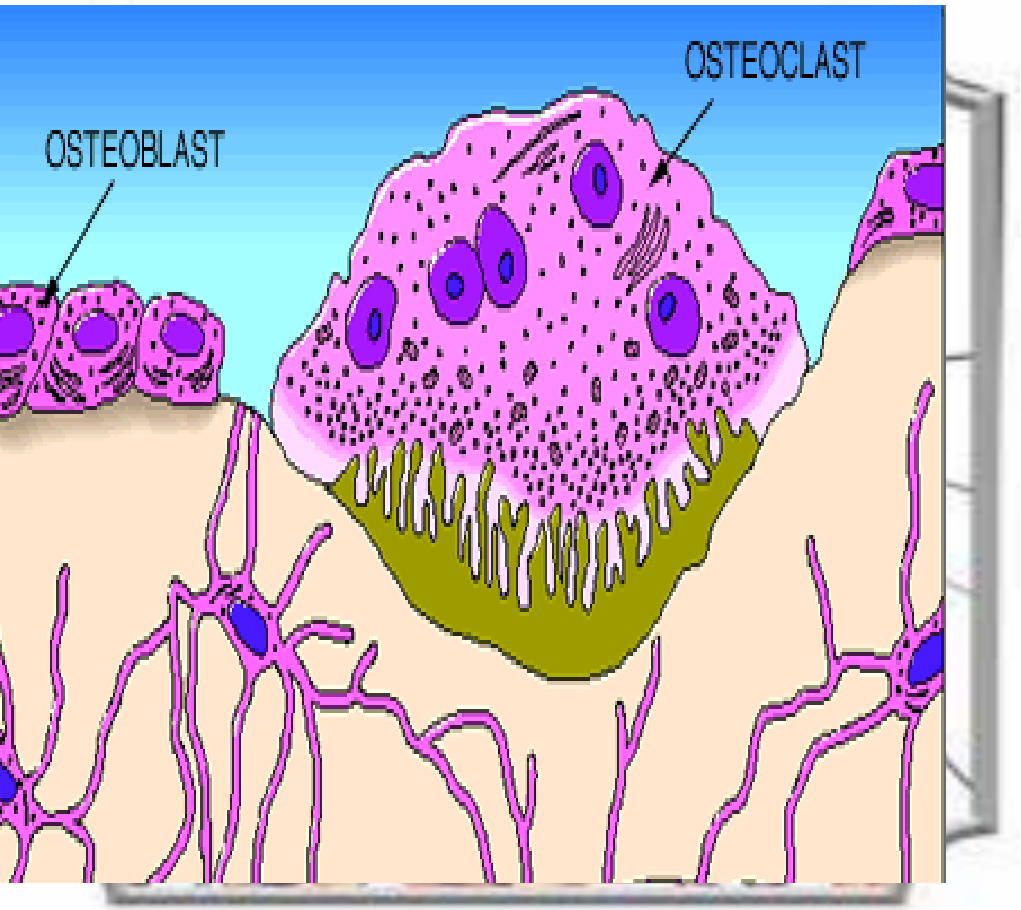
Physiology of Bone



Prof. faten zakareia
Professor of Physiology
College of Medicine
King Saud University

Lecture1:- Bone physiology (Referece book –Gyton 12 th edition,chapter 79 (p 955-966)

Objectives:-

At the end of this lecture the student should be able to:-

-Define bone and differentiate between types and sites of bone (cortical& trabecular)

-Appreciate differences between both types of bone in function

-know ca++ concentration and forms in the ECF& its relation to PO4

- differentiate bone cells &function of each

- know Bone remodelling & bone formation

- Define osteoporosis

- Appreciate effect of different hormones on bone physiology

Functions of bone:-

1-Supports soft tissue
2-Protects vital organs (cranium, thoracic cavity)
3-Contains bone marrow for blood cells synthesis تخليق
4-Reservoir of Ca++, PO4 to maintain constant concentrations of them in body fluids
5-Allows body movement

