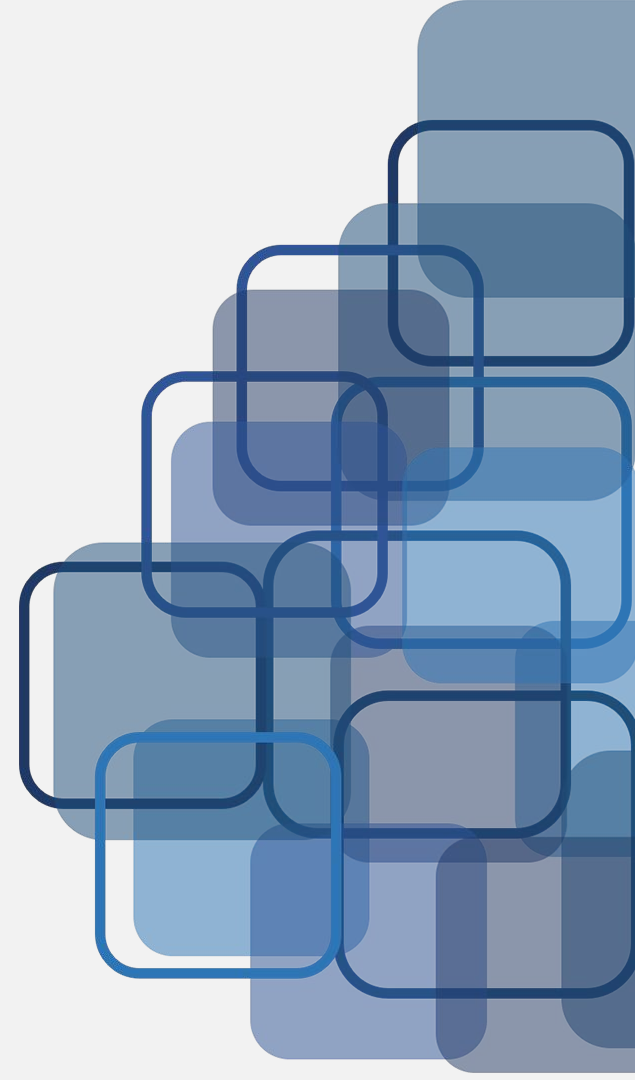


MED439
KING SAUD UNIVERSITY

Physiology 439

3

Physiology of bone



Editing file

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Red: Important
Black: In Male & Female slides
Blue: In male slides
Pink: In female slides
Gray: Notes & extra information



Objectives

- 01 Define bone and differentiate cortical & trabecular bone (sites and function of each).
- 02 State the normal levels and forms of Ca^{++} in the ECF and its relation to PO_4 .
- 03 Identify the bone cells and the function of each.
- 04 Define bone remodelling and explain the mechanism of bone formation.

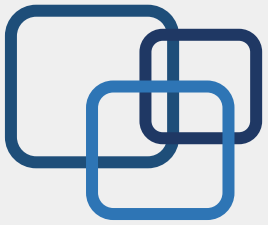
05 Define osteoporosis and states its causes.

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

07 Interpret the importance of the exchangeable calcium.

08 Discuss the effect of different hormones on calcium homeostasis.



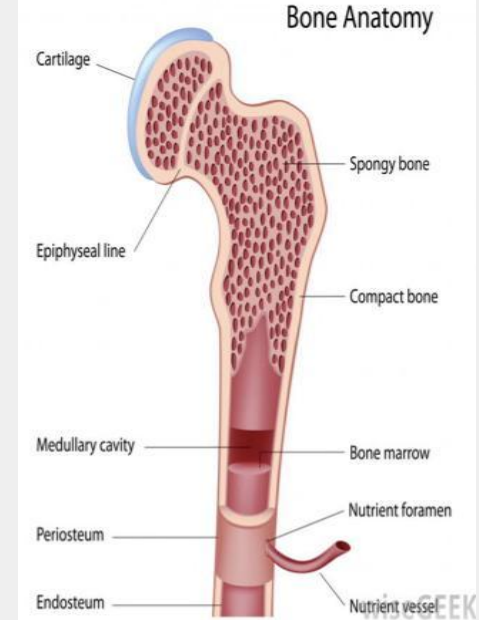


Physiology of bone

- ◆ Bone is a special form of **connective tissue**.
- ◆ It is well **Vascularized** with total blood flow of 200-400 mL/min in **Adult** human.
- ◆ The **ends** of each **long bone** is called **Epiphyses**.
- ◆ Epiphyses is **separated** from the shaft of the bone by a plate of **actively proliferating cartilage**, The **epiphyseal plate** (growth plate).
- ◆ Linear bone growth can occur **as long as the epiphyses are separated from the shaft of the bone**, but such growth ceases after the epiphyses unite with the shaft (Epiphyseal closure) , **at puberty** .

إذا اتحد الـ epiphyses مع الـ shaft واختفى الـ epiphyseal plate الي بينهم .. نمو العظم يوقف

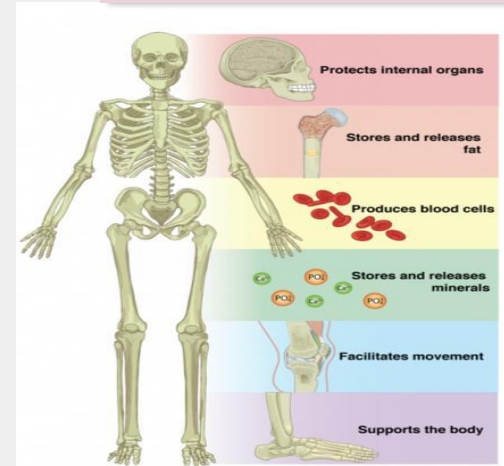
This picture was found in female slides

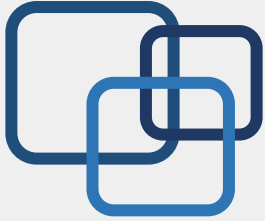


Functions of bone

- ◆ Is involved in the overall Ca^{++} and PO_4^- **Homeostasis**.
- ◆ **Protects** the vital organs.
- ◆ Permits **locomotion** and **support** against gravity.
- ◆ Contains the **bone marrow** (blood cells formation).
- ◆ Reservoir for calcium & Phosphate.

