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MSS

Musculoskeletal System

Pathology

Doctor 2018 | Medicine | JU

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-Musculoskeletal system is one of the most important systems due to its important functions.

- The diseases of MSS are very common such as Osteoporosis, Rheumatoid arthritis, bone and soft tissue tumors and so on ..

BONE FUNCTIONS:

1- Mechanical support. We can't walk and move without it ,(penguins lack knee joint that's why they can't walk the same way as we do)

2-Forces transmission. For example; your weight distributes all over the body toavoid the accumulation of the body weight on a specific joint.

3-Protection (the skull protects brain).

4-Mineral homeostasis. For example; calcium phosphorus metabolism is mainly controlled by the metabolism of the bone. Any problem in their metabolisms affects all the body; hypercalcemia and hypocalcemia are lethal.

5-Hematopoiesis (production of blood elements). Patient with severe disease in bone will develop **pancytopenia** (deficiency in bone marrow because of a bone disease which leads to a decrease in the number of white and red blood cells).

BONE STRUCTURE:

1-**Matrix** which is composed of two major substances:

- osteoid 35%: basic matrix material of the bone, organic material (mainly collagen type1 that gives the structural integrity of the bone), glycosaminoglycans & other proteins.

- minerals 65% (mainly calcium).

-Inorganic hydroxyapetite [Ca10(PO4)6(OH)2] **(the major component that makes the bone hard**).

2- **Cells**:

-Osteoblasts: the cells which form the bone

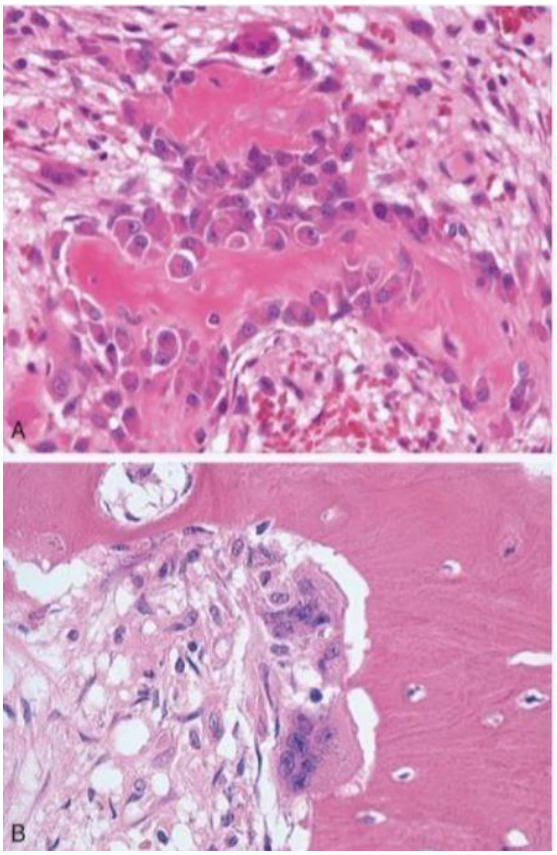
-Osteoclasts: Their major function is bone resorption. They are originated from macrophage system and they're usually large and multinucleated.

-Osteocytes: mature bone cells (low metabolic activity).

Note: the imbalance of osteoclastic vs osteoblastic activity causes a lot of diseases.

For example: at the age of 20 years the bone formation is actually more than the bone resorption, but at the age of (30-40) years the bone resorption is more than the bone formation and this causes problems.

Histlogical section:hematoxylin and eosin .



In picture A:

Pink material: osteoid (collagen type1+ glycosaminoglycans + hydroxyapatite).

Cells: osteoblasts(mononuclear), small in size, very active in forming bone.

In picture B:

Osteoclasts: originated from macrophage system, upon a certain stimulation monocytes turn into osteoclasts.

-Multinucleated, resorbing the bone.

-Types of bone:

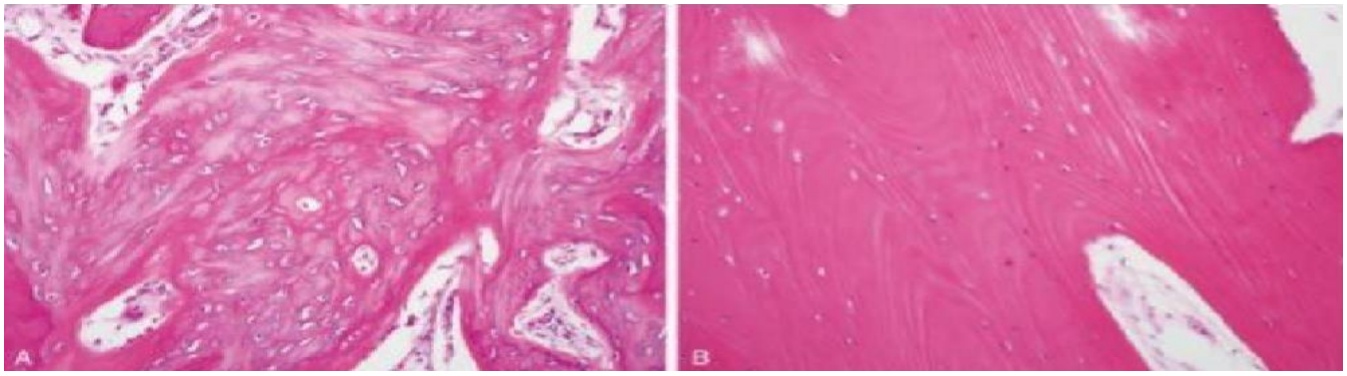
1-**lamellar bone**: adult mature bone.

2-**woven bone**: young fetal immature bone. (in fetus after birth then it will be converted into lamellar bone).

-The formation of lamellar bone is **slower** than the formation of woven bone but this gives us stronger structural stability.

-The presence of woven bone in adults is <u>ABNORML</u>; indicates pathology such as cancer or fracture.

Woven **Lamellar**



-Woven bone is more cellular and disorganized than lamellar bone. (you must differentiate between them)

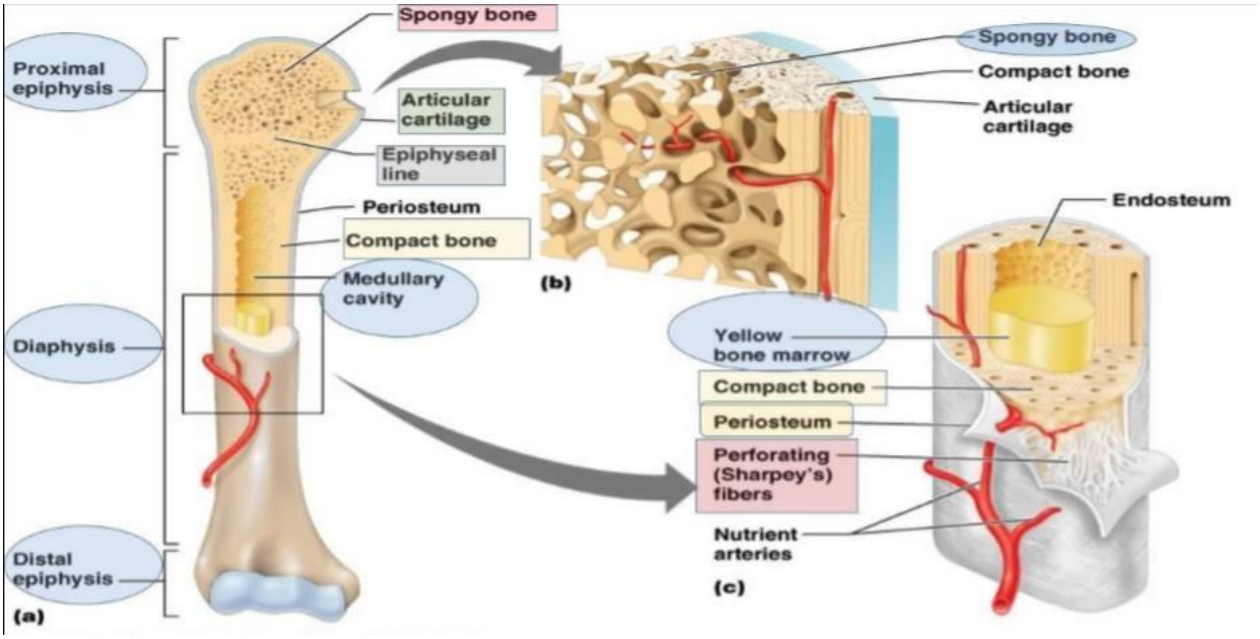
Structure of the typical long bone:

-Proximal and distal **epiphysis** and **diaphysis** (shaft) between them.

-Spongy bone surrounded by articular cartilage.

-Medullary cavity.

-Nutrient arteries exit from periosteum.



Notes:

1-The periosteum in children is thick and highly vascular, BUT in adults thin and less vascular.

