Editing File

Physiology of the Bone

Color Index:
-Main Text -Important -Notes
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Ty to Hasan Alsugahyir for sketch (MED445 inshallah) <3

Objectives

01 Define bone and differentiate cortical & trabecular bone (sites & function of each).

02 Identify the bone cells and the function of each.

03 Define bone remodeling and explain the mechanism of bone formation.

04 State the normal levels and forms of Ca^{2+} in the ECF and its relation to PO_4

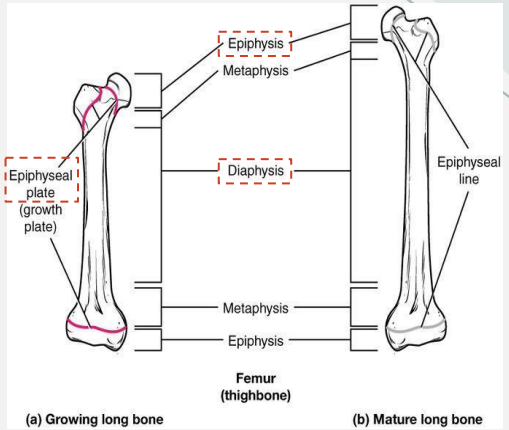
05 Interpret the importance of the exchangeable calcium.

06 Discuss the effect of different hormones on calcium homeostasis/bone physiology.

07 Define osteoporosis and state its causes.

Physiology of the Bone

Video

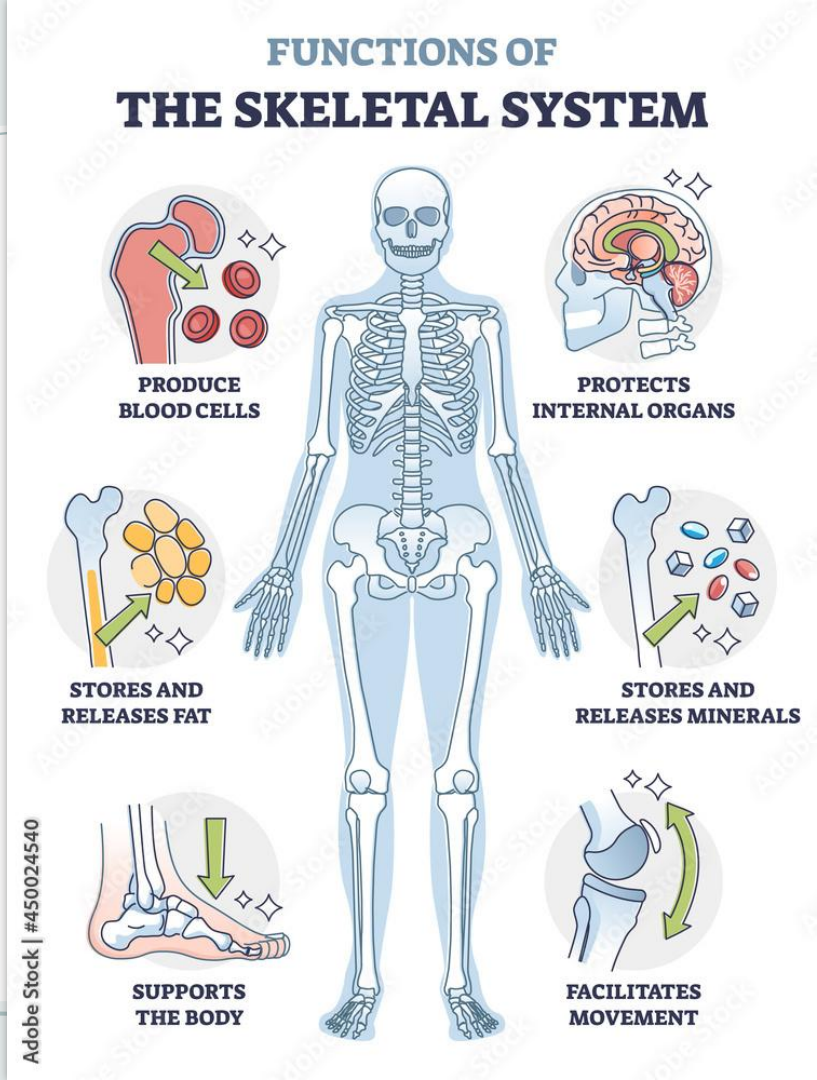


- Bone is a special form of connective tissue.
- Bone is well vascularized (rich in blood supply).
  Total blood flow: 200–400 mL/min in adult humans.
- Epiphyseal plate: an actively proliferating cartilage plate, which separates epiphyses (ends of each long bone) from shaft (diaphysis).
- As long as the epiphyses are separated from the shaft → linear bone growth can occur.
  Linear bone growth ceases/stops after epiphyses unite/combine with shaft(diaphysis) at puberty (epiphyseal closure).

