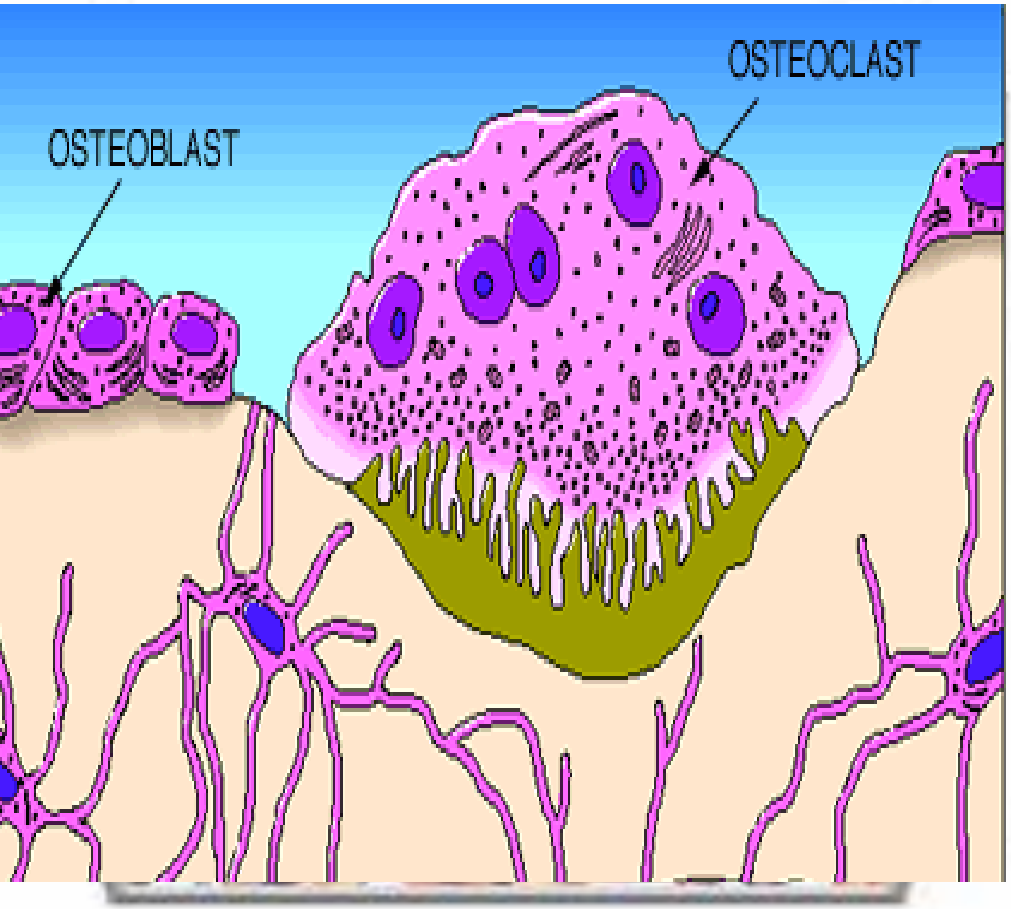
Physiology of Bone



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Lecture1:- Bone physiology

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

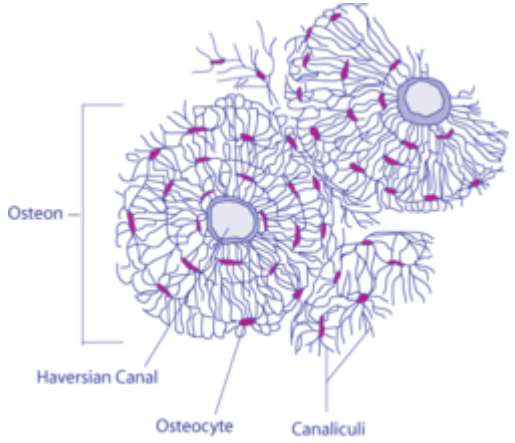
2-Protects vital organs (cranium, thoracic cavity)

