Physiology of the bone

We recommend you to study the 1st lecture of histology first.

Color index

- Important
- Further Explanation

Physiology Team 434
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Objectives

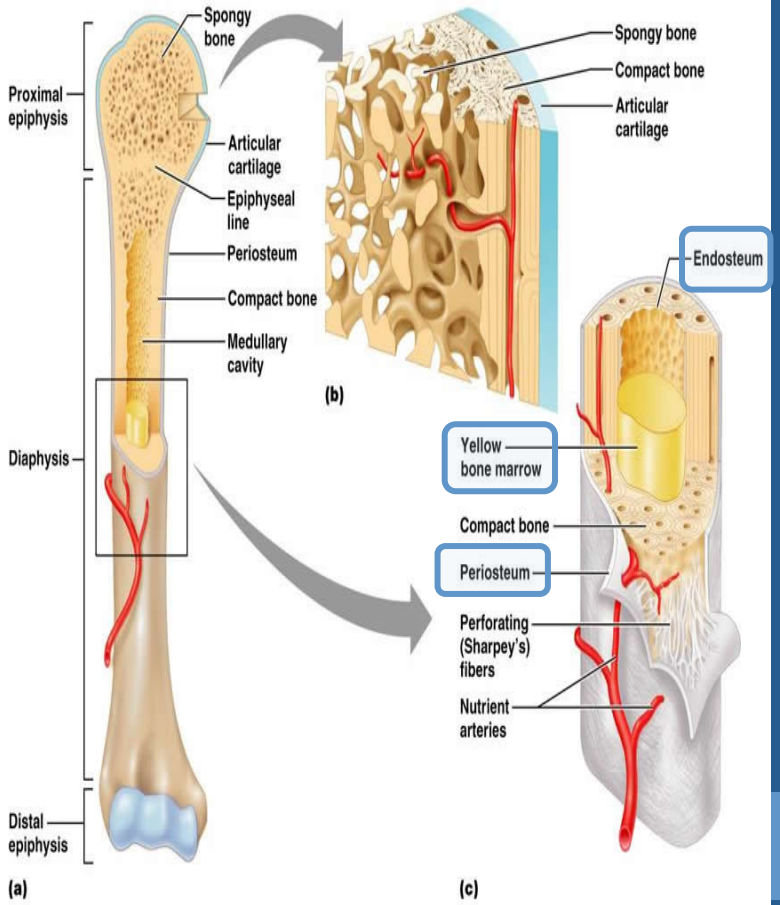
- Define bone and differentiate between types and sites of bone (cortical & trabecular)
- Appreciate differences between both types of bone in function
- know ca++ concentration and forms in the ECF& its relation to PO4
- differentiate bone cells &function of each
- know Bone remodelling & bone formation
- Define osteoporosis
- Appreciate effect of different hormones on bone physiology

Structure of bone:

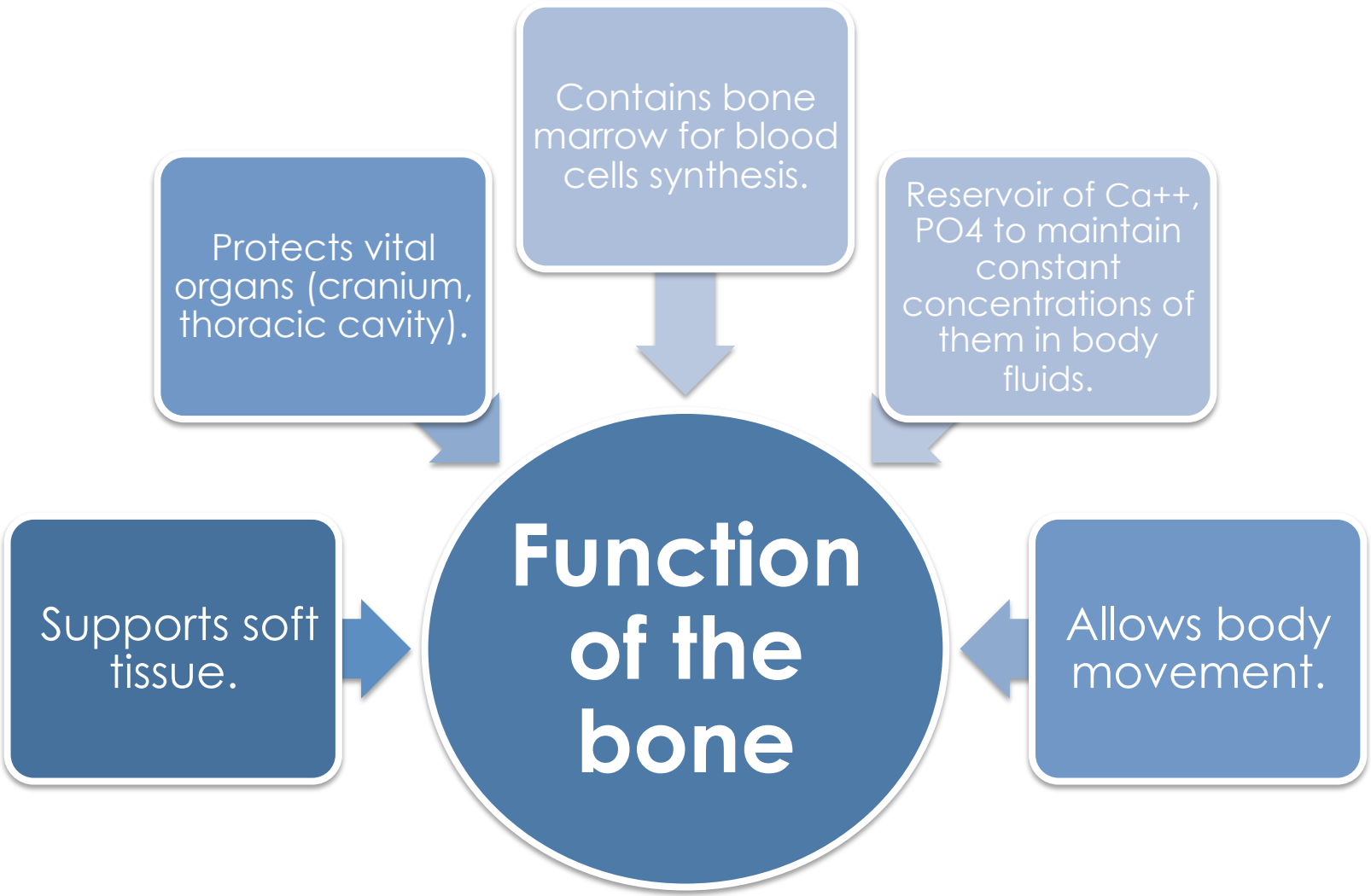
Bones are porous mineralized structures, **composed of** :

