# Connective tissue

- It is one of the basic tissue of the body designed primarily to connect and support various others tissues.

## General Features

- The connective and supportive tissues are derived from the mesoderm. However, the ectoderm of the head region may also contribute to their formation.
- The connective tissues are made up of three main components cells (widely separated from each other), fibers (different types), and amorphous ground substances.
- It is well vascularized.
- It performs many functions:
- Mechanical functions (connection, support, protection e.g., bone and cartilage).
- Body defenses (presence of phagocytes, presence of immunocompetent cells, physical properties of the ground substances which act against the spread of pathogenic organism.
- Storage (water and electrolytes, fat in adipose tissue).
- Temperature (heat) regulation (adipose tissue).
- Tissue repair (formation of scar tissue).

# Connective tissue proper

- Cells
- Fibers
- Amorphous ground substance

# Connective tissue cells

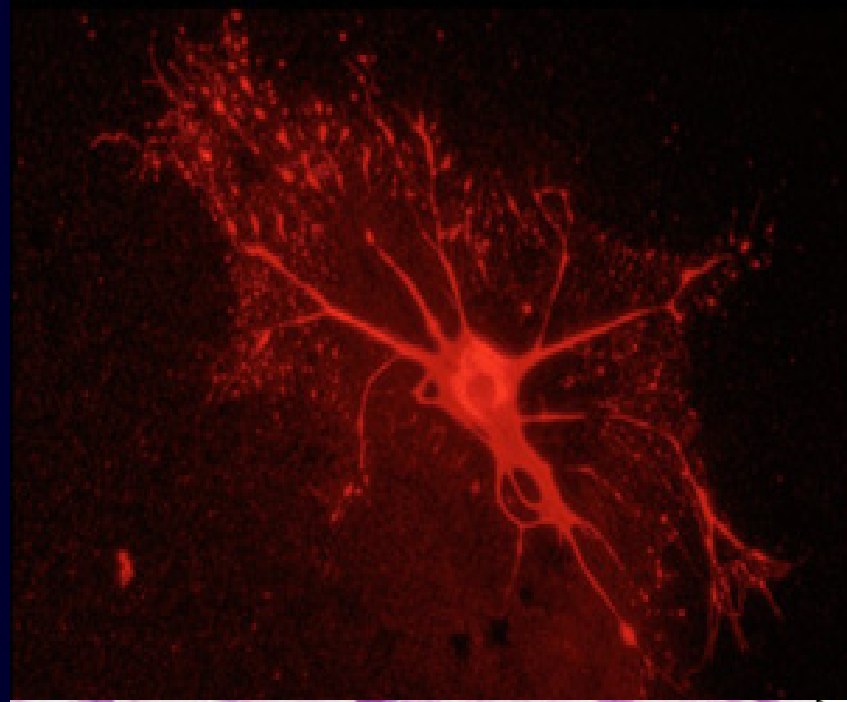
**The cells of the connective tissue are divided into two main groups:**

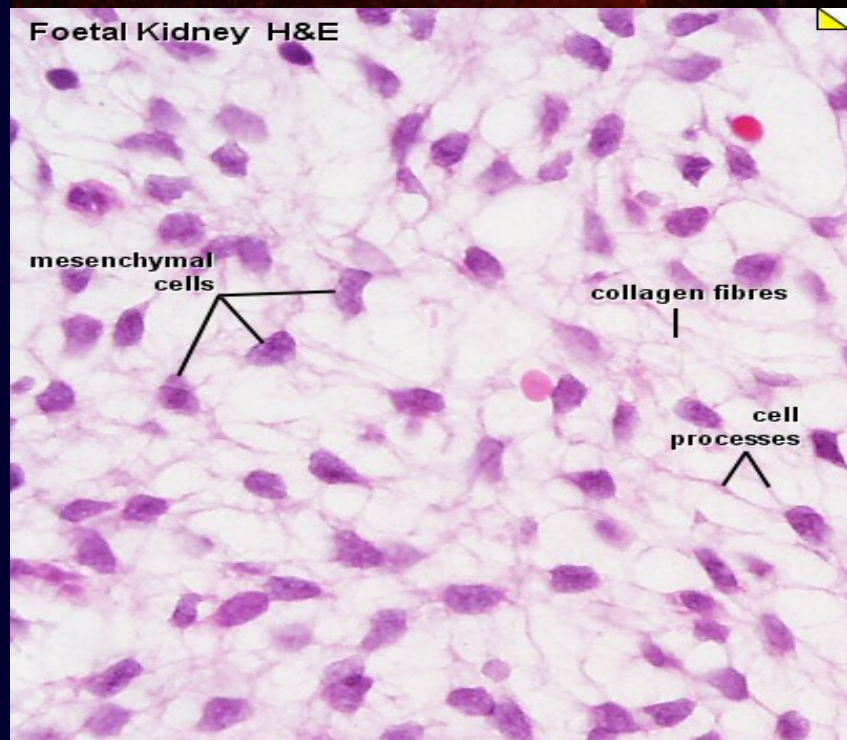
- **Fixed or permanent cell**
- **Free or visitant or wandering cells**

# Fixed or Permanent cell

# Mesenchymal cells

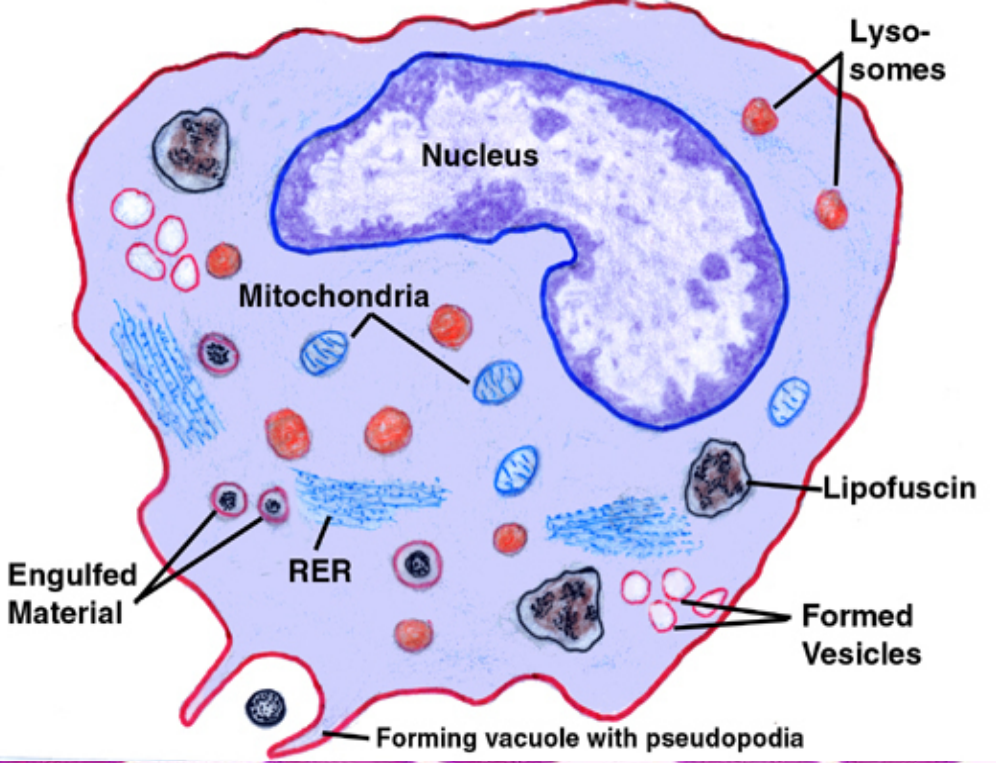
- They have an irregular stellate shape.
- Have delicate branching cytoplasmic processes
- The nucleus is pale and oval with dispersed chromatin and prominent nucleoli.
- The cytoplasm is basophilic
- Mesenchymal cells are relatively unspecialized and are capable of differentiation into all types of connective tissue cells including that of the skeleton and smooth muscles.

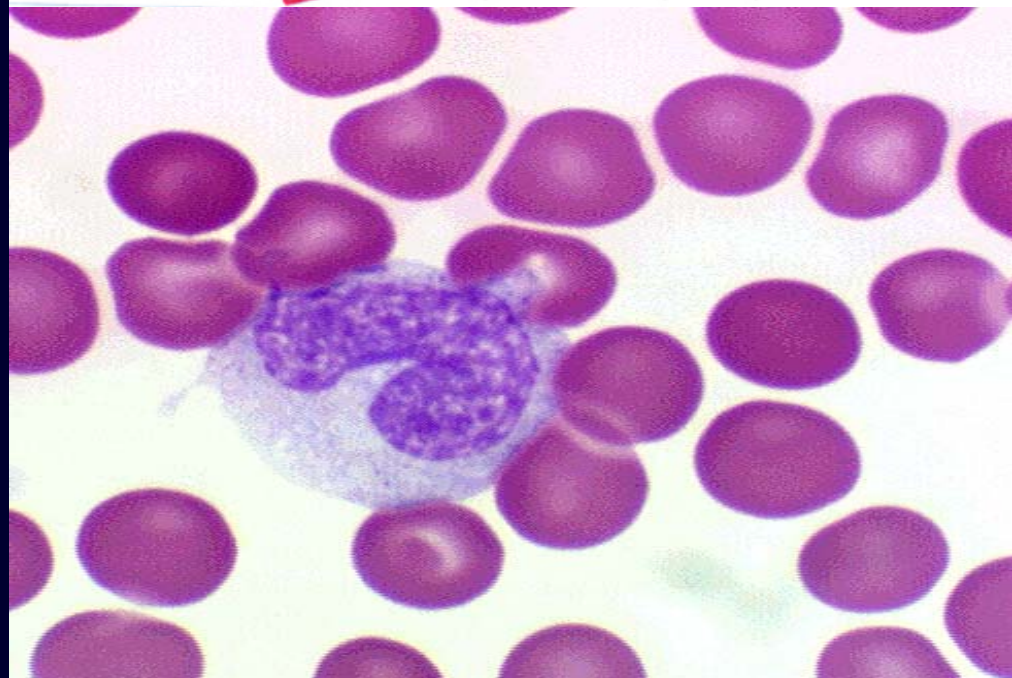




# Macrophage (histiocyte)

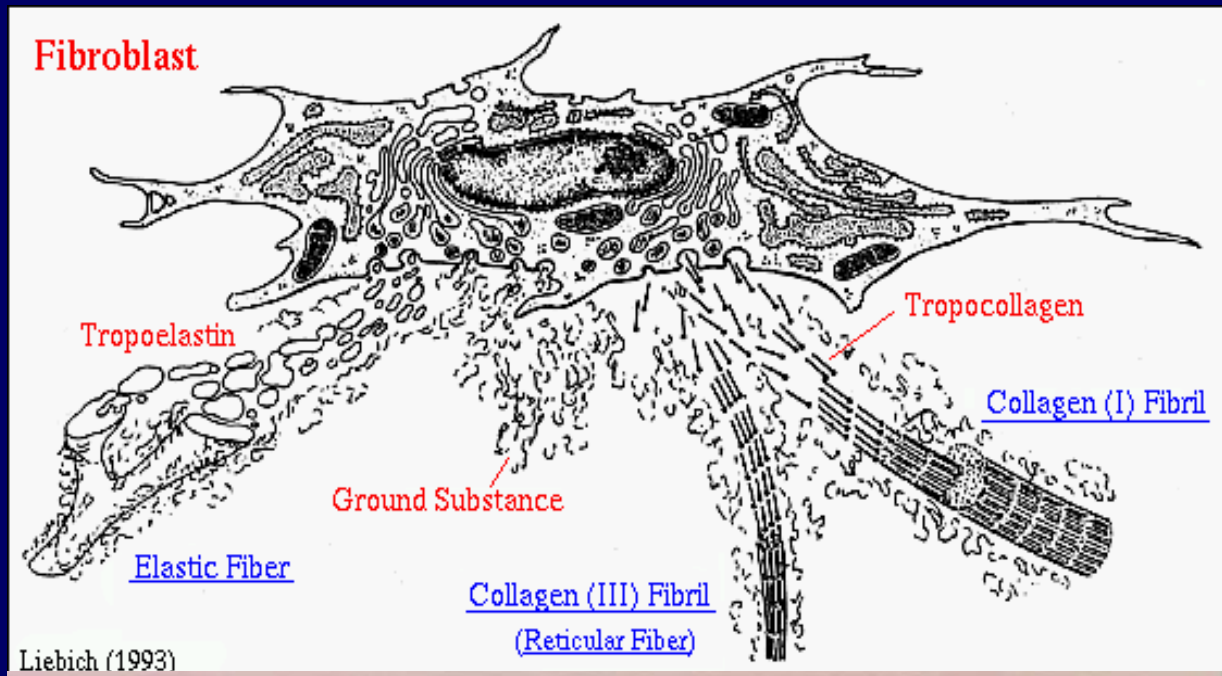
- Macrophage is derived from blood monocyte which migrate to CT and develop into these phagocytic cells.
- It is large irregular cell with eccentric oval or kidney shaped nucleus.
- It can be stained with vital stain as trypan blue.
- Phagocytosis and digestion of foreign materials
- and it plays important role in the defense mechanism of the tissues.

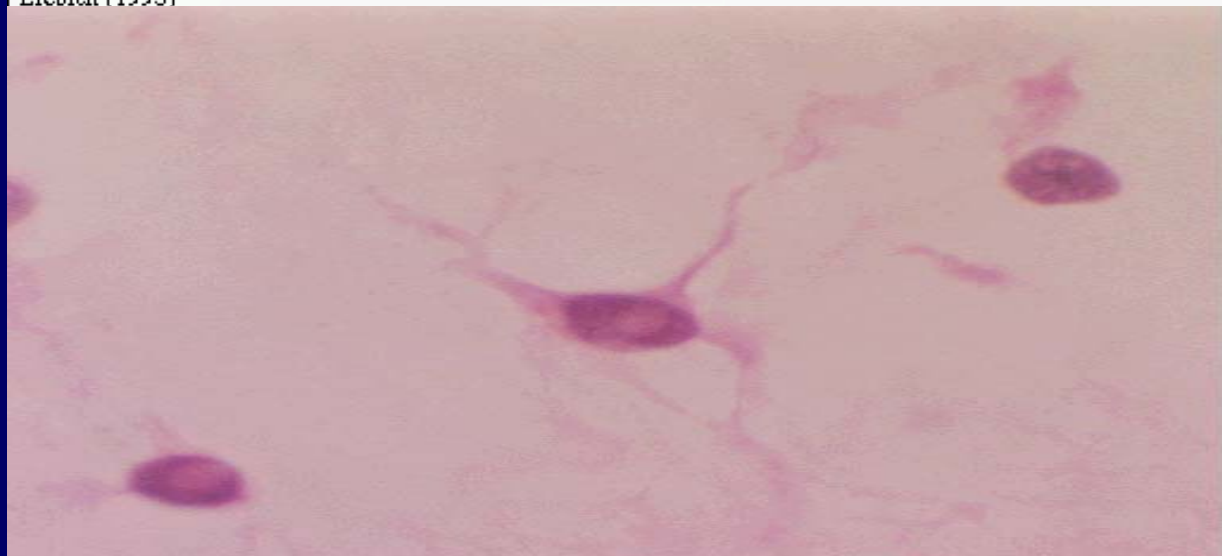


# Fibroblasts and Fibrocytes

- Fibroblasts are branched cells with long processes, with basophilic cytoplasm and large oval pale stained nucleus.
- It produces components of CT matrix and collagenic, elastic and reticular fibers.
- The fibrocyte is the old or inactive fibroblasts.
- They are spindle in shape with dark elongated nucleus and less basophilic cytoplasm.

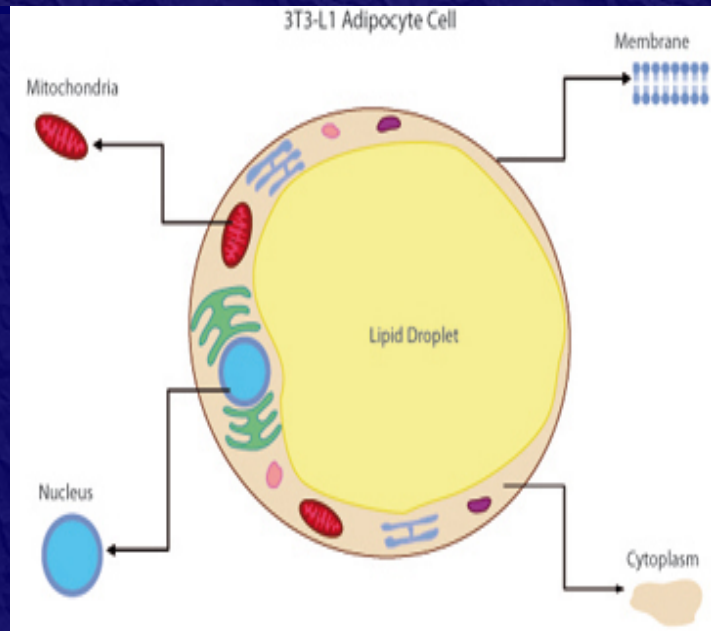


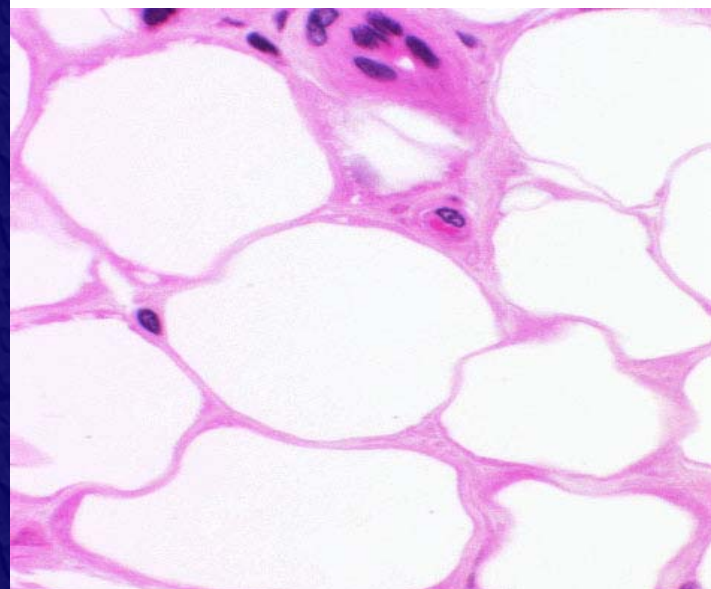



# Free, wandering or visitant cells of connective tissue

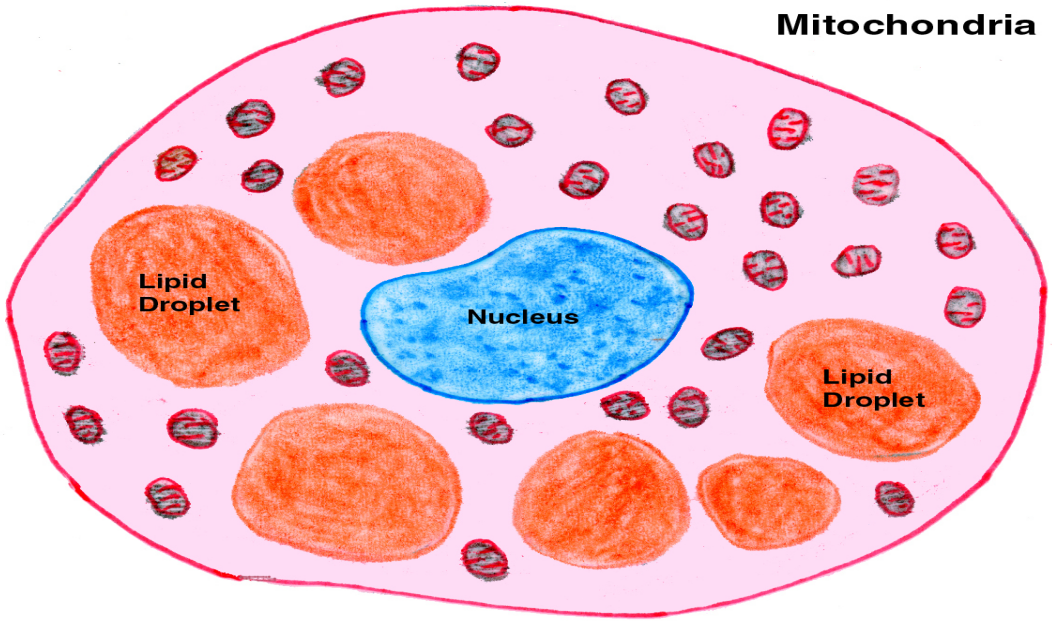
# Adipose cells (Adipocytes)

