بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

HISTOLOGY

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

FINAL | Lecture 1

Bone tissue pt.1

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Color coding used in the modified:

- *Black: the original slides*
- *Maroon: the doctor's explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

BONE TISSUE

Components

Bone : specialized type of connective tissue ,it has special feature which is the Matrix , it is the hardest type of CT due to the nature of its elements (especially ECM).

- **Bone matrix**

We said before that the matrix is consist of fibers and ground substance, but when we talk about bones we are talking about Organic and Inorganic parts of the matrix

- Organic
  - Collagen++
  - Proteoglycans
  - Glycoproteins

Organic includes the fibers and ground substance

- Inorganic

These are the ones that gave the bone its hardness and strength

  - Calcium hydroxyapatite +++

Small clusters of calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions start to form tiny crystals.
We'll discuss the structure and deposition in Osteogenesis process

Cells

Young and active

- Osteoblast
- Osteocytes
- Osteoclasts

Old and semi retired (low activity) not totally inactive ,it's important for the health of the bone ;if they die , the bone matrix undergoes degeneration and disintegration so it's essential for the maintenance of the life of the CT or Matrix

It is Monocyte-derived cell (monocytes are big cells found in the blood, with a kidney-shaped nucleus.)
This description is for the monocyte before the career shift. After the career shift, when these monocytes leave the bloodstream and move to the bone surface, a number of them will fuse together. The result is one large multi-nucleated cell, called an osteoclast .
It has a different function than other cells , During their differentiation, there is reprogramming of gene expression, with down regulation of immune-related genes " almost make the immune related genes silent " and up regulation of genes involved in bone resorption (breaking down of the matrix).

Functions

- Main constituent of the adult skeleton

Main function

- Provides solid support for the body, protects vital organs such as those in the cranial and thoracic cavities,

Brain :cranial cavity
Heart and lungs : thoracic cavity

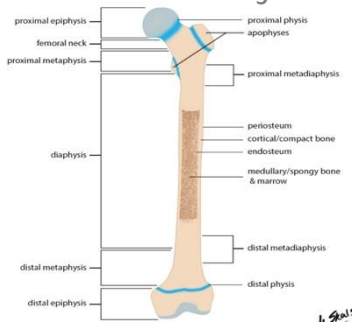
- Encloses internal (medullary) cavities containing bone marrow.

Bone is not entirely solid; it contains internal (medullary) cavities that house bone marrow (Bone marrow develops and plays a central role in hematopoiesis, producing blood cells within the medullary cavities of bone)

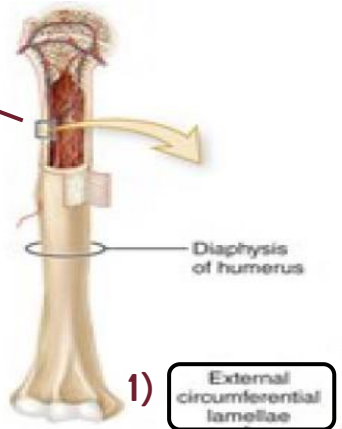
- Bone tissue also serves as a reservoir of calcium, phosphate, and other ions.

Bone stores calcium and phosphate in its matrix. When needed, osteoclasts release these ions. The body also maintains calcium levels by increasing intestinal absorption and reducing kidney excretion. If these aren't enough, bone resorption supplies extra calcium and phosphate.

Additional image



Humorous is a long bone, and long bone is one type of bones that its biggest dimension is the length "shaft"(diaphysis) and has two ends (epiphysis)
And the ribs are flat bones
They differ in the way of formation