Cells	Red or yellow bone marrow in the center of bone
Bone Matrix	Periosteum[1] & Endosteum[2].

A- **Calcified material**
deposits of calcium & phosphate salts mainly but there is magnesium,potassium & carbonate also).
B- **Collagen fibres**
C- **Lacunae.:** unfilled space or interval
D- **Canaliculi** : a small channel or duct.



1: a dense layer of vascular connective tissue enveloping the bones except at the surfaces of the joints.
2: is a thin layer of connective tissue that lines the surface of the bony tissue that forms the medullary cavity of long bones.

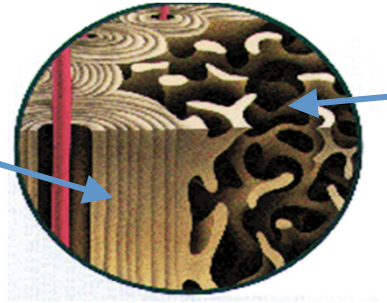

Contains bone marrow for blood cells synthesis.
Protects vital organs (cranium, thoracic cavity).
Reservoir of Ca++, PO4 to maintain constant concentrations of them in body fluids.
Function of the bone
Supports soft tissue.
Allows body movement.

Types of bones in the Human skeletal

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

Cortical bone 80%
(compact bone)

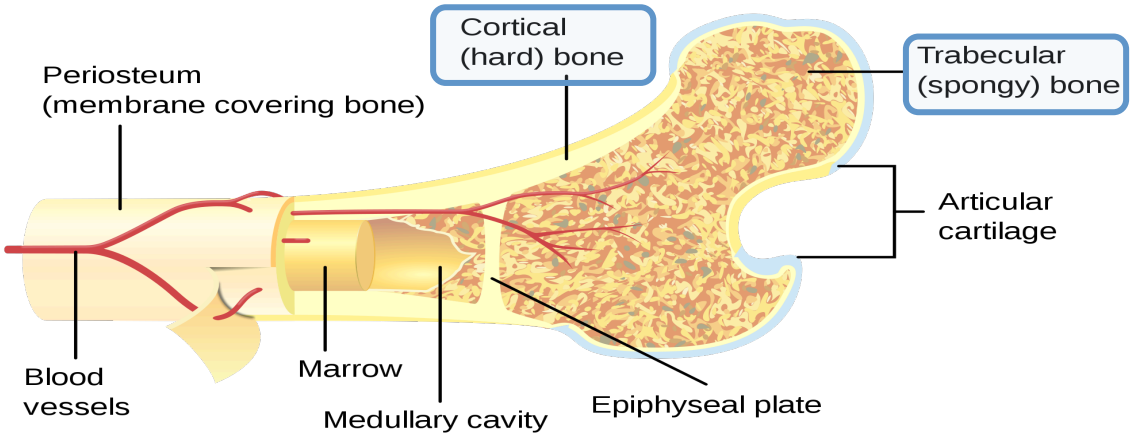
-Constitutes the dense concentric layers of long bones and the outer layer surrounding trabecular bone at ends of long bones



Trabecular bone 20%
(spongy bone)

-Present in the interior of skull, ribs vertebrae, pelvis ,epiphyseal and metaphyseal regions of long bones .

-Has five times greater surface area than cortical bone.
(80% of the bone surface area).



First type : Compact bone

* Its forms a protective outer shell around every bone in the body.
* Has a slow ca ++ turnover rate has high resistance to bending , and therefore present where bending would be undesirable (As in the middle of long bones).
* Structually we can see series of adjacent and overlapping bull's eye formations called osteons or Harvesian system .

