Pharmacology of Drugs Used in Calcium & Vitamin D Disorders

Objectives

By the end of lecture, the students will be able to:

- Recognize the common drugs used in calcium & vitamin D disorders.
- Classify them according to sources & Pharmacological effects.
- Detail the pharmacology of each drug regarding mechanism, clinical utility in affecting calcium & vitamin D.


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BONE

- Is a dynamic organ undergoing continuous remodeling process involving resorption of old bone by osteoclast & formation of new bone by osteoblast.
- The dominant site of calcium storage in the body is bone, which contains nearly 99.9% of body calcium.
- Although only a small fraction of total body calcium is located in the plasma, it is the plasma concentration of ionized calcium that is tightly regulated, primarily under the control of PTH and vitamin D.

The principal hormones involved in regulation of calcium metabolism & bone remodeling are:

- **Parathyroid hormone (PTH)**
- **Vitamin D**
- **Calcitonin**

PTH and vitamin D play central roles in the regulation of bone metabolism.

The target tissues regulate calcium homeostasis:

- **Bone** (Absorption and resorption)
- **Kidney (Reabsorption)**
- **Intestine** (Calcium absorption)

Parathyroid Hormone

Is released from the parathyroid gland in response to low plasma Ca^{2+} level.

Effects of PTH

BONE

Mobilization of Ca^{2+} and PO_4^{3-} from bone.

In response to hypocalcemia, PTH stimulates osteoclast cells to increase the outward flux of calcium to restore serum calcium level.