Structure of bone:-

Porous mineralized structure

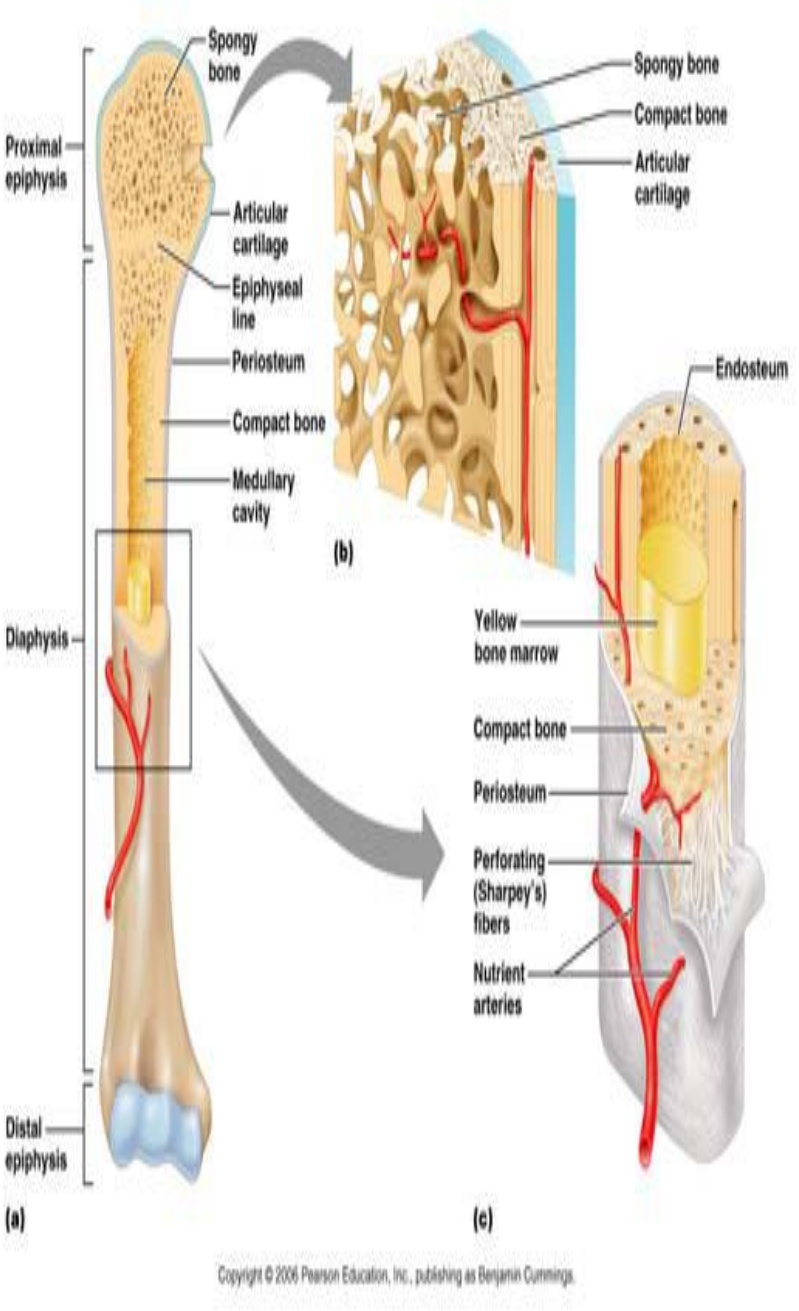
A-Cells ???