:439
إذا Epiphyses اتحد مع Shaft واختفى Epiphyseal plate اللي بينهم ← يوقف نمو العظم وهذا ما يحدث عند البلوغ.

Functions of Bone

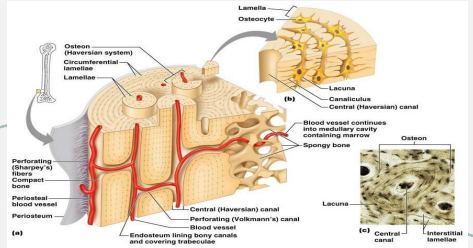
1. Involved in the overall Ca++ and PO4 homeostasis
2. Permits locomotion & support against gravity
3. Reservoir for calcium & phosphate
4. Contains the bone marrow (blood cells formation)
5. Protects the vital organs



Types & Structure of Bones

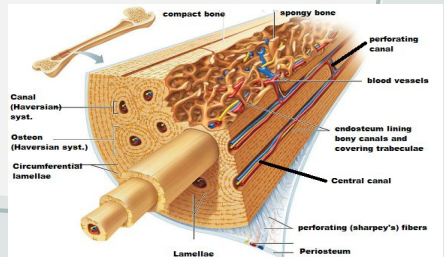
Cortical or Compact bones

- In the outer layer of most bones.
- 80% of the body bone (mass).
- Bone cells lie in lacunae. (cavity)
- Nutrients received by a way of canaliculi (channels) from haversian canals vessels.
- Has more bone tissue and less bone space.
- Has high resistance to bending and torsion.
- Composed of haversian systems/osteons.
    - Haversian systems: overlapping circular structure/formation.
    - Haversian systems: collagen that is arranged in concentric layers, around the haversian canals forming cylinders.
- Each osteon has osteonic/haversian canal (central canal).
    - Osteonic/haversian canal: central canal that contain blood vessels (capillaries - arterioles - venules), nerves, and Lymphatic.
- Composed of Matrix and Cells (next slide).



