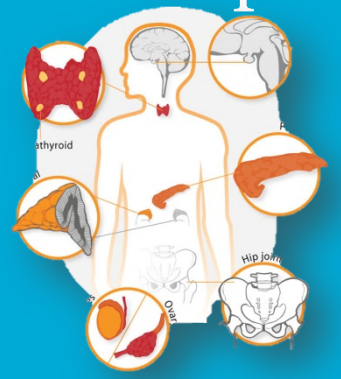
[lecture 3]

Vitamin D, Rickets and Osteoporosis



Endocrine system

Biochemistry Team

Teams

The Objectives

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

Red = Import-ant

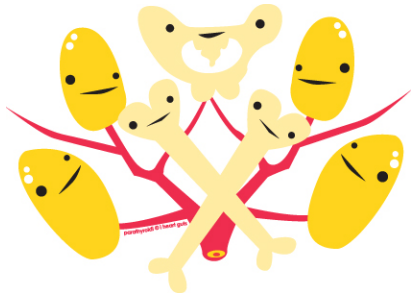
Blue = explain

Green = addition notes

Mind Map

Mind Map

- Vitamin D
  - Function
  - Metabolism
  - Regulation
- Osteomalacia and Rickets
  - Clinical feature
  - Diagnosis
- Osteoporosis
  - Diagnosis
  - Biochemical tests
  - Prevention
  - Treatment



Vitamin D

- 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 supplement

Vitamin D functions

- - Regulates **calcium and phosphorus** levels in the body (calcium homeostasis)
- - Promotes absorption of calcium and phosphorus from the intestine
- - Increases bone mineralization
- - Increases reabsorption of calcium and phosphorus by renal tubules
- - Maintains healthy bones and teeth

Vitamin D metabolism

1

1-Cholecalciferol(D3) is derived from 7-dehydrocholesterol in the skin by sunlight

2

2-In liver:

Cholecalciferol is converted to 25-hydroxycholecalciferol by the enzyme 25-hydroxylase

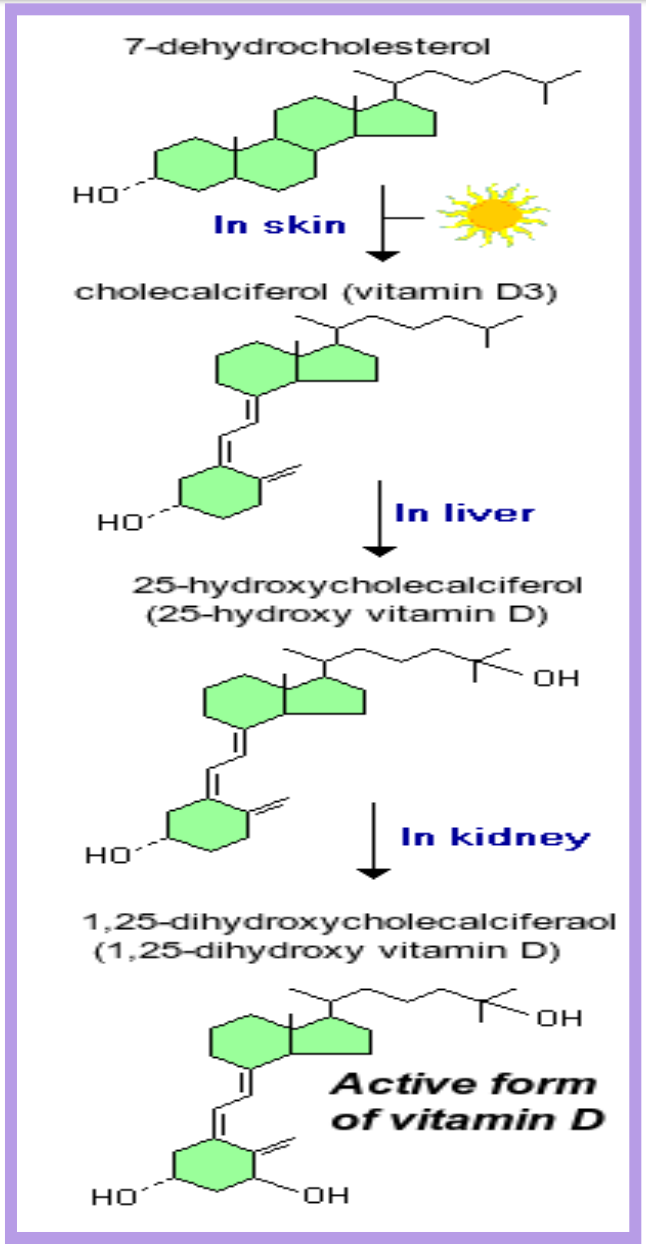
3

3-In kidneys:

The **1-a-hydroxylase enzyme converts 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol (biologically active)**

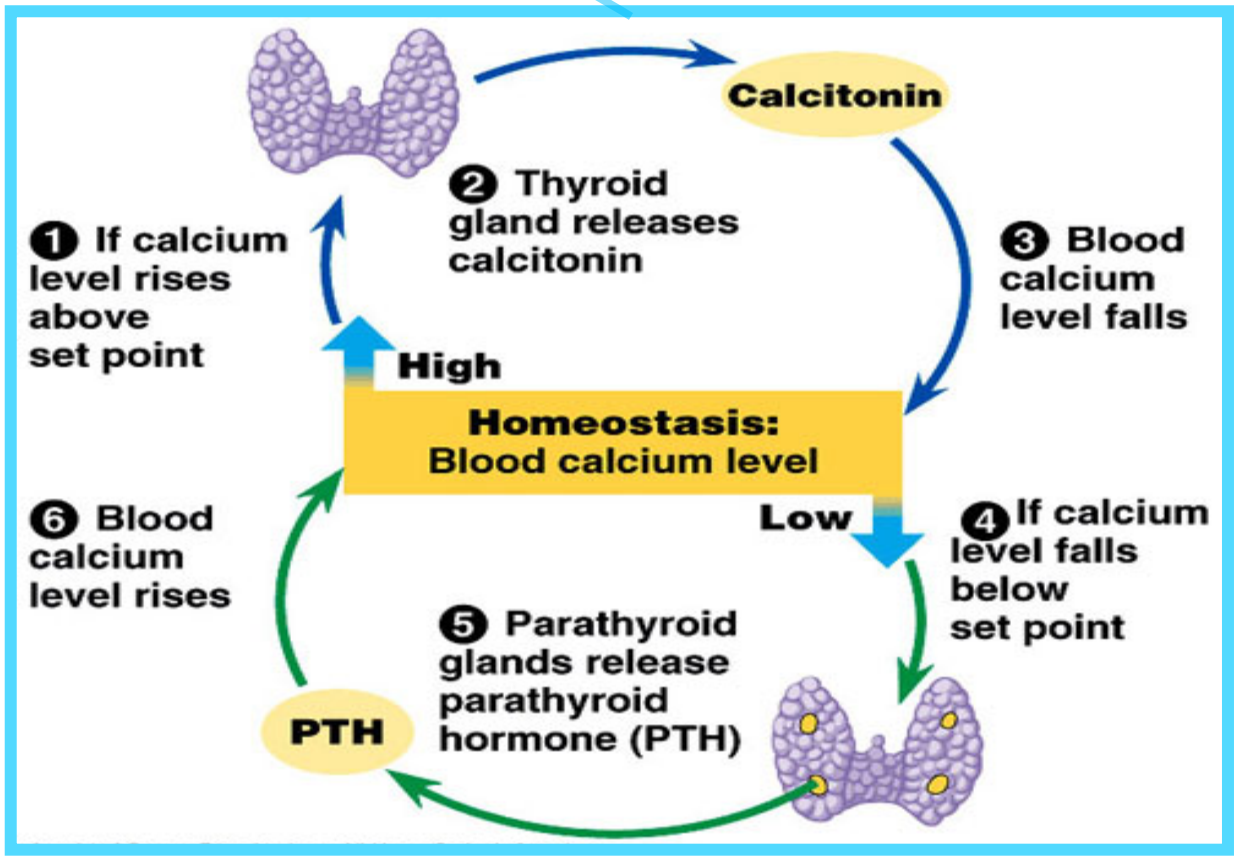
Active vitamin D is transported in blood by

gc-globulin protein



Vitamin D regulation and calcium homeostasis

- Vitamin D has essential role in calcium homeostasis
- **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



