Physiology of Bone

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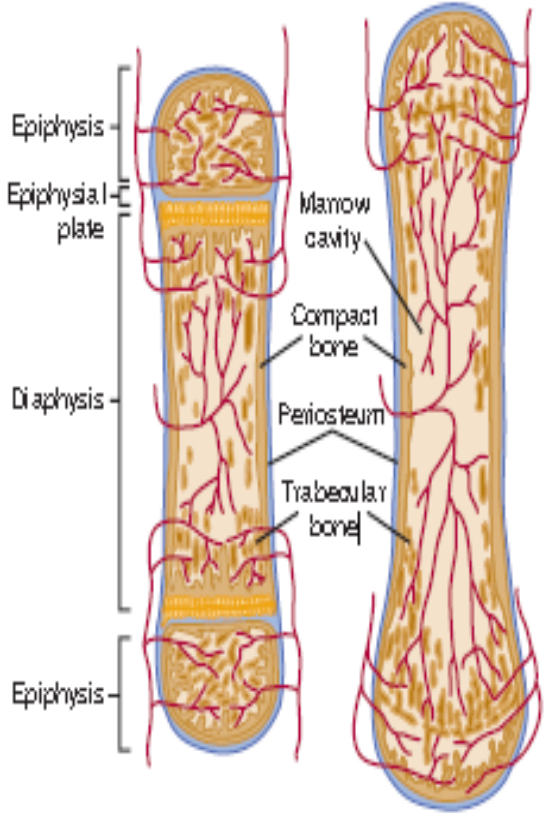
Objectives

By the end of the lecture you will be able to:

- Define bone and differentiate cortical & trabecular bone (sites and function of each).
- State the normal levels and forms of ca++ in the ECF and its relation to PO4.
- Identify the bone cells and the function of each.
- Define bone remodelling and explain the mechanism of bone formation.
- Discuss the effect of different hormones on bone physiology.
- Define osteoporosis.

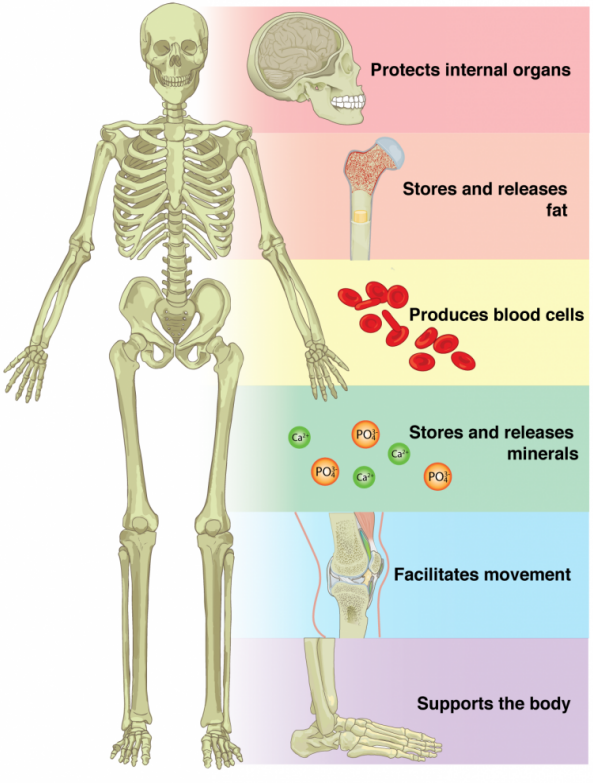
Physiology of Bone

- Bone is a special form of connective tissue.
- It is well vascularized with total blood flow of 200–400 mL/min in adult humans.
- The ends of each long bone**(epiphyses)** are separated from the shaft of the bone by a plate of actively proliferating cartilage, the **epiphysial plate.**
- Linear bone growth can occur as long as the epiphyses are separated from the shaft of the bone, but such growth ceases after the epiphyses unite with the shaft **(epiphysial closure).**



Functions of bone

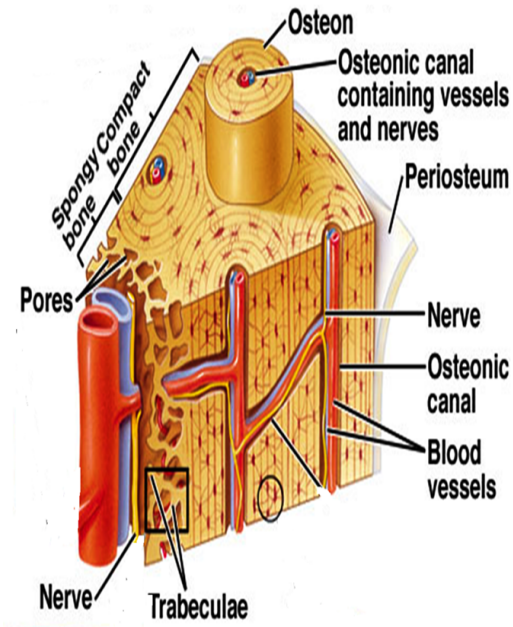
- Is involved in the overall Ca++ and PO4– homeostasis.
- Protects the vital organs,
- Permits locomotion and support against gravity.
- Contains the bone marrow (blood cells formation)
- Reservoir for calcium & phosphate

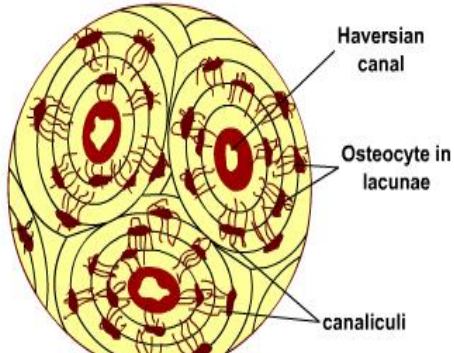


Types and structure of bone

Compact or cortical bone:

- In the outer layer of most bones is (80%) of the bones in the body.
- It has more bone tissue and less bone space
- Has high resistance to bending and torsion
- It is composed of overlapping circular structures (formations) called Haversain Systems or Osteons . Each osteon has a central canal called Osteonic Canal or Haversain Canal
- The Osteonic Canal contain blood vessels (capillaries, arterioles, venules), nerves and lymphatic's.
- Bone cell lie in lacunae
- They receive nutrients by way of canaliculi that ramify through out the compact bone

