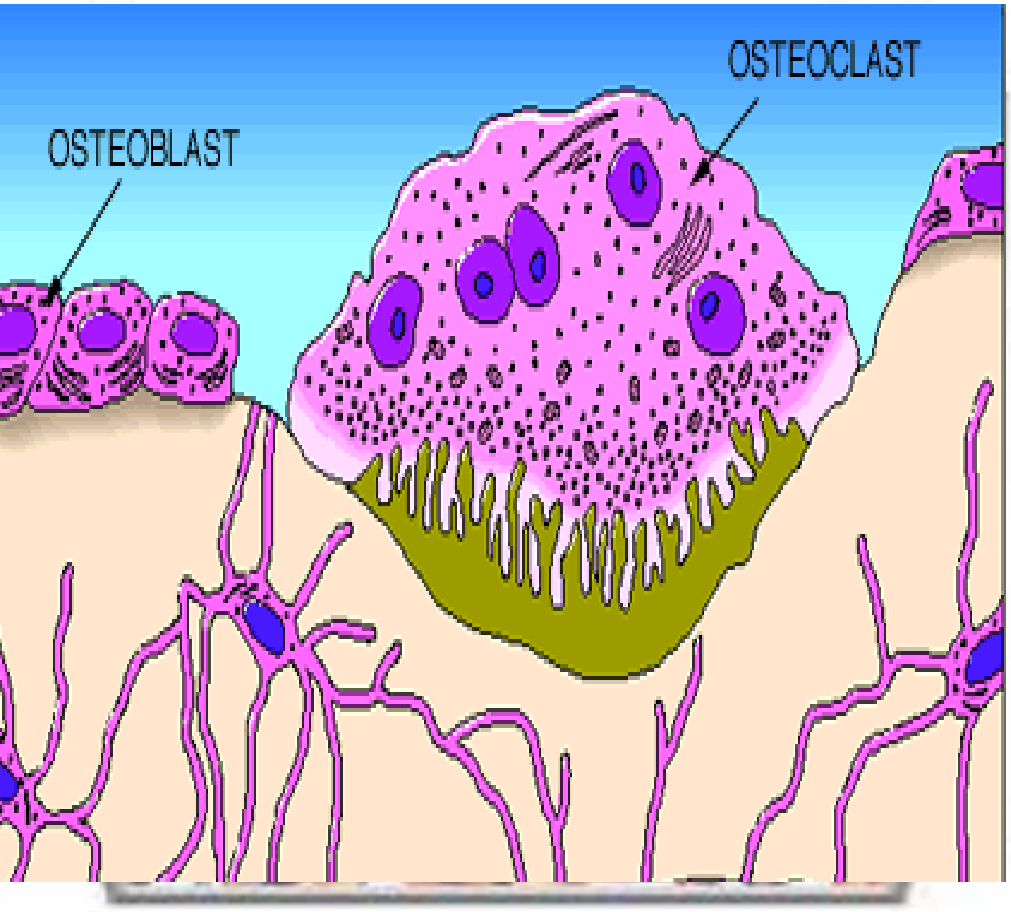
Physiology of Bone



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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 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