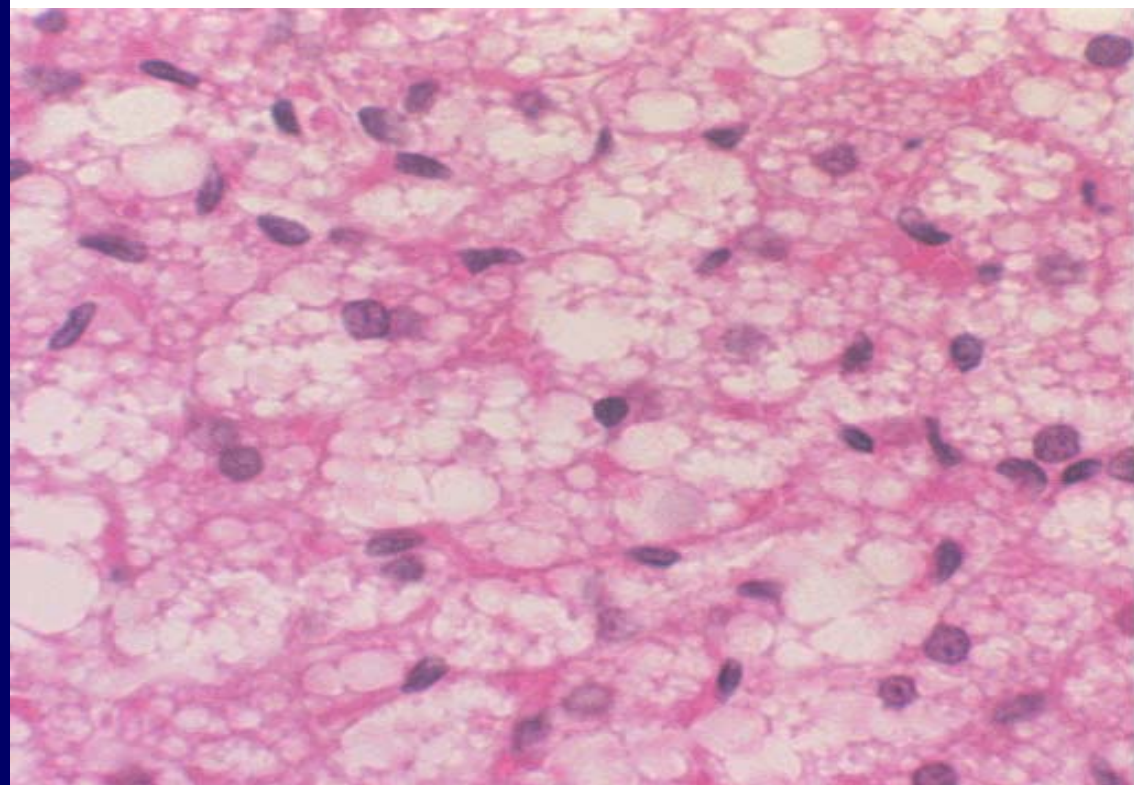
- The white adipocytes are polygonal or spherical in shape.
- The cell occupied by a single large lipid droplet surrounded by a thin rim of cytoplasm.
- The nuclei are flattened and displaced to on side.
- In H&E sections, fat is dissolved during the dehydration and clearing processes.
- Fat cells appear as large clear spaces surrounded by thin layer of cytoplasm giving the cells *a* signet ring appearance.



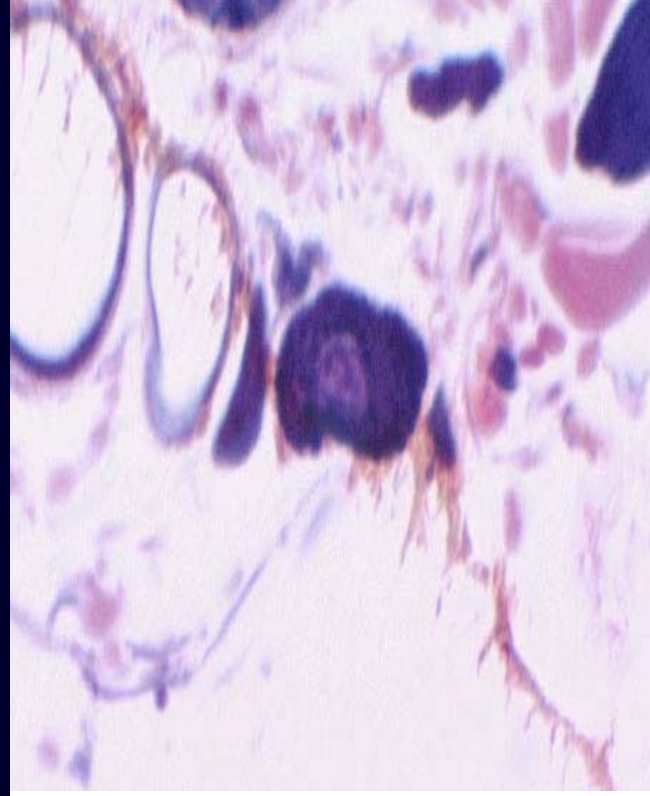
- The brown adipocytes
- Smaller than white one.
- The nuclei are oval, eccentricity located.
- Surrounded by a significant amount of strongly acidophilic cytoplasm.
- Multiple small lipid droplets.

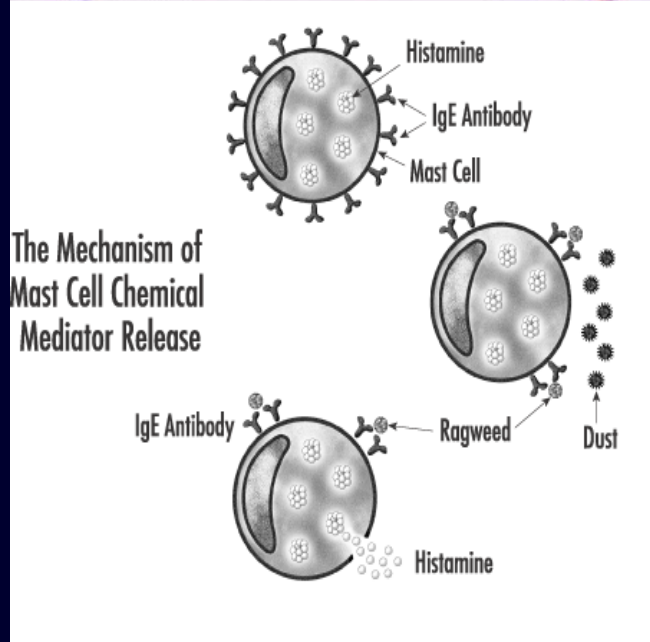


# Mast cells

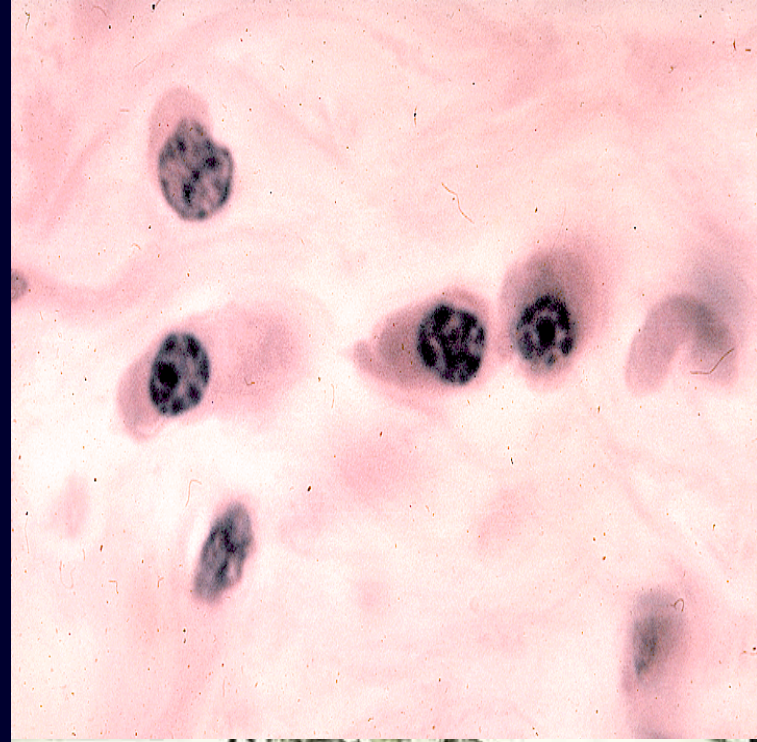
- Mast cells are found in the loose connective tissues specially that of the skin and intestine, particularly in association with blood vessels.
- They are large polymorphic, spherical or ovoid cells with spherical centrally located nuclei.
- The nuclei are completely obscured by numerous large metachromatic granules (they take a different color than that of the dye used. (e.g., when stained with toluidine blue they take red color). This property is known as metachromasia.
- The surface of the mast cell contains specific receptors for immunoglobulin E (IgE).
- In allergic and anaphylactic reactions, the interaction of foreign antigen with the antibody bound to the surface of mast cells induces the release of the chemical mediators stored in mast cell granules that promote the immediate hypersensitivity reaction or anaphylaxis.
- The granules of the mast cells contain histamine, heparin, ECF-A (eosinophil chemotactic factor for anaphylaxis) and serotonin.

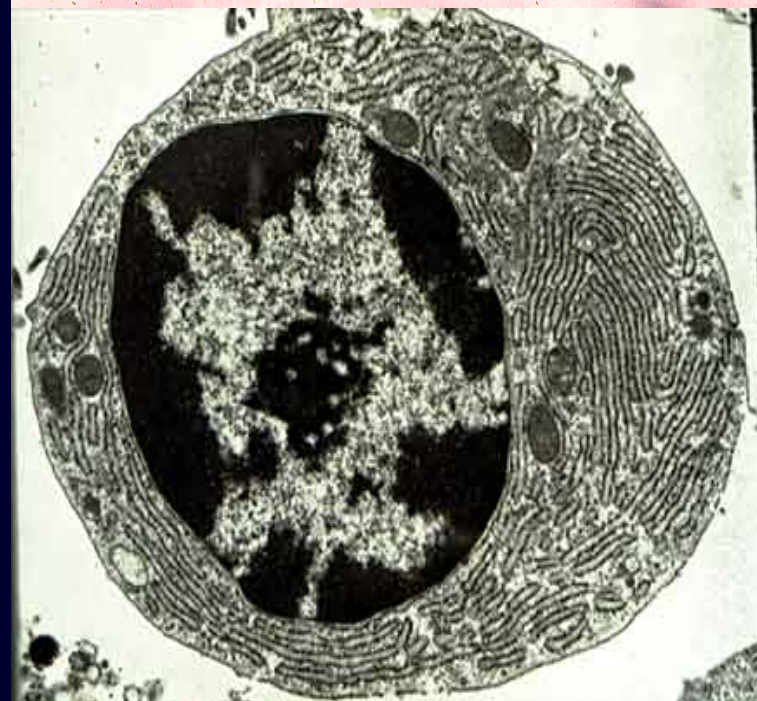




# Plasma cells

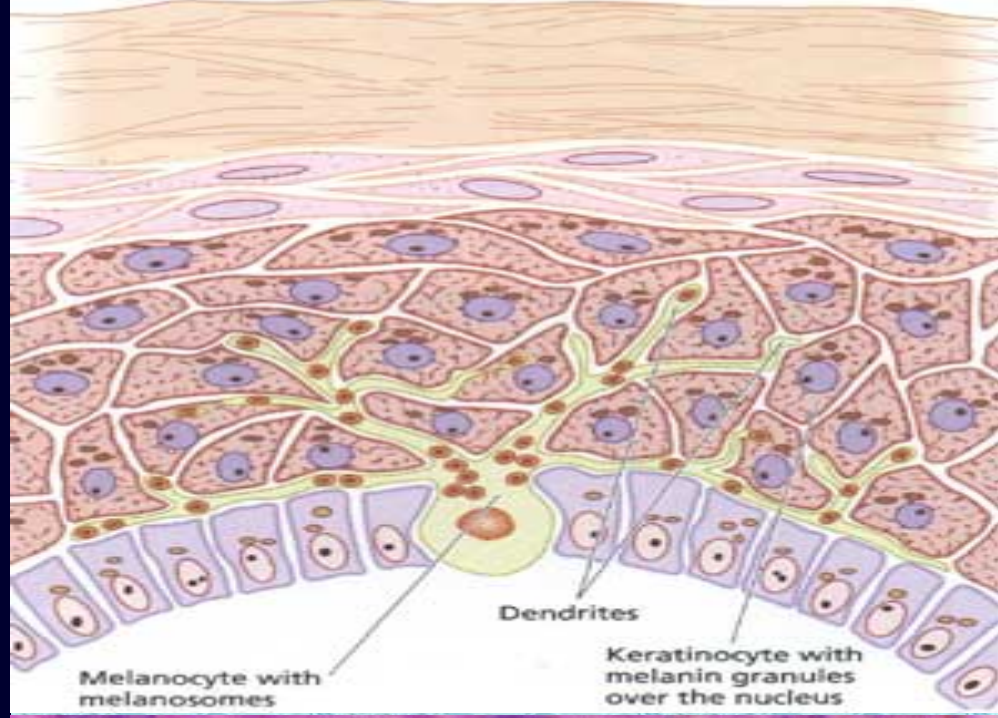
- Plasma cells are **spherical, oval or pear-shaped cells** with spherical, eccentric nucleus.
- The nuclear chromatin is condensed peripherally giving the nucleus a characteristic "**cartwheel**" appearance.
- The cytoplasm is **strongly basophilic** with a prominent negative Golgi image.
- **Production of antibodies**.

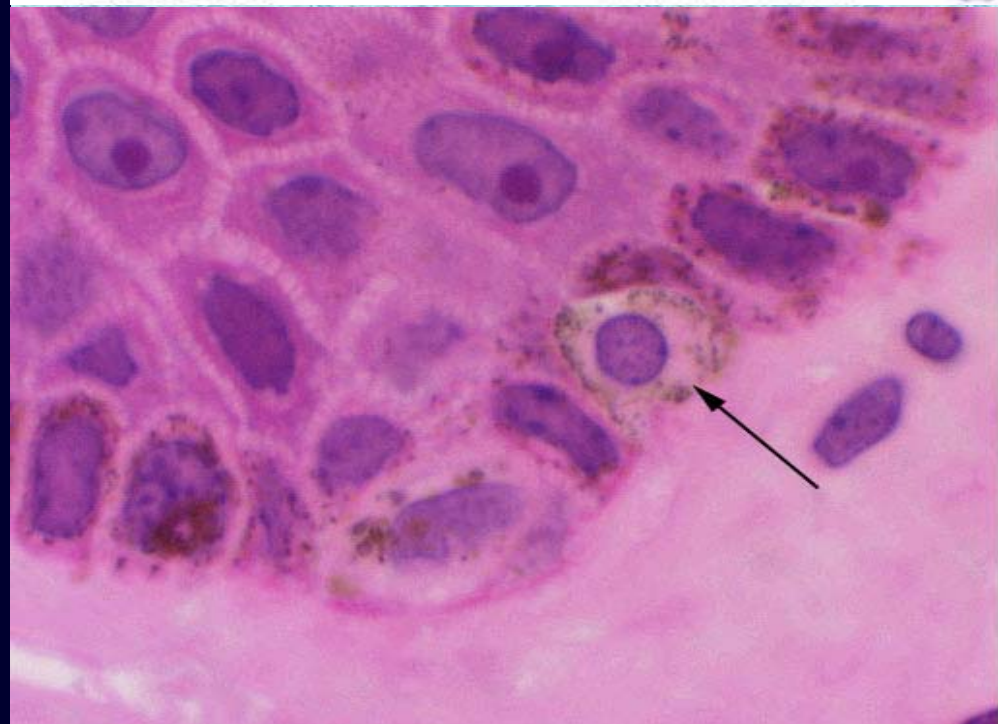




# Melanocytes

- They are large pigmented cells with numerous long branching processes.
- **The nucleus is spherical and central.**
- They carry melanin pigments.
- They occur in epidermis and iris.



# Blood leucocytes

- White blood cells migrate to CT where they perform their functions.
- They include:
- Lymphocytes
- Monocytes
- Granulocytes (especially eosinophils and neutrophils).

# Connective tissue fibers

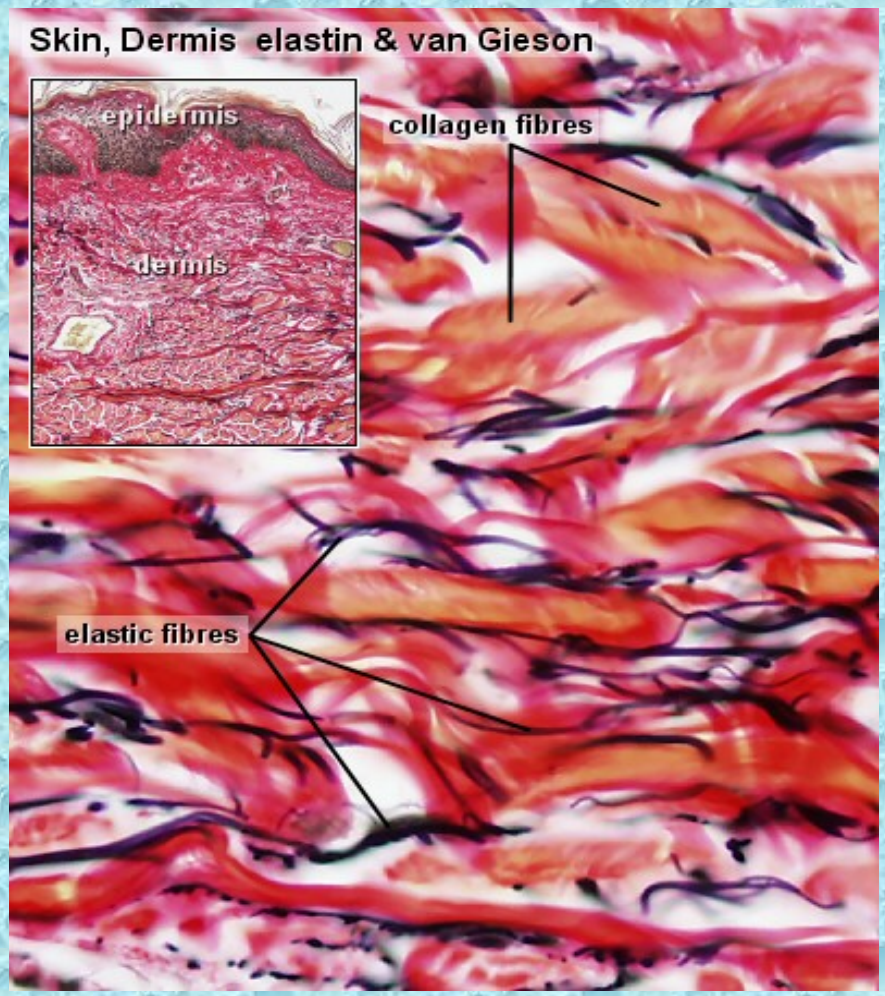
- White collagenous fibers
- Yellow elastic fibers.
- Reticular fibers.

# White collagenous fibers

- They are the most numerous fibers of CT.
- When present in great amount, they give the tissue a white color (e.g. tendon).
- They are inelastic, but highly resistant to stretch.
- They are formed of protein called collagen.
- They are wavy and present in bundles.
- They stain red with eosin.