This picture was found only in female slides

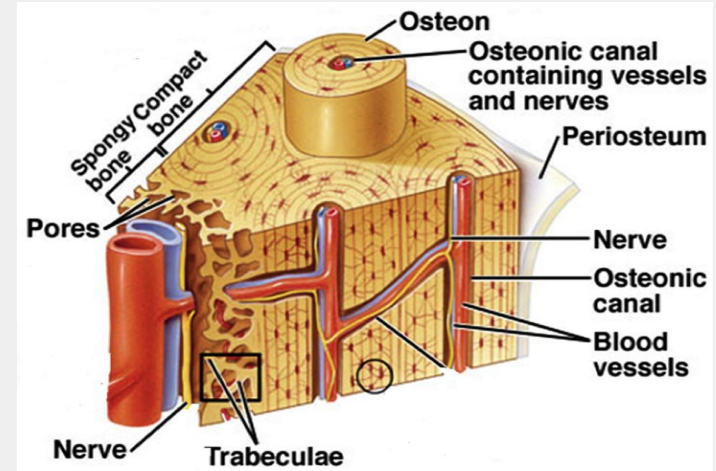


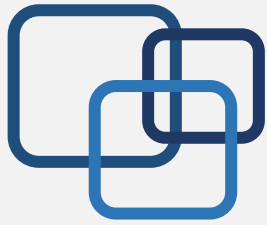


Types and structure of bone

Compact bone (Cortical):

- in **Outer layer** of most bones, 80% of the bones in the body.
- It has more bone tissue and less bone space.
- Has **high resistance** to bending and torsion.
- The bone cells lie in lacunae.
- It is composed of **Collagen** arranged in concentric layers **around the Haversian canals** forming cylinders (overlapping circular structures formations) called: **Osteons or Haversian systems**.
- Each Osteon has a central canal
- The **Osteonic canal** (Haversian canals) contain **blood vessels** (Capillaries! Arterioles, and Venules), **Nerves**, and **lymphatics**.
- **Compact bone** receive nutrients by way of canaliculi from **haversian canals**





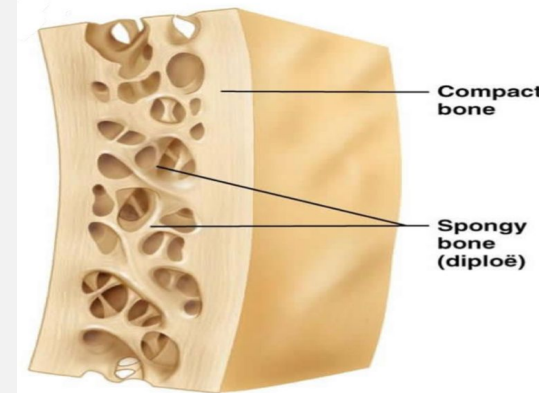
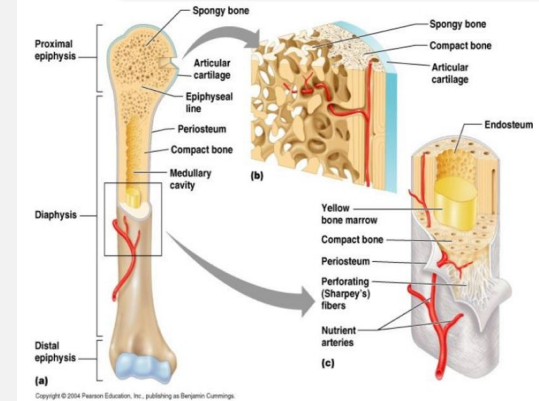
Types and structure of bone

Trabecular bone (Spongy):

- Inside the cortical bone, 20% of the body bones (skeletal mass).
- is made up of spicules OR plates.
- It has 5 times greater surface area than cortical bone.
- **Faster turnover** rate than cortical bone because of its large surface.
- More Important than cortical bone in terms of **calcium turnover**.
- Nutrients diffuse from bone extracellular.
- Compared to cortical bone it is:
 - 1- Less dense.
 - 2- More elastic.
 - 3- Higher turnover rate.
- The center of the bone contains Red, Yellow marrow, bone cells, and other tissues.

Bone turnover refers to the total volume of bone that is both resorbed and formed over a period of time

These two pictures was found in female slides





Composition of Compact bone

Organic Matrix 30%

Collagen fibers 90-95%:

Extended primarily along the lines of tensional force and give bone its powerful tensile strength.