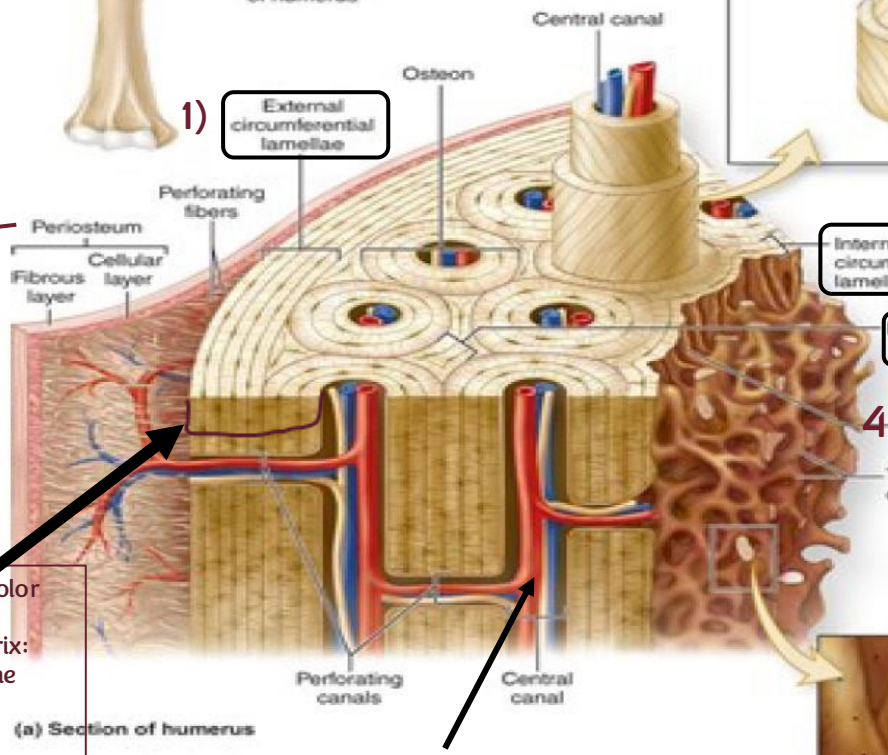
Every part of our body has covering either epithelium or connective tissue.
All bones are lined on their internal and external surfaces by layers of connective tissue containing osteogenic cells—endosteum on the internal surface surrounding the marrow cavity and periosteum on the external surface.
In bones ,due to their hard substance, they need a hard covering which is **periosteum** (peri= around, osteum = bone)
We also have **perichondrium** covering the cartilage