3-Contains bone marrow for blood cells synthesis خليق

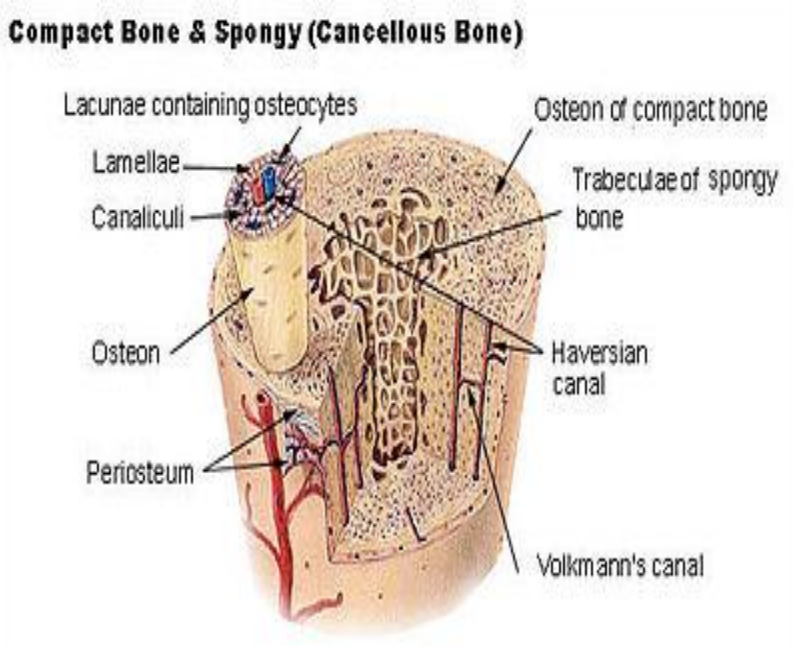
4-Reservoir of Ca++, PO4 to maintain constant concentrations of them in body fluids

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



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



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

Trabecular (spongy-Cancellous) Bone

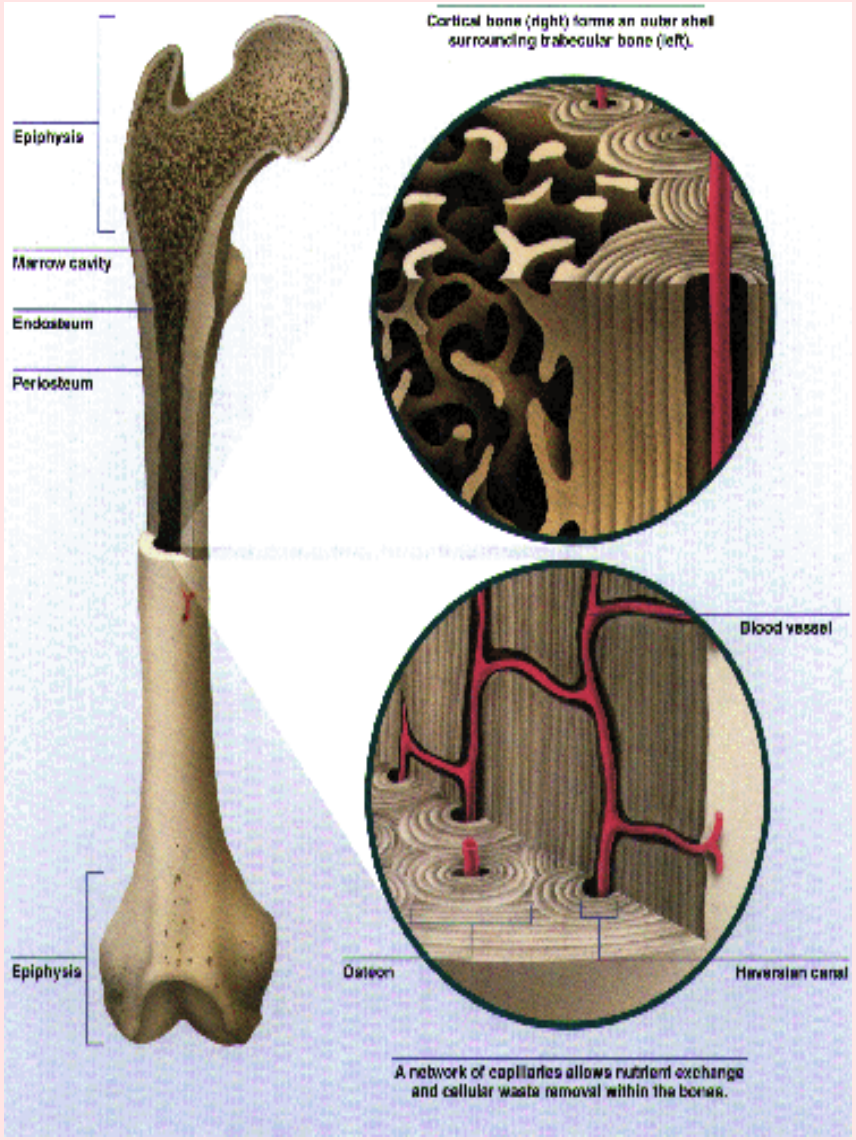
- -Rigid but appears spongy
- - Forms the interior scaffolding)(هيكل) which helps bone to maintain their shape despite compressive forces.
- **Compared to cortical bone it is:**

