# Physiology of the bone

- Color index:
  - Red: important
  - Green: doctor's notes
  - Grey: extra information
  - Pink: found only in female's slides
  - blue: found only in male's slides

Physiology 437 team work

# objectives:

**By the end of the lecture you will be able to:**

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

2- State the normal levels and forms of ca++ in the ECF and its relation to PO4.

3- Identify the bone cells and the function of each.

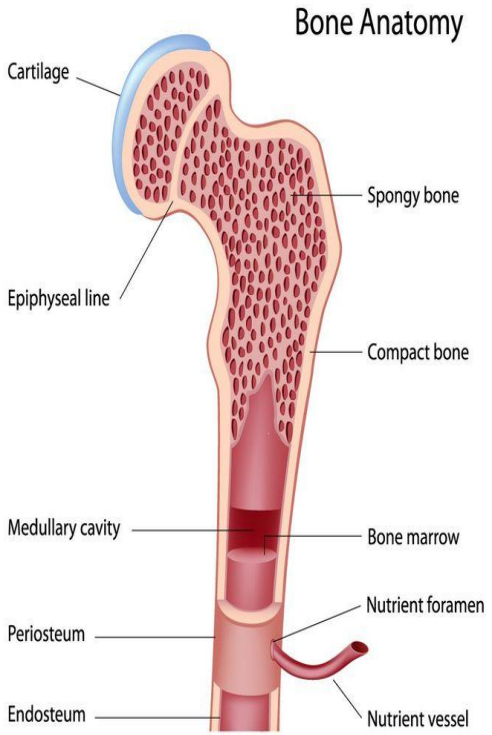
4- Define bone remodelling and explain the mechanism of bone formation.

5- Define osteoporosis.

6- Discuss the effect of different hormones on bone physiology.

# Physiology of bone

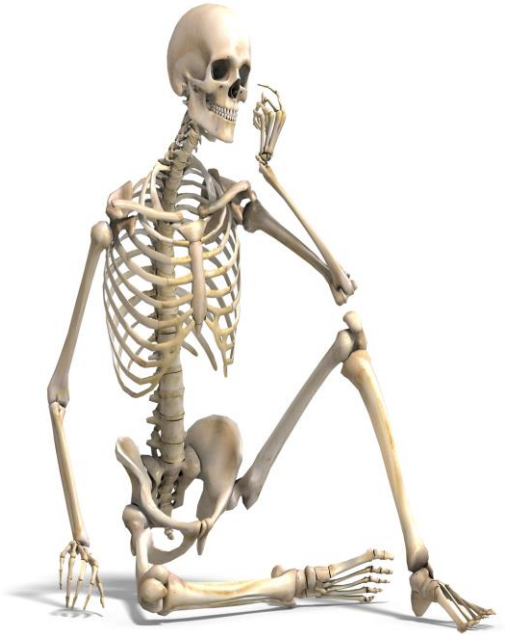
- Bone is a special form of connective tissue.
- It is well vascularized with total blood flow of 200–400 mL/min in adul humans.
- The ends of each long bone (**epiphyses**) are separated from the shaft of the bone by a plate of actively proliferating cartilage, the **epiphyseal plate.**
- Linear bone growth can occur as long as the epiphyses are separated from the shaft of the bone, but such growth ceases (stops) after the epiphyses unite with the shaft (**epiphyseal closure)***.*




*for interesting extra informations watch the video (2:51 mins)

# Function of bone

- Is involved in the overall Ca++ and PO4– homeostasis (regulation).
- Protects the vital organs,
- Permits locomotion and support against gravity.
- Contains the bone marrow (blood cells formation).
- Reservoir for calcium & phosphate .



# Types and structure of bone

## **Compact** or **Cortical** bone

-Compact or cortical bone: in the outer layer of most bones is (80%) of the bones in the body.

-the bone cells lie in lacunae. They receive nutrients by way of canaliculi from **haversian canals** vessels.

-Collagen is arranged in concentric layers, around the haversian canals forming cylinders called **osteons** or **haversian systems**. Imagine a bullseye, the collagen = rings and haversian canal is center of the the target.

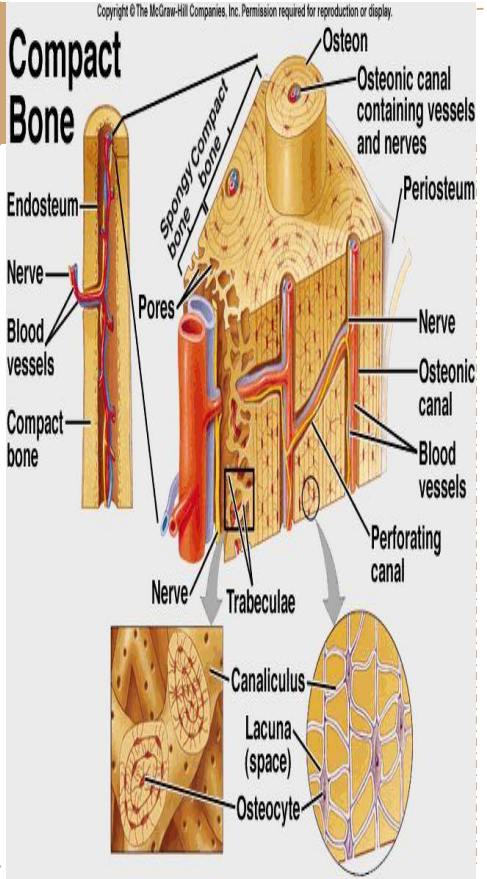
-It has more bone tissue and less bone space

-Has high resistance to bending and torsion (twisting)

-It is composed of overlapping circular structures (formations) called Haversian Systems or Osteons. Each osteon has a central canal called Osteonic Canal or Haversian Canal

- The Osteonic Canal contain blood vessels (capillaries, arterioles, venules ), nerves and lymphatics.

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

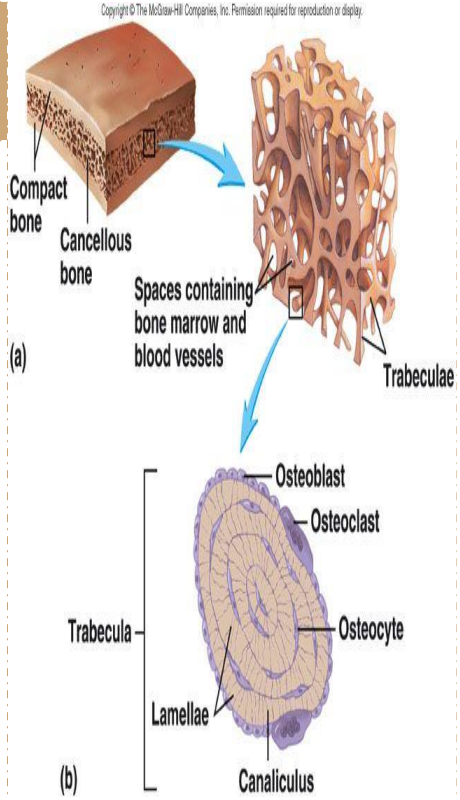


# Types and structure of bone

## **Trabecular** or **spongy** bone

inside the cortical bone, it is 20% of the body bone.
is made up of spicules (شويكات) or plates. Nutrients diffuse from bone extracellular fluid (ECF) into the trabeculae.

