MEDICINE
KING SAUD UNIVERSITY

Physiology Team 436

Physiology of Bone

Revised by
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Red: very important.
Green: Doctor's notes.
Yellow: numbers.
Gray: notes and explanation.

Physiology Team 436 – Musculoskeletal Block Lecture 1

Lecture: If work is intended for initial studying.
Review: If work is intended for revision.

Objectives

- Define bone (slide3) and differentiate cortical & trabecular bone (sites and function of each). (slide 5,8)
- State the normal levels and forms of ca++ in the ECF and its relation to PO4. (slide 9)
- Identify the bone cells and the function of each. (slide 9)
- Define bone remodelling and explain the mechanism of bone formation. (slide 16,17)
- Define osteoporosis. (slide 26,27)
- Discuss the effect of different hormones on bone physiology. (slide 21-25)

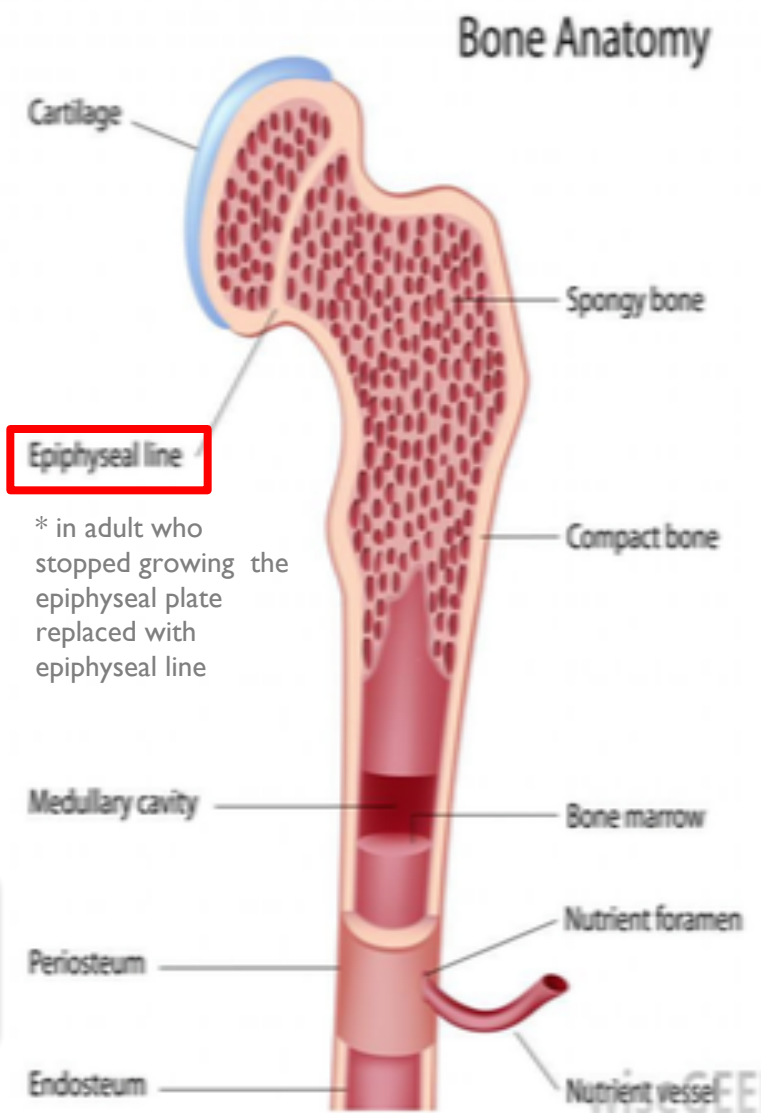
Physiology of Bone

- Bone is a special form of connective tissue.
- It is well vascularized with total blood flow of 200–400 mL/min in adult humans.

The epiphyseal plate : it is a plate of actively proliferating cartilage, it separates the ends (epiphysis) from the shaft of a long bone.

This separation allows linear bone growth.

Growth ceases (stops) after the epiphyses unite with the shaft **(epiphyseal closure).**



Functions of Bone:

1- Homeostasis of Ca++ and PO4.

2- Protects vital organs.

3- Permits locomotion and support against gravity.

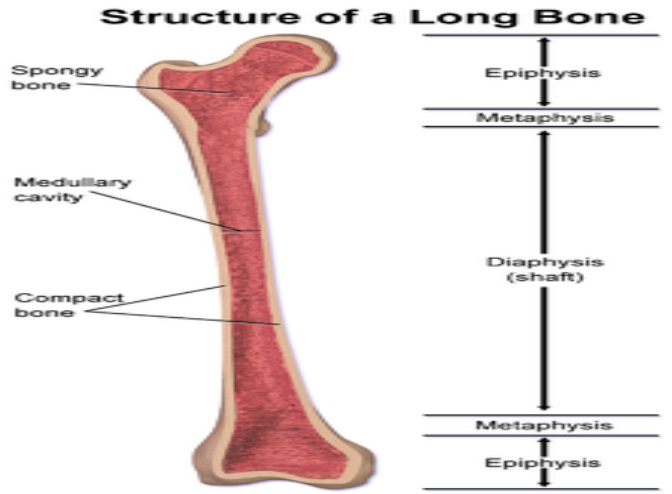
4- Formation of blood cells in the bone marrow.

5- Reservoir for calcium & phosphate.

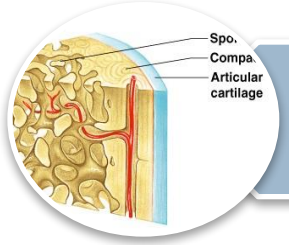
Types and structure of bone:

Types of bones

- 1- compact (cortical) 80%
- 2- spongy (trabecular) 20%

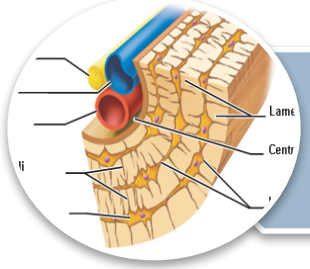


1- Compact Bone (Cortical Bone) 80%

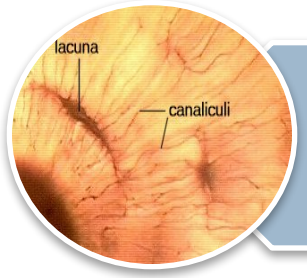


Site: in the outer layer of most bones, where there cells lie in lacunae (gaps).

Function: 80% of the body bone, it has high resistance to bending and torsion.



Compact bone has more bone tissue and less bone space.



Compact bone cells receive nutrients by way of **canaliculi** (a small channel or duct) from Haversian canals vessels.

Haversian System (Osteons)

Compact bone is formed of Haversian systems (Osteons)

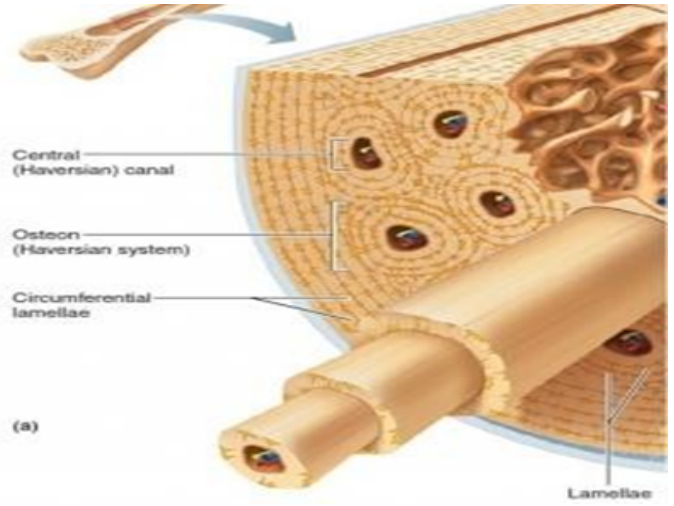
Osteons or Haversian systems are overlapping circular structures (formations)

Each osteon has a central canal called Osteonic Canal or Haversian Canal

The Osteonic Canal contains : blood vessels (capillaries, arterioles, venules), nerves and lymphatic's.

Between Haversian systems are concentric layers of mineralized bone called interstitial lamellae

Collagen is arranged in concentric layers, around the Haversian canals forming cylinders called osteons or Haversian systems.



للتوضيح :

- لدينا تركيب يسمى osteon وهو عبارة عن دوائر متداخلة وبأخر دائرة توجد قناة تسمى osteonic canal هذة القناة يوجد بها الأوعية الدموية.

