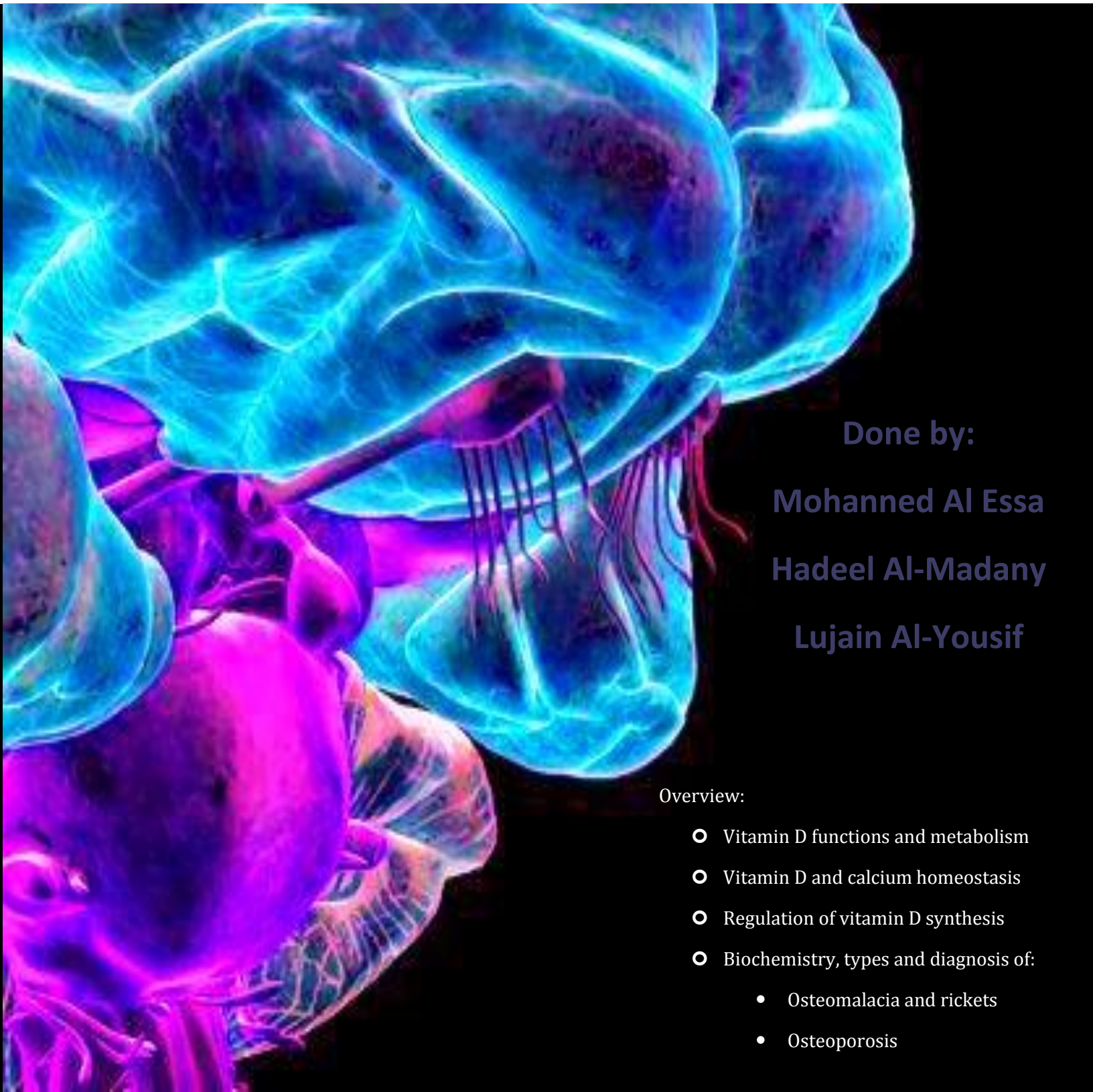
Vitamin D, Rickets and Osteoporosis



Done by:

Mohanned Al Essa

Hadeel Al-Madany

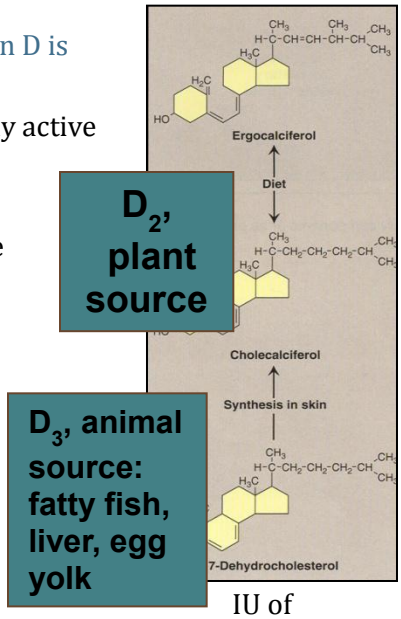
Lujain Al-Yousif

Overview:

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

D vitamins

- A group of sterols (lipid soluble) with a hormone-like function. "Vitamin D is considered a **steroid** hormone"
- **Calcitriol** (1, 25 diOH cholecalciferol = 1, 25 diOH D3) is the biologically active molecule.
- ***Vitamins D2 & D3***
  - Preformed Vitamin D in the diet: they are needed only in exposure to sunlight is limited.
  - They are also available as supplement
  - They are NOT biologically active
  - They are activated in vivo to the biologically active form
  - **Cholecalciferol** (vitamin D3) is synthesized in the skin by sunlight (UV)
  - **Ergocalciferol** (vitamin D2) is derived from ergosterol in lower animals and plants (from diet)
- ***Recommended dietary allowance (RDA):*** 5 mg cholecalciferol = 200 IU of vit D3 (or more) do not memorize it.
- D3 ⇆ D4 (vit. D3 can be converted into D4 and D4 into D3).



Functions:

- ✓ Regulates calcium and phosphorus levels in the body (calcium homeostasis)
- ✓ Maintains healthy bones and teeth

Through:

- Promoting absorption of calcium and phosphorus from the intestine
- Increasing reabsorption of calcium and phosphorus by renal tubules
- Increasing bone mineralization

Metabolism:

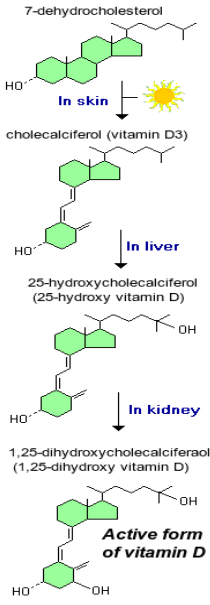
- **Cholecalciferol** is derived from **7-dehydrocholesterol** in the skin by ***sunlight***

In liver:

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

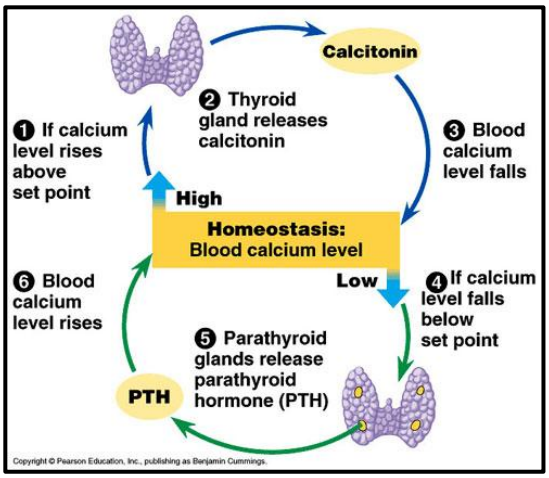
In kidneys:

- The ***1-a-hydroxylase*** enzyme **converts25-hydroxycholecalciferol** to 1**,25 dihydroxycholecalciferol** (biologically active)
- Active vitamin D is transported in blood by gc-globulin protein

