

# Parathyroid Gland & Calcium Metabolism

3 factors PTH, Vitamin D, Calcitonin

3 tissues Bone, Intestine, Kidneys

## Parathyroid Hormone (PTH)

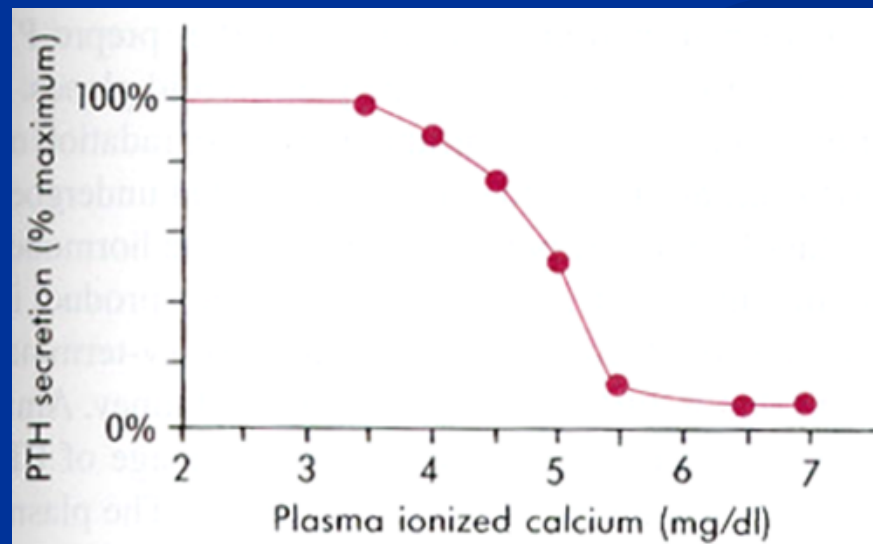
84 a.a peptide translated as a pre-prohormone

Regulation of synthesis & release:

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

Little if any regulation by  $\text{PO}_4^{--}$

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



- On bone (1° target tissue):

PTH ↑ resorption of  $\text{Ca}^{++}$  &  $\text{PO}_4^{--}$   
(cAMP) mediated effect

- On intestine:

