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Faculty of Medical Sciences
Integrated Academic Studies of Medicine
Department of Histology and Embryology

Connective tissues, blood and hemopoiesis

Cartilage

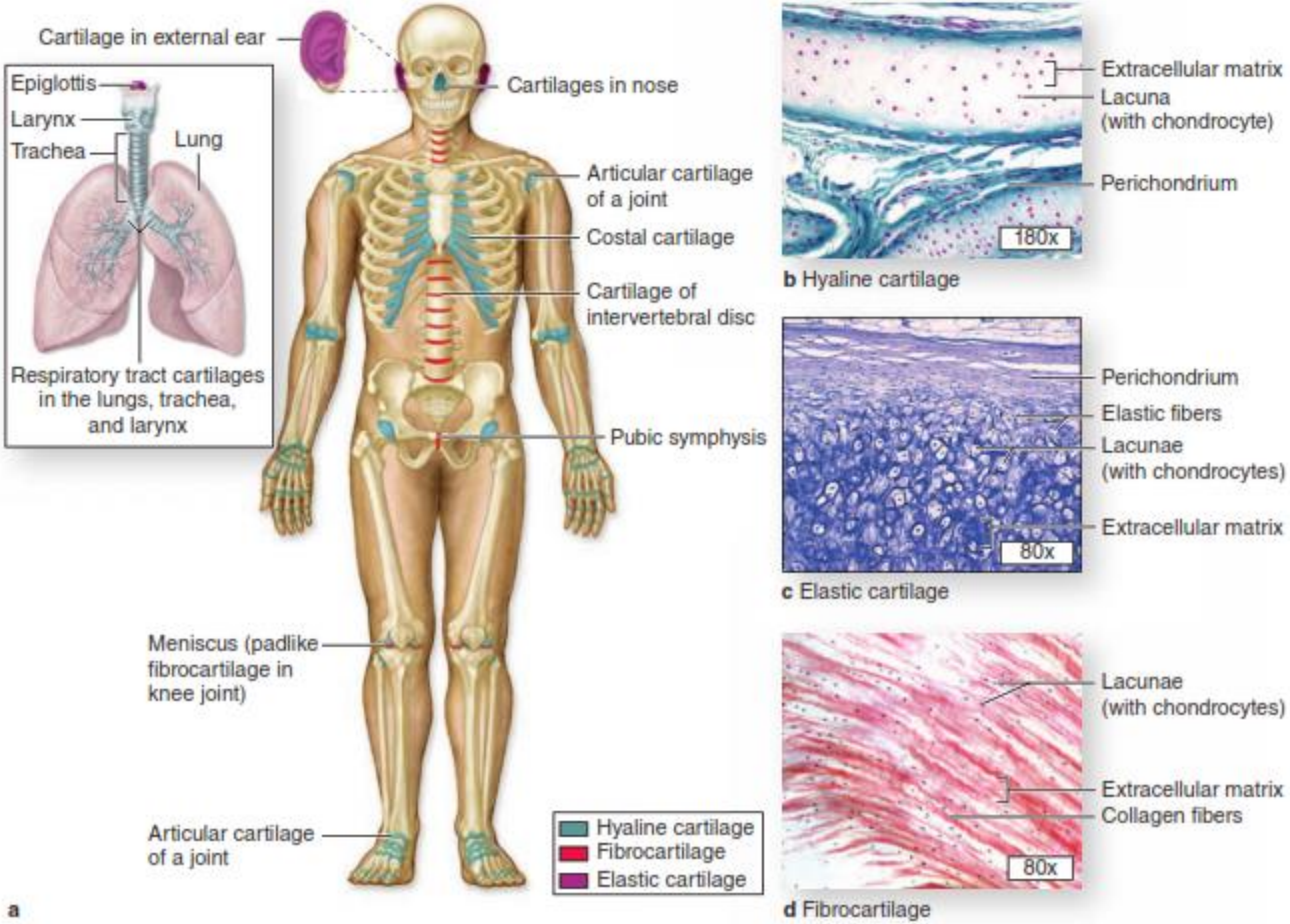
- Cartilage is a tough, durable form of supporting connective tissue, characterized by an extracellular matrix (ECM) with high concentrations of GAGs and proteoglycans, interacting with collagen and elastic fibers. Structural features of its matrix make cartilage ideal for a variety of mechanical and protective roles within the adult skeleton and elsewhere

- Specialized connective tissue whose main role is to provide support to soft tissues
- It is made up of cells - chondrocytes and a tough but flexible extracellular matrix
- Chondrocytes tend to group into smaller or larger groups

- They are located in small cavities called lacunae
- Around the cartilage there is an envelope made of dense connective tissue - the perichondrium

- Neither blood vessels nor nerves penetrate the cartilaginous tissue

- Cartilage cells are nourished by diffusion of substances from blood vessels of perichondrium


Cartilage in external ear
Epiglottis
Larynx
Trachea
Lung
Respiratory tract cartilages in the lungs, trachea, and larynx
Cartilages in nose
Articular cartilage of a joint
Costal cartilage
Cartilage of intervertebral disc
Pubic symphysis
Meniscus (padlike fibrocartilage in knee joint)
Articular cartilage of a joint
Hyaline cartilage
Fibrocartilage
Elastic cartilage
a
Extracellular matrix
Lacuna (with chondrocyte)
Perichondrium
180x
b Hyaline cartilage
Perichondrium
Elastic fibers
Lacunae (with chondrocytes)
Extracellular matrix
80x
c Elastic cartilage
Lacunae (with chondrocytes)
Extracellular matrix
Collagen fibers
80x
d Fibrocartilage