Ground substance 5-10%:

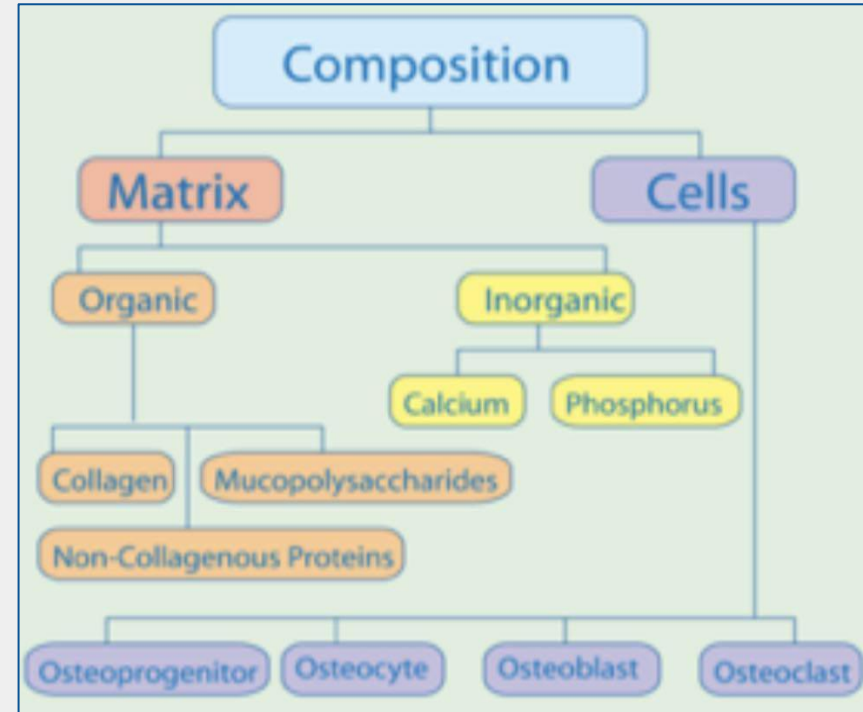
ECF, and Proteoglycans (Chondroitin Sulphate, Hyaluronic acid)

Bone salts 70%

Crystalline salts of Ca^{++} and PO_4^- (Hydroxyapatite)
The ratio of Ca/P ratio is 1.3 - 2 or 1.5 - 2.

Mg^+ , Na^+ , K^+ , Carbonate ions are also present.

Newly formed bone have a considerably higher percentage of matrix in relation to salts.



Bone Cells

Osteoblast are the bone forming cells that **secrete collagen** forming a matrix around themselves which then calcifies and when **surrounded by calcified matrix** the are called **Osteocytes**.

Osteoprogenitor cell is like the stem cell in blood.

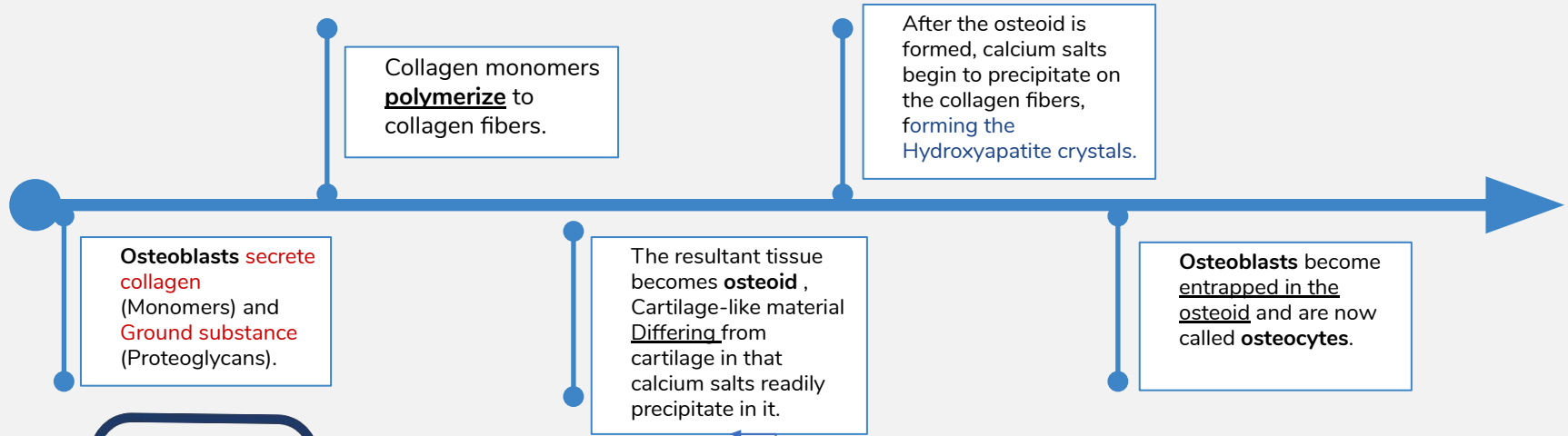
Osteoblasts regulate concentration of Ca and Phosphate in bone fluid.

Osteocytes send processes into the canaliculi that ramify throughout the bone.

Osteoclasts are **multinuclear** cells that **erode and resorb** previously formed bone. They **Phagocytose** bone and **Digesting it in their cytoplasm.**