Effects of PTH.. Continue

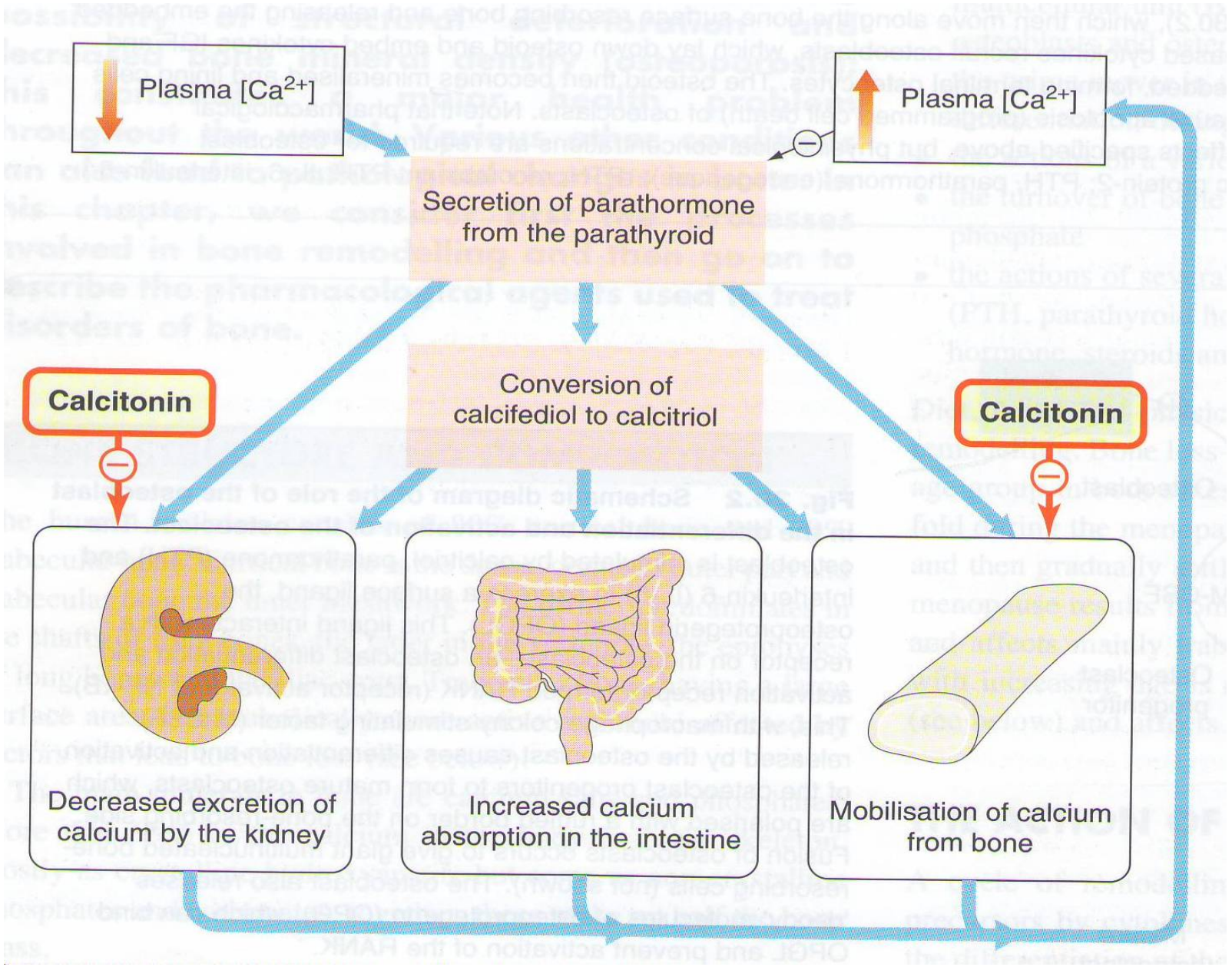
Kidney

- ↑ Ca^{2+} reabsorption.
- ↑ formation of calcitriol which is the active form of vitamin D.

Effects of PTH.. Continue

GIT

- ↑ **absorption of Ca^{2+}**


Plasma [Ca2+]
Plasma [Ca2+]
Secretion of parathormone from the parathyroid
Conversion of calcifediol to calcitriol
Calcitonin
Calcitonin
Decreased excretion of calcium by the kidney
Increased calcium absorption in the intestine
Mobilisation of calcium from bone

Effects of PTH.. Continue

Daily, intermittent administration of PTH for 1 to 2 hours/day leads to a net stimulation of bone formation.

Continuous exposure to elevated PTH leads to bone resorption and risk of fracture.

RESPONSE TO PTH

PTH

Intermittent

↑ Osteoblast number/function

Bone formation

Bone mass/strength

Continuous

↑ Osteoclast

↑ Bone resorption

↑ Serum Ca^{++}

Clinical Uses

Treatment of severe osteoporosis.

Resistance cases failed to response to other medications.

Teriparatide

Synthetic polypeptide form of PTH (PTH analogue).

It belongs to a class of antiosteoporosis drugs, the so-called “anabolic” agents.

Given, once/ daily/ subcutaneous injection.

Teriparatide

Therapeutic effects of teriparatide depend upon the pattern of systemic exposure.

Once-daily administration → stimulates new bone formation by preferential stimulation of osteoblastic activity over osteoclastic activity.

By contrast, continuous administration → may be detrimental to the skeleton because bone resorption may be stimulated more than bone formation.

Therapeutic uses of Teriparatide

- **Should not be used routinely due to carcinogenic effects.**
- **Use in severs osteoporosis or patients not responding to other drugs.**
- **For treatment of osteoporosis in people who have a risk of getting fracture (increase bone mass & strength)**
- **Good for postmenopausal osteoporosis.**

Side effects of Teriparatide

- **Carcinogenic effect (osteosarcoma).**
- **Diarrhea, Heart burn, Nausea.**
- **Headache, Leg Cramps.**
- **Hypotension when standing.**
- **Elevated serum calcium can occur in some cases can lead to kidney stones.**

Contraindications of Teriparatide

Should not be used by people with increased risk for bone tumors (Osteosarcoma) including:

- **People with Paget's disease of bone.**
- **People who had radiation treatment involving bones.**
- **Children not recommended.**

Vitamin D

Vitamin D is a steroid hormone that is intimately involved in the regulation of plasma calcium levels.