B-Bone matrix

Calcified material(**deposits of calcium & phophates salts mainly but there is magnesium ,potassium &carbonate**),collagen fibres lacunae, Canaliculi

c-Periosteum & Endosteum

d- **red or yellow marrow in** the center of the bone



The human skeleton is actually made up of 2 types of bones:

(1) **Cortical bone (compact bone)** → 80 %

-Constitutes the dense concentric layers of long bones

-Also outer layer surround trabecular bone at ends of long bones

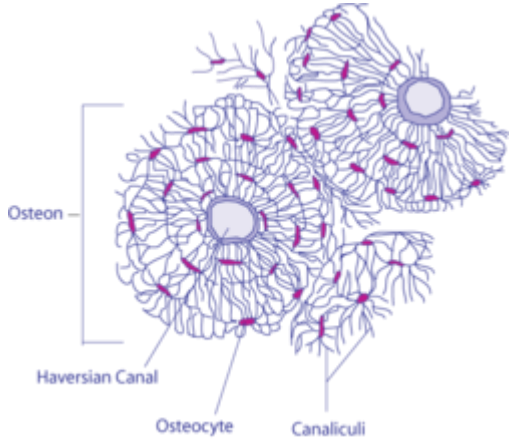
(2) **Trabecular bone (spongy)** → 20%

-Present in the interior of skull, ribs, vertebrae, pelvis and (in long bones present only in epipheseal and metaphysal regions)

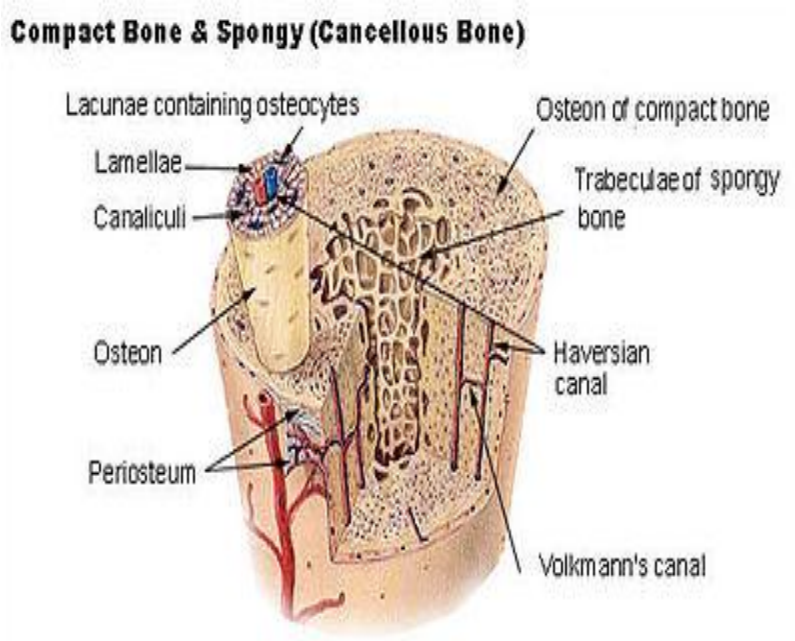
It has five times greater surface area than cortical bone (80% of the bone surface area).

Compact bone

- (غلاف)-Forms a protective outer shell around every bone in the body.
- دوران معدل-has a slow ca ++ turnover rate
- تقويس-Has high resistance to bending
- present where bending would be (undesirable as in the middle of long bones.)



- -There is a series of adjacent bull's eye **osteons or Harvesian** called **systems**.



- **Osteon** is composed of a central - vascular channel called the Harvesian canal, surrounded by a kind of tunnel of concentric lamellae of نفق mineralized bone,.
- Harvesian canal can contain capillaries, aterioles, venules, nerves and possibly lymphatics.

