

MSS



Sheet no.1

Pathology



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★ The Bone functions ★

1_mechanical support .

2- Forces transmission.

-if you carry something in your head, this weight will be equally distributed all your bony structures.

3-protection

-brain is protected by the skull , plevic organs are protected by pelvic bones.

4- Mineral homeostasis

-calcium and phosphorus metabolism is mainly controlled by physiology of bone .

5-hematopoiesis

-the bone marrow is one of the main sources of hematopoiesis

→ any disease will affect the bone , it will affect most of its functions .

★ bone structure

1- matrix (osteoid 35% and minerals 65%)

-✓osteoid ; organic type 1 collagen (the major component of osteoid and one of the strongest types of collagen) and glycosaminoglycans and other proteins.

-✓Inorganic hydroxyapatite $\{Ca_{10}(po_4)_6(oh)_2\}$

-✓woven & lamellar bone ...depending on the type of matrix and the arrangement of matrix & cells.

2- cells ;

A-Osteoblast ; it is act as a stem cells ; it will form bone .. " sometimes these cells it will increase in fracture or healing or in an abnormal conditions (such as osteoblastoma).

→ high activity of these cells = more bone formation

b-Osteoclasts; resorbs the bone "originate from macrophage - monocyte system "

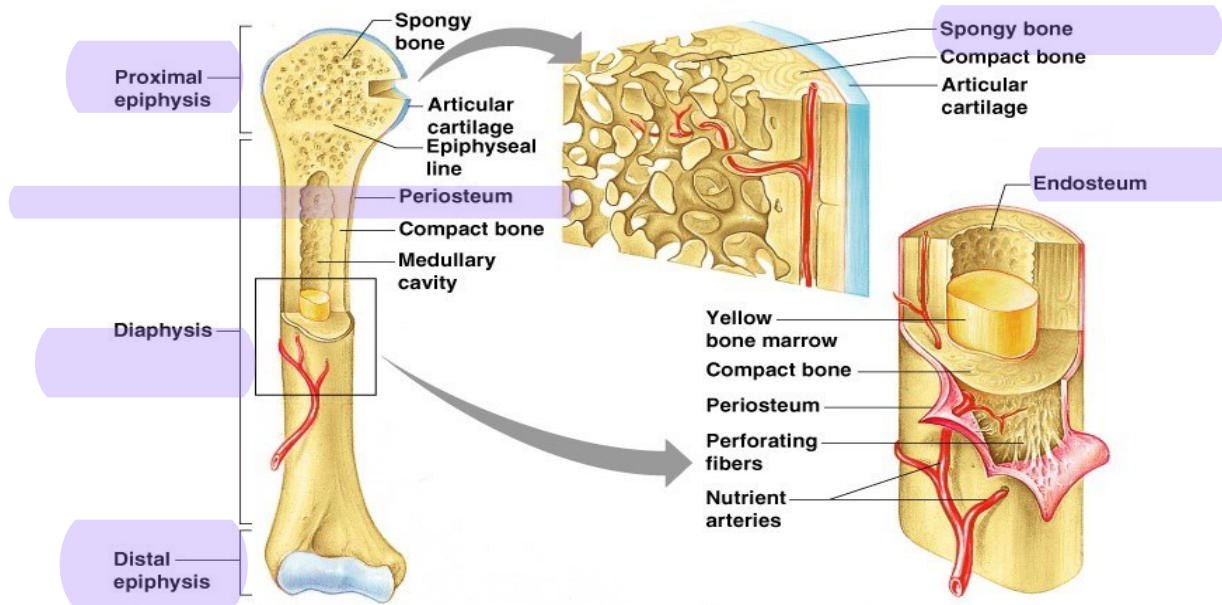
→ sometimes we need these cells in remodeling .

→ They are major player in the **OSTEOPROSIS**

C-Osteocyte ; mature bone cells

→ less active ; small in size ; does not have too many cytoplasmic organelles for metabolic activity .

★ structure of a typical Long Bone ;



Notes on the figure ;

- periosteum ; which is the outer part which contain nerves
- epiphyseal plate ; where the growth occurs .
- proximal and distal epiphysis.
- compact bone ; below the periosteum and before getting into spongy bone marrow & it is very hard
- Medullary cavity ; which contain bone marrow particles where the major hematopoiesis occurs.
- Diaphysis ; in the middle , located between the proximal & distal epiphysis
- The blood supply is in Endosteum (which is the inner part of the compact bone)