باختصار تنتشر وتتشعب
البروزات في باقي أنحاء العظم
عن طريق الـ Osteocytes

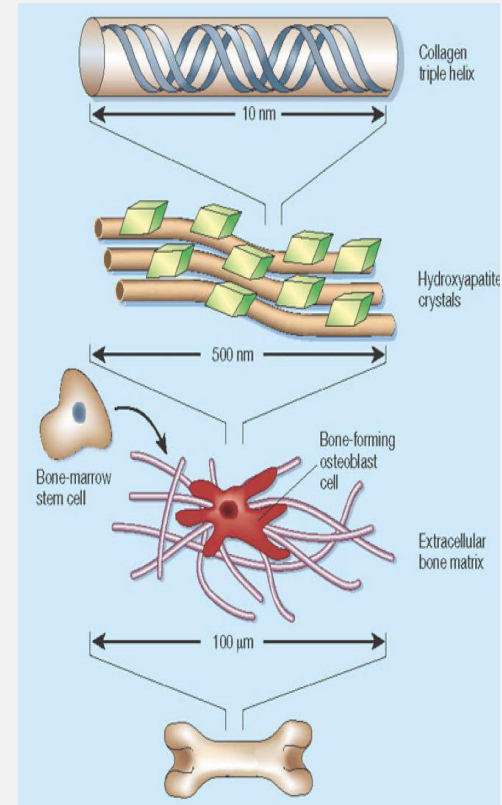
Mechanism of Bone Calcification



Osteoid نسيج يشبه الغضروف (مائل الكالسيوم) ، مهياً لترسب أملاح الكالسيوم عليه

Tensile and Compressional strength of bone

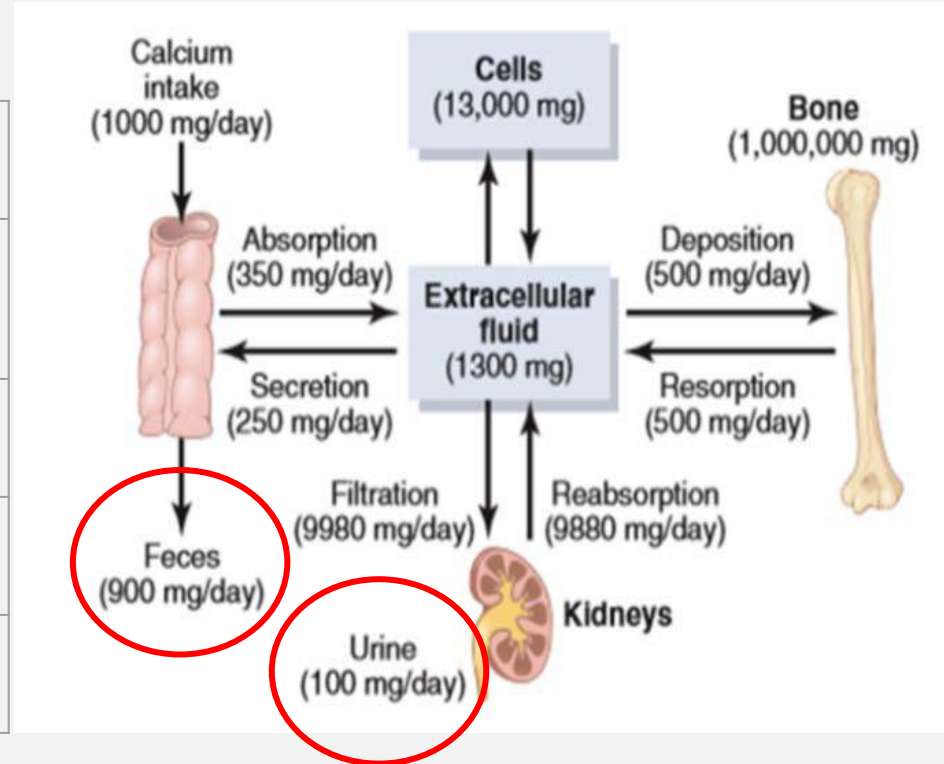
- The **collagen fibers** of bone, like those of tendons, have great **tensile strength**.
- The **Calcium salts** have great **compressional strength**.
- These combined properties plus the degree of bondage between the collagen fibers and the crystals provide a **bony structure** that has **BOTH** extreme tensile strength **AND** extreme compressional strength.
- N.B **Hydroxyapatite** crystals **fail to be formed in normal tissues EXCEPT** in bone despite the High level of Ca & P ions due to the presence of an **inhibitor of precipitation called Pyrophosphate**.



Calcium Homeostasis in human body

- 1.5% of body weight is Calcium.
- About 1100 - 1300 gm,
- 99% is in the skeleton.

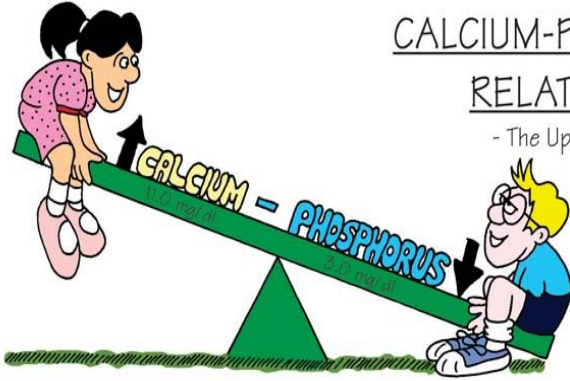
	Calcium	Phosphorus
Total body content	1,300 g	600 g
Relative tissue distribution		
Bones & teeth	99%	86%
Extracellular fluid	0.1%	0.08%
Intracellular fluid	1.0%	14%