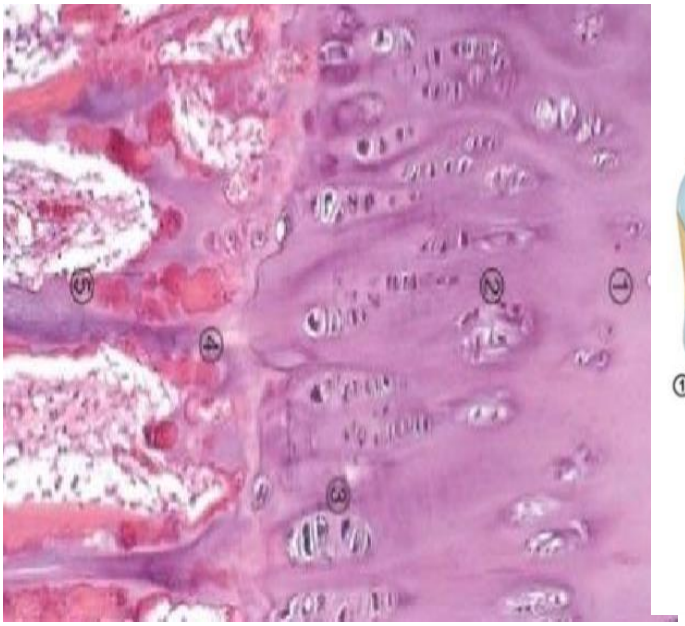
2- The sensitive part of the bone is the periosteum (full of neurons) so the irritation of periosteum is painful.

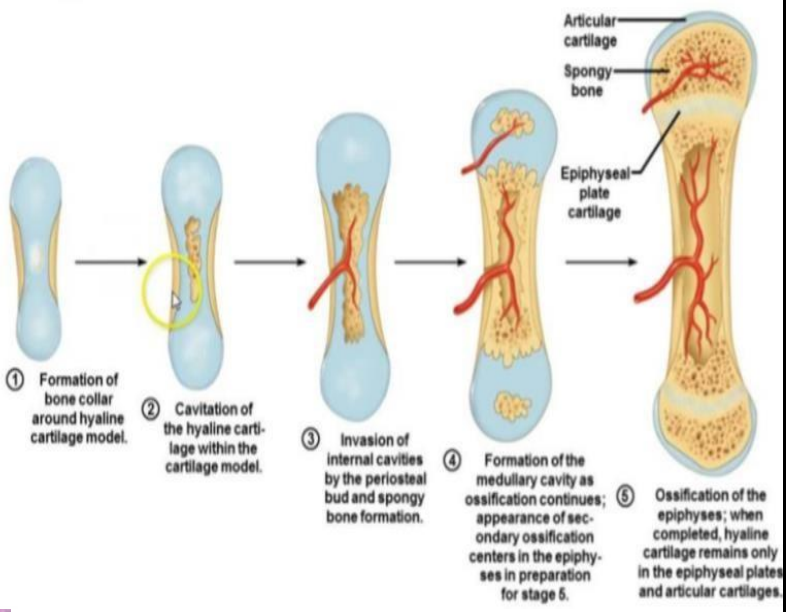
3- The structures of the bone are important because there are specific diseases that affect certain structures (for example osteosarcoma can't be found in diaphysis it is only found in epiphysis or the metaphysis, on the other hand (Ewing sarcoma) always affects the diaphysis.

Development of bone

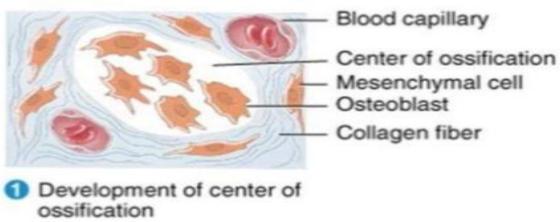
In the embryo, the **long bones** are cartilage at first, then the cartilage will turn into bone by a process called **endochondral ossification**.

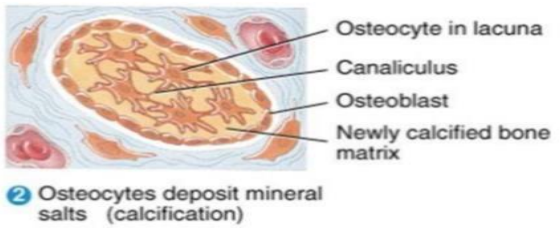
➔ Basically, under certain cytokines, growth factors and proper environmental stimulations the chondrocytes turn into osteoblast until the bones are completely formed except some areas remain cartilage for specific functions. (endochondral ossification is the major method of bone formation)