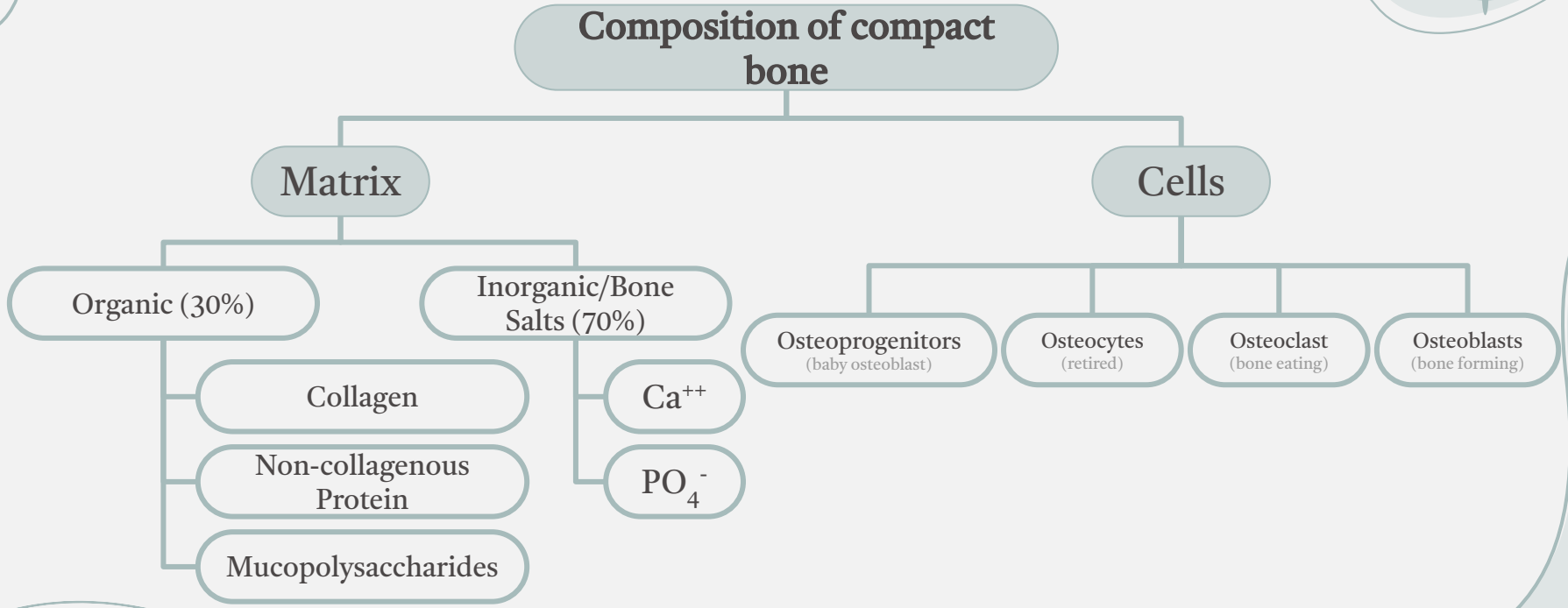
Trabecular or Spongy bones

- Inside the cortical bone.
- 20% of the body bone (skeletal mass).
- Made up of spicules or plates.(not concentric)
- Nutrients diffuse from bone extracellular fluid (ECF) into the trabeculae.
- Has 5 times greater surface area than cortical bone
    - Large surface → faster turnover rate than cortical bone → more important than cortical bone in terms of Ca++ turnover.(Ca production cycle)
- Compared to cortical bone, it is:
    - Less dense
    - More elastic
    - Higher turnover rate
- Center of the bone contains:
    - Red marrow
    - Yellow marrow
    - Bone cells
    - Other tissue
- More space less tissue.

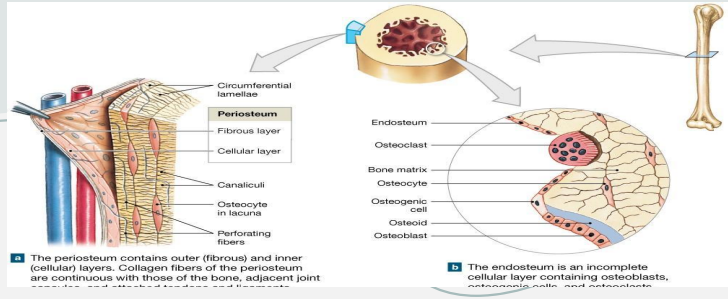


Overview (Detailed in the next 2 slides)

Video



Matrix



Matrix

Organic Matrix (30%)

1) **Collagen fibers** (90-95%):
   - Extend primarily along the lines of tensional force.
   - Gives the bone its powerful tensile strength.
2) **Ground substance** (5-10%):
   - Soft gelatinous medium of ECF and proteoglycans (chondroitin sulphate & hyaluronic acid)

Inorganic Matrix (Bone Salts) (70%)

- **Crystalline salts:** Ca^{++} and PO_4^- (hydroxyapatite).
  - Ca/P ratio: (1.3 - 2). Ca is more than PO4
- Mg^+, Na^+, K^+, Carbonate ions are also present.
- **NB:** newly formed bone have a considerably higher percentage of organic matrix in relation to salts.

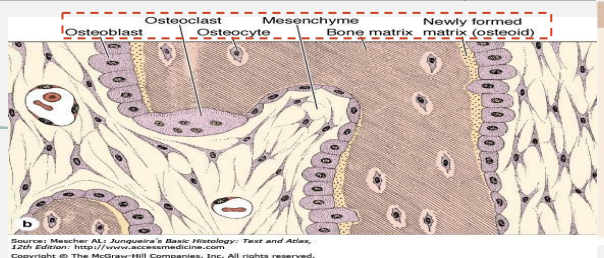
Cells

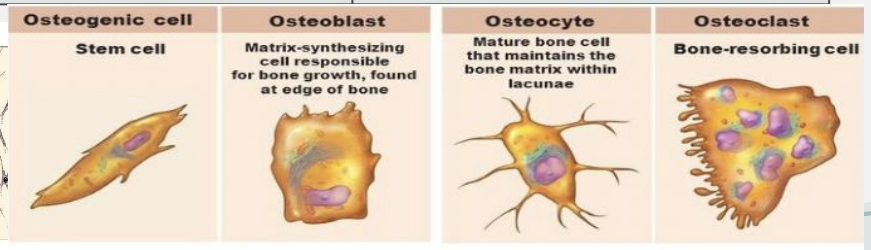
Video

OsteoBLAST	OsteoCYTES	OsteoCLASTS (bone eating cell)
• Bone forming cells. • Secrete collagen forming a matrix around themselves which then calcifies. • Regulate Ca and Phosphate concentration in bone fluid.	• When the osteoblasts get surrounded by osteoid, they are called **osteocytes.** (they are osteoblasts surrounded by osteoid) • Send processes into the canaliculi that ramify (make branches) throughout the bone.	• Multinuclear cells that erode and resorb previously formed bone. • Phagocytose bone, digesting it in their cytoplasm. • Derivative of monocytes/macrophages

Osteoid: The newly formed matrix and the only area where calcification occurs.