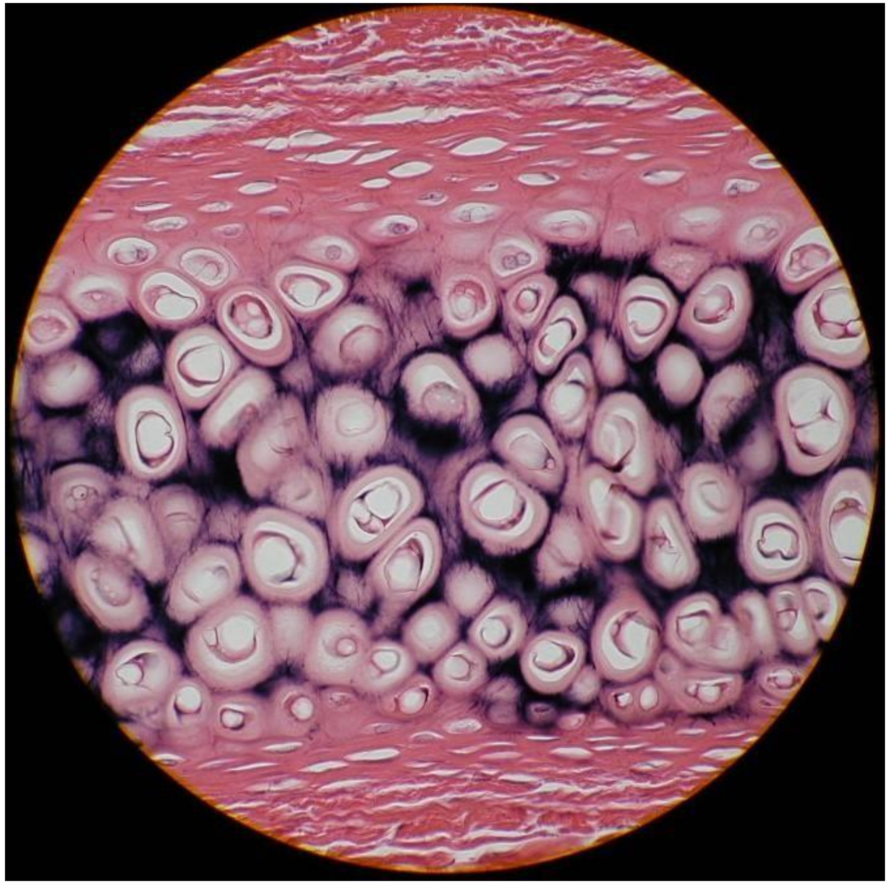
Perichodrium

*Cartilage is surrounded by the perichondrium, a sheath of dense connective tissue permeated with blood vessels and nerves. In mature cartilage, the perichondrium is compact, and two layers can be observed in the growing cartilage:

- Outer fibrous
- Internal cellular

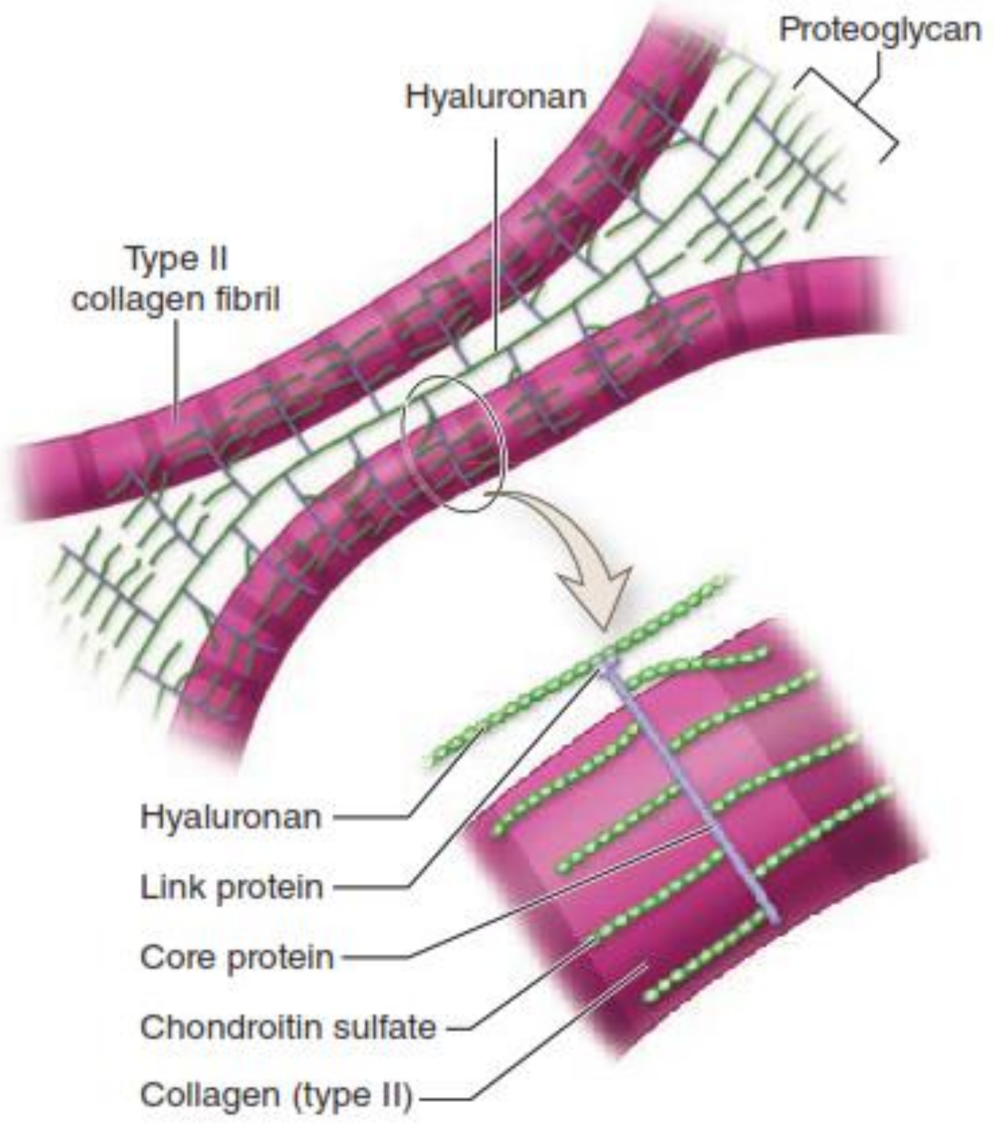
*The outer layer of the perichondrium contains fibroblasts and collagen fibers, and the inner layer contains stem cells of cartilage tissue - chondrogenic cells