Trabecular (spongy-Cancellous) Bone

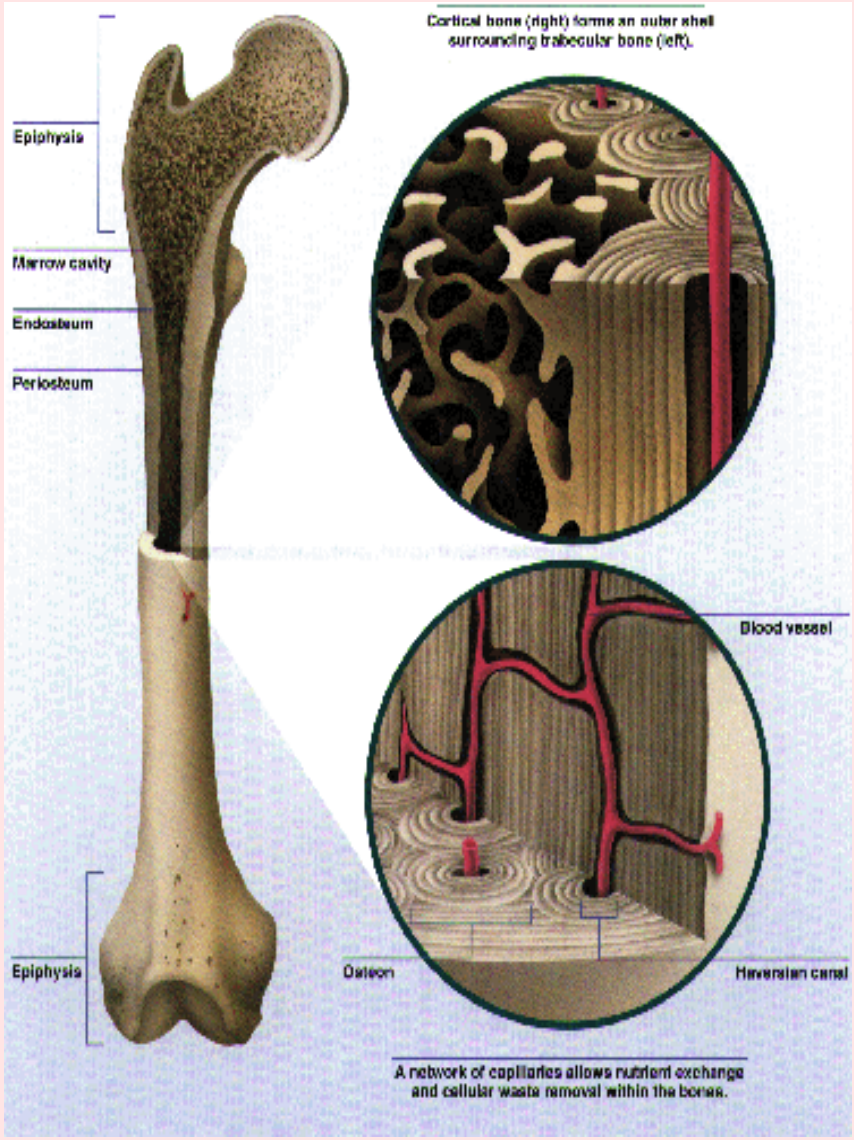
- Rigid but appears spongy
-)(هيكل)- Forms the interior scaffolding which helps bone to maintain their shape despite compressive forces.
- **Compared to cortical bone it is:**

(1) less dense

(2) more elastic

(3) greater surface area

(4)it has high calcium turnover rate because of the greater surface area



Calcium Homeostasis

Extracellular Fluid (ECF) Calcium

Normal Ca^{2+} level in plasma ranges from **8.5-10 mg/dL**

(mean 9.4 mg/dL) It exists in fractions

:(1) **Free ionized calcium** → **50%** of total ECF calcium, diffusable through capillary membrane

(2) **Protein-bound calcium** → **40**%, (non diffusable through capillary membrane**)**

a-90% bound to albumin

b- Remainder bound to globulins

Alkalosis increases calcium binding to protein and decreases ionized calcium

(3**) Calcium bound to serum constituents** → **10%** (citrate & phosphate) (not ionized- diffusable)

-Only the free, ionized Ca^{2+} is biologically active

Q-What are Ca++ functions?

Q-What is effect of hypo and hypercalcaemia on central nervous system?

Phosphate (PO_4):

-

-Calcium is tightly regulated with Phosphorous in the body.

-85% of PO_4 in bone

-’15% in cells

- less than 1% in ECF In forms as H2P04 , HPO4

PO_4 normal plasma concentration is **3.0-4.5 mg/dL**.

Ca++ x PO4 = constant (solubility product)

-if any one increase it should precipitate in bone مترسب

Bone& Ca++

-70% of Bone is formed of calcium (99% of the Calcium of bone in form of hydroxyapatite crystal) & phosphate salts **($CaP0_4$ and hydroxide)**)

- Calcium salts in bone provide structural integrity of the skeleton

-About 99% of Ca of our body is in bone.

