Parathyroid Gland & Calcium Metabolism

3 factors PTH, Vitamin D, Calcitonin

3 tissues Bone, Intestine, Kidneys

Parathyroid Hormone (PTH)

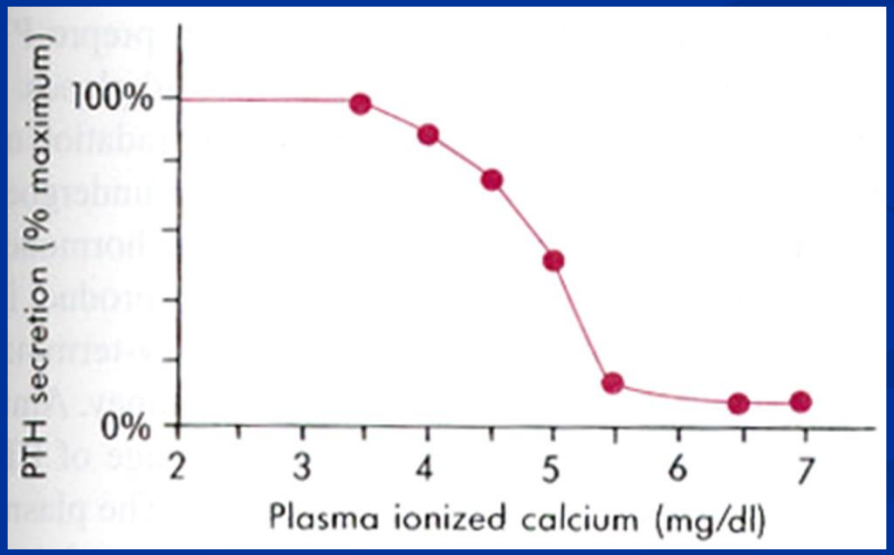
84 a.a peptide translated as a pre-prohormone

Regulation of synthesis & release:

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

Little if any regulation by PO_4^{--}

- 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^{--}

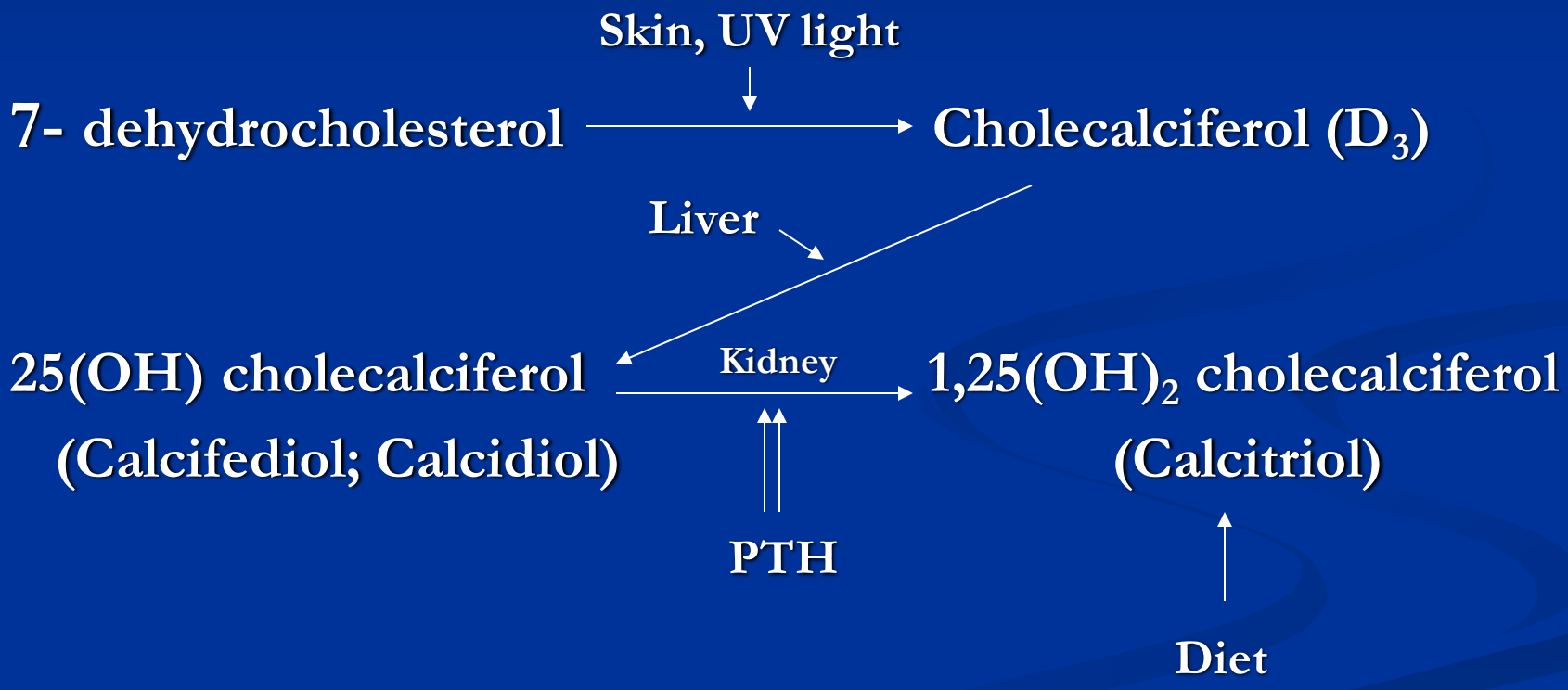
An indirect effect through ↑ vitamin D synthesis

- On kidneys:

↑ reabsorption of Ca^{++}, ↑↑↑ excretion of PO_4^{--}

(cAMP mediated effect)

- Synthesis of vitamin D



Vitamin D (Normal daily requirement 400 IU/day)

- On intestine (1º 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:

↑ [Ca^{++}] → ↑ calcitonin; ↓ [Ca^{++}] → ↓ calcitonin

- Effects:

On bone: ↓ bone resorption (↓Ca^{++}&PO_4^{--}movement)

On kidneys: ↑ Ca^{++}& PO_4^{--} excretion

? On intestine: ↓ 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
$[Ca^{++}]$	↑	↑	↓
$[PO_4^{--}]$	↓	↑	↓

- 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 [Ca^{++}]
- ↑ blood [PO_4^{--}]
- ↓ urinary [cAMP]
- ↓ urinary [PTH]
- ↓ urinary [Ca^{++}]
- ↓ urinary [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:

- 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 [PO_4^{--}]
- ↑ urinary [cAMP]
- ↑ urinary [PTH]
- ↑ urinary [Ca^{++}]
- ↑ urinary [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 1º hyperparatyroidism & 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 deminaralization 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