Osteomalacia and Rickets

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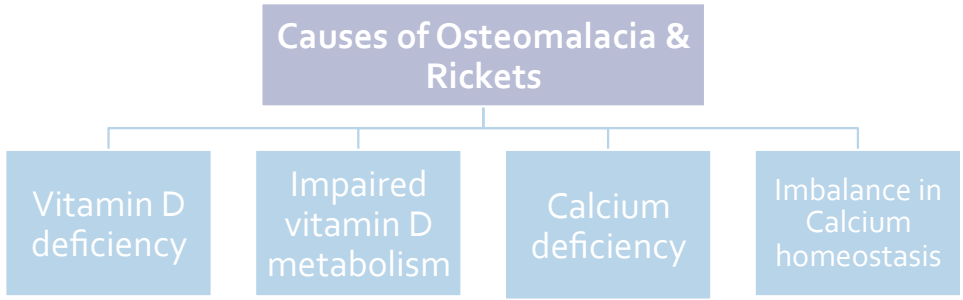
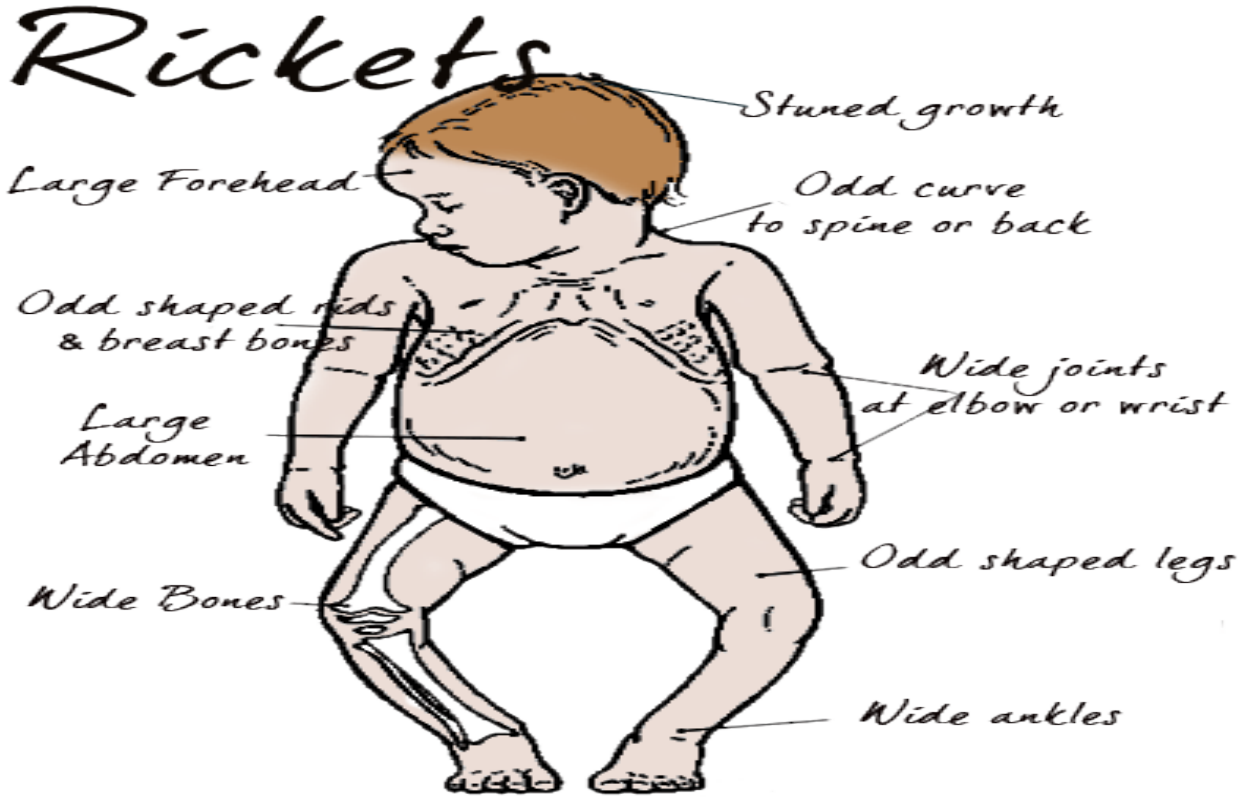
- Osteomalacia: defective bone mineralization in adults
- - (softening of the bone in adult) (demineralization)
- Rickets: defective bone and cartilage mineralization in children
- -(softening of the bone in children) (defect in mineralization)