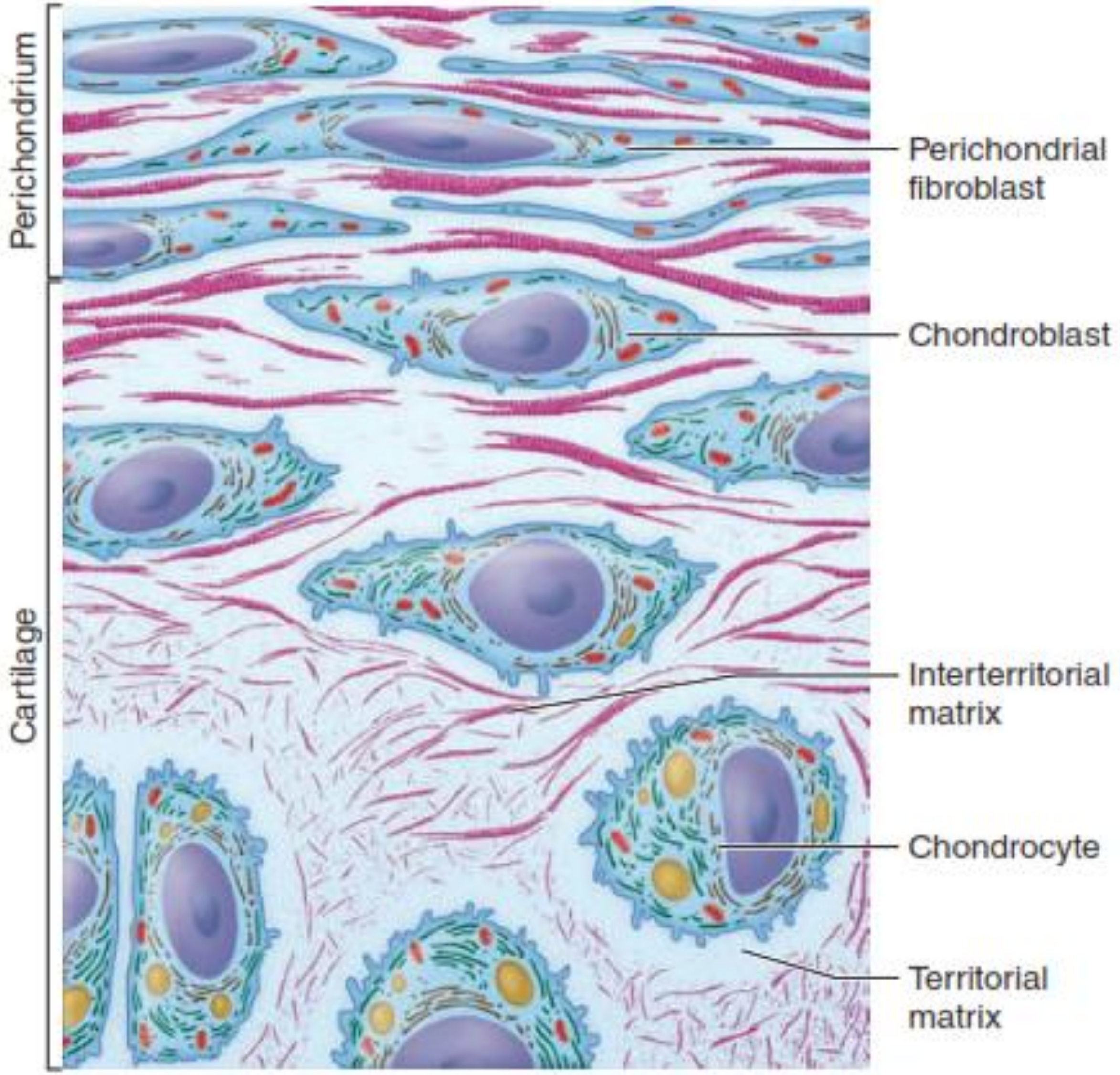
*Cartilaginous cells are nourished by diffusion of metabolites from the capillaries of the perichodrium.



Cartilage cells

- Cartilage contains three types of cells that belong to the same cell line:
  - Chondrogenic cells – the inner layer of the perichondrium
  - Chondroblasts – on the surface of the cartilage
  - Chondrocytes - in the depth of the cartilage
- The main morphological characteristics of chondrogenic cells are a flattened shape, a dark oblong nucleus and weakly expressed organelles, which indicates their inactivity

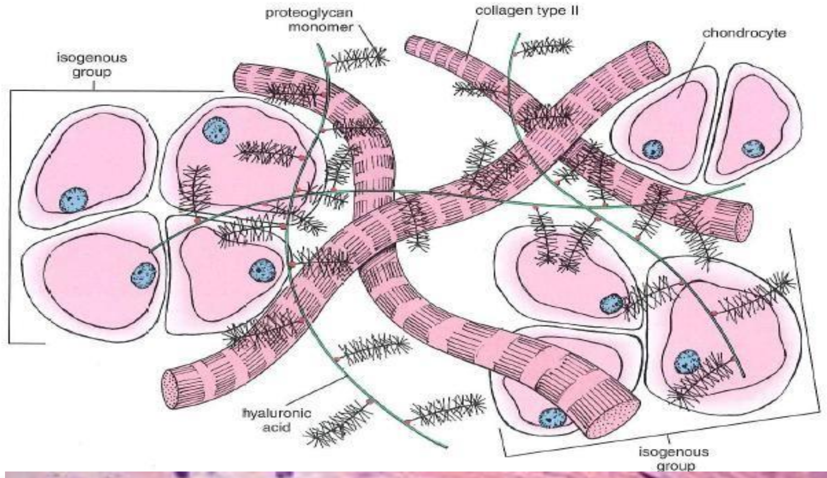

Proteoglycan
Hyaluronan
Type II
collagen fibril
Hyaluronan
Link protein
Core protein
Chondroitin sulfate
Collagen (type II)