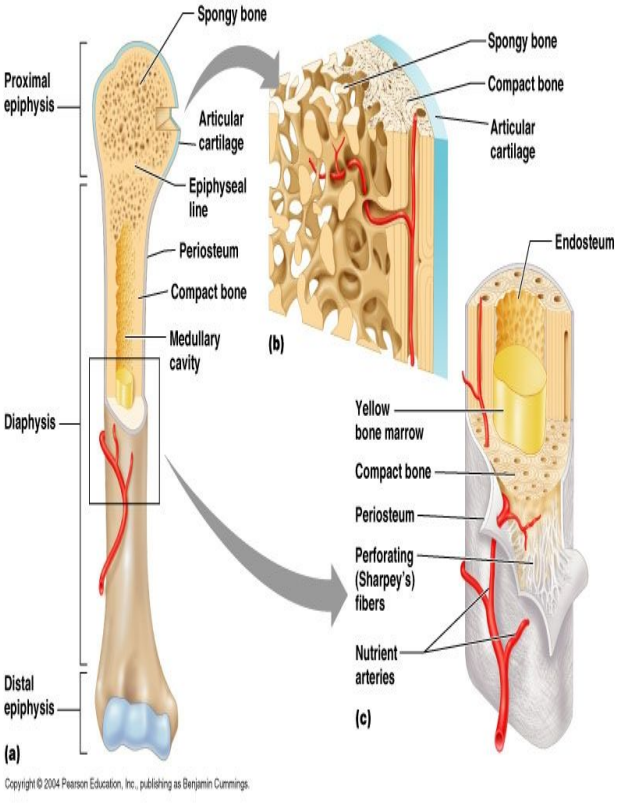




Types and structure of bone -2

Trabecular or spongy bone:

- Inside the cortical bone, is 20% of the body bones
- Is made of spicules or plates
- Though it represents only 20% of the skeletal mass, it has 5 times greater surface area than cortical bone
- Because of its large surface, it has faster turnover rate than cortical bone ; hence it is more important than cortical bone in terms of calcium turnover
- Compared to cortical bone , it is:
- (1) less dense,
- (2) more elastic and
- (3) has a higher turnover rate than compact bone .
- The nutrient is diffused from bone ECF into trabiculae



Composition of Compact Bone

(30%) is organic Matrix : composed of

a-Collagen fibers 90-95%: extend primarily along the lines of tensional force and give bone its powerful tensile strength.

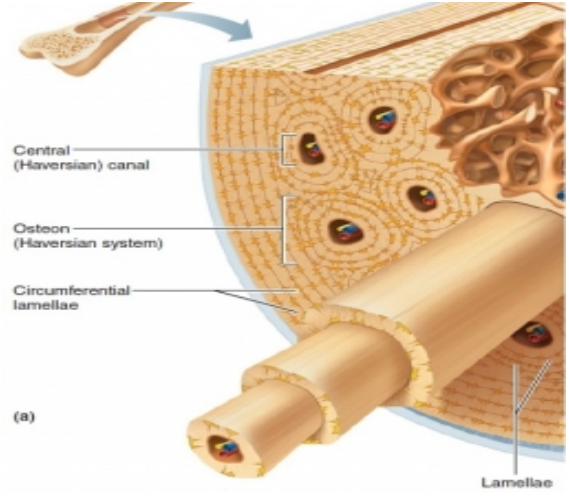
b- Ground substance 5-10% of

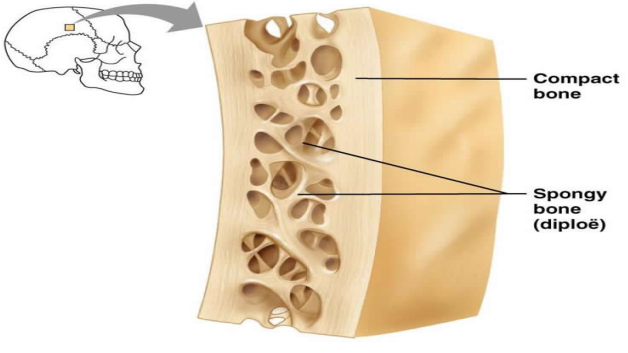
ECF and Proteoglycans (chondroitin sulphate and hayluronic acid)

(70%) is bone Salts :

- **Crystalline salts of Ca++ & PO4 (Hydroxyapatite) the ratio of Ca/P ratio is 1.3-2).**
- **Mg+, Na+, K+, Carbonate ions are also present.**

NB: newly formed bone have a considerably higher percentage of matrix in relation to salts.



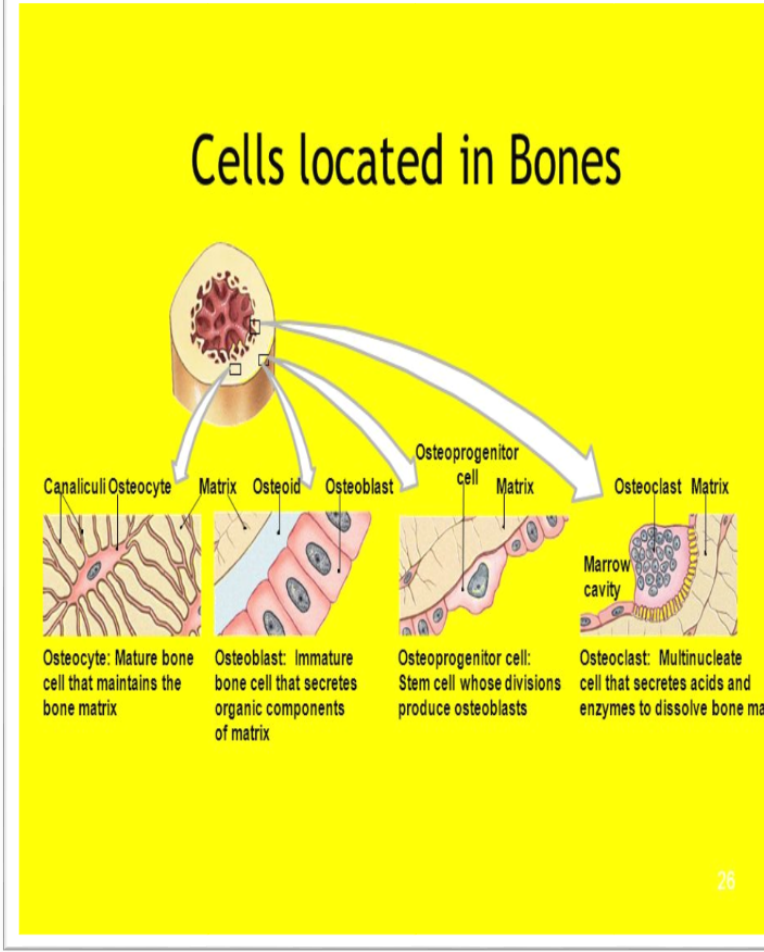


Bone cells

Osteoblasts are the bone forming cells that secrete collagen forming a matrix around themselves which then calcifies and when surrounded by calcified matrix, they are called **Osteocytes** and send processes into the canaliculi that ramify throughout the bone.

