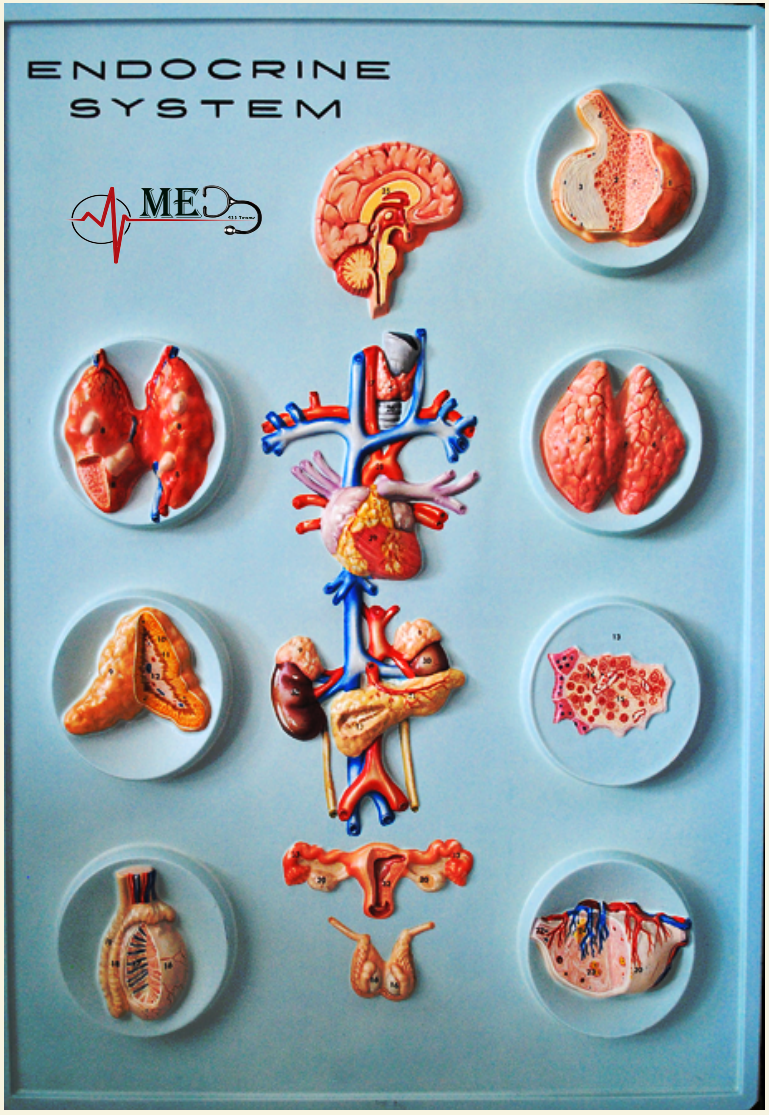


LECTURE 3 :

Vitamin D, Rickets and Osteoporosis

Objectives:

- Vitamin D functions and metabolism
- Vitamin D and calcium homeostasis
- Regulation of vitamin D synthesis
- Biochemistry, types and diagnosis of:
  - A- Osteomalacia and rickets
  - B- Osteoporosis

Background

- Vitamin D is considered a **steroid hormone**
- Cholecalciferol (vitamin D3) is synthesized in the **skin by sunlight (UV)**
- The biologically active form is:
  - **1,25-dihydroxycholecalciferol (calcitriol)**
- **Ergocalciferol (vitamin D2) is derived from ergosterol** in lower animals and plants
- D3, D2 are also available as supplements

