Intestine, Kidneys

Parathyroid Hormone (PTH)

84 a.a peptide translated as a pre-prohormone

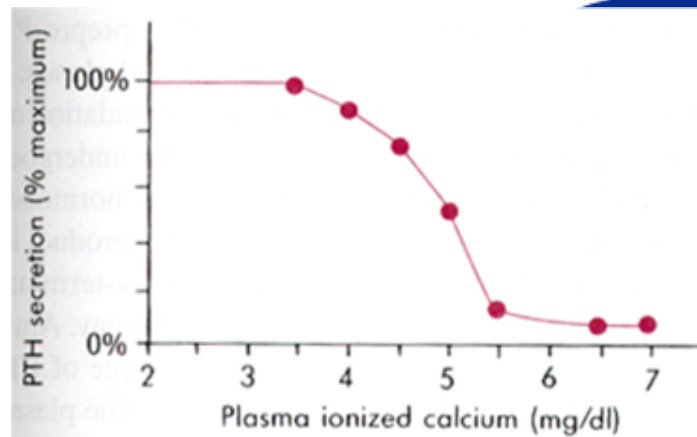
Regulation of synthesis & release:

$\downarrow [Ca^{++}] \Rightarrow \uparrow PTH; \uparrow [Ca^{++}] \Rightarrow \downarrow PTH$

Little if any regulation by PO_4^{--}

Originated from larger precursor (pre-parathyroid hormone) that Cleaved in rough endoplasmic reticulum into pro-parathyroid hormone then in golgi apparatus to parathyroid hormone

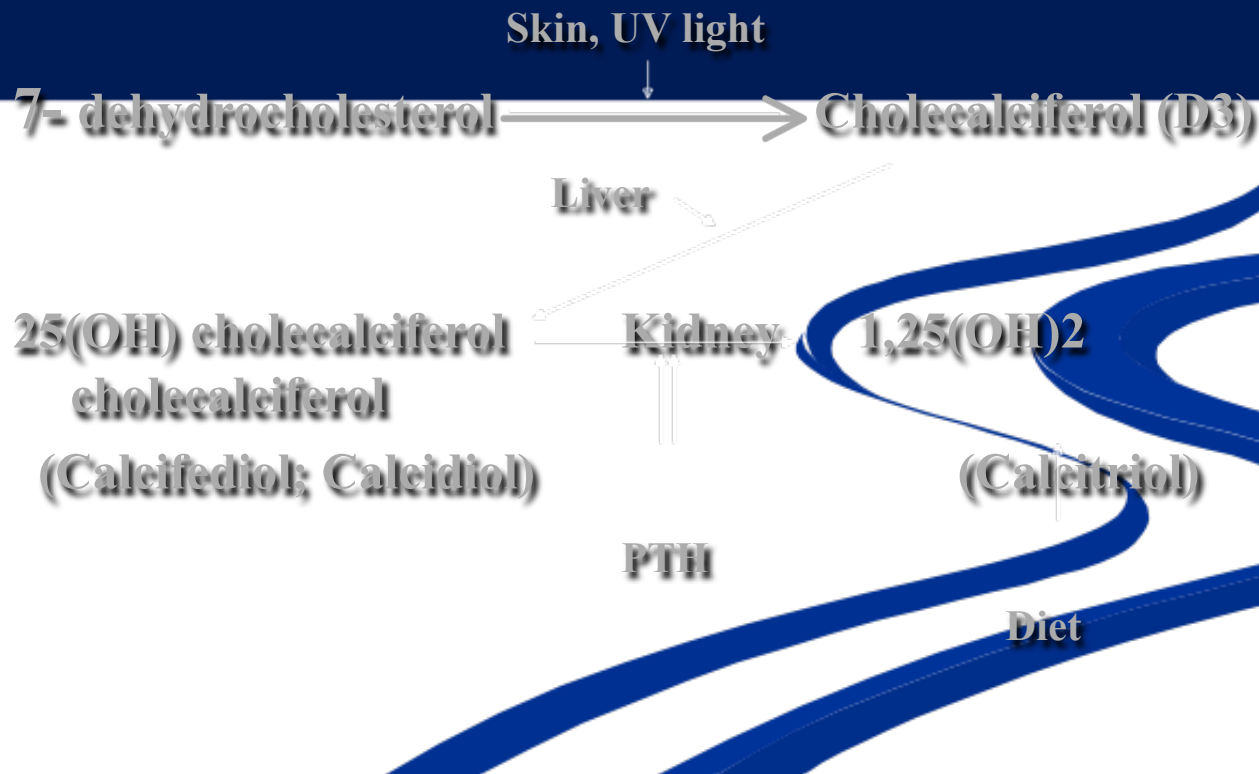
- **Maximum secretion of PTH occurs at plasma Ca^{++} below 3.5 mg/dl**
- **At Ca^{++} above 5.5 mg/dl, PTH secretion is maximally inhibited**



