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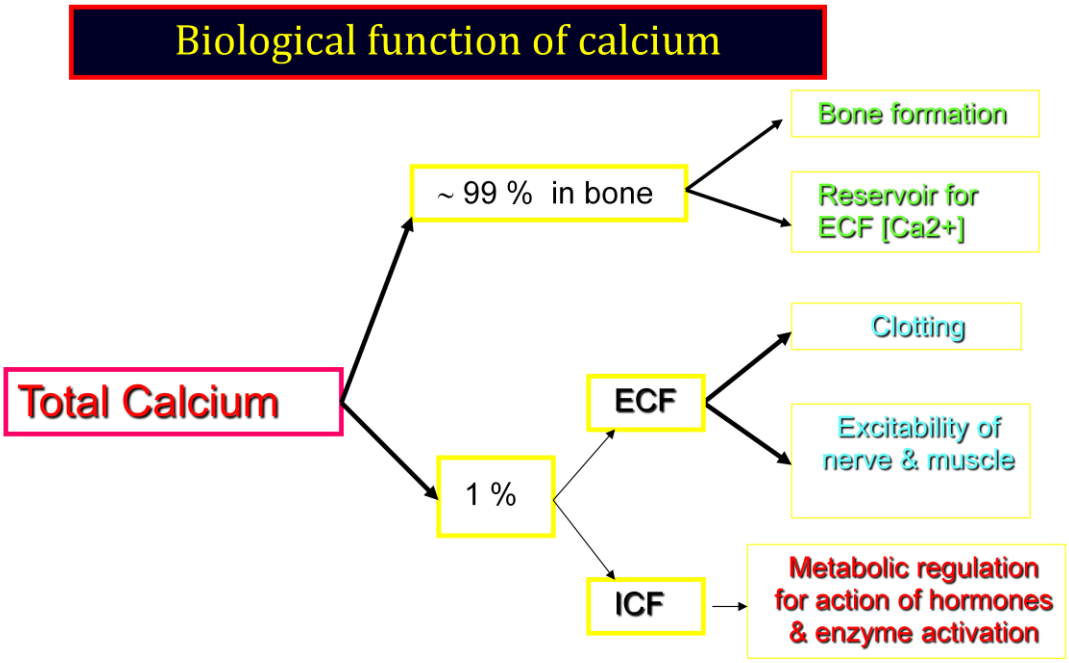
Special thanks to :

Badra'a

❖ **Calcium is the most abundant mineral in the body:**
(1 kg) in a 70 kg man.

✓ ~ 99% of the body's calcium is present **in the bone**, where it is combined with phosphate .



Calcium balance:

- In adults: normally, **calcium intake = output** .
- In infancy and childhood: **input > output** → positive balance , due to active skeletal growth.
- In old age: calcium **output > input** → negative balance; marked in women after menopause, → postmenopausal osteoporosis.

Plasma [Ca^{2+}] is regulated by:

✓ PTH
✓ 1,25 DHCC
✓ Calcitonin

@ Parathyroid hormone (PTH) is the principal acute regulator of plasma [Ca^{2+}].

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 and D2 are available as **supplement**

- ✓ Ca in the bone **99 %** .... after that Na
- ✓ In the lab we measured D2 to used it in montreing the pt.
- ✓ Vit D is toxic when it take in excessive amount .it is not like vit C the excessive amount will be secretion !
  - The more form of vit D in the body and stored form is **25-hydroxycholecalciferol** and that what we measured In the lab !