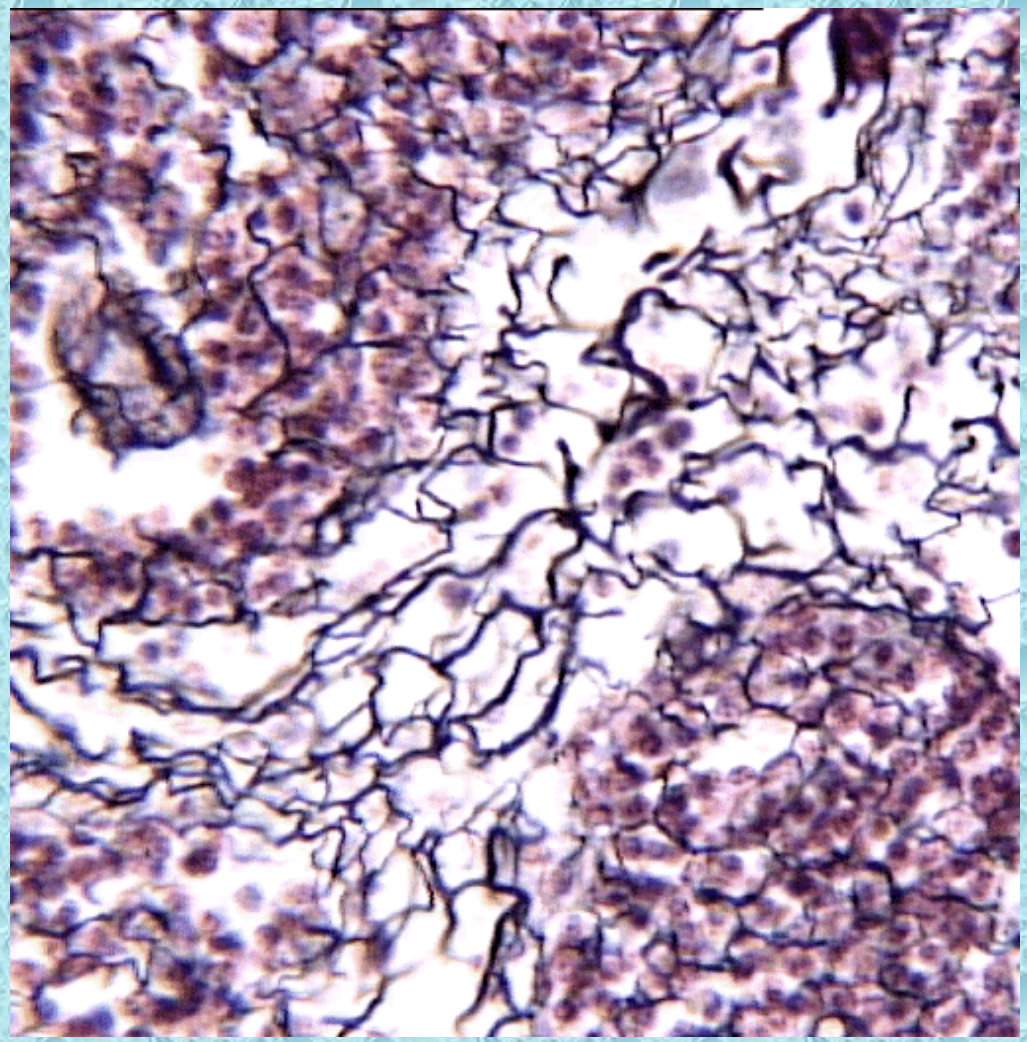
# Yellow elastic fibers

- Elastic fibers are fine, usually present singly and can branch and anastomose.
- When present in large amounts, they give the tissue a yellow color.
- They are soft, flexible and elastic.
- They are formed of a protein called elastin.
- They stain brown with orcein.



# Reticular fibers

- They are very fine fibers, branch and reunite to form a network.
- They are composed of especial type of collagen protein.
- They stain black with silver.



# Ground substance

- It is an amorphous substance, present in-between the CT cells.
- The CT fibers are embedded in it.
- It is composed of glycoproteins and glycosaminoglycans.
- It is secreted by fibroblasts.
- It can be stained metachromatically with toluidine blue.
- It binds CT cells and fibers together.

# Types of connective tissue

I. CT proper

II. Supporting CT

# Types of connective tissue

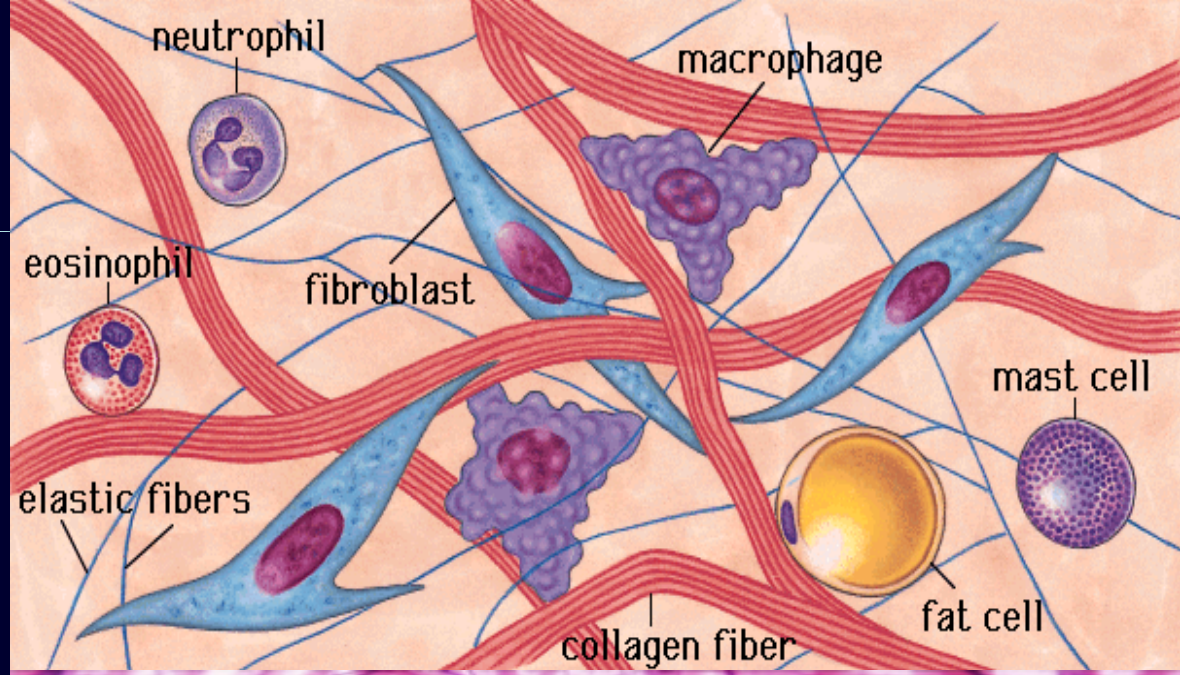
I. CT proper
- -Loose CT
- -Dense CT

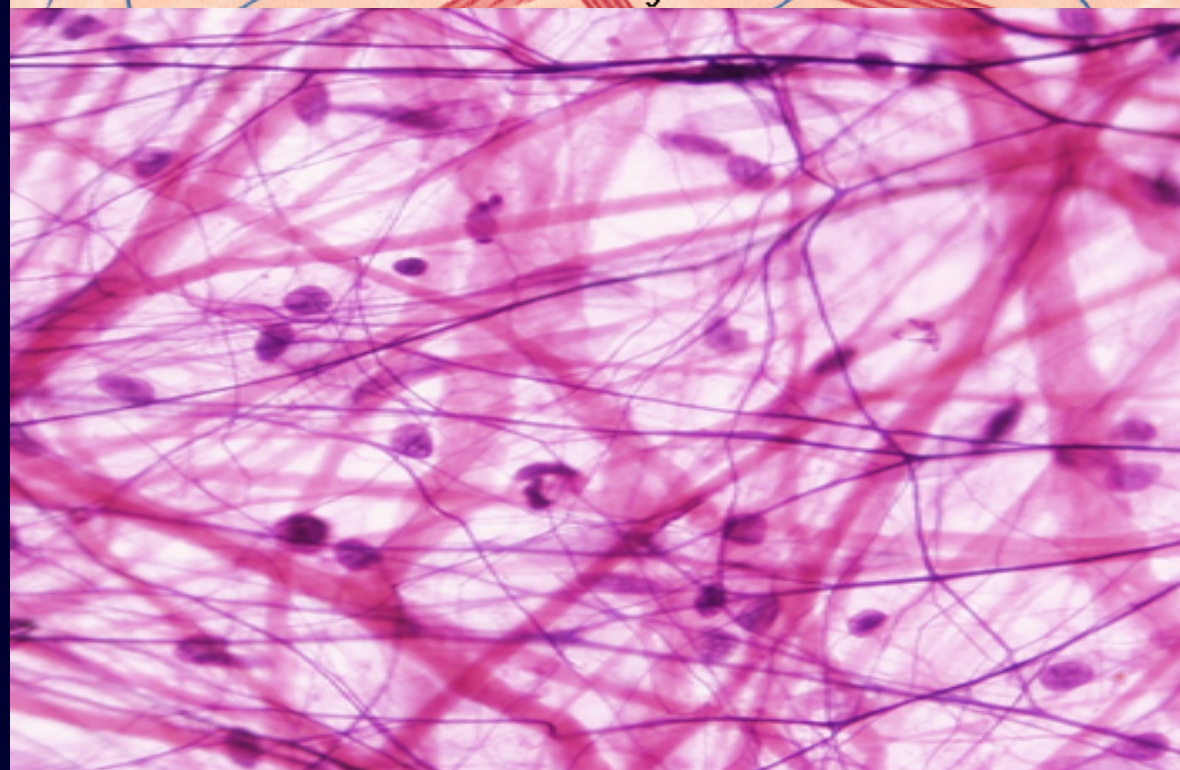
II. CT with special properties
- -Yellow elastic tissue
- -Reticular CT
- -Mucoid CT
- -Adipose tissue

III. Supporting CT
- -Cartilage
- -Bone

# 1. Loose CT

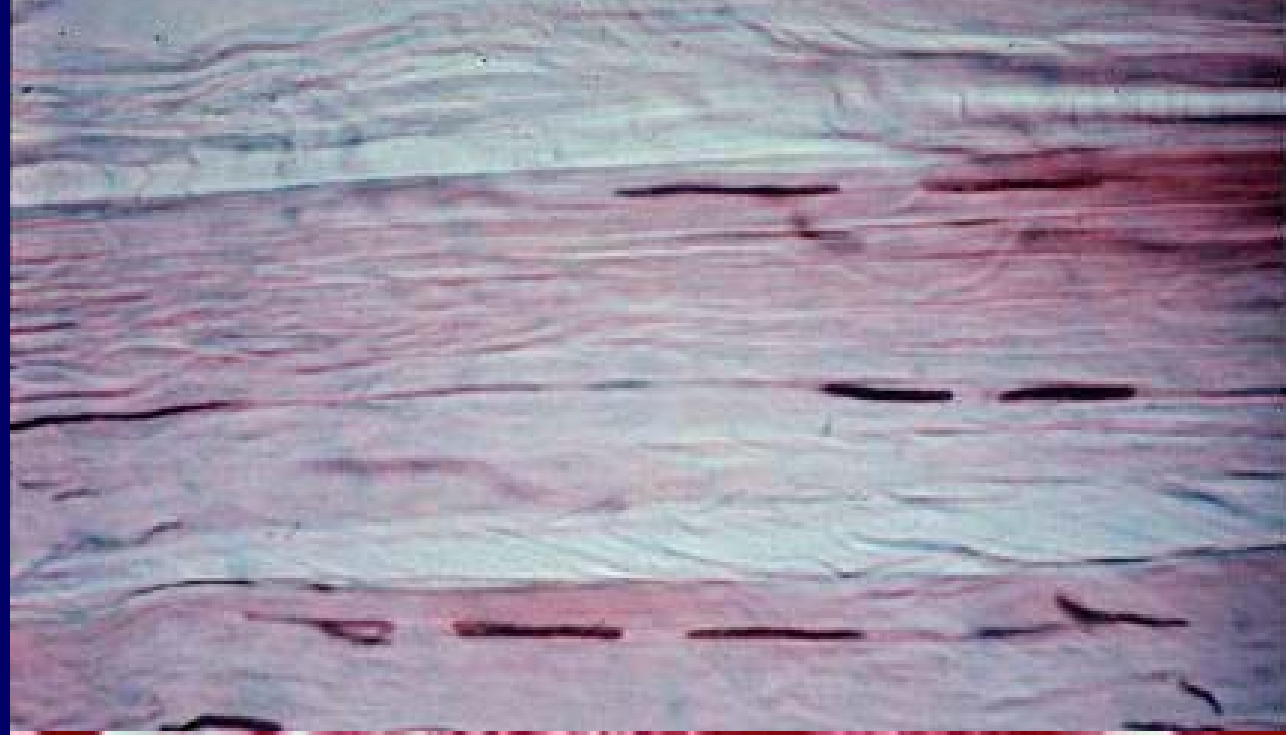
- It is delicate, flexible and contains all constituents of CT (cells, fibers and ground substances.
- Sites: between muscles, in dermis, in hypodermis, and around blood and lymph vessels.



# 2. Dense CT

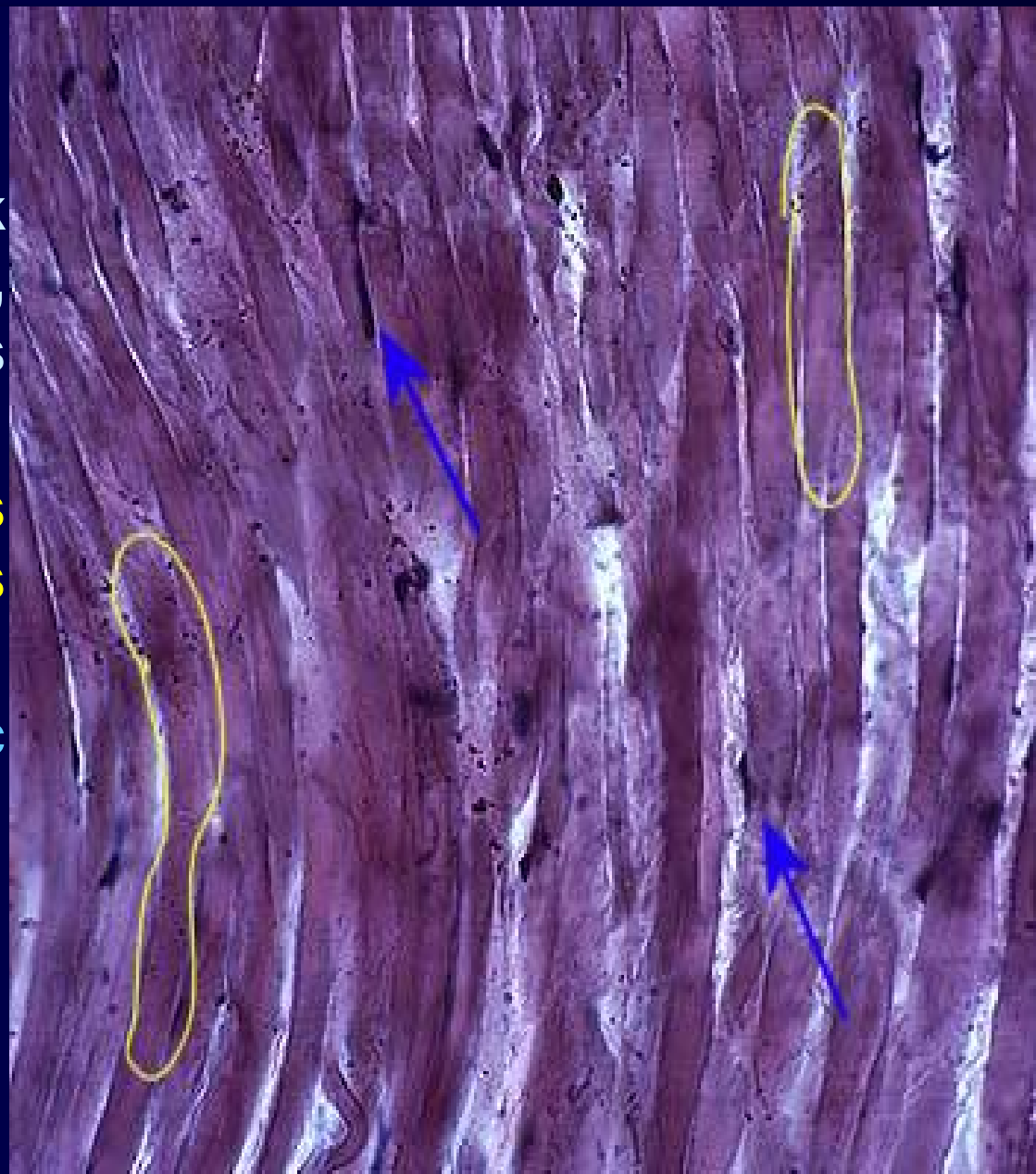
- There is abundance of collagen fibers separated by fibroblasts. It may be:
- 1. Dense regular CT: The collagen bundles are arranged in regular pattern. Example tendon.
- Dense irregular CT: the collagen bundles run in different directions. Example in dermis of the skin.



# II. CT with special properties

## 1. Yellow Elastic Tissue

- Formed of thick parallel, elastic fibers, thin collagen fibers and fibroblasts.
- On gross examination, it is yellow in color.
- It is present in elastic ligaments.

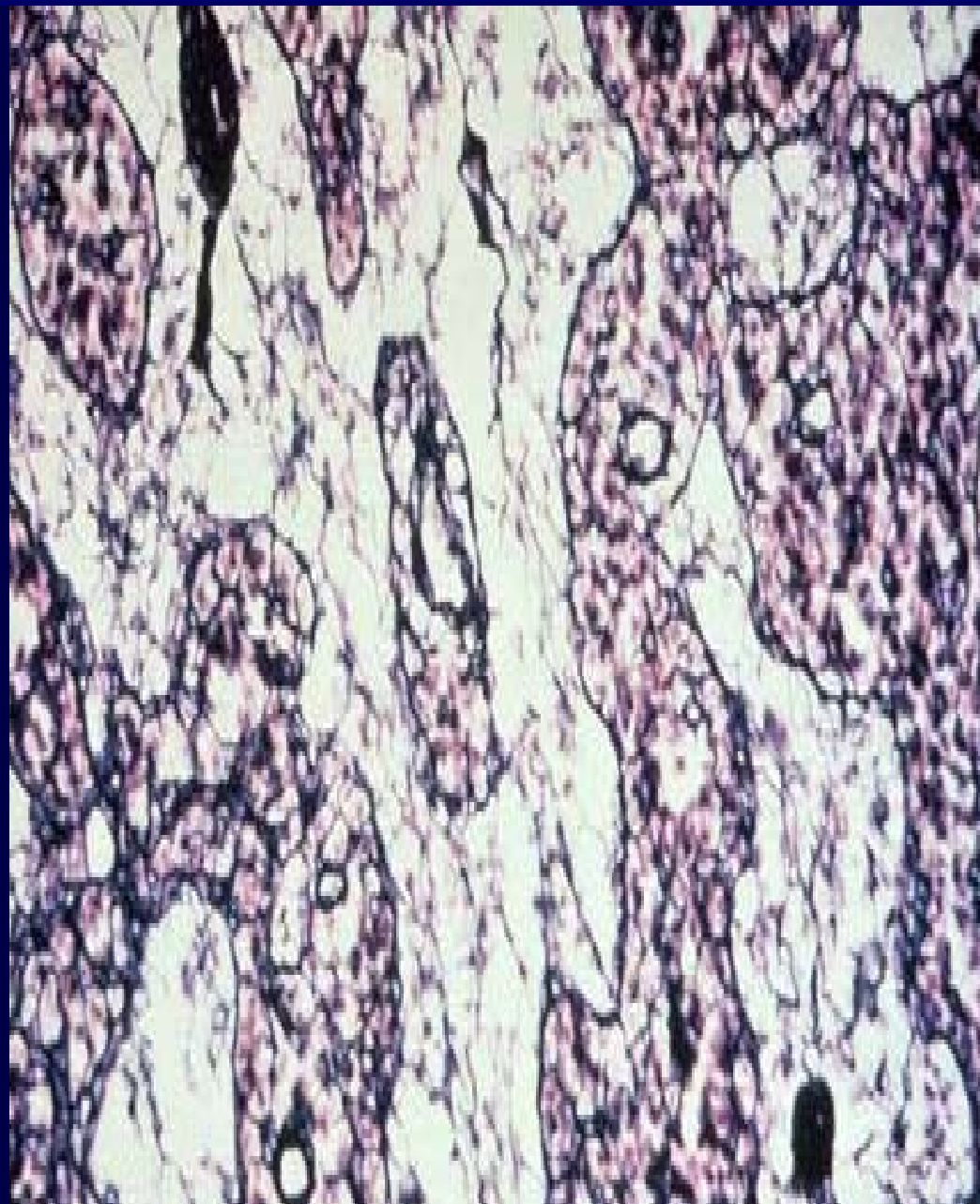


# II. CT with special properties

## 2. Reticular tissue

- Formed of a network of reticular cells and specialized fibroblasts called reticular cells.