Each osteon is composed of a central vascular channel called the Haversian canal . surrounded by circles of concentric lamella of minerlized bone
Between each osteon are interstitial lamellae
Harvesian canal can contain capillaries , aterioles, venules, nerves and (possibly) lymphatics.

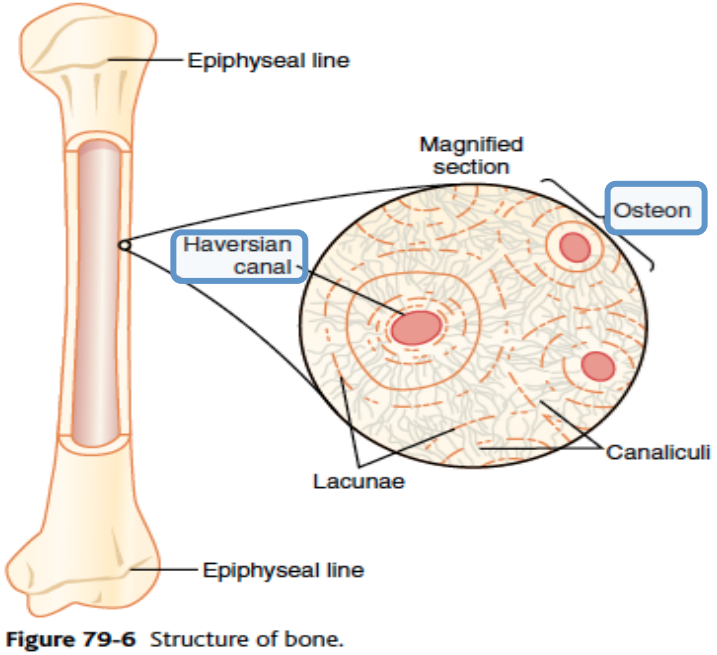


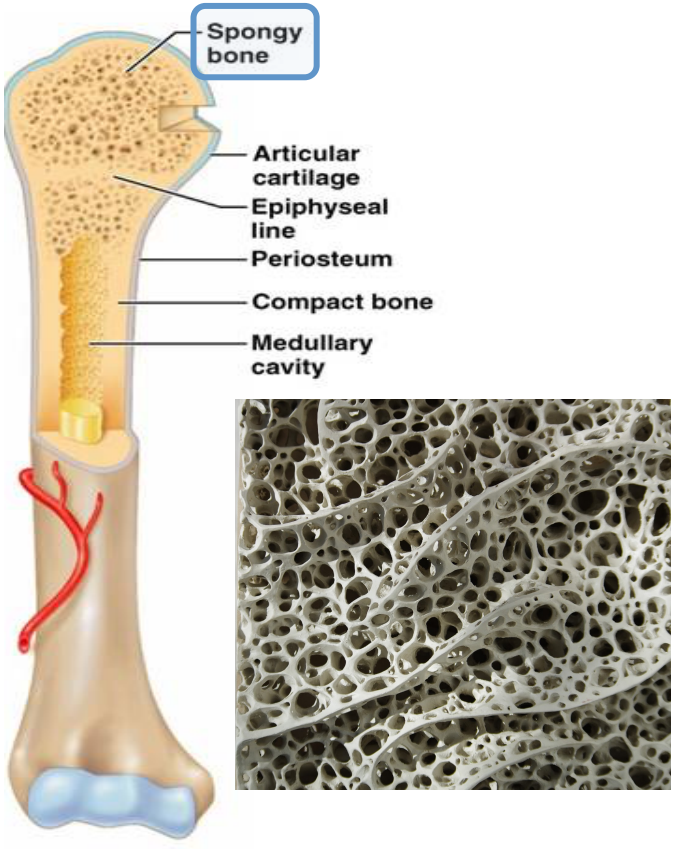
Figure 79-6 Structure of bone.

Osteons system is only found in compact bone

Turnover is the ability to exchange Ca between bone and blood

Second type **Trabecular (spongy/cancellous) Bone**

* **Rigid but appears spongy .**
* 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 (flexible).
  (3) greater surface area.
  (4) it has high calcium turnover rate because of the greater surface area .



Calcium Homeostasis

Extracellular Fluid (ECF) Calcium:

- Normal Ca2+ level in plasma ranges from 8.5-10 mg/dL (mean 9.4 mg/dL)
- **It exists in three fractions :**

1) Free Ionized calcium → 50% of total ECF calcium

*Diffusible through capillary membrane (Only biologically active & produce all functions)

2) Protein-bound calcium → 40% of total ECF calcium

*Non-diffusible throughapillary membrane.

* 90% is bound to albumin , rest is bound to globulins.