- **On bone (1° 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)

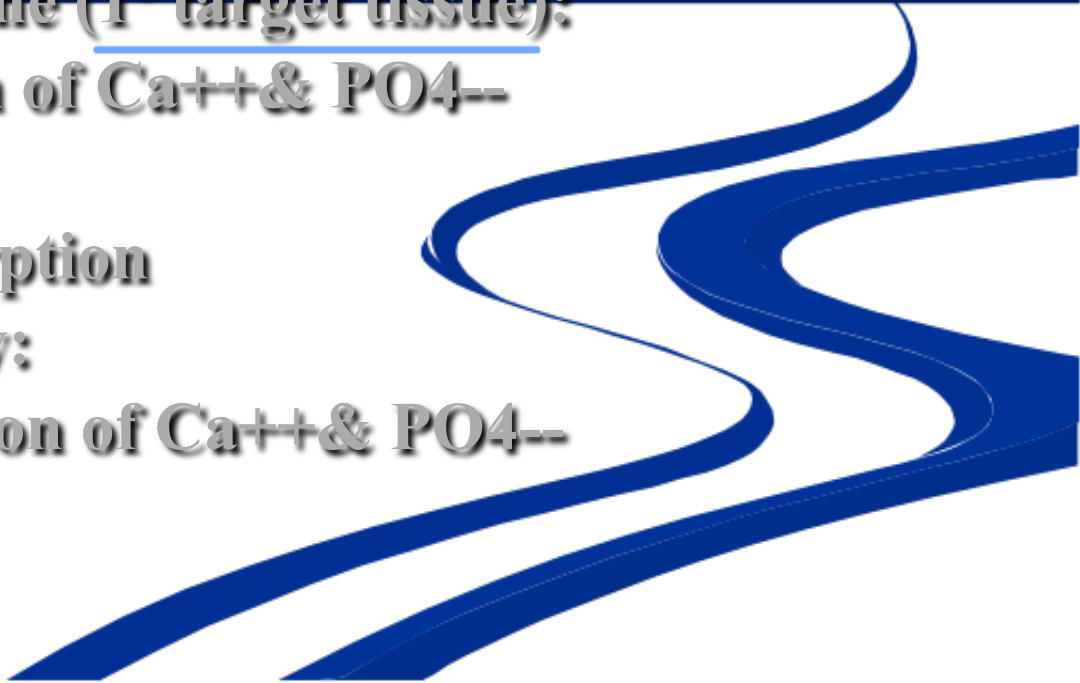
The effect of PTH on kidney result in increasing the release of phosphate (exceeding the absorption of it under the effect of vit D & resorption from bone)

- Synthesis of vitamin D**



The first step in vit D synthesis: in skin
 First step in activation occurs in liver
 The least : in kidney.

Vitamin D (Normal daily requirement 400 IU/day)

- **On intestine (1° target tissue):**
↑ absorption of Ca^{++} & PO_4^{--}
 - **On bone:**
↑ bone resorption
 - **On kidney:**
↑ reabsorption of Ca^{++} & PO_4^{--}
- 

Calcitonin (32 a.a peptide)

Synthesized and released from parafollicular cells of the thyroid

- **Regulation of synthesis & release:**
 $\uparrow [Ca^{++}] \Rightarrow \uparrow \text{calcitonin}; \downarrow [Ca^{++}] \Rightarrow \downarrow \text{calcitonin}$
- **Effects:**
 - On bone: \downarrow bone resorption ($\downarrow Ca^{++}$ & PO_4^{--} movement)**
 - On kidneys: $\uparrow Ca^{++}$ & PO_4^{--} excretion**
 - ? On intestine: $\downarrow Ca^{++}$ & PO_4^{--} 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)

Bronchospasm

Depression, anxiety, abdominal pain

Cataract...


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

Paresthesia

Median nerve is compressed at the wrist, resulting in numbness or pain



- **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...

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)-recently approved in the management of osteoporosis; given SC

small doses

عاده ما نجربهم
الكثير منهم
ممكن

Hypersecretion (hyperparathyroidism):

- **Causes:**

- **1° hyperparathyroidism (adenomas)**

- **2° hyperparathyroidism**

2° to any cause of hypocalcemia

e.g. malabsorption syndrome, renal disease...

- **3° 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 1° hyperparathyroidism & cancer of parathyroid gland**

- **Other drugs effective in the management of hypercalcemia:**

- **Diuretics**

- e.g. Furosemide (\uparrow Ca^{++} excretion)

- **Plicamycin; inhibits bone resorption**

- **Biophosphonates** (To treat osteoporosis)

- Etidronate, Pamidronate...**

- \uparrow bone formation and \downarrow 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

- Biophosphanates

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