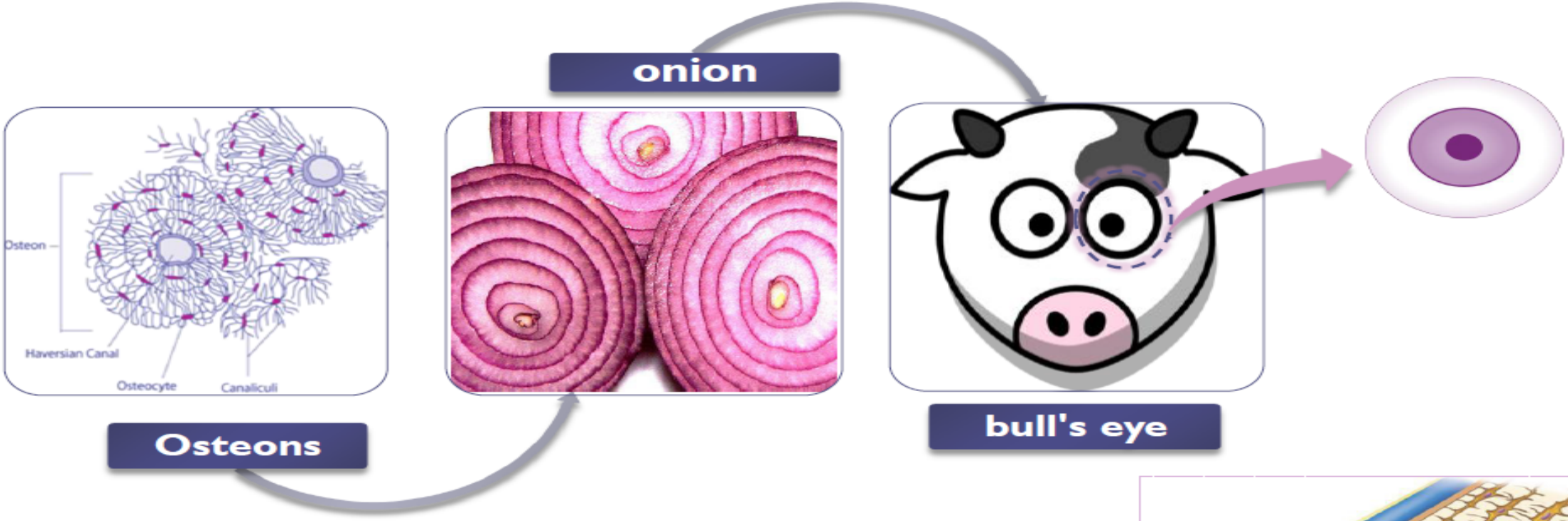
- ال compact Bone يتكون من أكثر من ال osteons متجاورة فنسمي -هذا التجمع – أو النظام ب Haversian System

- هذا النظام لا يوجد إلا بال compact Bone وهو ما يعطيه الصلابة

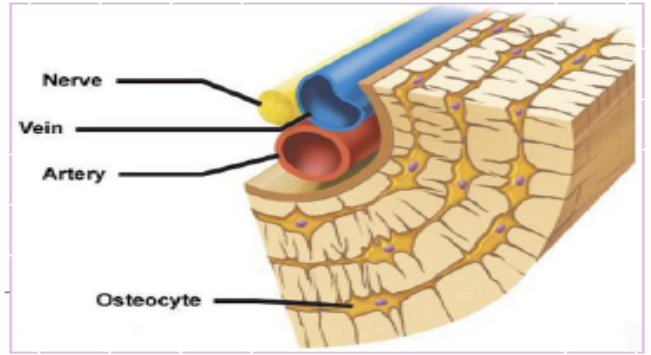
Haversian system is the fundamental functional unit of much compact bone.

Extra Notes
"compact bone"

From 435

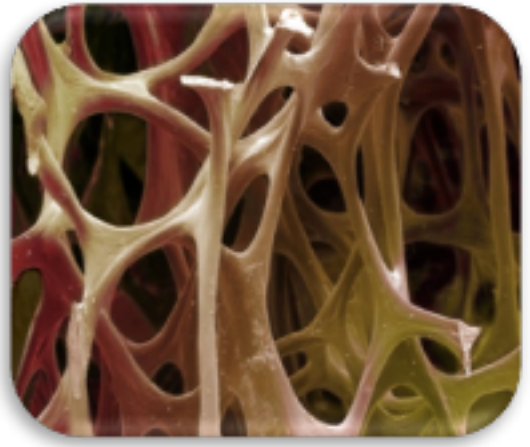


- Cortical = cortex = قشرة خارجية
- Osteons resemble : cow's eye .
- Concentric lamellae "onion-like" = صفائح متحدة المركز
- Hervesian system has central canal " hervesian canal" that consist of blood vessels, nerves, venules and arteries.



2- Spongy Bone (Trabecular Bone) 20%

- **Site : inside the cortical bone .** Remember : compact bone Is forming the OUTSIDE layers of Bones, while the spongy forms the INSIDE layers of the bones.
- Though it represents only 20% of the skeletal mass, it has 5 times greater surface area than cortical bone.
- Function : Because of its large surface, it has faster turnover rate than cortical bone; hence it is more important than cortical bone in terms of calcium turnover.
- made up of spicules or plates.
- Nutrients diffuse from extracellular fluid (ECF) of bone, into the trabeculae.
- The center of the bone contains red, yellow marrow, bone cells and other tissues.



Compared to cortical bone , it is:
(1) less dense, (2) more elastic and (3) has a higher turnover rate than compact bone.

Calcium turnover:
حركة الكالسيوم من العظم للدم والعكس

NOTE : ال compact Bone يشكل 80% من عظام الجسم كلها ولكن ال spongy bone يشكل 80% من العظم الواحد فيأخذ مساحة أكبر بالعظم الواحد ، غالباً يكون الجزء الأكبر من ال FLAT BONES ولهذا السبب لها مساحة كبيرة.

Composition of Compact Bone (Cortical Bone)

Bone Cells:	Matrix:
1) Osteoblasts: immature bone forming cells that: - Secrete collagen -> forming a matrix around themselves -> which then calcifies. - Then when the bone forming cells are surrounded by calcified matrix they are called **osteocytes**. - **Function:** regulating Ca and Phosphate concentration in bone fluid.	**1) Organic matrix**: 30% (contains carbon) A- Collagen fibers Type I (90-95%): extend along the lines of tensional force to give the bone its tensile strength. (more in next slide) B- Ground substance 5-10% of ECF and Proteoglycans (chondroitin sulphate and hayluronic acid).
2) Osteocytes: are mature osteoblasts surrounded by calcified matrix. (more explanation in next slide) They send processes into the canaliculi that ramify throughout the bone.	**2) Bone salts**: 70% (Inorganic) - Crystalline salts of Ca++ & PO4 (Hydroxyapatite). - The ratio of Ca/P ratio is 1.5 – 2. - Other secondary components: Mg+, Na+, K+, Carbonate ions Exception: Newly formed bones have a higher percentage of matrix (collagen) in relation to salts.
3) Osteoclasts: multinuclear cells **Function :** that erode and resorb previously formed bone, by phagocytosis and digesting it in their cytoplasm.	

Ratio is 1.3 – 2 in boys slide .

Mechanism of Bone Calcification

Osteoblasts: secrete **collagen** (monomers) and ground substance (**proteoglycans**).

The collagen monomers polymerize to **collagen fibers.**

The resultant tissue becomes **osteoid**, a cartilage-like material.

It differs from cartilage in that calcium salts readily precipitate in it. (has ability to be calcified).

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

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

*للتوضيح : ال osteoblast في النسيج العظمي تفرز collagen حول نفسها بعدها راح يصير في النسيج collagen fibers وعندها يسمى هذا النسيج ب osteoid ، ثم يبدأ الكالسيوم بالترسب والأرتباط بالكولاجين مما يكون hydroxyapatite crystals.

حين تنتهي هذة العملية يكون قد تكون حول ال ostoblast ال osteoid فتنتهي مهمتها فتتحول لل Inactive form اللي هو الosteocytes

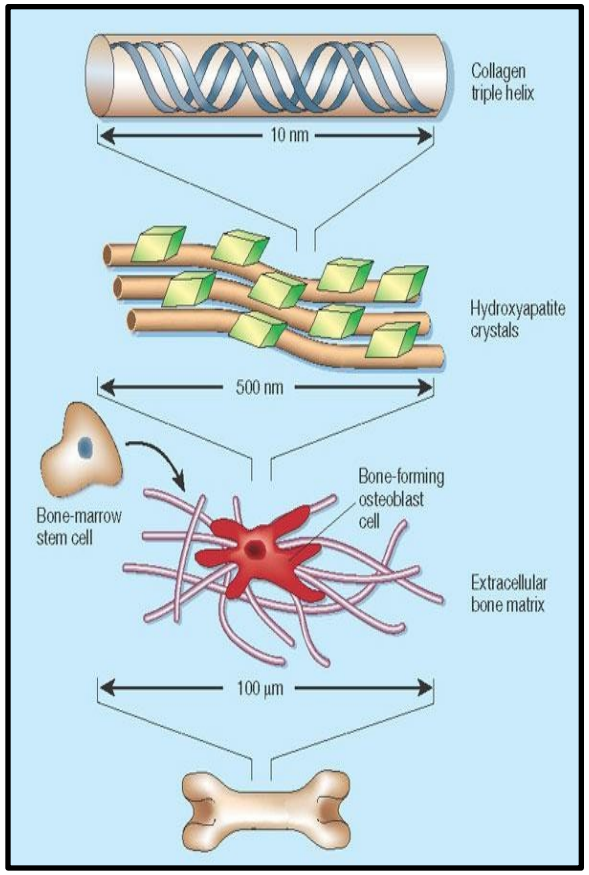
Tensile and Compressional Strength of Bone

1) Collagen Fibers like those of tendons have great **tensile** strength.