When osteoblasts are surrounded by calcified matrix, they are called osteocytes.





Mechanism of Bone Calcification

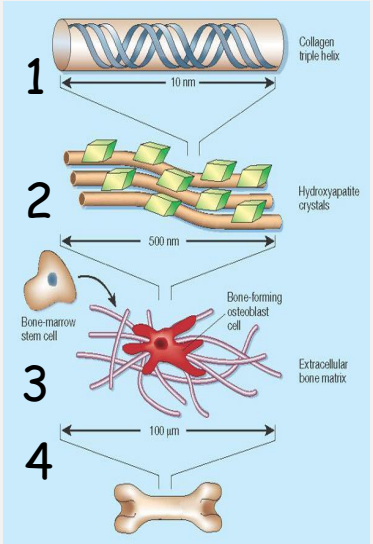
Video

1. Osteoblasts **secrete** collagen (monomers) and ground substance (proteoglycans). Collagen monomers **polymerize** to collagen fibers.

2. Resultant tissue: osteoid. (bone without salts)
   - **Osteoid:** a cartilage-like material differing from cartilage in that calcium salts readily precipitate in it.

3. Osteoblasts become **entrapped** in the osteoid and are now called osteocytes.

4. After the osteoid is formed, calcium salts begin to **precipitate** on the collagen fibers forming **hydroxyapatite crystals**.

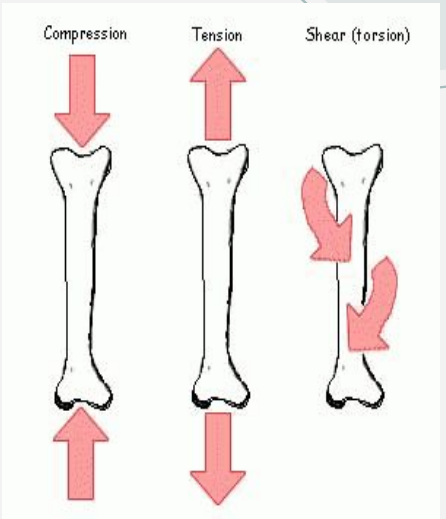


Tensile & Compressional Strength of Bone

- **Collagen fibers** of bone (like those of tendons) have great **tensile strength.**
  - **Tendons:** C.T. that connect muscle to bone, capable of withstanding tension.

- **Calcium salts** have great **compressional strength.**

- These combined properties + degree of bondage between collagen fibers and crystals → bony structure that has: extreme **tensile** strength + extreme **compressional** strength.



Tensile → tension (شد).

Compressional → compression (ضغط).

الكولاجين فايبرز ← عظامنا ما تنكسر لما تنشد.
الكالسيوم ← العظام ما تنكمش لما تنضغط.

Precipitation of Calcium in non-osseous tissue under abnormal conditions

Normal

Hydroxyapatite or calcium salts do not precipitate in plasma, ECF, or normal tissues (except bone), despite the high levels of Ca & P ions, due to the presence of the inhibitor factor called pyrophosphate.

Abnormal

Under abnormal conditions, pyrophosphate disappears from tissue allowing precipitation of Ca and P. This can happen in:

- Arterial walls, in arteriosclerosis and cause the arteries to become bone like tubes.
- Degenerating tissue
- Old blood clots

Mechanisms of bone calcification

The mechanisms that cause calcium salts to be deposited in the osteoid is not fully understood. The regulation of this process depends to a great extent on pyrophosphate, which inhibits hydroxyapatite crystallization and calcification of the bone.
The levels of pyrophosphate, in turn are regulated by at least three other molecules secreted by osteoblasts.

1) **Tissue Nonspecific Alkaline Phosphatase (TNAP):** which breaks down pyrophosphate. Its secreted by the osteoblasts into the osteoid to neutralize the pyrophosphate. Once the pyrophosphate has been neutralized, the natural affinity of the collagen fibers for calcium salts causes the hydroxyapatite crystallization. Decrease pyrophosphate -> increase calcification

2) **Nucleotide Pyrophosphatase Phosphodiesterase 1 (NPP1):** which produces pyrophosphate outside the cell. Increase pyrophosphate -> decrease calcification

3) **Ankylosis Protein (ANK):** Contributes to the extracellular pool of pyrophosphate by transporting it from the interior to the surface of the cell. Increase pyrophosphate -> decrease calcification

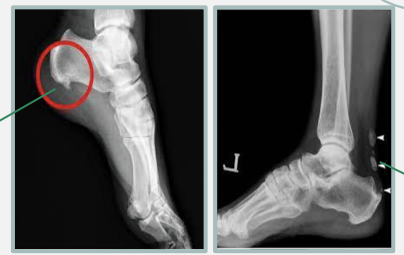
Mechanisms of bone calcification cont..