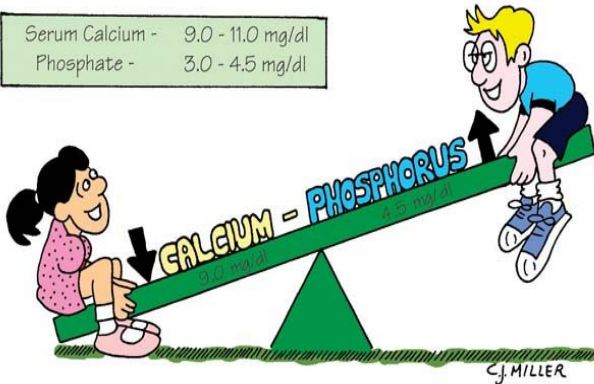
Serum Calcium and Phosphate

CALCIUM-PHOSPHORUS RELATIONSHIP

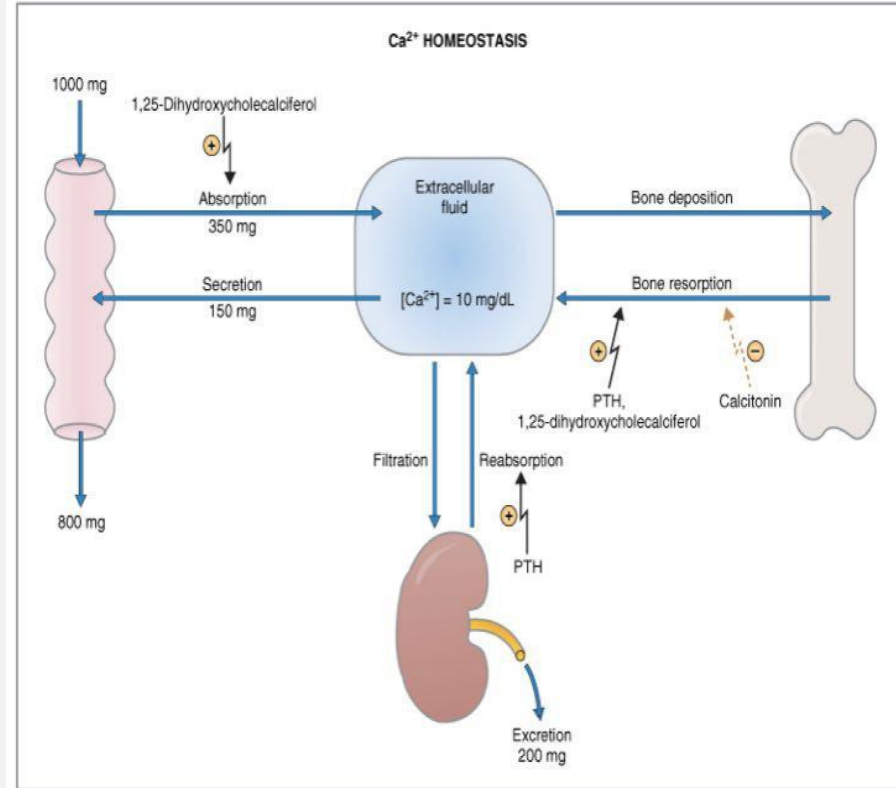
- The Ups and Down -



Serum Calcium -	9.0 - 11.0 mg/dl
Phosphate -	3.0 - 4.5 mg/dl



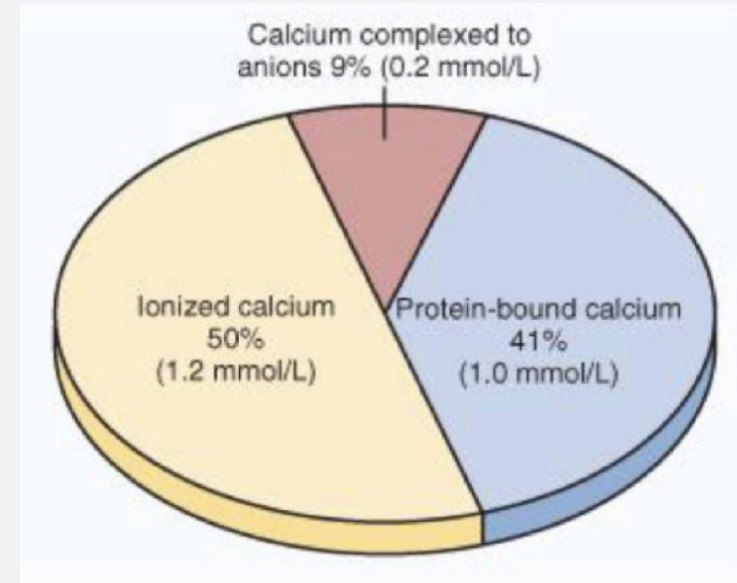
C.J. MILLER



Plasma Calcium

- Plasma calcium level: 9 - 11 mg/dl. Average: 9.4 mg/dl
- 59% (Diffusible) = Ionized + Complexed
- 41% (Non diffusible) = Protein bound

- Plasma calcium level is important to know if calcium level is normal or not.



Calcium exchange between Bone and ECF

01

The bone contains a type of exchangeable calcium that is **always** in **equilibrium** with the Ca^{++} ions in the ECF

02

It normally amounts to about **0.4-1%** of the total bone calcium.

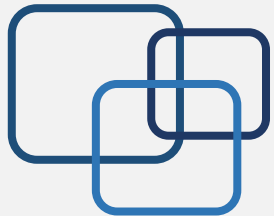
الـ Exchangeable Calcium
عبارة عن كالسيوم أقل ارتباطاً بالعظم
وقابل للإفصال في حال حصل خلل في
تركيز الكالسيوم في الـ ECF

03

This calcium is a form of **readily mobilizable** salt such as **CaHPO_4** and other amorphous calcium salts.

04

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



Remodeling of Bone

Bone is continually deposited by **osteoblasts**, and absorbed where **osteoclasts** are active.

Osteoblasts

The renewal rate is about 4% per year for compact bone and 20% per year for trabecular bone.

العظام تستمر في التجدد بنسبة بسيطة "تقريبًا ثابتة" في الحالات الطبيعية (ليس فقط في حالات الكسور أو الأمراض) ويحدث لكل أنواع العظام (Compact and Trabecular)

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

Osteoblasts are found on the outer surfaces of the bones and in the bone cavities.