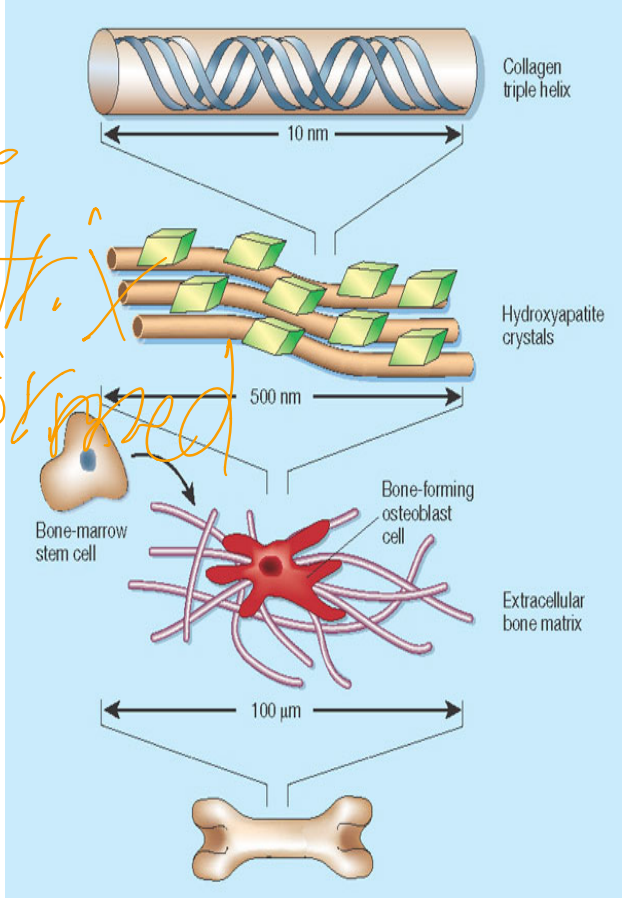
Osteoblasts regulate Ca and Phosphate concentration in bone fluid.

Osteoclasts are multinuclear cells that erode and resorb previously formed bone. They phagocytose bone, digesting it in their cytoplasm.



Mechanism of Bone Calcification -1

- ***Osteoblasts*** secrete *collagen* (monomers) and *ground substance* (proteoglycans).
- The collagen monomers polymerize to collagen fibers.
- The resultant tissue becomes ***osteoid***, a cartilage-like material differing from cartilage in that calcium salts readily precipitate in it.
- Osteoblasts become entrapped in the osteoid and are now called ***osteocytes***.
- After the osteoid is formed, calcium salts begin to precipitate on the collagen fibers forming the ***hydroxyapatite crystals***.



Mechanism of Bone Calcification -2

- The mechanism that causes calcium salts to be deposited in the osteoid is not fully understood,
- The regulation of this process depend to a great extent on pyrophosphate, which inhibits hydroxyapatite crystallization and calcification of the bone.
- The levels of pyrophosphate, in turn, are regulated by at least three other molecules.
- 1-Tissue nonspecifc alkaline phosphatase (TNAP), which breaks down pyrophosphate is secreted by the osteoblasts into the osteoid to neutralize the pyrophosphate, and once the pyrophosphate has been neutralized, the natural affinity of the collagen fibers for calcium salts causes the hydroxyapatite crystallization.

Mechanism of Bone Calcification -3

- Osteoblasts also secretes at least two other sub stances that regulate bone calci fcation:
- (1) Nucleotide pyrophosphatase phosphodiesterase1 (NPP1), which produces pyrophosphate outside the cells,
- (2) Ankylosis protein (ANK), which contributes to the extracellular pool of pyrophosphate by transporting it from the interior to the surface of the cell.
- Deficiencies of NPP1 or ANK cause decreased extracellular pyrophosphate and excessive calcification of bone, such as bone spurs, or even calcification of other tissues such as tendons and liga-ments of the spine, which occurs in people with a form of arthritis called ankylosing spondylitis.

Tensile and Compressional Strength of Bone

- The collagen fibers of bone, like those of tendons, have great tensile strength, whereas the calcium salts have great compressional strength.
- These combined properties plus the degree of bondage between the collagen fibers and the crystals provide a bony structure that has both extreme tensile strength and extreme compressional strength.
- **N.B:** hydroxyapatite crystals fail to be formed in normal tissues except in bone despite the high levels of Ca & P ions due to the presence of ***pyrophosphate.***

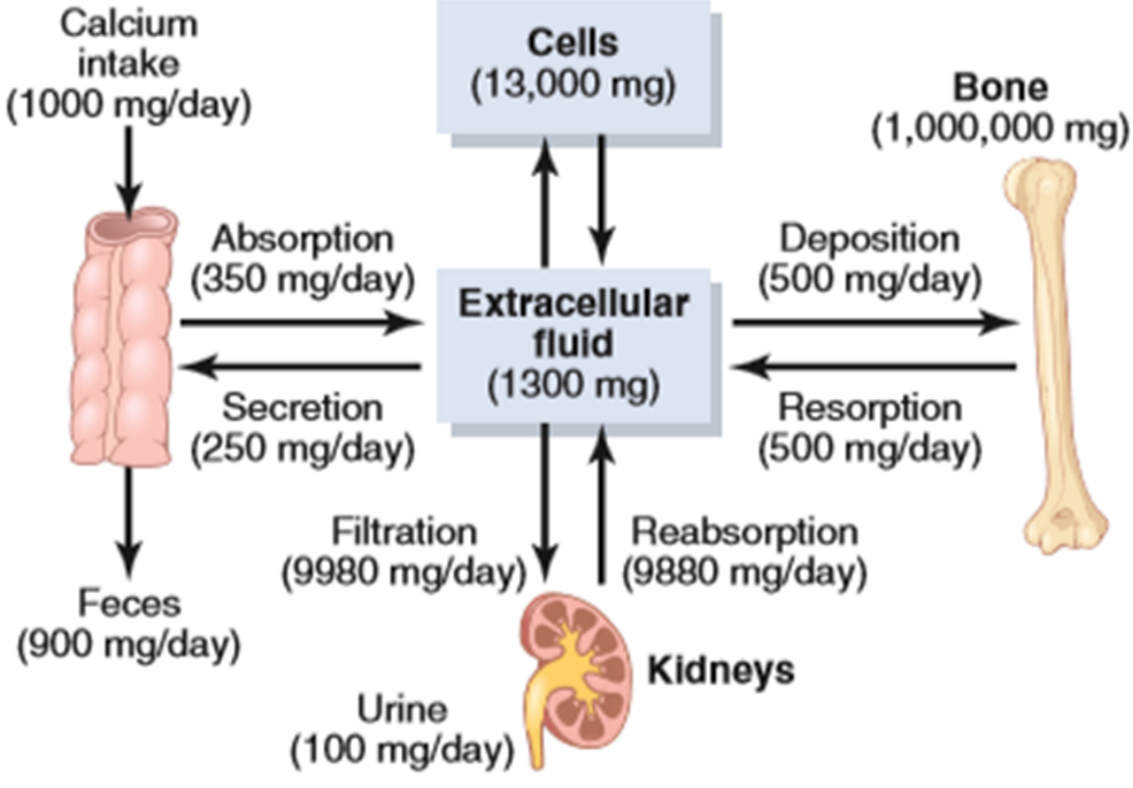
Body Calcium levels

- 1.5% of body weight is Calcium,
- about 1100 -1300 gm.
- 99% is in the skeleton.