2) Calcium salts have great **compressional** strength.

These combined properties plus the degree of bondage between collagen and crystals provide the bony structure that has the tensile and compressional strength.

هذه الصورة تخص السلايد اللي قبل.



N.B: hydroxyapatite crystals fail to be formed in normal tissues except in bone, despite the high levels of Ca & P ions, due to the presence of an inhibitor of precipitation called **pyrophosphate.**

للتوضيح: لماذا لا يتكون الhydroxyapatite crystals في الأنسجة الأخرى غير العظام ؟ مع الرغم من وجود الكولاجين والكالسيوم فيهم ؟ لأن الأنسجة الأخرى تحتوي على مثبط لأرتباط الكالسيوم بالكولاجين يسمى ب pyrophosphate

Calcium Levels

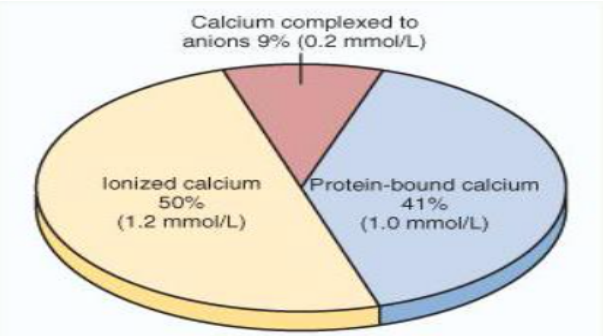
Body Calcium Levels:
نسبته في الجسم ككل

→ 1.5% of body weight
1100 to 1300 grams

Calcium Levels:

- **Intracellular calcium** → 99% is in the skeleton.
- **ECF calcium:**
  - Plasma calcium level : (9 -11 mg/dl)
    Average: 9.4 mg/dl
  - 59% (diffusible) = ionized + Complexed
  - 41% (non diffusible) = protein bound

	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%

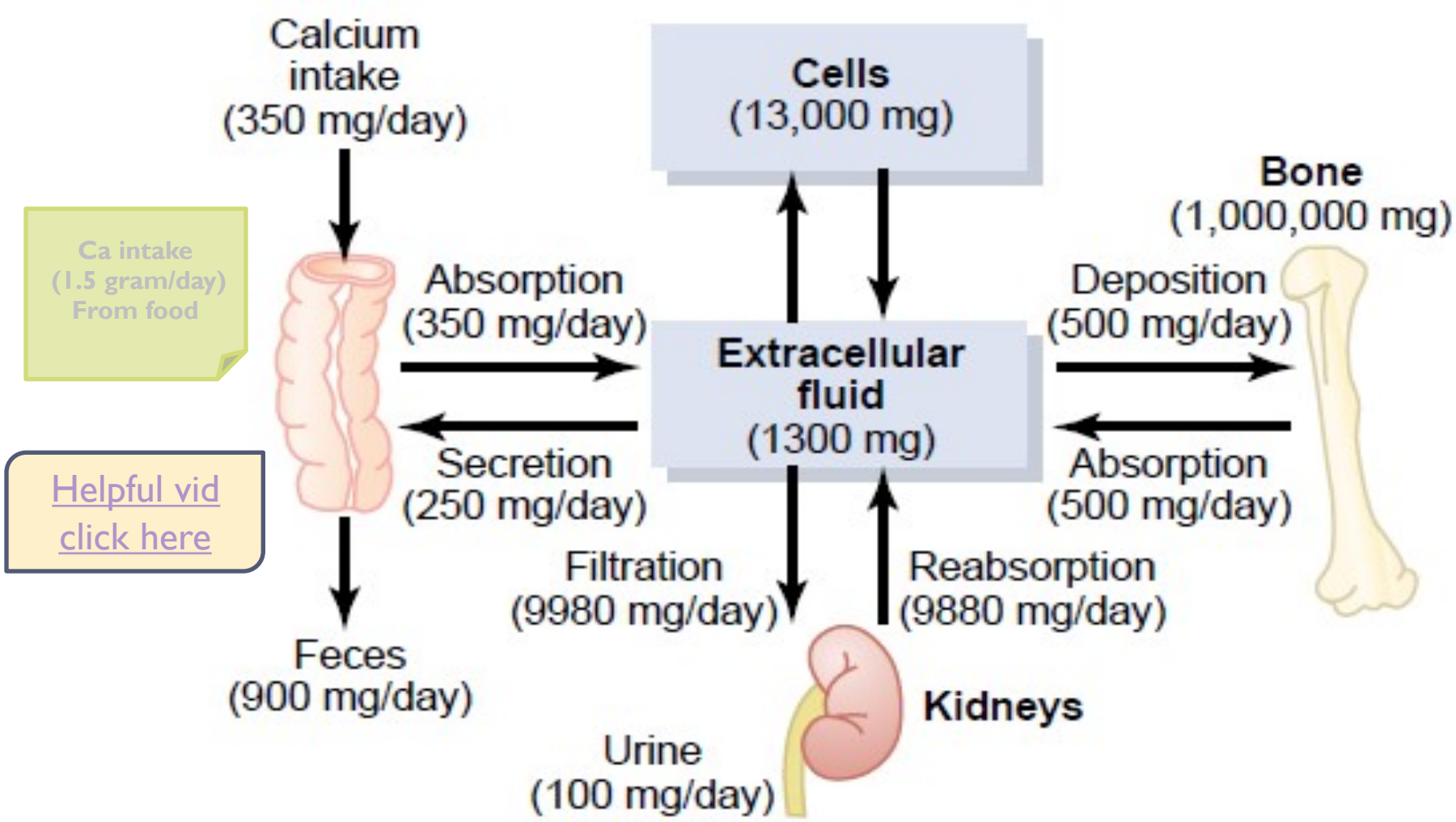


Calcium complexed anions:
يكونdiffusible ولكن لا يدخل في metabolic or biologic reactions.
Anions
EX :(PO4 , CO2)

Ionized calcium :
يكونdiffusible و يدخل في metabolic or biologic reactions
Ex:blood coagulation or muscle contraction.

Protein-bound calcium :
يكونBound وليسdiffusible ولا يدخل فيMetabolic reaction ولكنه يكون مثل المخزن للكالسيوم .

Calcium Homeostasis in Human Body



Ca intake (1.5 gram/day) From food

Helpful vid click here

Calcium enters our bodies from food then it is absorbed in the intestine to the ECF . It will either be deposited in the bone or in the cells; the excess is going to be excreted by the kidney

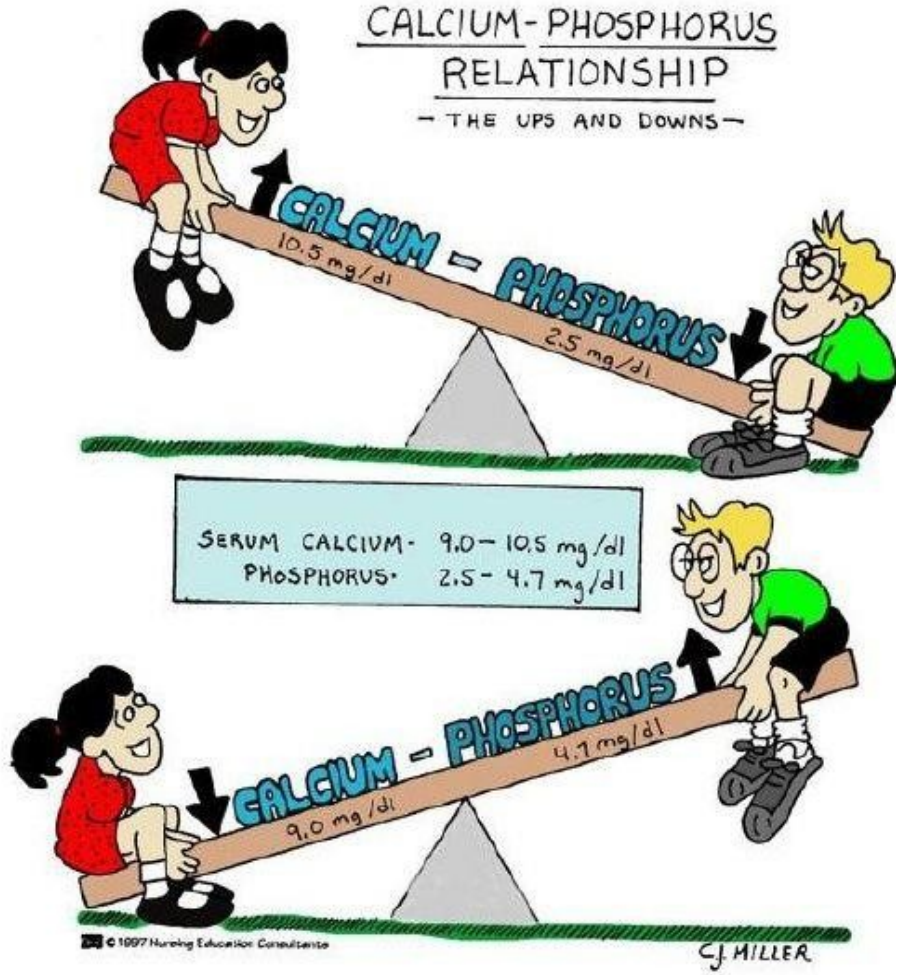
There is an exchange of Ca between the structures which is responsible for Ca homeostasis.