- about 0.1% in ECF

- 1% of our body Ca is in cells organells

- F

BONE GROWTH:-

Growth occurs at epiphyseal طولي Linear plates.المشاشي

-Increase in width occurs at periosteum غشاء العظم

-During growth , bone mass increases and bone formation exceeds امتصاص Resorption

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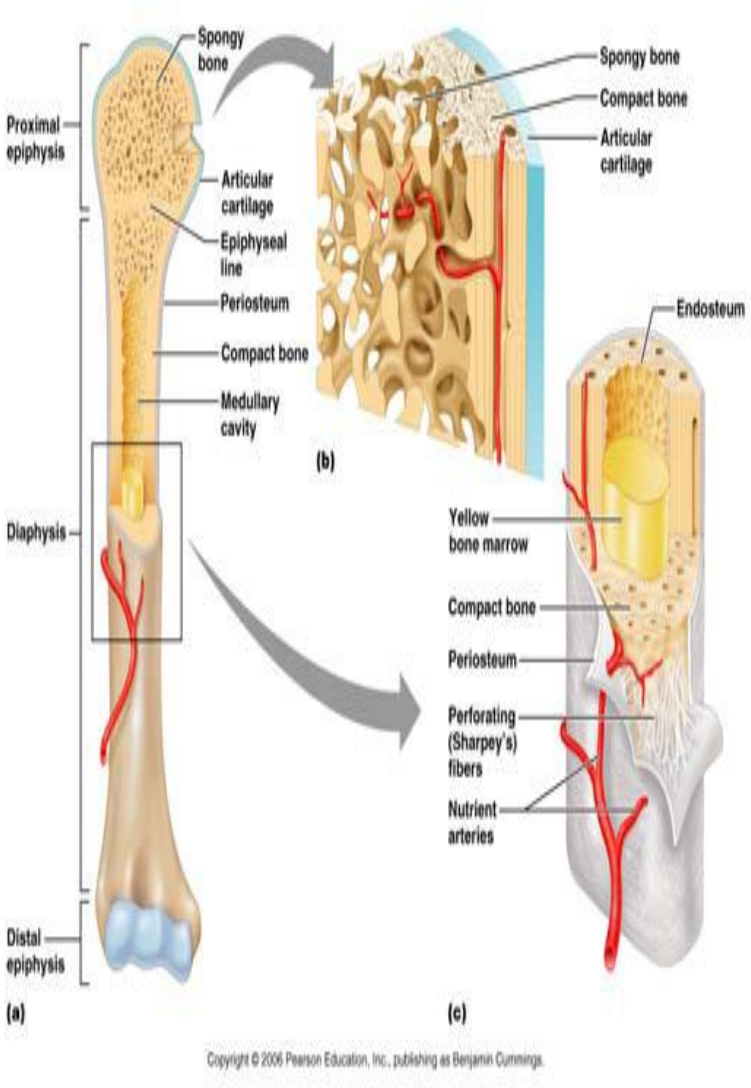
- 10% of total adult bone mass turns over each year during remodeling process إعادة تشكيل -

Once adult bone mass is achieved **equal rates of formation and resorption to** maintain bone mass

-At about 30 years old , rate of resorption begins to exceed formation and bone mass slowly decreases.



Bone Cells

There are three types of bone cells:

Osteoblast :

Bone forming cell present on outer surface of bone and in bone cavities

-secretes collagen forming bone matrix around themselves then they calcified (on which Ca^{++} and PO_4 يترسب precipitate)

(2) Osteocytes :

Mature bone cell derived from osteoblasts.

It is enclosed in bone matrix.

Q - What is the function of osteocytes ?

A -Transfer of calcium from bone canaliculi to the ECF

(3) Osteoclast :

large phagocytic multinucleated ,its activity controlled by Parathormone hormone

-function is to resorb the formed bone. HOW?