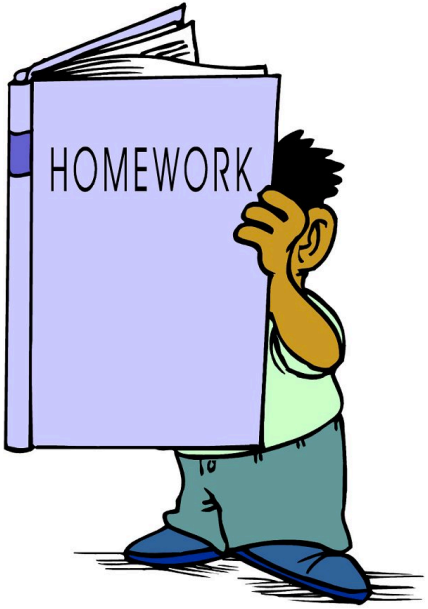
Alkalosis increases calcium binding to protein and decreases ionized calcium.

3) Calcium bound to serum constituents → 10%

*citrate & phosphate.

*Non- ionized/diffusable.

2 questions were given by Prof. Faten Zakareia as Homework



Q1-What are the functions of Ca++?

Helps build and maintain bones, helps ward off osteoporosis, contraction of skletal cardiac and smooth muscles, blood clotting and transmission of nerve impulses.

Q2-What is effect of hypocalcemia and hypercalcaemia on central nervous system?

Hypocalcemia[1]: cause the nervous system to become more excited.
Hypercalcemia[2] : cause progressive depression of the nervous system.

1: Hypocalcemia -> **decrease** in calcium concentration

2: Hypercalcemia -> **increase** in calcium concentration

Phosphate (PO4)

85% in bone	15% in cells	< 1% in ECF in H2PO4 and HPO4 forms

*Calcium is tightly regulated with Phosphorous in the body.

*Normal plasma concentration is 3.0-4.5 mg/dL. PO4.

*If any one increase it should precipitate in bone .

Ca++ x PO4 = constant (solubility product)

Calcium and phosphate are inversely proportional.

Bone & Calcium

* 70% of bone is formed of Calcium & Phosphate salts.

Phosphate salt : $CaPO_4$ & hydroxide

99% of calcium of the bone in form of hydroxyapatite crystal

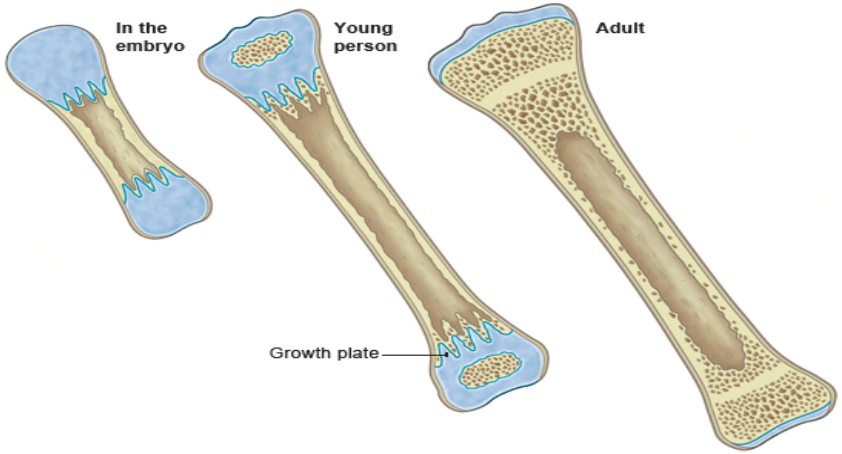
*Calcium salts in bone provide structural integrity of the skeleton.
*Calcium in our body is distributed as following :
- 99% in bones -0.1% in ECF -1% in cells organelles

*Exchangeable Ca++ of bone (0.4 – 1% of total bone Ca++) has rapid buffering mechanisms to keep ECF Ca++ levels constant , if ECF Ca++ falls below normal , this Ca will be moved from bone into ECF.

Bone Growth

Growth occurs at

- Epiphyseal → **Linear growth**
- Periosteum → **Width.**



* During growth: -bone mass increases and -Bone formationexceeds Resorption .

*__10%__ of total adult bone mass turns over each year during remodeling process

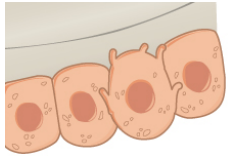
* Once adult bone mass achieve equal rates of formation and resorption the bos maintained

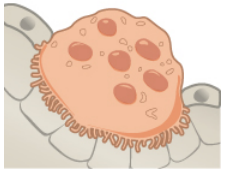
* At about 30 years old , rate of resorption begins to exceed formation and bone mass slowly decreases .

BONE CELLS

There are three types of bone cells :

YouTube **Helpful video**
http://www.youtube.com/watch?v=78RBpWSOI08&index=2&list=PL353EE41649BF2338&channel=Amgen





1)Osteoblast :

*Bone-forming cell, present on outer surface of bone and bone cavities (periosteum & endosteum)

***Function**

- secrets unclassifid collagen (which forms matrix called osteoid) around themself becoming trapped , qucescent & now calleded osteocytes .

2) Osteocyte :

*Mature bone cell derived from osteoblasts.

*It is enclosed in bone matrix.