NOTE: No calcium = No blood coagulation

Serum Calcium and Phosphate

Calcium and phosphate in the body react in opposite ways : as blood calcium levels rise, phosphate levels fall and vice versa

إذا زاد الكالسيوم يقل الفسفور و العكس بحيث أن مجموعهم يكون ثابت (علاقة عكسية)



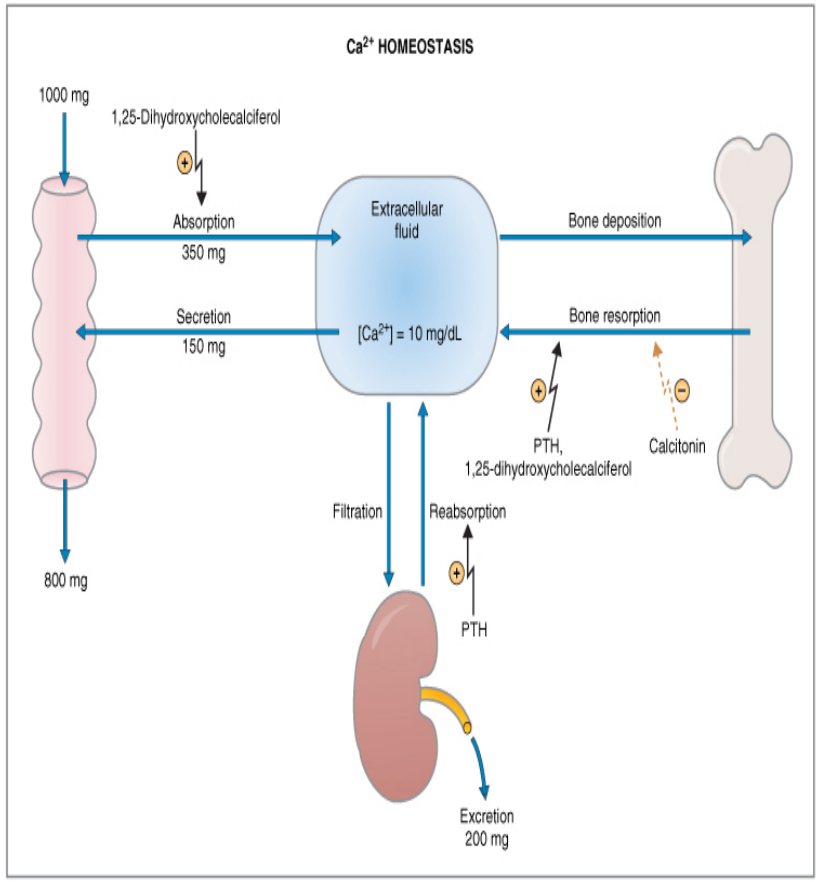


Figure 9-34 Ca^{2+} homeostasis in an adult eating 1000 mg/day of elemental Ca^{2+}. Hormonal effects on Ca^{2+} absorption from the gastrointestinal tract, bone remodeling, and Ca^{2+} reabsorption in the kidney are shown. PTH, Parathyroid hormone.

Exchangeable Calcium

- The bone contains a type of exchangeable calcium that is always in equilibrium with the Ca++ ions in the ECF.
- Calcium Exchange Between Bone and ECF.
- Normally,its amount is about (0.4-1%) of the total bone calcium
- This calcium is a form of readily mobilizable salt such as CaHPO4 and other amorphous calcium salts يعني يقدر انه يطلع من العظم بسهولة
- The importance of exchangeable calcium is that it provides a rapid buffering mechanism to keep the Ca++ ions concentration in ECF from rising to excessive levels or falling to very low levels under transient conditions of excess or decreased availability of calcium.

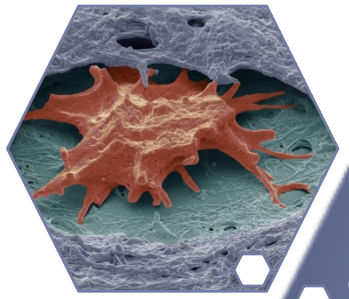
أهمية ال Exchangeable calcium أنه بمجرد إنخفاض تركيز الكالسيوم في الجسم الدم يتحرر من العظم ويرفع مستوى الكالسوم، والعكس صحيح فعد إرتفاع الكالسيوم في الدم علطول يرجع يرتبط بالعظم .

Deposition and Absorption of Bone (Bone Remodeling)

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

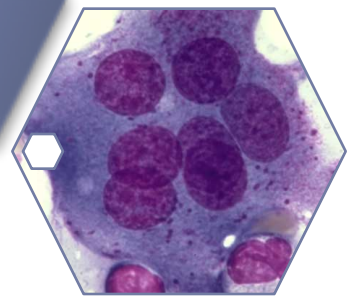
A small amount of osteoblastic activity occurs on about 4% of all bone surfaces at any given time in an adult, so that at least some new bone is being formed constantly (باستمرار).

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



Bone is continually deposited by osteoblasts

Absorbed where osteoclasts are active



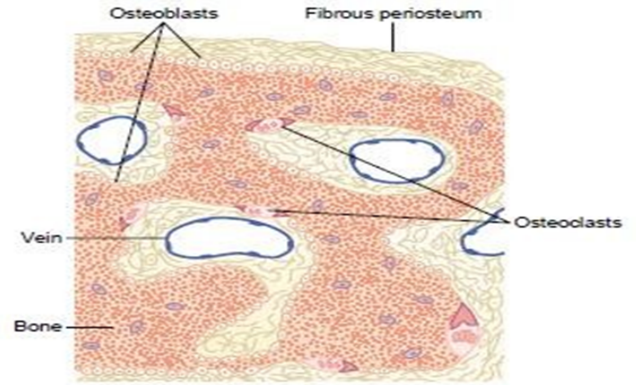
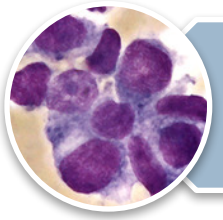


Figure 79–4

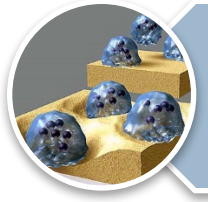
Osteoblastic and osteoclastic activity in the same bone.

Bone Absorption or Resorption

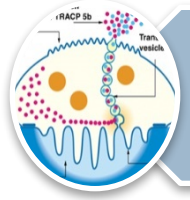


Osteoclasts are large phagocytic multinucleated cells,

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



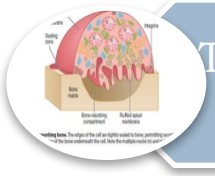
The shape of the bone can be rearranged for proper support of mechanical forces by deposition and absorption of bone in accordance with stress patterns.



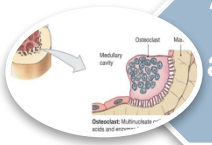
The osteoclasts secrete two types of substances:

1-proteolytic enzymes from the lysosomes

2-several acids from the mitochondria and secretory vesicles.



The enzymes dissolve the organic matrix, and the acids cause solution of the bone salts.



The osteoclastic cells also phagocytose minute particles of bone matrix and crystals, dissoluting them and releasing products (like: Ca) into the blood.