Canaliculi

- fluid-containing channels called the **canaliculi**.

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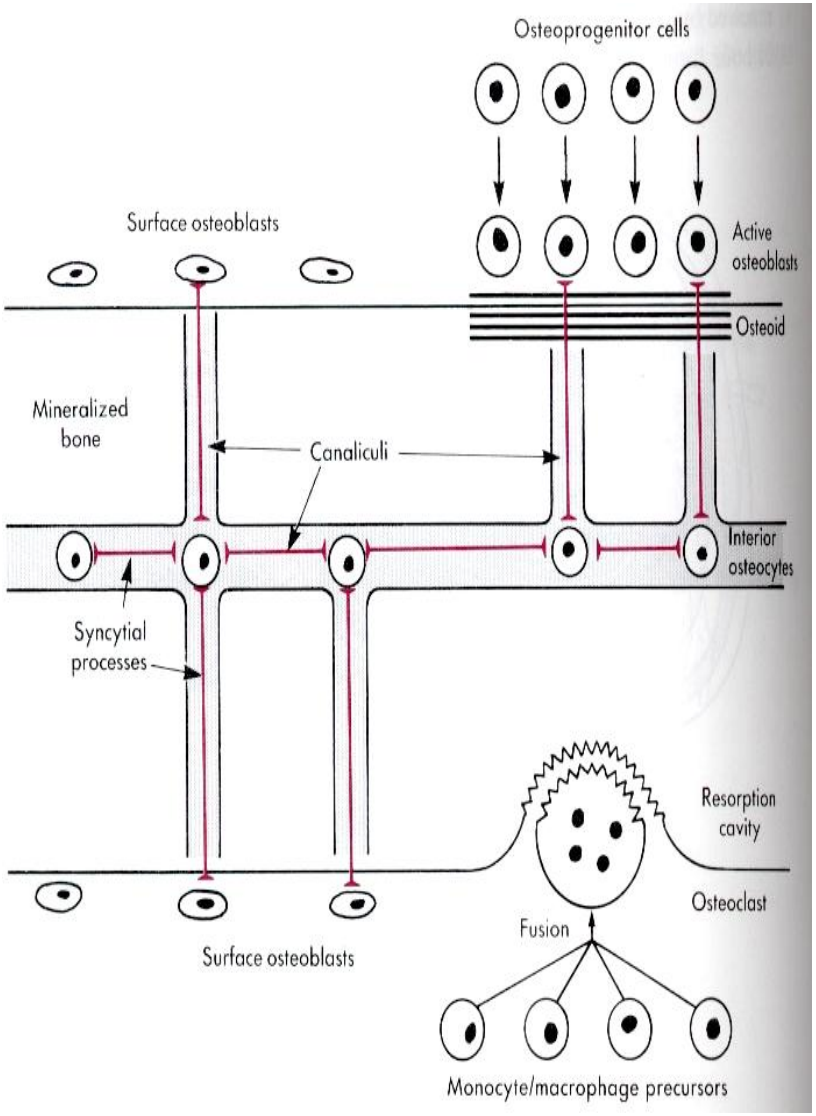
-Interior osteocytes remain connected to surface cells (osteoblasts) via syncytial cell processes.

- Osteocytes transfer calcium from large surface area of the interior of canaliculi to the ECF



Bone formation

- 1-Bone formation begins when Active **osteoblasts** synthesize uncalcified Collagen (raws) of an organic صفائفfibrils to form matrix called Osteoid. **called osteocytes)**
- 2- Then **Mineralization** (Deposition & precipitation of Calcium & Phosphate on the Osteoid collagen fibers forming hydroxyaptite crystals over a period of weeks or months)

Control of bone resorption ارتشاف

Bone resorption of Ca^{++} occurs by two mechanims :

(1**) Osteocytic osteolysis** → rapid and transient effect
(2) **Osteoclasitc resorption** → slow and sustained mechanism **.**

-What is the effect of (PTH) & vitamin D & Ostrogen in bone resorption?

1-Osteocytic Resorption (osteolysis)

- by osteocytes.