They are normally active on less than 1% of the bone surfaces of an adult.

The osteoclasts secrete two types of substances:

Normally active to phagocytosis the old bones, dead bone, etc.

several acids from the mitochondria and secretory vesicles.

proteolytic enzymes from the lysosomes

solution of the bone salts.

dissolve the organic matrix.

The function of Substances:

The bone remodeling process

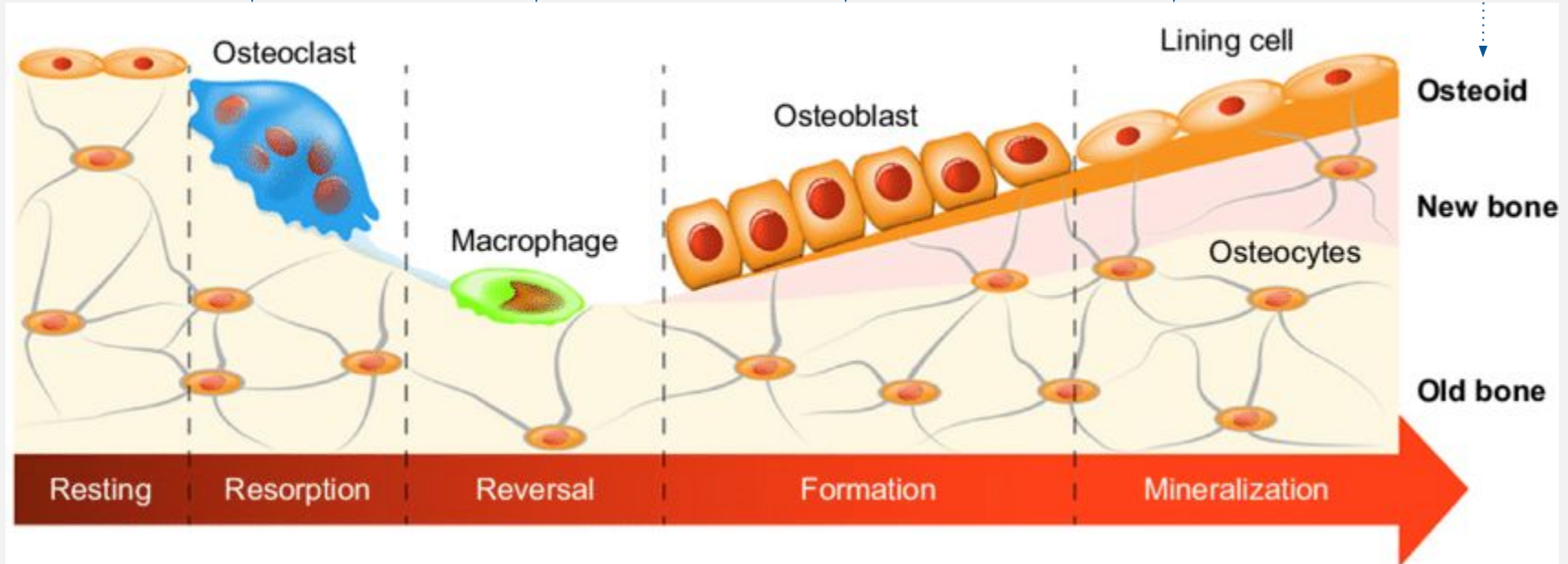
Osteoclasts cells are phagocytose the old bone, that called "resorption"

then macrophages cleans the area and remove the osteoclasts with their substances

Osteoblasts cells are forming new bone and producing new matrix

Osteoblasts cells will complete their life cycle and go through the new bone in form "osteocytes"

made of bone collagen without deposit the calcium and phosphate



Importance of Continual Bone Remodeling



Control of the Rate of Bone Deposition by Bone "Stress"

1

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

2

The **shape of the bone** can be rearranged for **proper support** of mechanical forces.

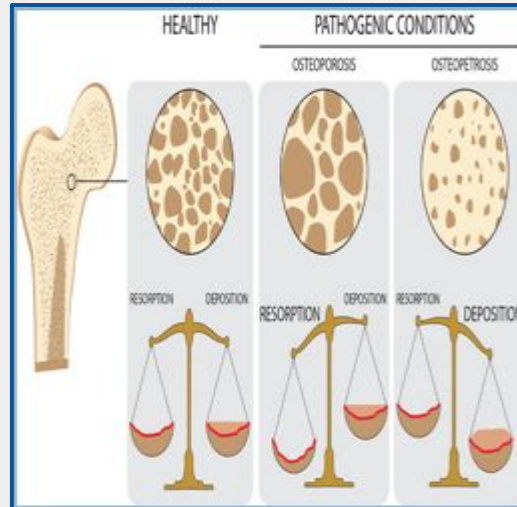
3

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

As we said in previous slide: the old bone is phagocytosis osteoclasts, while the new Organic matrix is produced by osteoblasts

The **bones of children** are less brittle due to more remodeling in the children.

بما أن العظام تتأثر قوتها بمقدار الضغط عليها فهذا يعني أن عظام الرياضيين أقوى، بينما العظام التي لا تستعمل "مثل العظام مع الجبيرة بعد الكسور" تصبح أضعف بسبب عدم استعمالها



Bone is **deposited** in proportion to the **load** that it must carry.

هذا يعني أن زيادة الضغط على العظام يحفز ترسب الكالسيوم وبالتالي الكالسيوم يرفع الصلابة والقوة للعظم المتأثر بالضغط

Continual **physical stress** stimulates osteoblastic **deposition** and **calcification** of bone.