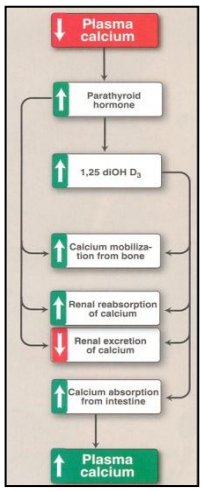


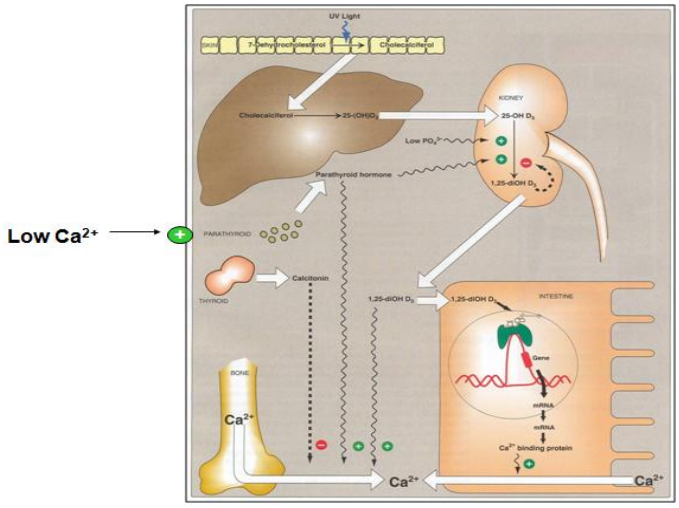
The last step is the regulatory stage.

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





Diseases caused mainly by decreased physical activity, decreased exposure to sunlight and to a little extent, decreased calcium intake (calcium deficiency mainly in vegetarians) or imbalance of calcium homeostasis.

Osteomalacia and Rickets

- Osteomalacia: defective bone mineralization in adults
- Ricket: defective bone and cartilage mineralization in children
- Due to:
  - Vitamin D deficiency
  - Impaired vitamin D metabolism (includes any defect/deficiency in the enzymes)
  - Calcium deficiency
  - Imbalance in calcium homeostasis
- Before introduction of vitamin D-supplemented milk, children with insufficient exposure to sunlight developed Vit D deficiency due to impaired intestinal absorption of calcium
- Not common these days as foods (milk, oils) are now supplemented with vitamin D
- ***Serum levels of 25-hydroxycholecalciferol is low in these patients***
- **Osteomalacia and Rickets** : serum level of Alkaline phosphatase activity +PTH are increased (the rest are decreased).
- In severe forms:
  - Serum calcium falls (hypocalcemia) not a good marker

- PTH secretion increases
- Alkaline phosphatase increases (not specific)

Vitamin-D-dependent rickets types 1 and 2 (genetic disorders)

- Rare bone diseases
- Due to:
  - Defects in vitamin D synthesis: **type 1** (can be overcome by high doses of Vit D)
  - Defects in vitamin D receptor: **type 2** (cannot be overcome by high doses of Vit D, as the hormone is unable to act)

Clinical Features:

Rickets	Osteomalacia
Soft bones	**Soft bones**
Skeletal deformity (bowed legs)	**Bone pain**
Bone pain	**Bone fractures**
Increased tendency of bone fractures	**Compressed vertebrae**
Dental problems	**Muscle weakness**
Muscle weakness	
Growth disturbance	

Diagnosis:

- Measuring serum levels of:
  - 25-hydroxycholecalciferol it is the form that we measure in a blood test.
  - PTH
  - Calcium
  - Phosphate
  - Alkaline phosphatase

Osteoporosis

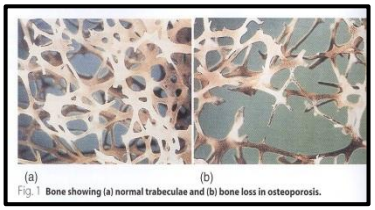


Fig. 1 Bone showing (a) normal trabeculae and (b) bone loss in osteoporosis.