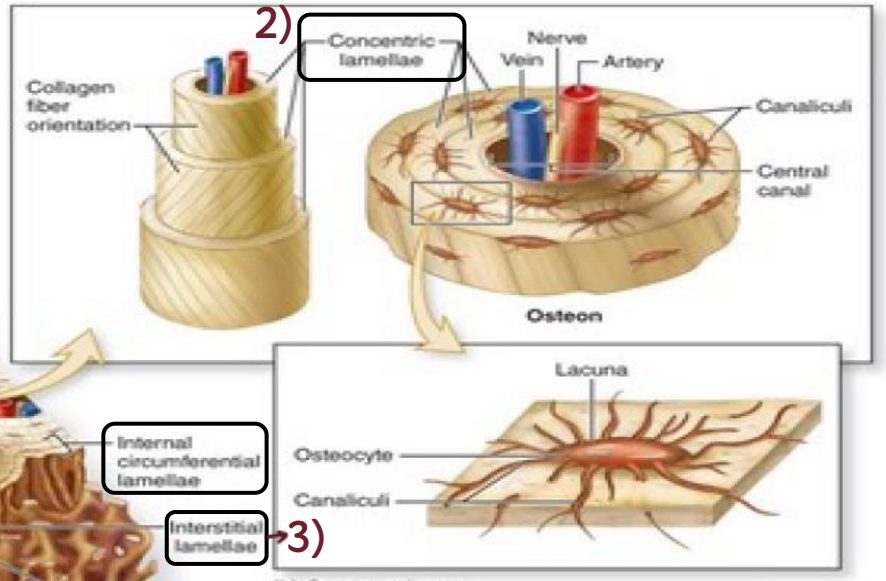
Bone

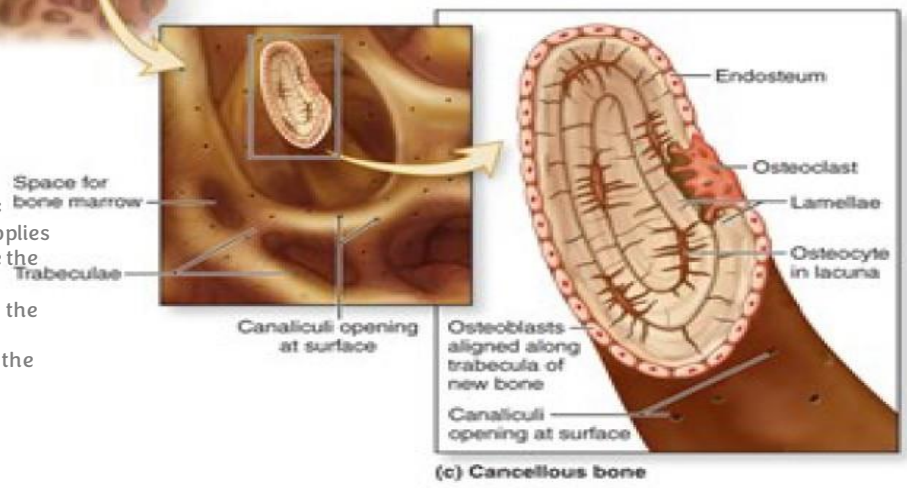
Internal organization of the bone :

Because of its hardness, bone cannot be sectioned routinely. Bone matrix is usually softened by immersion in a decalcifying solution before paraffin embedding, or embedded in plastic after fixation and sectioned with a specialised microtome.

These are connective tissues called **lamellae** (صفائح)(matrix = the yellow color in the image) and they have different shapes and locations .
We have 4 types of lamellae which are bone cells are surrounded by matrix:
1.External or outer circumferential lamellae : beneath the periosteum at the periphery
2.Concentric lamellae : surround central canals
3. Interstitial lamellae: fill spaces between osteons
4. Inner circumferential lamellae : same as the external but in the inner part with spongy part surrounded with medullary cavities , and with the compact part of the bone .(compact and spongy are two different types of bones)
-An osteon (or Haversian system) is the fundamental functional unit and the structural building blocks of bones, contain blood vessels, nerves, and osteocytes, providing structural strength and supporting bone remodelling and consisting of concentric layers of bone matrix, called lamellae (Concentric lamellae), surrounding a central canal.
<u>These cells are surrounded by hard matrix , so the cells are osteocytes which are the old and semi-retired cells .</u>