The bones of **athletes** become considerably **heavier** than those of non athletes. (the bone of the leg in the cast becomes thin and up to 30 % decalcified within a few weeks)

Bone stress also determines the **shape of bones** under certain circumstances. (e.g. Healing of fractures may start angulated in children then become straight).

In healthy individual there's balance between resorption by osteoclasts and deposition by osteoblasts, but if there's more resorption that lead to osteoporosis, and more deposition lead to osteopetrosis



Repair of a Fracture Activates Osteoblasts

Fracture of a bone activates all the periosteal and intrasosseous **osteoblasts** involved in the break.

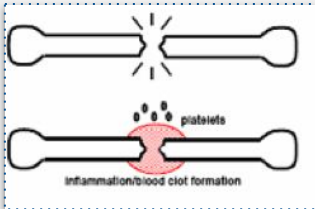
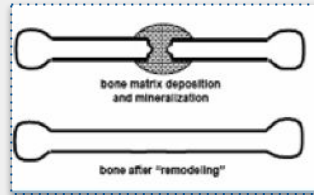
Large numbers of new osteoblasts are formed from osteoprogenitor cells, which are bone stem cells in the surface tissue lining bone, called the "bone membrane".

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 a callus.

الكسر راح ينشّط الـ
Osteoblasts
الموجودة في
Periosteum and intrasosseous
Inflammation وبيصير في مكان الكسر

The osteoprogenitors are responsible for producing new osteoblasts, they are found in bone membrane "The periosteum"

في مكان الكسر راح يتكون عندنا
group of osteoblasts that make osteoblastic
tissue and produce new organic matrix
وراح يكون عبارة عن
soft bone
ولكن خلال فترة قصيرة راح يترسب عندنا الكالسيوم
وبيتحول العظم إلى
Hard bone
وهذي العملية نسميها
Callus



Hormonal Control

of Calcium Metabolism & Physiology of Bone

1, 25 dihydroxycholecalciferol:
a steroid hormone formed from Vitamin D.

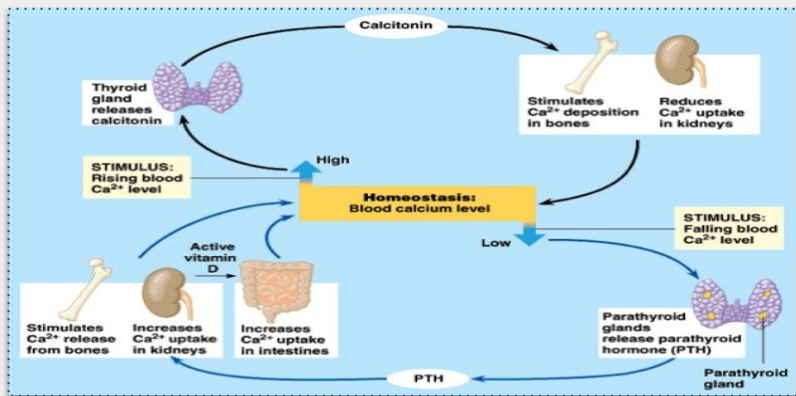
Parathyroid hormone (PTH):
secreted by parathyroid gland.
when the blood Ca level is low

Increase Ca absorption (indirect via 1,25 dihydroxycholecalciferol)

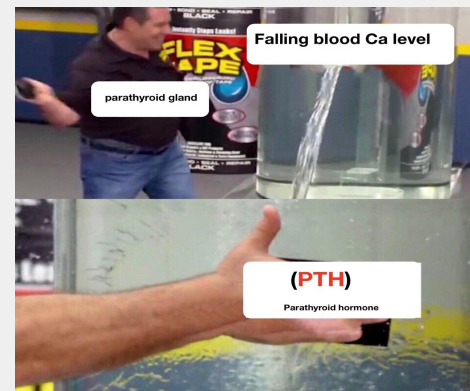
Calcitonin: secreted by c-cells in the thyroid gland.
when the blood Ca level is high (**inhibit osteoclasts while osteoblasts continue to lock calcium in bone matrix.**)

To a lesser extent ;
Glucocorticoids, GH, estrogens & various growth factors.

