

Physiology Team

430

Musculoskeletal Block

1st lecture

Physiology Bone

إعداد

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* هذا العمل شامل لجميع نقاط المحاضرة مع بعض الإضافات للتوضيح

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^{++} , PO_4 to maintain constant concentrations in body fluids
- * Allows body to move

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Structure of bone : BONE MATRIX & BONE CELLS

BONE MATRIX

	Organic matrix	Inorganic component
Made	collagen	CaPO ₄ crystals
Called	Osteoid	hydroxyapatite
Makes	30 %	70 %

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BONE CELLS

three types (Osteoblast , Osteocytes , Osteoclast)

Osteoblast	Osteocytes	Osteoclast
<ul style="list-style-type: none"> * Differentiated bone forming cell * It secretes bone matrix (mainly collagen) on which Ca^{++} and PO_4 precipitate. 	<ul style="list-style-type: none"> * the mature bone cell * It is enclosed in bone matrix. 	<ul style="list-style-type: none"> * Bone-resorbing cell * Inorganic bone is composed of hydroxyapatite and organic matrix is composed primarily of collagen

Types of Bone

two Types (Cortical bone , Trabecular bone)

1) Cortical bone :

- * Constitutes the dense , concentric layers of long bones
- * **Comprises 80 % of total body bone mass**
- * Has a slow turnover rate
- * 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 .
- * 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, arterioles, venules), nerves and possibly lymphatics.
- * Between Harvesian system are interstitial lamellae (concentric layers of mineralized bone).
- * Lamellar bone gets its strength from its plywood-like from being composed of parallel layers of bone alternate in orientation by 90 degrees.

2) Trapecular 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
- * 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 , ↓ 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 .

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Calcium

- * Bone serves as a major reservoir for Ca⁺⁺ storage
- * However , very little Ca²⁺ can be released from it .
- * Most of the Calcium in our bodies is found as hydroxyapatite , HA { i.e., calcium phosphate/hydroxide compound } , crystals.

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Extracellular Fluid (ECF) Calcium

- * Ca⁺⁺ level in plasma is 8.5-10 mg/dL .
- * It exists **in 3 fractions** :

	Ionized calcium	Protein-bound calcium	Calcium bound to serum constituents
Of total ECF calcium	50 %	40 %	10%
Some points	Only the free (Ca ²⁺) , is biologically active	Of Protein-bound calcium : 1) 90 % bound to albumin 2) 10 % bound to globulins	(citrate & phosphate)

- * 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

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During growth

- * rate of bone formation **exceeds** يفوق bone 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 resorption begins to **exceed** formation and bone mass slowly **decreases** .

خلال مرحلة النمو : معدل تكوين العظام يفوق معدل نقصان العظم
عندما يصل الانسان الى عمر ٣٠ يبدأ معدل نقصان العظم يفوق معدل
تكوين العظم وبالتالي يؤدي إلى نقصان كتلة العظم

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Phosphate

- * PO₄ plasma concentration is **3.0-4.5** mg/dL.
(**87%** diffusible , **13%** non-diffusible)

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Bone formation

- * Bone formation begins when : **active osteoblasts synthesize collagen fibers** . (that form the organic matrix called osteoid)
- * Calcium phosphate is deposited on the osteoid and making it is mineralized.

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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 مؤشرات of osteoblast activity .

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Bone Resorption:

* This process **does not** merely extract إنتزاع calcium, it destroys entire matrix of bone and diminishes يقلل bone mass.

* Cell responsible for sustained resorption is the **osteoclast** .

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Bone resorption of Ca⁺⁺ by two mechanisms :

(A) osteocytic osteolysis :

* This involves transfer of calcium from Canaliculi (القنوات الدقيقة) to extracellular fluid via activity of osteocytes.

* It is a fast (rapid) and transient effect.

(B) osteoclastic resorption is slow and sustained mechanism .

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What is the Role of Canaliculi ?

* Canaliculi are minute fluid-containing channels within the bone unit

* Interior osteocytes remain connected to surface cells via syncytial cell processes.

* This process permits تعطي تصريح transfer of calcium from enormous هائل surface area of the interior to extracellular fluid.