- Not common these days → because food (milk, oil) are now supplemented with vitamin D
- Serum level of 25-hydroxycholecalciferol is low
- In sever cases :
  - ↓serum Calcium (hypocalcaemia)
  - ↑ PTH secretion (because of low Ca^{+2})
  - ↑ Alkaline phosphatase (alkaline phosphate isoenzyme is a marker for turnover (increase in "children" and "Osteomalacia and Rickets")



Vitamin-D-dependent rickets type 1 and 2 :

-it is a Rare disease due to genetic disorders

1) defects in Vitamin D synthesis
2) defects in Vitamin D receptor (no hormone action)

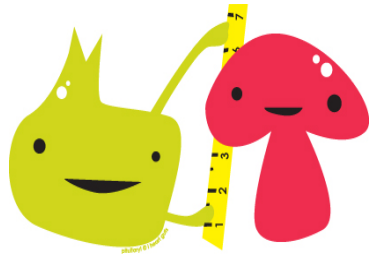
Clinical features	Rickets	Osteomalacia
Soft bone	✓	✓
Skeletal deformity (bowed legs)	✓	
Bone pain	✓	✓
Increase tendency of bone fracture	✓	✓
Dental problem	✓	
Muscle weakness	✓	✓
Growth disturbance	✓	
Compressed vertebrae		✓

Diagnosis

Measuring serum level of :

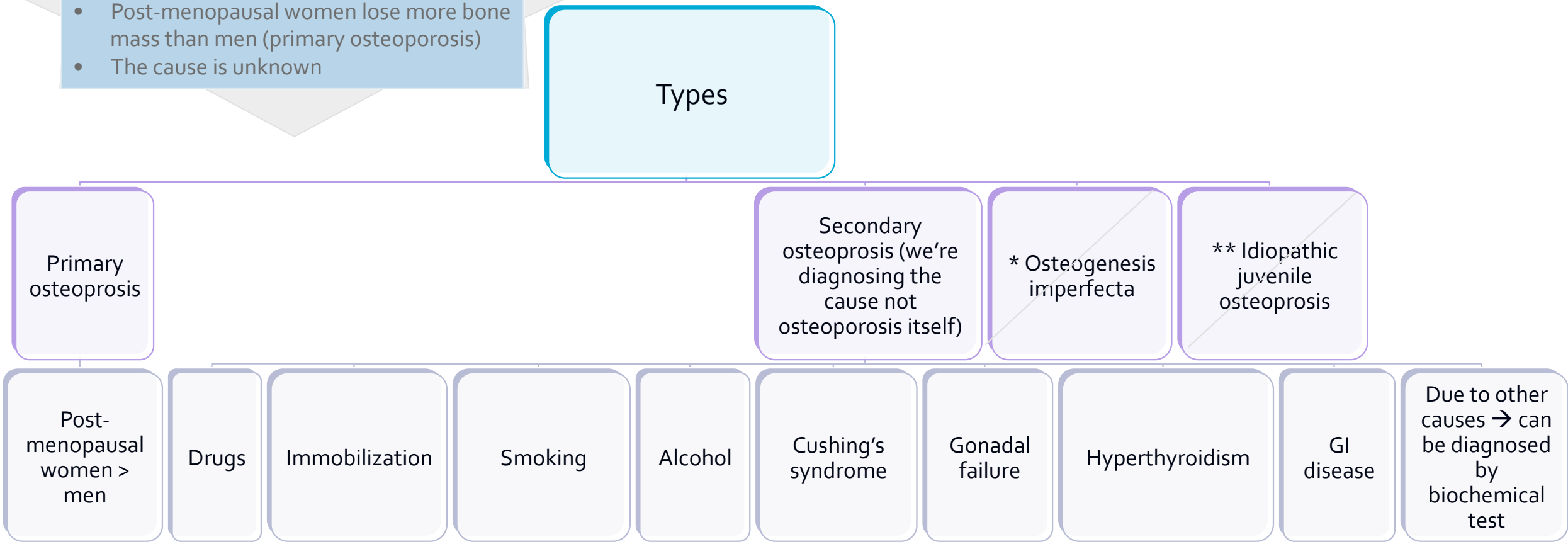
- 25-hydroxycholecalciferol
- PTH
- Ca^{+2}
- Phosphate
- Alkaline phosphate

