Physiology of Bone

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

- Define bone & differentiate between types of bone (cortical & trabecular)
- State Ca^{++} concentration and its forms in the ECF ; its relation to PO_4
- Differentiate between the types of bone cells & appreciate their functions .
- Describe bone formation & remodeling
- Understand what is osteoporosis
- Appreciate the effects of different hormones on bone

- Functions of bone

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

✓ Protects vital organs

✓ Provides support for soft tissues

✓ Allows & facilitates movement

✓ Contains bone marrow

✓ Reservoir for Calcium & Phosphate

Structure of Bone •

(1) 30% of bone → is organic matrix (made mainly of collagen) .

✓ It is called osteoid ,

(2) 70% of bone → is inorganic (mineral) bone , made mainly of $CaPO_4$ crystals (with some calcium carbonate crystals , in addition) .

✓ It is called Hydroxyapatite

Bone Cells

- Are 3 types :

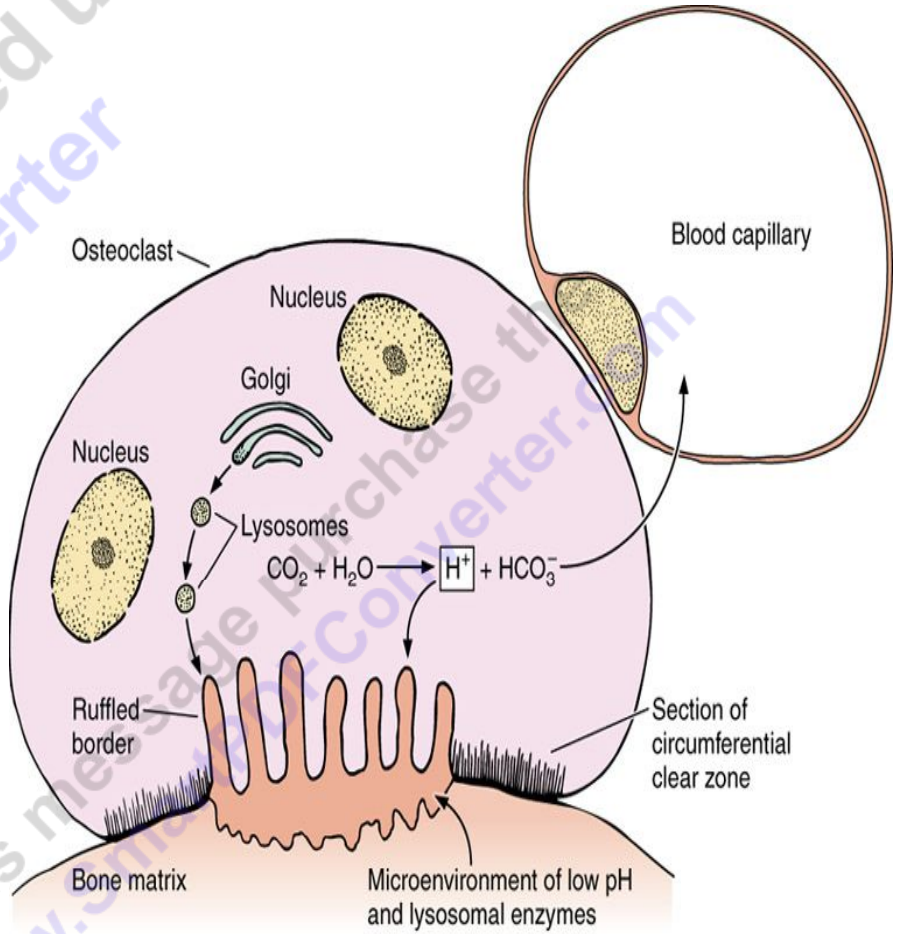
(1) Osteoblasts :

- Bone-forming cells that are responsible for →
- (1) production of a bone matrix (osteoid)
- (2) Mineralization of this matrix : by depositing on it $CaPO_4$ (calcium phosphate) and calcium carbonate crystals
- N.B. : Hydroxyapatite → is the $CaPO_4$ (calcium phosphate) and calcium carbonate that are precipitated/deposited on the osteoid .