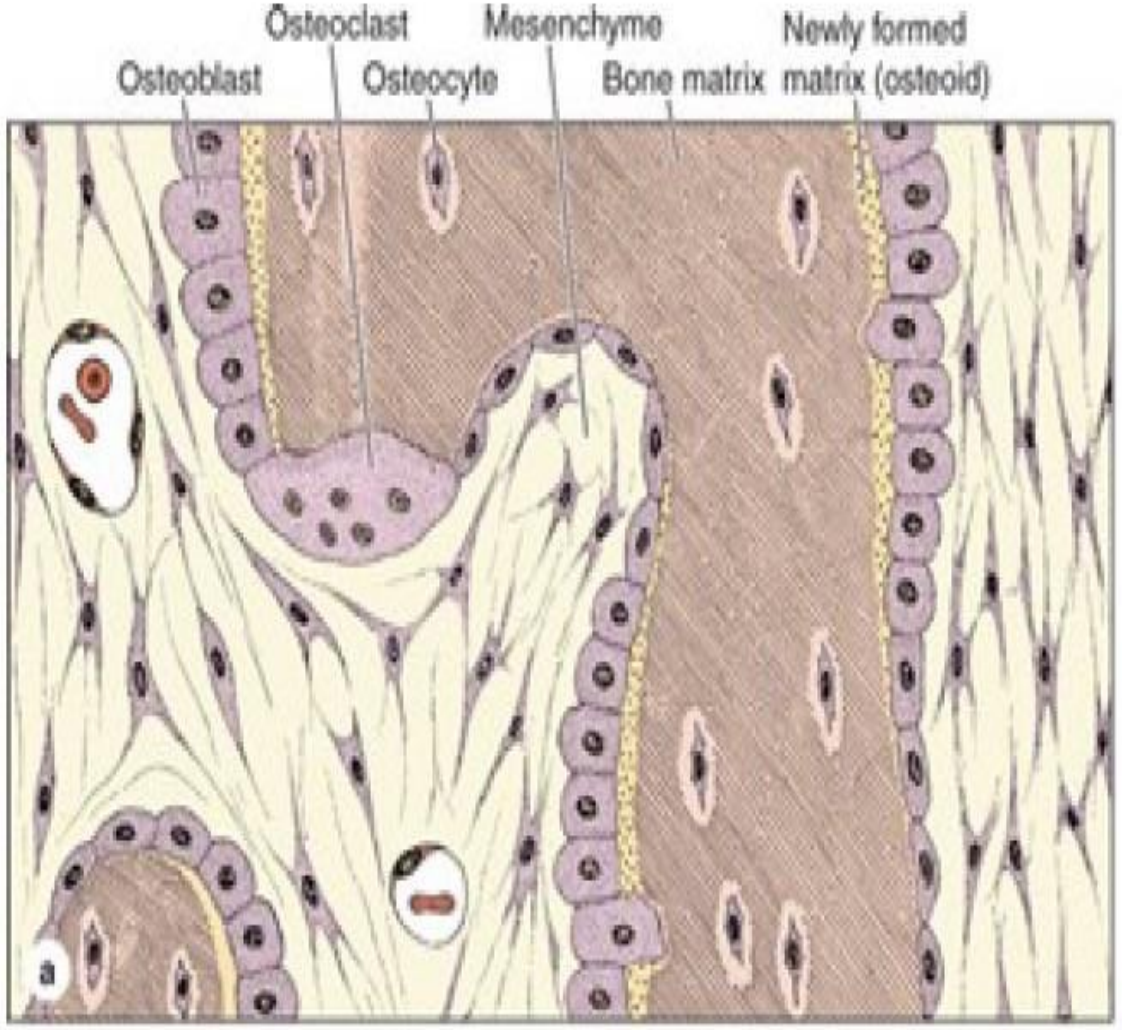


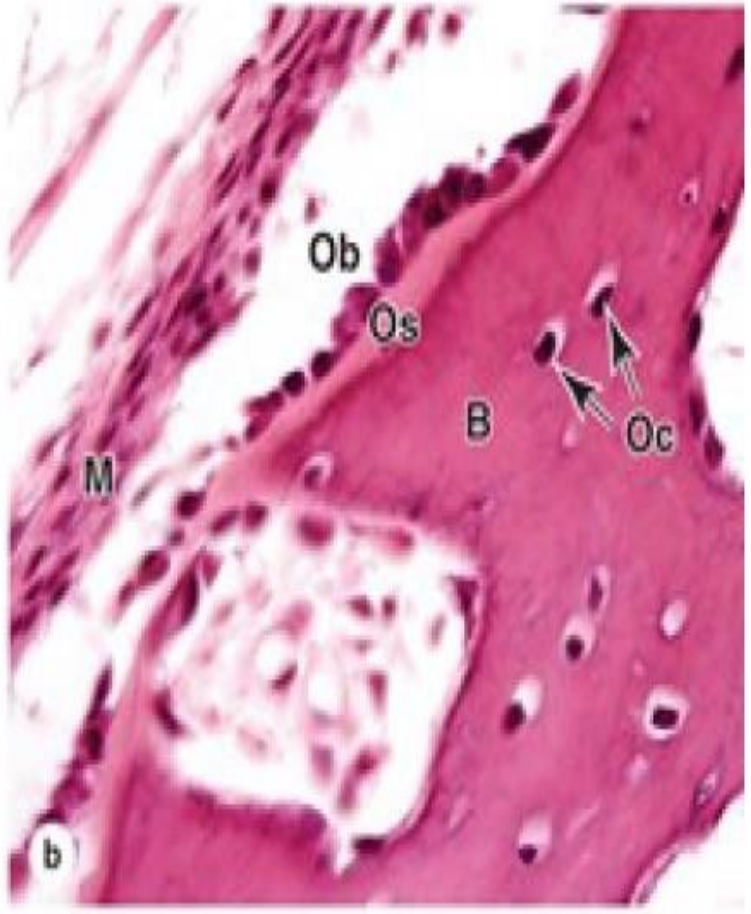


It is highly organized and highly vascularized
The bone is supplied with blood from three main sources:
1. Nutrient artery: The main blood supply of the bone, Supplies Bone marrow, Inner part of compact bone, Divides inside the bone into branches
2. Periosteal arteries: Come from the periosteum, Supply the Outer part of compact bone
3. Metaphyseal & Epiphyseal arteries : Supply the ends of the bone (Metaphysis, Epiphysis)