***Function**

-Transfer of calcium from bone canaliculi to the ECF

3) Osteoclast :

large phagocytic multinucleated cell derived from monocytes.
its activity controlled by Parathormone hormone

***Function:**

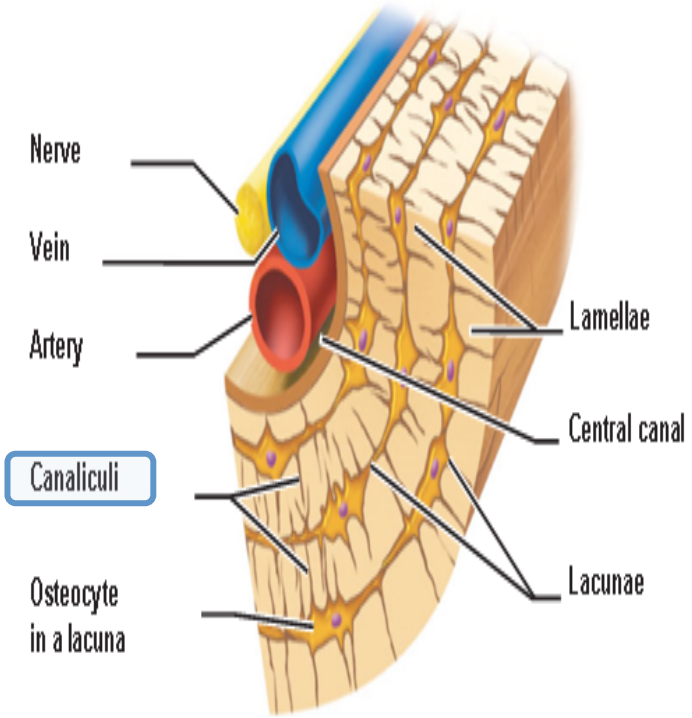
Bone-resorbing (removing)cell -Osteoclasts secrete enzymes that dissolve the matrix of old bone tissue and acids that dissolve bone salts

CANALICULI

*Fluid-containing channels called the canaliculi.

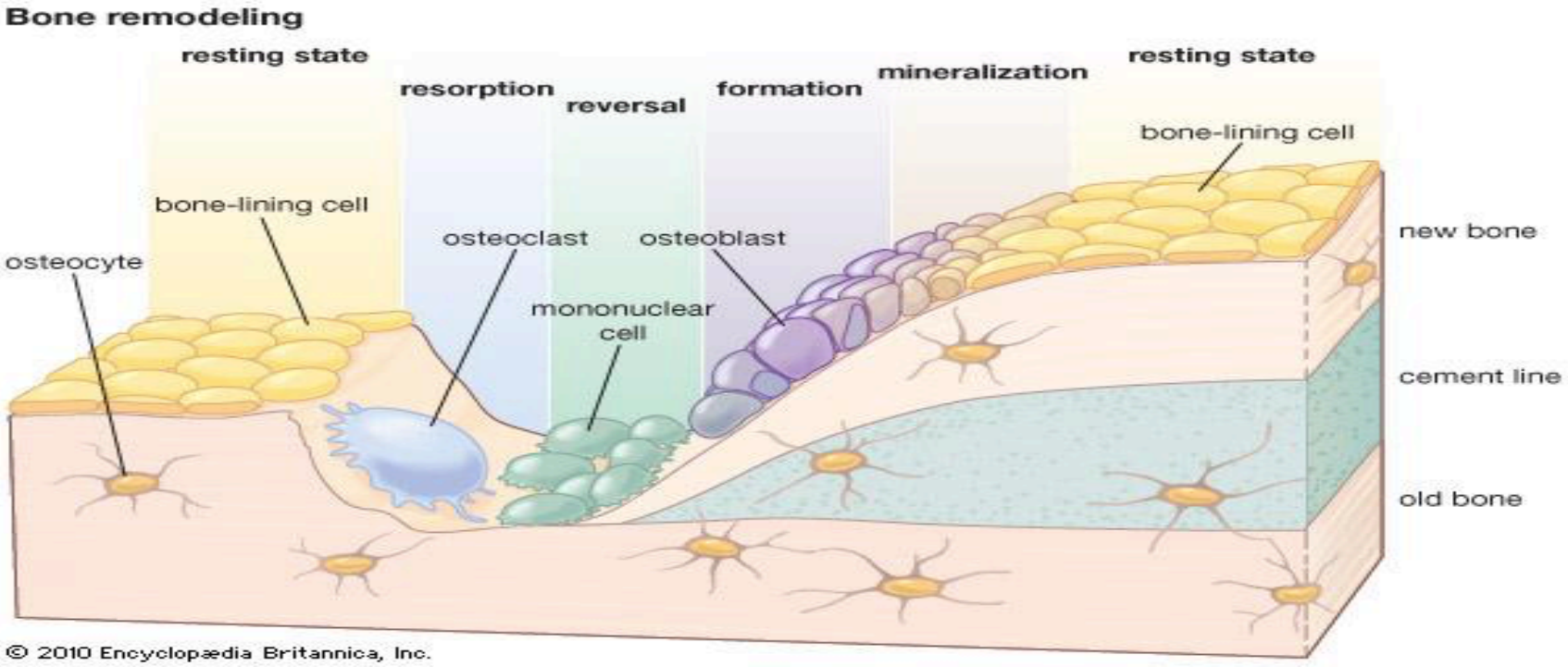
*Canaliculi traverse the mineralized bone.

