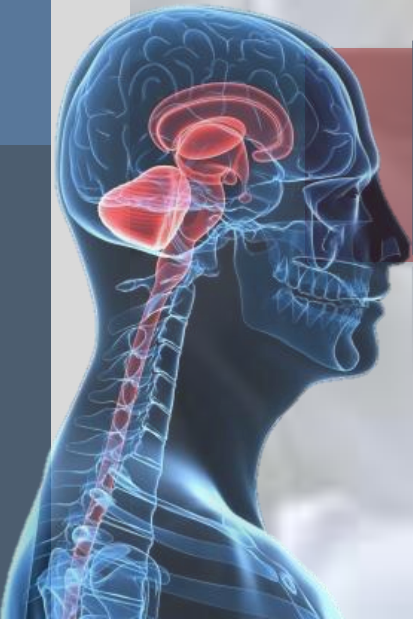


King Saud University
College of Medicine
2nd Year, Endocrine
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L4 Pharmacology of drugs used in calcium & vitamin D disorders

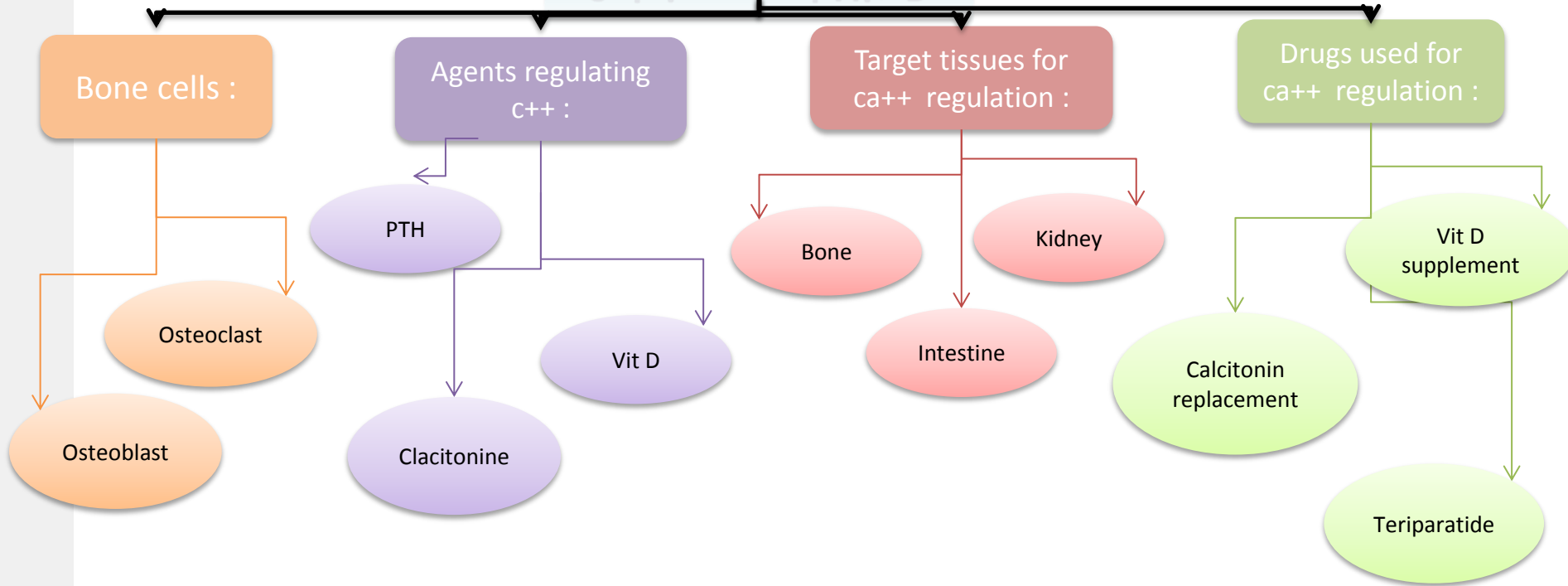




Objectives

- ✓ 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.

Calcium and Vit D



BONE

- Is a dynamic organ undergoes 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 (99.9% of body calcium).