Value of Continual Bone Remodeling (أهمية إعادة تشكيل العظم)

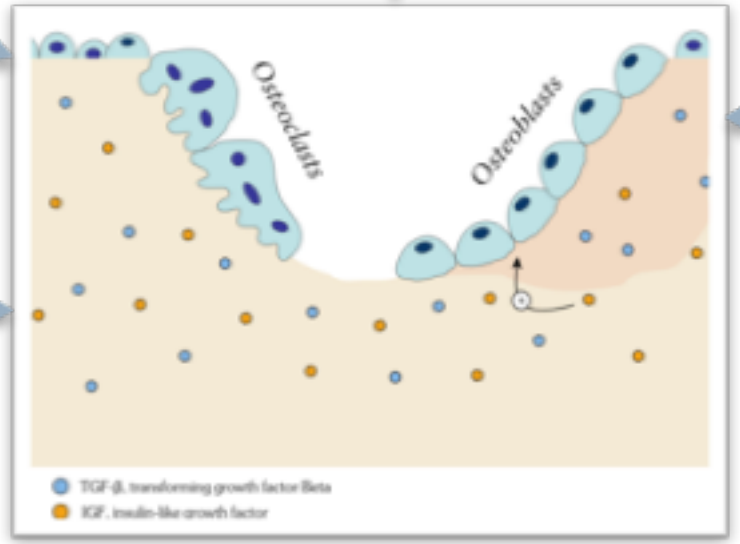
The shape of the bone can be rearranged for proper support of mechanical forces by deposition and absorption of bone in accordance with stress patterns

old bone becomes relatively brittle(هش) and weak; therefore, new organic matrix is needed as the old organic matrix degenerates . In this manner, the normal toughness(المتانة) of bone is maintained.

Video

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

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



عشان كذا الناس اللي تبذل مجهود أكبر و تشيل أشياء ثقيلة و تمشي أكثر تكون العظام عندهم أقوى

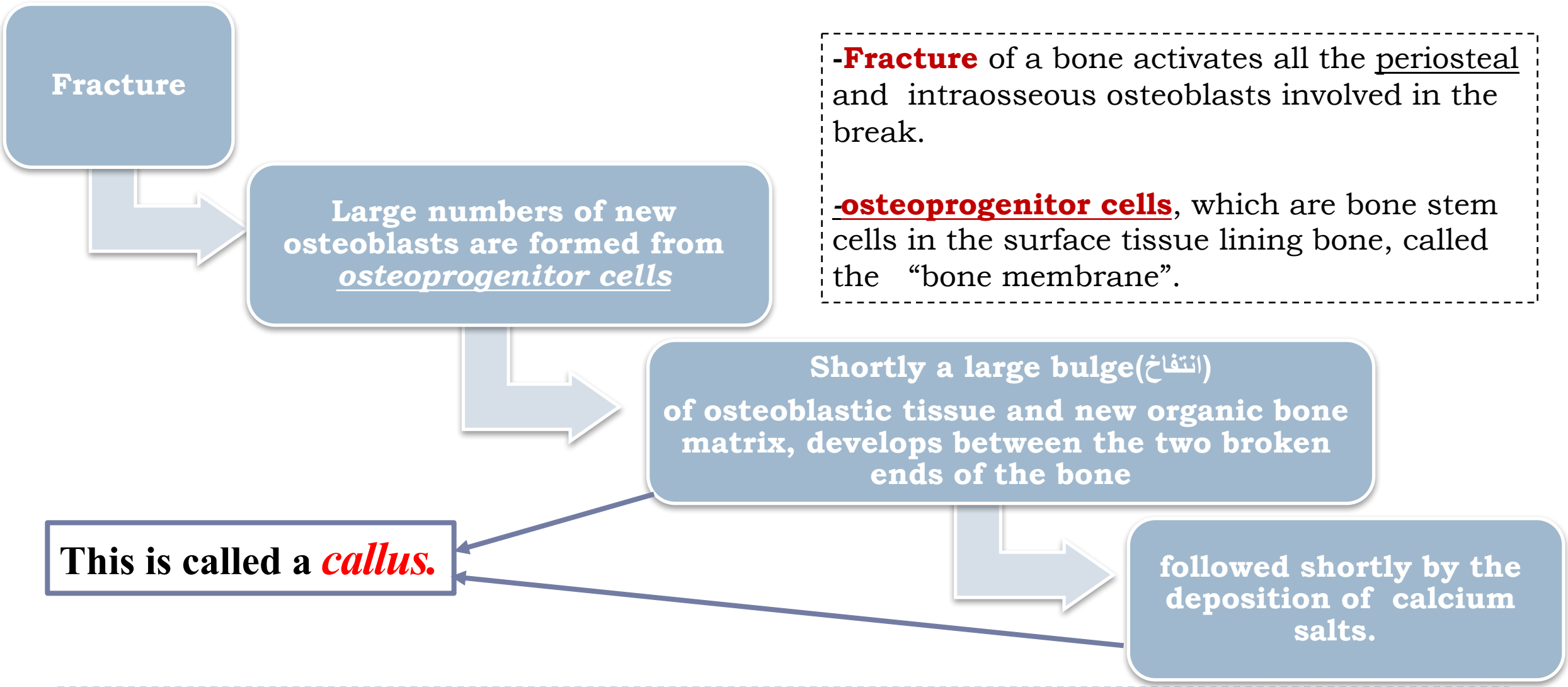
Control of the Rate of Bone Deposition by Bone “Stress”

كل ما زاد الstress
Bone deposition يزيد
و راح يكون العظم اثقل

- Bone is deposited in proportion to the load that it must carry.
- Continual physical stress stimulates osteoblastic deposition and calcification of bone.
- The bones of athletes become considerably heavier than those of no athletes. Also, 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).

وجدوا ان الأطفال اول ما يحصل لهم كسر ممكن الهيلينق للعظم يكون على هيئة انقل يعني ما يكون ستراايت ولكن مع مرور الوقت يكون الطفل يمشي على رجله المكسوره فراح يبدأ ال Deposition يسوي remodeling في هذي الأنقل مما يخليها ترجع ستراايت و طبيعية .

Repair of a Fracture Activates Osteoblasts

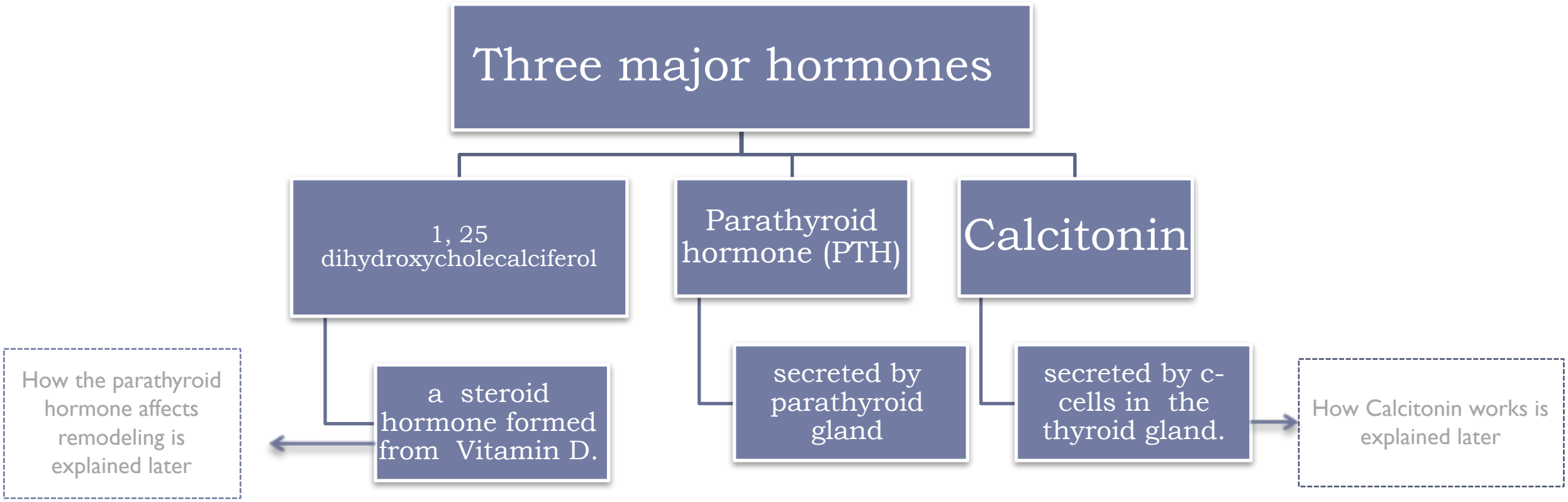


-**Fracture** of a bone activates all the periosteal and intraosseous osteoblasts involved in the break.