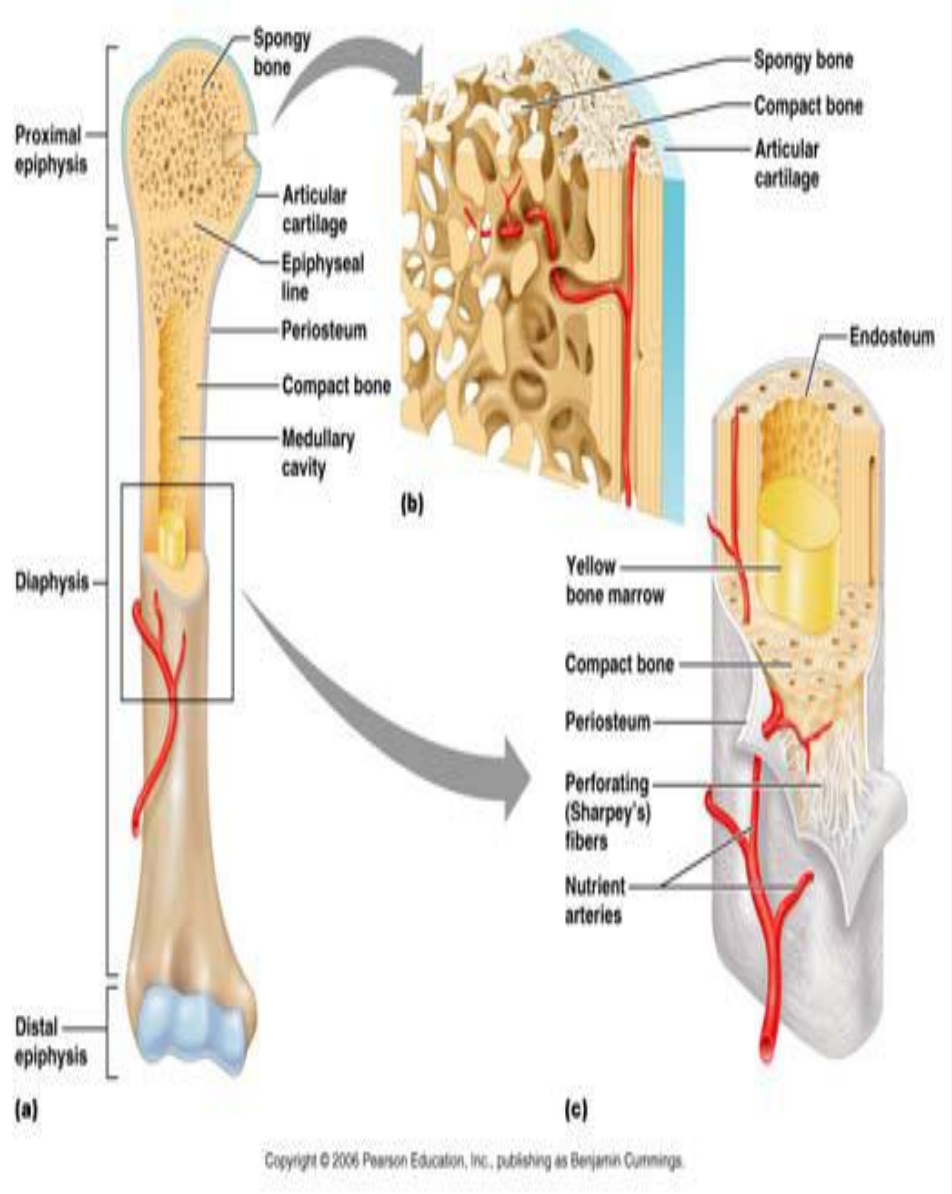
Calcified material,

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).


Spongy bone
Proximal epiphysis
Articular cartilage
Epiphyseal line
Periosteum
Compact bone
Medullary cavity
Diaphysis
Distal epiphysis
(a)
Spongy bone
Compact bone
Articular cartilage
(b)
Endosteum
Yellow bone marrow
Compact bone
Periosteum
Perforating (Sharpey's) fibers
Nutrient arteries
(c)
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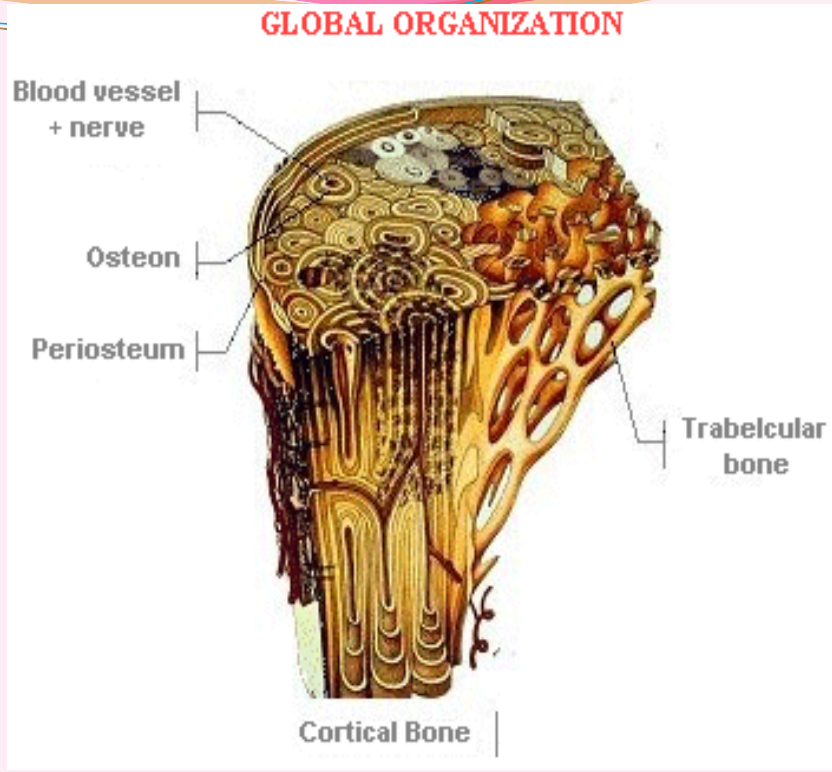
Compact bone