(2) Osteoclasts (Bone-Res orbing cells) :

- Remove bone tissue.
- This process is called Bone Resorption
- This process involves removal of both →
- (1) osteoid matrix , &
- (2) minerals (hydroxyapatite)
- Thus , bone resorption by

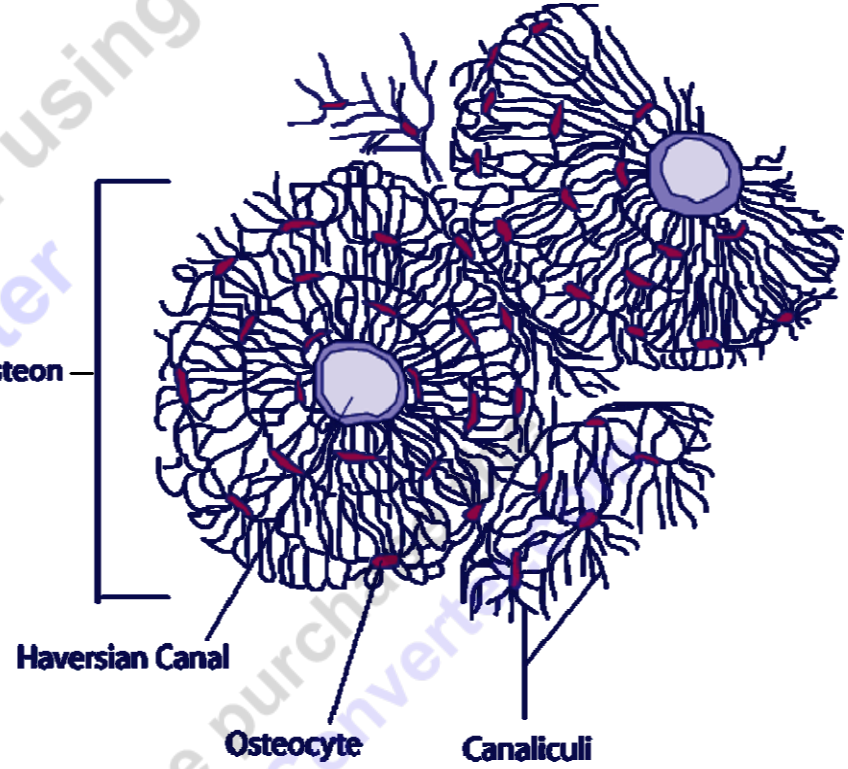
osteoclasts does not merely extract calcium, but it destroys the matrix & demineralizes bone →thereby diminishes total bone mass.

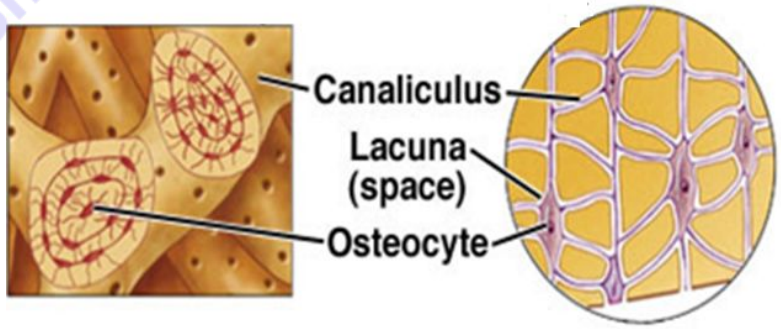


Parathyroid hormone (PTH) promotes (encourages) bone resorption

(3) Osteocytes :

- When Osteoblasts secrete collagen (osteoid matrix),they become trapped in their own secretion
- When they become trapped in the matrix , they change into osteocytes & become embedded into small holes called" Lacunae "(singular : Lacuna)
- Osteocyte is the most abundant cell in compact bone .
- Each osteocyte sends, from its cell-body , long cytoplasmic extensions that connect it to other osteocytes .
- These cytoplasmic extensions extend into & occupy tiny canals called canaliculi
- Canaliculi are used for exchange of minerals (Calcium & Phosphate),nutrients and waste products through gap junctions