Note :

* Both mechanisms are stimulated by **Parathyroid Hormone(PTH)** . so, PTH **inhibits** bone-formation .

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Bone remodeling:

What is the meaning of bone remodeling ?

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 resting → osteoclasts

Mechanism :

- * 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.

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Bone remodeling affected by :

- 1- PTH.
- 2- 1,25 Dihydroxycholecalciferol.
(stimulate activity & formation of osteoclasts)
- 3- Calcitonin. (inhibits activity & formation of osteoclasts)

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Osteoporosis

- * The total bone mass of humans peaks **يصل ضروته** 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. **سن اليأس**
- * Bone resorption **exceeds** formation.
- * osteoporosis means → Reduced bone **density** and **mass**.
- * This leads to increased susceptibility **حساسية** to fracture
- * It occurs earlier in life for women than men but eventually both genders succumb to it.

Problem :

The rate of osteoclastic resorption exceeds deposition of new bone.

Cause:

loss of anabolic steroids as estrogen & testosterone which stimulate osteoblastic activity

result : bone becomes weak & Ca^{++} is lost from skeleton

Hormonal control of Calcium

3 principal hormones regulate Ca^{++} and three organs mthat function in Ca^{++} homeostasis.

- (1) Parathyroid hormone (PTH),
- (2) 1,25-dihydroxycholecalciferol (Vitamin D), and
- (3) Calcitonin, regulate Ca^{++}

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1) Parathyroid hormone (PTH) :

Inhibits bone formation

Increases plasma Ca^{++} levels

decrease **plasma phosphate levels** by :

(A) **directly acting** on bone → activate osteoclasts → stimulate Ca^{++} resorption

(B) **acting on kidney** → stimulate Ca^{++} reabsorption in the distal tubule → inhibit reabsorption of phosphate (thereby promoting its excretion).

(C) **acting indirectly on kidney** → change vitamin D inactive form into the active form

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2) 1,25 dihydroxy cholecalciferol (Vitamin D) :