Bone cells

1. Osteoblast
2. Osteocytes
3. Osteoclasts





This image is a representation on how the bone looks like on a certain stage, these 2 images are the same (one is animated and the other is under the microscope)

Explaining the previous slide:

- Osteocytes are imprisoned in the matrix, while osteoblasts (not yet imprisoned) are found on top of the surface, after they release the matrix and completely surround themselves they get trapped, becoming osteocytes. Osteoclasts are found on top of the surface of the matrix.

- The image is a representation of osteogenesis which takes place by 2 mechanisms: 1)indirectly within the mesenchyme. 2)Hyaline cartilage is formed from the mesenchyme, and it will be removed and replaced by bone.

- So the mesenchymal cells differentiate to become osteoblasts, and the osteoclasts come from the blood stream as monocytes and they fuse to create the osteoclasts (which is huge and multi-nucleated).

- The osteoblasts start to lay down the first form of bone, which could be said to be the immature type of bone , it is called osteoid (it looks different than the bone matrix when using H&E stain because it's not fully developed yet).

- The osteoblasts are more than the osteocytes in the image, which means that not all osteoblasts will be trapped in the future and become osteocytes. When the osteoblasts synthetic activity is completed, some of them will become osteocytes and the rest (majority) undergo apoptosis (الموت الخلوي), which explains the huge difference in numbers between osteoblasts and osteocytes, And a small number of them flatten to cover the matrix and become bone lining cells.

- Most of the osteoblasts should undergo apoptosis to get rid of the cells and keep the matrix healthy and solid, so the number of the cells should be minimized when they're done with their synthetic activity, and another type of cells is formed which is called bone lining cells but they're quite small in number and flat.

- The osteoid will go through Mineralization (adding inorganic substances to the osteoid to make it closer to the mature

Cells

- Osteocytes are found in cavities (lacunae) between bone matrix layers (lamellae), with cytoplasmic processes in small canaliculi that extend into the matrix.
- Osteoblasts growing cells which synthesize and secrete the organic components of the matrix
- Osteoclasts which are giant, multinucleated cells involved in removing calcified bone matrix and remodeling bone tissue