- Many recent studies suggest that Osteocytes →
- (1) Have mechanosensory mechanisms → i.e., acts as receptors for mechanical stresses & strain .
- (2) Regulate amounts of calcium & phosphate being transported in either direction (from ECF to bone ; or from bone to ECF) ,
- (3) Act as regulators of osteogenesis (bone formation)

  & osteolysis (bone resorption) → by translating the degree & type of mechanical strain into biochemical signals .
- Depending on the degree & type of strain , the bidchemical signals can result in
- <u>(I) increased rate of osteogenesis (bone formation) by →</u>

  (1) stimulating osteoblasts , &

  (2) increasing rate of transfer of calcium & phosphate from ECF to bone, →

or

<u>(II) increased rate of osteolysis (bone resorption) by →</u>

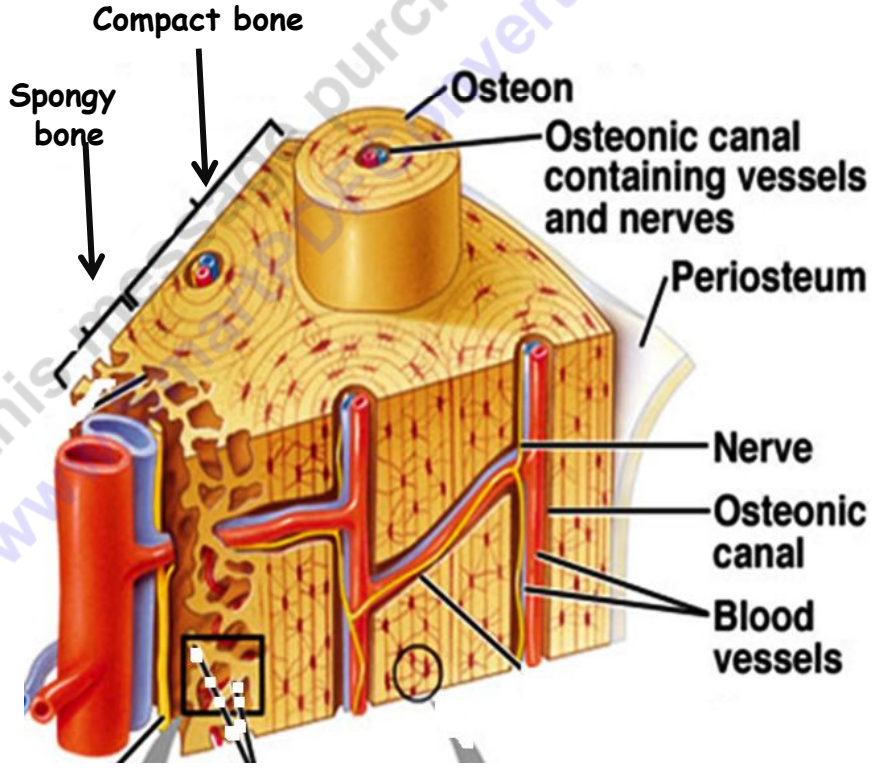
(1) stimulating osteclasts, &

(2) increasing rate of transfer of calcium & phosphate from bone to ECF

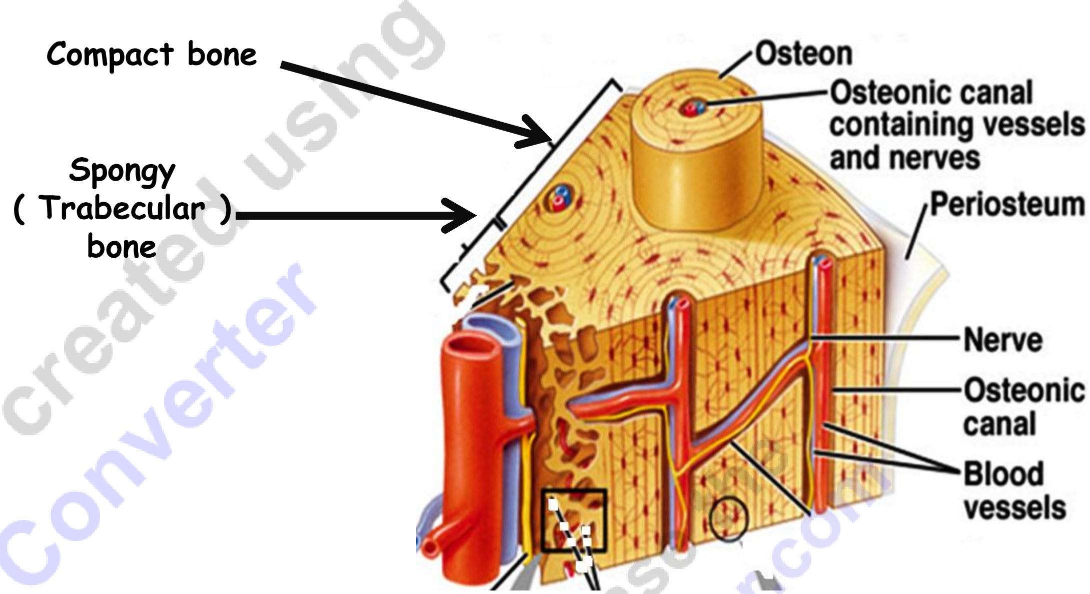
Types of Bone (According to Macroscopic Structure)