Though it represents only 20% of the skeletal mass, it has 5 times greater surface area than cortical bone يأخذ مساحة كبيرة لكن بكثافة قليلة
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 compared to cortical bone , it is:
(1) less dense,
(2) more elastic and
(3) has a higher turnover rate than compact bone .
The center of the bone contains red, yellow marrow, bone cells and other tissues.



# Composition of Compact Bone

## A) Matrix

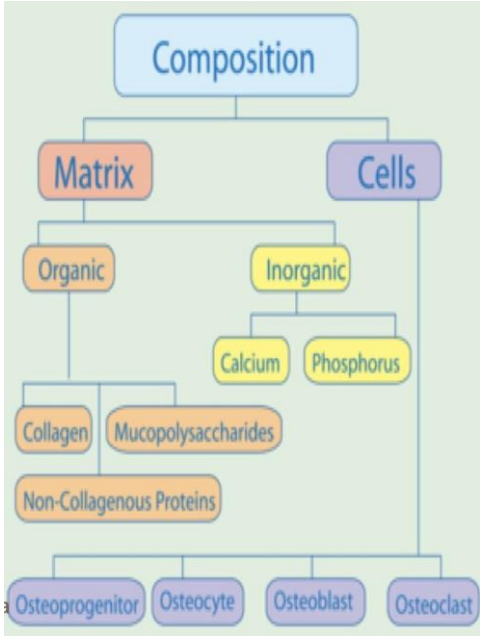
**30% is organic Matrix:** composed of

A) **Collagen fibers 90-95%**: extend primarily along the lines of tensional force and give bone its powerful tensile strength.
B) **Ground substance 5-10%**: ECF and Proteoglycans* hyaluronic acid.

*are proteins that fill up the bone extracellular matrix and regulate collagen fibrillogenesis.

**70% is bone Salts:**

- Crystalline salts of Ca++ and PO4 (**Hydroxyapatite**) the ratio of Ca/P ratio is 1.5-2).
- Mg+, Na+, K+, Carbonate ions are also present.




NB: newly formed bone have a considerably higher percentage of matrix in relation to salts. (Which is why newborn's bones are soft)

Organic matrix makes the bone **soft**, bone salts are inorganic substances that make the bone **hard**.

# B) Bone Cells

Note osteoblast and osteocyte are forming cells but osteoclasts are destructing cells

**Osteoblasts**

Functioning cells.

Are the bone forming cells that secrete collagen forming a matrix around themselves which then calcifies.

- Osteoblasts regulate **Ca** and **Phosphate** concentration in bone fluid.

*Calcification*

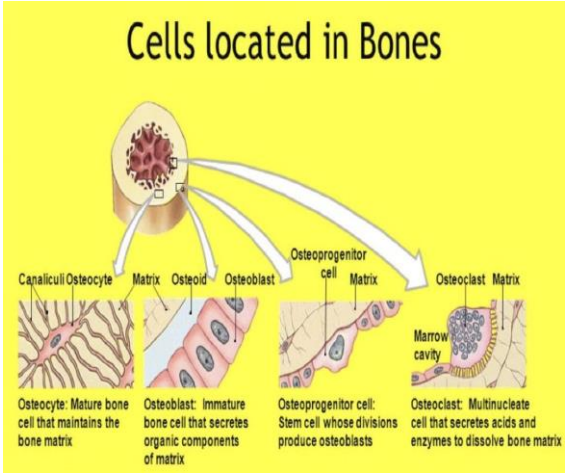
**Osteocytes**

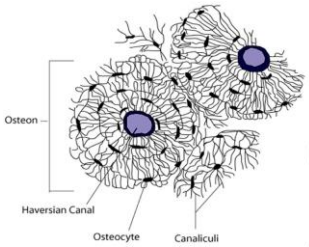
None functioning, give the bone its strength.

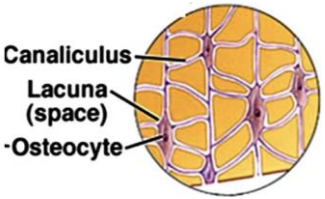
are surrounded by calcified matrix, and send processes into the canaliculi that ramify (branch out) throughout the bone.

**Osteoclasts***

Are <u>multinuclear</u> cells that erode and resorb previously formed bone. They phagocytose bone, digesting it in their cytoplasm.




*rich in lysosomes

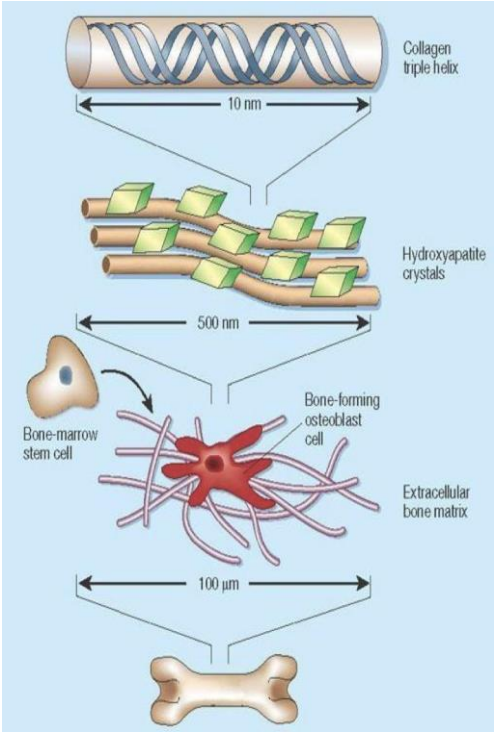
# Mechanism of Bone Calcification

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

The collagen monomers polymerize to collagen fibers.

The resultant tissue becomes **osteoid**, a cartilage-like material differing from cartilage in that calcium salts readily precipitate in it.

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




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

- From 436

*للتوضيح :ال osteoblastفي النسيج العظمي تفرز حول نفسها collagenبعدها راح يصير في النسيج fibers collagenوعندها يسمى هذا النسيج ب osteoid، ثم يبدأ الكالسيوم بالترسب والأرتباط بالكولاجين مما يكون . crystals hydroxyapatiteحين تنتهي هذة العملية يكون قد تكون حول ال lostoblastال osteoidفتنتهي مهمتها فتتحول لل Inactive formاللي هو الosteocytes

# 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.

- Pyrophosphate is protective against calcification of the soft tissues.
- Deficiency of pyrophosphate (Inhibitor of precipitation) leads to extra articular calcifications,
  for example: calcifications in the form of stones in the kidney.