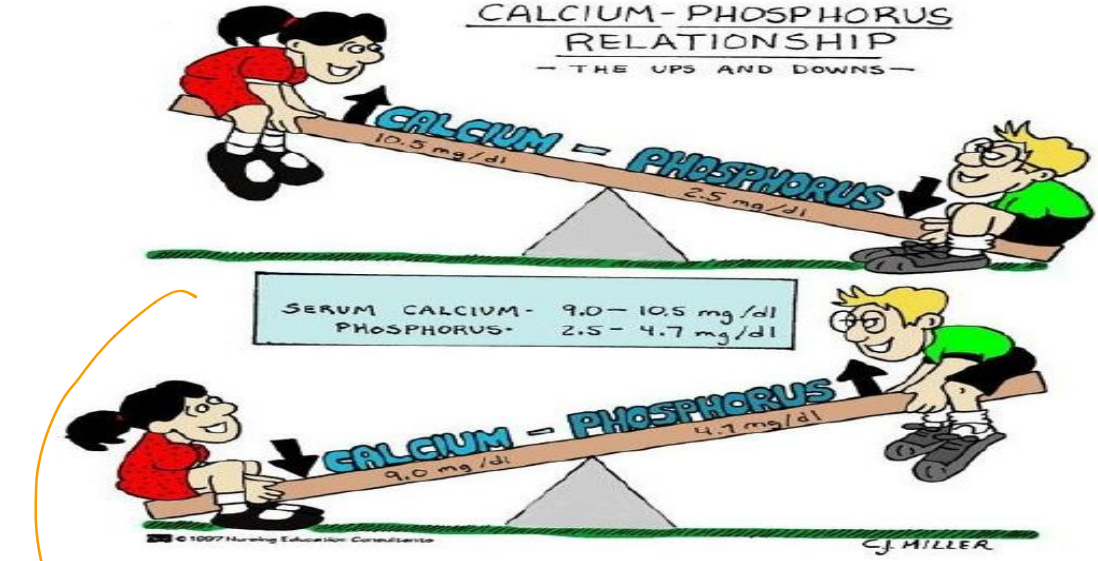
TABLE 36.1 Body Content and Tissue Distribution of Calcium and Phosphorus in a Healthy Adult

	Calcium	Phosphorus
Total Body Content	1,300 g	600 g
Relative Tissue Distribution (% of total body content)		
Bones and teeth	99%	86%
Extracellular fluid	0.1%	0.08%
Intracellular fluid	1.0%	14%

Calcium homeostasis in human body



Serum calcium and Phosphate

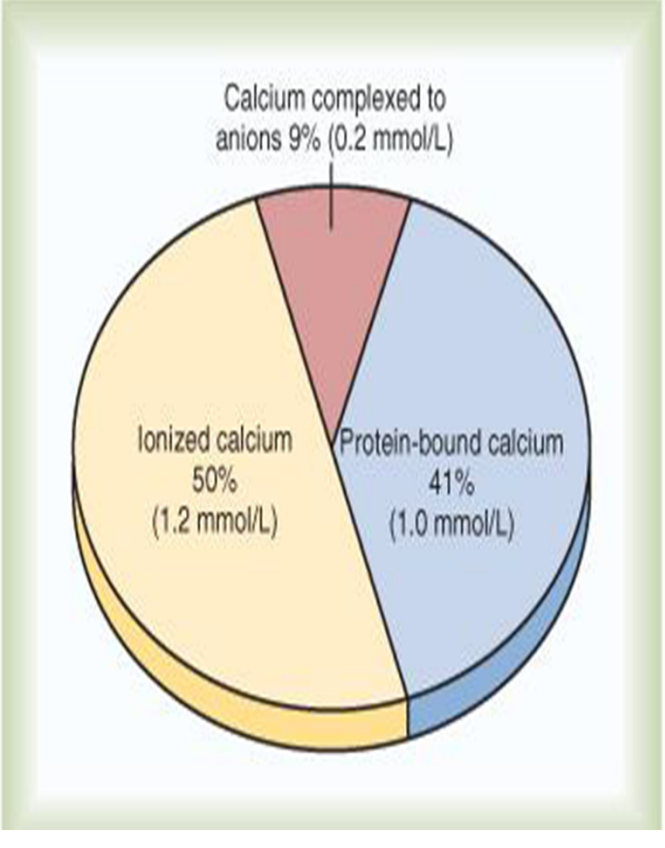


should always be maintained

Plasma Calcium

Plasma calcium level:

- **(9 -11 mg/dl) average :9.4 mg/dl**
- **59% (diffusible)= Ionized + Complexed**
- **41% (non diffusible)= protein bound**

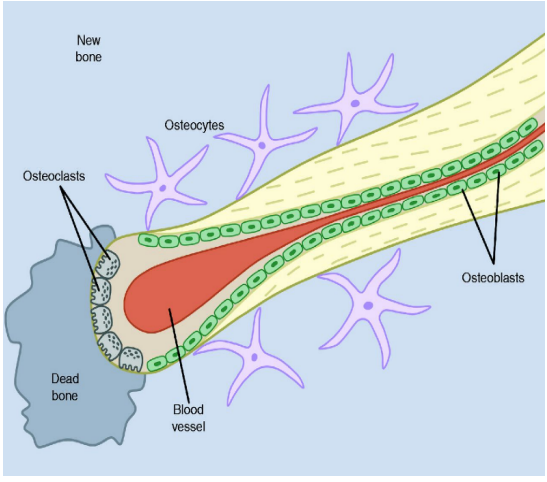


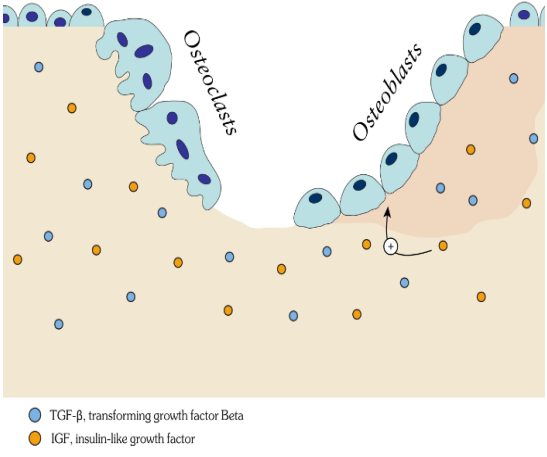
Calcium Exchange Between Bone and ECF

- The bone contains a type of *exchangeable* calcium that is always in equilibrium with the Ca++ ions in the ECF
- It normally amounts to about (0.4-1%) of the total bone calcium.
- This calcium is a form of readily mobilizable salt such as $CaHPO_4$ and other amorphous calcium salts.
- The importance of exchangeable calcium is that it provides a rapid *buffering* mechanism to keep the Ca++ ions concentration in ECF from rising to excessive levels or falling to very low levels under transient conditions of excess or decreased availability of calcium.