(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**
- It exists in fractions :
- (1) Free ionized calcium → **50%** of total ECF calcium
- (2) Protein-bound calcium → **40%**
  - -90% bound to albumin
  - - Remainder bound to globulins
- Alkalosis increases calcium binding to protein and decreases ionized calcium
- (3) Calcium bound to serum constituents → **10%** (citrate & phosphate)
- **Only the free, ionized Ca^{2+} is biologically active.**

- **PO_4 :-**
- Calcium is tightly regulated with Phosphorous in the body.
- PO_4 normal plasma concentration is **3.0-4.5 mg/dL**.
- 1- **13 %** Non- diffusable protein bound (85-90 % is found in bone.)
- 2- **87** % Diffusable form (52% ionized & rest bound to ions)
- 2- small amount in ATP, cAMP and proteins compounds
- **Ca++ x PO4 = constant (solubility product)**
- -if any one increase it should precipitate مترسب in bone

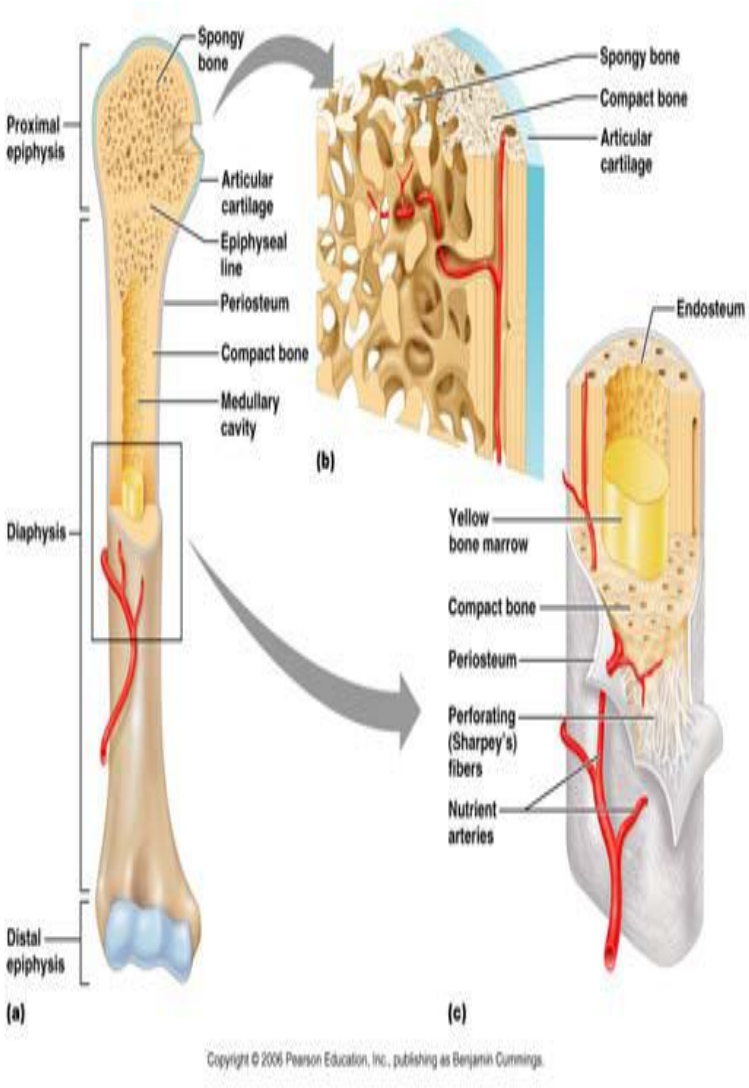
- **Bone& Ca++:-**

-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. Whereas < 1% of our body Ca is in ECF , if it falls below normal,Ca will move from bone into ECF**

- **BONE GROWTH:-**
- -Linear طولي growth occurs at epiphyseal المشاشيplates.
- -Increase in width occurs at periosteum
- غشاء العظم
- -During growth , rate of bone formation exceeds resorptionامتصاص and bone mass increases.
- -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:

(1) Osteoblast :

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

(2) Osteocytes :

- is the **mature bone cell** .
- 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 :

- is a large multinucleated cell derived from monocytes
- -function is to resorb يرتشف the formed bone. (secrete Hcl to acidify area of bone to dissolve hydroxyapatite & acid proteases digest collagen)

Canaliculi

Within each bone unit is minute fluid-containing channels called the **canaliculi**.