- It is present in lymphoid organs and bone marrow.

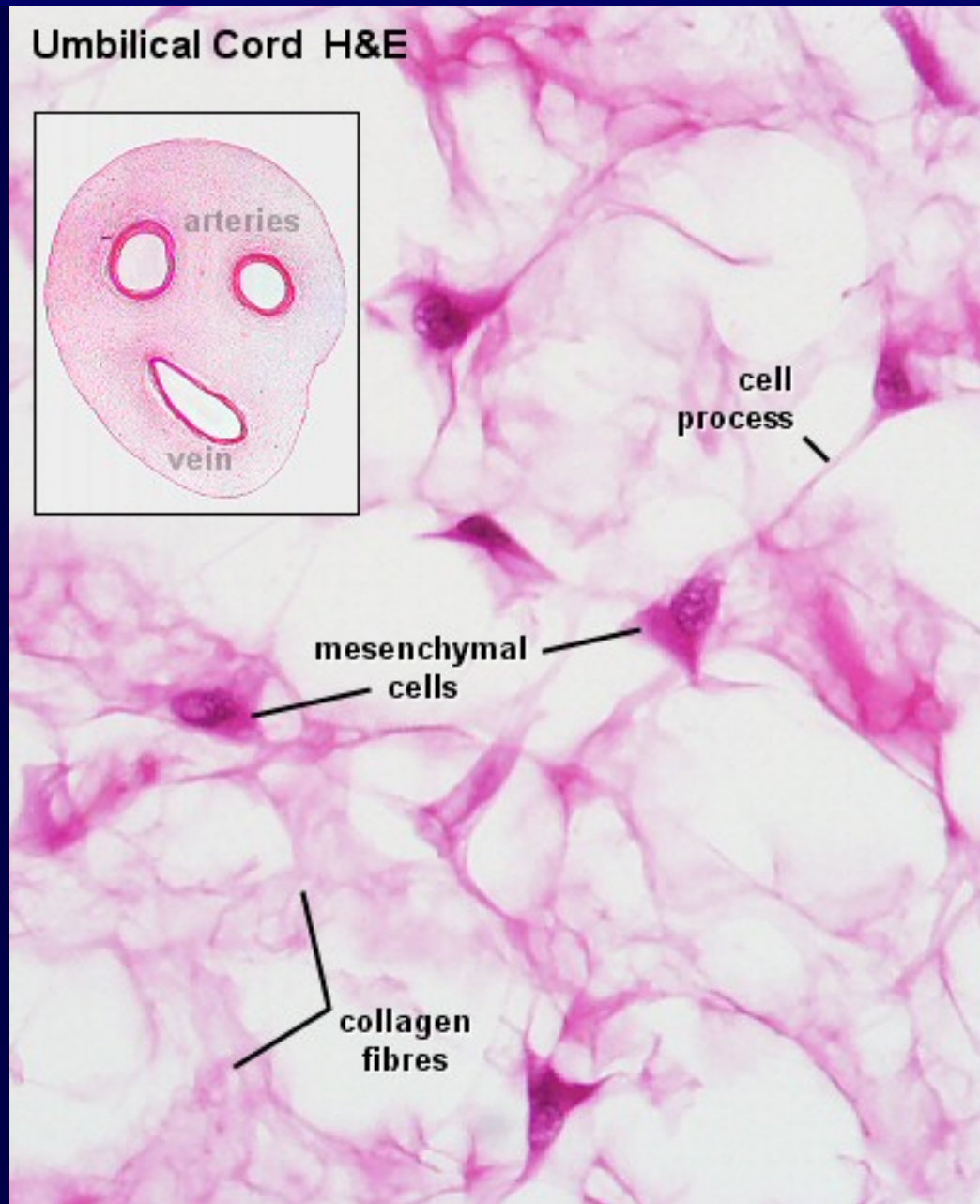


# CT with special properties

### 3. Mucoid CT

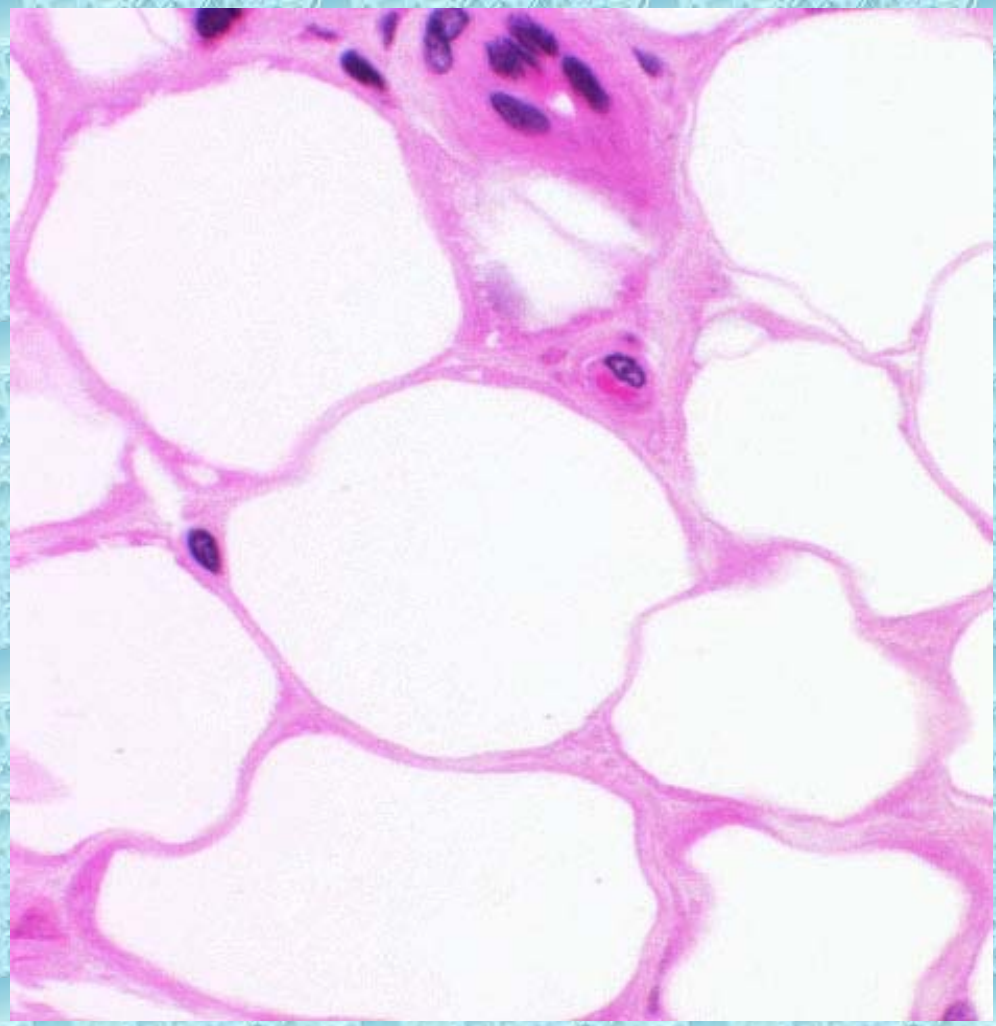
- Formed of abundance of jelly-like ground substance, collagen fibers and fibroblasts.

- It is present in umbilical cord and pulp of the teeth.



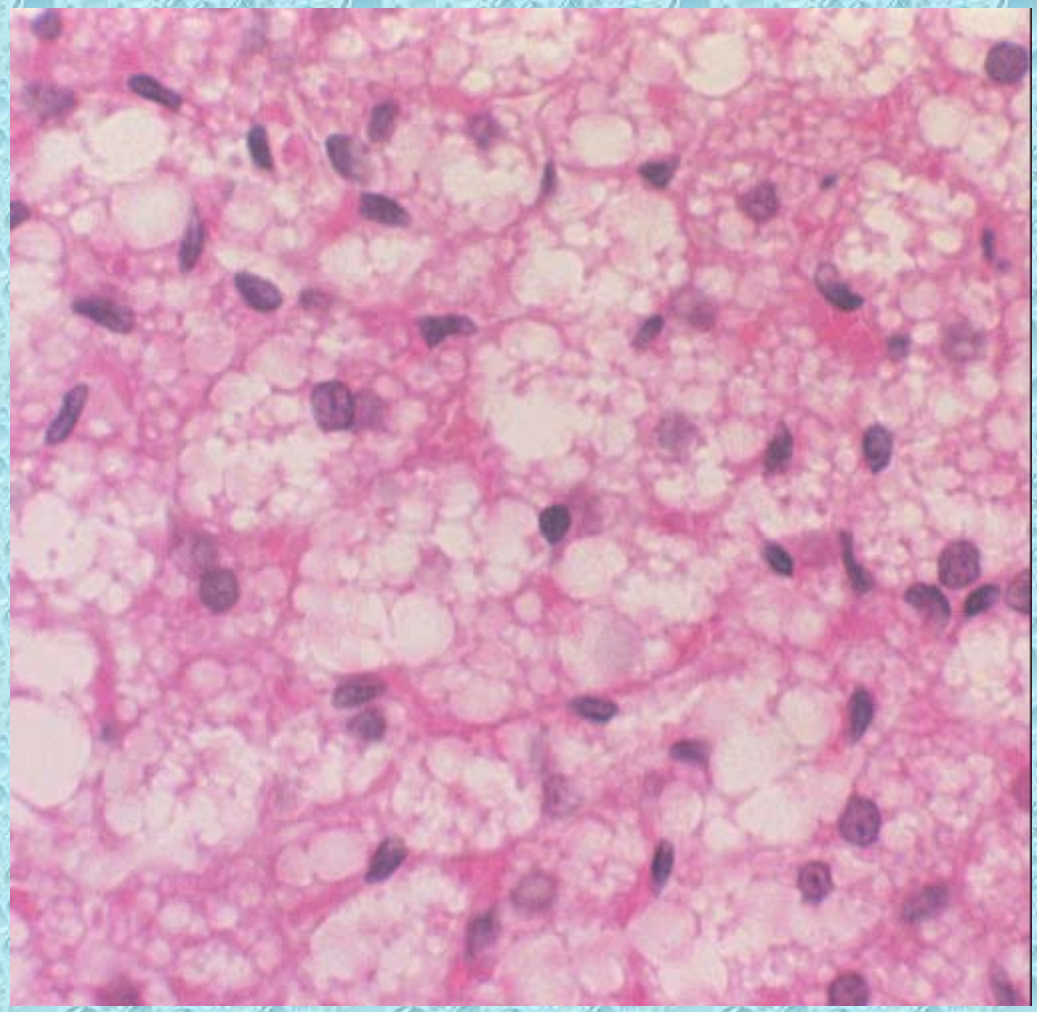
# White adipose tissue

- It is composed of cells that contain one large central droplet of fat (unilocular fat cells) and it represents most of the adipose tissue in humans.
- The unilocular fat cell is large and spherical.
- Their cytoplasm forms a thin ring surrounding the single fat droplet.
- The nucleus is flat and eccentric.



# Brown adipose tissue

- It is composed of cells that contain numerous lipid droplets (multilocular fat cells) and is present in few sites in the human.
- The multilocular adipose cell is polygonal, smaller than the unilocular fat cell and contains many lipid droplets of different sizes.
- The nucleus is spherical and central.



# III. Adult supportive tissues
## Cartilage and Bone

- The cartilage is a semi-rigid, flexible, avascular form of connective tissue designed to perform a supportive function.
- It is composed of cells and matrix (fibers and amorphous ground substance).

# Types of cartilage

I. Hyaline cartilage

II. Elastic cartilage

III. Fibrocartilage

# Hyaline cartilage

The hyaline cartilage consists of:

**Perichondrium**

- It is a vascular connective tissue capsule that invests the external surface of cartilage.
- It is composed of two layers: a) Outer fibrous layer, composed of dense irregular connective tissue containing blood vessels and nerves.

b) Inner cellular or chondrogenic layer made up of chondroblasts that are actively involved in production of matrix during cartilage growth and regeneration.

**3. Matrix**

- The hyaline cartilage matrix is an amorphous gel consists mainly of sulfated glycosaminoglycans that are strongly basophilic, PAS positive and metachromatic.
- It contains collagen fibrils.

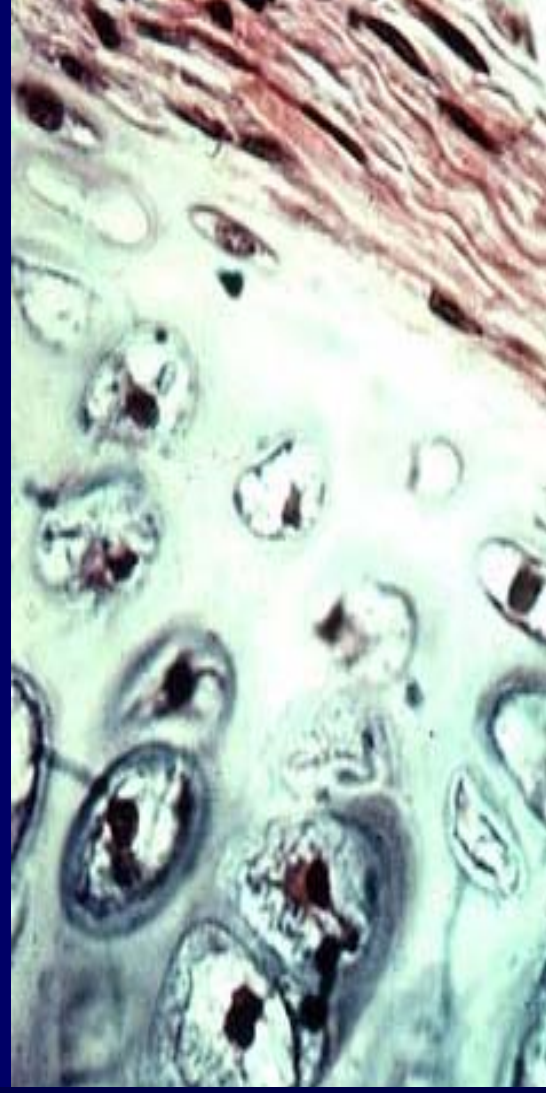
**2. Cartilage cells**

*a.* **Chondroblasts (cartilage forming cells)**

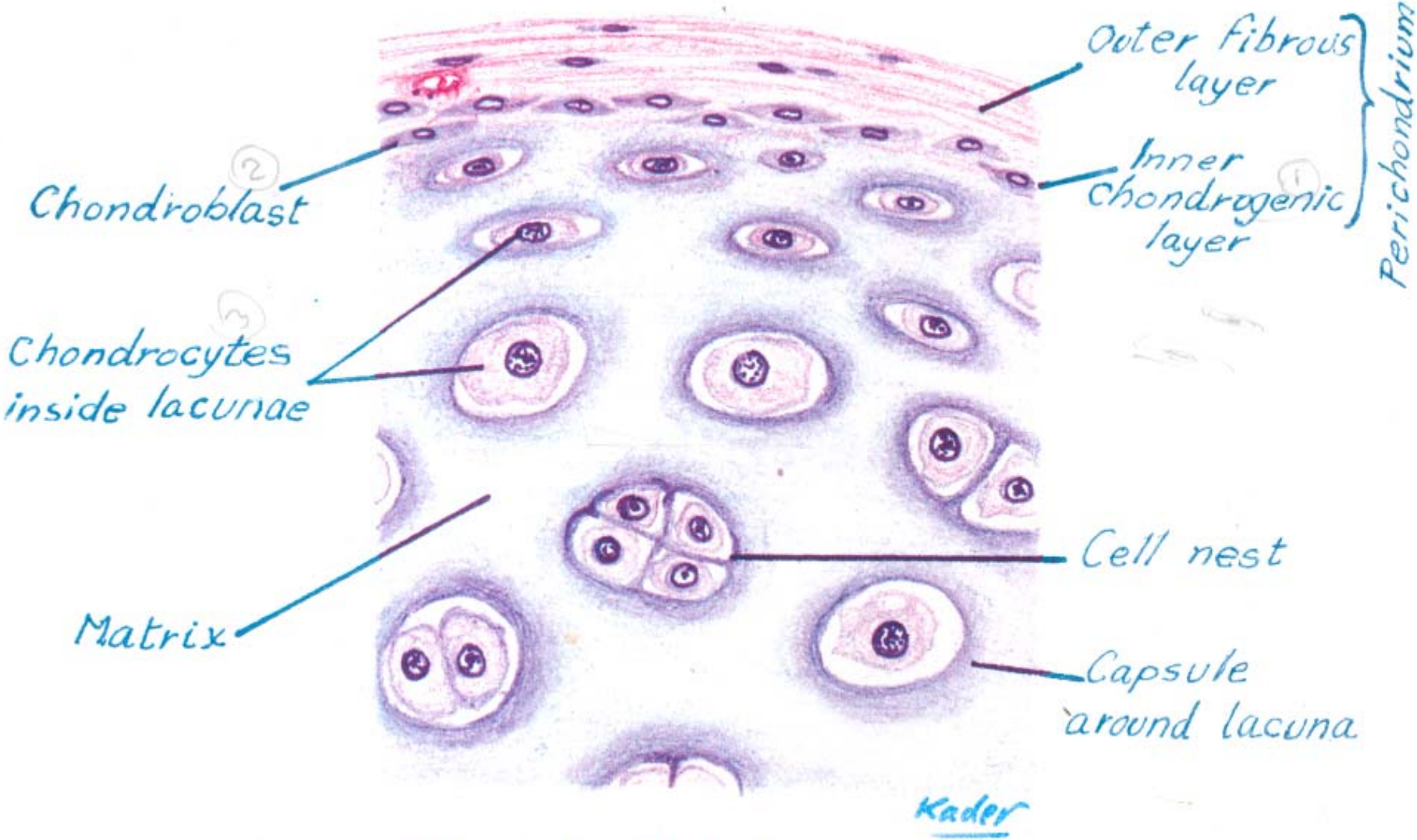
- Found mainly in the inner chondrogenic layer of the perichondrium.
- Oval or spindle-shaped cells with oval pale nuclei.
- The cytoplasm is basophilic rich in ribosomes, rER and Golgi saccules.
- They secrete matrix around themselves and become deeply buried in the cartilage matrix where they are called chondrocytes.

**b. Chondrocytes (mature cartilage cells)**

- They are located in tiny spaces within the cartilage matrix known as lacunae.
- Some lacunae contain only one cell; others contain two, four, or sometimes six cells.
- These multicellular lacunae are called cell nests or isogenous groups because each cluster is the progeny of one cell.



•The hyaline cartilage occurs in many places such as articular surface, fetal skeleton, nasal septum, larynx, trachea and bronchi.




(Costal Cartilage, T.S.)