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

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

In liver:

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

Vitamin D metabolism

in the skin

- Cholecalciferol is derived from **7-dehydrocholesterol** by sunlight

In liver:

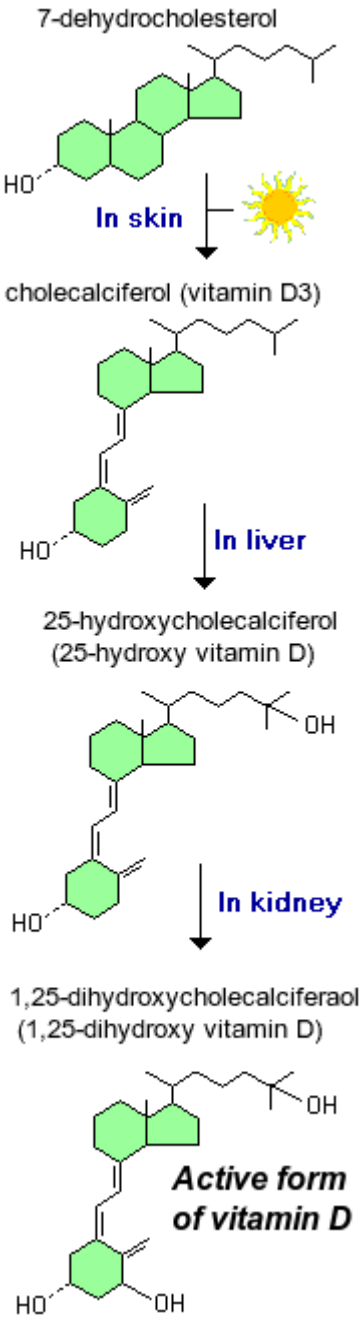
- Cholecalciferol is converted to **25-hydroxycholecalciferol** by the enzyme 25-hydroxylase

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



1-a-hydroxylase supplement give it to renal problem pt (nephropathy) .. (diabetic –old pt)!

To converts 25-hydroxycholecalciferol **to 1,25-dihydroxycholecalciferol** !

***in the kidney (very regulated organ):**

- 1-when phosphate is low that stimulate convention of 25-hydroxycholecalciferol **to 1,25-dihydroxycholecalciferol** (biologically active) ! (**direct**)

2- when ca is low stimulate PTH which stimulate 1-a-hydroxylase to convert 25-hydroxycholecalciferol **to 1,25-dihydroxycholecalciferol** (biologically active) (**indirect**)

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 homeostasis

+ve in children and infant b/c they will need it in growth !