Deficiencies of NPP1 or ANK cause:

Decreased extracellular pyrophosphate

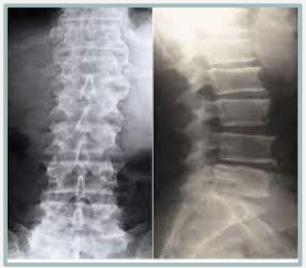
- Excessive calcification of bone, such as bone spurs.

- Calcification of other tissues such as tendons and ligaments of the spine, which occurs in people with a form of arthritis called ankylosing spondylitis



Bone spur

Calcification of achilles tendon



Ankylosing spondylitis

Remodeling of bone

Bone is continually deposited by osteoblasts, and absorbed where osteoclasts are active. The renewal rate is about 4% per year form compact bone and 20% per year for trabecular bone.

Osteoblasts

- Found on the outer surface and in the cavities of bones.
- A small amount of osteoblastic activity occurs on about 4% of all bone surfaces at any given time in an adult , so that at least some new bone is being formed constantly.

Osteoclasts

- Osteoclasts are large phagocytic multinucleated cells.
- they are normally active in less than 1% of the bone surfaces of an adult.

The osteoclasts secrete two types of substances:

1) Proteolytic enzymes from the lysosomes ⇨ dissolve the organic matrix (like collagen).
2) Several acids from the mitochondria and the secretory vesicles ⇨ cause solution of bone salts (hydroxyapatite).

The osteoclasts also phagocytose minute particles of bone matrix and crystals, dissolute them and release the products into the bloodstream.

Importance of continuous bone remodeling

01
Bone adjusts its strength in proportion to the degree of bone stress and it thickens when subjected to heavy loads.

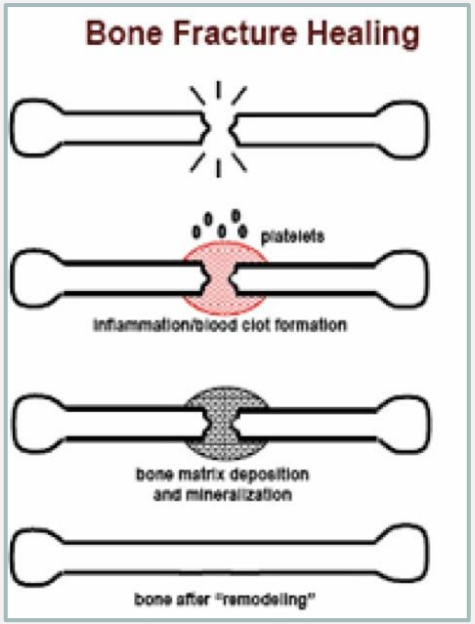
02
The shape of the bone can be rearranged for proper support of mechanical forces by deposition and resorption of bone in accordance with stress patterns.

03
Because the old bone becomes relatively brittle and weak, new organic matrix is needed to maintain the normal toughness of bone.

04
Therefore, the bones of children are less brittle in comparison with the bones of the elderly, due to more remodeling in children.

Repair of a Fracture Activates Osteoblasts

- Fracture of a bone activates all the periosteal and intraosseous osteoblasts involved in the break.
- Large numbers of new osteoblasts are formed from osteoprogenitor cells, which are bone stem cells in the surface tissue lining the bone, called the “bone membrane”
- Shortly a large bulge of osteoblastic tissue and new organic bone matrix, develops between the two broken bone ends followed shortly by the deposition of calcium salts, this is called callus.



