Physiology of Bone

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● Functions of bone

- Bone is a living, growing tissue which has several functions :

✓ Supports soft tissue
✓ Protects vital organs (cranium, thoracic cavity)
✓ Contains bone marrow
✓ Reservoir of Ca++, PO4 to maintain constant concentrations in body fluids
✓ Allows body to move

Structure of Bone

● Bone Matrix

- Made of organic & inorganic components

(A) Organic matrix →

- made of collagen ,
- called osteoid ,
- makes 30% of bone , on which is laid the →

(B) Inorganic (mineral) component →

- called hydroxyapatite ,
- made of $CaP0_4$ crystals ,
- constitutes the remaining 70% of bone matrix

Bone Cells

- There are three types of bone cells:

(1) Osteoblast :

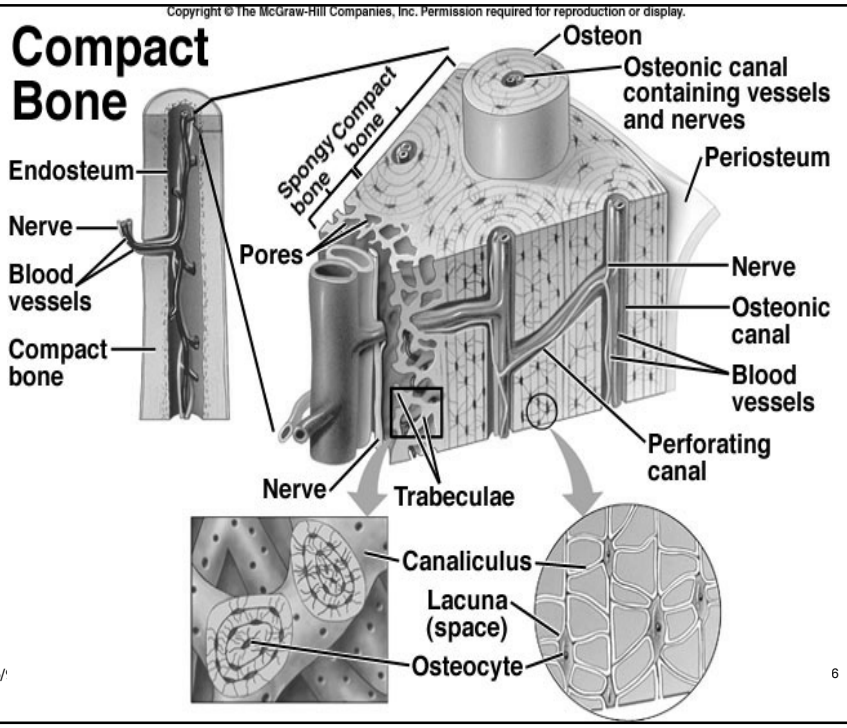
- Differentiated bone forming cell .
- It secretes bone matrix (mainly collagen) on which Ca^{++} and PO_4 precipitate.

(2) Osteocytes :

- is the mature bone cell .
- It is enclosed in bone matrix.

(3) Osteoclast :

- Bone-resorbing cell
- Inorganic bone is composed of hydroxyapatite and organic matrix is composed primarily of collagen .

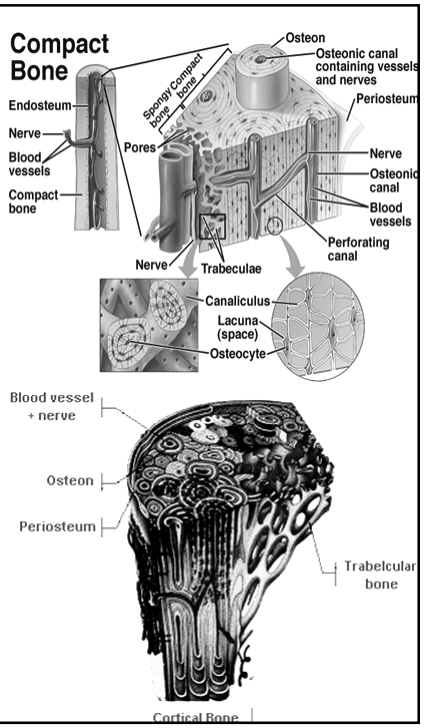


Types of Bone

- There are two types of bone in the human skeleton :
- (1) Cortical bone :
- Constitutes the dense , concentric layers of long bones
- Comprises 80 % of total body bone mass
- Has a slow turnover rate
- (2) Trabecular bone :
- Comprises 20% of total bone mass
- Present in the interior of flat bones (skull, ribs, vertebrae, pelvis) , and also present in epiphyseal and metaphysal regions of long bones
- Though it represents only 20% of the skeletal mass, it has 5 times greater surface area than cortical bone
- Because of its greater surface area & accessibility , it has a faster turnover rate than cortical bone ; hence it is more important than cortical bone in terms of calcium turnover