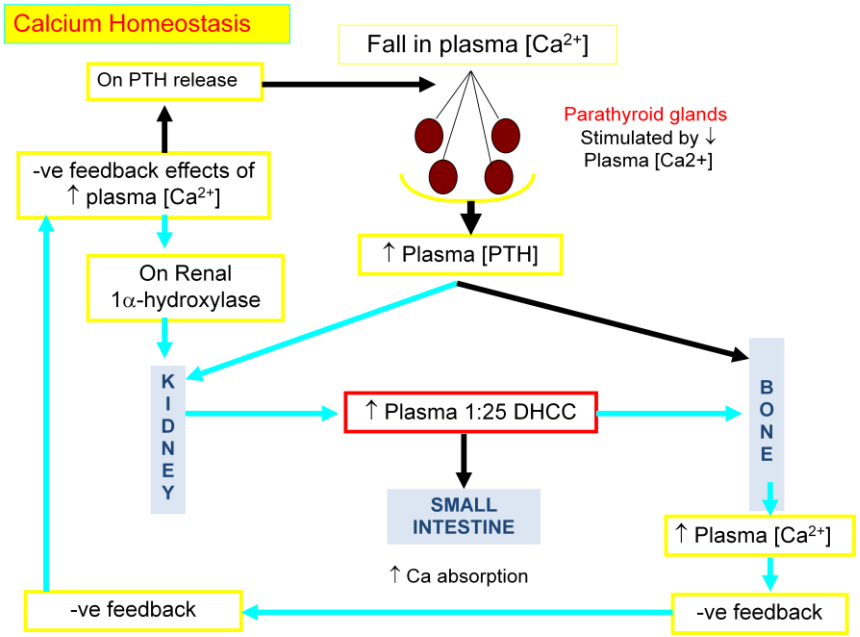
-ve in old resorption of the bone more

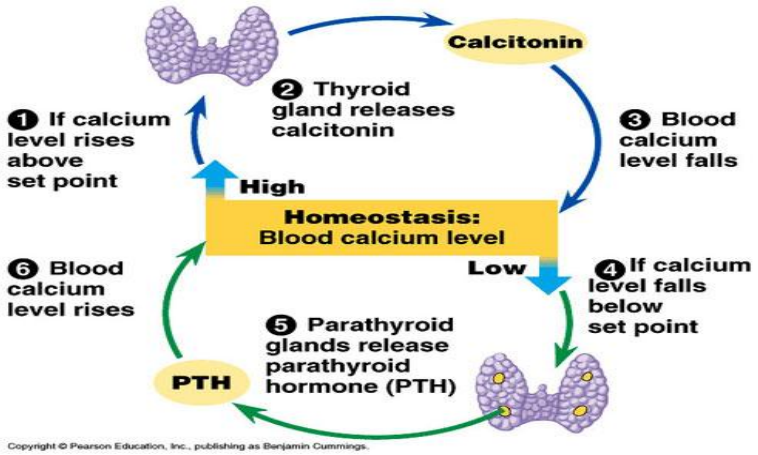
- **Calcium absorption in the gut:**
  - Indirectly depends on PTH
  - Directly depends on vitamin D

Role of vitamin D (1:25 DHCC) (Calcitriol):

- **Stimulates GI absorption of both calcium and phosphate** through synthesis of a Ca^{2+}-binding protein in the intestinal epithelial cell necessary for Ca^{2+} absorption .
- **Stimulates bone resorption**.

- Net effect of calcitriol : ↑ serum calcium
  ↑ serum phosphate
- Deficiency of 1: 25-DHCC ➔ defective bone mineralization.





Calcium homeostasis

Calcitonin

- **Calcitonin** is

  The only Hypocalcemic hormone

  - **a peptide hormone**
  - **secreted by the parafollicular or "C" cells** of the thyroid gland
  - **released** in response to high plasma calcium
- **Net result of its action** → ↓ plasma calcium & phosphate

Calcitonin ➔ ↓ plasma [Ca^{2+}] by:

↓ **osteoclast activity**

↓ **renal reabsorption of calcium and phosphate**.

Rickets

- **Defects of bone and cartilage mineralization in children (osteomalacia in adults)**
- Due to:
  - Vitamin D deficiency
  - Impaired vitamin D metabolism
  - Calcium deficiency
  - Disturbance in calcium homeostasis
- Not a common disease as foods (milk, oils) are now supplemented with vitamin D

1-Vitamin D deficiency = nutrational Rickets

Due to:

- malapsorption
- do not come under the sun
- low ca intake

2-Impaired vitamin D metabolism = renal Rickets

- They donot have the active form of vit D "1-a-hydroxylase enzyme deficieny"

- **In severe forms of rickets:**
  - Serum calcium falls (hypocalcemia)
  - PTH secretion increases
  - Alkaline phosphatase increases

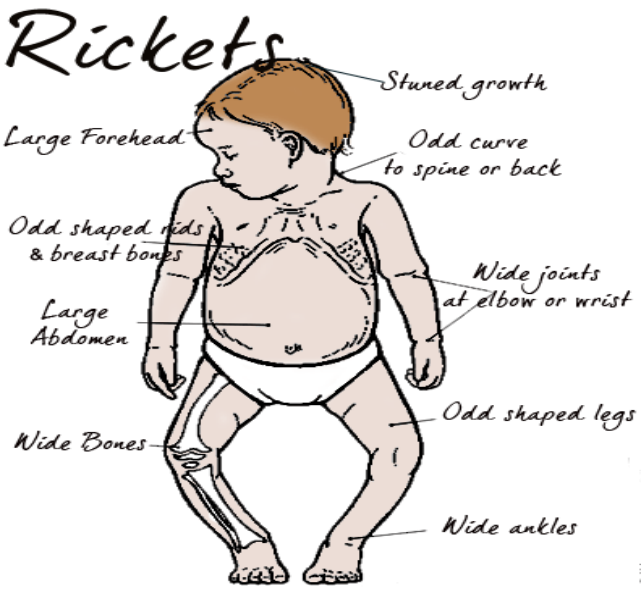
> ✓ Alkaline phosphatase found in the liver , bone , placenta
> ✓ In Rickets b/c bone try to build new bone cell **that cause Alkaline phosphatase increases**