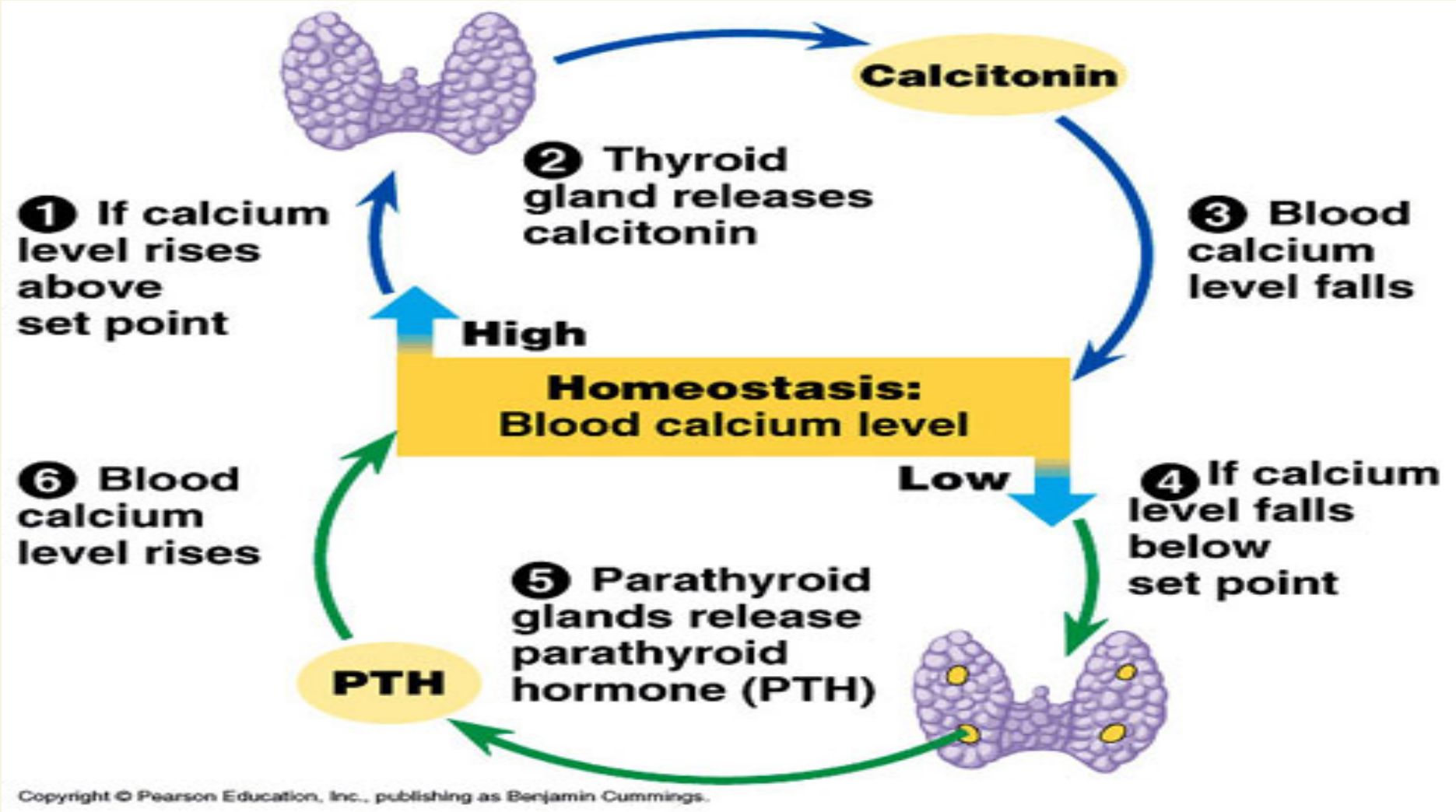
Functions

- Regulates calcium and phosphate levels in the body (**calcium homeostasis**) by increasing uptake of calcium and phosphate by the intestine
- Increasing reabsorption of calcium and phosphate by renal tubules
- Stimulating resorption of bone when blood calcium is low
- Increase bone mineralization