1-stimulates bone resorptionn by mobilizing Ca^{2+} from bone

2- stimulate absorption of Ca^{2+} from the intestine

(1) & (2) lead to **increased** blood Ca^{2+} level

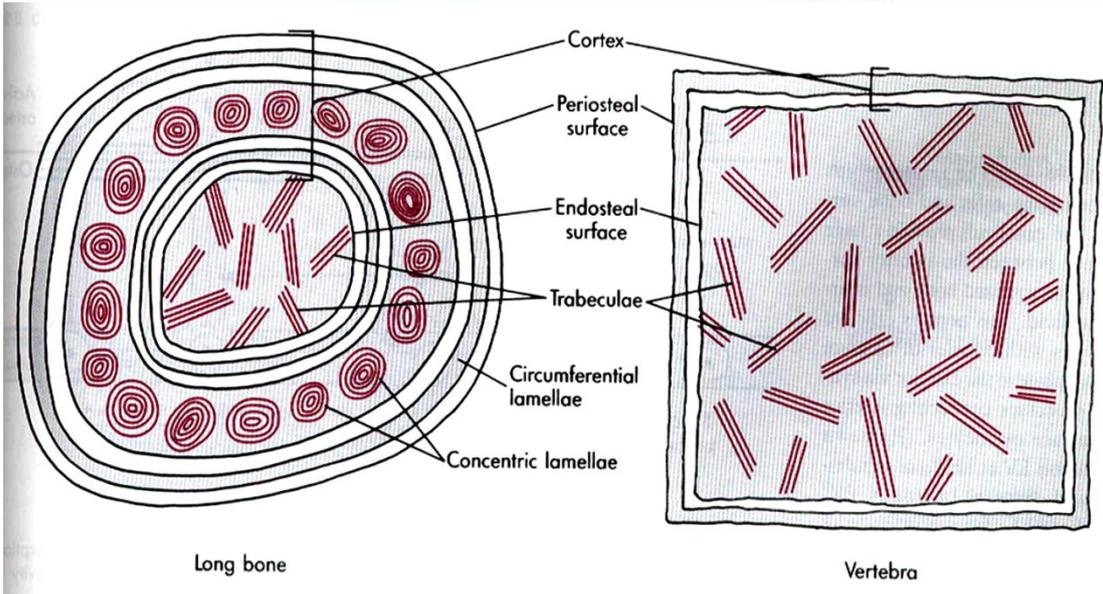
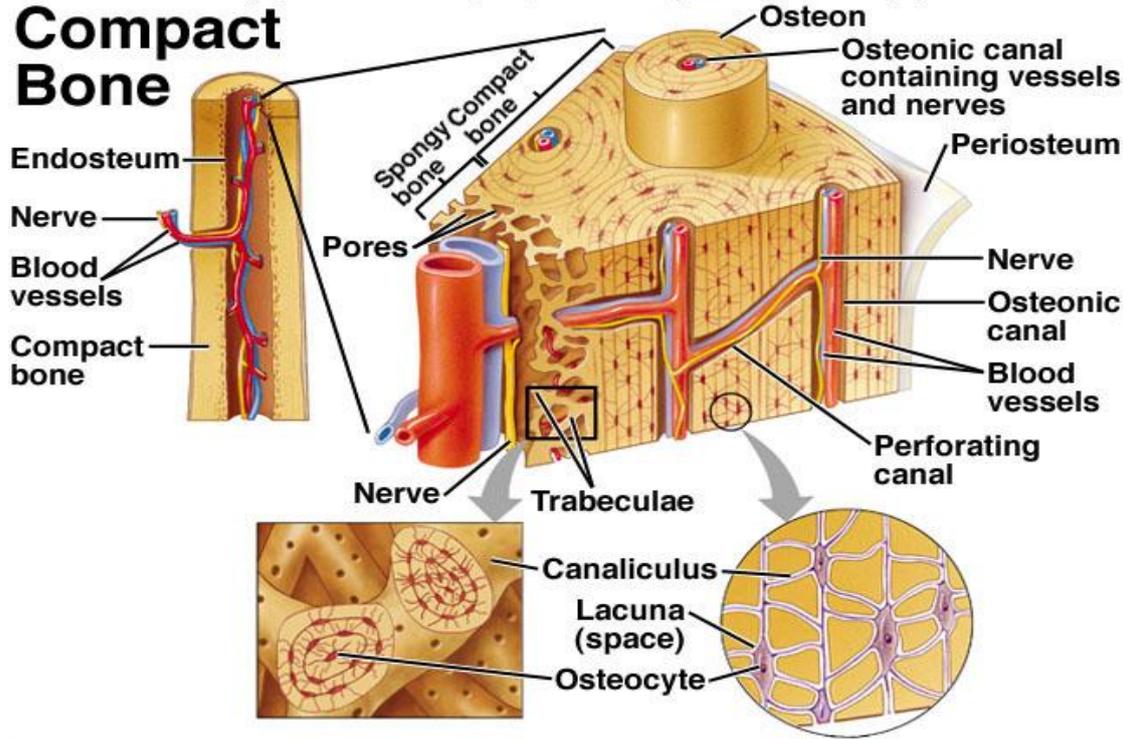
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3) Calcitonin :