# HYALINE CARTILAGE

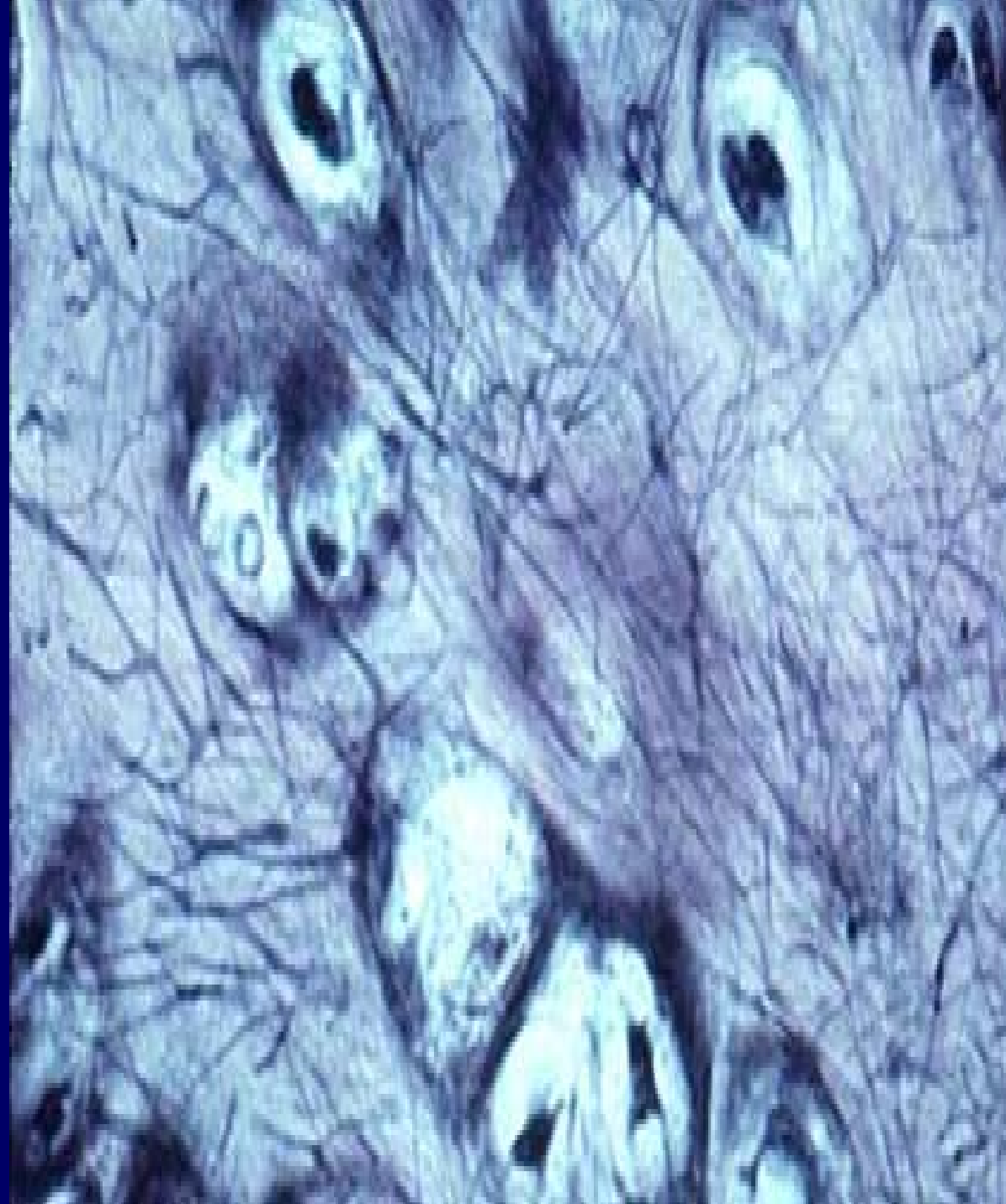
# Elastic cartilage

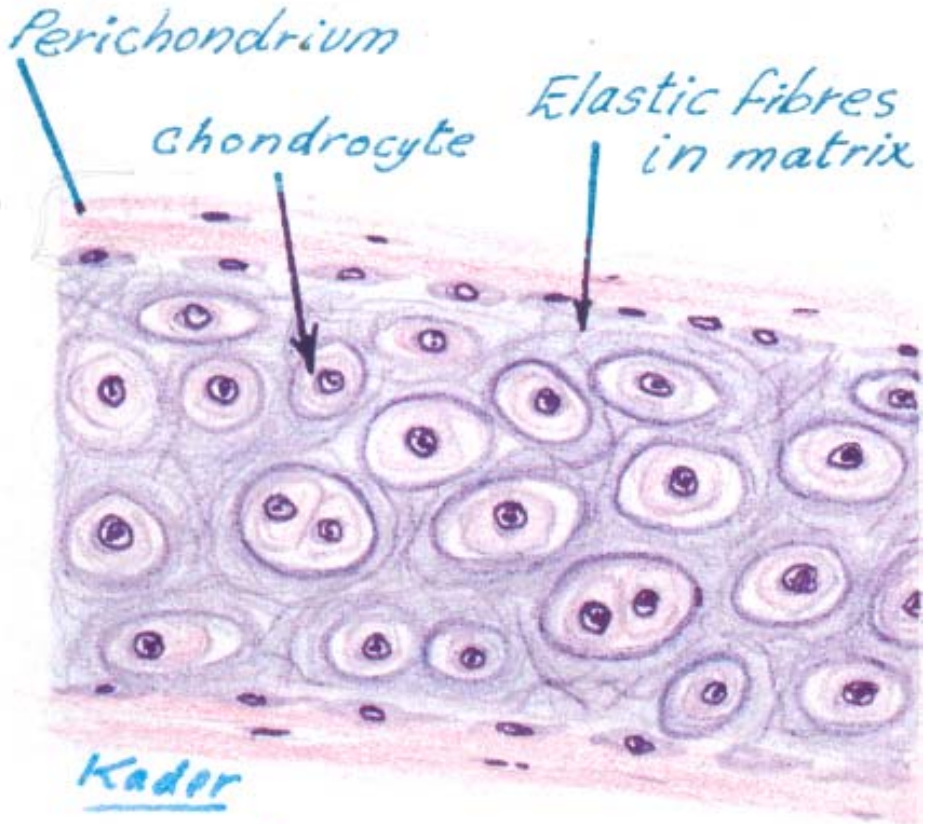
- The histological structure of the elastic cartilage is similar to that of the hyaline cartilage except:

1) cell nests are few.

2) The matrices contain a dense network of elastic fibers that are visible in H&E sections.

- The elastic cartilage occurs in the external ear and external auditory canal, the epiglottis, corniculate and cuneiform cartilage of the larynx.



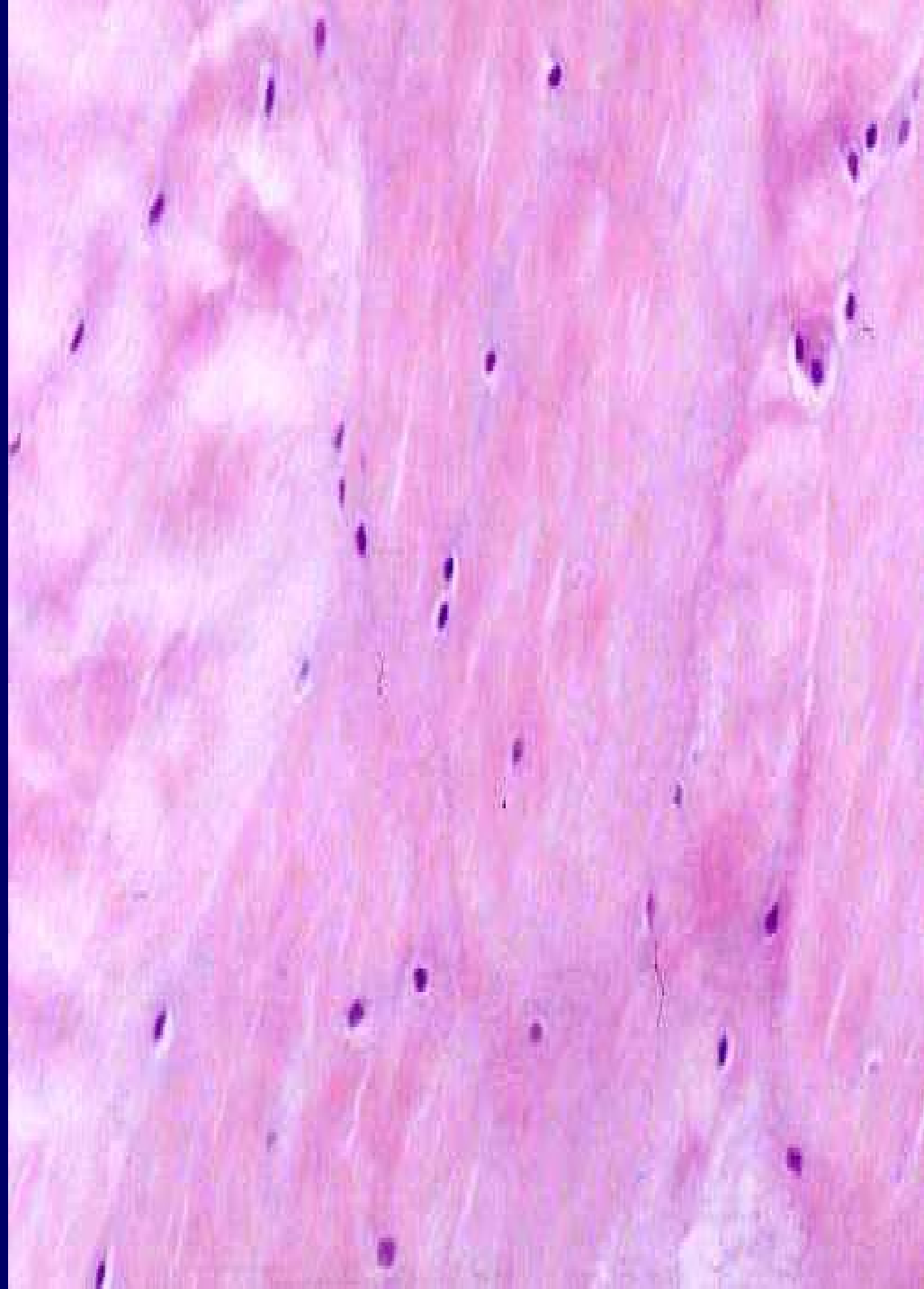


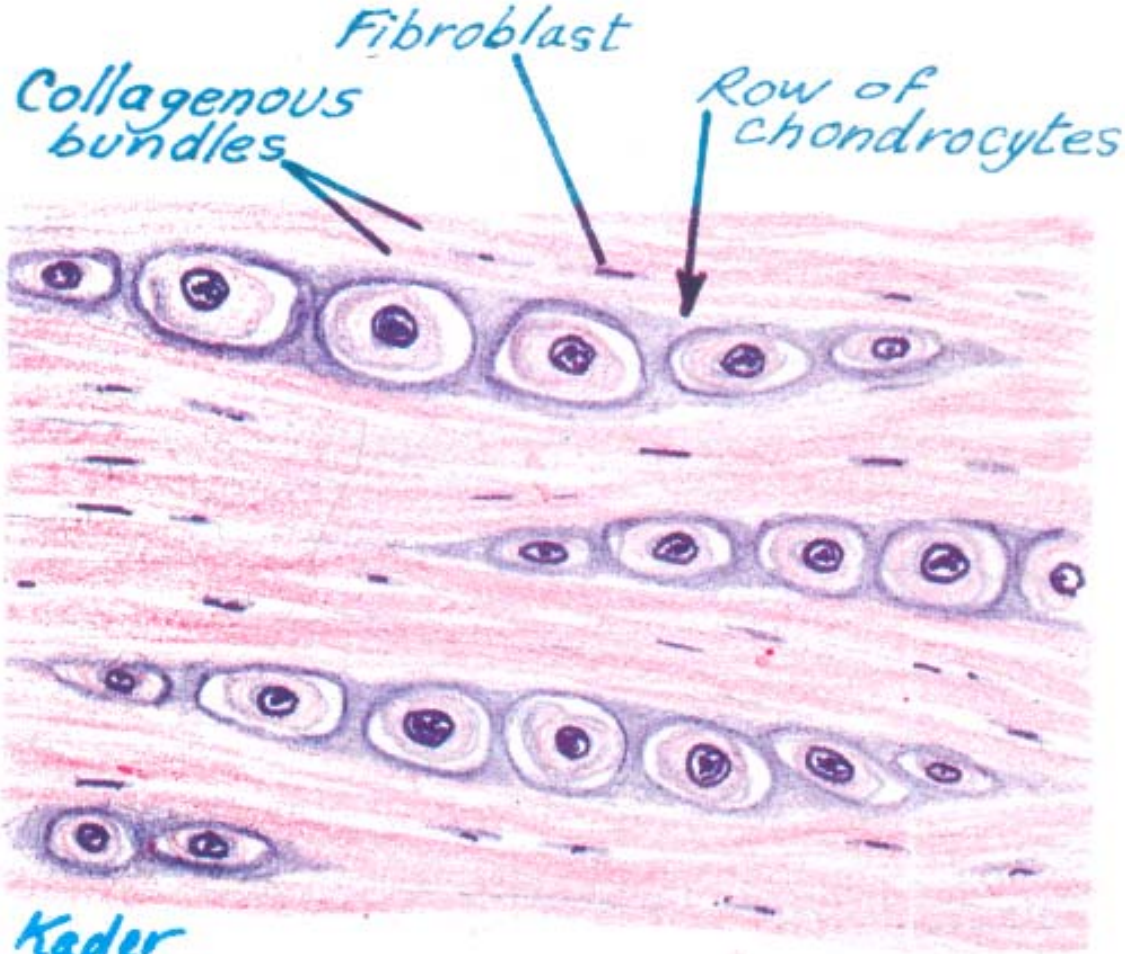

(Ear Pinna)

# YELLOW ELASTIC FIBRO-CARTILAGE

## Fibrocartilage

- It is a transitional form between hyaline cartilage and dense regular connective tissue.
- It consists of regular parallel bundles of collagen fibers separated by encapsulated chondrocytes that occur singly, in pairs or sometimes form rows.
- The ground substances are little and only found around the chondrocytes.
- The fibrocartilage is found in the intervertebral discs, menisci of the stifle joint and at the attachment of tendons and bones.






(Intervertebral Disc)

# WHITE FIBRO-CARTILAGE

# Bone

- The bone is a specialized form of connective tissue in which the extracellular components are mineralized.

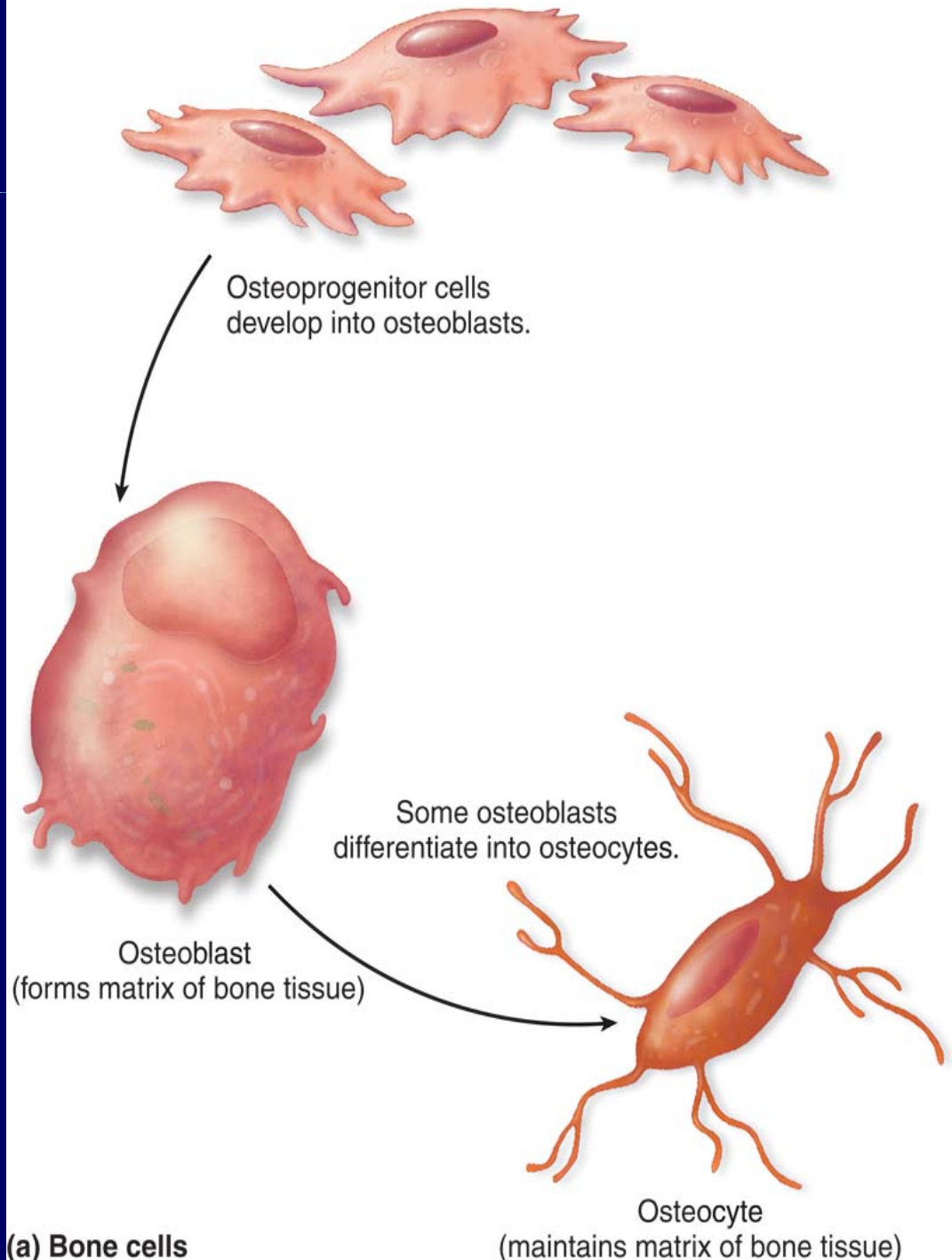
# Bone

- Cells (osteogenic cells, osteoblasts, osteocytes, osteoclasts).
- Matrix (a mixture of collagen fibers, ground substance and mineral salts).

# Bone Cells

## Osteogenic cells

- They are undifferentiated cells found in the endosteum, the inner osteogenic layer of the periosteum and the lining of the osteonal canal.
- The cells have pale-staining oval or elongated nuclei.
- Little acidophilic or faintly basophilic cytoplasm.
- They develop from the mesenchymal cells
- Capable in times of need (i.e. bone growth or fracture repair) to divide and transform into any of the other bone cells.