-Osteocytes digest mineralized bone & transfere calcium & Po4 from canaliculi to ECF

-Does not decrease bone mass

- reduce calcium & Po4

-Removes calcium from recently formed crystals

- Quick process begins in minutes.

(2) **Osteoclasitc resorption :-**

-

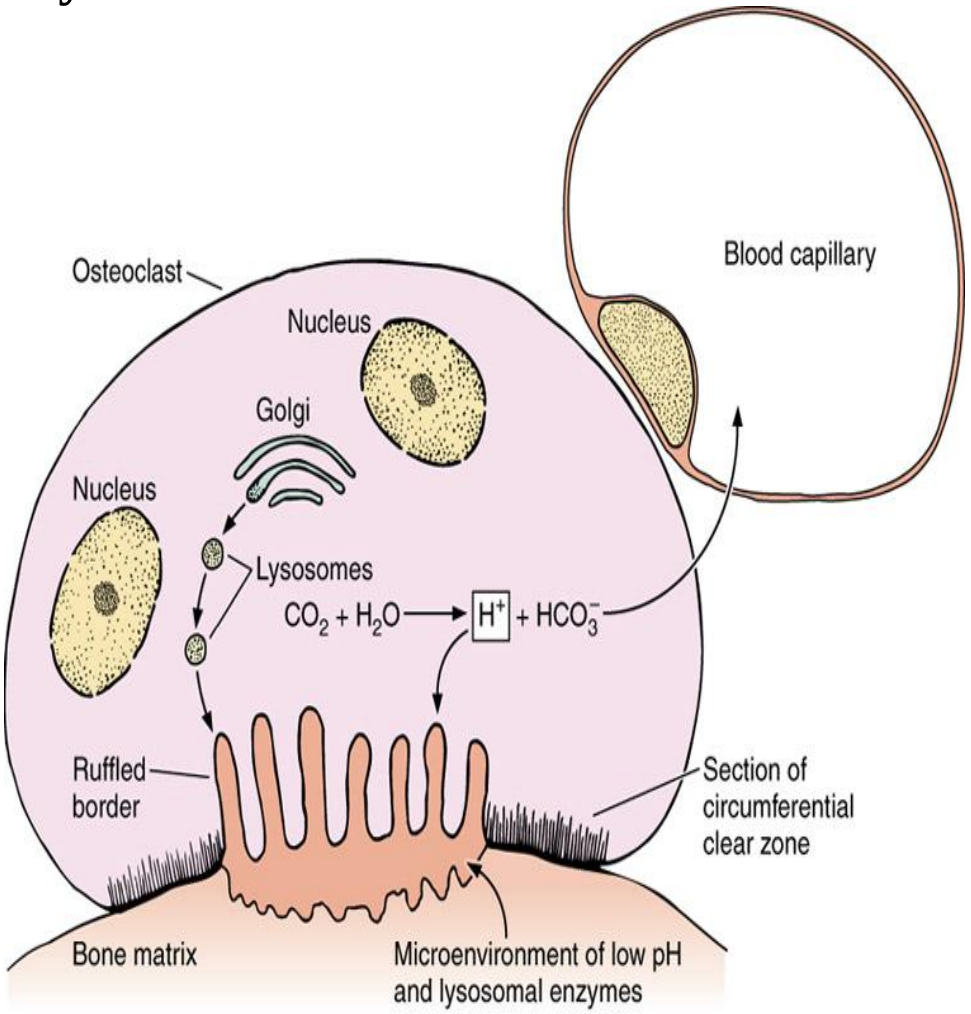
--slow and sustained needs several **days or weeks .**

- destroys matrix of old bone

- diminishes bone mass & not calcium & Po4

- By osteoclasts.

(acidify area of bone to dissolve hydroxyapatite by Hcl then lysosomes & acid proteases digest collagen)



Bone remodeling (اعادة تشكيل)

-What is the meaning of bone resorbtion?

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-Endocrine signals to resting **osteoblasts** generate paracrine signals to osteoclasts)

-Osteoclasts digest and resorb an area of mineralized bone.(how?)