Deposition and Absorption of Bone
(Remodeling of Bone)

- Bone remodeling is s refers to the continuous processes of bone absorption (by osteoclasts) & then its deposition (by osteoblasts) .
- Osteoblasts are found on the outer surfaces of the bones and in the bone cavities.
- A small amount of osteoblastic activity occurs on about 4% of all bone surfaces at any given time in an adult), so that at least some new bone is being formed constantly.
- The renewal rate is about 4% per year for compact bone and 20% per year for trabecular bone.





Cont.….Bone resorption

- **Osteoclasts** are large phagocytic multinucleated cells
- They are normally active on less than 1% of the bone surfaces of an adult.
- The osteoclasts secrete two types of substances:
- proteolytic enzymes from the lysosomes
- several acids from the mitochondria and secretory vesicles.
- The enzymes dissolve the organic matrix, and the acids cause solution of the bone salts.
- The osteoclastic cells also phagocytose minute particles of bone matrix and crystals, dissoluting them and releasing the products into the blood.
- Remodeling cycle takes around 100 days

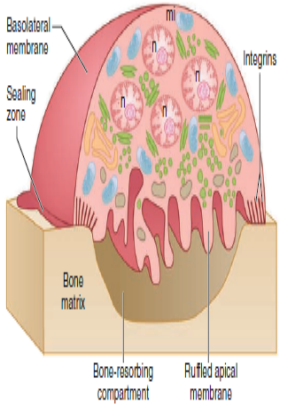
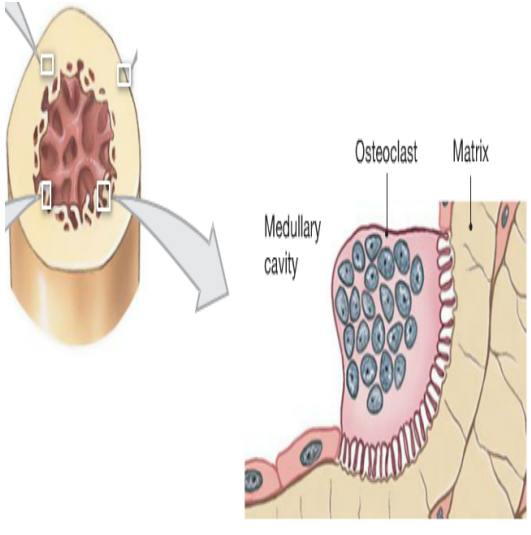


FIGURE 21-10 **Osteoclast resorbing bone.** The edges of the cell are tightly sealed to bone, permitting secretion of acid from the ruffled apical membrane and consequent erosion of the bone underneath the cell. Note the multiple nuclei (n) and mitochondria (mi). (Used with permission of R. Baron.)



Osteoclast: Multinucleate cell that secretes acids and enzymes to dissolve bone matrix

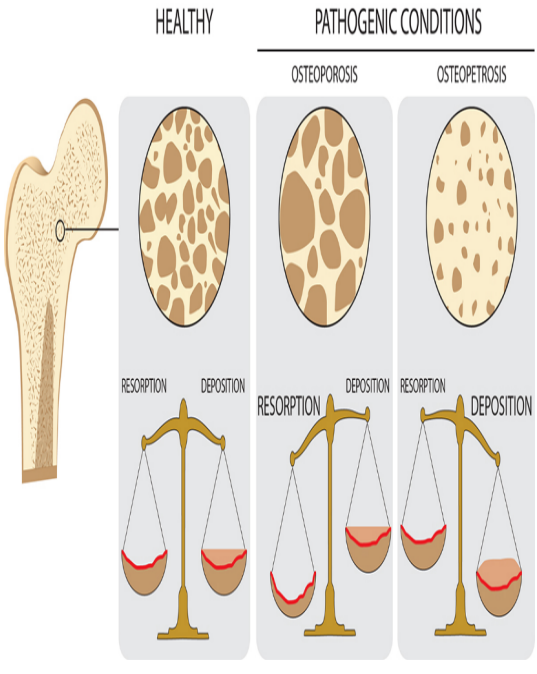
Value of Continual Bone Remodeling

1- Bone adjusts its strength in proportion to the degree of bone stress and it thicken when subjected to heavy loads.

2- The shape of the bone can be rearranged for proper support of mechanical forces by deposition and absorption of bone in accordance with stress patterns.

3- Because old bone becomes relatively brittle and weak, new organic matrix is needed as the old organic matrix degenerates. In this manner, the normal toughness of bone is maintained.

Therefore, the bones of children are less brittle in comparison with the bones of the elderly, due to more remodeling in the children.

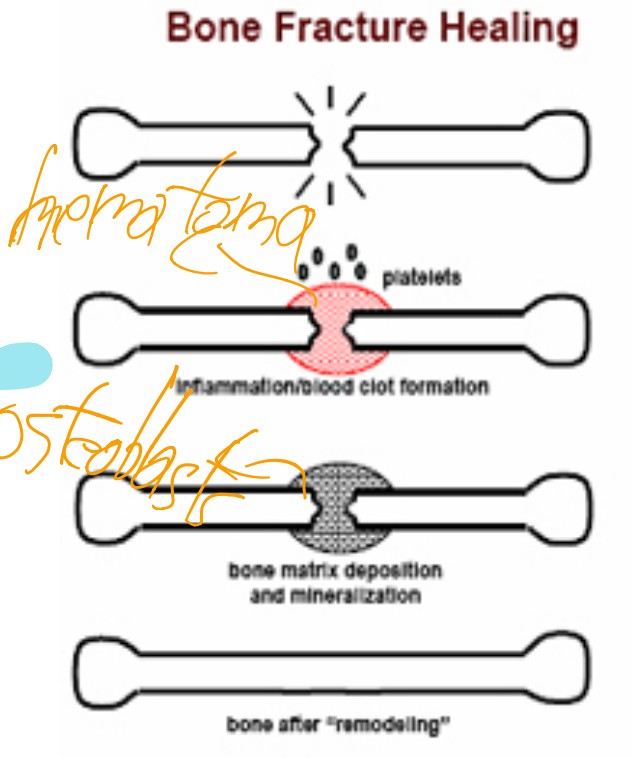


Control of the Rate of Bone Deposition by Bone "Stress"

- Bone is deposited in proportion to the load that it must carry.
- Continual physical stress stimulates osteoblastic deposition and calcification of bone.
- The bones of athletes become considerably heavier than those of no athletes. Also, the bone of the leg in the cast becomes thin and up to 30 % decalcified within a few weeks.
- Bone stress also determines the shape of bones under certain circumstances. (e.g. Healing of fractures may start angulated in children then become straight).