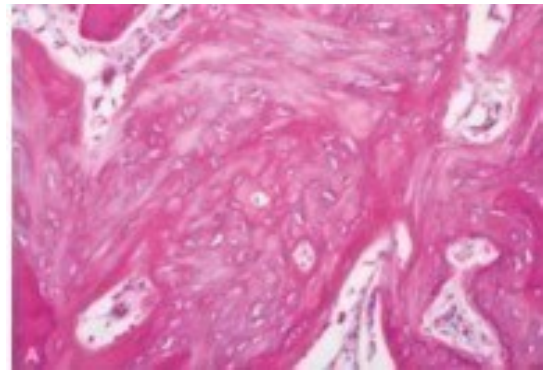
we prefer this division of bone because there are diseases or fractures occurs that can affects the proximal epiphysis , some of them affects diaphysis and some of them affects metaphysis , so the location of pathology inside the bone also important and determinant of different diagnosis

- The density of the bone inside determines if you have osteoporosis or not

★ woven bone & Lamellar bone

Woven Bone ;

- ➔ More cellular and disorganized the
- ➔ The trabeculae is more wide the
- ➔ The arrangement between cells and type 1 collagen is haphazard



- ➔ in early young born in children and in certain diseases.

- in adults if we see woven bone something wrong or abnormal is going on , whether its malignancy or fracture site

Lamellar Bone ;

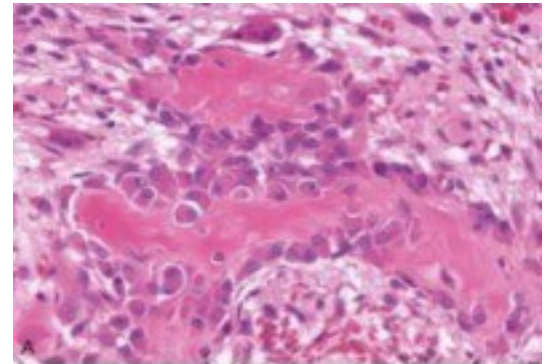
- ➔ The cells are more linear and organized.
- ➔ Less cells
- ➔ Main structure of mature long bones strong & more collagen



Osteoblasts & osteoclasts

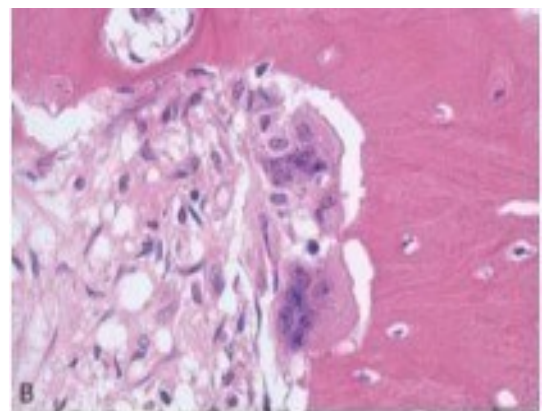
1-osteoblasts

- ➔ Smaller cells
- ➔ Mono nuclear cells
- ➔ The nuclear cytoplasmic ratio a little bit higher
- ➔ They form bone elements , lying down the young osteoid material , we can see it in osteoblastoma or osteoblastic cancer or at the site of fraction & in the new bone and children.



2- osteoclastic

- ➔ Big cells
- ➔ They eat up mature bone
- ➔ Multi nucleated giant cells "each osteoclast can have up 100-150 nuclei.
- ➔ Giant cell tumor of bone and osteoclastoma are names for tumors in osteoclasts , as it is needed in remodeling .

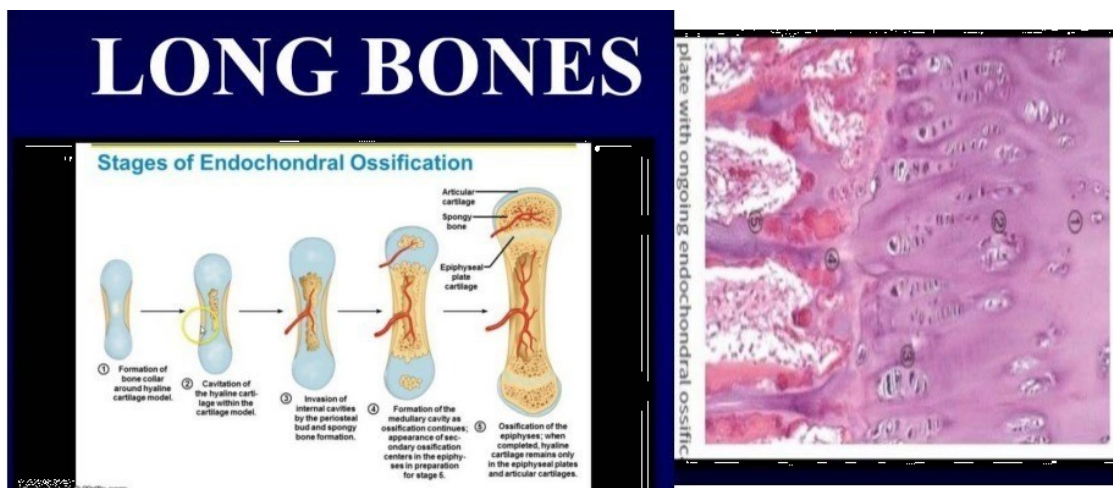


➤ The development of the bone

- There are two major ways where the development of bone occurs:

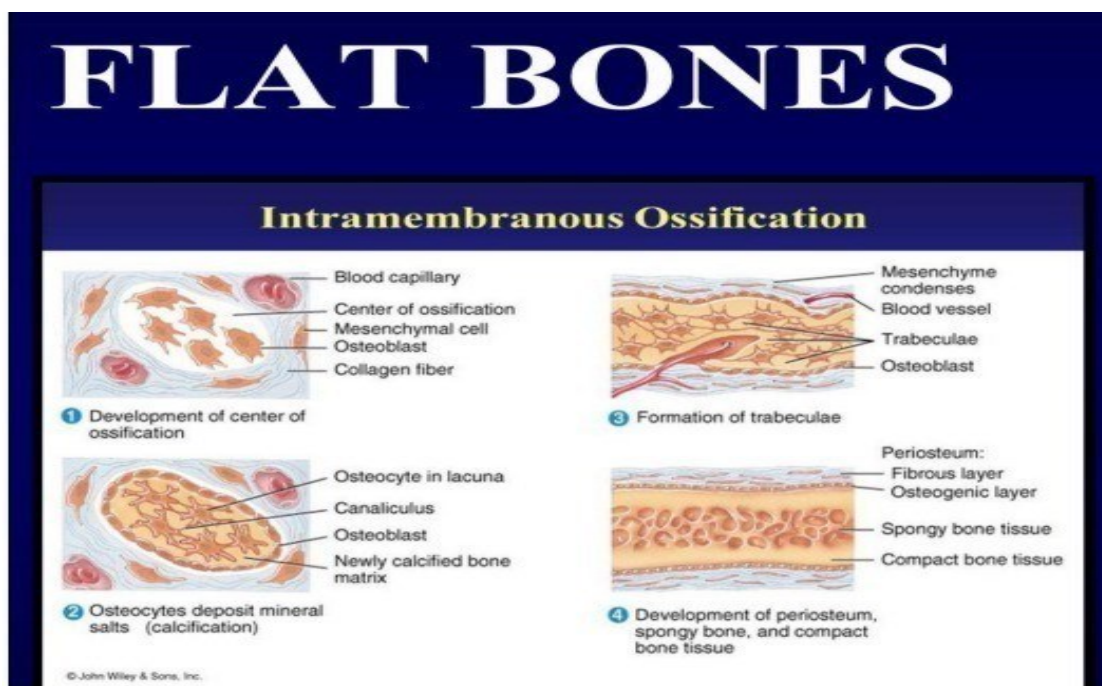
1- Endochondral ossification

From its name, indicates formation of bone from young mature cartilage from in utero until mature bone in adults. It is the main process where long bone is formed. This process starts with cartilage and then the endochondral ossification starts in the center until most of your long bone is replaced by mature bone and there is only a remnant of articular cartilage at both ends



2-Intra membranous ossification

Formation of flat bones like a clavicle, scapula, pelvic bone doesn't require Cartilage and The bone is formed by intra-membranous ossification. In this process we don't pass through cartilage formation, it starts with soft tissue membranes with stem cells between them (based on stimulating of stem cells which are recruited to the specific bone)



➤ Homeostasis & remodeling

- ✓ Continuous and dynamic complex process even in adult mature Skeleton (microscopic level).
- ✓ Peak bone mass is reached in early adulthood after completion of skeletal growth [between (20-30)]. Then it starts to decrease depending on nutrition and athletic activity.
- ✓ Resorption > bone formation on 4th decade [the main pathogenesis of the major metabolic syndrome of osteoporosis].

Very important Table

	+ Osteoclast differentiation	- Osteoclast differentiation	
More Resorption	PTH parathyroid hormone IL-1 Steroids	BMPs (bone morphogenic proteins) Sex hormones (estrogen & test.)	Less resorption

✓ patients who have either. endogenous steroid production or exogenous steroid usage for disease , autoimmune diseases or cancer they will have more osteoclastic activity and more bone resorption , that is why people who are taking steroids are advised to take vitamin D and calcium products

used by ATHLETES to increase bone and muscle mass.
 - this is a reason why women are more susceptible to osteoporosis especially menopausal women.

The Balance between bone formation [osteoblasts] and bone resorption [osteoclasts] is very critical in the understanding of many diseases like osteoporosis [the bone and the bone matrix gets less and the bone becomes weaker and exposed to many diseases and fractures].

✓ Macrophages-colony stimulating factors (M-CSF) are cytokines secreted by stromal cells (undifferentiated) upon specific stimulation RANK ligand.