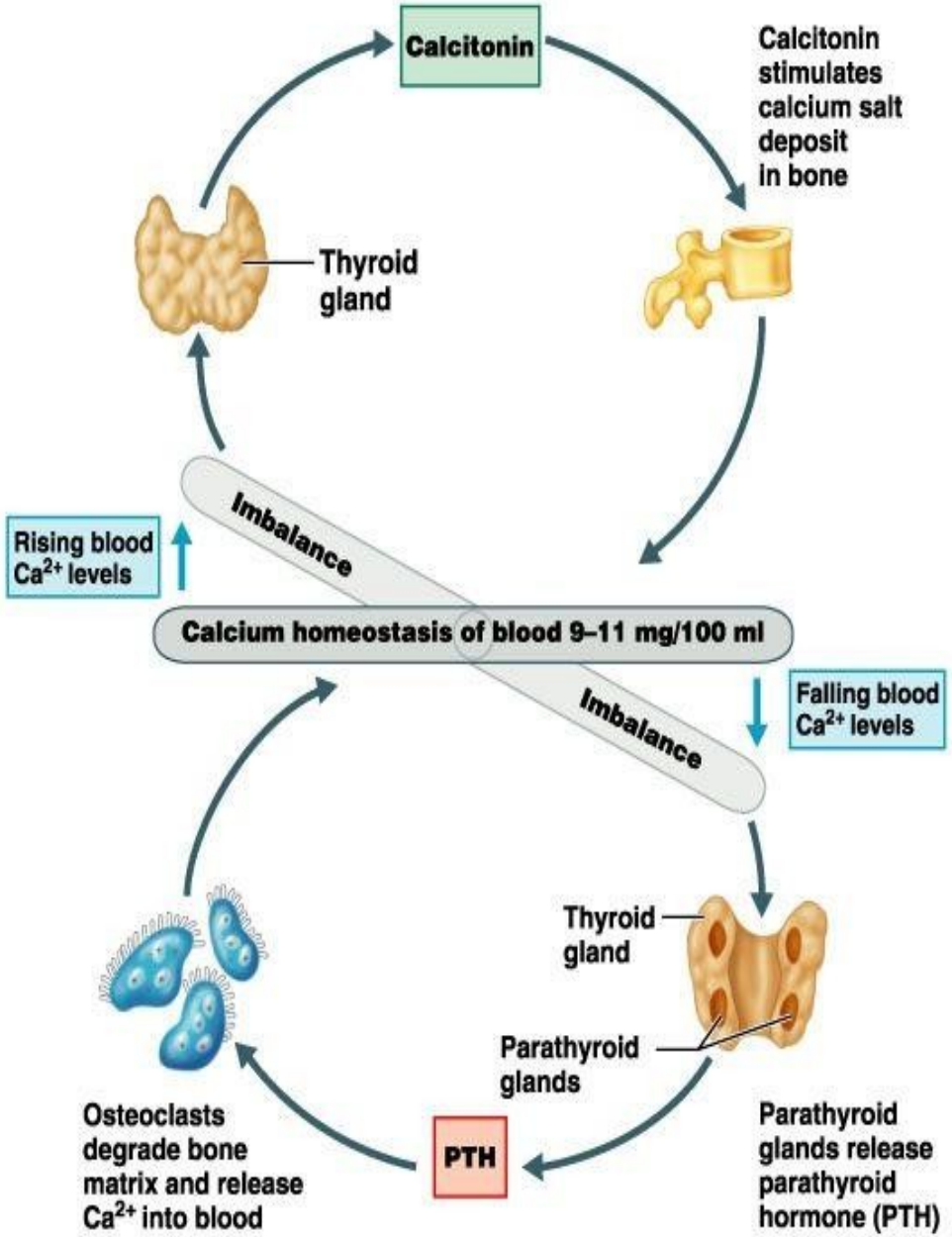
-**osteoprogenitor cells**, which are bone stem cells in the surface tissue lining bone, called the "bone membrane".

Periosteum: is a membrane that covers the outer surface of all bones

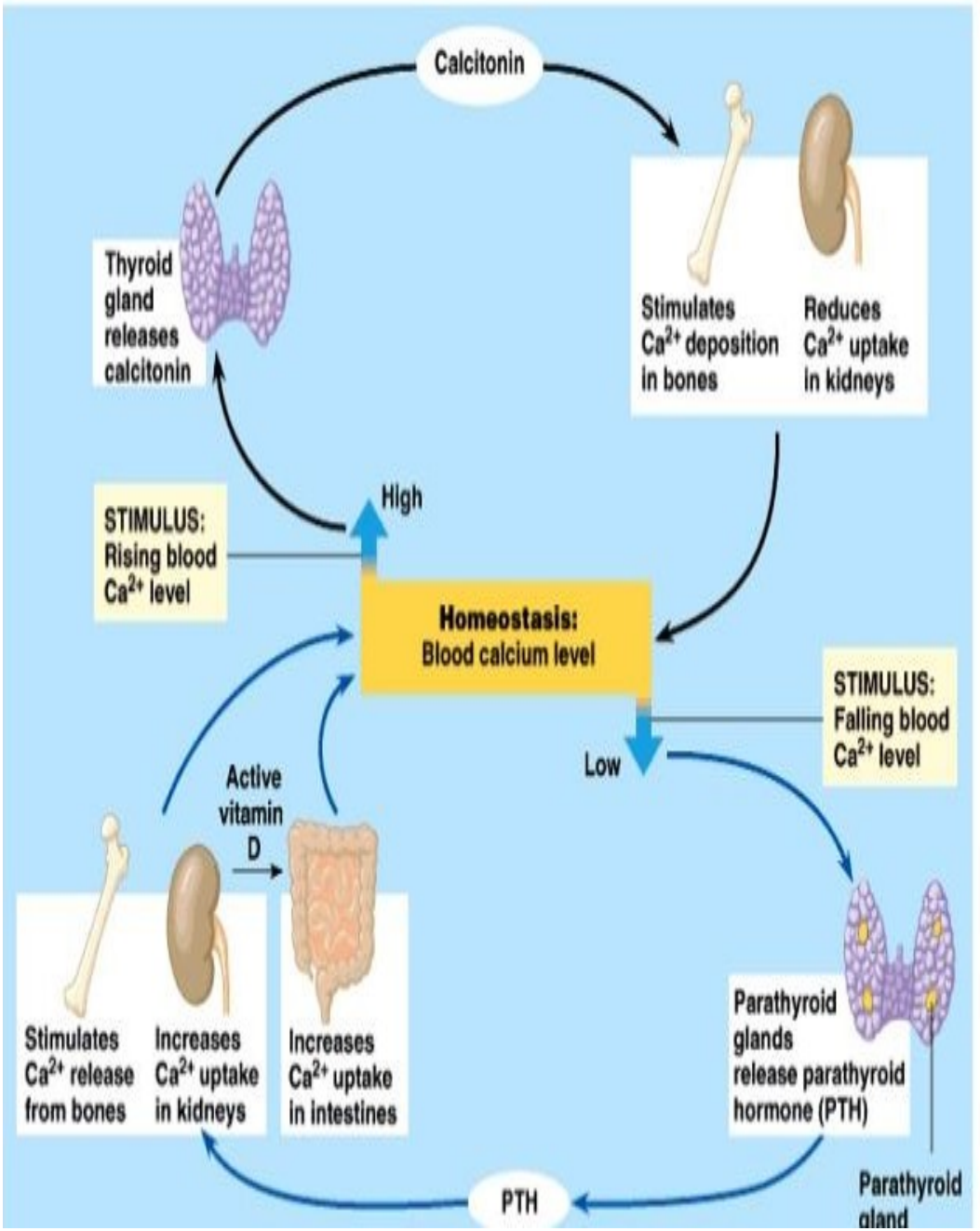
Hormonal Control of Calcium Metabolism & Physiology of Bone



To a lesser extent ; Glucocorticoids, GH, estrogens & various growth factors also affect Calcium Metabolism.



- If the Ca level in blood is high the thyroid gland will release calcitonin which will stimulate the Ca deposition in bone and reduce Ca uptake in kidney.
- If the Ca level in blood is low the parathyroid gland will release PTH which will stimulate Ca release from bone and increase Ca uptake in kidney and increase Ca uptake in intestines .



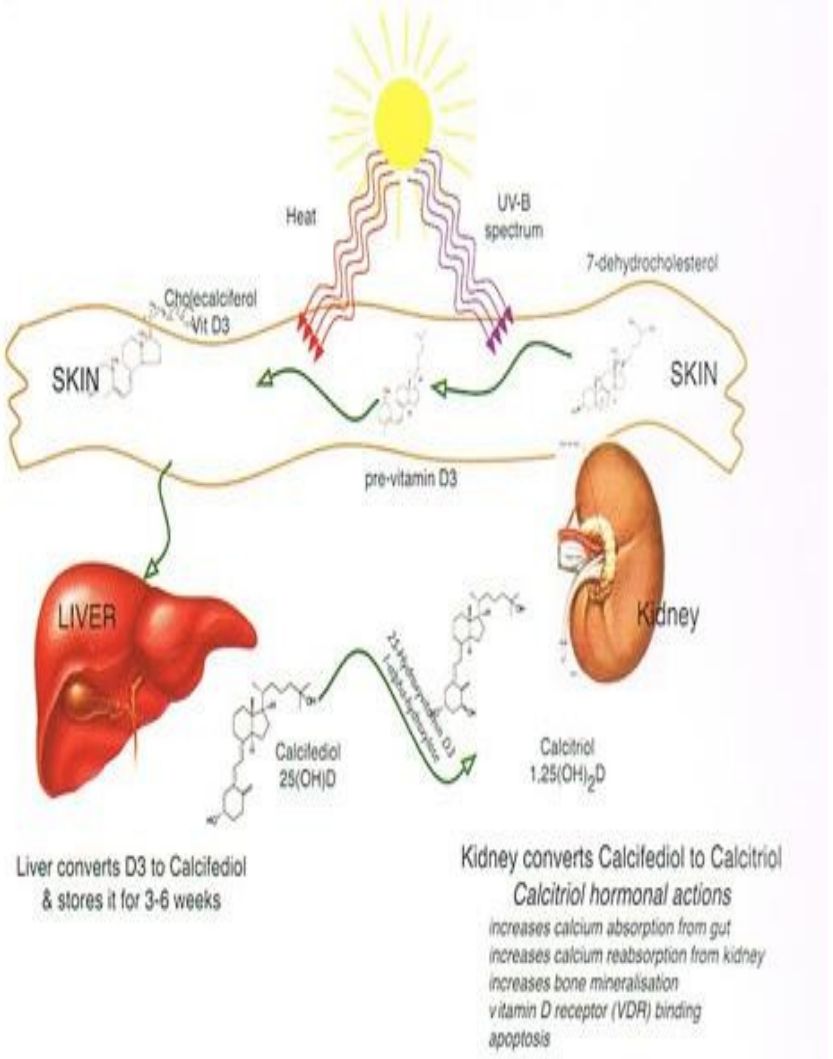
Vitamin D

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



Parathyroid Hormone (PTH)