**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.***

- **From 436:**

للتوضيح :لماذا لا يتكون ال **crystals hydroxyapatite** 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

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

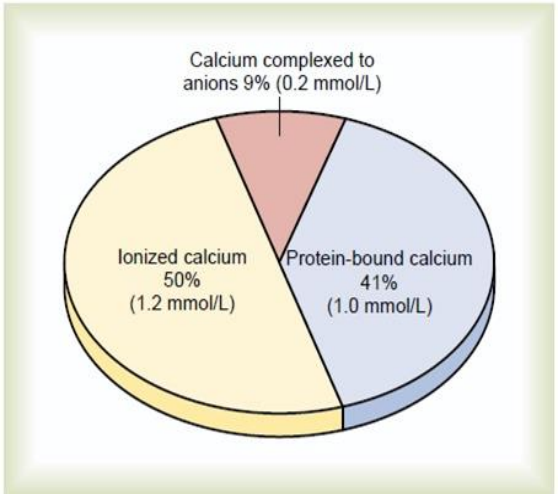
**Plasma Calcium (9 -11 mg/dl) average: 9.4 mg/dl**

- protein bound (non diffusible) 41%
  - In plasma (storage sites)
- *Balance*
- (diffusible) 59%
  - Used in Ca functions because it can cross capillary wall.
  - Ioinized 50%
  - Complexed 9%

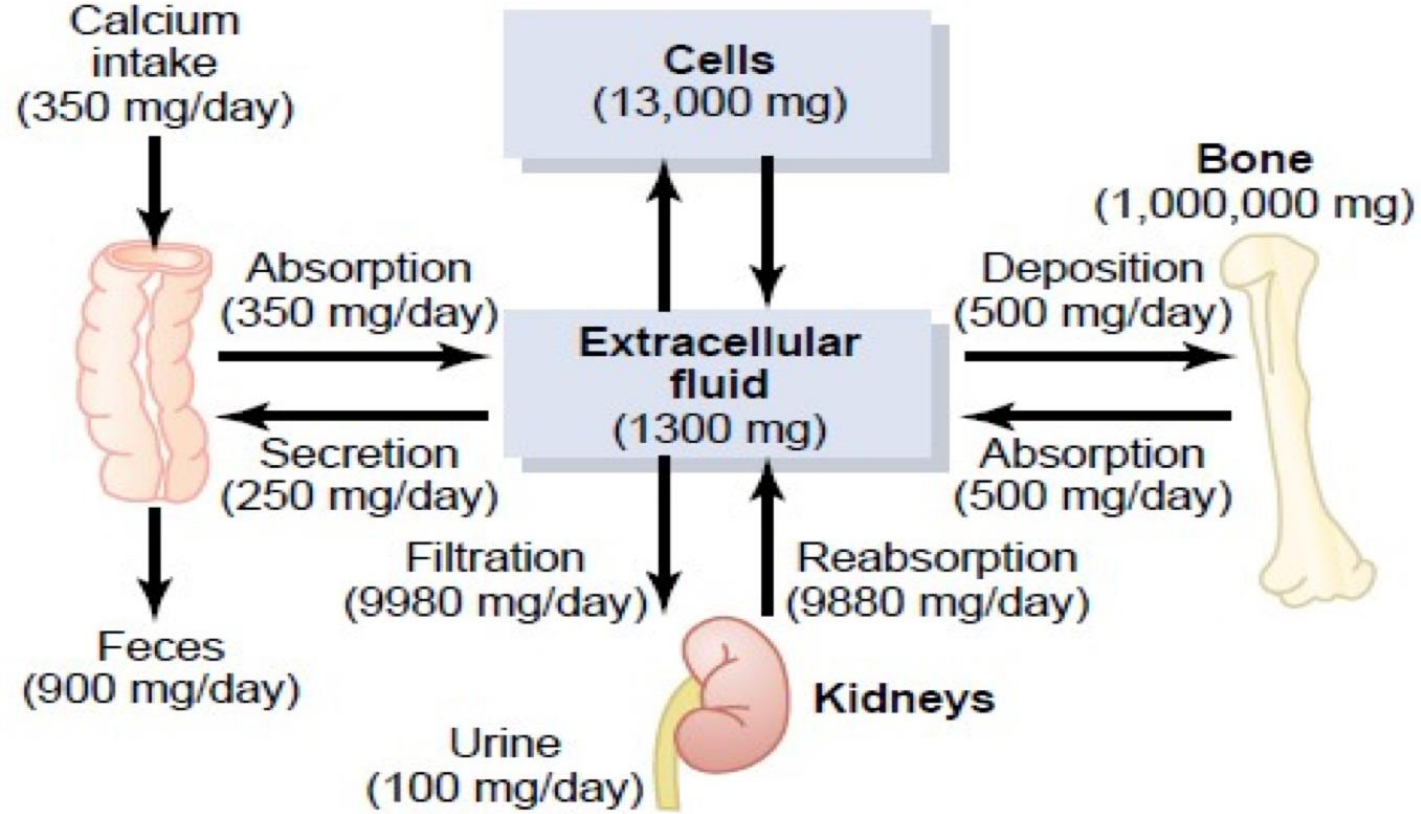
The following was only found in female's slides

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

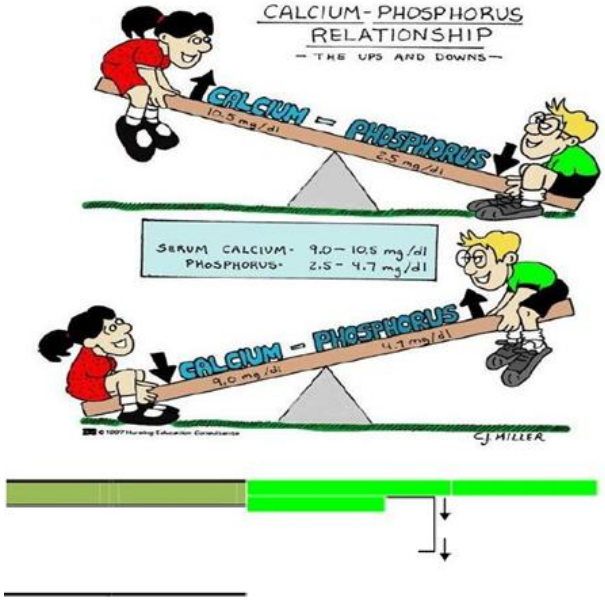
| | Calcium | Phosphorus |
|---|---|---|
| Total Body Content | 1,300 g | 600 g |
| Relative Tissue Distribution (% of total body content) | | |
| Bones and teeth | 99% | 86% |
| Extracellular fluid | 0.1% | 0.08% |
| Intracellular fluid | 1.0% | 14% |