Helpful video for Osteomalacia and Rickets Disease : http://education-portal.com/academy/lesson/osteomalacia-and-rickets-causes-and-symptoms.html



Osteoporosis

- Reduction in bone mass per unit volume
- Bone matrix composition is normal but it is reduced (bone mineral density is normal in composition but reduced in the amount)
- Post-menopausal women lose more bone mass than men (primary osteoporosis)
- The cause is unknown



* Osteogenesis imperfecta is a rare form of osteoporosis that is present at birth

** diopathic juvenile osteoporosis is rare. It occurs in children between the ages of 8 and 14 or during times of rapid growth.

Osteoporosis

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Diagnosis

- Serial measurement of bone density
- No specific biochemical tests to diagnose or monitor primary osteoporosis (no biochemical markers)
- The test results overlap in healthy subjects and patients with osteoporosis

Prevention

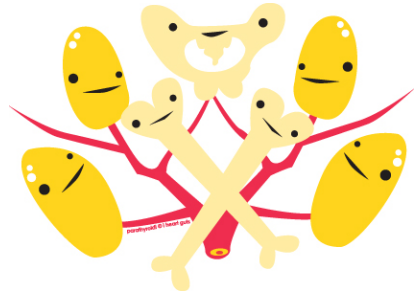
- Prevention from childhood is important
- Good diet and exercise
- Hormone replacement therapy in menopause (estrogen)

Common biochemical test

- Hydroxyproline (bone resorption)
- Alkaline phosphate (bone turnover)
- Osteocalcin (bone formation) "osteoblast make osteocalcin"

Treatment

- In confirmed case of osteoporosis → treatment options are unsatisfactory
- Oral Ca^{+2} , Estrogen , fluoride therapy may be beneficial



summary

- Osteomalacia: defective bone mineralization in adults
- Rickets: defective bone and cartilage mineralization in children
  - Causes :
    * Vitamin D deficiency * Impaired Vitamin D metabolism
    * Calcium deficiency * Imbalance in calcium homeostasis

- Diagnosis by measuring serum level of :
  *25-hydroxycholecalciferol * PTH
  *Calcium * Phosphate * Alkaline phosphatase

- Osteoporosis :
  - 1/ primary (genetic defect)
  - 2/secondary : Drugs ,alcohol , smoking , GI disease … etc

- Treatment
  - In confirmed cases of osteoporosis → treatment options are unsatisfactory

Doctor's extra notes

•Under normal condition vitamin D increases the activity of osteoblast to promote bone formation and increase the activity of alkaline phosphatase to increase local bone concentration of phosphorus ,but when hypocalcium occurs vitamin D will promote bone resorption to increase blood $Ca2+$ to normal levels .