- Canaliculi traverse تعبر خلال the mineralized bone.

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

- Osteocytes transfer calcium from bone canaliculi to the ECF

-These processes permits transfer of calcium from (large)surface area of the interior of canaliculi to extracellular fluid

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Bone formation

- 1-Bone formation begins when Active **osteoblasts** synthesize uncalcified Collagen fibrils to form arrays صفائف(raws)of an organic matrix called the osteoid.
- 2- Then mineralization (Deposition of Calcium &
- Phosphate on the Osteoid Matrix)

Mineralization

- Requires adequate Calcium and phosphate
-Dependent on Vitamin D
- Alkaline phosphatase and osteocalcin play roles in bone formation(their plasma levels are indicators of osteoblast activity).

Control of bone resorption ارتشاف

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

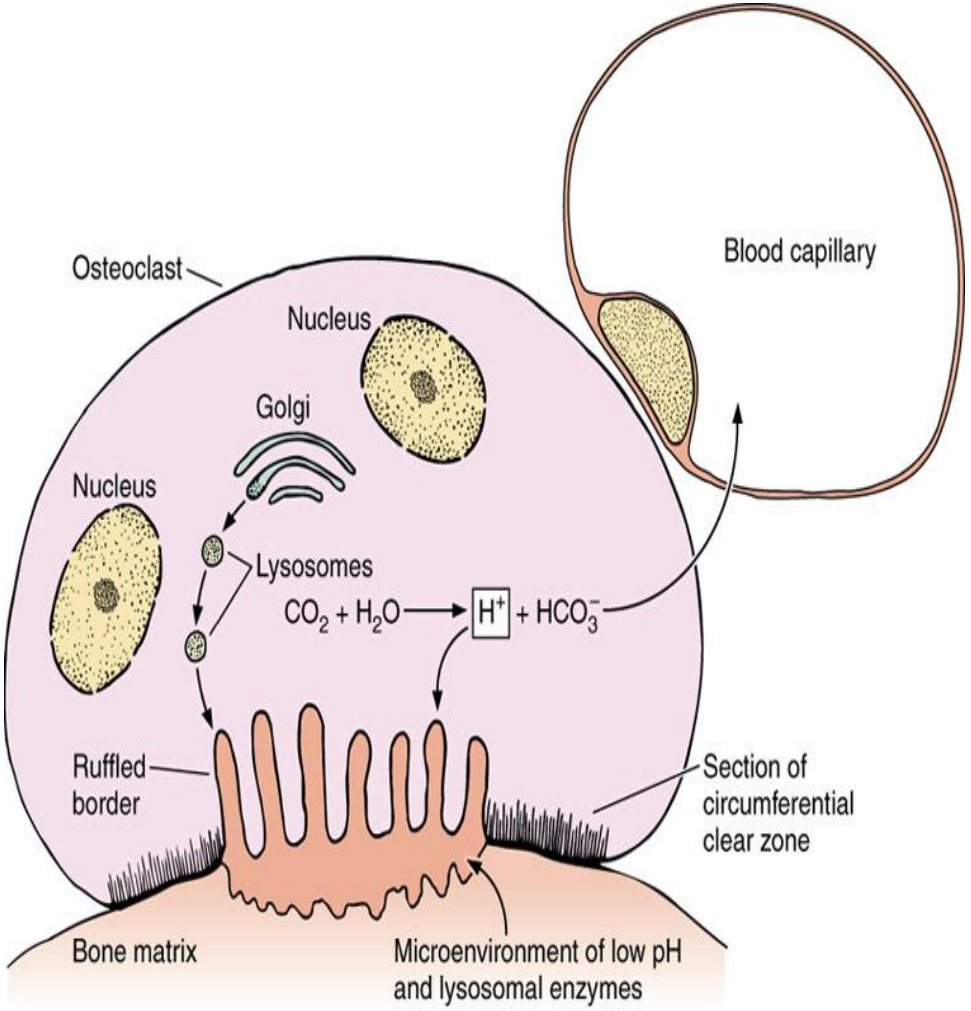
- (1) osteocytic osteolysis → this is a rapid and transient effect
- (2) osteoclasitc resorption → is slow and sustained mechanism .
- Both are stimulated by Parathyroid Hormone (PTH) .