Osteoblasts

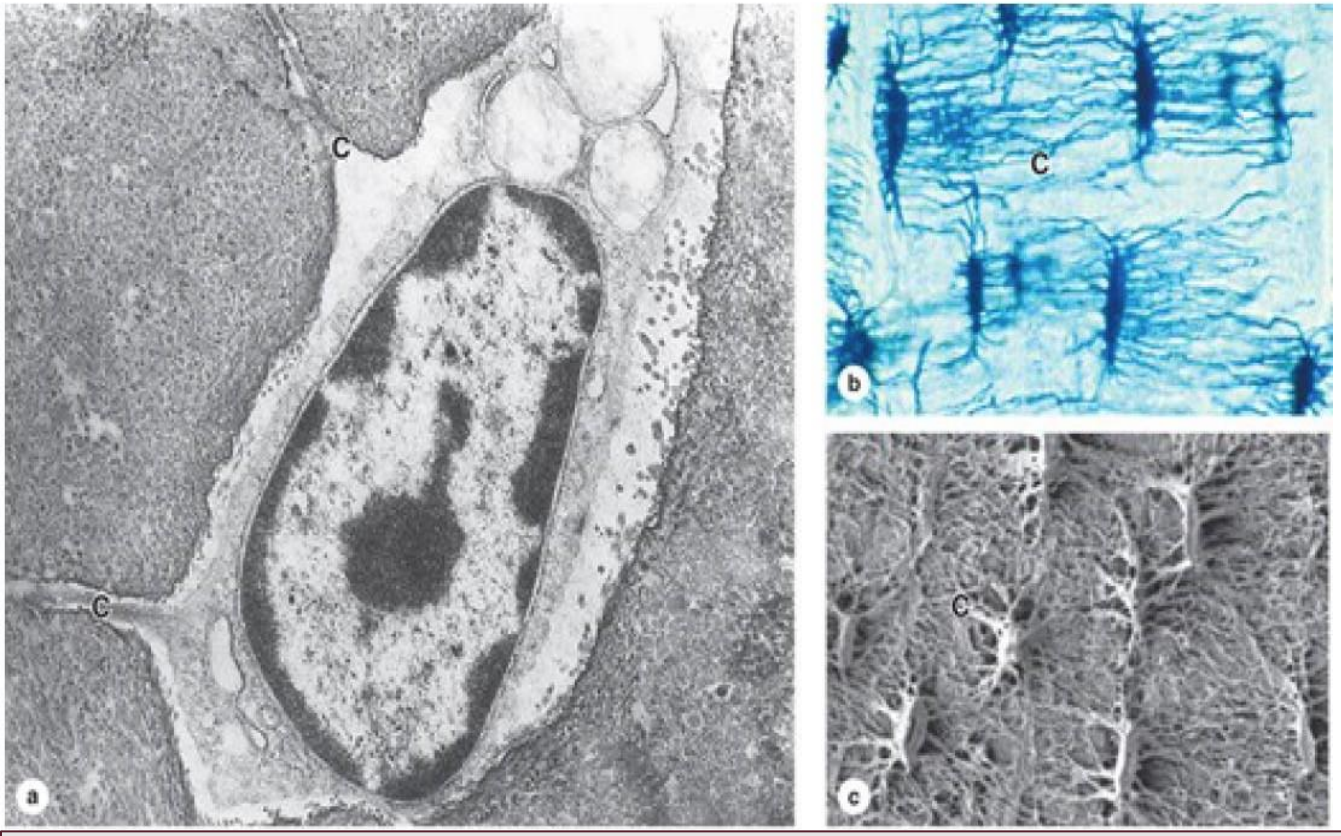
- **Originating from mesenchymal stem cells.**
- **Produce the organic components of bone matrix**
- **Located exclusively at the surfaces of bone matrix.**
- Active ones are located exclusively at the surfaces of bone matrix (integrins)

Osteoblasts

When their synthetic activity is completed:

- Some osteoblasts differentiate as osteocytes entrapped in matrix-bound lacunae.
- Some flatten and cover the matrix surface as bone lining cells
- The majority undergo apoptosis.

Osteocytes



(A) Is taken with TEM. The matrix is dense and is dark-grayish, the lacuna is a bit lighter and the canaliculi are visible too, the osteocyte is found inside the lacuna. The nucleus is in the middle and it contains the genetic material inside.
(B) It is injected with stain (so it can travel through all the spaces) so that you are able to see the extensive network between the cells. If we had the double amount of the cells that will minimize the amount of bone matrix making it weaker.
(C) SEM of the lacunas with the osteocytes inside, and it shows the extensive network between the cells through their canals.

- Surrounded by the material they secrete and then differentiate as osteocytes.
- Processes in canaliculi 250-300 nm.
- Osteocytes communicate with one another and with nearby osteoblasts and bone lining cells via gap junctions at the ends of their processes
- The most abundant cells in bone (IN ADULTS ONLY, but during growth period we have a lot more osteoblasts than osteocytes).
- Exhibit significantly less RER, smaller Golgi complexes, and more condensed nuclear chromatin than osteoblasts
- Maintain the calcified matrix, and their death is followed by rapid matrix resorption