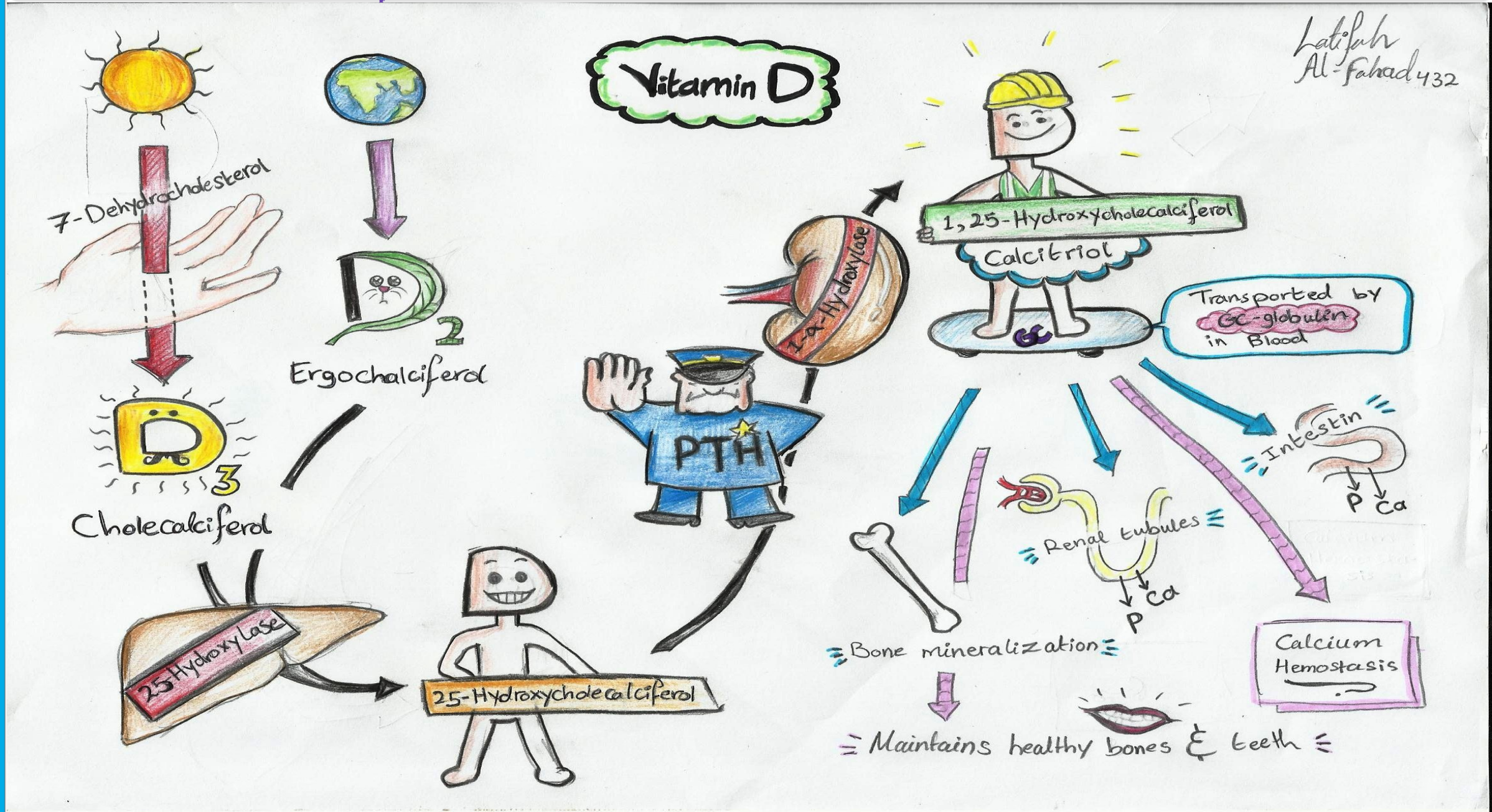
•25-hydroxycholecalciferol is the major storage form and the one measured in the blood.

•1-a-hydroxylase is regulated:

- ↓ PO_4^{3-} directly activates it
- ↓$Ca2+$ indirectly activates it through release of parathyroid hormones

Summary

Special thanks to Latifah Al-Fahad



Test your knowledge ..!

A-12-months old female , presented to the clinic with bowed legs ,Dental problems and growth disturbance , what is the most likely diagnose :

1) Osteomalacia
2) Rickets
3) Osteoporosis
4) Hypothyroidism

B-Primary Osteoporosis may be caused by :

1) Smoking
2) Drugs
3) Immobilization
4) Post-menopausal

C- calcium homeostasis is maintained by:

1) PTH and calcitonin
2) Cholesterol and calcium
3) Vitamin D and vitamin C
4) Vitamin C and PTH

D- The precursor of bile salts, vitamin D and sex hormones:

1)Tyrosine
2)Cholesterol
3)Glucose
4)Glutamate

E- The most potent Vitamin D metabolite is :

1) 25-Hydroxycholecalciferol
2) 1,25-Dihydroxycholecalciferol
3) 24, 25-Dihydroxycholecalciferol
4) 7-Dehydrocholesterol

F- 25-Hydroxylation of vitamin D occurs in :

1) Skin
2) Liver
3) Kidneys
4) Intestinal mucosa

A-(2) B-(4) C-(1) D-(2) E-(2) F-(2)

Biochemistry
Team

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