# Osteoblasts (bone forming cells)

- They are small, ovoid branching cells.
- During active bone formation, they are arranged in an epithelial-like layer of cuboidal cells connected to each other by short slender processes.
- The nucleus is oval, eccentric (at the cells end away from the bone surface), and euchromatic with prominent nucleolus.
- The cytoplasm is deeply basophilic and shows a negative Golgi image near the nucleus.
- Osteoblasts are responsible for the formation of organic components of bone matrix (osteoid tissue).
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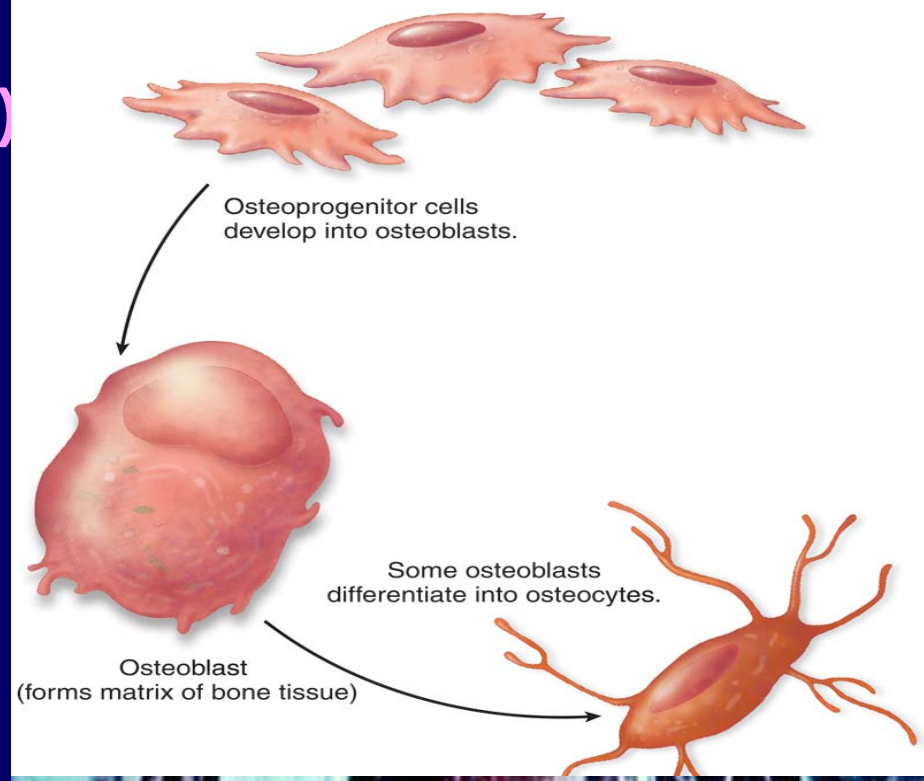
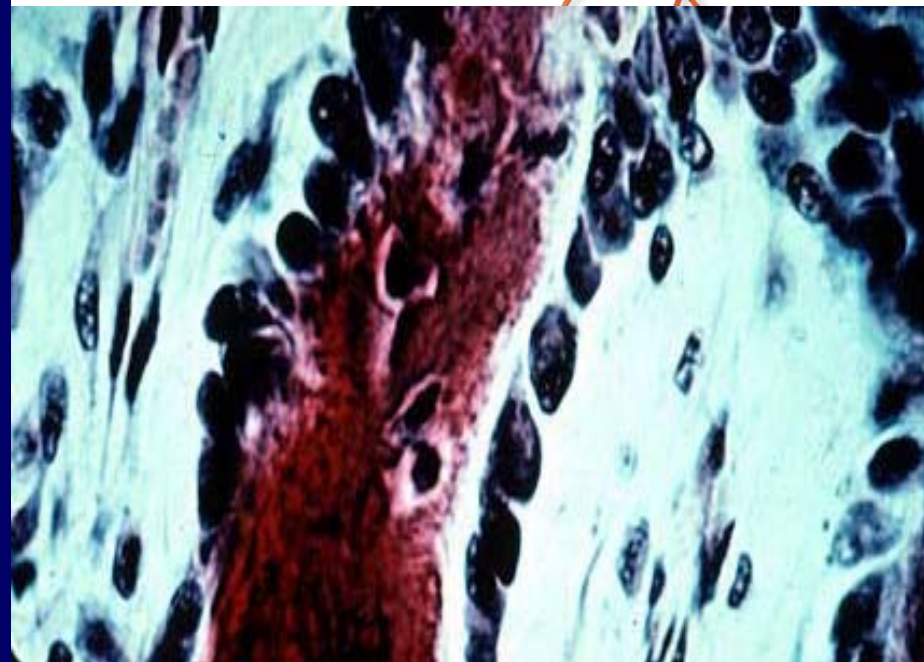
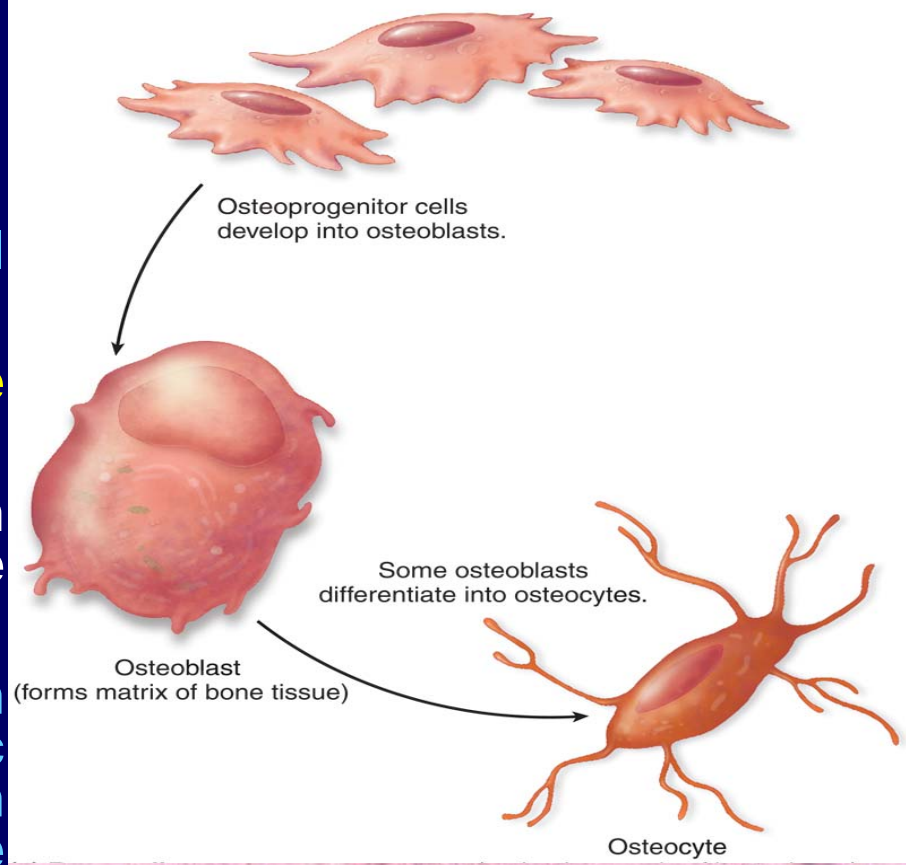
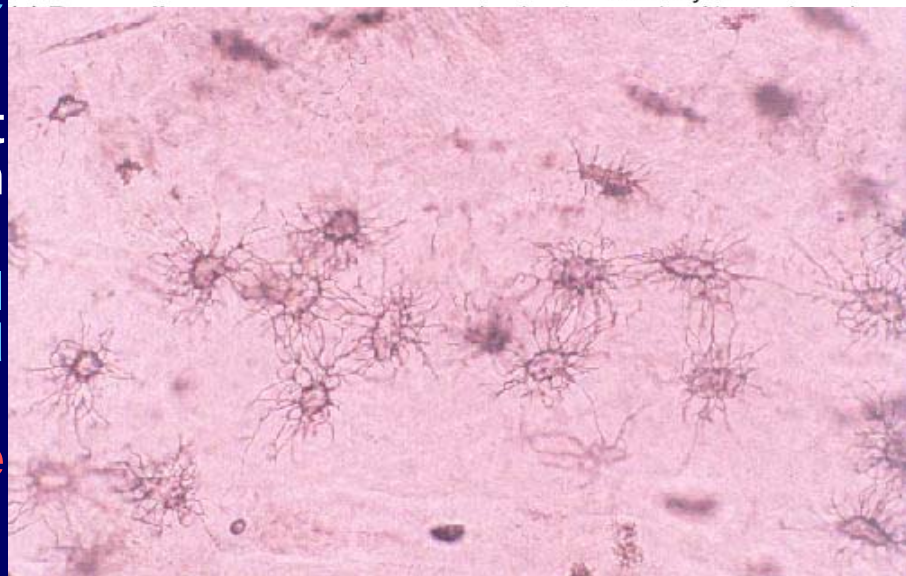


# Osteocytes (mature bone cells)

- The osteocytes are the principal cells of mature bone.
- They are located inside lacunae within calcified bone matrix.
- They are less active than osteoblasts and can not divide inside their lacunae.
- The cell body is flattened with numerous cytoplasmic processes that extend through tiny channels within the bone matrix called canaliculi.
- The processes of the adjacent cells are interconnected with each other via gap junctions.
- Permitting flow of ions and small molecules between blood and osteocytes.
- Preserve and maintain the integrity of the bone matrix.

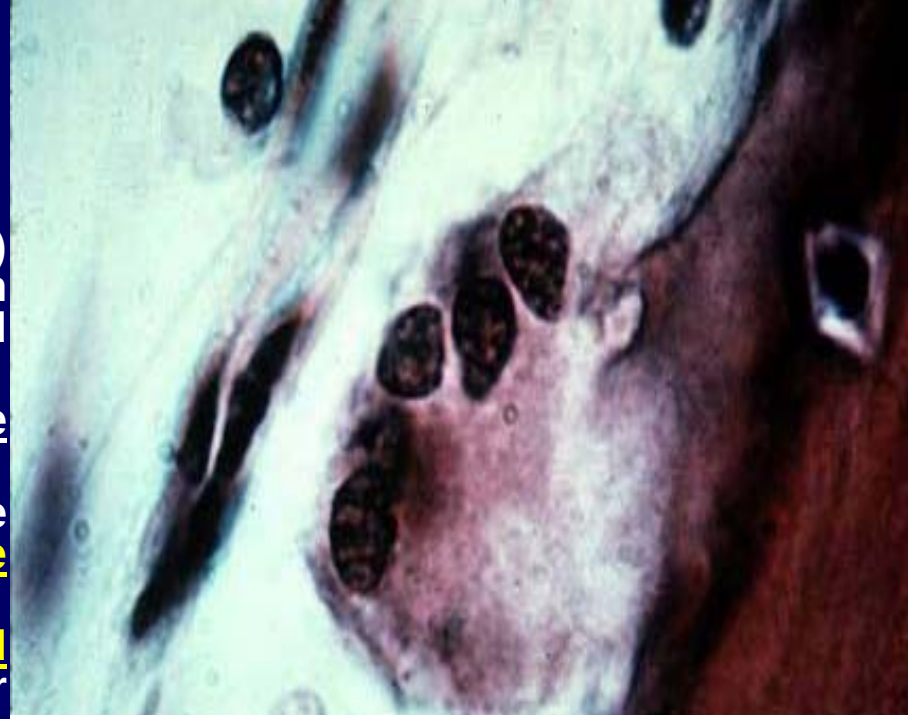


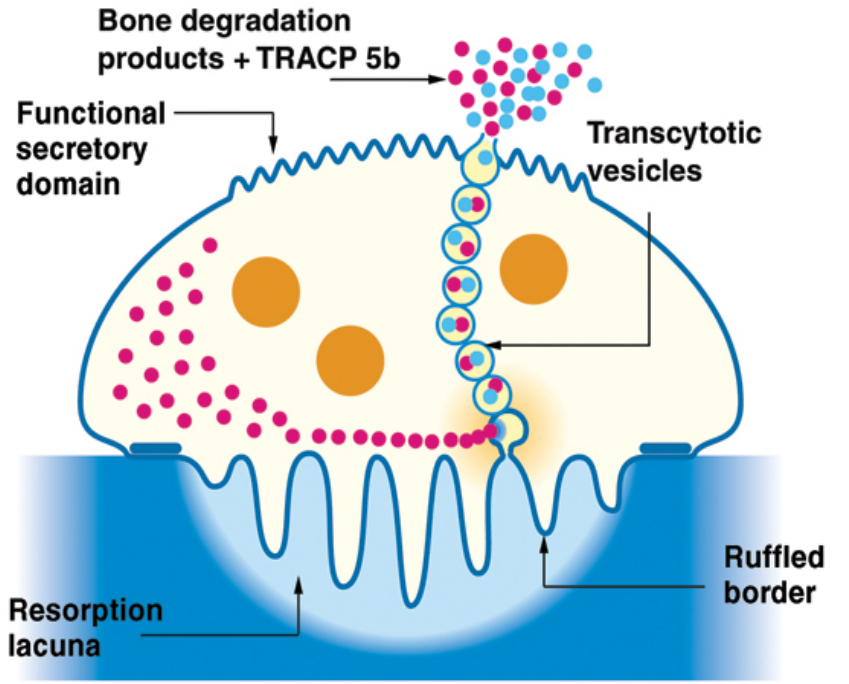



# Osteoclasts

- They are large (about 50 μm) multinucleated cells lining in depressions on the bone surface called Howships lacunae.
- With LM, the cell has an irregular shape with an acidophilic foamy cytoplasm.
- The part of the cell border facing the bone surface has striated border-like structure.
- Osteoclasts originate from blood monocytes, which fuse with each other to form multinucleated osteoclast.
- Degradation of mineralized bone matrix through:

1. Focal decalcification through production of organic acids (carbonic, lactic and citric) to generate local acidic environment capable of dissolving calcium from the bone matrix.
- 2. Extracellular digestion of the organic components of the bone matrix through liberation of acid hydrolase to the extracellular matrix.





# Bone matrix

- **It consists of organic and inorganic elements:**

**1. Organic matrix**

- **It is made up of a mixture of glycoprotein ground substance and type I collagen.**

**2. Inorganic matrix**

- **It consists of mineral salts, mainly calcium phosphate that is deposited as submicroscopic hydroxyapatite crystals within the collagen fibers.**

# Types of bone

- Compact Bone
- Spongy or Cancellous Bone

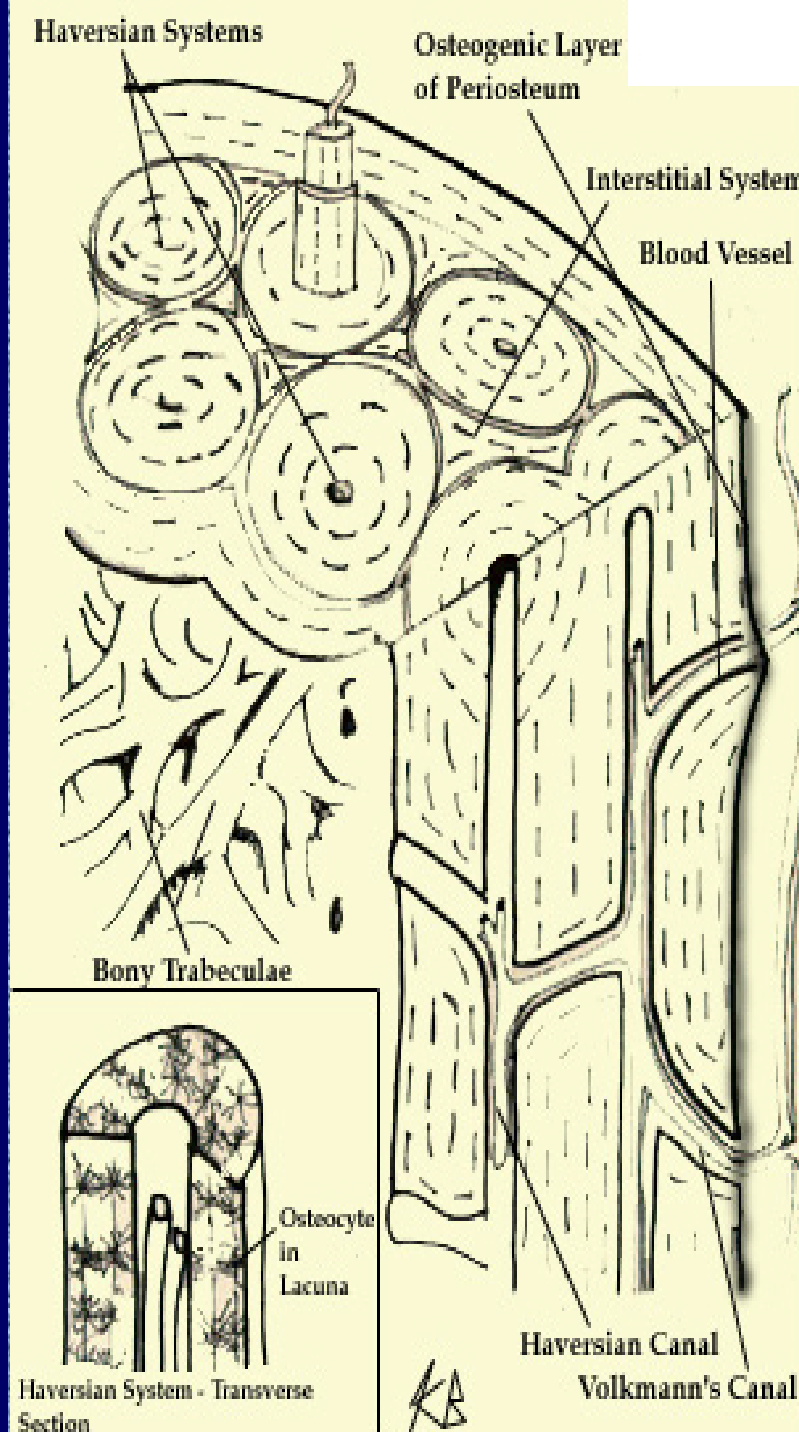
# Compact bone

**Dense wall of the shaft.**

- **Diaphysis of the long bone.**
- **It consists of the following layers:**

**1) Periosteum**

- **It is a tough connective tissue layer invests the outer surface of bone.**
- **It consists of two layers: a) outer fibrous layer of dense irregular connective tissue and blood vessels.**
- **b) Inner cellular or osteogenic layer formed of osteoblasts.**
- **It is absent on the articular surface covered by hyaline cartilage.**
- **2) Outer circumferential lamellae**
- **They are bony lamellae (thin layer of calcified matrix separated by lacunae interconnected by canaliculi) arranged parallel to the outer surface of the bone.**



# Compact bone

## 3) Osteon (Haversian system)

- It is the structural unit of the compact bone.
- It is a cylindrical structure about 0.4 mm in diameter that runs parallel to the long axis of the bone.

It consists of:

- a. Central canal or Haversian canal
- It is a longitudinal canal containing blood and lymphatic vessels and nerves.

b) Haversian lamellae (or concentric lamellae)

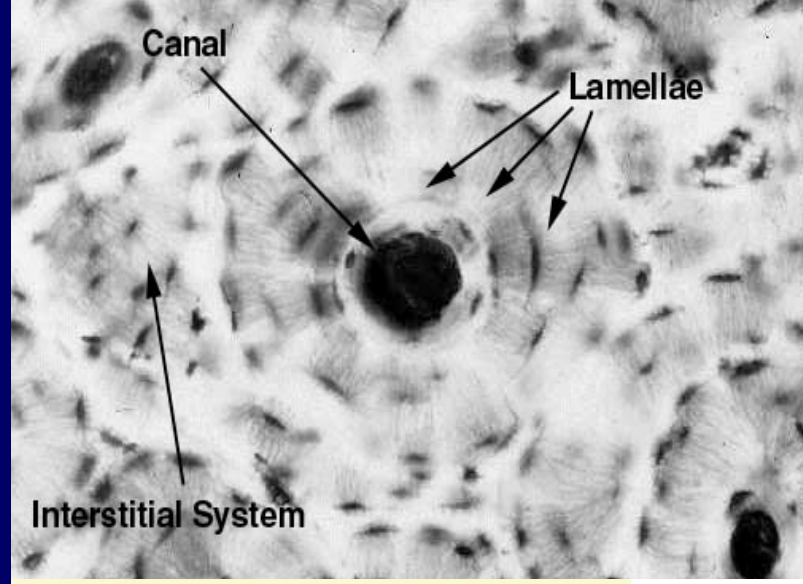
- They are about 4-20 bony lamellae that are concentricity arranged around the central canal.

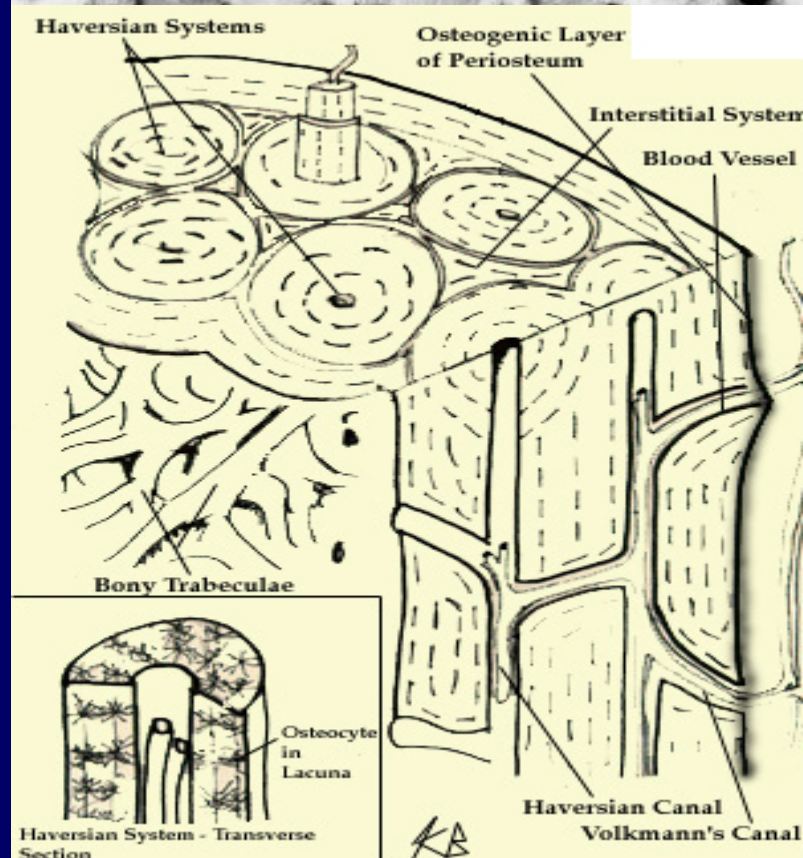
c) Osteocytes

- They are trapped inside lacunae located within or between the concentric lamellae.

d) Canaliculi

- They are tiny tubules radiate from each lacuna to anastomose with those of the adjacent lacunae.