The principal agents involved in calcium metabolism & bone remodeling are :



Exerting their effect on :
Bone
Kidney
GIT

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

1- PARATHYROID HORMONE (PTH)

Released from the parathyroid gland
in response to **hypocalcemia**.
(to restore normal plasma Ca)

Bone: (increase activity of osteoclast)

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

Kidney :

↑ Ca^{2+} reabsorption (decrease excretion)
↑ formation of calcitriol which is the active form of vitamin D

GIT: (increase Ca^{2+} intestinal absorption)

↑ absorption of Ca^{2+}

Parathyroid Hormone (PTH)

1- Continuous exposure to elevated PTH leads to **bone resorption** (increase activity

Of osteoclast and it will increase outward of Ca^{2+} so it will use in hypocalcaemia)

2- Daily intermittent administration of PTH leads to **bone formation**(give 1 or 2 hour in day maximum and it will increase the activity of osteoblast then increase bone formation and bone mass so it use in severe osteoporosis)

(because by intermittent administration, we firstly activate osteoclast then osteoblast will take over to compensate leading to more bone formation).

Response to PTH

Clinical Uses:

(depend on mood of administration)

1. Treatment of **severe osteoporosis** .

2. **Resistance cases** failed to response to other medications.

2- TERIPARATIDE

- Synthetic polypeptide form of PTH and affects calcium homeostasis in the same way as PTH.

Clinical Uses

1. Osteoporosis in **postmenopausal women** at high risk of fracture.
2. **Hypogonadal osteoporosis** in men at high risk of fracture

Side Effects

1. **Carcinogenic** effect (osteosarcoma)
2. Diarrhea, heart burn, nausea (gastric upset ,abdominal pain)
3. Headache & Hypotension
4. Elevated serum calcium can occur in some cases can lead to **kidney stones** (because it is increase Ca^{2+} level)

Routes of administration

Given daily Subcutaneous injection (with different dose)

Contraindications

1. **People having bone tumors**
2. Paget's disease of bone (abnormal metabolic bone disease unknown etiology)
3. People who had radiation treatment involving bones
4. Children
5. People who have liability to form renal stone (genetic ,type of food)

3-VITAMIN D

- Vitamin D: it has 2 forms:

- Vitamin D2** (Ergocalciferol): is the prescription form of vitamin D & is also used as food additive.
- Vitamin D3** (Cholecalciferol): is usually for vitamin D- fortified milk & foods & also available in drug combination products. **Both of them are routinely added to calcium supplements** and milk for the purpose of preventing rickets in children and osteomalacia in adults. (abnormal polymineralization : decrease in Ca^{2+})