# Calcium homeostasis in human body



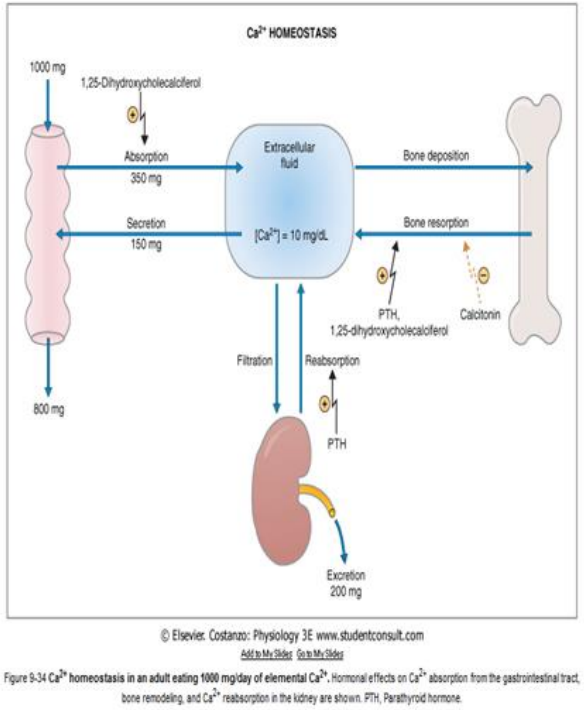
# Serum calcium phosphate




**Calcium and phosphorus relationship**

If the calcium get increase the phosphorus will decrease

If the calcium get decrease the phosphorus will increase




Calcium and phosphorus in the body have an inversely proportional relationship. When one increases, the other decreases.

اذا زاد الكالسيوم يقل الفسفور و العكس صحيح، الأهم في الاخير يكون مجموعهم ثابت.

Calcium is more than phosphorus in the serum because it is needed in many cellular processes like nerve conduction and blood coagulation.

# Calcium Exchange Between Bone and 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 readily mobilizable salt such as CaHPO4 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 ECF from rising to excessive levels or falling to very low levels under transient conditions of excess or decreased availability of calcium.

Important to keep the calcium homeostasis.This form of calcium is mobilizable (قابل للحركه) , this calcium is combined with phosphate but this is a different combination than the one in the Hydroxyapatite. Hydroxyapatite is more solid and stable , therefore it is not considered exchangeable.

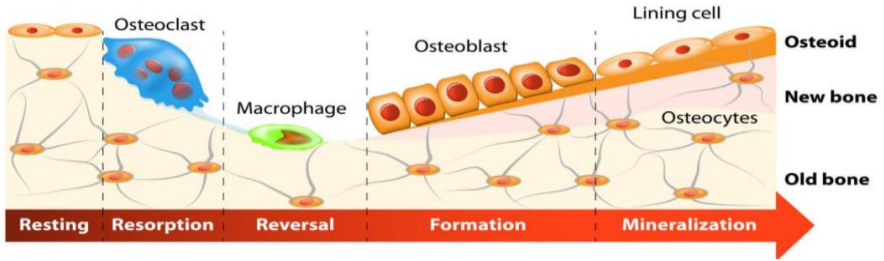
# Remodeling of Bone

العمليتين .عملية تجديد للعظام الاحلال و التجديد يشتغلون مع بعض.

# Deposition and Absorption of Bone

Bone remodeling is the continuous process of bone absorption (by osteoclasts,) and then its deposition (by osteoblasts.)

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

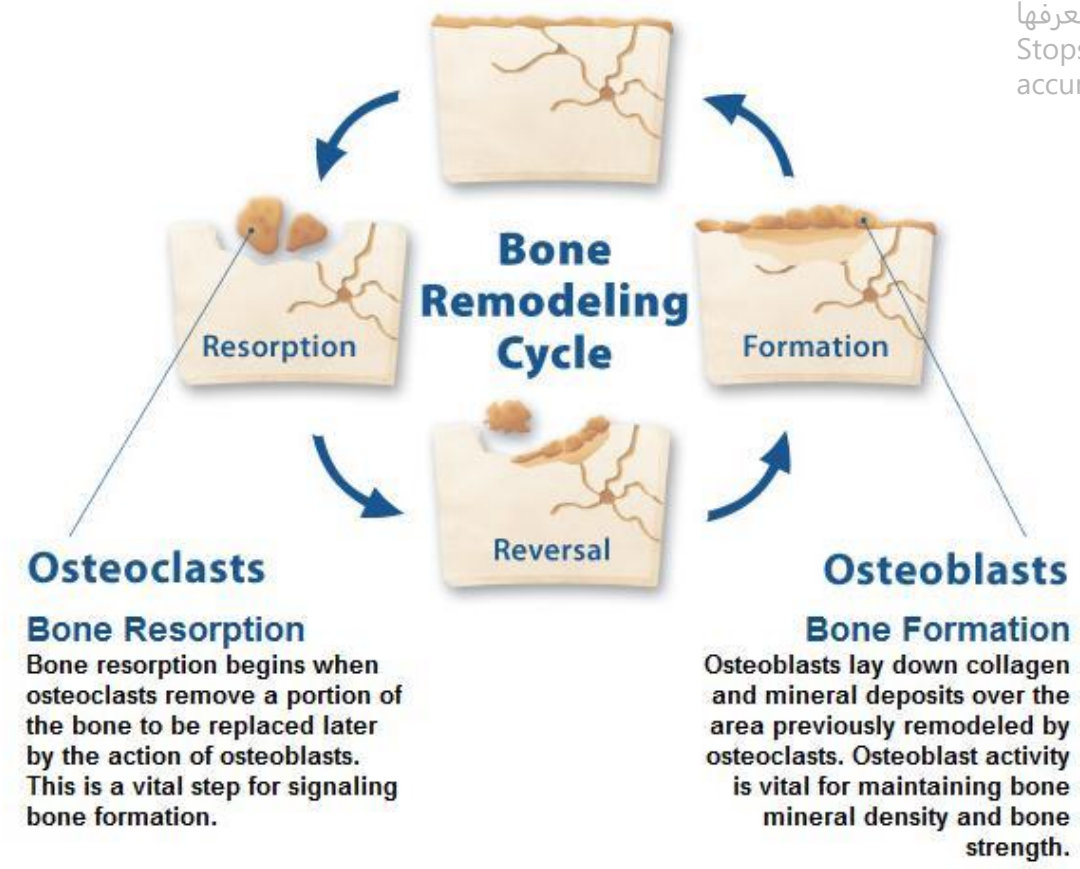



**Osteoblasts:**

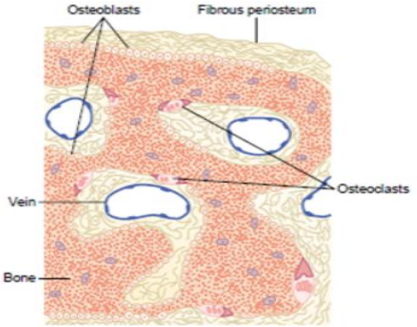
- Osteoblasts are found on the outer surfaces of the bones and in the bone cavities.
- A small amount of osteoblastic activity occurs on about 4% of all bone surfaces at any given time in an adult, so that at least some new bone is being formed constantly.
- The renewal rate is about 4% per year for compact bone and 20% per year for trabecular bone.