# Compact bone

- The cytoplasmic processes of the osteocytes pass in the canaliculi.
- Communicate via gap junction with the processes of adjacent cells and with the extravascular fluid in the center canal.

**4) Interstitial lamellae**

- They are bony lamellae occupying the spaces between the osteons.

**5) Volkman's canal (transverse canal)**

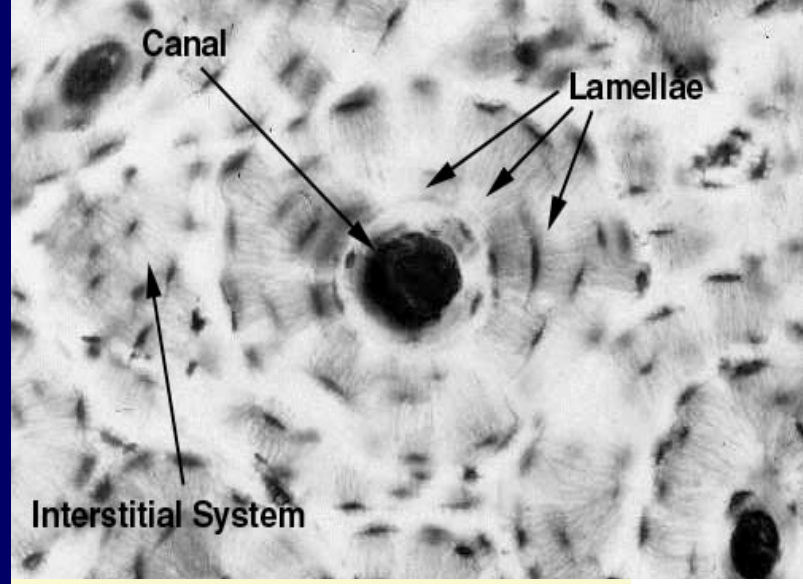
- It is transverse or oblique canals connect between:
- Two Haversian canals.
- Or between the Haversian canal and periosteum.
- Unlike the Haversian canal, they are not surrounded by concentric bony lamellae.

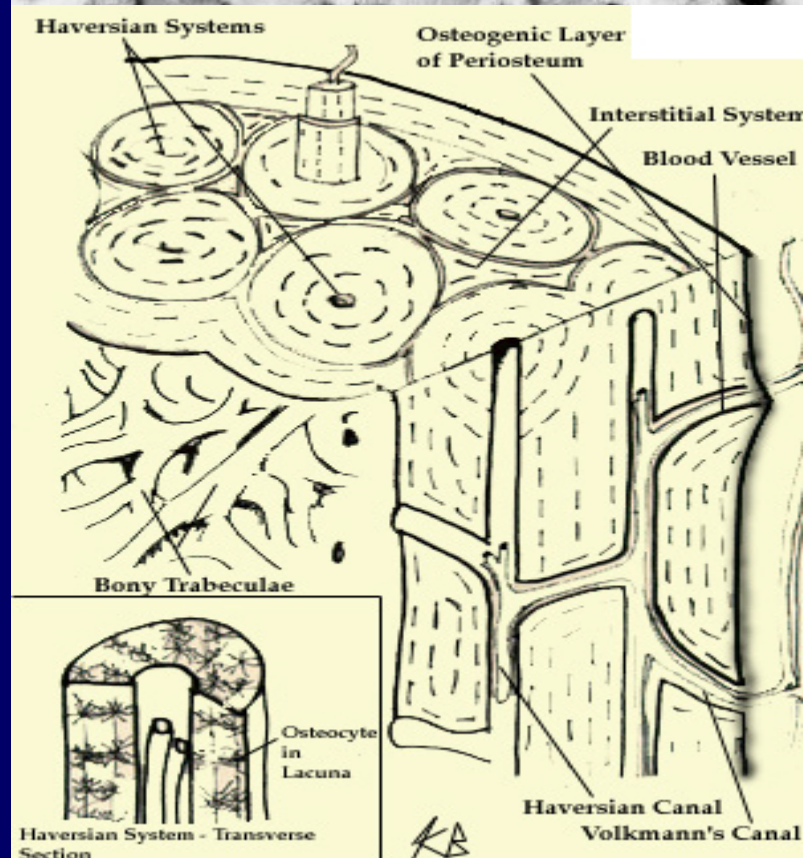
**6) Inner circumferential lamellae**

- They are bony lamellae arranged parallel to the inner surface of the bone.

**7) Endosteum**

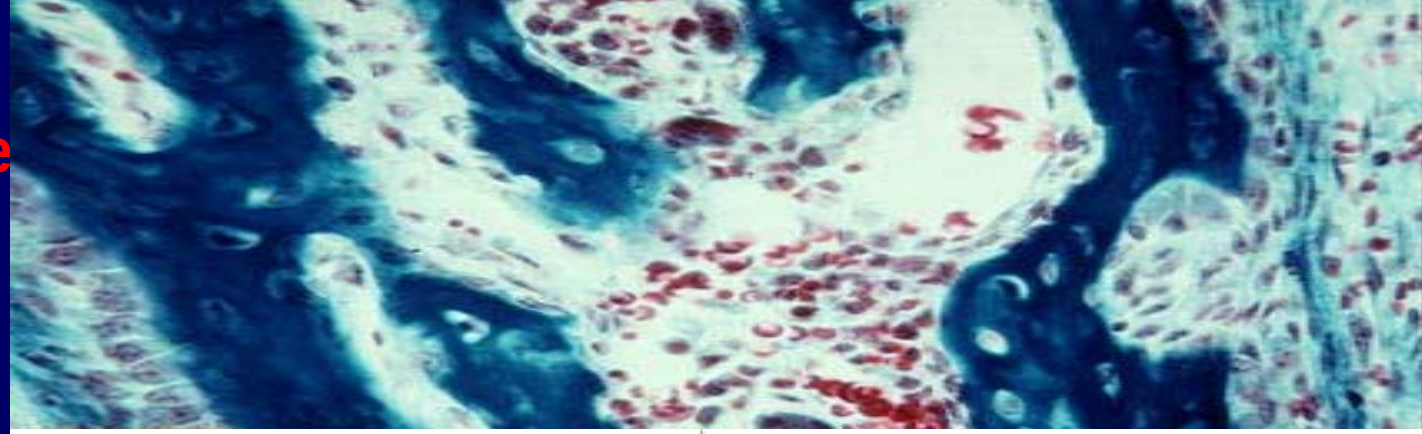
- It invests the inner surface of the bone (marrow cavity) and is formed of only osteogenic layer that is responsible for growth of bone, continuous remodeling and fracture repair.

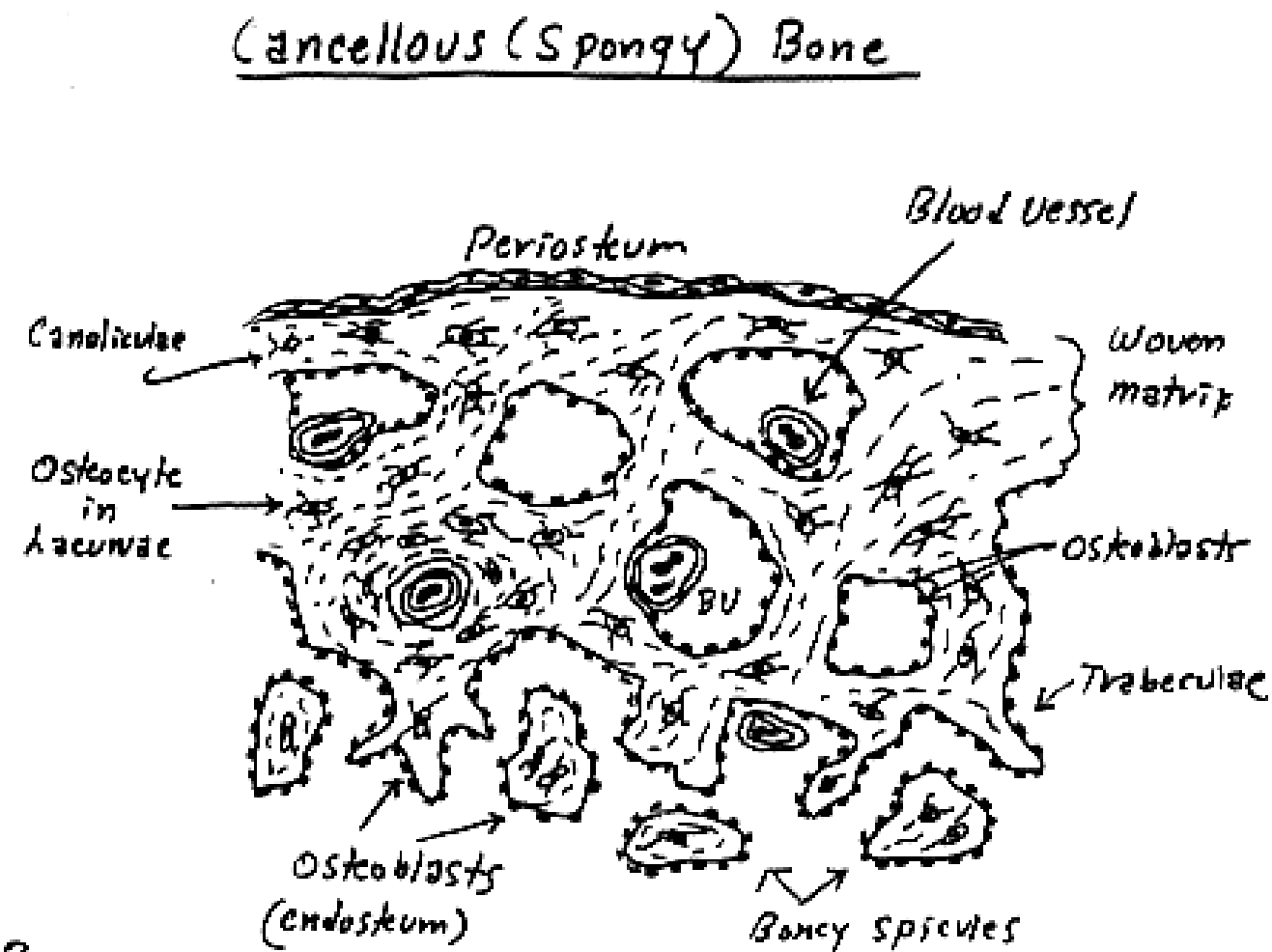


# Cancellous or spongy bone

- A network of bony trabecullae.
- Separated by interconnecting spaces containing bone marrow.
- The trabecullae are thin and composed of bone matrix.
- With lacunae containing osteocytes that exchange metabolites via canaliculi with blood sinusoids in the marrow cavity.





# Blood

- **Blood consists of free cells suspended in a fluid medium called plasma.**
- **The volume of blood in healthy adult human is 5-6 liters.**

**Blood cells:**

- **They constitute 45% of total blood volume and include:**

1. **Red blood cells (corpuscles) or erythrocytes.**
2. **White blood cells or leukocytes.**
3. **Platelets.**

# Blood

**Blood plasma:**

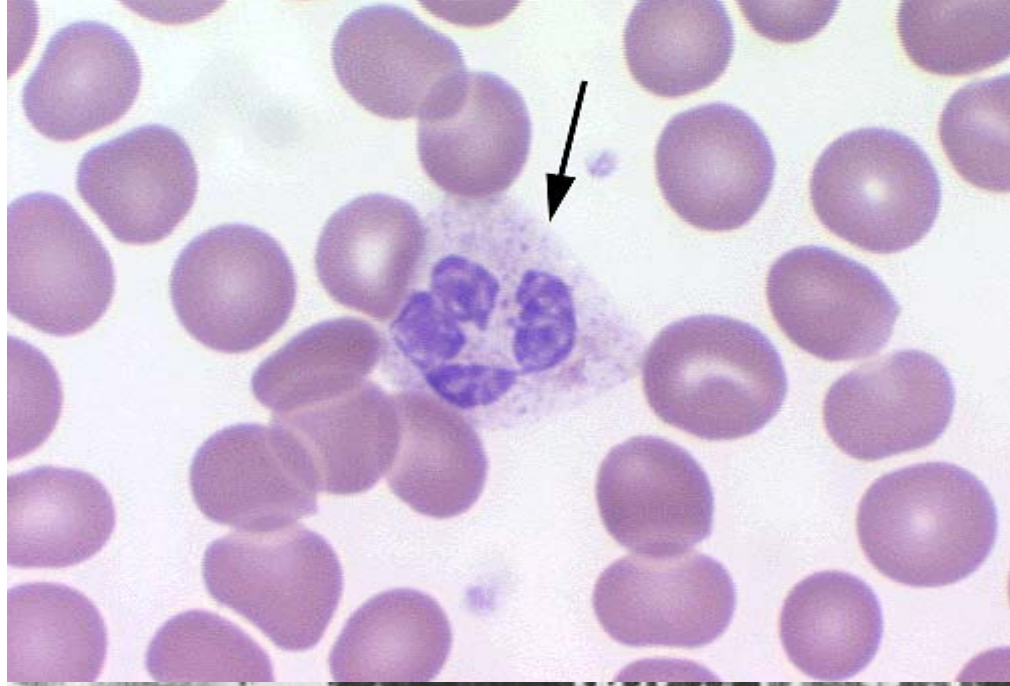
- **Plasma is a yellowish fluid, constitutes 55% of the total volume.**
- **It consists of:**
- **Water 90%**
- **Plasma proteins (albumin, globulin, fibrinogen and prothrombin) 7%.**
- **Small amount of Ca, sodium chloride, bicarbonate and phosphate.**

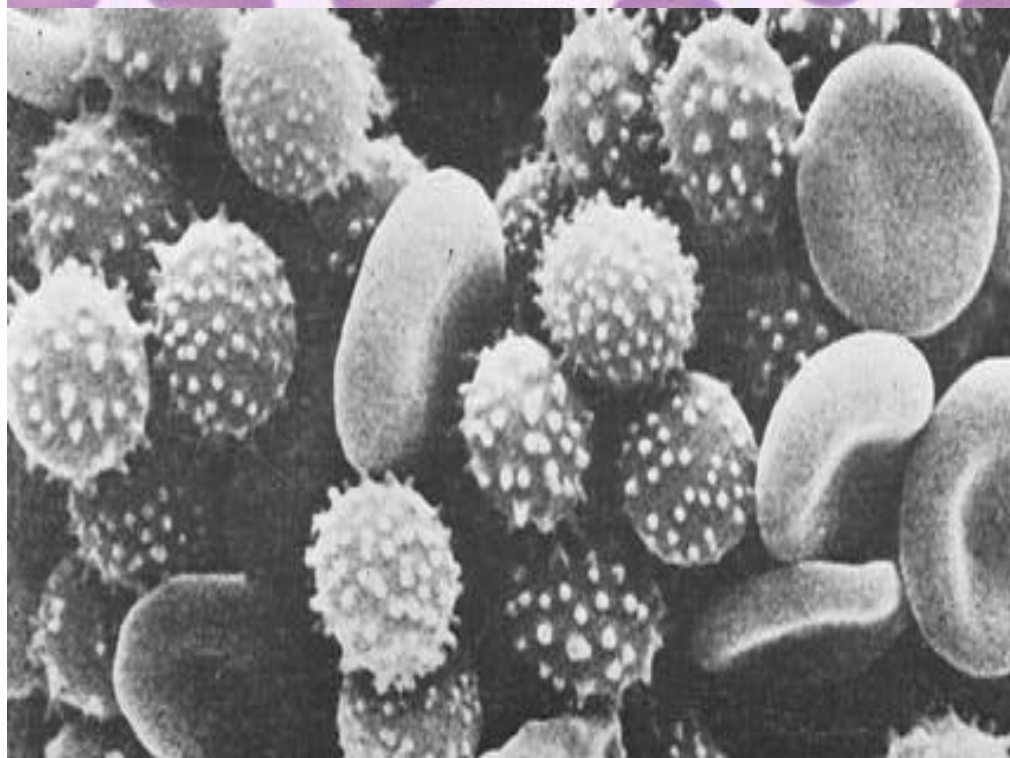
**Functions of the blood:**

1. **Transport oxygen, carbon dioxide and hormones.**
2. **Maintenance of acid-base balance.**
3. **Removal of waste products of cell metabolism.**
4. **Control body temperature.**
5. **Defense against infection.**

# Erythrocytes

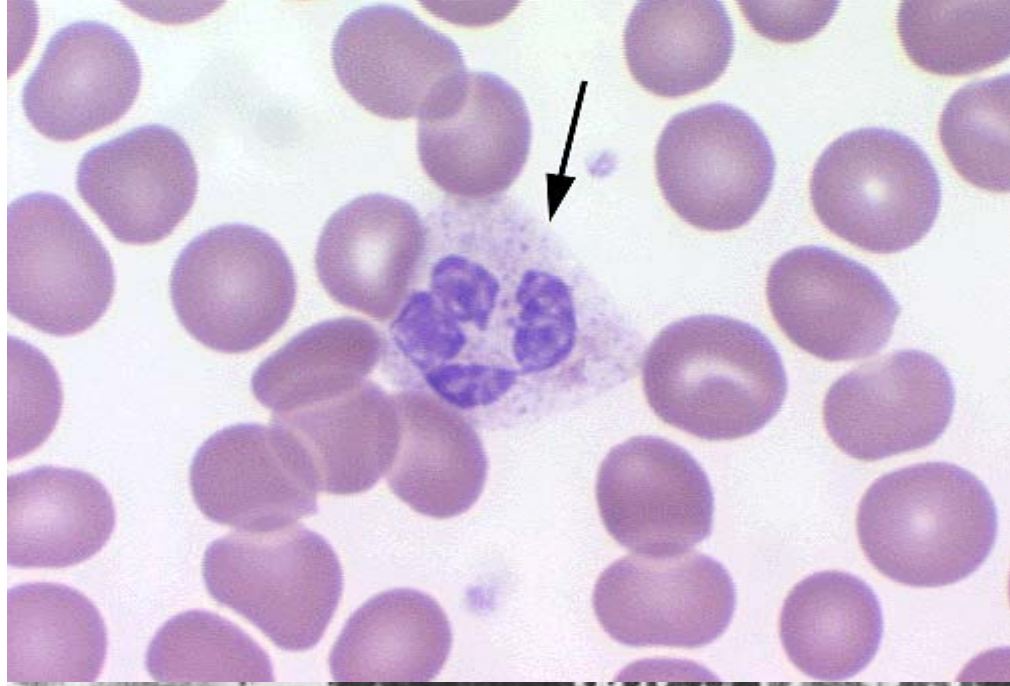
- They are not true cells, as they have no nuclei or organoids.
- The cytoplasm contains only hemoglobin surrounded with cell membrane.
- The normal count of erythrocytes is 5 million/cubic millimeter of blood in males, and 4.5 millions/cubic millimeter of blood in females.
- They are biconcave discs of about 7.2 micron in diameter and 1.9 micron in thickness.