1-Osteocytic osteolysis

- Cell responsible for resorption is the **osteocyte**.
- Activity of **osteocytes** digest mineralized bone area then calcium transfer from canaliculi to extracellular fluid
- Does not decrease bone mass.
- Removes calcium **from most recently formed crystals**
- **Quick process.**

(2) Osteoclasitc resorption → is slow and sustained mechanism .

- - destroys matrix of old bone
- - diminishes bone mass.
- Cell responsible for resorption is the **osteoclast**.
- (acidify area of bone to dissolve hydroxyapatite by Hcl then lysosomes & acid proteases digest collagen)



Bone remodeling

- **Remodeling (اعادة تشكيل)** means continuous deposition of newbone by osteoblasts & absorption of old bone by osteoclasts
- -Endocrine signals to resting **osteoblasts** generate paracrine signals to osteoclasts
- **Osteoclasts** digest and resorb an area of mineralized bone.
- Local macrophages clean up debris.
- Then **osteoblasts** are recruited to site and deposit new matrix which will be mineralized.
- New bone replaces previously resorbed bone.

Bone remodling affected by;-

1-mechanical stress on bone stimulates formation of stronger bone

2- Parathyroid hormone (PTH)& 1,25 DIHYDROXYCHOLECALCIFEROL stimulates osteoclastic activity & formation of osteoclasts

Osteoporosis

- The total bone mass of humans peaks at 25-35 years of age.
- Men have more bone mass than women.
- A gradual decline occurs in both genders with aging, but women undergo an accelerated loss of bone due to increased resorption during peri-menopause
- قبل سن اليأس
- Bone resorption exceeds formation.

- **Osteoporosis :-**
- **-**Reduced bone density and mass
- -Susceptibility to fracture.
- -Earlier in life for women than men
- **-The rate of osteoclastic resorption exceeds deposition of new bone**
  - Cause/ loss of anabolic steroids as estrogen & testosterone which stim osteoblastic activity
  -bone becomes weak & ca++ is lost from skeleton
- **Reduced risk by:**
  - High Calcium in the diet
  - habitual exercise
  - avoidance of smoking and alcohol intake
  - avoid drinking carbonated soft drinks

Hormonal control of Calcium

Three principal hormones regulate Ca^{++}

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

(2) ingested in the diet

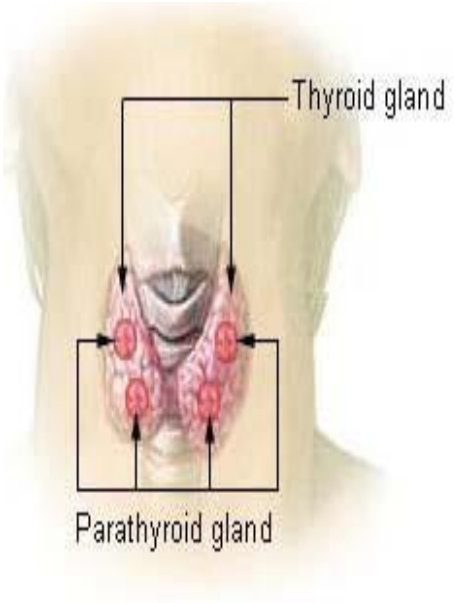
- In liver Vit D3 converted to 25 hydroxycholecalciferol , in kidney
- **PTH** convert it to **1,25 dihydroxycholecalciferol (active form)**

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

- **- stimulate absorption of Ca^{2+} from the intestine**
- **- stimulate Ca reabsorption in kidneys**
- **- help in bone formation**
- **- mobilize ca++ from bone into plasma by increasing number of osteoclasts to increase plasma Ca^{++} levels (only when it drops)**

2-Parathyroid Hormone (PTH) Action

- Parathormone from parathyroid gland
- Functions:-
- - To increase plasma Ca^{++} levels when it drops and decrease plasma phosphate levels.
- 1- acts directly on the bones to stimulate Ca^{++} resorption by activating osteoclasts
- 2- on kidney to stimulate Ca++ reabsorption in the distal tubule & to inhibit reabosorptioin of phosphate (thereby stimulating its excretion).
- 3-PTH also acts indirectly on kidney by activation of 25-(OH) -D into 1,25-$(OH)_2$-D(active vit D)



3-Calcitonin

- Calcitonin is synthesized and secreted by the parafollicular cells of the thyroid gland (C cells)
- -Calcitonin acts to decrease plasma Ca^{++} levels.
- The major stimulus of calcitonin secretion is a rise in plasma Ca^{++} levels
- -it suppresses osteoclastic activity and number in bone
- -it increases osteoblastic activity to mineralize bone