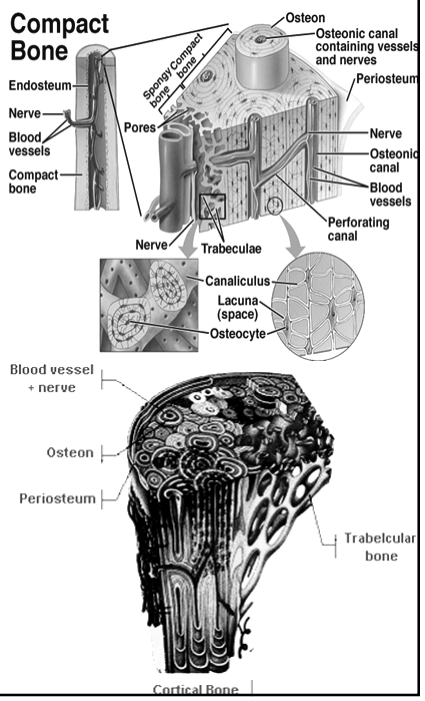
Cortical Bone (1)

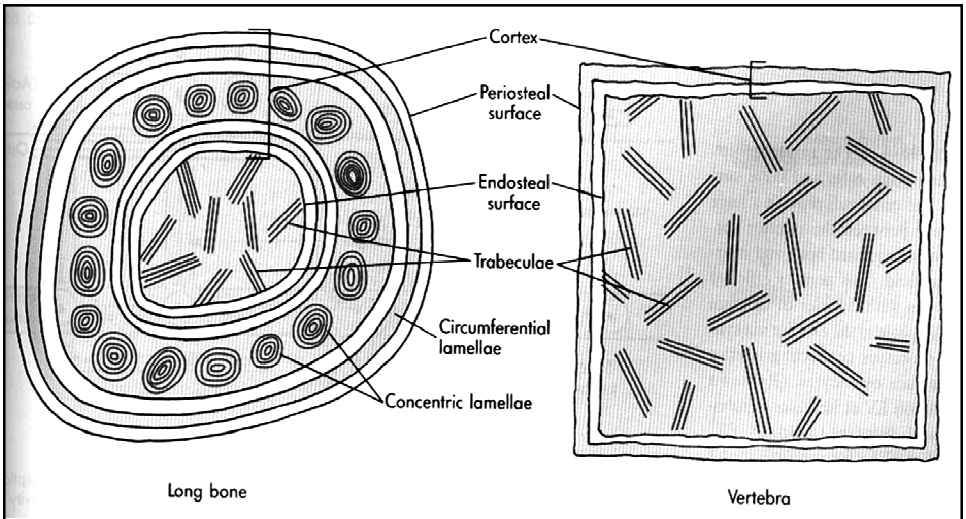
- Also called compact bone, because it forms a protective outer shell around every bone in the body.
- Has high resistance to bending and torsion , & therefore it provides strength in areas where bending would be undesirable , such as in the middle of long bones.
- It has a series of adjacent and overlapping circular formations called Harvesian Systems or Osteons .



Cortical Bone (2)

- Each Harvesian System (Osteon) is composed of a central vascular channel surrounded by a tunnel, called the Harvesian Canal.
- The Harvesian Canal contain blood vessels (capillaries, aterioles, venules), nerves and possibly lymphatics.
- Between Harvesian system are interstitial lamellae (concentric layers of mineralized bone).





- Lamellar bone gets it strength from its plywood-like from being composed of parallel layers of bone alternate in orientation by 90 degrees.