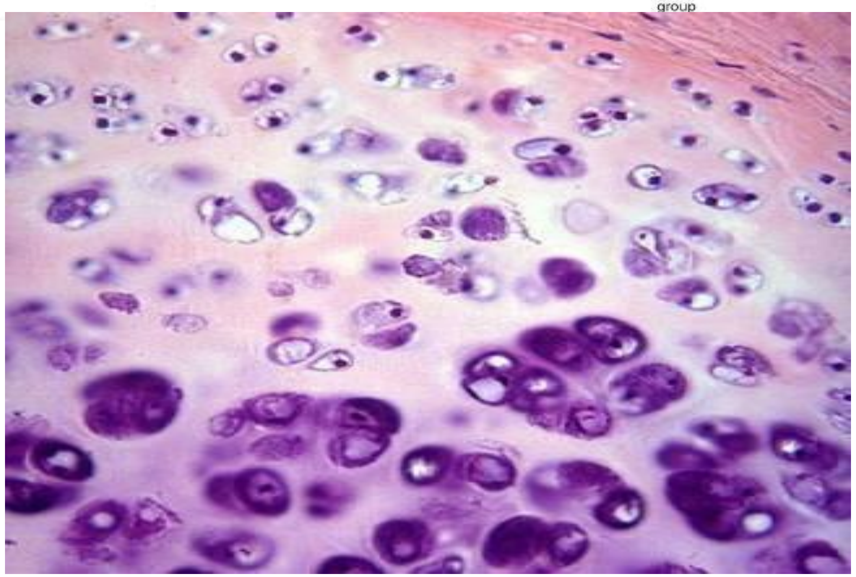

Perichondrium
Cartilage
Perichondrial
fibroblast
Chondroblast
Interterritorial
matrix
Chondrocyte
Territorial
matrix

- In growing cartilage, chondrogenic cells are activated and differentiate into immature cartilage cells called chondroblasts
- The nucleus of the chondroblast is oval and bright, and the cytoplasm is filled with secretory organelles
- Chondroblasts synthesize and secrete extracellular matrix around themselves. When they are completely surrounded by cartilage cells can be considered mature and are called chondrocytes

Cartilage cells - chondrocytes

- Weakly expressed organelles and a lower level of activity than chondroblasts.
- The cavities in which the mature cartilage cells are located are called lacunae.
- Within the lacuna, chondrocytes can divide and form groups in which the cells are arranged in a row or in the form of a cluster.
- A cluster of chondrocytes in one lacuna is designated as an isogenic group
- The narrow band of the extracellular matrix that surrounds the isogenic groups is slightly darker colored and called territory, while the rest of the matrix is lighter in color and called interterritory
- Isogenic group and territory together they form a chondron





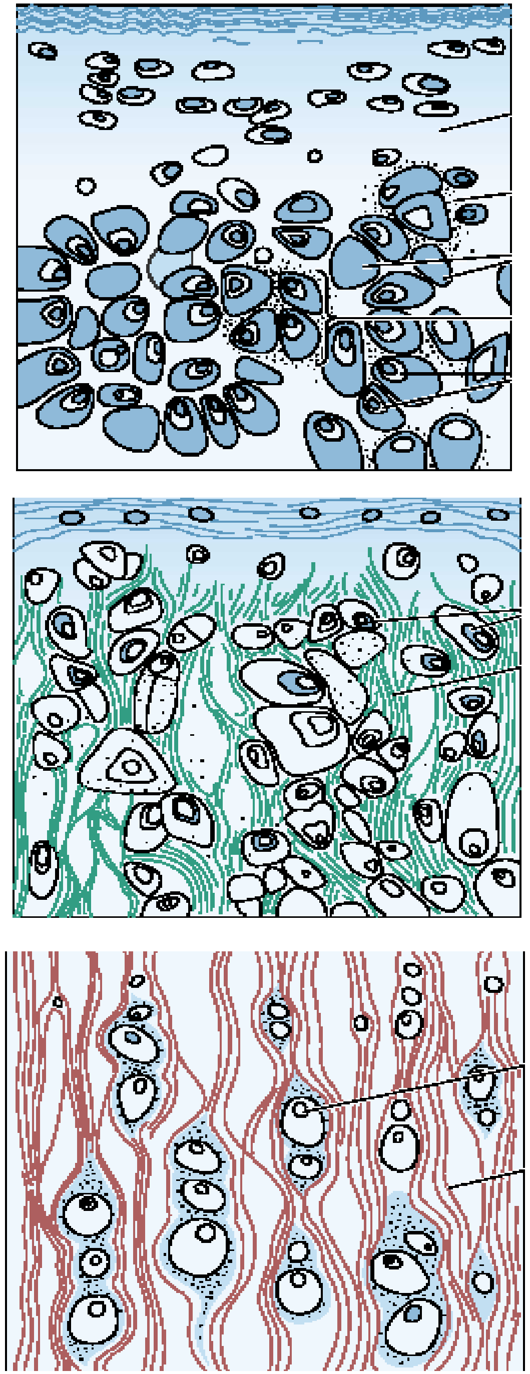
Types of cartilage

There are three types of cartilage in the human body:

Hyaline

Elastic

Fibrous



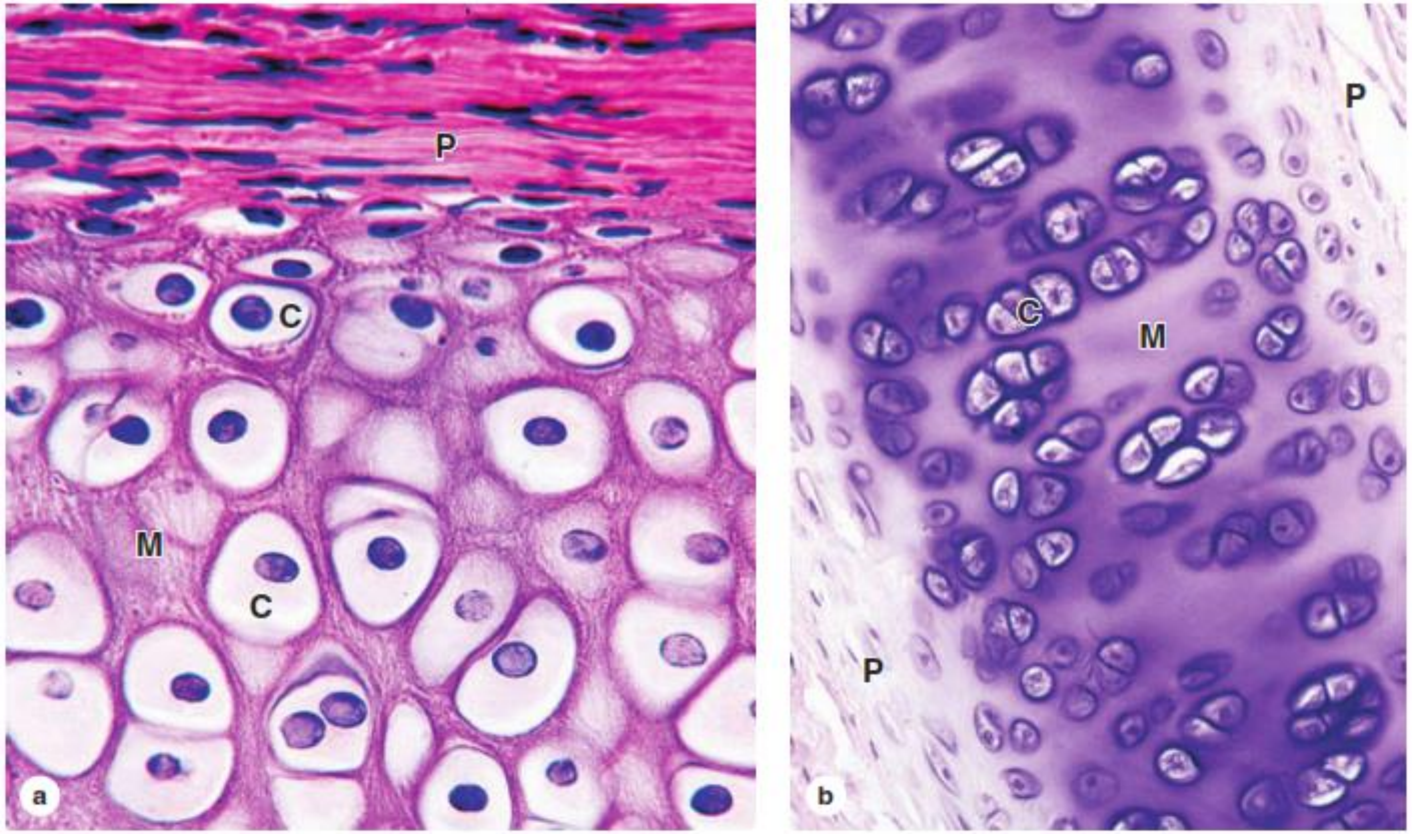
- The differences between them are related primarily to the type and amount of fiber contained in ECM

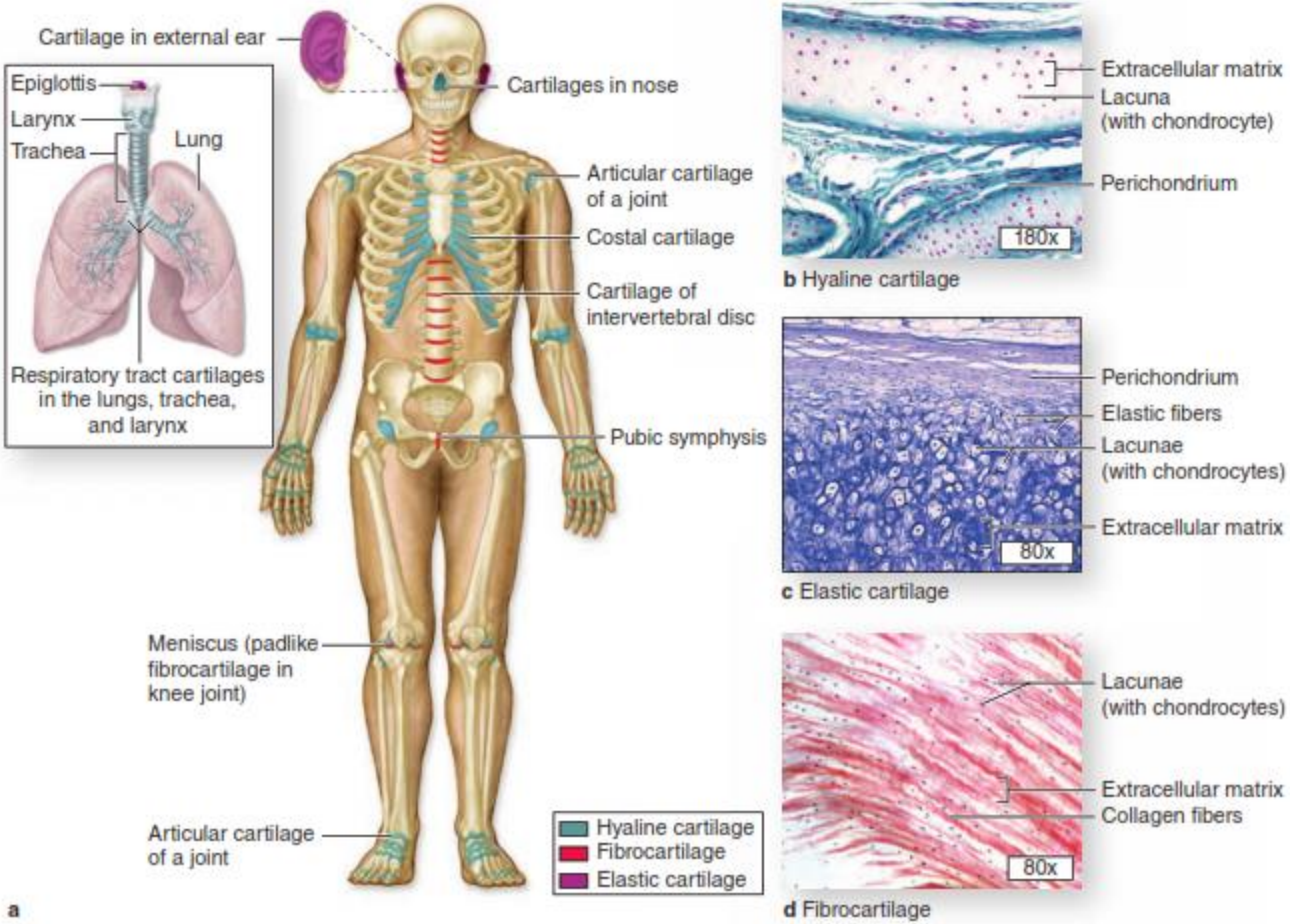
- Hyaline cartilage contains fibers made of collagen type II, elastic, in addition to collagen, it also contains a network of elastic fibers, while the fibrous type is dominated by collagen type I fibers