Osteocytes

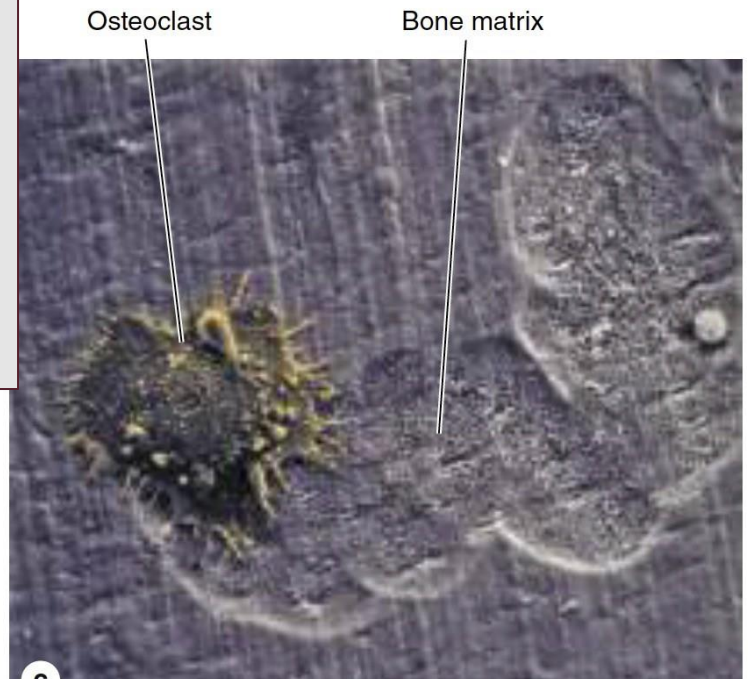
- These are the old and semi-retired (not engaged in synthetic activity but they oversee the health of the matrix).If these cells die, a disintegration in the matrix happen.

- Mechanostats(مستشعرات ميكانيكية) : the osteocytes are important for the maintenance of the bone matrix. Muscles are inserted on bone and the attachment and constant pulling of muscles on the bones is sensed by the osteocytes, which gives the mechanostats (osteocytes) energy to excite them which will make sure that the matrix is optimally mineralized (that's why someone doing a lot of physical activity has healthy bones). On the other hand, someone who doesn't do much physical activity, so the mechanostats lack excitation from the pulling that comes from the muscles, which would decrease the mineralization of the bone matrix, making it lighter and less mineralized matrix (their bones look like the bones of people who are diagnosed with osteoporosis هشاشة العظام). That's why it's always advised to keep moving and running because it would influence the strength of the bones.