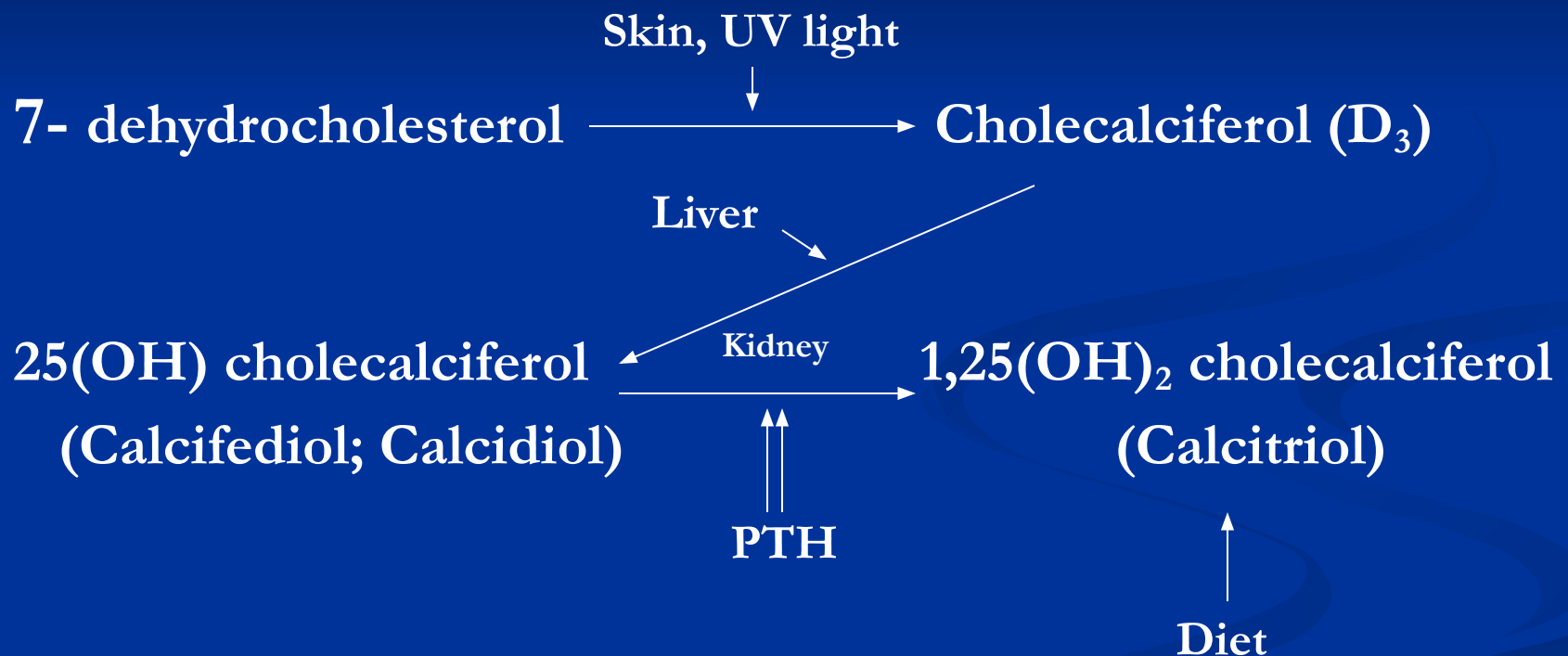
↑ absorption of  $\text{Ca}^{++}$  &  $\text{PO}_4^{--}$

An indirect effect through ↑ vitamin D synthesis

- On kidneys:

↑ reabsorption of  $\text{Ca}^{++}$ , ↑↑↑ excretion of  $\text{PO}_4^{--}$   
(cAMP mediated effect)

## ■ Synthesis of vitamin D



**Vitamin D** (Normal daily requirement 400 IU/day)

- On intestine (1° target tissue):

- ↑ absorption of  $\text{Ca}^{++}$  &  $\text{PO}_4^{--}$

- On bone:

- ↑ bone resorption

- On kidney:

- ↑ reabsorption of  $\text{Ca}^{++}$  &  $\text{PO}_4^{--}$

## Calcitonin (32 a.a peptide)

Synthesized and released from parafollicular cells of the thyroid

- Regulation of synthesis & release:

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

- Effects:

On bone:  $\downarrow$  bone resorption ( $\downarrow \text{Ca}^{++}$  &  $\text{PO}_4^{--}$  movement)

On kidneys:  $\uparrow \text{Ca}^{++}$  &  $\text{PO}_4^{--}$  excretion

? On intestine:  $\downarrow \text{Ca}^{++}$  &  $\text{PO}_4^{--}$  absorption

- May be more important in regulating bone remodeling than in  $\text{Ca}^{++}$  homeostasis:

Evidence: Chronic excess of calcitonin does not produce hypocalcemia and removal of parafollicular cells does not cause hypercalcemia

- PTH and Vitamin  $\text{D}_3$  regulation dominate



PTH

Vit. D

Calcitonin

[Ca<sup>++</sup>]

↑

↑

↓

[PO<sub>4</sub><sup>-</sup>]

↓

↑

↓

- 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,  $\alpha$ -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<sub>x</sub> of hyperparathyroidism:**

- Low Ca<sup>++</sup> diet
- Na<sup>+</sup> phosphate
- Steroids e.g. Prednisolone... ↓ Ca<sup>++</sup> 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 ( $\uparrow \text{Ca}^{++}$  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<sub>x</sub>:

- Salmon calcitonin (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, orally

Etidronate, alendronate, residronate, pamidronate...