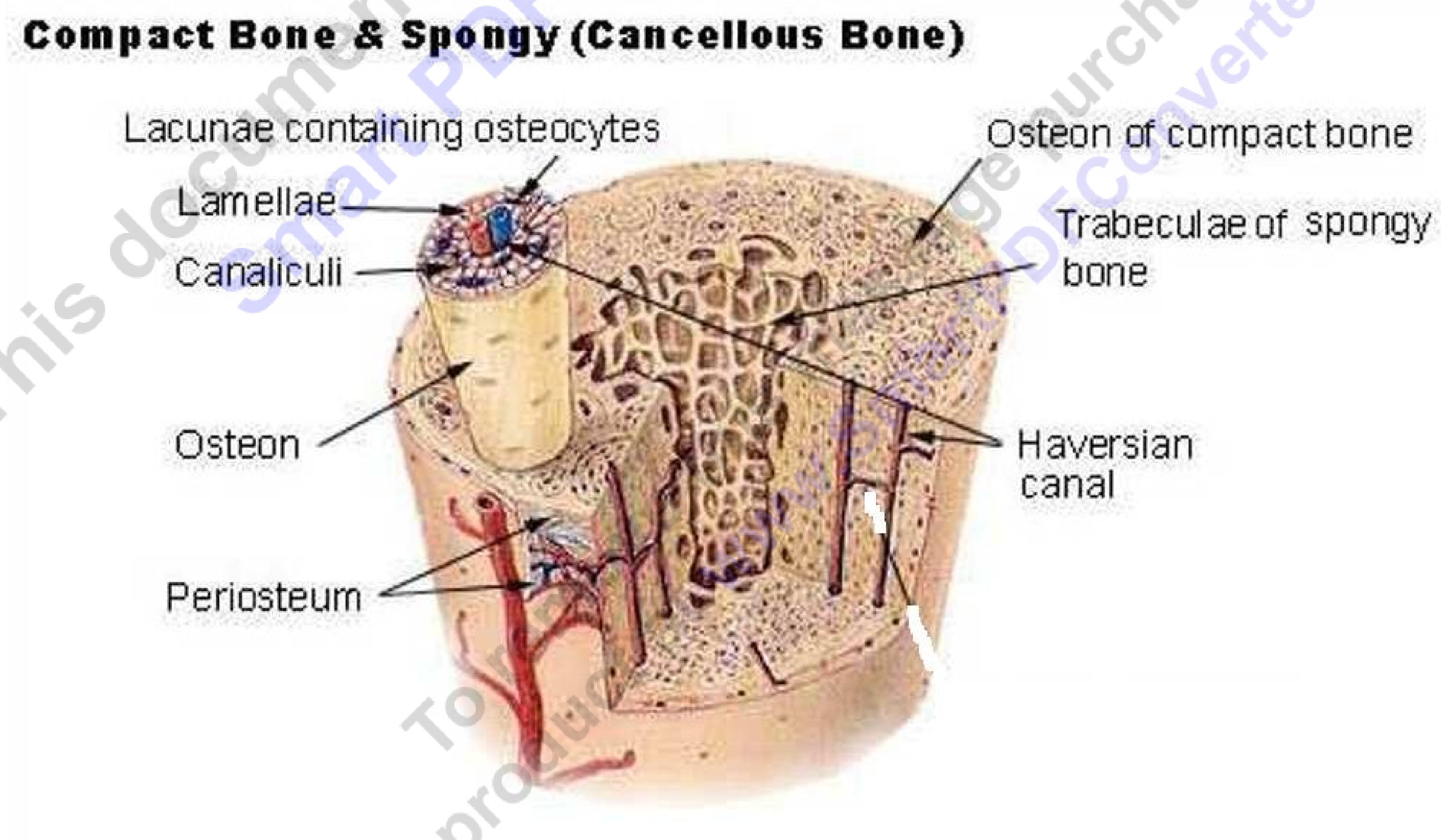
- **(1) Compct (Cortical) bone**

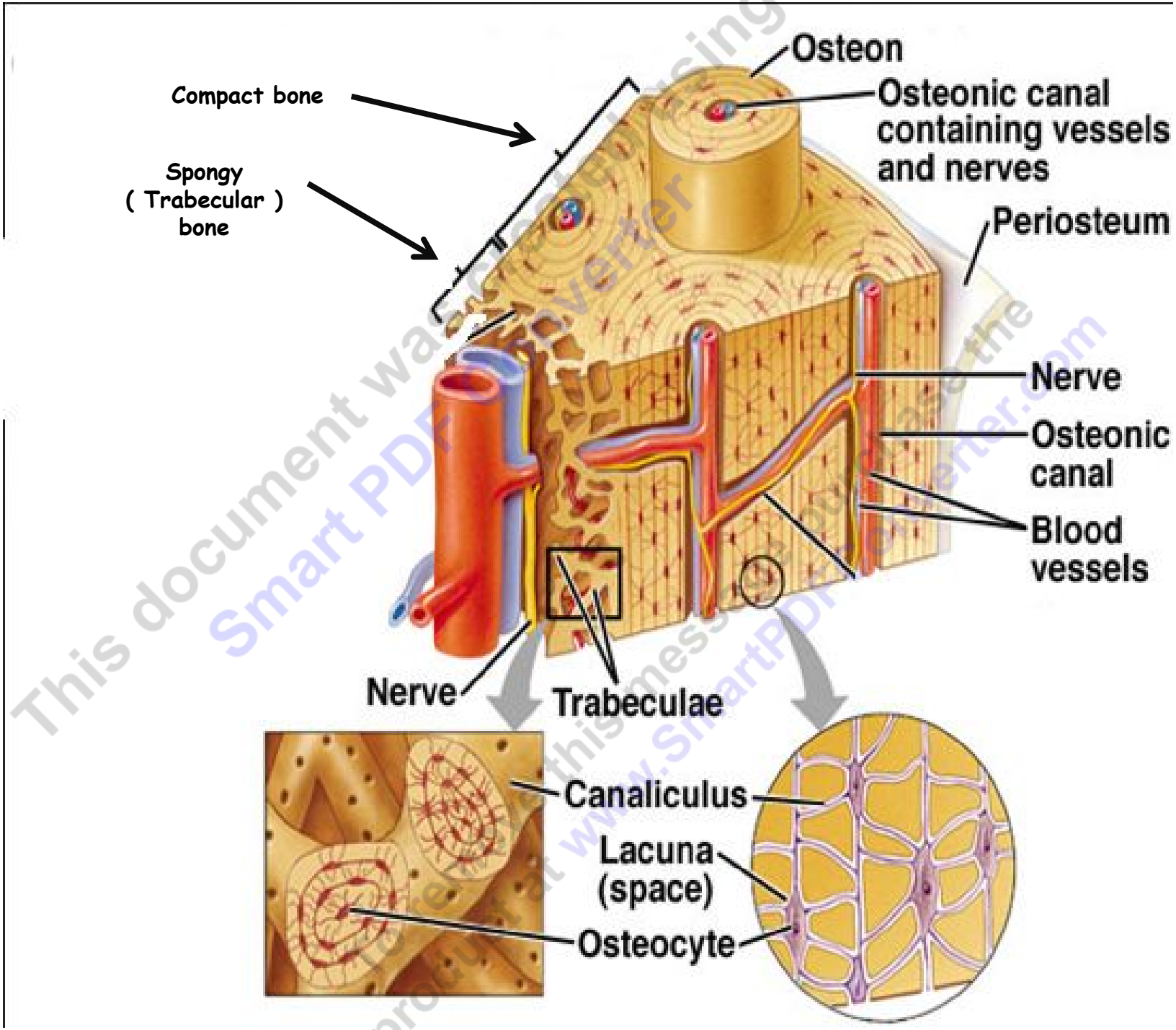
- The part of a bone where bone substance to bone space relation is a bigger quantity is called compact bone.
- This means that there is more bone tissue and less empty space.
- Made of dense , concentric layers , & present on the exterior of bones , constituting their outer protective layer
- Has high resistance to bending and torsion & therefore it provides strength in areas where bending would be undesirable , such as in the middle of long bones.
- Constitutes 80 % of total body bone mass
- Has a slow turnover rate
- It has a series of adjacent circular formations called Harvesian Systems or Osteons