- **Cholecalciferol (Vitamin D3) skin**
- **Ergocalciferol (Vitamin D2) plants**
- **Vitamin D2** is the prescription form of vitamin D & is also used as food additive (milk).
- **Vitamin D3** is usually for vitamin D- fortified milk & foods & also available in drug combination products.
- **Vit D2 and Vit D3 have equal biological activities.**

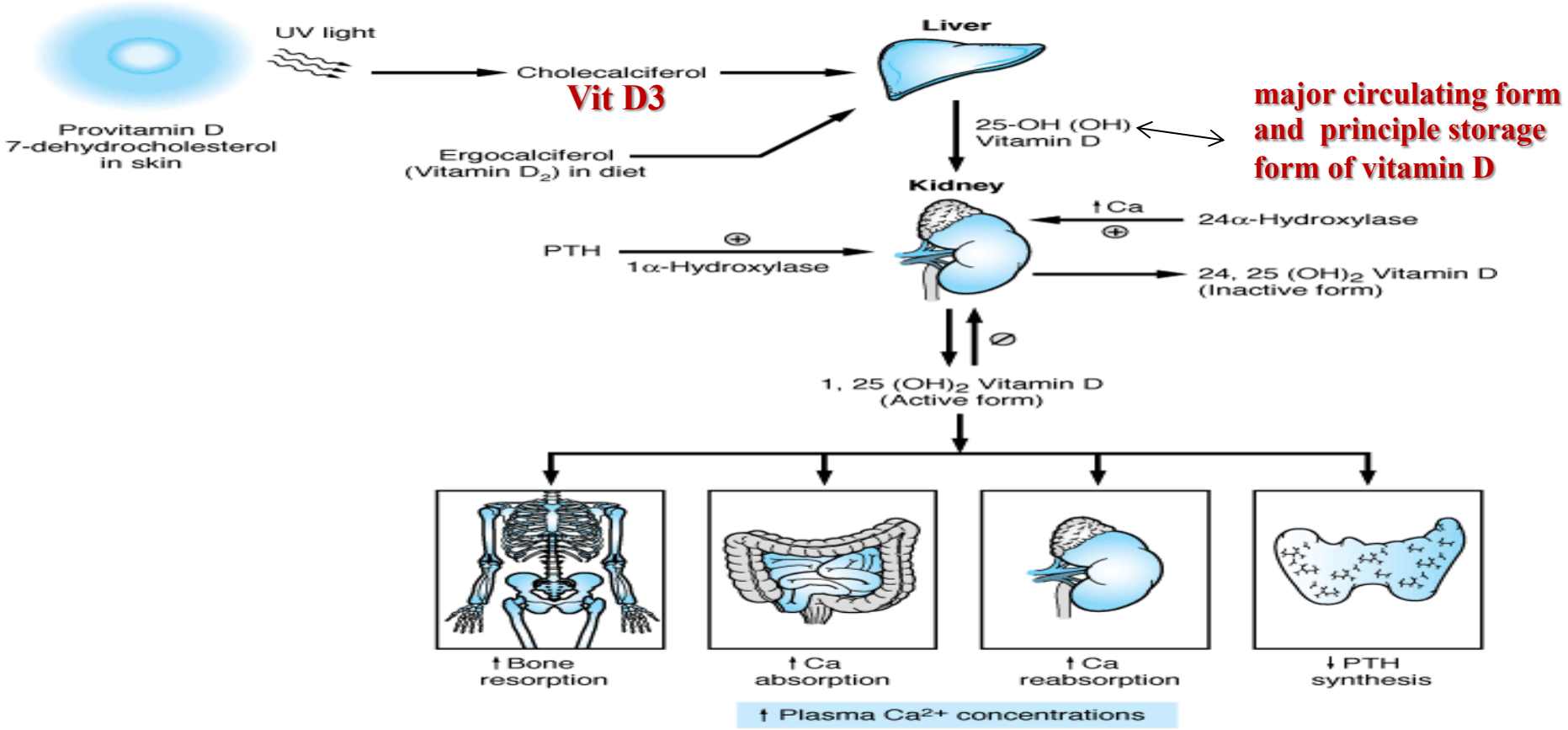
Sources of Vitamin D

D2 ***Diet as in***

- Milk
- Egg yolk
- Fish oils

Note both D2 and D3 travel to the liver and then converted to active from in the kidneys see next slide

Calcium and Vitamin D



Source: Molina PE: *Endocrine Physiology, 3rd Edition:*
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Vitamin D increases bone resorption, increases Ca^{2+} absorption from the intestine, increases renal Ca^{2+} reabsorption, and decreases the production of PTH by the parathyroid glands. The overall effect of vitamin D is to increase plasma Ca^{2+} concentrations.