They don't have direct role

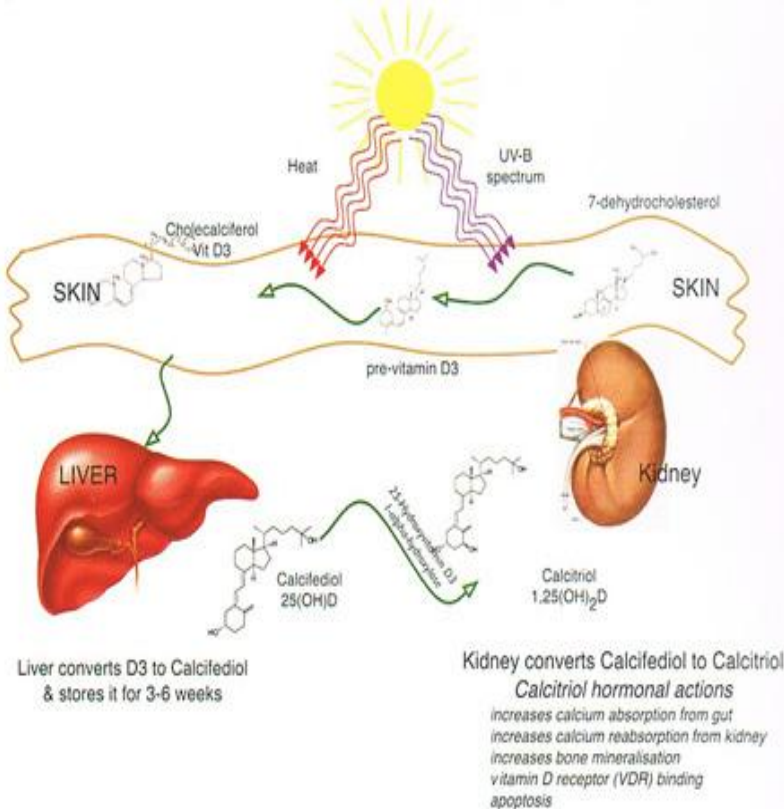


شرح الصورة
بإختصار عشان بصير عندنا توازن داخل الجسم نحتاج مستوى الكالسيوم يكون ثابت وهذا الثبات يحصل من خلال الهرمونات بحيث لما ينخفض الكالسيوم راح يُفرز PTH from Parathyroid gland ولما يكون عندنا ارتفاع راح يُفرز Calcitonin from C-cell





Vitamin D



VITAMIN D – ACTION OF CALCITRIOL



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

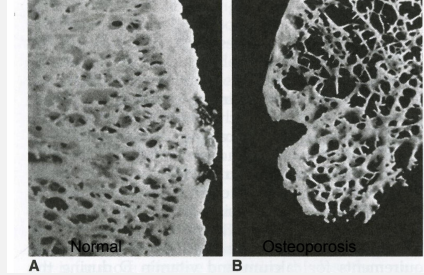
➤ Mineralization of bone at low doses

➤ Mobilization of calcium from bone at high doses

➤ Increased reabsorption of calcium and phosphorus

➤ Decreased excretion of calcium and phosphorus

Osteoporosis



meaning: reduced bone density and mass.

Is caused by a relative excess of osteoclastic function . Loss of bone matrix is marked . Matrix and mineral are both lost and there is a loss of bone mass due to :

Lack of physical stress

Malnutrition, lack of vitamin C

Old age, Postmenopausal lack of estrogen.

Cushing's syndrome.

Complications of Osteoporosis:

The incidence of fractures is increased particularly in the **distal forearm** (colles fracture), **vertebral body**, and **hip**. These areas have a high content of trabecular bone, which is more active metabolically, it is lost more rapidly.

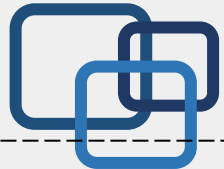
Fractures of the **vertebrae** with kyphosis produces “widow’s hump” in elderly women with osteoporosis.

Fractures of the **hip** in elderly are associated with a mortality rate of 12–20%, and 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.

S U M M A R Y

- Bone is a special form of connective tissue.
- Involved in the body homeostasis (Ca^{++} & PO_4^- Homeostasis).
- There are two types of bone structure (Compact & Trabecular).
- Bone is composed of 30% organic matrix and 70% bone salts.
- Osteocyte is mature bone cell that maintains the bone matrix
- Osteoblasts secrete collagen (monomers) and ground substance (Proteoglycans).
- Collagen fibers are responsible for tensile extreme strength and calcium salts are responsible for extreme compressional strength.
- 99% of the body calcium in the skeleton and teeth .
- Calcium and Phosphate in serum have an inverse relationship.
- The diffusible plasma calcium can move freely inside and outside of the cell because they are an ionized.
- The importance of exchangeable calcium is that it provides a rapid buffering.
- Bone is continually deposited by osteoblasts, and absorbed where osteoclasts are active “this process called the bone remodeling process “ both types of bone cells are found in the bone surface.
- The rate of deposition is affecting by the stress on bone.
- There are a lot of hormones that maintain the blood calcium level.
- The osteoporosis is condition happen when there is increasing in absorption (reduce bone mass) and it has complications .



MCQs

Q1: After the osteoid is formed, calcium salts begin to precipitate on the collagen fibers forming the

A) Exchangeable Calcium	B) Hydroxyapatite crystals	C) Osteocytes	D) All of them
-------------------------	----------------------------	---------------	----------------

Q2 : Collagen fibers are responsible for which of the following EXTREME strength?

A) Tensile	B) Compressional	C) Both	D) None
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Q3 : Which of the following percentage that describe bone and teeth calcium?

A) 99%	B) 51%	C) 0.1%	D) 0.01%
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Q4 : The several acids which produce from osteoclasts are cause:

A) solution of the bone collagen.	B) dissolve the organic matrix.	C) solution of the bone salts.	D) dissolve the inorganic matrix.
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Q5 : In repair of a fracture there are Large numbers of new osteoblasts are formed from:

A) Osteoclasts cell	B) osteoprogenitor cell	C) Osteocytes cell	D) osteoporosis
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Q6 : If there is decreasing of blood calcium level that lead to release:

A) Calcitonin	B) Parathyroid hormone (PTH)	C) 1, 25 dihydroxycholecalciferol	D) both B and C
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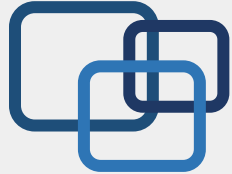
SAQs

Q1: What are the bone functions?

Q2: what are the causes of osteoporosis?

MCQs key answer :
6) D
5) B
4) C
3) A
2) A
1) B

SAQ answer key :
1) Protects vital organs, Stores and releases P04 + Ca
Produces blood cells, Facilitates movement, Supports the body. (Slide 3)
2) Lack of physical stress, Malnutrition, lack of vitamin C, Old age, Postmenopausal lack of estrogen, Cushing's syndrome.



THANK
you 😊

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