	Hyaline Cartilage	Elastic Cartilage	Fibrocartilage
Main features of the extracellular matrix	Homogeneous, with type II collagen and aggrecan	Type II collagen, aggrecan, and darker elastic fibers	Type II collagen and large areas of dense connective tissue with type I collagen
Major cells	Chondrocytes, chondroblasts	Chondrocytes, chondroblasts	Chondrocytes, fibroblasts
Typical arrangement of chondrocytes	Isolated or in small isogenous groups	Usually in small isogenous groups	Isolated or in isogenous groups arranged axially
Presence of perichondrium	Yes (except at epiphyses and articular cartilage)	Yes	No
Main locations or examples	Many components of upper respiratory tract; articular ends and epiphyseal plates of long bones; fetal skeleton	External ear, external acoustic meatus, auditory tube; epiglottis and certain other laryngeal cartilages	Intervertebral discs, pubic symphysis, meniscus, and certain other joints; insertions of tendons
Main functions	Provides smooth, low-friction surfaces in joints; structural support for respiratory tract	Provides flexible shape and support of soft tissues	Provides cushioning, tensile strength, and resistance to tearing and compression

Hyaline cartilage

* The most common type of cartilage in the human body.
* In the embryonic period, it builds the temporary skeleton of the fetus, which is gradually replaced by bone tissue in the fetus
* In adults, hyaline cartilage is present on the articular surfaces of movable joints, in the airways and on the edges of the ribs
* On a fresh section, the extracellular matrix is transparent like glass, hence the name hyaline (Greek: hyalos - glass) cartilage. In hyaline cartilage as a rule, isogenic groups are circular in shape and contain 2, 4, 8 or more cells

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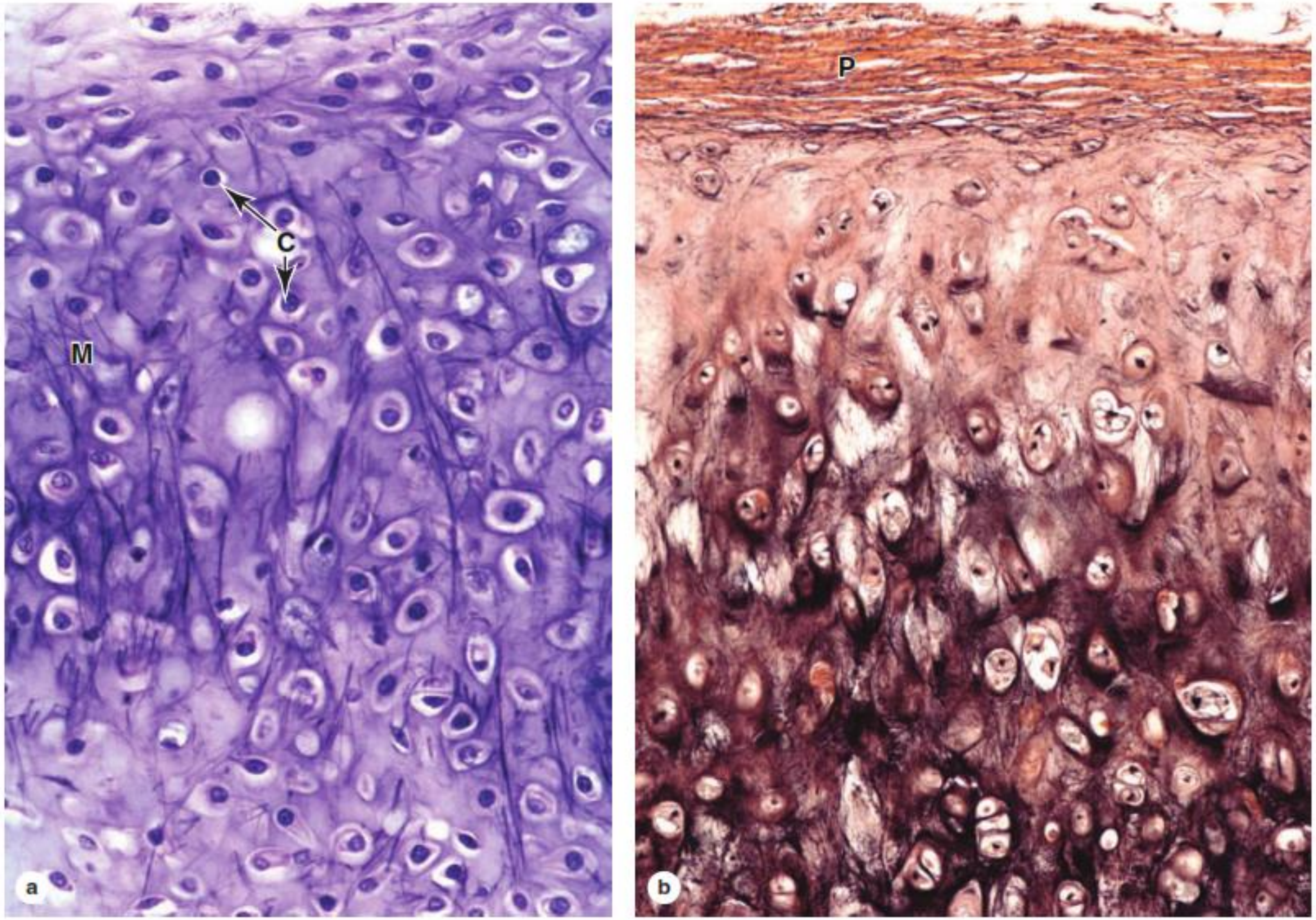
Hyaline cartilage

- The basic substance contains proteoglycans, glycoproteins and water
- Cartilage proteoglycans join together to form giant supramolecules - proteoglycan aggregates that have the greatest influence on the physical properties of cartilage (strength, flexibility, resistance to pressure)
- The most important proteoglycan is aggrecan
- Glycoproteins include: ancorin, tenascin and fibronectin
- 60-80% of hyaline cartilage is water, which is mostly, but not all, bound to aggrecan-hyaluronan aggregates, which enables the transport of substances through tissue matrix