✓ RANK ligand and its receptors are one of the current target for treatment by specific drugs that enhance its action or block the receptor of this ligand.

✓ This stimulation makes the stem cell active so it will be differentiated into osteoclast precursor then it will be converted into mature osteoclast that goes to the bone and does its function (bone resorption). In the mature osteoclast, the cytoplasm will increase and the size of nucleus will decrease

There is another another endogenous factor can block this process by blocking the RANK-RANK ligand receptor interaction which is osteoprotegerin so it inhibits the maturity of osteoclast

There is endogenous balance between these two processes, and you can between these two processes and you can alter this balance with or against osteoclast activity according to your needs

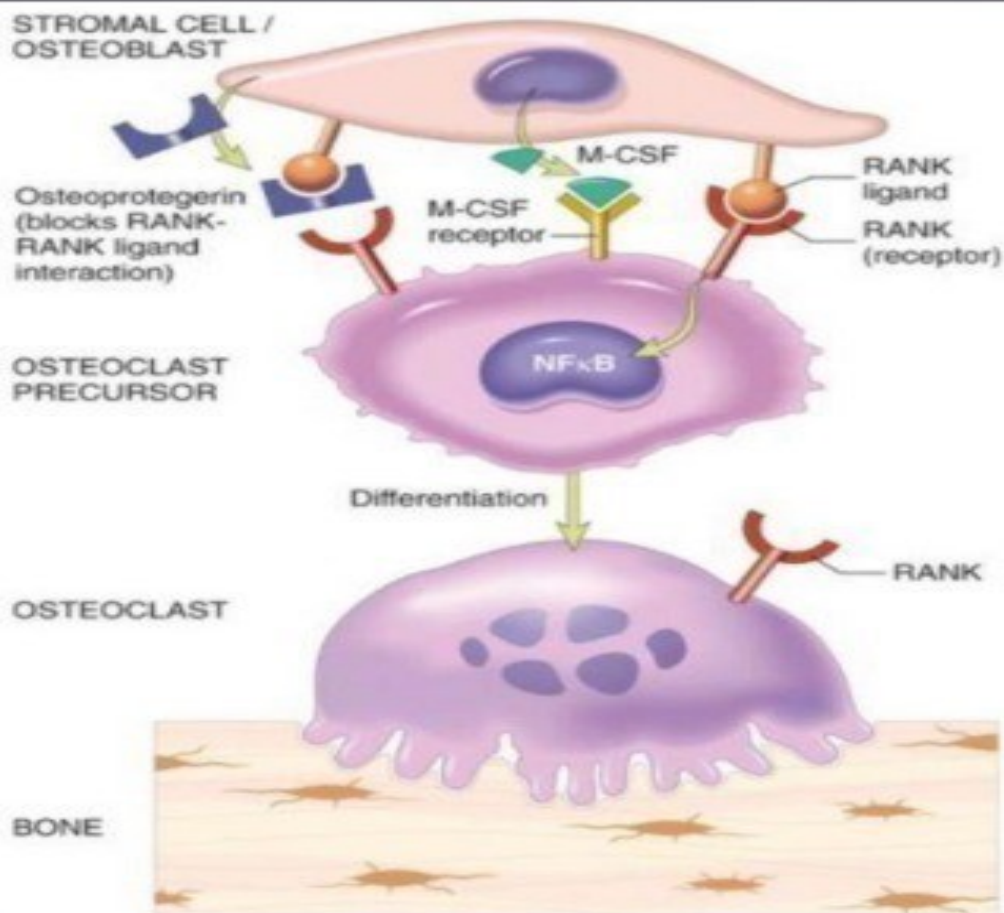


FIG. 21.4 Paracrine molecular mechanisms that regulate osteoclast formation and fun...

Past papers on this lecture

1. Which of the following is true regarding lamellar bone :

- a. It is found in the fetus
- b. Fibers are disorganized
- c. Has stronger structural integrity than woven bone
- d. It's formation is rapid

2. Which of the following is true about osteocytes?

- a. They are large and multinucleated
- b. They have high metabolic activity
- c. They are mature bone cells
- d. They are essential for bone resorption

3. Which of the following is false regarding bone?

- a. Lamellar bone is the mature bone
- b. Formation of woven bone is much faster than lamellar bone
- c. Both types have similar composition at general
- d. The presence of woven bone in adults is normal

4. Which one of the following statements best describe bone structure and its Physiology ?

- a. The osteoid constitutes 85% of the matrix.
- b. Type II collagen is the main protein in matrix
- c. Lamellar bone is less cellular than woven bone
- d. Osteocytes are large multinucleated cells
- e. Osteoclasts are small bone forming cells

Ans: 1-c. 2-c. 3-d. 4-c.

The End