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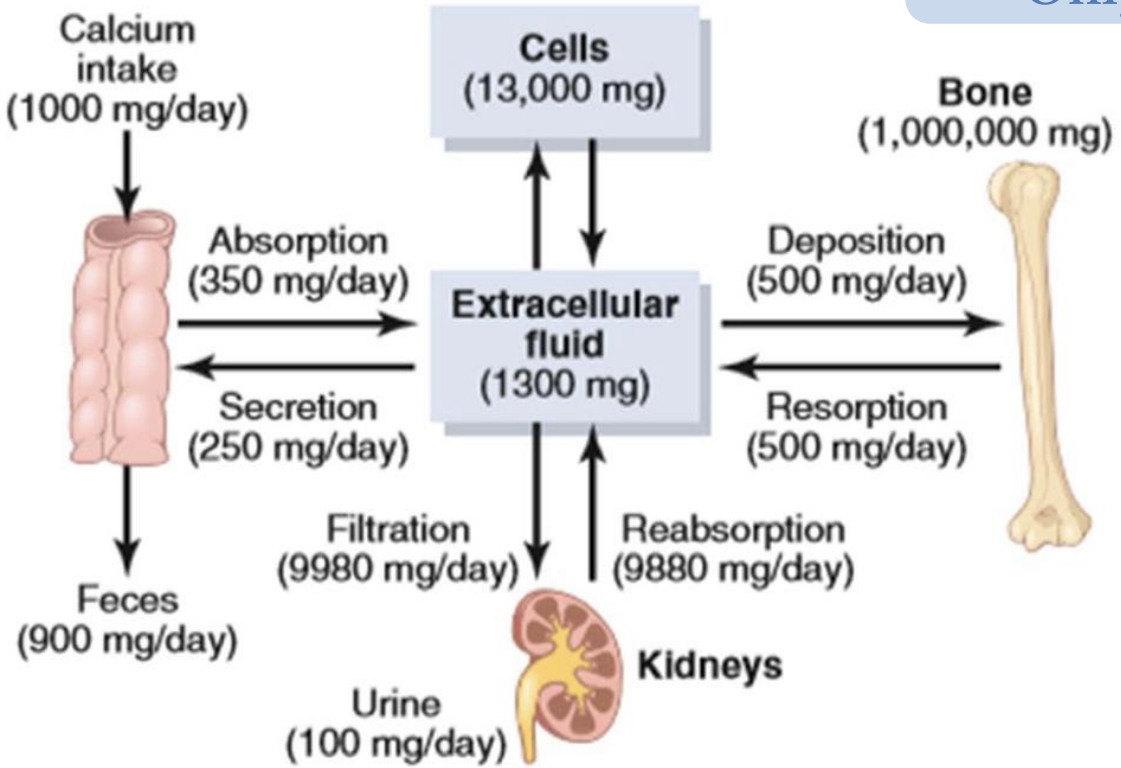
- Know that in normal circumstances calcium inside = calcium outside

Calcium Homeostasis in Human Body



Body calcium levels

- 1.5% of body weight is calcium.
- About 1100 - 1300 gm.
- 99% is in the skeleton.
- Average plasma calcium level: 9.4 mg/dl.
- Plasma calcium level: 9 - 11 mg/dl.
- 50%: Ionized + diffusible
- 9%: Non ionized and complexed to anion (citrate & phosphate)
- 41%: Non ionized & (non diffusible) = protein bound

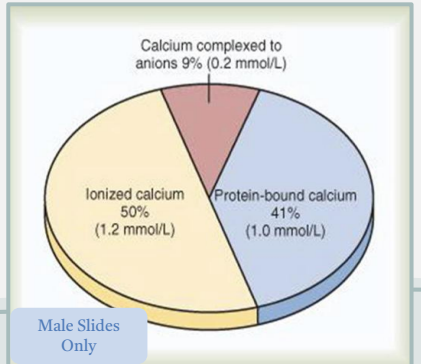


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TABLE 36.1 Body Content and Tissue Distribution of Calcium and Phosphorus in a Healthy Adult

	Calcium	Phosphorus
Total Body Content	1,300 g	600 g
Relative Tissue Distribution (% of total body content)		
Bones and teeth	99%	86%
Extracellular fluid	0.1%	0.08%
Intracellular fluid	1.0%	14%

Note: Phosphate is usually half the calcium.

Calcium exchange between the bone & ECF

The bone contains a type of exchangeable calcium that is always in equilibrium with the Ca++ ions in the ECF. It normally amounts to about (0.4 - 1 %) of the total bone calcium.

This calcium is a form of freely mobilizable salt such as calcium hydrogen phosphate ($CaHPO_4$) and other amorphous calcium salts.

The importance of exchangeable calcium is that it provides a rapid buffering mechanism to keep the Ca++ ions concentration in the ECF from rising to excessive levels or falling to very low levels under transient conditions of excess or decreased availability of calcium.

Hormonal control of calcium metabolism & physiology

Three major hormones are concerned:

Parathyroid hormone (PTH)
Secreted by parathyroid gland in response to low serum calcium levels.

1,25 dihydroxycholecalciferol
A steroid hormone formed from vitamin D, it stimulates Ca++ & phosphate absorption from intestine and kidney.