*For more understanding (extra):

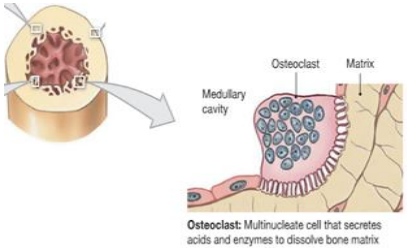
Remodeling of bone = ينحتوا العظام الى الosteoclasts شكلها الطبيعي اللي نعرفها
Stops over deposition and accumulation of bone



# Osteoclasts




- Osteoclasts are large phagocytic multinucleated cells
- They are normally active on less than 1% of the bone surfaces of an adult.
- The osteoclasts secrete
- two types of substances:




| | Proteolytic enzymes | Several acids |
|---|---|---|
| Location of origin | from the lysosomes | from the mitochondria and secretory vesicles |
| purpose | dissolve the organic matrix | solution of the bone salts |

- The osteoclastic cells also phagocytose minute particles of bone matrix and crystals, dissoluting them and releasing the products into the blood.

# Value of Continual Bone Remodeling

1. Bone adjusts its strength in proportion to the degree of bone stress and it thicken when subjected to heavy loads. (more stress = stronger)
2. 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.
3. Because old bone becomes relatively brittle (هش) and weak, new organic matrix is needed as the old organic matrix degenerates. In this manner, the normal toughness of bone is maintained.
(فتتحلل العظام القديمة، وتستبدل بالجديدة .بسبب الاستعمال المتكرر للعظام، العظام القديمة تضعف.)
4. Therefore, the bones of children are less brittle than the bones of the elderly, due to more remodeling in the children.

عملية التجديد عند الاطفال اعلى من الكبار في السن.

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

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

+

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

+

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

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

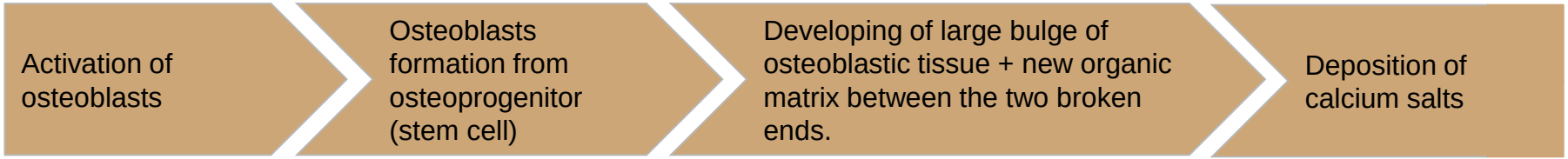
Bone stress=continual use of bone, so when we are wearing a cast the bone is immobilized and so no stress is on it = no need for it to be thick and it becomes thinner and lighter

# 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 bone, called the "bone membrane".

-Shortly a large bulge of osteoblastic tissue and new organic bone matrix, develops between the two broken ends of the bone followed shortly by the deposition of calcium salts. This is called a ***callus**.** Callus is not final stage of bone healing, fracture can re-occur to the same area even with callus if no caution is taken.




*callus means the bony healing tissue which forms around the ends of broken bone

# Hormonal Control of Calcium Metabolism & Physiology of Bone

Three major hormones

Active Vitamin D

***1, 25 dihydroxycholecalciferol***

a steroid hormone formed from Vitamin D.

***Parathyroid hormone (PTH)***

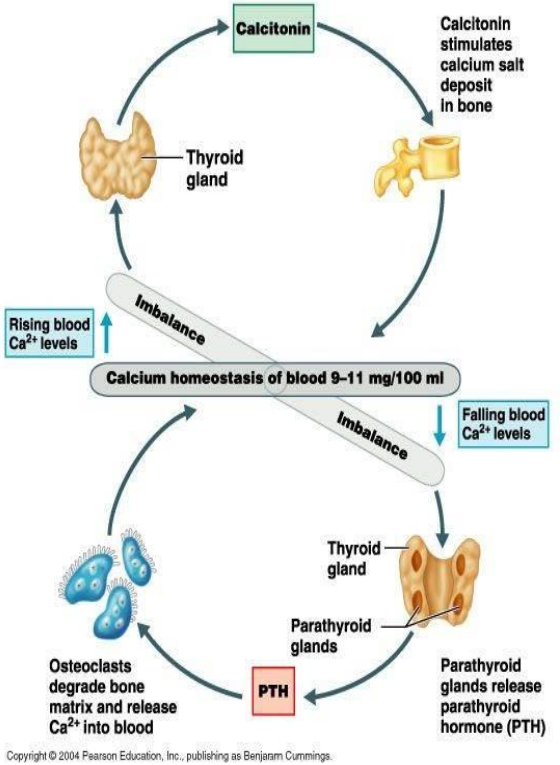
secreted by parathyroid gland

Main goal of PTH is to work when the serum level of Calcium is low.