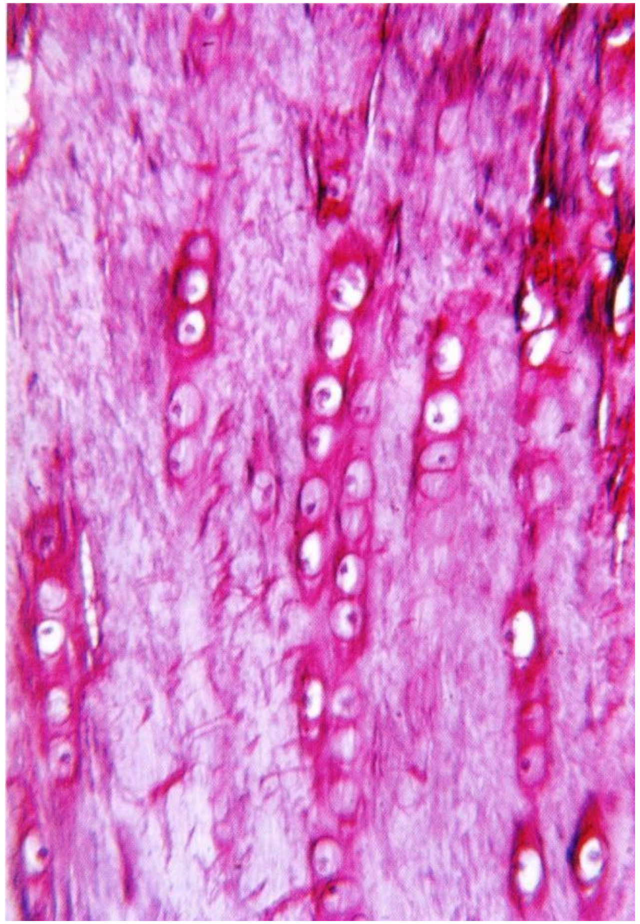
Elastic cartilage

- It is found in the auricle, external ear canal, auditory tube and larynx
- Chondrocytes in elastic cartilage are more numerous, larger and usually form small isogenic groups with two cells each in the lacuna
- In addition to collagen fibers, the extracellular matrix also contains a rich network of elastic fibers
- Elastin makes up this cartilage pliable and gives it a yellow color



Fibrous cartilage

- It is found in the intervertebral discs, the symphysis of the groin, the menisci of the knee joint and at the point of attachment of tendons and ligaments to the bone.
- The only type of cartilage it does not possess perichondrium
- It contains a little basic substance and a big amount of type I collagen fibers
- Collagen fibers are organized into bundles that give the cartilage its whitish color
- Chondrocytes are placed between bundles of collagen fibers as single cells or grouped in the form of a string
- Chondrocytes resemble fibrocytes, from which they differ in their oval shape



Histogenesis and cartilage growth

- At the site of cartilage tissue formation, the cells proliferate and create a cell cluster within the mesenchyme, which is called a chondrogenic blast, and the space it occupies is called a chondrification center.
- Cells in the blastema begin to form a cartilaginous matrix and become Chondroblasts

- Cartilage grows in two ways:
- Appositional growth - new cartilage tissue is created from the surface of existing cartilage
- Interstitial growth - new tissue is created inside the existing one

- Cartilage regeneration is limited and is better in children, while in adults it is slow and incomplete - regeneration is carried out through the perichondrium

Bone tissue

- Bone tissue is a supportive connective tissue with a mineralized intercellular matrix and numerous roles:

- Providing support and enabling movement

- Protection of vital organs in the cranial and thoracic cavity

- Storage of minerals, primarily calcium and phosphorus

- It is made of organic and inorganic material
- Its hardness is given by calcium phosphate precipitated in the form of hydroxyapatite crystals

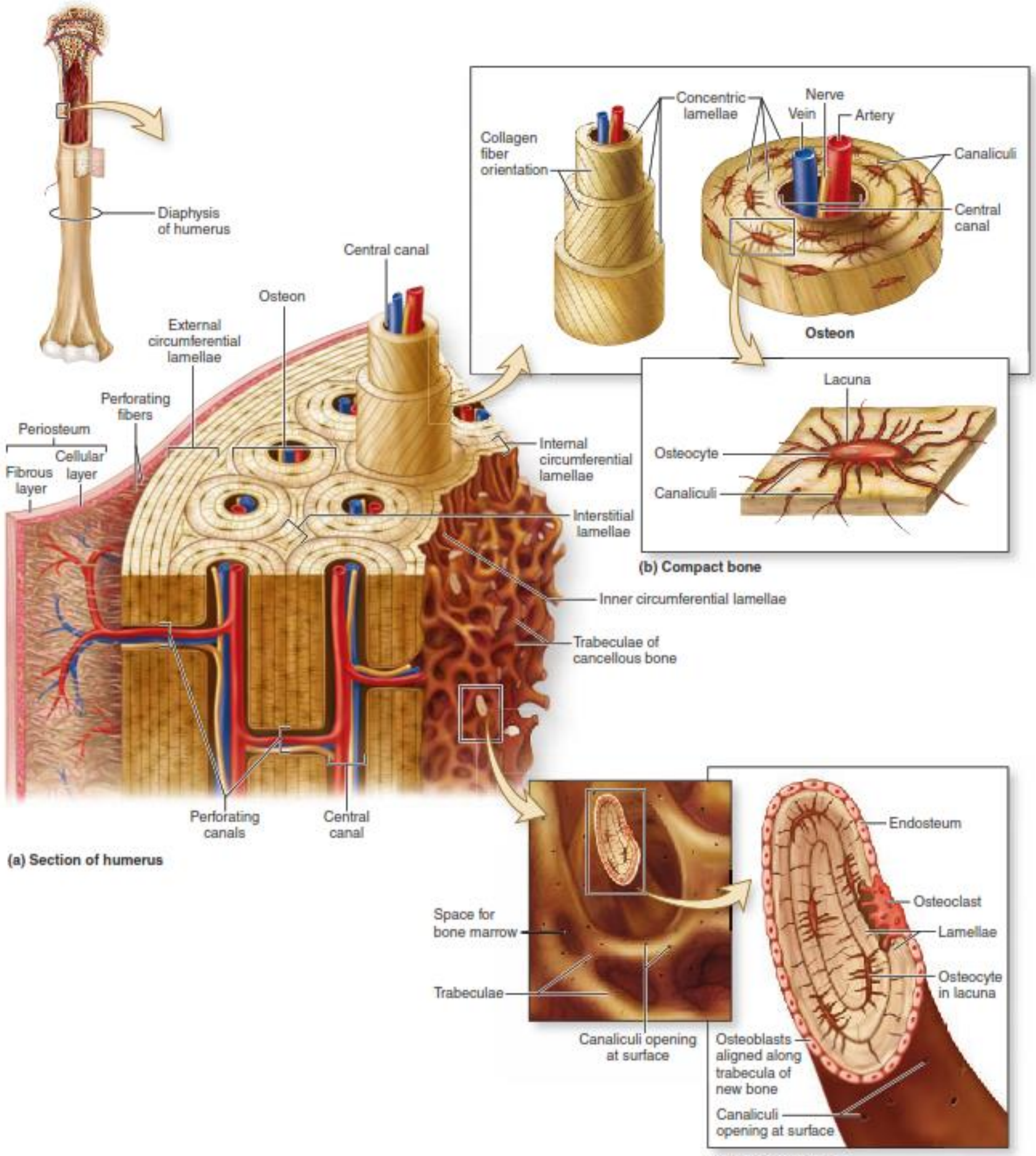
- Its strength is given by the collagen fibers in which these crystals are incorporated