Calcium and Vitamin D.. Continue

Sunshine: **Cholecalciferol (D3)**

Generated in the skin from 7-dehydrocholesterol by the action of ultraviolet radiation (sunshine).

Vitamin D Metabolism

The initial transformation of D3 occurs in **liver** to (Calcifediol) the main storage from of Vit D in our body.

In the **Kidney**: **Parathyroid Hormone** stimulates the formation of active form of vitamin D **(Calcitriol)**

Effects of Vitamin D

Bone: Activation of osteoblast cells.

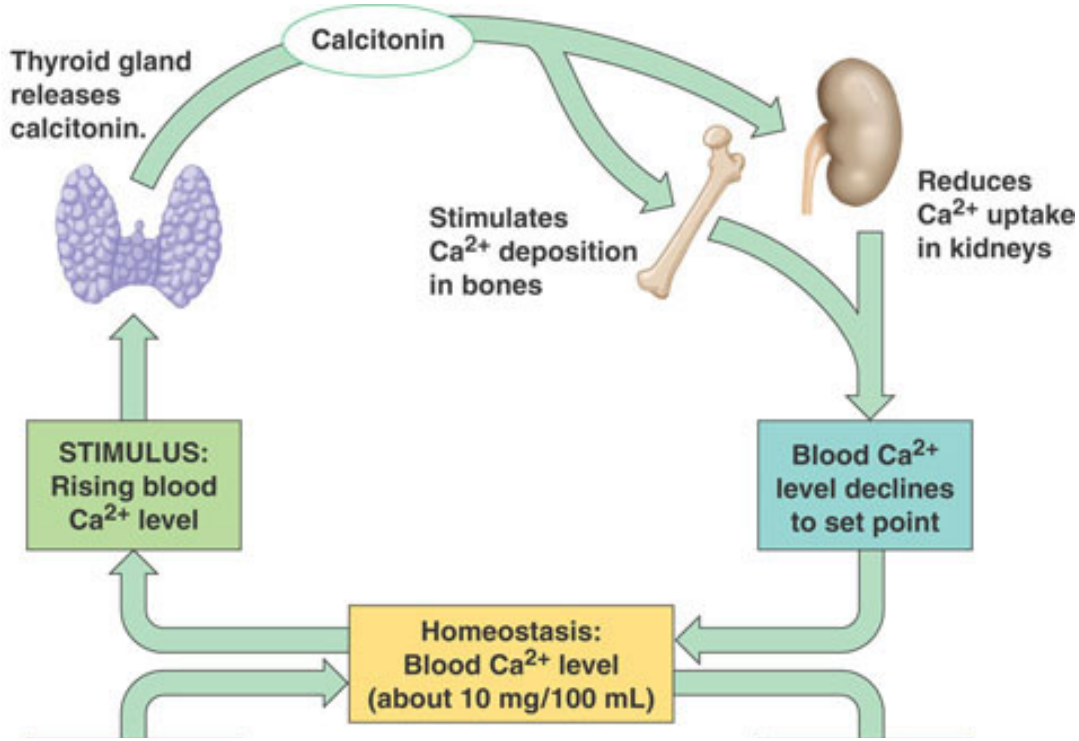
Kidney: Increased reabsorption of Ca^{2+} & PO_4.

GIT: Increased absorption of Ca^{2+}.

Calcitonin

Produced by the parafollicular cells (C cells) of the thyroid gland. It is released when there is an elevated level of Ca^{2+} in the blood.

Calcitonin does not appear to be critical for the regulation of calcium homeostasis even if thyroid gland is removed



Effects of Calcitonin

Bone: **Decrease bone resorption by inhibiting osteoclast activity.**

Kidney: **Decreases reabsorption of Ca^{2+} & PO_4, thus increasing their excretion.**

Clinical uses of Calcitonin (it has lower efficacy compared to other drugs)

- **Osteoporosis (major indication; alternative to other drugs)**
- **Hypercalcemia** (short-term treatment of hypercalcemia of malignancy), Pagets disease.
- **Routes of administration**

  S.C, Nasal spray

Adverse effects of Calcitonin

- Nausea
- local inflammation (Injection)
- Flushing of face & hands
- Nasal irritation

Thank You.

Treasure your Bones!