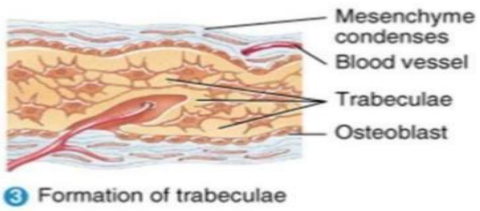


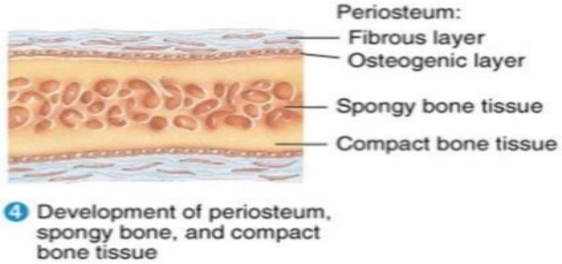


➔ The other way of bone formation is **intramembranous ossification**, which is the formation of flat bones (ex: skull,mandible).









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In this process we don't pass through cartilage formation , it starts with soft tissue membranes with stem cells between them (that's why is its called intramembranous ossification) those cells after being stimulated by cytokines are turned into osteoblast ❼ forming bone without passing through cartilage formation.

HOMEOSTASIS & REMODELING

The bone and bone marrow are responsible for the balance and homeostasis of calcium, phosphorous and other minerals keeping them in normal levels. Continuous and dynamic complex process even in adult mature skeleton (microscopic level).

-Needs cytokines and growth factors, etc..

-**Peak bone mass** is reached in early adulthood after completion of skeletal growth, but this **does not mean** that your metabolic processes of activities including bone marrow formation, hematopoiesis and bone homeostasis or remodeling will stop.

- Resorption will be more than bone formation on 4th decade. **What can you do**?

Slowdown and delate the intensity in this process by multiple factors such as drinking milk.

-The activity and the presence of good active osteoclast and their stimulatory factors and their inhibitory factors are the **major player** of this process.

+ Osteoclast differentiation	- Osteoclast differentiation
PTH Parathyroid hormone **IL-1** **Steroids**	**BMPs (bone morphogenic proteins)** **Sex hormones (estrogen & test.)**

Increase the resorption (weaken the bone)

- **Steroids** are very common drugs; are given for patients with autoimmune diseases (asthma for example), so the steroids stimulate the osteoclastic differentiation making the bone resorption higher.
- Patients with long term steroids therapy **have a higher risk of osteoporosis**.

Dicrease the activity of bone resorption(dicreasee the weakness).

- There are some drugs which mimics the action of **BMPs** to dicrease the activity of osteoclasts or to treat postmenopausal osteoporosis.
- When the **estrogen** level drops in postmenopausal women, the osteoclastic activity will be increased and this one of the risk factor of the presence of the postmenopausal osteoporosis.

- **What is the source of osteoclasts?**

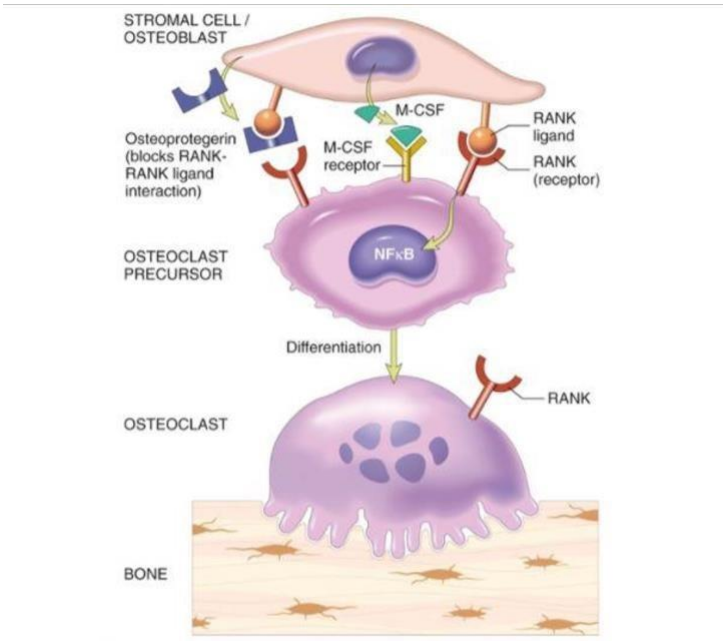
Macrophages-colony stimulating factors (M-CSF) are cytokines secreted by stromal cells (undifferentiated) upon specific stimulation **RANK ligand.**

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 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 alter this balance with or against osteoclastic activity according to your needs.



Notice that after differentiation , the nucleus to cytoplasm ratio decreases .

GOOD LUCK