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



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

	Bone Formation	Bone Resorption	Bone Remodeling
Function		Transfer of *Ca++* from *bone fluid* to *blood*.	Maintain normal toughness of bone (new bone replaces resorbed bone).
Mechanism	1-*Begins:* When active osteoblasts synthesize uncalcified/raw collagen to form matrix called (*Osteoid*) 2-*Mineralization:* Deposition & precipitation of *calcium* & *phosphate* on Osteoid collagen fibers. 3-*Hydroxyapatite crystals* form in weeks/months.	1-*Osteocystic osteolysis:* Rapid and tRansient effect. 2-*Osteoclastic resorption:* Slow and Sustained.	1-*Endocrine signals* to resting osteoblasts generates paracrine signals to osteoclasts (differentiation & maturation). 2-*Osteoclasts digest* and resorb (by acids & enzymes) 3-Local *Macrophages clean* debris. 4-*Osteoblasts recruited* to site & deposit new matrix that will be mineralized. 5-*Osteocytes* (osteoblasts in bone matrix) form system of interconnected cells spread all inside bone.
Bone Cells	*Osteoblasts:* 1-Synthesize uncalcified/raw collagen 2-Secrete *Alkaline Phosphate* & *Osteocalcin*	*Osteoclasts/Osteocytes:* Break down bone and release minerals.	1-*Osteoblasts:* a)Deposition of new bone & matrix. b)Secrete factor to help in maturation of osteoclasts. 2-*Osteoclasts:* Digest & resorb area of mineralized bone.
Requirements	1-Adequate *Vitamin D*. 2-*Alkaline Phosphate* & *Osteocalcin* (secreted by osteoblasts): Bone formation (their plasma levels are indicators of osteoblast activity.	1-Parathyroid Hormone *(PTH)* & *Vitamin D*: Stimulate PRODUCTION of mature osteoclasts. 2-*Ostrrogen*: Stimulate OPG factor (osteoprotegrin) that INHIBITS formation of osteoclasts.	Affected by: 1-*Mechanical Stress on Bone:* Stimulates formation of stronger bones (athletes have heavier & stronger bones). 2-*(PTH)* & *1,25 Dihydroxycholecalciferol* (active form of *Vit D*): Stimulate activity & FORMATION of osteoclasts. 3-*Calcitonin:* INHIBITS activity & formation of osteoclasts.



YouTube Helpful video

http://www.youtube.com/watch?v=0dV1Bwe2v6c&index=3&list=PL353EE41649BF2338

Bone Resorption

Osteocytic Resorption (osteolysis)

*By **osteocytes.**

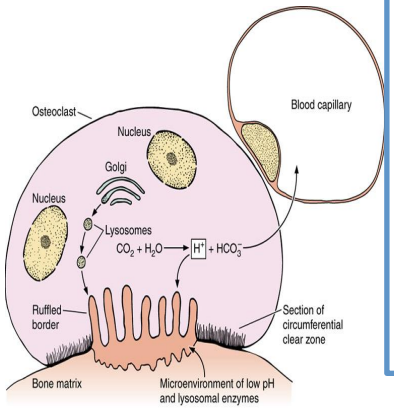
*They digest mineralized bone & transfer calcium & Po4 from canaliculi to ECF.

*Does not decrease bone mass.

*Reduce calcium & Po4.

*Removes calcium from recently formed crystals.

*Quick process begins in minutes.



Osteoclasitc Resorption

*By **osteoclasts.**

*They acidify area of bone to dissolve hydroxyapatite by Hcl then lysosomes & acid proteases digest collagen.

* Destroys matrix of old bone - diminishes bone mass & not calcium & Po4.

*Slow and sustained needs several days or weeks .

Osteoporosis[1]

*Diminished bone matrix (not from poor calcification as in rickets or osteomalacia[2])
*The rate of osteoclastic resorption exceeds deposition of new bone by osteoblastic activity. (Rate of resorption is more than the rate of formation)
*During childhood, bone formation exceeds resorption and the total bone mass peaks at 25-35 years of age.
Thereafter , because of falling levels of the anabolic steroids (oestrogen & progesterone , which stimulate osteoblasts) (Increase of the rate of formation)

*Osteoporosis → reduced bone density and mass
*This leads to increased susceptIbility to fracture. Osteoporosis occurs earlier in life for women than men (Especially women around menopause) but, eventually both genders succumb to it.
***Osteoclastic bone resorption is : slow process that reduce bone-mass**