Calcitonin
Secreted by c-cells in the thyroid gland in response to high serum calcium levels.

To a lesser extent: Glucocorticoids, Growth hormones (GH), estrogens and various growth factors also affect calcium metabolism.

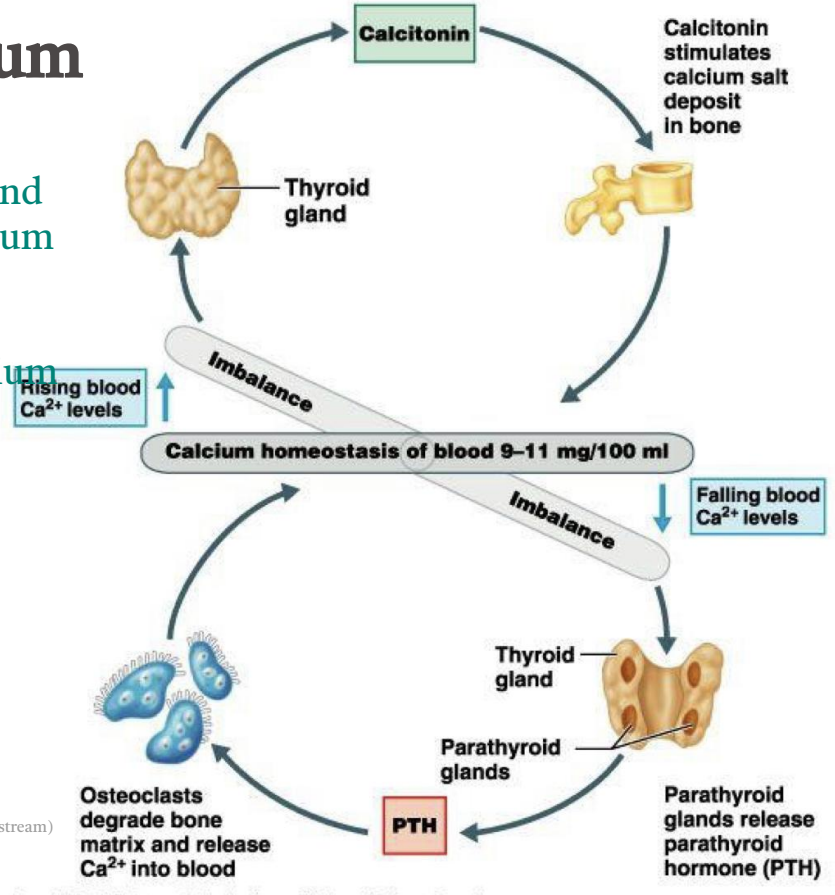
Hormonal control of plasma calcium

Hypocalcemia leads to the stimulation of PTH from your parathyroid gland, PTH works on inhibiting osteoblasts and increasing the activity of osteoclasts in order to raise calcium levels.

Osteoclasts work on breaking down bone, thus more calcium is released into the blood.

Hypercalcemia leads to the release of Calcitonin from the thyroid gland.

Calcitonin functions:
- osteoclasts ⇩
- intestinal absorption ⇩
- osteoblasts ⇧
- excretion of calcium by the kidney ⇧ (reduces the amount reabsorbed into bloodstream)



Special thanks to team 443

Vitamin D

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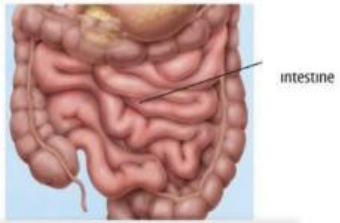
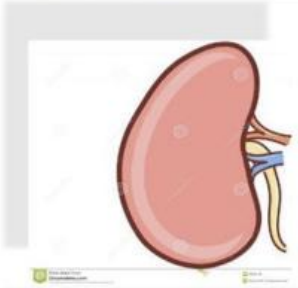
Vitamin D - ACTION OF CALCITRIOL