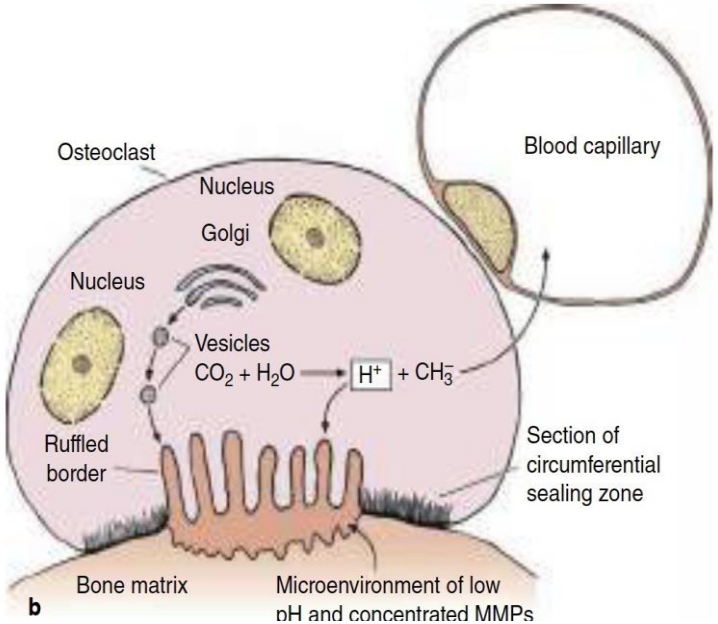
Osteoclast

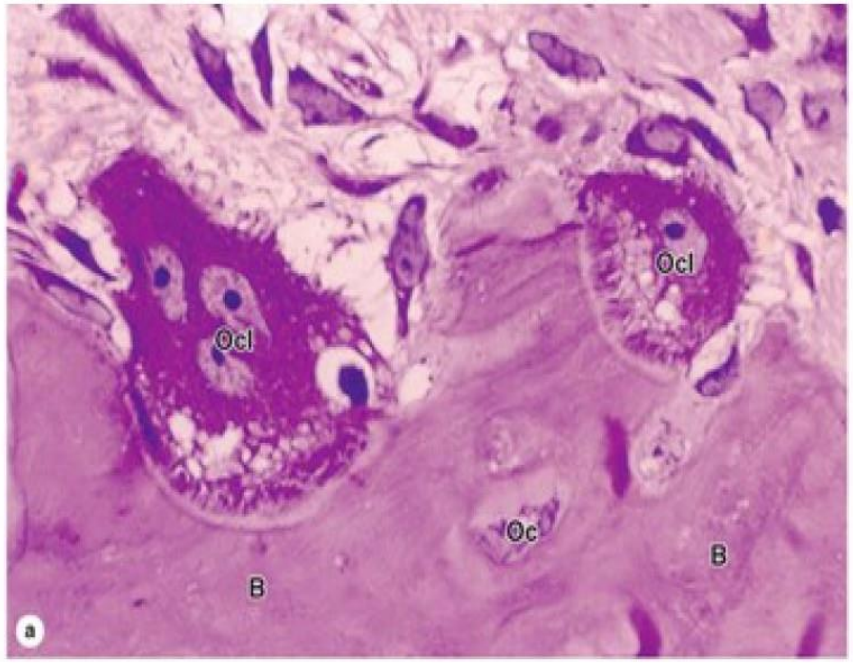
- Very large, motile cells with multiple nuclei.
- Resorption cavities (Howship lacunae)
- Osteoclast's circumferential sealing zone where integrins tightly bind the cell to the bone matrix.
- The sealing zone surrounds a ruffled border of microvilli and other cytoplasmic projections close to this matrix.

Taken with SEM. Colored with photoshop. You can see its footprint behind it and it's traveling through the bone matrix because the genes that are responsible of mobility are still active so they can liberate the inorganic components.



During embryogenesis, the first form bone is formed (which is not ideal but good for that period of time, it is not optimally mineralized and the direction of collagen is not optimal). In order to create a more optimal and mature structure of bone, we need to get rid of what we have which is done by osteoclasts, then the osteoblasts will build a new form of bone which is more optimal.





Osteoclasts

The bone is in a constant state of remodeling, which means the matrix is reformed regularly.

When looking in bone sections , you can find small osteons, larger ones and intermediate ones, that is because of the remodeling of the bone, the smaller osteons are newer while the larger ones are older, so bone usually keeps removing osteons and creates new ones.
When we keep doing physical activity (keeping interaction between muscle and bones), this will be transcribed into changing the direction of the osteons to make a healthier type of bone

The image (B) from last slide: you can see a huge osteoclast. In order to release the inorganic components ,they have to create isolated environments because it involves releasing enzymes within those environments. The cell creates a structure that looks like microvilli that is surrounded by the sealing zone, which prevents leaking of enzymes and the low pH fluids to the surroundings. Once the osteoclast is done, it will move and create another sealing zone and create another ruffled border to start working again.

Osteon

Osteon (Haversian system):

- Complex of concentric lamellae
- 100-250 µm in diameter
- Surrounding a central canal that
- Contains small blood vessels, nerves, and endosteum

Periosteum & Endosteum

- **External and internal surfaces of all bones**
- **Periosteum is a dense connective tissue, containing mostly bundled type I collagen, but also fibroblasts and blood vessels**
- **Type I collagen (Fibrillar collagens types I, II, and III).**
- Bone is vascularized by small vessels that penetrate the matrix from the periosteum.
- Endosteum covers all trabeculae around the marrow cavities.

QUIZ TIME!!

For any feedback, scan the code or click on it

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

Additional Resources:

رسالة من الفريق العلمي:

قال رسول الله -صلى الله عليه وسلم- : "عجبا لأمر المؤمن إن أمره كله له خير، وليس ذلك لأحد إلا للمؤمن، إن أصابته سراء شكر فكان خيرا له، وإن أصابته ضراء صبر فكان خيرا له" 💙