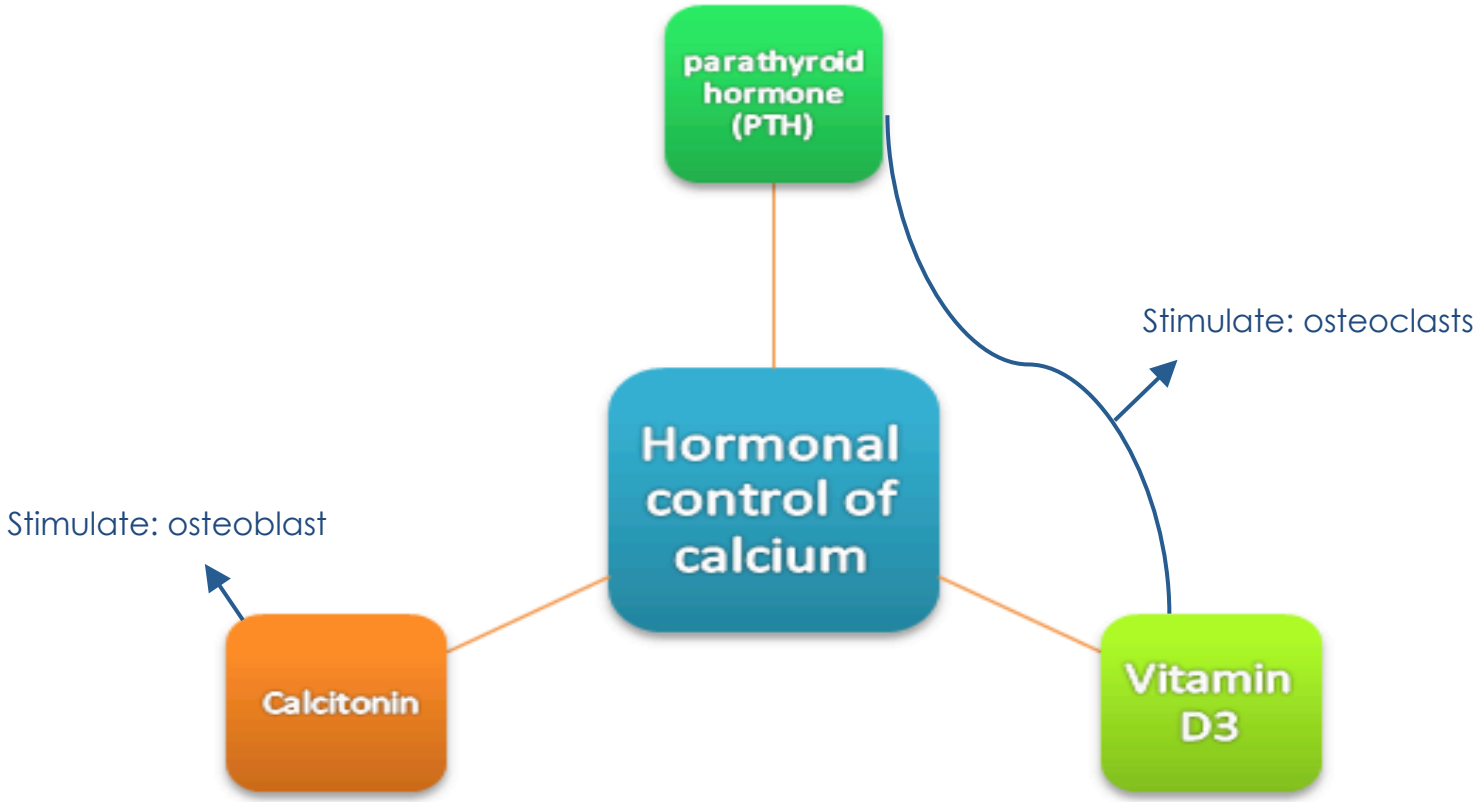
reduced risk by:

1- high calcium in the diet. 2- Habitual exercise. 3- Avoidance of smoking,
4- Alcohol and drinking carbonated soft drinks

1: osteoporosis: refers to the degeneration of already constructed bone.(هشاشة العظام)
2: osteomalacia: is an abnormality in building process of bone.(لين العظام)

What happens to our grandma's ? =)

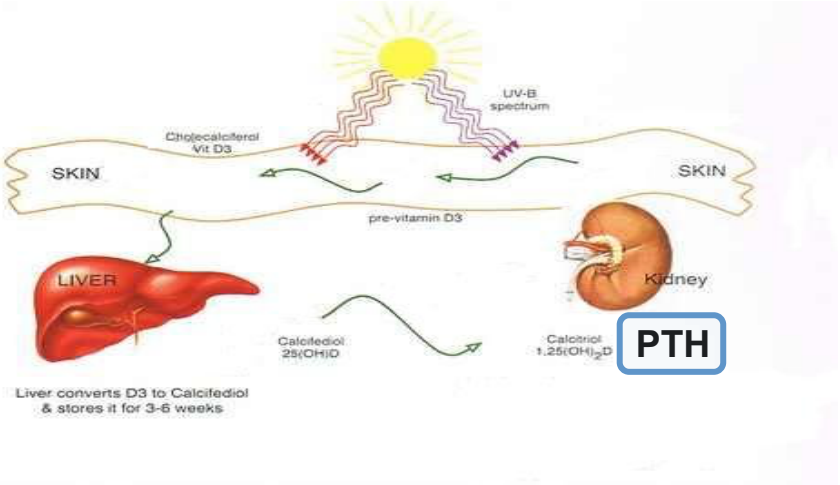
1. loss of anabolic steroids as estrogen and testosterone which stimulate osteoblastic activity and decrease osteoclastsic activity
2. lack physical stress
3. old age and decreased growth H
4. malnutrition and vit D deficiency
5.smoking, carbonated soft drinks and alcohol



They regulate Ca++ resorption, absorption and excretion from the 3 organs:
(bone, kidney and intestine)

Vitamin D

*The main action of active Vitamin D (1,25 dihydroxycholecalciferol) is :
*Stimulate absorption of Ca2+ & PO4 from the intestine (calbindin protein)
*Stimulate Ca reabsorption in the distal tubules in kidneys
*Help in bone formation & resorption (large amounts of vit D cause bone absorption, it increases calcium
*Transport through cell membranes to outside bone, but in small amounts stimulates bone calcification as it increases calcium absorption from intestine & kidney also increases calcium transport through cell membranes to inside bone to osteoblast & osteocyte membranes.