Repair of a Fracture Activates Osteoblasts

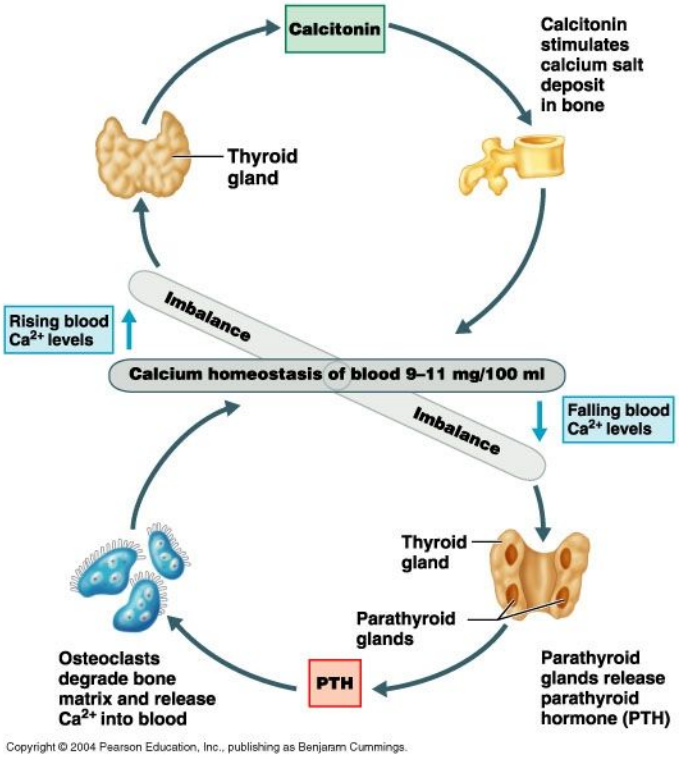
- Fracture of a bone activates all the periosteal and intraosseous osteoblasts involved in the break.
- Large numbers of new osteoblasts are formed from *osteoprogenitor cells*, which are bone stem cells in the surface tissue lining bone, called the "bone membrane.
- Shortly a large bulge of osteoblastic tissue and new organic bone matrix, develops between the two broken ends of the bone followed shortly by the deposition of calcium salts. This is called a *callus*.



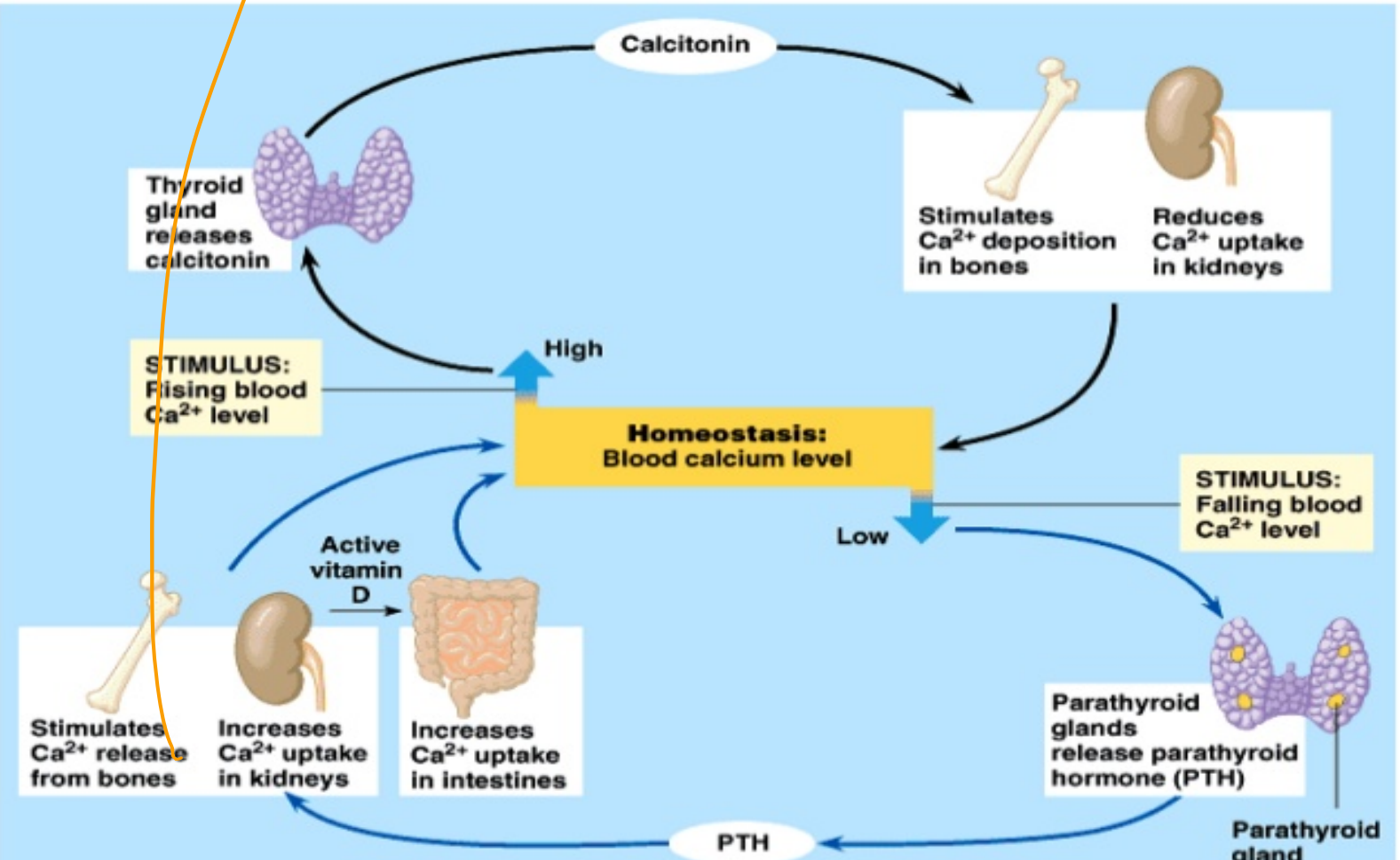
Hormonal Control of Calcium Metabolism & Physiology of Bone

Three major hormones are concerned :

- *1, 25 dihydroxycholecalciferol*: a steroid hormone formed from Vitamin D.
- *Parathyroid hormone (PTH)*: secreted by parathyroid gland
- *Calcitonin:* secreted by c-cells in the thyroid gland.
- To a lesser extent ; Glucocorticoids, GH, estrogens & various growth factors also affect Calcium Metabolism.