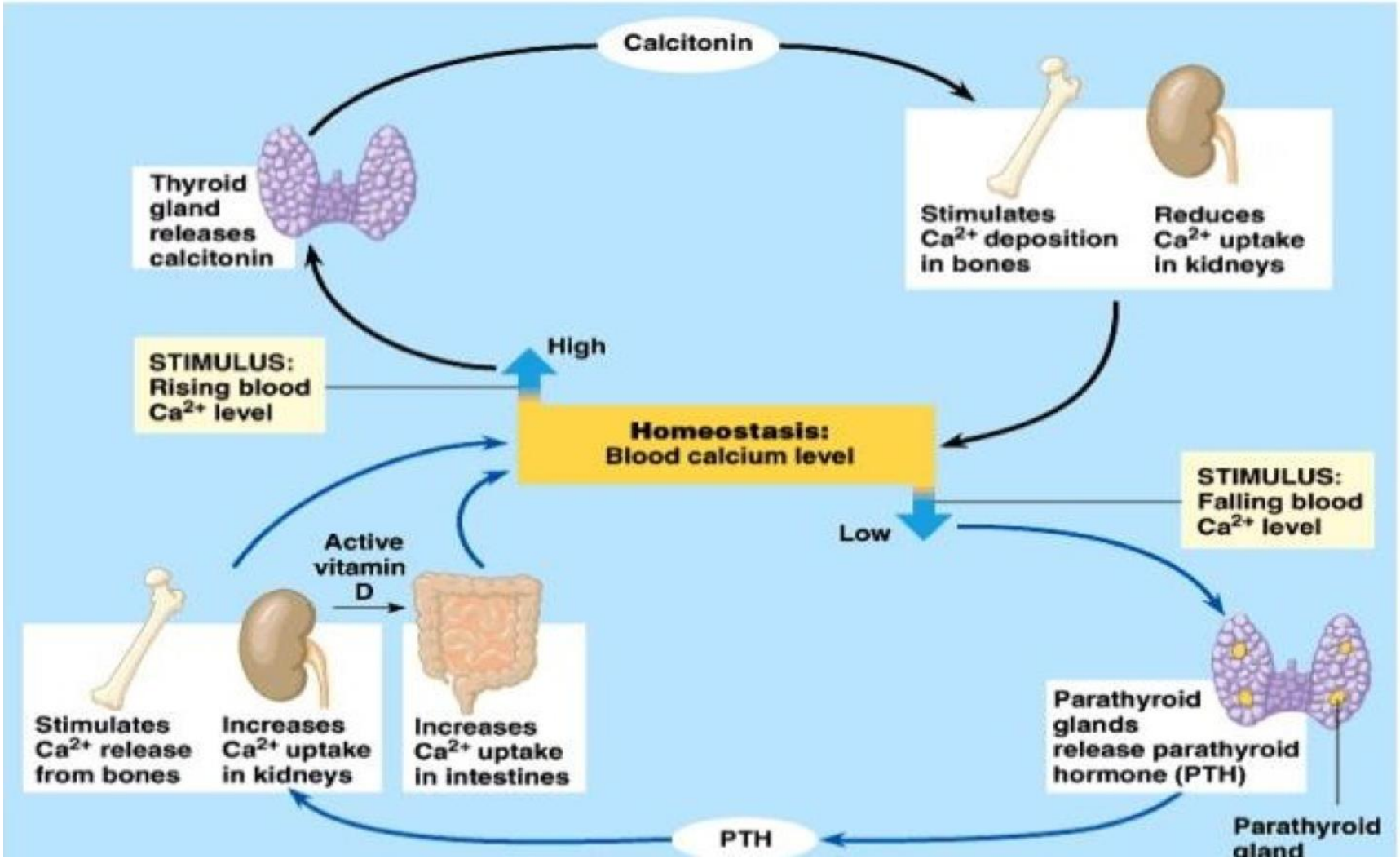
***Calcitonin***

secreted by c-cells in the thyroid gland.

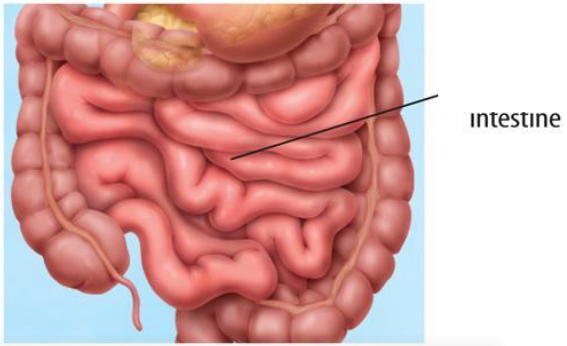
Main goal of calcitonin is to work when the serum level of Calcium is high.



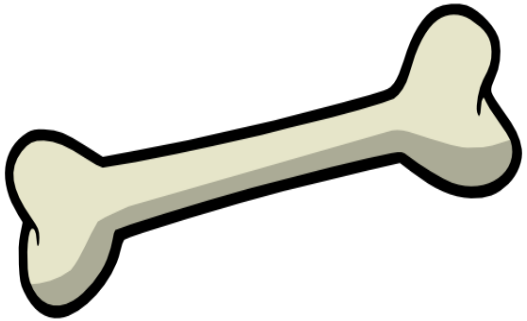

-To a lesser extent; Glucocorticoids, GH, estrogens & various growth factors also affect Calcium Metabolism.


Calcitonin
Thyroid gland releases calcitonin
Stimulates $Ca^{2+}$ deposition in bones
Reduces $Ca^{2+}$ uptake in kidneys
STIMULUS: Rising blood $Ca^{2+}$ level
High
Homeostasis: Blood calcium level
STIMULUS: Falling blood $Ca^{2+}$ level
Low
Active vitamin D
Stimulates $Ca^{2+}$ release from bones
Increases $Ca^{2+}$ uptake in kidneys
Increases $Ca^{2+}$ uptake in intestines
Parathyroid glands release parathyroid hormone (PTH)
PTH
Parathyroid gland

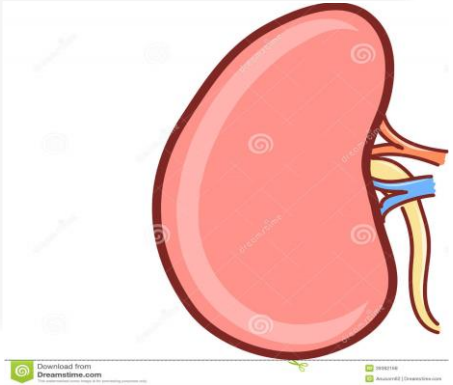
# Vitamin D - ACTION OF CALCITRIOL




-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

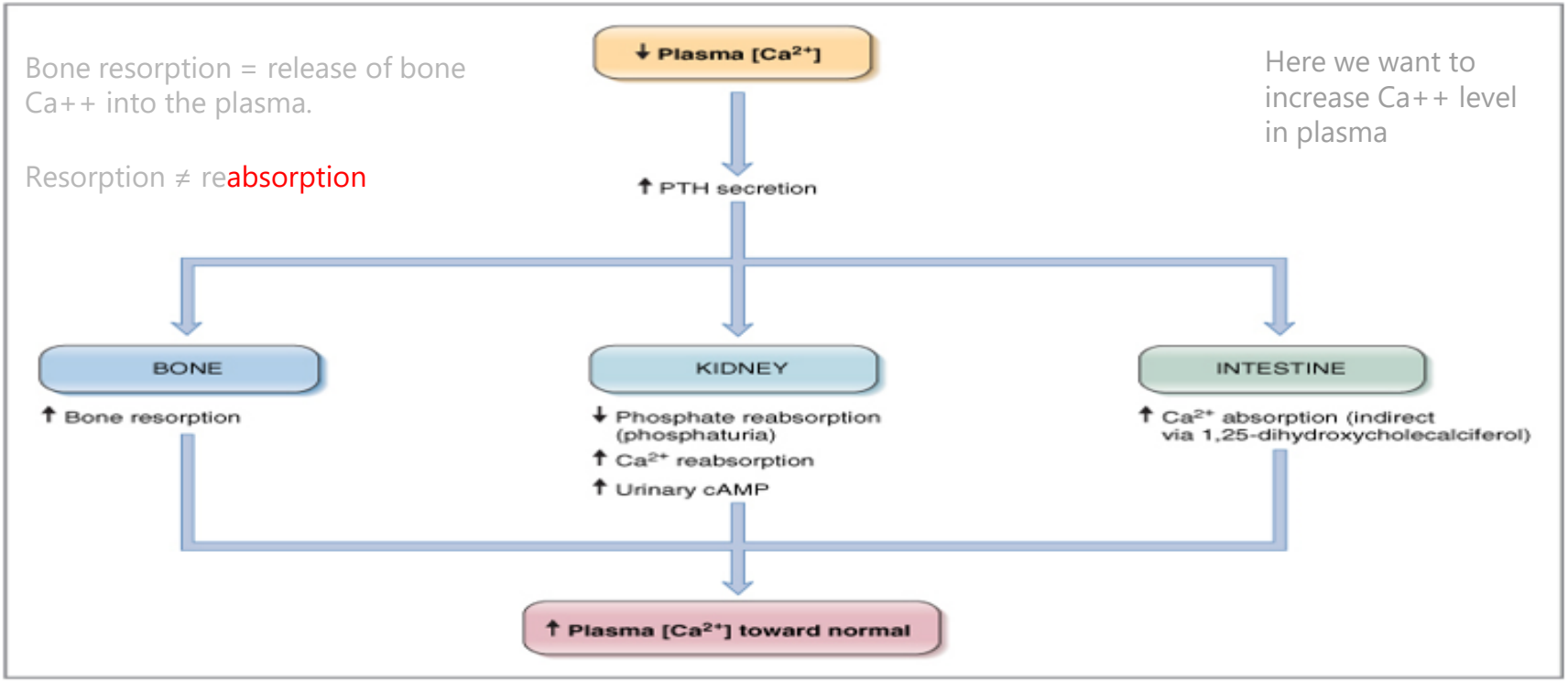



-increased reabsorption of calcium and phosphorus
-decreased excretion of calcium and phosphorus

# Parathyroid Hormone (PTH)

Bone resorption = release of bone Ca++ into the plasma.