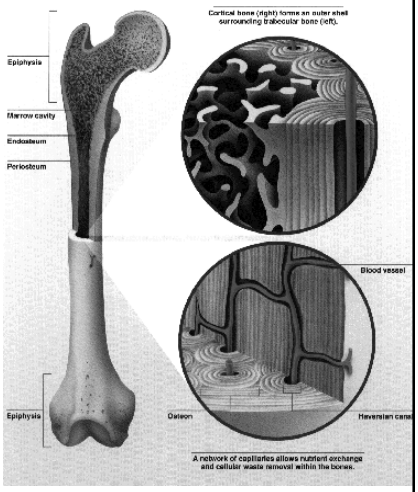
Trabecular Bone (1)

- Trabecular bone has spongy appearance but actually it is rigid .
- It is composed of bundles of short and parallel strands of bone fused together.
- It forms the interior scaffolding ١ , which helps bone to maintain their shape despite compressive forces.
- 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.

Calcium

- Bone serves as a major reservoir for Ca^{++} storage
- However , very little Ca^{2+} can be released from it .
- Most of the Calcium in our bodies is found as hydroxyapatite , HA { i.e., calcium phosphate/hydroxide compound } , crystals.

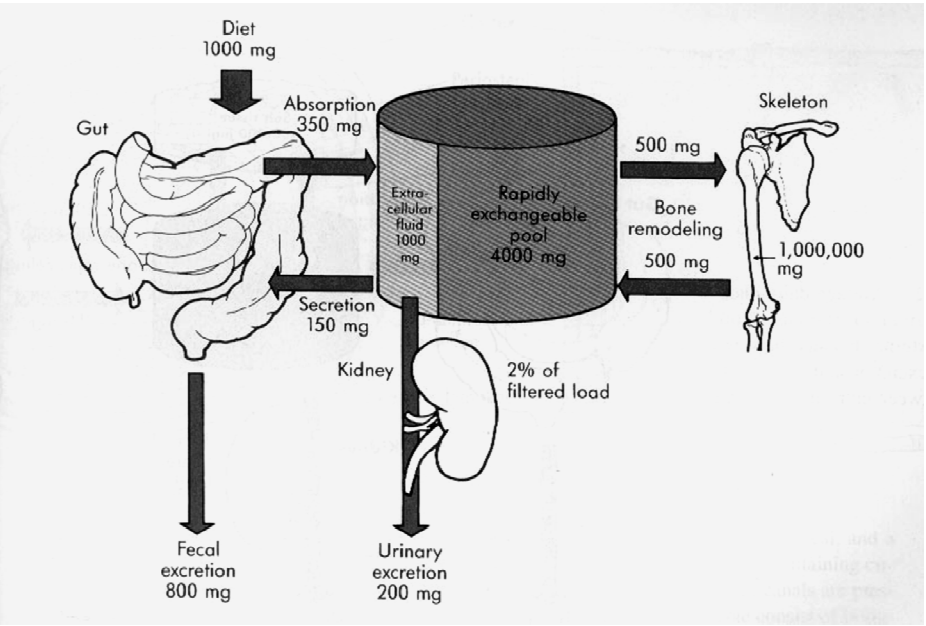
Extracellular Fluid (ECF) Calcium

- Ca^{++} level in plasma is 8.5-10 mg/dL .
- It exists in 3 fractions :
- (1) Ionized calcium → 50% of total ECF calcium
- (2) Protein-bound calcium → 40% of total ECF calcium
    - 90% of the protein-bound calcium is bound to albumin,
    - the remaining 10% is bound to globulins
- (3) Calcium bound to serum constituents (citrate & phosphate) → 10%
- Only the free, ionized Ca^{2+} { (1) above } is biologically active.

- Binding of calcium to albumin is pH-dependent
- Alkalosis increases calcium binding to protein → thereby decreases ionized calcium level
- Calcium is tightly regulated with Phosphorous in the body.
- Phosphorous is an essential mineral necessary for ATP, cAMP second messenger systems, and other roles

- During growth , rate of bone formation exceeds resorption and skeletal mass increases.
- Linear growth occurs at epiphyseal plates.
- Increase in width occurs at periosteum
- Once adult bone mass is achieved equal rates of formation and resorption maintain bone mass until age of about 30 years when rate of resportion begins to exceed formation and bone mass slowly decreases.