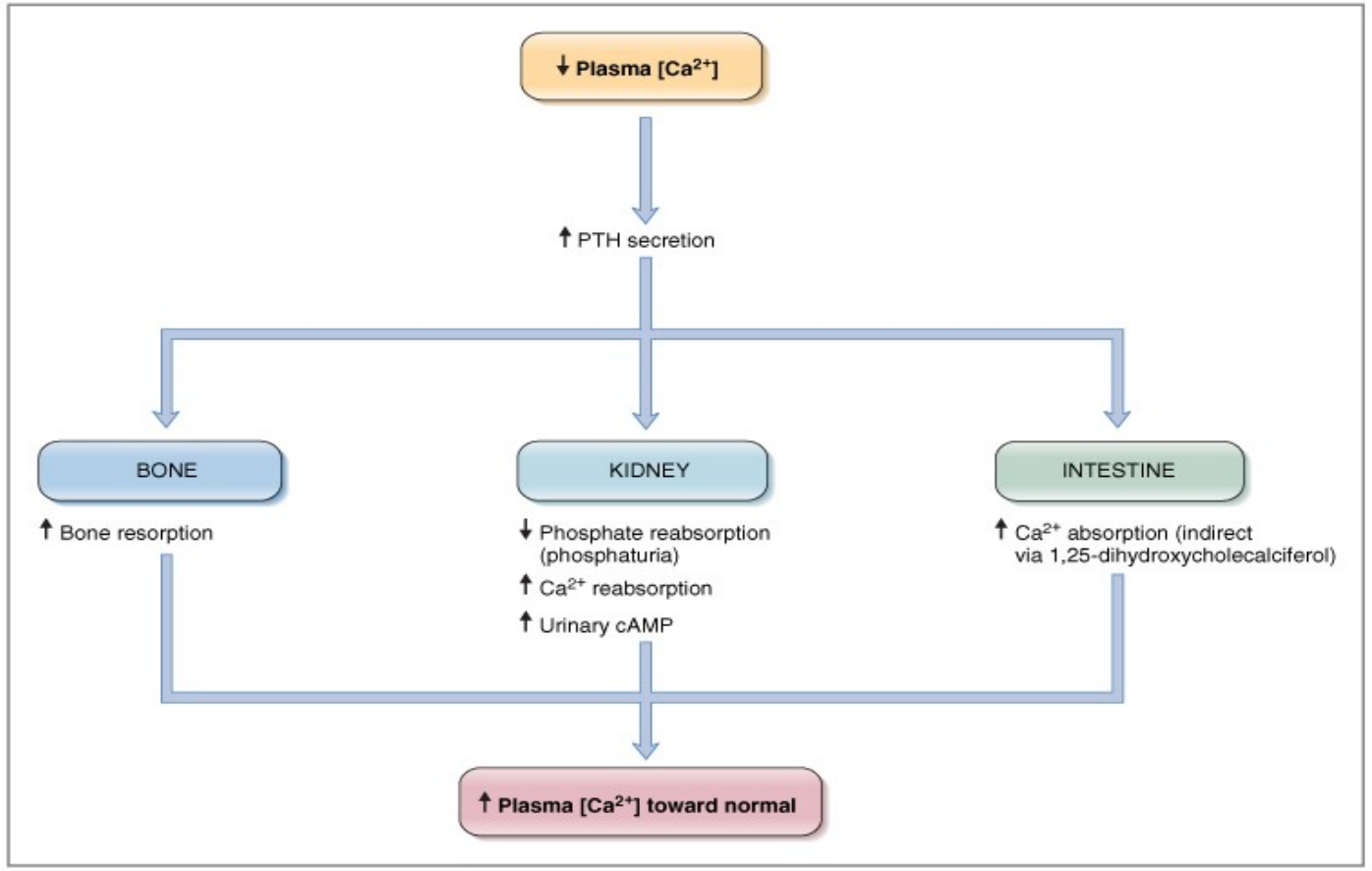
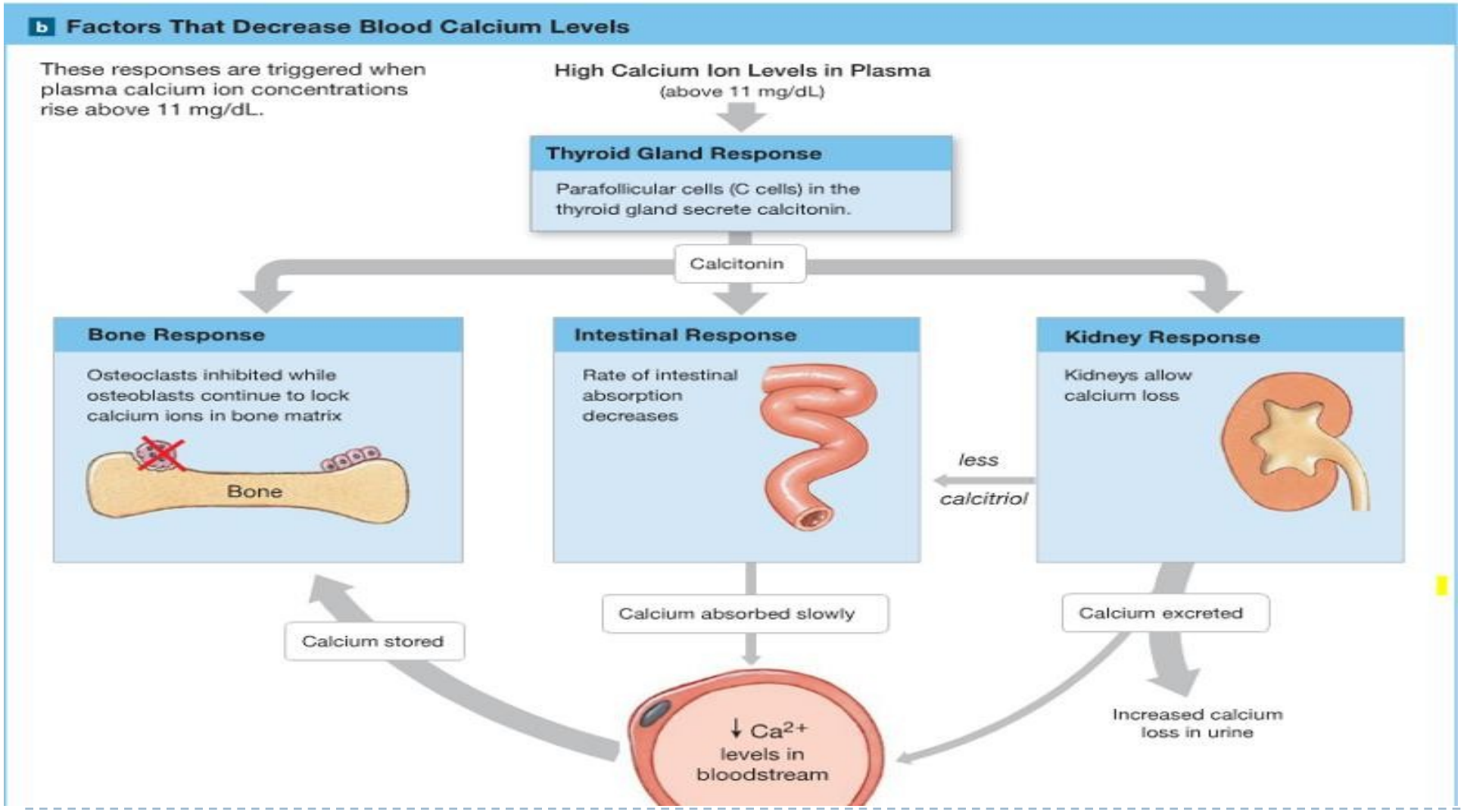


Figure 9-37 **Regulation of PTH secretion and PTH actions on bone, kidney, and intestine.** cAMP, Cyclic adenosine monophosphate; PTH, parathyroid hormone.

how does the parathyroid hormone affect remodeling ?
1) Increase absorption of ca++ in intestine.
2) Increase absorption of ca++ in kidney.
3) Stop phosphate absorption
4) Stimulate the kidney to produce 1,25 dihydroxycholecalciferol 5) In bone increase formation & activation of osteoclast which resorption to the bone and release ca++ to blood.