- Each osteon has a central " osteogenic canal " containing blood vessels & nerves .
- Between the osteons are concentric layers of bone called Lamellae .







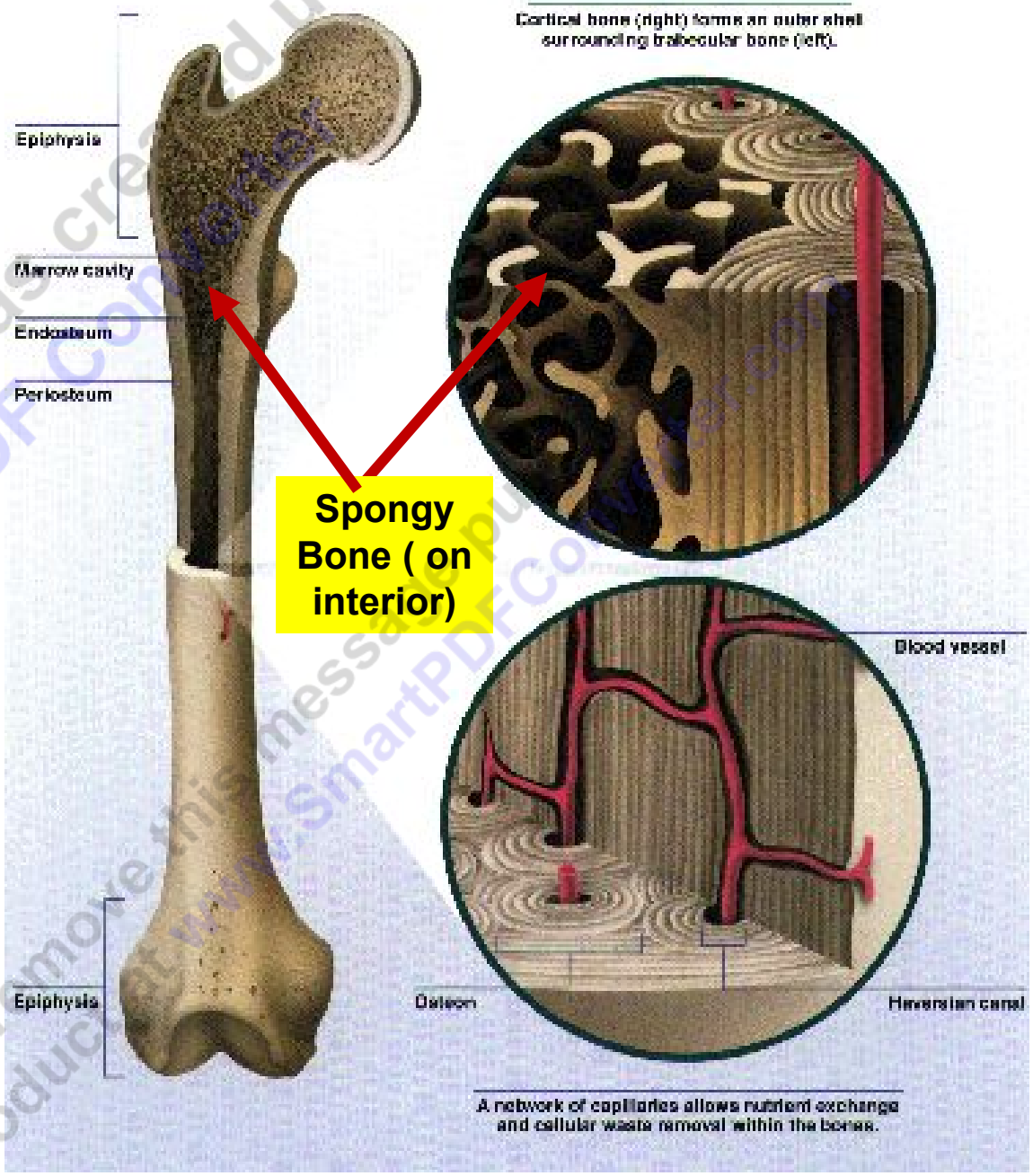
(2) Spongy (Trabecular) Bone

- The part of a bone where bone substance to bone space ratio is a smaller quantity.
- This means that there is more empty space and less bone tissue.
- Present in the interior bones
- Comprises 20% of total bone mass
- Compared to cortical bone , it is:

(1) less dense,

(2) more elastic and

(3) has a higher turnover rate than compact bone .



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 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
  (most of it is bound to albumin , & a much smaller frcation is bound to globulins)
- (3) Calcium bound to serum 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 , the rate of bone formation exceeds its resorption → hence skeletal mass increases.
- Increase in bone length (longitudinal or linear growth) occurs at the epiphyseal plates , &
- Increase in bone 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
- After that , the rate of resportion begins to exceed formation and bone mass slowly decreases.

Phosphate

- PO_4 plasma concentration is 3.0-4.5 mg/dL.
- Most of it is diffusible and much less of it is non-diffusible (protein- bound),
- Diffusible PO_4 :
- 52% is ionized & the rest is combined to different ions
- Non-iffusible PO_4 :
- This is protein-bound to proteins .
- Most of the bond phosphate is present in bone , & the rest of it is present in ATP, cAMP, and other compounds

Bone formation (Osteogenesis)

- Mainly 2 stages →
- (1) Osteoblasts synthesize collagen fibers that form the organic matrix called osetoid)
- (2) Mineralization (deposition of calcium & phosphate on the osteoid matrix)
- Mineralization requires adequate calcium and phosphate , & is dependent on Vitamin D
- Plasma levels of Osteocalcin (produced by osteoblasts) is indicators of level of osteoblastic activity .