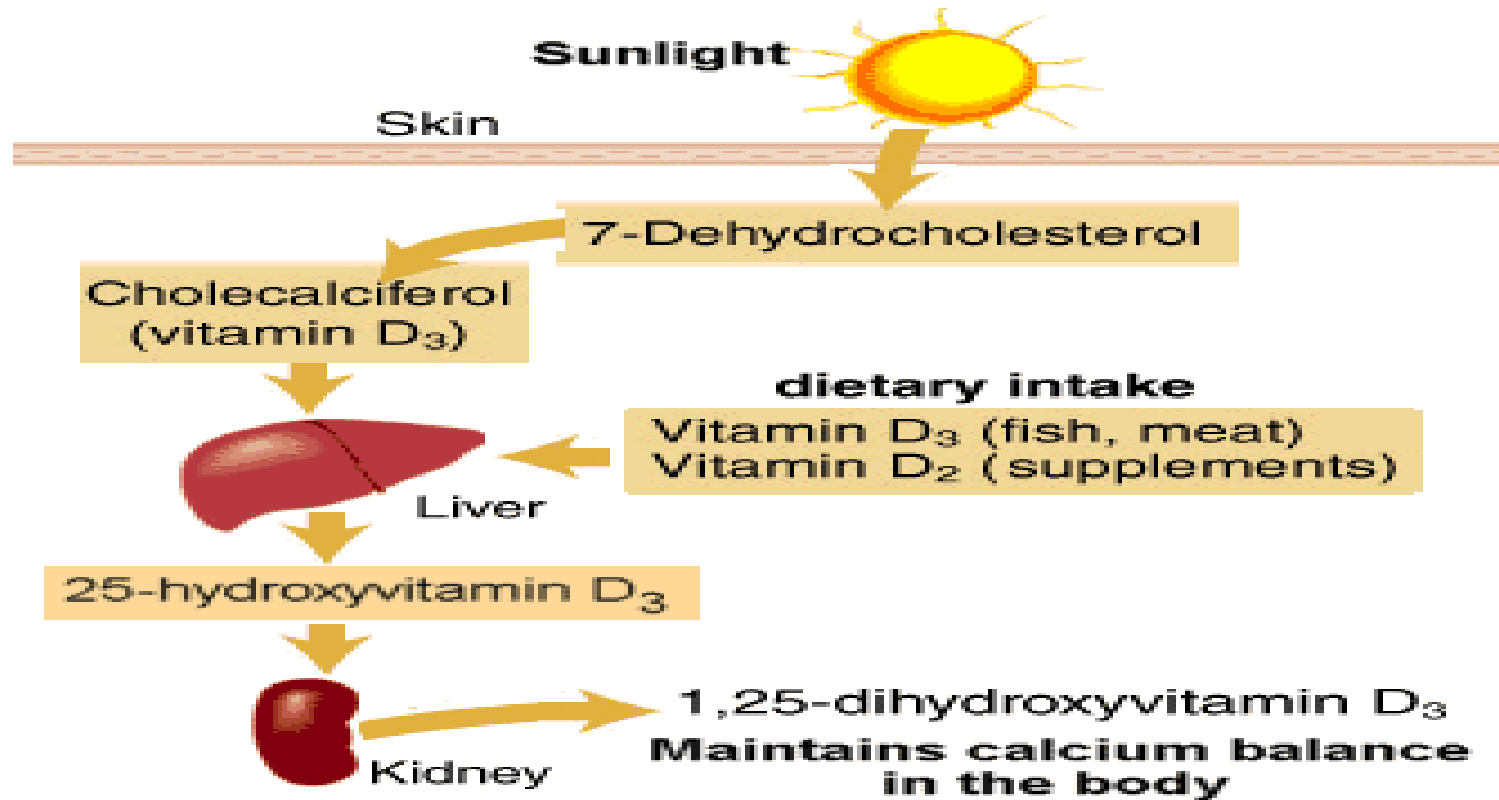
- **Sources of Vitamin D :**

- Vit.d2** :from diet such as ;egg youlk ,fishoil,milk
- Vit.d3**:sunchine , generated in the skin from 7-dehydrocholestrol by the action of ultraviolet light.

Note: - Vitamin D3 may be less toxic than D2 because higher concentrations of D2 circulate in the blood when consumed (compared to vitamin D3).

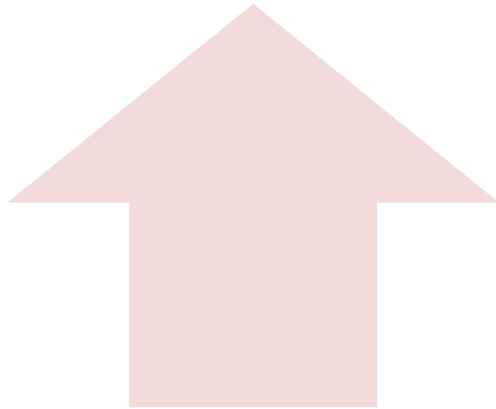
-Vitamin D3 is the more potent form of vitamin D, which is a potential benefit.

VITAMIN D METABOLISM

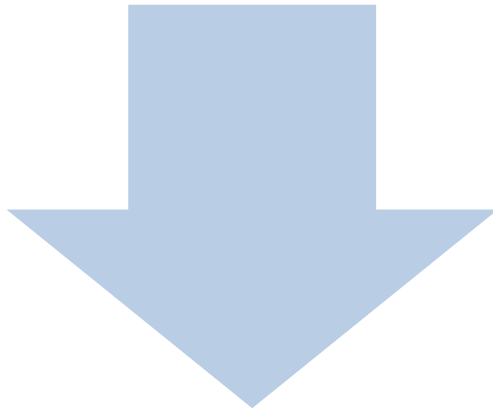


Vitamin d formed in the skin by 7-dehydroxycholesterol . by the effect of sunlight it will converted into cholecalciferol(vit.d3)which goes to the liver .dietary intake is also goes to the liver. So , liver converts all forms of vit.d into 25-hydroxyvitamin D3 . In kidney , PTH stimulate formation of the active form of vit.d which is (calcitriol) { 1,25-(OH)₂ D₃ } .