Calcitonin Hormone

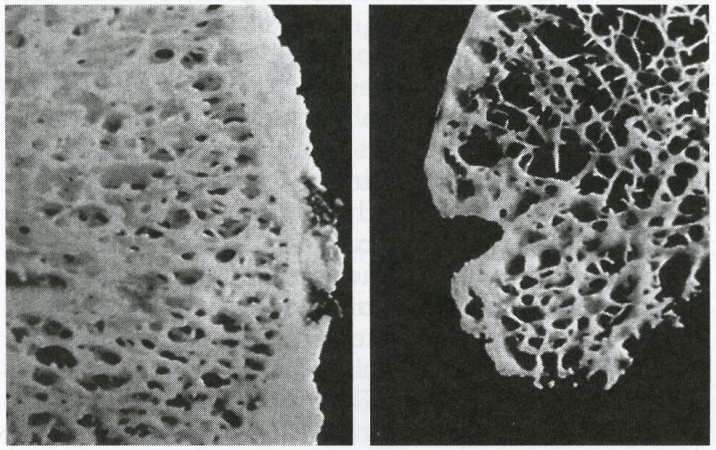


How does Calcitonin work ?

1) Inhibit absorption of ca++ in intestine.
   2)Inhibit absorption of ca++ in kidney.
2) 3) Activate osteoblast to increase the ca++ inside the bone.

Osteoporosis

- Osteoporosis means : reduced bone density and mass.
- Caused by a relative excess of osteoclastic function. Bone matrix and mineral are both lost.



• Difference between normal bone **(A)** and osteoporotic bone **(B).**

Loss of bone mass is due to :

1. Lack of physical stress
2. Malnutrition, lack of vitamin C
3. Old age, Postmenopausal lack of estrogen
4. Cushing's syndrome.

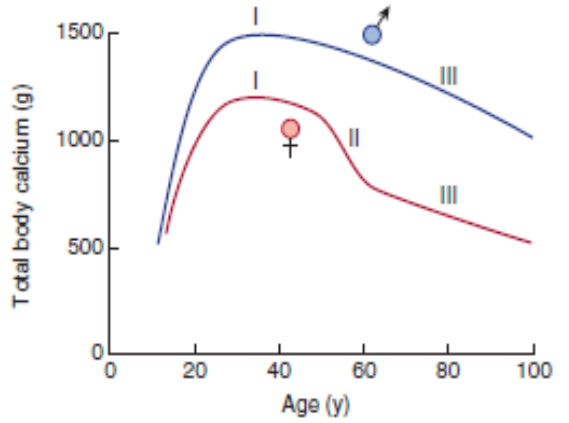


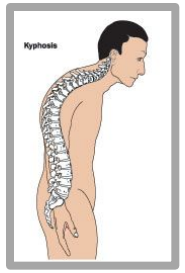
FIGURE 21–12 Total body calcium, an index of bone mass, at various ages in men and women. Note the rapid increase to young adult levels (phase I) followed by the steady loss of bone with advancing age in both sexes (phase III) and the superimposed rapid loss in women after menopause (phase II). (Reproduced with permission from Evans TG, Williams TF (eds): Oxford *Textbook of Geriatric Medicine*. Oxford University Press; 1992.)

Complications of Osteoporosis

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

2. Fractures of the vertebrae with kyphosis produces "widow's hump" in elderly women with osteoporosis.

3. Fractures of the hip in elderly are associated with a mortality rate of 12–20%, half of those who survive require prolonged expensive care.



Prevention (may help prevent or slow the progress of osteoporosis):

- Increased intake of calcium.
- Moderate exercise.

Extra Slide: (Answer to one of Dr. Samy Azer's questions regarding: Rank Ligand (RANKL) and Osteoprotegerin (OPG))

Question:

Question 4: Osteoprotegerin (OPG) plays a significant role in the pathogenesis of osteoporosis by:

a) Inhibiting bone resorption.
b) Acting as "a decoy receptor" for RANK, preventing it from binding the RANK receptor on osteoclasts precursors.
c) Stimulating osteoclast differentiation.
d) Enhancing the production of the tumour necrosis factor (TNF) receptor.
e) Stimulating the production of NF_{kB}.

To understand:

Ligand: is a small molecule that binds with a larger protein molecule;

For example: an extracellular chemical messenger binding with a plasma membrane receptor.

Special thanks to Leena Alwakeel!

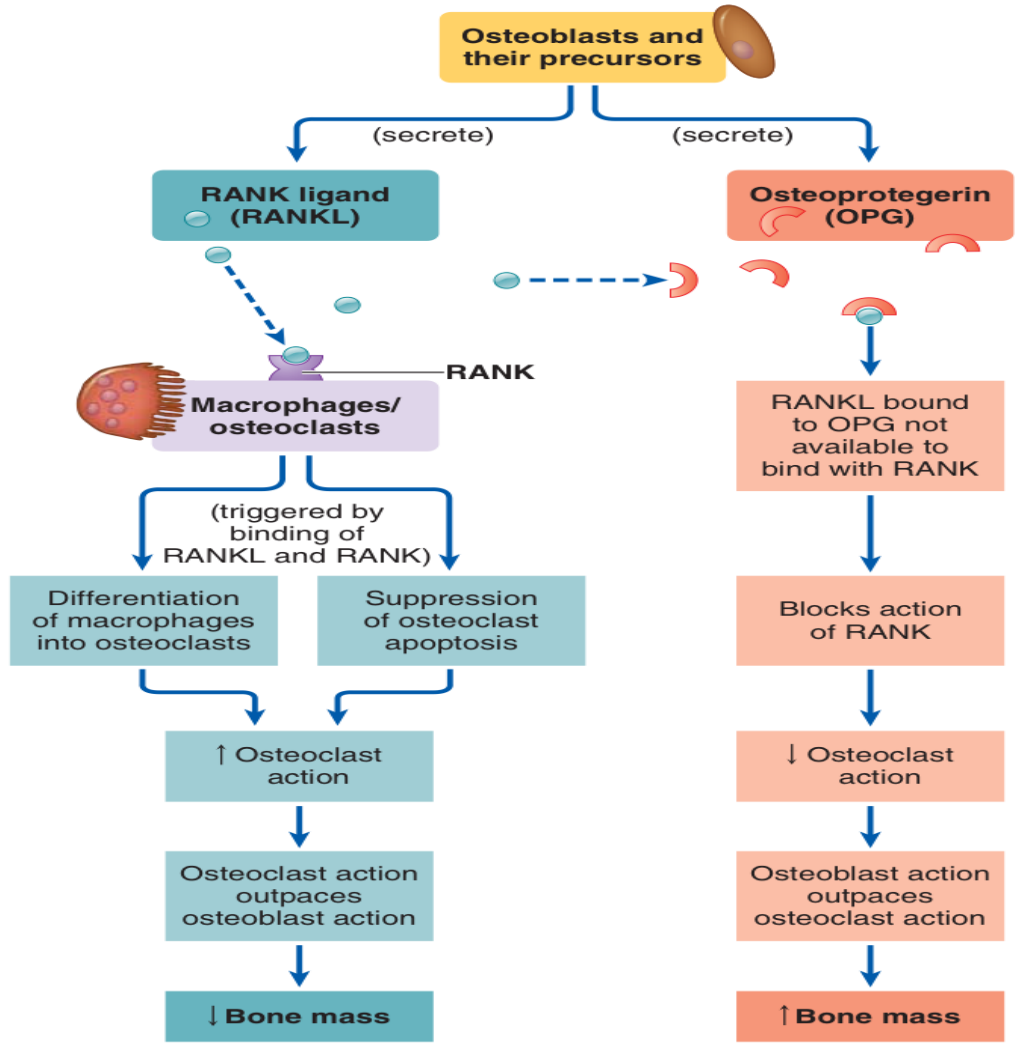


FIGURE 19-22 Role of osteoblasts in governing osteoclast development and activity.

Quiz

- https://www.onlineexambuilder.com/bone-physiology/exam-116528

Link to Editing File

(Please be sure to check this file frequently for any edits or updates on all of our lectures.)

References:

- Girls' and boys' slides.
- Guyton and Hall Textbook of Medical Physiology (Thirteenth Edition.)

Thank you!

اعمل لترسم بسمة، اعمل لتمسح دمعة، اعمل و أنت تعلم أن الله لا يضيع أجر من أحسن عملا.

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