Resorption ≠ reabsorption

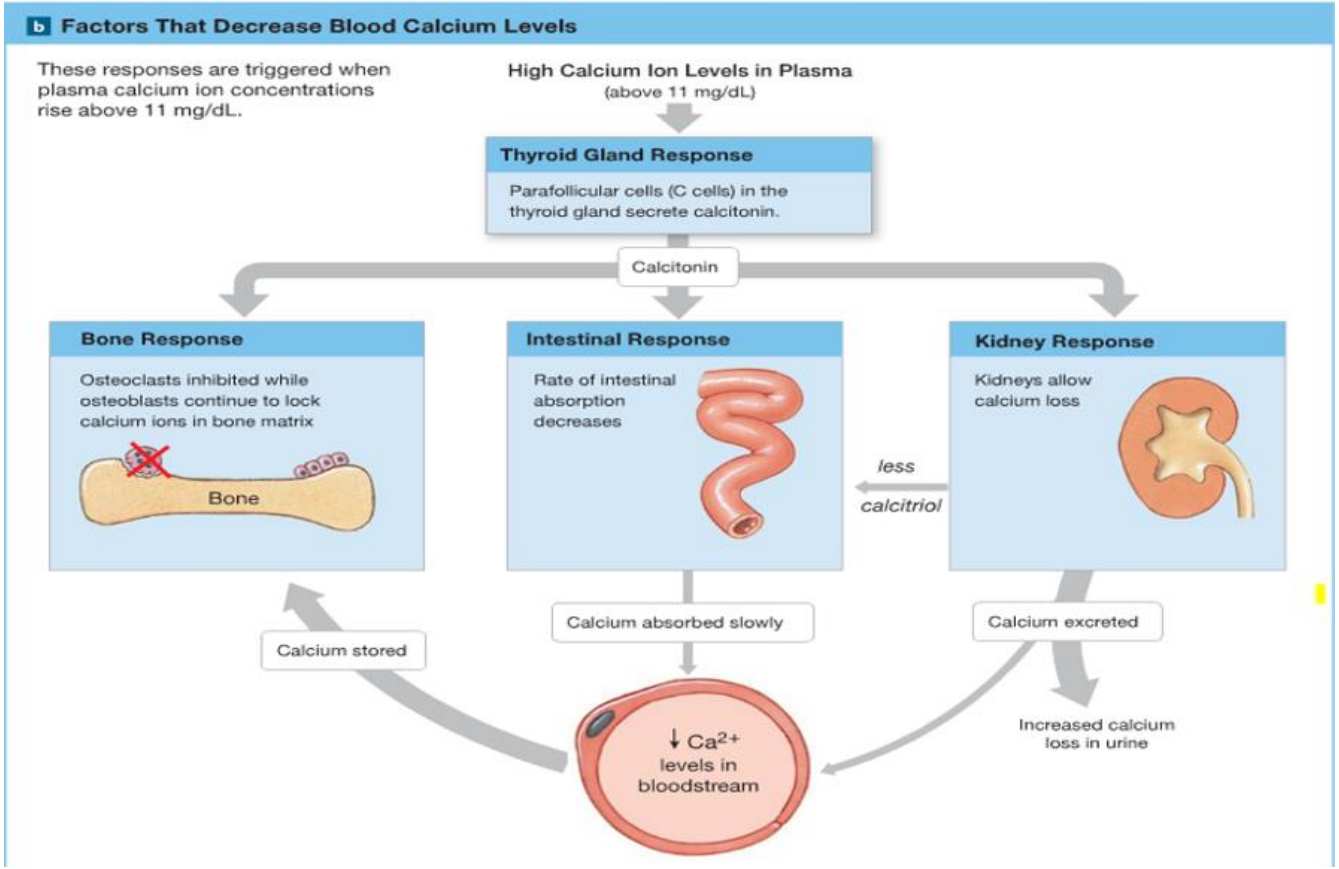



Here we want to increase Ca++ level in plasma



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

# Calcitonin Hormone

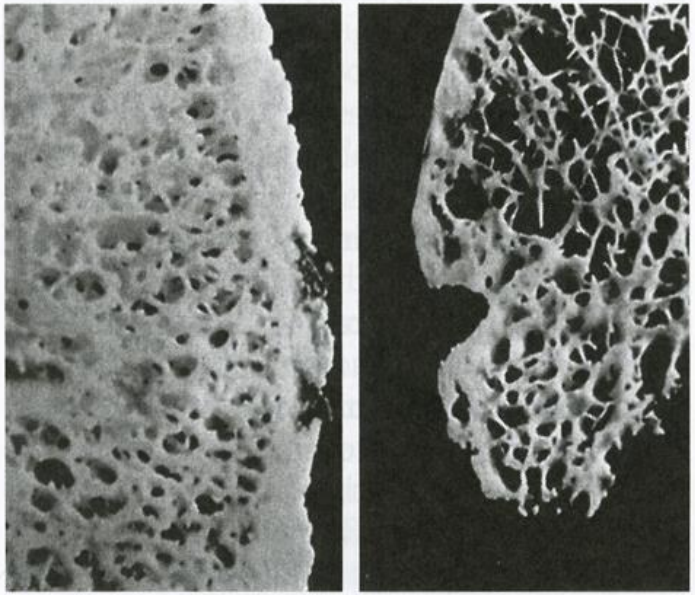


# Osteoporosis

- **Osteoporosis:** means reduced bone density and mass
- Is caused by decrease of osteoblastic activity or occasionally due to 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. |

# Osteoporosis




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

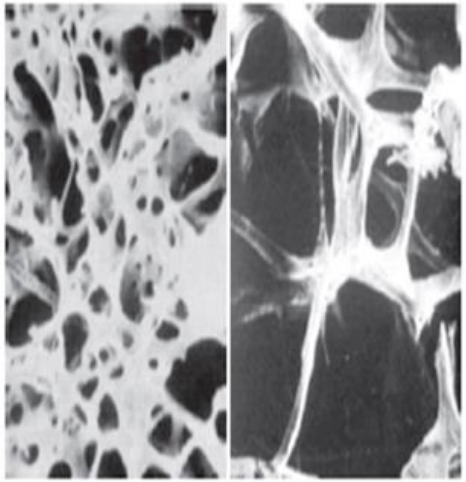


**FIGURE 21–11 Normal trabecular bone (left) compared with trabecular bone from a patient with osteoporosis (right).** The loss of mass in osteoporosis leaves bones more susceptible to breakage.