Vitamin-D-dependent rickets types 1 and 2 :

- Rare bone diseases due **to genetic disorders**
- Defects in vitamin D synthesis
- Receptor defects that do not allow vitamin D to act

Clinical features

- Soft bones
- Skeletal deformity (bowed legs)
- Bone pain
- Increased tendency of bone fractures
- Dental problems
- Muscle weakness
- Growth disturbance



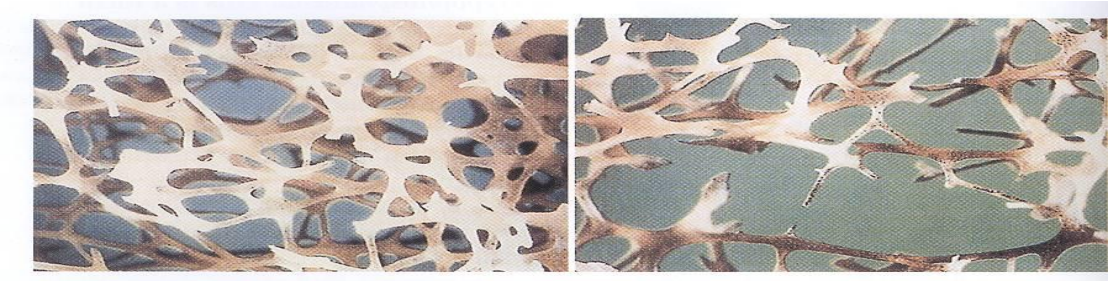
Diagnosis:

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

Osteoporosis

Ca and phosphate are normal but the matrix is reduce !

- 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



(a) (b)

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

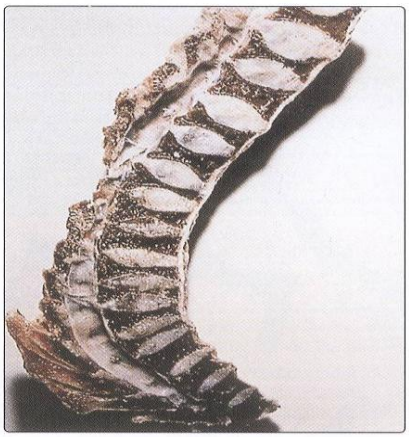


Fig. 2 **Crush fractures of vertebral bodies in a patient with osteoporosis.**

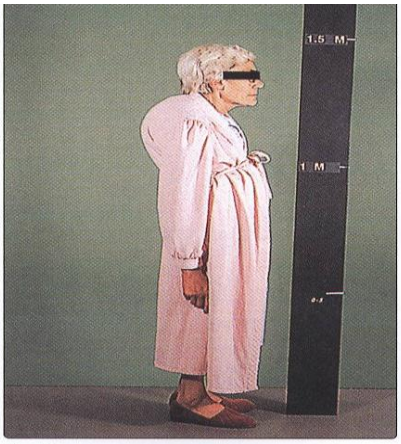


Fig. 3 **Elderly woman with so-called 'Dowager's hump' from collapsed vertebrae due to osteoporosis.**

Secondary osteoporosis may be caused by:

- Drugs
- Immobilization
- Smoking
- Alcohol
- Cushing's syndrome
- Gonadal failure
- Hyperthyroidism
- GI disease

Diagnosis

- Serial measurements 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 tests:

- ❖ Hydroxyproline (bone resorption)
- ❖ Alkaline phosphatase (bone turnover)
- ❖ Osteocalcin (bone formation)

of bone density do it **after 30** then every 2 years !

– Secondary osteoporosis (**due to other causes**) can be diagnosed by biochemical tests

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**