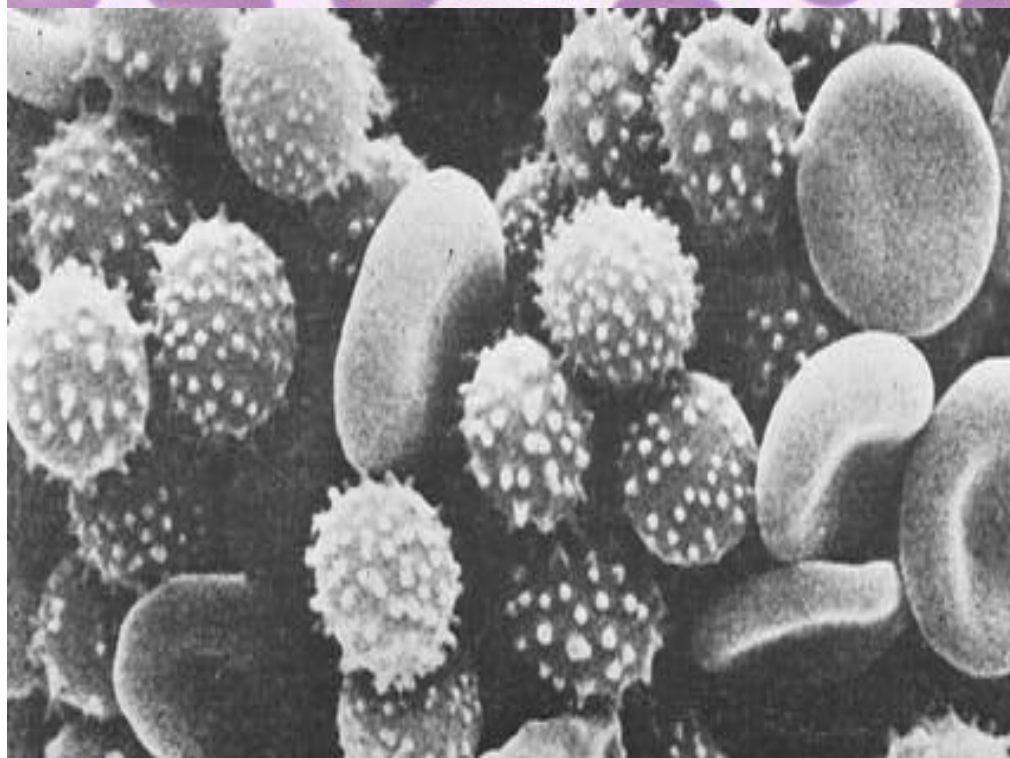




# Erythrocytes

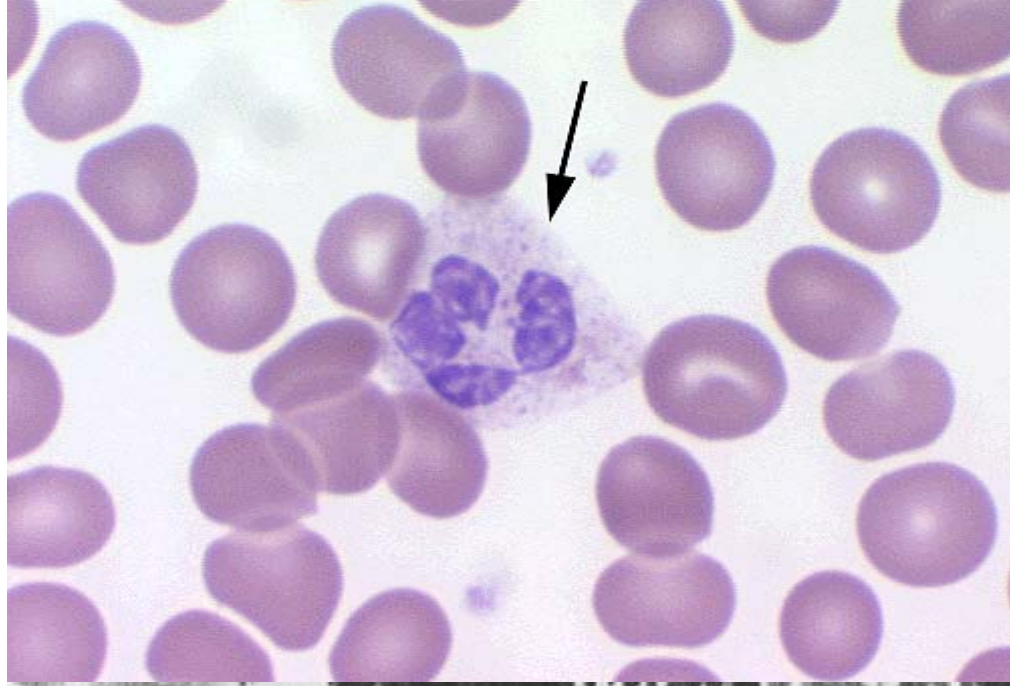
- RBCs, sometimes adhere together via their concave surface forming the so called rouleaux.
- This phenomenon occurs when the circulation is slow.
- Decrease in number of RBCs is known as anemia.
- Increase in number of RBCs is known as polycythaemia.
- In macrocytic anemia, diameter of RBCs increases, while in microcytic anemia, their diameter decreases.

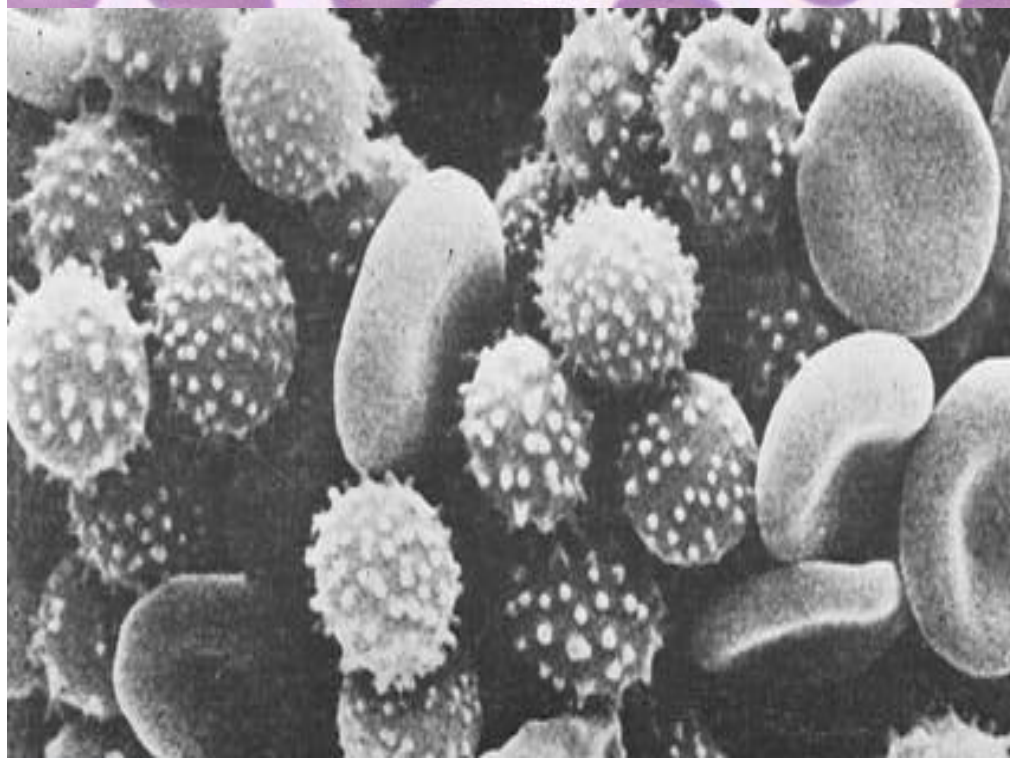


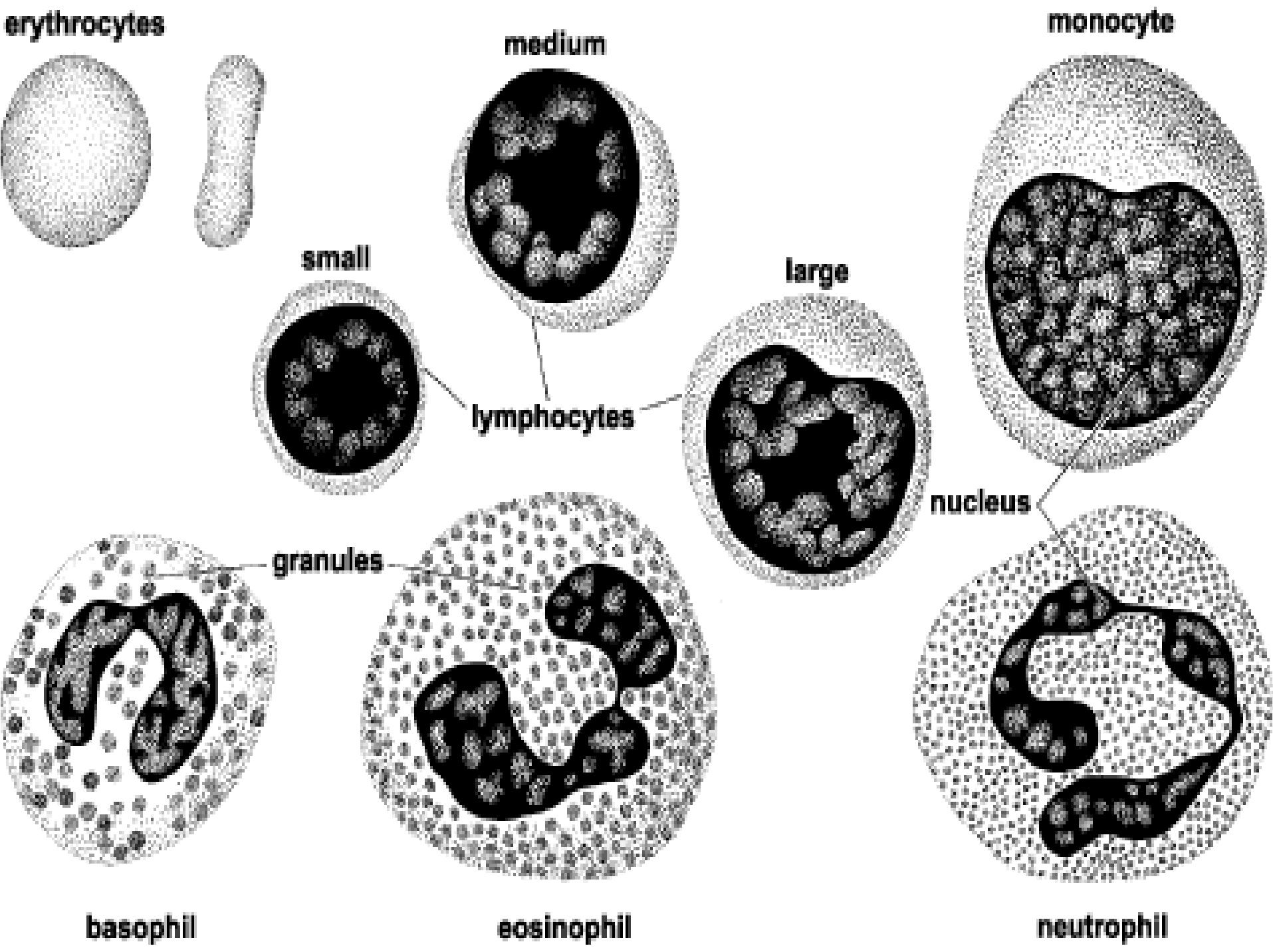


# Erythrocytes

- **In different diseases, abnormal size of RBCs may appear and this is called anisocytosis.**
- **Life-span of RBCs is 100-120 days after which they are destroyed by macrophages in spleen and liver.**
- **Transport of oxygen from lung to tissue and carbon dioxide from tissue to lung.**

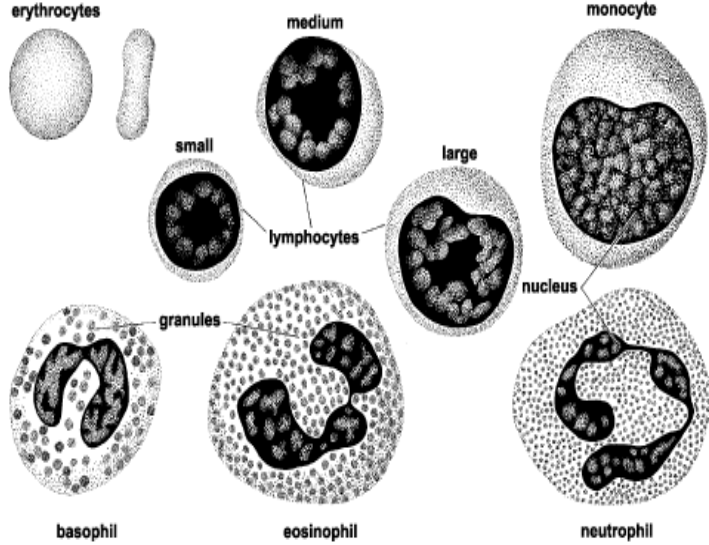




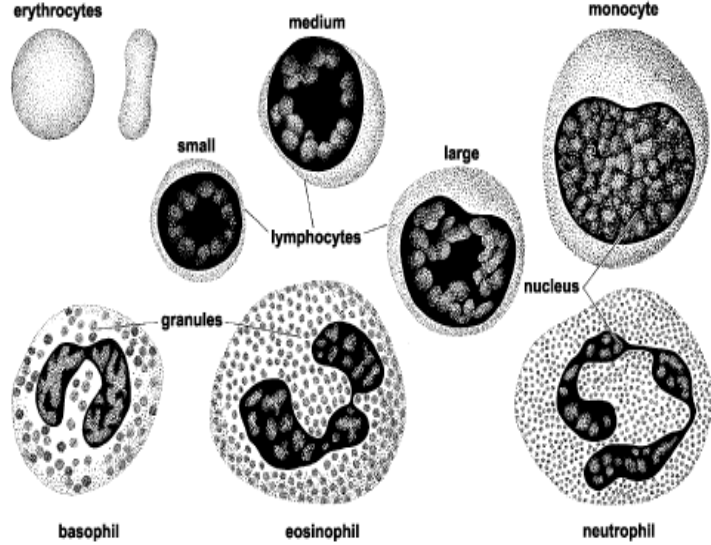

erythrocytes
medium
monocyte
small
large
lymphocytes
nucleus
granules
basophil
eosinophil
neutrophil

| LEUKOCYTES | RBCS |
| --- | --- |
| -True cells with nuclei and organelles. | -Bags containing hemoglobin. No nuclei or organelles. |
| - Don't form rouleaux. | -Form rouleaux in slow streams. |
| -Five types classified into: 3 granular and 2 non-granular. | -One type only, with clear homogenous cytoplasm |
| Color: Colorless, but when condensed they appear white. | -Greenish yellow, but when condensed they appear red. |
| -Number: in thousands (4000-10 000l $mm^3$). | -In millions (4.5 -5.5 million/$mm^3$). |
| Size: Larger (7-20 μm) | -Smaller (6-9 μm) |
| Staining: Granules and cytoplasm of different types have specific reactions. | -Acidophilic due to hemoglobin. |
| -Domain of function: extracellular. | - Inside blood vessels. |
| -Different defensive functions for the different types. | - One function mainly gaseous exchange. |
| -Origin from myeloid and lymphoid tissues. | - From myeloid tissue only. |
| _life span: shorter (few days), but T-lymphocytes can live for years. | -Longer life span (120 days). |

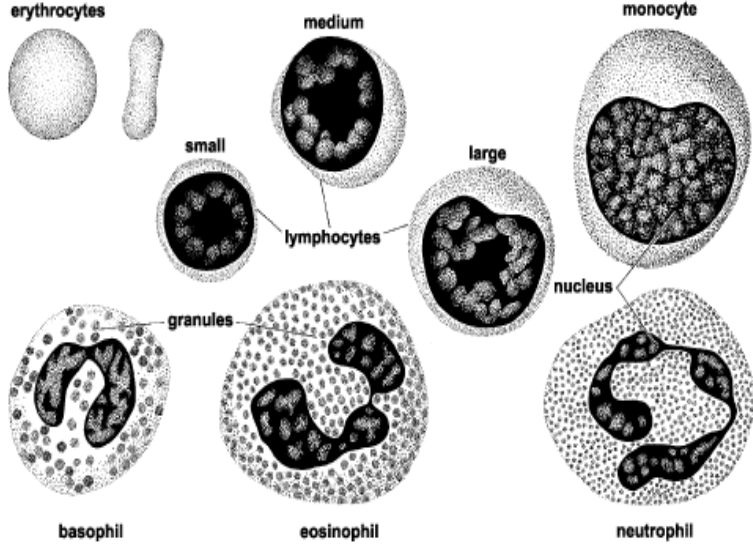
| | NEUTROPHILS | EOSINOPHILS | BASOPHILS |
|---|---|---|---|
| Percentage | 60-70% | 1-5% | 0.5-1% |
| Size | 10-12μm. | 12-15 μm | 10-12 μm |
| Nucleus | -Multilobed (1-5 deeply stained lobes attached by delicate strands). | Bilobed, or horse shoe shaped, and less deeply stained. | Irregular, lightly stained and obscured by Cytoplasmic granules. |
| Cytoplasm | Contains fine Neutrophilic and azurophilic granules. Specific granules are fine and have little affinity to staining dye. They contain bactericidal enzymes. | Irregular boundary, packed with large refractile acidophilic granules. | Contains large basophilic granules (metachromatic). |



| | NEUTROPHILS | EOSINOPHILS | BASOPHILS |
|---|---|---|---|
| Cytoplasm | Non specific (azurophilic) granules are large granules stain reddish purple with basic dye methelene azure. The contain hydrolytic enzymes | | |
| Functions | Phagocytosis, they are called microphages and they are the first line of defense against bacterial infection. An increase in the number of neutrophils is called neutrophilia. Thic occur in acute Pyogenic inflammations. A decrease in their number is called neutropenia. This occur in influenza, typhoid fever, ,easles and tuberculosis. | Secrete histaminase which play an active role in allergy and parasitic infestation. An increase in the number of eosinophil is called is called eosinophilia, this occurs in allergic, parasitic and some skin diseases. A decrease in their number is called eosinopenia. This occur after cortisone treatment and acute infections. | An increase in basophils is called basophilia. It occurs in small pox and chicken pox. |
| Life span | 3-5 days | 8-12 days | 12-15 days |



| | LYMPHOCYTES | | MONOCYTES |
|---|---|---|---|
| | Small | Large | |
| Percentage | T-lymphocytes (75%) B-lymphocytes (25%) | 8% of lymphocytes | 3-8 % |
| Size | 6-8 micron. | 10-12 micron. | 12-20 micron. |
| Nucleus | Small spherical and Deeply stained. | Large indented And Lightly stained. | Large indented or horse-shoe and paler than that of the lymphocytes. |
| Cytoplasm | Non-granular, forms a little rim around the nucleus, and stain pale blue. | Non granular, Abundant and stains faintly Blue (clear glass appearance) | Non-granular, abundant and stain grayish blue (frosted glass appearance). |




•**Functions of Lymphocytes:** They are principally involved in the immune response of the body.

•An increase in the number of lymphocytes occurs in chronic inflammations, as in tuberculosis and syphilis.

•It also occurs in whooping cough and lymphatic leukemia.

| | LYMPHOCYTES | | MONOCYTES |
|---|---|---|---|
| | Small | Large | |
| Percentage | T-lymphocytes (75%) B-lymphocytes (25%) | 8% of lymphocytes | 3-8 % |
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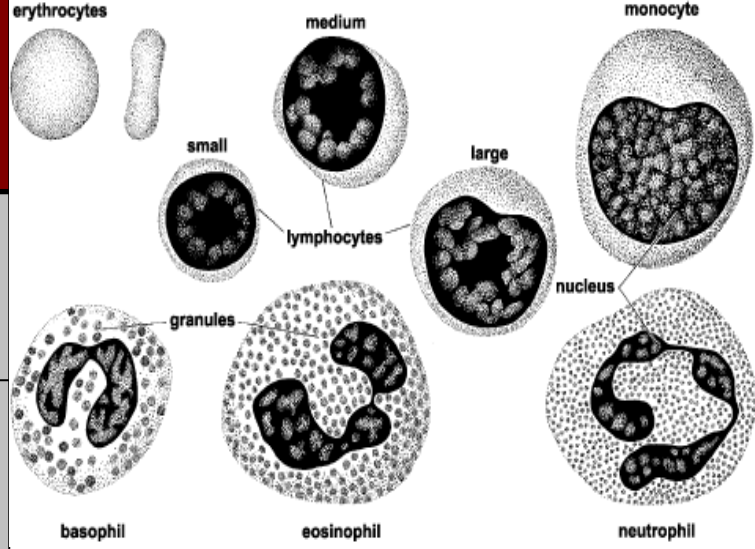


## Functions of monocytes:

- In the CT they change to macrophages which are highly phagocytic cells.
- They increase in number in malaria, typhoid, and monocytic leukemia.
- Monocytes circulate in blood for three days after which they leave blood to the CT, where they differentiate into macrophages.

# Blood Platelets

- Small fragments of cytoplasm of megakaryocytes in bone marrow.
- 2-5 microns.
- 150000-400000/cubic millimeter of blood.
- Bounded by cell membrane, have no nuclei.
- Each platelets has a central dark region called granulomere and peripheral pale non-granular region called hyalomere.
- Function: form clots and stop bleeding from cut end of blood vessels.