EFFECT OF ACTIVE METABOLITE OF VITAMIN D



- 1- Increase bone resorption
- 2- Increase serum calcium and phosphate by promoting their uptake from GIT



- 1- Decrease renal excretion of both electrolytes
- 2- Inhibit PTH formation (negative feedback)

4-CALCITONIN

Definition	Released from the parafollicular cells (C cells) of the thyroid gland in response hypercalcemia .
Effects on	Bone : Decrease bone resorption by inhibiting osteoclast activity . Kidney : Decreases reabsorption of Ca^{2+} & PO_4 , thus increasing their excretion .
Clinical uses	Osteoporosis , Hypercalcemia , Hypercalcemia due to Paget's disease
Routes of administration	S.C , Nasal spray(calcitonin salmon)
Side effects	Nausea ,local inflammation (injection) ,Flushing of face & hands , Nasal irritation ,headache.

SUMMARY

HORMONE	Source	MOA	EFFECTS OF HORMONES		
			INTESTINE	BONE	KIDNEY
Parathyroid (PTH)	parathyroid gland	↑ Blood Ca^{+2} level in response to hypocalcemia	↑ absorption of Ca^{+2}	↑ bone resorption ↑ Osteoclasts	↑ Ca^{2+} reabsorption ↑ formation of active vit. D
Vitamin D	D2: Diet D3:Sunshine	↑ Blood Ca^{+2} level in response to hypocalcemia	↑ absorption of Ca^{+2} & phosphate	↑ bone resorption ↑ Osteoclasts	↑ Ca^{2+} reabsorption Note: On parathyroid gland: Inhibit PTH formation
Calcitonin	Parafollicular cells (C cells) of the thyroid gland	↓ Blood Ca^{+2} level in response to hypercalcemia	-	↓ bone resorption by inhibiting osteoclast activity	↓ reabsorption of Ca^{+2} & PO_4 (↑ excretion)

SUMMARY

DURG	MOA	ROUTE	USES	SIDE EFFECT	Contraindications
Parathyroid	↑ Blood Ca ⁺² level	-	-severe osteoporosis -Resistance cases failed to response to other medications	- Note: when PTH given - <u>Intermittent</u> → ↑ osteoblast → Bone formation - <u>Continuous</u> → ↑ osteoclast → bone resorption → ↑ blood Ca ⁺²	-
Teriparatide Synthetic PTH.	↑ Blood Ca ⁺² level	daily Subcutaneous injection	-Osteoporosis in postmenopausal women -Hypogonadal osteoporosis in men	-Carcinogenic effect -Diarrhea, heart burn, nausea Headache -Hypotension -kidney stons	-children People having: -bone tumor -Paget,s disease -bone radiation treatment
Vitamin D	↑ Blood Ca ⁺² level	-	added to calcium supplements to prevent rickets & osteomalacia	-	-
Calcitonin	↓ Blood Ca ⁺² level	-Subcutaneous injection -nasal spray (calcitonin salmon)	-Osteoporosis -Hypercalcemia -Hypercalcemia due to Paget's disease	-Nausea - local inflammation (injection) -Flushing of face & hands -Nasal irritation	-

Quiz yourself

1\ The trigger for PTH secretion :

- A. Hypocalcaemia
- B. Hypocalcaemia
- C. Hyperkalemia
- D. Hypokalemia

2\ A person who was diagnosed with osteoporosis , he was given a medication to treat it, but there was no improvement , what is the drug of choice in this case :

- A. Vit D
- B. Thyroxin
- C. PTH
- D. Calcitonine

3\ The cell which is responsible for bone resorption is :

- A. Osteoblast
- B. Osteoclast
- C. Osteocyte
- D. Osteogenic cells

4\ Which of the following hormones that stimulate the formation of calcitrol :

- A. Aldosterone
- B. Calcitonin
- C. PTH
- D. Thyroid hormone

5\ A person was referred to orthopedic clinic and diagnosed with osteoporosis, the doctor prescribed a drug for him, after that he developed nausea and flushing of the hands and face, what is the drug that caused these signs to appear :

- A. Calcitonin
- B. PTH
- C. Vit D
- D. methomazole

6\ A 56 years old woman who had her last period about 5 years old, she is complaining from osteoporosis for 3 years, she was given a drug for it. Which of the following is the drug in her case :

- A. PTH
- B. Teriparatide
- C. Biphosphonate
- D. Estrogen analoges

7\ A patient came to the hospital with hypotension and headache, some investigation was done (Blood testes), they found that his serum calcium level is elevated. Which of the following drugs has this side effect :

- A. Calcitonin
- B. Levothyronin
- C. Propranolol
- D. Teriparatide

Answers:

1.B

2.C

3.B

4.C

5.A

6.B

7.D

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We hope that we made this lecture easier for you
Good Luck !