

Parathyroid Gland & Calcium Metabolism

3 factors PTH, Vitamin D, Calcitonin

3 tissues Bone, Intestine, Kidneys

Parathyroid Hormone (PTH)

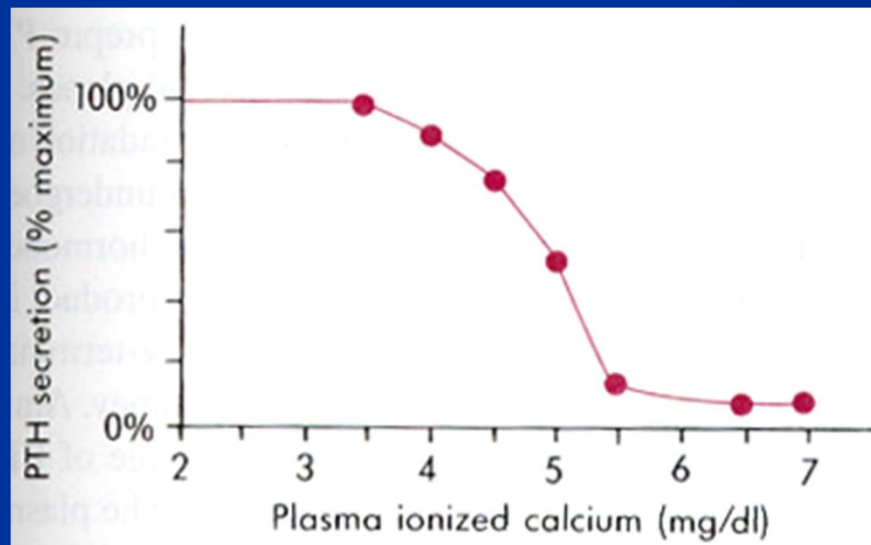
84 a.a peptide translated as a pre-prohormone

Regulation of synthesis & release:

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

Little if any regulation by PO_4^{--}

- 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:

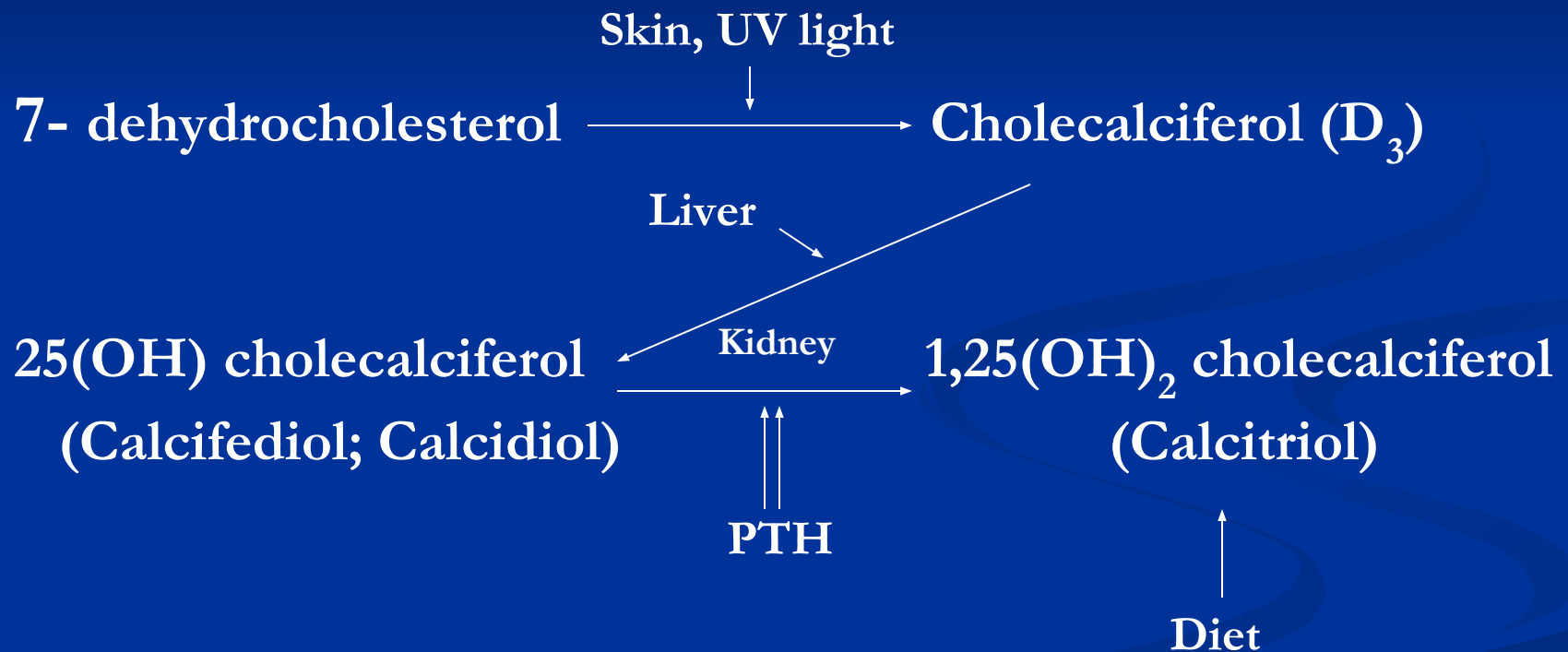
↑ absorption of Ca^{++} & PO_4^{--}

An indirect effect through ↑ vitamin D synthesis

- On kidneys:

↑ reabsorption of Ca^{++} , ↑↑↑ excretion of PO_4^{--}
(cAMP mediated effect)

■ Synthesis of vitamin D



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 D_3 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)

■ 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...

■ Lab. Tests (hypoparathyroidism):

- ↓ blood $[\text{Ca}^{++}]$
- ↑ blood $[\text{PO}_4^{--}]$
- ↓ urinary [cAMP]
- ↓ urinary [PTH]
- ↓ urinary $[\text{Ca}^{++}]$
- ↓ urinary $[\text{PO}_4^{--}]$

■ **R_x 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

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 $[\text{Ca}^{++}]$
- ↓ blood $[\text{PO}_4^{--}]$
- ↑ urinary [cAMP]
- ↑ urinary [PTH]
- ↑ urinary $[\text{Ca}^{++}]$
- ↑ urinary $[\text{PO}_4^{--}]$

Bone x-ray → bone decalcification

■ **R_x of hyperparathyroidism:**

- Low Ca⁺⁺ diet
- Na⁺ phosphate
- 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

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...

■ R_x:

- 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