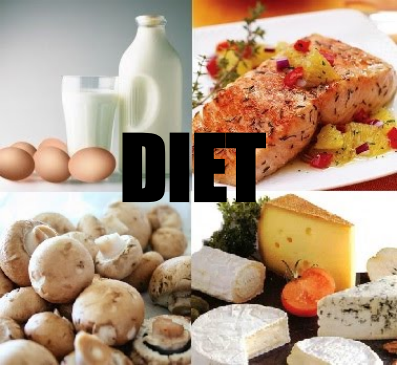
Regulation

- Calcium homeostasis is maintained by **parathyroid hormone (PTH) and calcitonin**
- Vitamin D synthesis is **strictly controlled in the kidneys by PTH**
- **Hydroxylation of 25-hydroxycholecalciferol is PTH-dependent in kidneys**
- Calcium absorption in the gut:
  - **Indirectly** depends on PTH
  - **Directly** depends on vitamin D

Calcium homeostasis

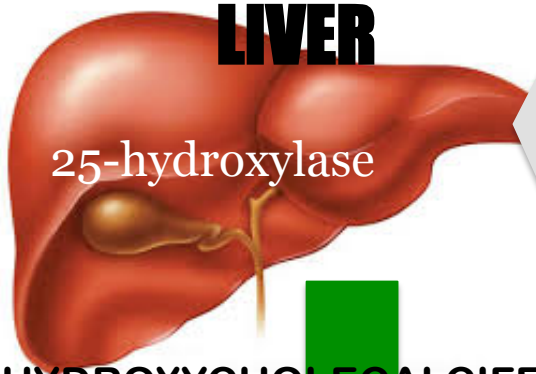


Vitamin D metabolism



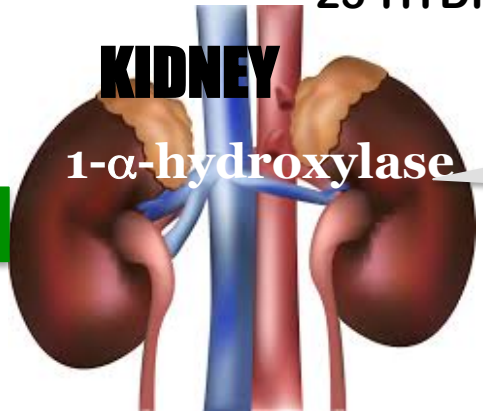
Cholecalciferol is derived from 7-dehydrocholesterol[1] in the **skin** by sunlight

CHOLECALCIFEROL



Cholecalciferol is converted to 25-hydroxy-cholecalciferol by the enzyme 25-hydroxylase

25-HYDROXYCHOLECALCIFEROL



1,25-DIHYDROXYCHOLECALCIFEROL (BIOLOGICALLY ACTIVE)

- The 1-a-hydroxylase enzyme converts 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol (**biologically active**)
- Active vitamin D is transported in blood by gc-globulin protein

1: Derivative of cholesterol

	Osteomalacia	Rickets disease
Definition	Defective bone mineralization in **adults**	Defective bone and cartilage mineralization in **children**
Causes	**Vitamin D deficiency, Impaired vitamin D metabolism, Calcium deficiency, Imbalance in calcium homeostasis**	
Notes	❑ **Not common these days** as foods (milk, oils) are now supplemented with vitamin D ❑ Serum levels of 25-hydroxycholecalciferol is low in these patients ❑ In severe forms: (**hypocalcaemia**), **PTH increases, Alkaline phosphatase increases**	
Clinical features	○ Soft bones ○ Bone pain ○ Bone fractures ○ Compressed vertebrae ○ Muscle weakness	○ Soft bones ○ Bone pain ○ Increased tendency of bone fractures ○ Muscle weakness ○ Skeletal deformity (**bowed legs**) ○ Dental problems ○ Growth disturbance
Diagnosis	Measuring serum levels of: **25-hydroxycholecalciferol => low** **Phosphate => low**	**PTH => high** **Alkaline phosphatase => high** **Calcium => low**

Vitamin-D-dependent rickets types 1 and 2:

- Rare bone diseases due to genetic disorders

Occur due to :