Suppresses osteoclasts

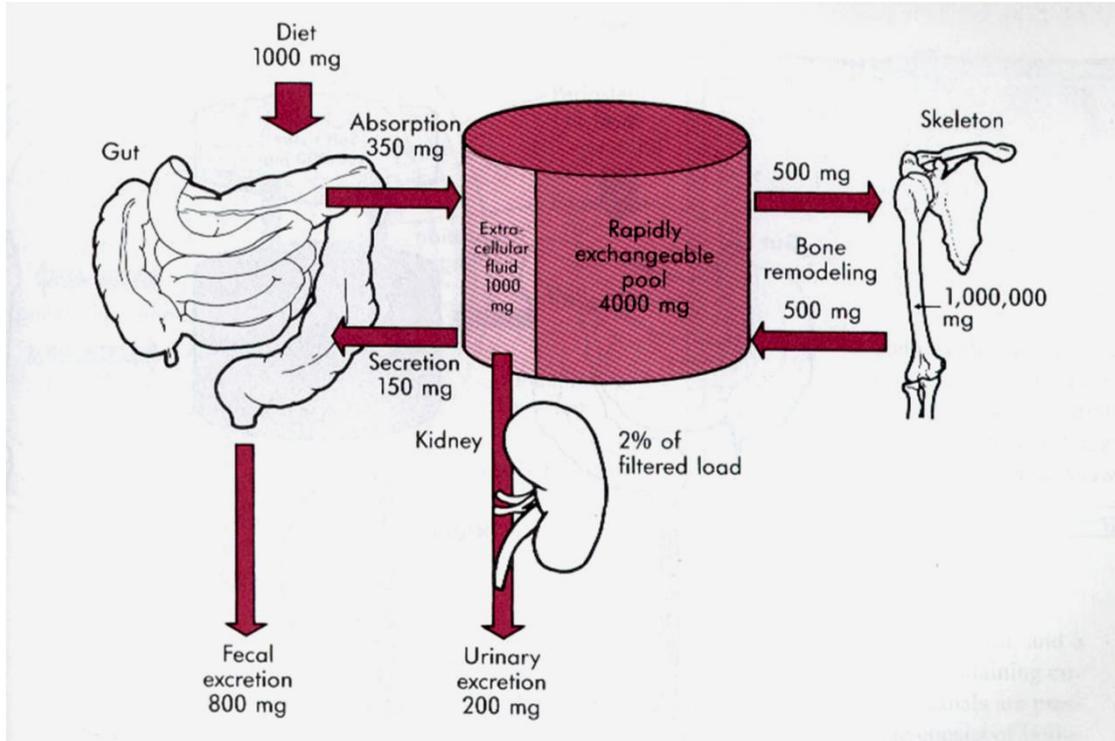
stimulates osteoblasts

Compact Bone



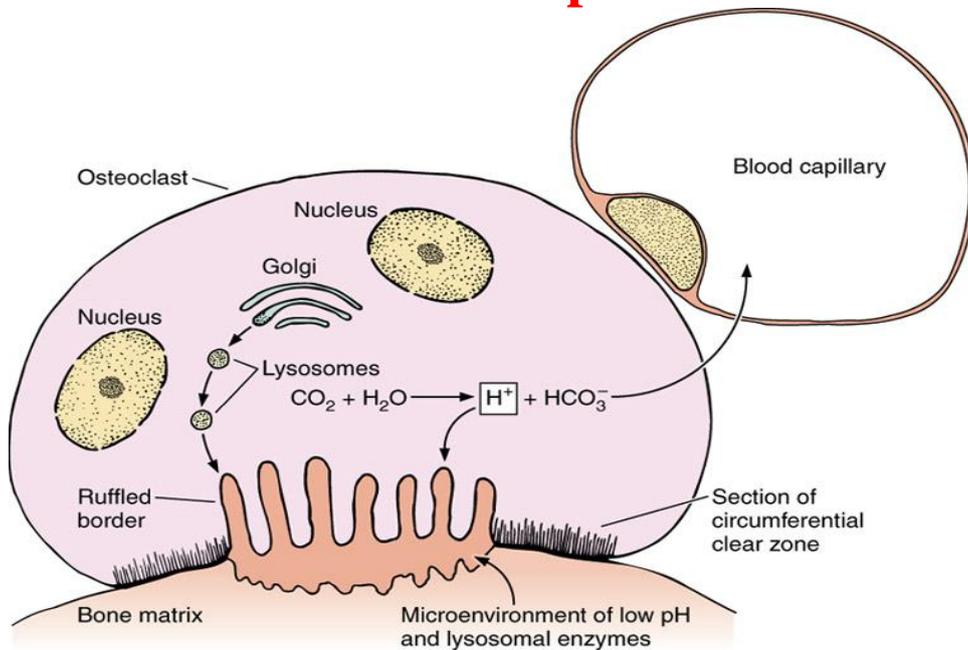
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Calcium turnover



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Bone Resorption



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Osteoclasts and Ca⁺⁺ resorption