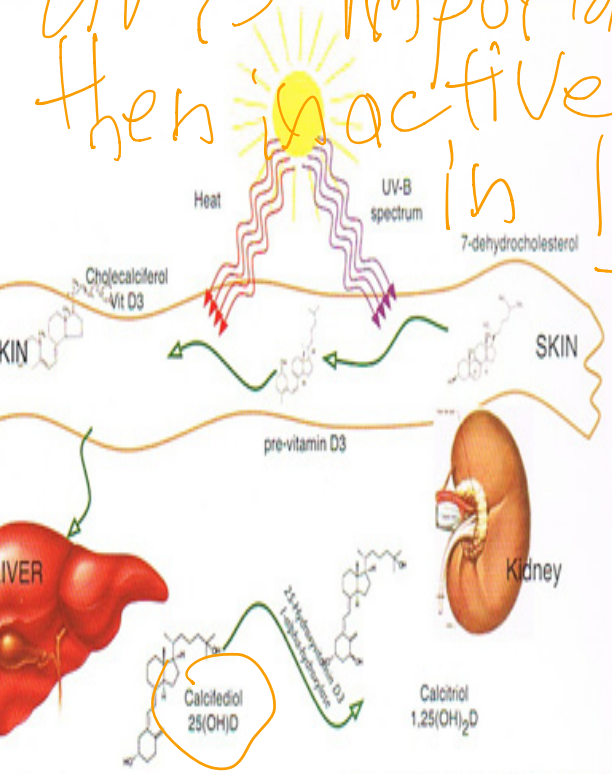


Hormonal control of plasma calcium



Vitamin D

UV is important for Body to form D then inactive vitamin in skin is activate in liver & kidney to Calcitriol (1,25 di-OH)



onverts D3 to Calcifediol
tores it for 3-6 weeks

Kidney converts Calcifediol to Calcitriol

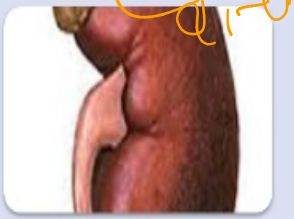
Calcitriol hormonal actions

increases calcium absorption from gut
increases calcium reabsorption from kidney
increases bone mineralisation
vitamin D receptor (VDR) binding
apoptosis

VITAMIN D- ACTION OF CALCITRIOL

- Increases the intestinal absorption of calcium and phosphate by increased synthesis of calcium binding protein (calbinding D28k)

- Mineralization of bone at low doses
- Mobilization of calcium from bone at high doses



- Increased reabsorption of calcium and phosphorus
- Decreased excretion of calcium and phosphorus

Parathyroid Hormone (PTH)