- Defects in vitamin D synthesis
- Defects in vitamin D receptor (no hormone action)

Osteoporosis

Definition	Reduction in bone mass per unit volume (Bone matrix composition is normal but it is reduced)
Primary osteoporosis	Post-menopausal women (They lose more bone mass than men)
Secondary osteoporosis	1. Drugs 2. Immobilization 3. Smoking 4. Alcohol 5. Cushing' s syndrome 6. Hyperthyroidism 7. Gonadal failure 8. GI disease
Diagnosis	•Serial measurement of bone density •No specific biochemical tests to diagnose or monitor primary osteoporosis •The test results **overlap** in healthy subjects and patients with osteoporosis
Common biochemical test	❑ Hydroxyproline (bone resorption) ❑ Osteocalcin (bone formation)
Prevention[1]	•Good diet and exercise prevent osteoporosis later •Hormone replacement therapy in menopause prevents osteoporosis
Treatment	•In confirmed cases: treatment options are unsatisfactory •Oral calcium, estrogens, fluoride therapy may be beneficial

Summary

❑Vitamin D is considered as a steroid hormone

1,25-dihydroxycholecalciferol (calcitriol) is the active form of vitamin D (made in the kidneys)

- Vitamin D regulates calcium homeostasis, increase bone mineralization and increase renal reabsorption of Calcium and phosphorus.

❑ Calcium homeostasis is maintained by parathyroid hormone (PTH) and calcitonin.

- Calcium absorption in the gut depends Indirectly on PTH and Directly on vitamin D .

❑Osteomalacia: defective bone mineralization in adults

❑Rickets: defective bone and cartilage mineralization in children

-They are not common nowadays because of vitamin D supplements

❑Osteoporosis: Reduction in bone mass per unit volume

- Can occur as a complication of (Cushing's, Hyperthyroidism, GIT diseases)

Hormone replacement therapy in menopause prevents osteoporosis

TEST YOURSELF!

1. Calcium homeostasis is maintained by?

A. Vitamin D and Vitamin C .
B. Cholesterol and Calcium.
C. Vitamin D only.
D. PTH and Calcitonin.

2. The precursor of bile salts, sex hormones and vitamin D is

A. Diosgenin.
B. Campesterol.
C. Cholesterol.
D. Ergosterol.

3. The most potent Vitamin D metabolite is

A. 25-Hydroxycholecalciferol.
B. 1,25-Dihydroxycholecalciferol.
C. 24, 25-Dihydroxycholecalciferol.
D. 7-Dehydrocholesterol.

4. 25-Hydroxylation of vitamin D occurs in

A. Skin.
B. Liver.
C. Kidneys.
D. Intestinal mucosa.

5. Osteoporosis may occur as a complication of which of The following:

A. Cushing's syndrome
B. Heart failure
C. Intake of oral contraceptives
D. None

1. D	2. C	3. B	4. B	5. A	6.B	7. A	8. B	9.D	10. B

6. 10 months Old female, presented to the clinic with bowed legs, dental problems and her growth profile is disturbed, what is the most likely diagnoses?

A. Osteomalacia.
B. Rickets.
C. Osteoporosis.
D. Hypothyroidism.

7. The cause of primary Osteoporosis is?

A. Unknown.
B. Unhealthy diet.
C. Fat accumulation.
D. Diabetes.

8- The prevalence of osteoporosis is higher in postmenopausal women than men due to the fact:

A. They have increased PTH activity
B. They lose more bone mass
C. Increased activity of osteoclasts
D. Intake of estrogen supplements.

9. The hydroxylation step of vitamin D in the liver is carried by:

A- 25-dehydroxylase
B- 1-a-hydroxylase
C- 1,25 hydroxylase
D- 25-hydroxylase

10. Calcium absorption in the gut depends DIRECTLY on:

A- PTH
B- Vitamin D
C- Calcitonin
D- Parietal cells

THANK YOU ...

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