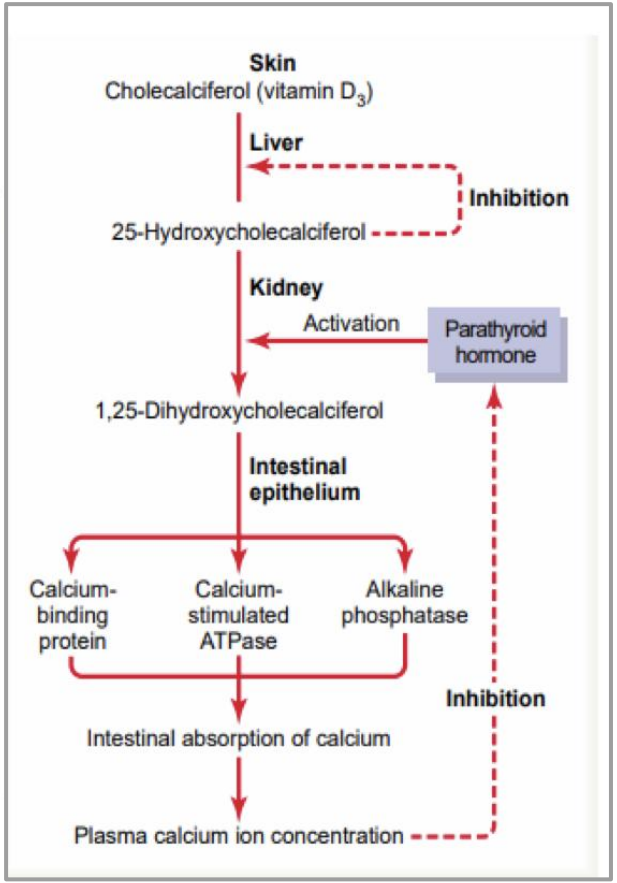


-Increases the intestinal absorption of calcium and phosphate by increased synthesis of calcium binding protein (calbindin D28k)

-Mineralization of bone at low doses
-Mobilization of calcium from bone at high doses



-increased reabsorption of calcium and phosphorus
-decreased excretion of calcium and phosphorus



Osteoporosis

Osteoporosis: reduced bone density and mass.
In a person with osteoporosis the osteoblastic activity in the bone is usually less than normal (depressed activity of osteoblast), and consequently the rate of bone osteoid deposition is depressed. But occasionally caused by loss of osteoclast activity.
Loss of bone matrix , mineral & mass is marked.
It results from diminished organic bone matrix rather than from poor bone calcification.

Causes of Osteoporosis

- Lack of physical stress on bones.
- Malnutrition
- Lack of vitamin C
- Old age
- Postmenopausal lack of estrogen
- Cushing's syndrome characterized by abnormally high cortisol levels.

"More plates on the bar = more calcium in the bones"

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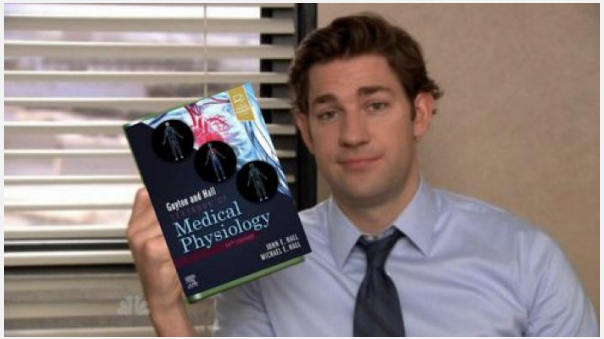
Complications of osteoporosis

- The incidence of fractures is increased particularly in the distal forearm (colle's fracture), vertebral body & hip. These areas have a high content of trabecular bone, which is more active metabolically, it is lost more rapidly.
- Fractures of the vertebrae with kyphosis produces "widow's hump" in elderly women with osteoporosis.
- Fractures of the hip in elderly are associated with a mortality rate of 12 - 20%, & half of those who survive require prolonged expensive care.
- Increased intake of calcium and moderate exercise may help prevent or slow the progress of osteoporosis.

You can find the pages related to this lecture from (Guyton) here

Note: Guyton has extra information that might not be with us, but if you want to learn more about the topic make sure to check it out :3



Thanks to team 443 <3

MCQ

Q1: Collagen fibers are responsible for which of the following?			
A- Tensile strength	B-compressional strength	C- Both	D- None
Q2: which of the following cells is responsible for bone resorption?			
A- Osteons	B- Osteoblasts	C- Osteoclasts	D- Osteocytes
Q3: which of the following is one of the characteristics of osteoclast?			
A- in the periosteum	B- Arise from osteocytes	C- Can divide	D- Multinucleated
Q4: which of the following gives bones compressional strength?			
A- Collagen	B- Ca	C- Osteoblast	D- Proteoglycans

1: A 2: C 3: D 4: B

SAQ

Q1: Name the types of bones?
A1:
Cortical (compact)
Trabecular (spongy)

Q2: what are the cells found in compact bone?
A2:Osteoprogenitors
Osteocytes
Osteoblasts
Osteoclasts

Q3: list 3 substances that regulate bone calcification?
A3: slide 12

Q4: under abnormal conditions where can calcification occur?
A4: slide 11

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