- -forms a protective outer shell (غلاف) around every bone in the body.
- -has a slow ca ++ turnover دوران معدلrate
- -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

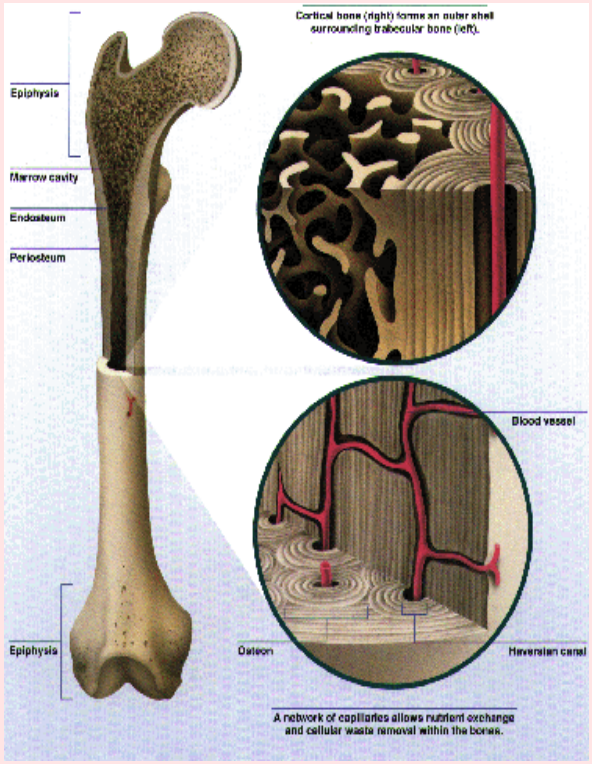
- -Rigid but appears spongy
- - Forms the interior scaffolding)(هيكل) which helps bone to maintain their shape despite compressive forces.
- **Compared to cortical bone it is:**

(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 PO_4 = 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($CaPo_4$ 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 Ca is in ECF ,if it falls below normal,Ca will move from bone into ECF

- **BONE GROWTH:-**
- -Linear طولي growth occurs at epiphysealالمشاشي plates.
- Increase in width occurs at periosteumغشاء 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 resportion 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

-

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

- 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** 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-PTH & 1,25 DIHYDROXYCHOLECALCIFEROL stimulates osteoclastic activity & formation of osteoclasts