- **Osteogenesis imperfecta (brittle bone disease)**

- is a genetic bone disorder where there is defective osteoid formation .
- Thus they have weak bones, that are susceptible to repeated fractures.
- Patients have short stature ,
- blue sclera ,
- bowed legs ,
- kyphosos or scolipsis

Bone remodeling

- Q : What is the meaning of bone remodeling ?
- Answer : it means the continuous & lifelong processes of bone absorption (by osteoclasts) & then its deposition (by osteoblasts) .
- Osteoclasts digest and resorb and area of mineralized bone & then local macrophages clean up debris.Thereafter , osteoblasts are recruited to site and deposit new matrix which will be mineralized. In this way new bone replaces previously resorbed bone
- Remodeling responds to functional demands of the mechanical loading . It depends , in addition , on complex signaling pathways .
- These signaling pathways include the action of several hormones such as Parathyroid Hormone (PTH), Vitamin D , Growth hormone , and Calcitonin
- The process of bone remodelling also controls the reshaping or replacement of bone following injuries such as fractures and micro-damage which occurs during normal activity.
- In the first year of life, almost 100% of the skeleton is replaced. In adults, remodeling proceeds at about 10% per year.
- An imbalance in the regulation of bone remodeling's two sub-processes, bone resorption and bone formation, results in many metabolic bone diseases, such as osteoporosis

Osteoporosis هشاشة العظام

- Osteoporosis means → Reduced bone density and mass
- 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
- This leads to increased susceptibility to fracture.
- It occurs earlier in life for women than men but eventually both genders succumb to it
- 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-roch diet & calcium suuplements in diet
  - habitual exercise
  - avoidance of smoking and alcohol intake
  - avoid drinking carbonated soft drinks

- Thanks