Calcium turnover



Phosphate

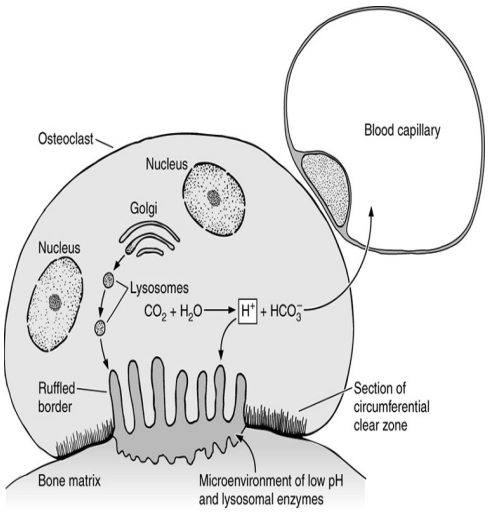
- PO_4 plasma concentration is 3.0-4.5 mg/dL.
- 87% of it is diffusible and 13% non-diffusible,
- Diffusible PO_4 :
- 52% is ionized & the rest is combined to different ions
- Non-iffusible PO_4 :
- This is protein-bound .
- 85-90% of it is present in bone.
- The rest of the protein-bound is present in ATP, cAMP, and other compounds

Bone formation

- Bone formation begins when active osteoblasts synthesize collagen fibers (that form the organic matrix called osetoid)
- Calcium phosphate is deposited on the osteoid → thereby making it s mineralized
  - Mineralization (Deposition of Calcium & Phosphate on the Osteoid Matrix)
- 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 .

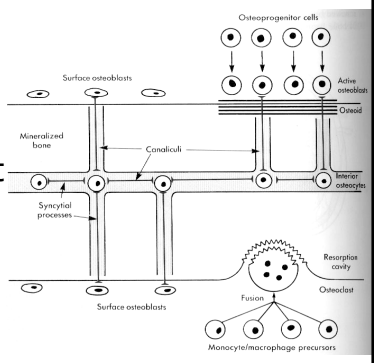
Bone Resorption

- This process does not merely extract calcium, it destroys entire matrix of bone and diminishes bone mass.
- Cell responsible for <u>sustained</u> resorption is the osteoclast .



Control of Bone Formation and Resorption

- Bone resorption of Ca^{++} by two <u>mechanims :</u>
- <u>(A) osteocytic osteolysis →</u>
- This involves transfer of calcium from canaliculi to extracellular fluid via activity of osteocytes.
- It is a fast (rapid) and transient effect ,
- Canaliculi are minute fluid-containing channels within the bone unit
- Interior osteocytes remain connected to surface cells via syncytial cell processes.
- This process permits transfer of calcium from enormous surface area of the interior to extracellular fluid.



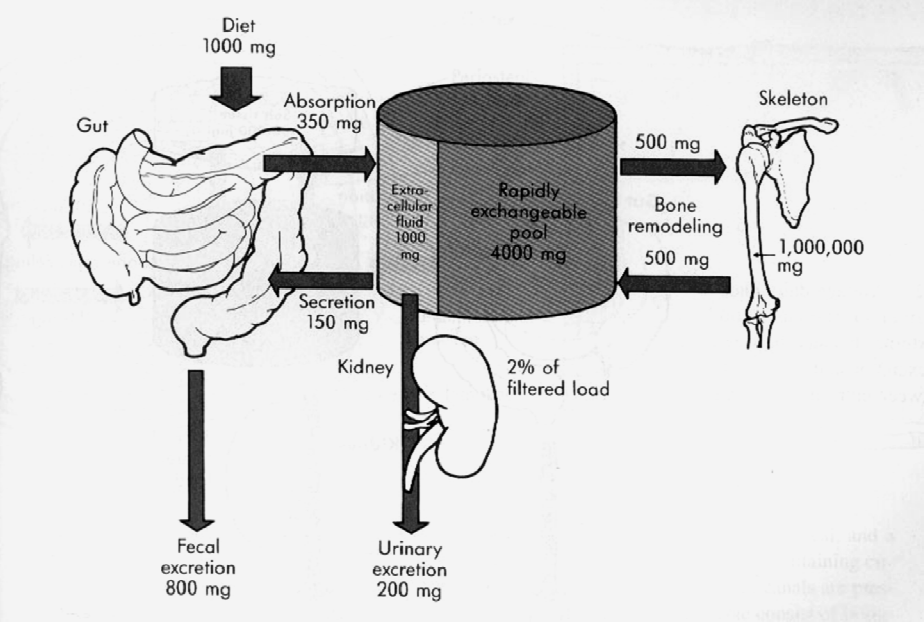
Control of Bone Formation and Resorption (2)

- Summary : Q → What is the function of osteocytes ?
- Answer : Transfer of calcium from canaliculi to the CSF
- (B) osteoclasitc resorption
- is slow and sustained mechanism .
- Both are stimulated by Parathyroid Hormone (Parathormone , PTH) .
- Hence PTH inhibits bone-formation .