3- CALCITONIN inhibits activity& formation of osteoclasts

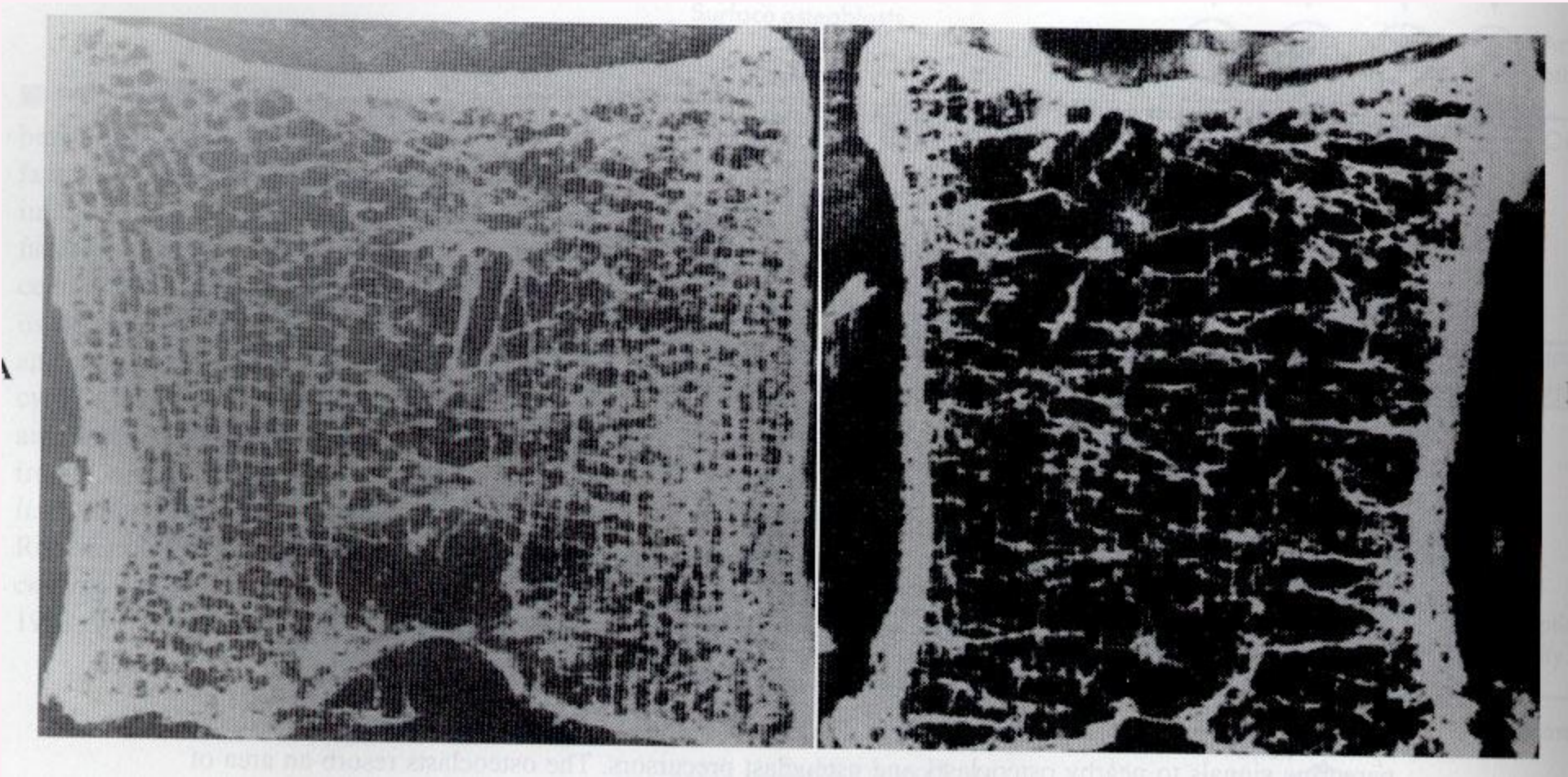
Osteoporosis

- 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

Vertebrae of 40- vs. 92-year-old women

Note the marked loss of trabeculae with preservation of cortex.



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).

Table 48-1 Major effects of various hormones on bone

Bone formation	*Bone resorption*
Stimulated by	**Stimulated by**
Growth hormone (constant)	Parathyroid hormone (constant)
Insulin-like growth factors	Vitamin D
Insulin	Cortisol
Estrogen	Thyroid hormone
Androgen	Prostaglandins
Vitamin D (mineralization)	Interleukin-1
Transforming growth factor-β	Interleukin-6
Skeletal growth factor	Tumor necrosis factor α
Bone-derived growth factor	Tumor necrosis factor β
Platelet-derived growth factor	
Calcitonin	
Parathyroid hormone (intermittent)	
Inhibited by	**Inhibited by**
Cortisol	Estrogen
	Androgen
	Calcitonin
	Transforming growth factor-β
	γ-Interferon
	Nitric oxide

Hormonal control of bones

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

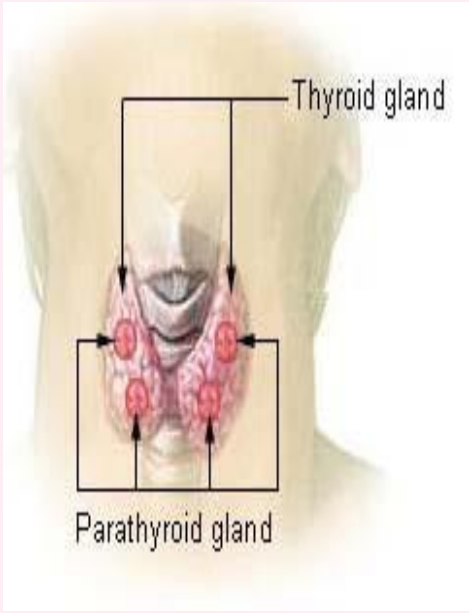
- In liver Vit D3 converted to 25 hydroxycholecalciferol , in kidney
- **PTH** convert it to **1,25 dihydroxycholecalciferol (active form)**

- 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