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

- **Secondary osteoporosis may be caused by:**
  - Drugs
  - Immobilization
  - Smoking
  - Alcohol
  - Cushing's syndrome
  - Gonadal failure
  - Hyperthyroidism
  - GI disease

Diagnosis

- Serial measurement of bone density
- No specific biochemical tests to diagnose or monitor primary osteoporosis
- Secondary osteoporosis (due to other causes) can be diagnosed by biochemical tests
- The test results overlap in healthy subjects and patients with osteoporosis

Common biochemical tests:

- Urinary Hydroxyproline (bone resorption)
- Alkaline phosphatase (bone formation)
- Osteocalcin (bone formation)

Biochemistry Diagnosis is Unremarkable in Osteoporosis

Prevention

- Prevention from childhood is important
- Good diet and exercise prevent osteoporosis later
- Hormone replacement therapy in menopause prevents osteoporosis

Treatment

- In confirmed cases of osteoporosis
  - Treatment options are unsatisfactory
- Oral calcium, estrogens, fluoride therapy may be beneficial

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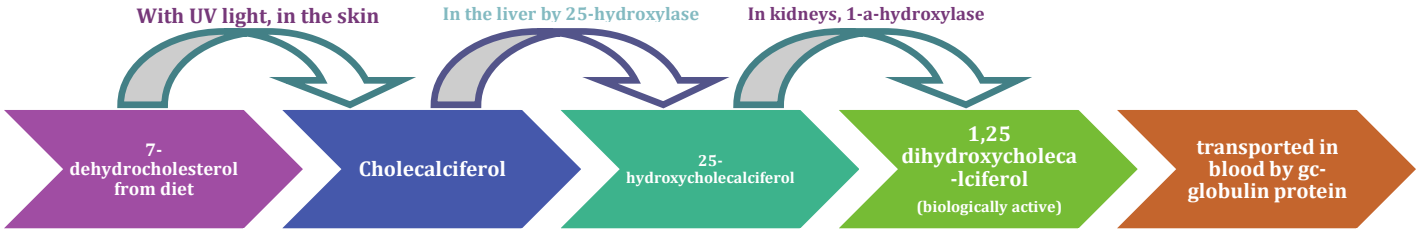
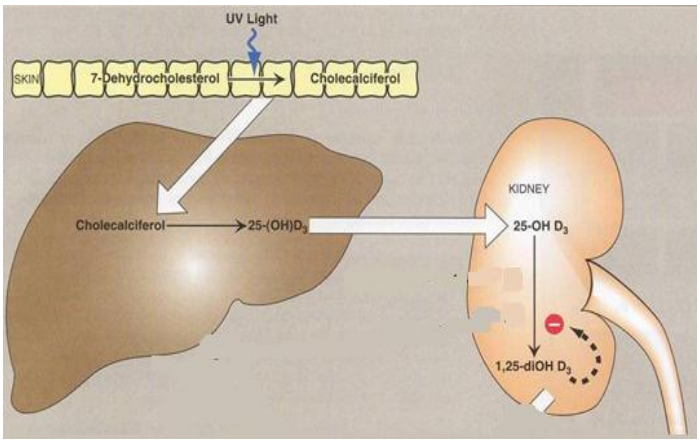
Summary

Functions of Vit. D:

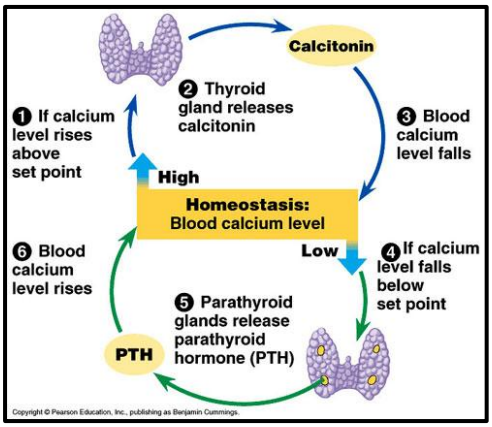
- Regulates calcium and phosphorus levels in the body (calcium homeostasis)
- Promotes absorption of calcium and phosphorus from the intestine
- Increases bone mineralization
- Increases the reabsorption of calcium and phosphorus by renal tubules
- Maintains healthy bones and teeth

Metabolism:





Vitamin D regulation and Calcium homeostasis:



- **Osteomalacia**: defective bone mineralization in adults
- **Ricket:** defective bone and cartilage mineralization in children

Diagnosis:

- Measuring serum levels of:
  25-hydroxycholecalciferol- PTH – Calcium – Phosphate - Alkaline phosphatase

Osteoporosis

- Reduction in bone mass per unit volume
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