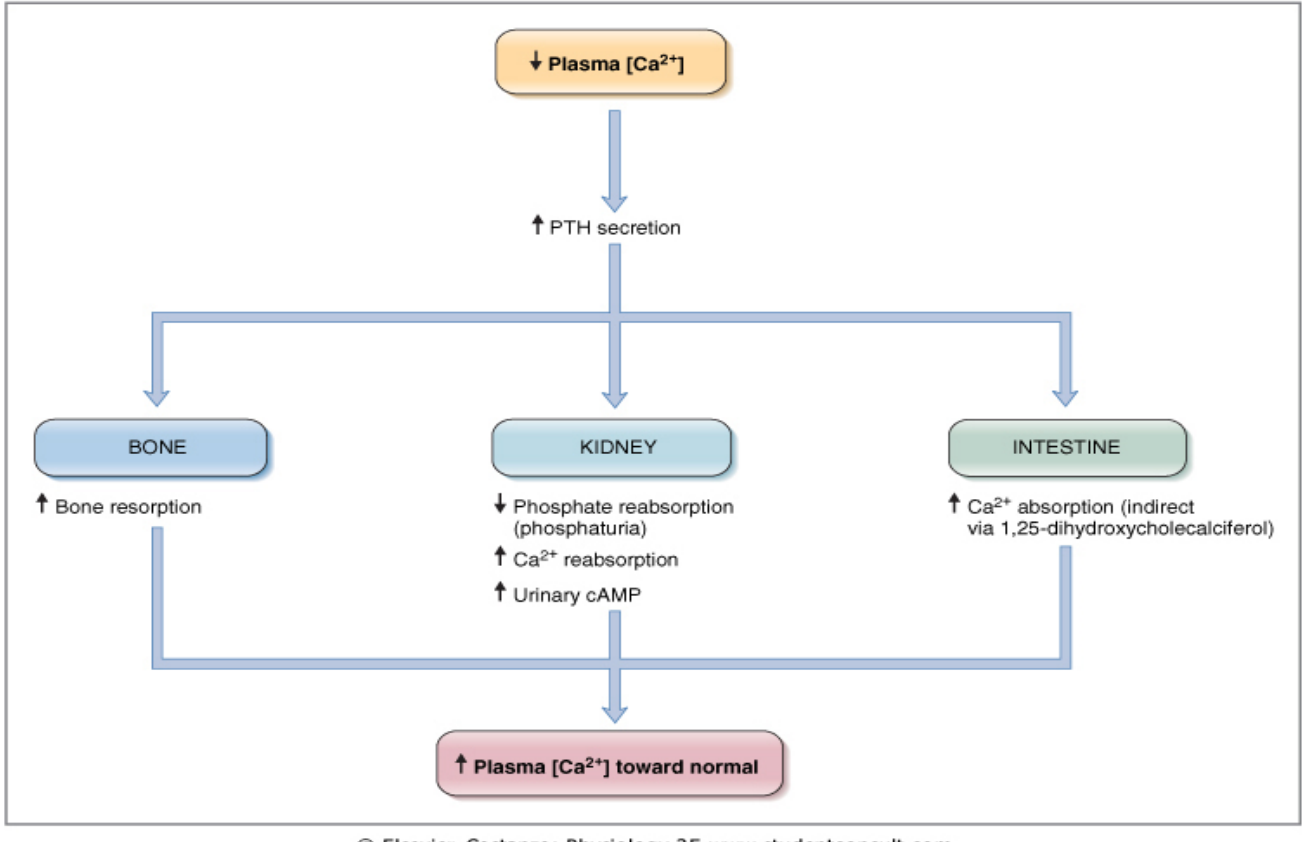
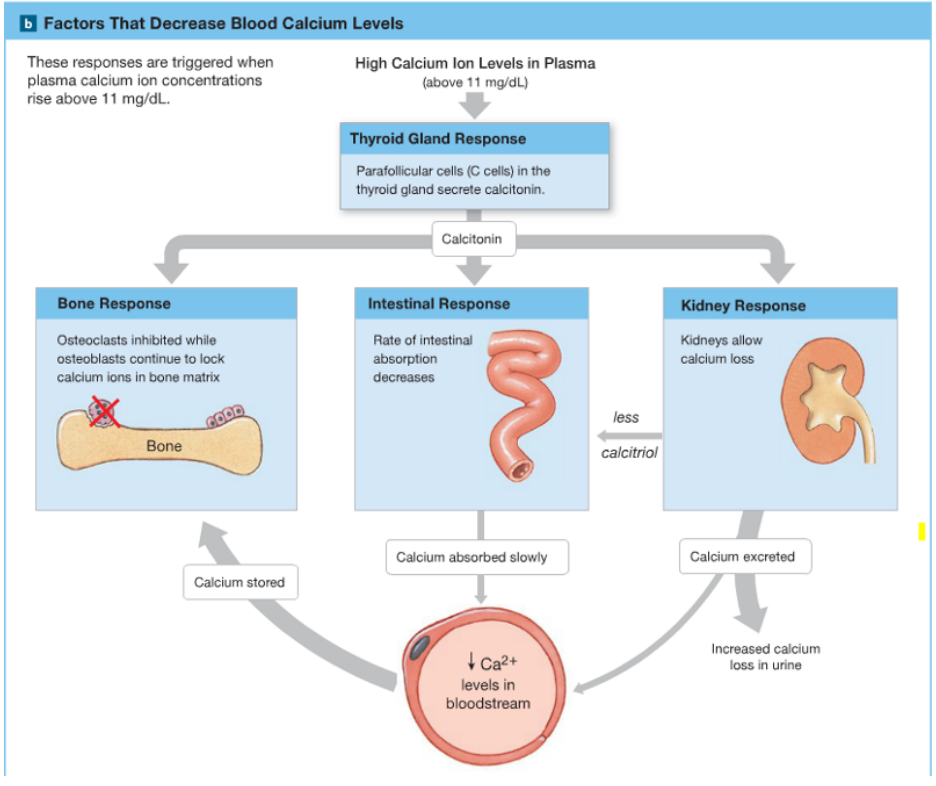
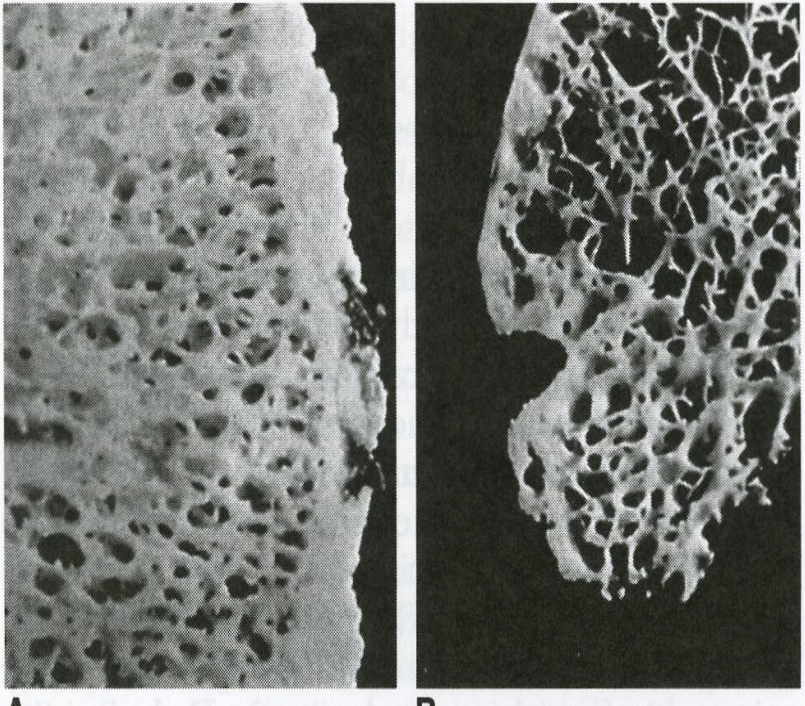


Figure 9-37 **Regulation of PTH secretion and PTH actions on bone, kidney, and intestine.** cAMP, Cyclic adenosine monophosphate; PTH, parathyroid hormone.

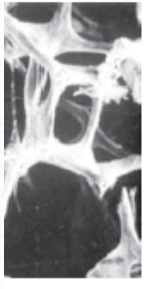
Calcitonin Hormone



Osteoporosis



• Difference between normal bone **(A)** and osteoporotic bone **(B).**



ne (left) compared with porosis (right). The loss usceptible to breakage.

Osteoporosis

- **Osteoporosis:** means reduced bone density and mass
- Is caused by a relative excess of osteoclastic function. Loss of bone matrix is marked. Matrix and mineral are both lost and there is a loss of bone mass. Due to :
- Lack of physical stress
- Malnutrition
- lack of vitamin C
- Old age
- Postmenopausal lack of estrogen
- Cushing's syndrome.

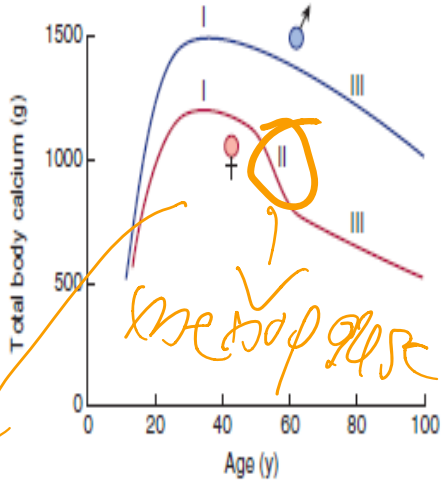


FIGURE 21–12 Total body calcium, an index of bone mass, at various ages in men and women. Note the rapid increase to young adult levels (phase I) followed by the steady loss of bone with advancing age in both sexes (phase III) and the superimposed rapid loss in women after menopause (phase II). (Reproduced with permission from Evans TG, Williams TF (eds): Oxford *Textbook of Geriatric Medicine*. Oxford University Press; 1992.)

Complications of Osteoporosis

- The incidence of fractures is increased particularly in the distal forearm (Colles fracture), vertebral body, and hip. These areas have a high content of trabecular bone, which is more active metabolically, it is lost more rapidly.
- Fractures of the vertebrae with kyphosis produces “widow’s hump” in elderly women with osteoporosis.
- Fractures of the hip in elderly are associated with a mortality rate of 12–20%, and half of those who survive require prolonged expensive care.
- Increased intake of calcium and moderate exercise may help prevent or slow the progress of osteoporosis,

THANK YOU