- Local macrophages clean up debris.

-Then **osteoblasts** are recruited to site & deposit new matrix

-What is the role os osteocytes?

-New bone replaces resorbed bone.

-Figure 79-5 •

Bone remodling affected by;-

1-Mechanical stress on bone stimulates formation of stronger bone

2- Parathyroid hormone (PTH) & 1,25 dihydroxycholecalciferol

3- Calcitonin

Osteoporosis :-

-Reduced bone density & mass

- diminished bone matrix ( )

-bone becomes weak & ca++ is lost from skeleton.

-Earlier in life for women than men.Why ?

-The rate of osteoclastic resorption exceeds deposition of new bone by osteoblastic activity .What are the causes?

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Reduced risk by:

--High Calcium in the diet

--habitual exercise

--avoidance of smoking & alcohol intake & drinking carbonated soft drinks

Hormonal control of Calcium

1-Parathyroid hormone (PTH)
2- 1,25-dihydroxycholicalcefirol (active form of Vitamin D3)
(cholicalcefirol = Vitamin D3)
3- Calcitonin
- They regulate Ca^{++} resorption, absorption and excretion from the three organs that function in Ca^{++}homeostasis (bone, kidney and intestine).

-1-Vitamin D

-**Humans acquire vitamin D from two sources**.

-1-produced in the skin by ultraviolet radiation on cholesterol to form Vit D3(cholecalciferol) (exposure to sun ultravioletprevents vit D defeciency)

2- ingested in the diet-

-**In liver:**- Vit D3 converted to 25 hydroxycholecalciferol ,

in kidney :- Parathormone (PTH) convert it to **1,25 dihydroxycholecalciferol (active form)**

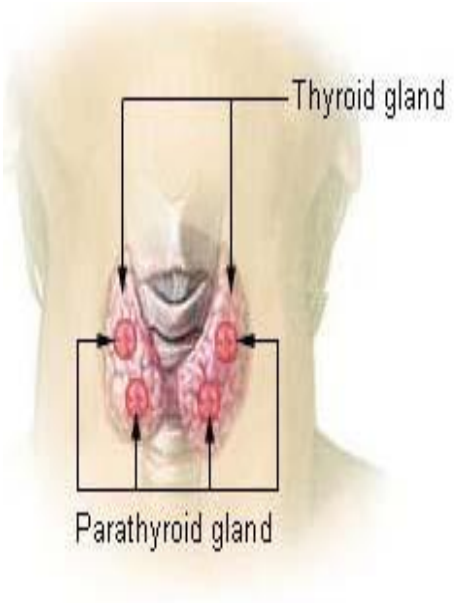
The main action of active Vitamin D (1,25 dihydroxycholecalciferol)

- stimulate absorption of Ca^{2+} & PO4 from the intestine
- stimulate Ca reabsorption in kidneys
- help in bone formation & absorption(large amounts of vit D cause bone absorpion, but in small amounts stimulates bone calcification as it increase calcium absorption

- Mobilize ca++ from bone into plasma by increasing number of osteoclasts to increase plasma Ca^{++} levels (only when it drops

2-Parathyroid Hormone (PTH)

Parathormone from parathyroid gland



Functions:-

- increase plasma Ca^{++} levels when it drops and decrease plasma phosphate levels by:

1- acts directly on the bones to stimulate Ca^{++} absorption from bone & bone resorption by activating osteoclasts

2- on kidney to stimulate Ca++ reabsorption & prevents its execretion & inhibit reabosorption of phosphate .

3- acts indirectly on kidney by activation of 25-(OH)-D into 1,25-$(OH)_2$-D (active vit D)

4-on intestine to stimulate Ca++ reabsorption

3-Calcitonin

-Calcitonin is from parafollicular cells of the thyroid gland (C cells)

-Calcitonin acts to decrease plasma Ca^{++} levels.

-Stimulated by a rise in plasma Ca^{++} levels

- suppresses osteoclastic activity

-decrease formation of new osteoclasts

-it increases osteoblastic activity