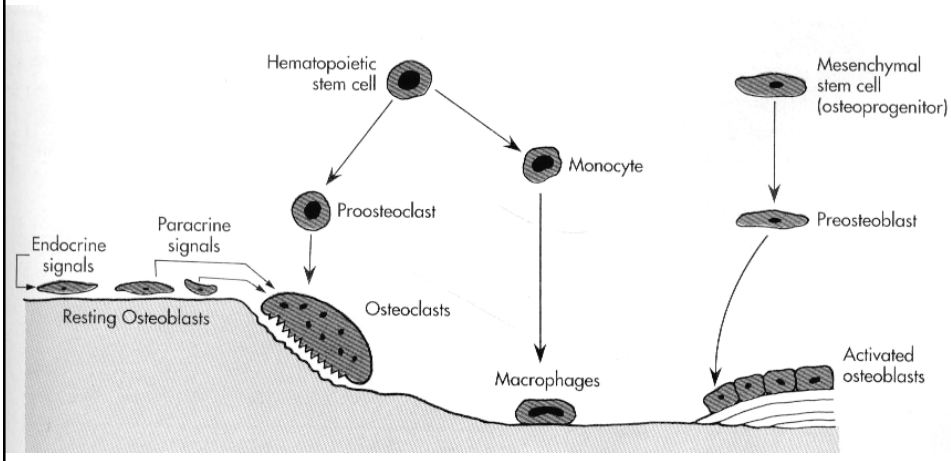
Bone remodeling

- Q : What is the meaning of bone remodeling ?
- Answer : it means the continuous processes of bone absorption (by osteoclasts) & then its deposition (by osteoblasts) .
- 10% of total adult bone mass turns over each year during remodeling process
- Endocrine signals to resting osteoblasts generate paracrine signals to osteoclasts
- Osteoclasts digest and resorb and 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.

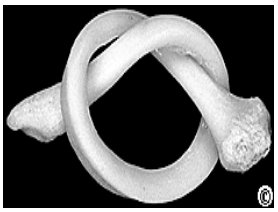
Calcium turnover



Osteoclasts and Ca++ resorption



Bone remodling affected by;-



1-mechanical stress on bone stimulates formation of stronger bone
2- PTH and 1,25 Dihydroxycholecalciferol stimulate activity & formation of osteoclasts
3- Calcitonin inhibits activity & formation of osteoclasts

Osteoporosis (1)

- 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 perimenopause.
- Bone resorption exceeds formation.
- osteoporosis means → Reduced bone density and mass:
- This leads to increased susceptibility to fracture.
- It occurs earlier in life for women than men but eventually both genders succumb to it

Osteoporosis (2)

- The rate of osteoclastic resorption exceeds deposition of new bone
- Cause → loss of anabolic steroids as estrogen & testosterone which stimulate osteoblastic activity → as a result : bone becomes weak & ca^{++} is lost from skeleton
- How to reduced its risk:
  - calcium suuplements in diet
  - habitual exercise
  - avoidance of smoking and alcohol intake
  - avoid drinking carbonated soft drinks

Hormonal control of Calcium

- 3 principal hormones regulate Ca^{++} and three organs that function in Ca^{++} homeostasis.
- (1) Parathyroid hormone (PTH),
- (2) 1,25-dihydroxycholecalciferol (Vitamin D), and
- (3) Calcitonin, regulate Ca^{++}
- 1,25 dihydroxy cholecalciferol (Vitamin D) :
- (1) Its main action is to stimulates bone resorptionn . by mobilizing Ca^{2+} from bone
- (2) stimulate absorption of Ca^{2+} from the intestine
- (1) & (2) above lead to increased blood Ca^{2+} level

- Parathyroid hormone (PTH) :
- Inhibits bone formation
- Increases plasma Ca^{++} levels and decrease plasma phosphate levels by :
- (1) directly acting on bone to activate osteoclasts → stimulate Ca^{++} resorption
- (2) acting on kidney to stimulate Ca++ reabsorption in the distal tubule & to inhibit reabosorptioin of phosphate (thereby promoting its excretion).
- (3) acting indirectly on kidney to change vitamin D inactive form into the active form

- Calcitonin :
- Suppresses osteoclasts & stimulates osteoblasts

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