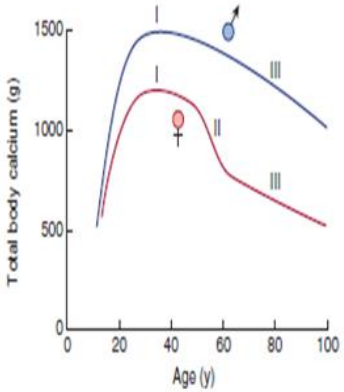



**FIGURE 21–12 Total body calcium, an index of bone mass, at various ages in men and women.** Note the rapid increase to young adult levels (phase I) followed by the steady loss of bone with advancing age in both sexes (phase III) and the superimposed rapid loss in women after menopause (phase II). (Reproduced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

# Complications of Osteoporosis

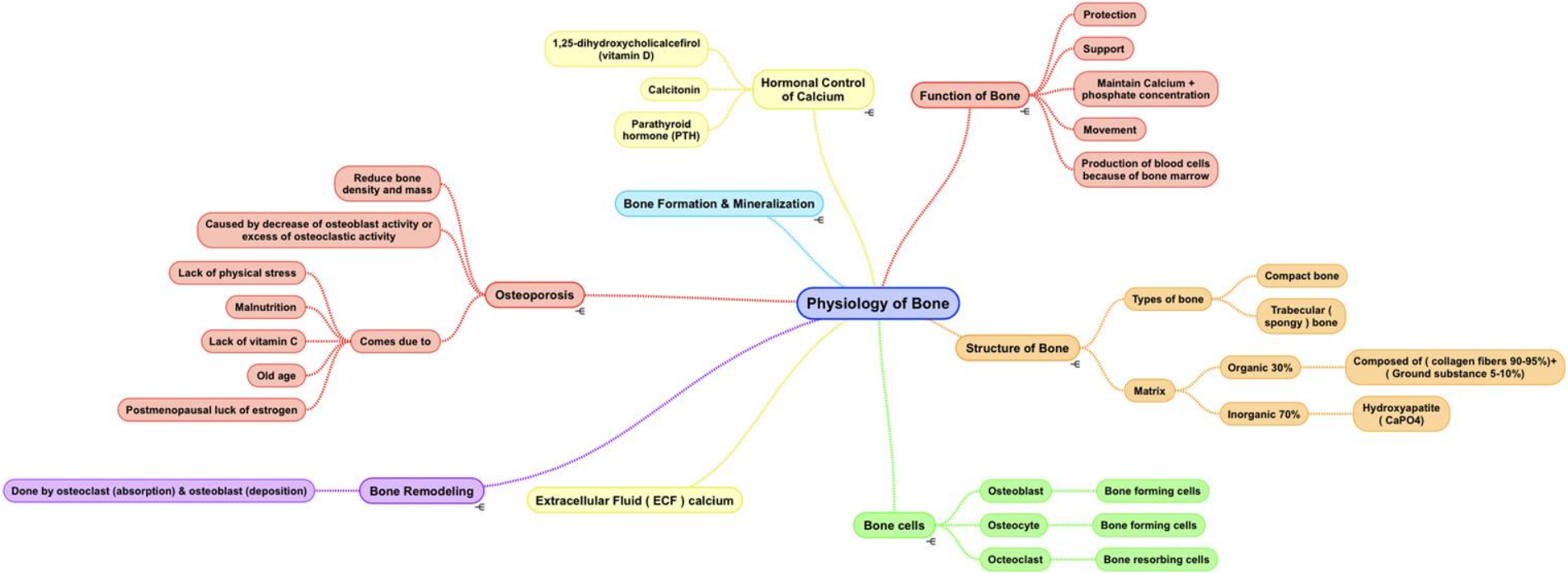
- The incidence of fractures is increased particularly in the :

  1.distal forearm (Colles fracture)  2.vertebral body  3.hip.

**WHY?:** 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. (Kyphosis is the extreme curvature of the back)
- 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.

# Summary


Physiology of Bone
Function of Bone
Protection
Support
Maintain Calcium + phosphate concentration
Movement
Production of blood cells because of bone marrow
Hormonal Control of Calcium
1,25-dihydroxycholicalcefirol (vitamin D)
Calcitonin
Parathyroid hormone (PTH)
Bone Formation & Mineralization
Osteoporosis
Reduce bone density and mass
Caused by decrease of osteoblast activity or excess of osteoclastic activity
Comes due to
Lack of physical stress
Malnutrition
Lack of vitamin C
Old age
Postmenopausal luck of estrogen
Structure of Bone
Types of bone
Compact bone
Trabecular ( spongy ) bone
Matrix
Organic 30%
Composed of ( collagen fibers 90-95%)+ ( Ground substance 5-10%)
Inorganic 70%
Hydroxyapatite ( CaPO4)
Bone Remodeling
Done by osteoclast (absorption) & osteoblast (deposition)
Extracellular Fluid ( ECF ) calcium
Bone cells
Osteoblast
Bone forming cells
Osteocyte
Bone forming cells
Octeoclast
Bone resorbing cells

# Quiz

1) Which one of these are multinuclear cells that phagocytose bone?
A. osteoblasts
B. osteoclasts
C. osteocytes

2) Calcium salts have great tensile strength.
A. True
B. False

3) Body weight calcium in a healthy adult :
A. 1900 g
B. 700 g
C. 1300 g
D. 2100 g

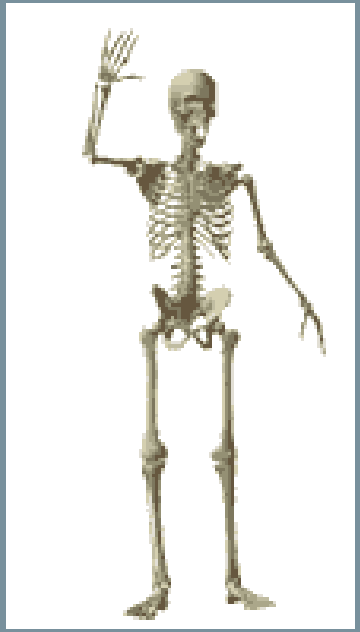
Correct answers:
1: B
2: B
3: C

**Female's team:**

1. Ahad Algrain
2. Hadeel
3. Maha Alnahdi
4. Majd AlBarrak
5. Rahaf Alshammari
6. Rinad Alghoraiby
7. Munira Alhadlg
8. Sarah AlBlaihed

**Male's team:**

1. Anas Alsaif
2. Mohammed Alhassan
3. Omar Alfawzan
4. Saad Alhadab
5. Anas alsuwaida
6. Khaled alogaili



**Team Leaders:**
Abdulhakim AlOnaiq
Alanoud Salman

**contact us at:**

physiologyteam437@gmail.com

@physio437

**editing file**