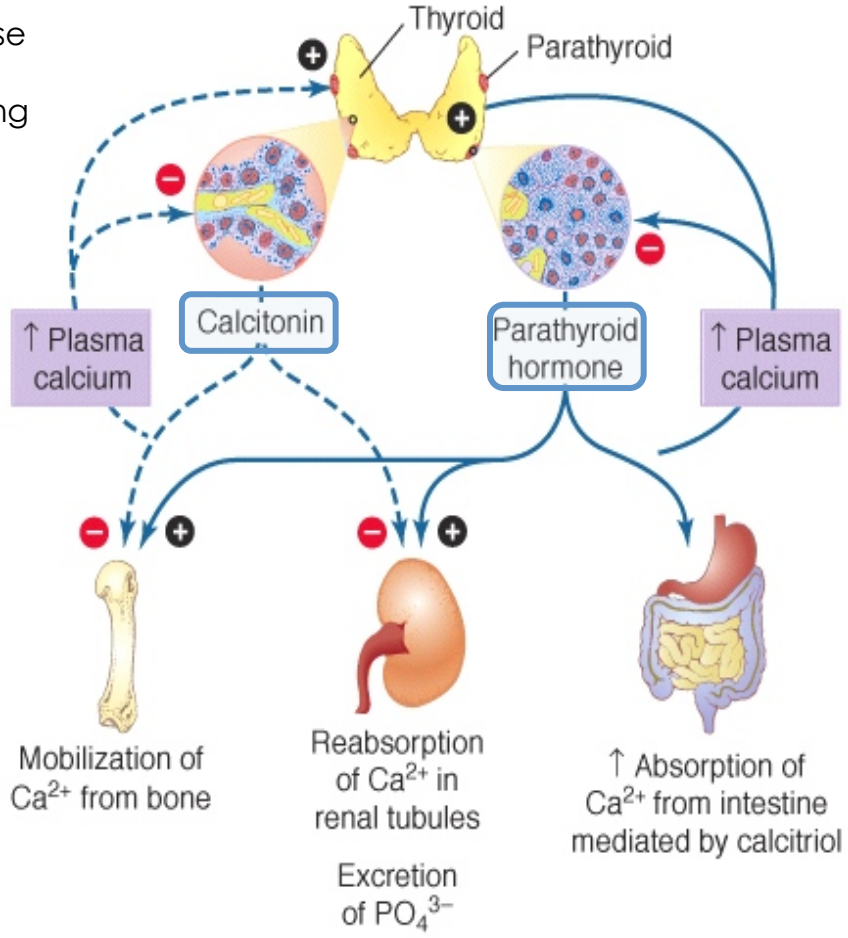
Vit.D and Calcium are inversely proportional to each other. When Calcium rate increase in blood Vit.D decrease the absorption from kidney, intestine and bones.

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

Parathyroid hormone (PTH) Breaking

*Increase plasma Ca++ levels when it drops and decrease plasma phosphate levels
*Act on the bones to stimulate Ca absorption by activating osteoclasts.
*Act on kidney (distal tubule) to stimulate Ca++ reabsorption, and inhibit reabsorption of phosphate and

indirectly by activation of 25-(oh)-D into 1,25-(OH)2-D (thereby stimulating its excretion)
*On intestine to stimulate Ca++ reabsorption



Calcitonin Building

*From parafollicular cells of the thyroid gland. (C cells).
- decrease plasma Ca++ levels
- increases osteoblastic activity
- decrease → formation of new osteoclasts (osteocytic osteolysis)
- Stimulated by rise in plasma Ca++ levels.

(over long period decreased osteoclasts activity are followed with decreased number of osteoblasts → little effect on bone)

MCQs

1) Where we can find the cortical bone:

a. it is found in the interior of the skull.
b. it is found in the outer shell of all bone and also the shafts in long bone.
c. it is found in the interior of long bones
d. only in the heads of long bones.

2) Which of these condition might cause depression of the nervous system:

a. hypercalcemia
b. hypernatremia
c. hypocalcemia
d. hyponatremia

3) Which of these type of bone cells has the ability to absorb the bone

a. osteoblast
b. osteoclast
c. osteocyte
d. osteogenic

4) The cause of osteoporosis is mainly due to deficiency of Vit D :

a. True
b. False

5) The action of parathyroid hormone:

a. Decrease calcium and phosphate absorption of the bone
b. increase the excretion of calcium by the kidneys
c. increase the excretion of phosphate by the kidneys
d. Act on the intestine to inhibit the Ca absorption

Answer:
1. B
2. A
3. B
4. B
5. C

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