Bone tissue

- In the case of demineralization, the bone becomes flexible like a tendon, and with the removal of the organic substrate, the bone becomes brittle and easily broken.
- In the human body, only enamel and dentin are harder than bone, and only cartilage better withstands mechanical stress
- The outer surface of the bone is covered by a layer of dense connective tissue (periosteum), and the inner endosteum

- Osteogenic cells are found in these bone sheaths

- Inside the bone tissue there are cavities (lacunae) in which they are located mature bone cells - osteocytes



(a) Section of humerus

(b) Compact bone

(c) Cancellous bone

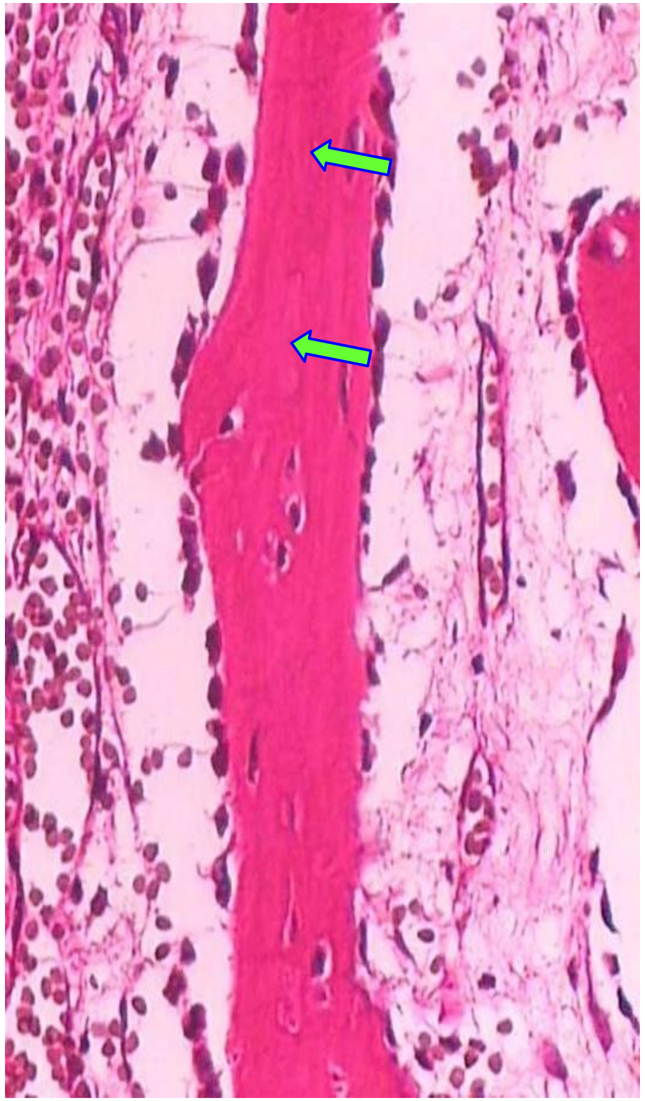
Bone tissue cells

- In the functional sense, four types of cells belong to the bone tissue:
- Osteoprogenitor cells
- Osteoblasts
- Osteocytes
- Osteoclasts
- Osteoprogenitor cells, osteoblasts and osteocytes represent the same type of cell that is in different stages of maturity and activity
- Osteoclasts belong to a special cell line

Bone tissue cells - osteoblasts

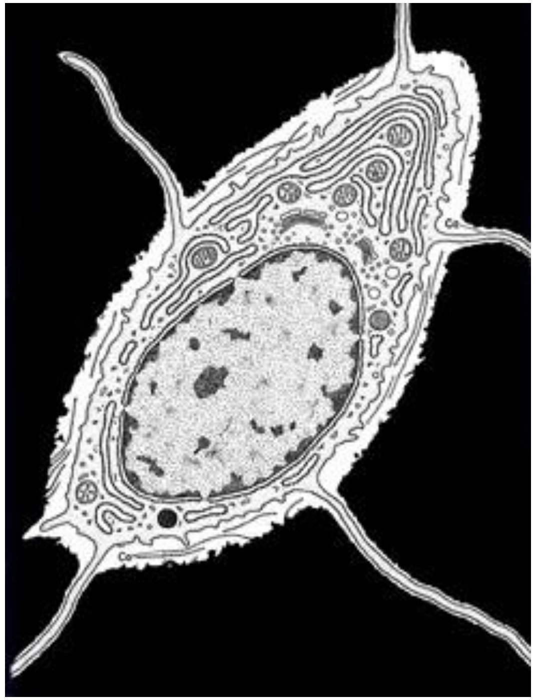
- Young bone cells located on the surface of bone tissue
- They differ from osteoprogenitor cells by their larger dimensions, oval shape, and numerous micro pitches, light round nucleus and well developed organelles, especially those responsible for protein synthesis (granulated ER, Golgi complex)

- They secrete osteoid - an organic part outside the cell matrix, and help in its mineralization.
- Some osteoblasts remain during the secretion "trapped" in the matrix they create around themselves and they become osteocytes



Bone tissue cells - osteocytes

- Mature bone cells "trapped" in the mineralized bone matrix
- They are located in small cavities called lacunae
- There is one osteocyte in each lacuna
- Adjacent lacunae are interconnected narrow bone canals (canaliculi ossei)
- Osteocytes are smaller than osteoblasts and have the shape of a plum stone

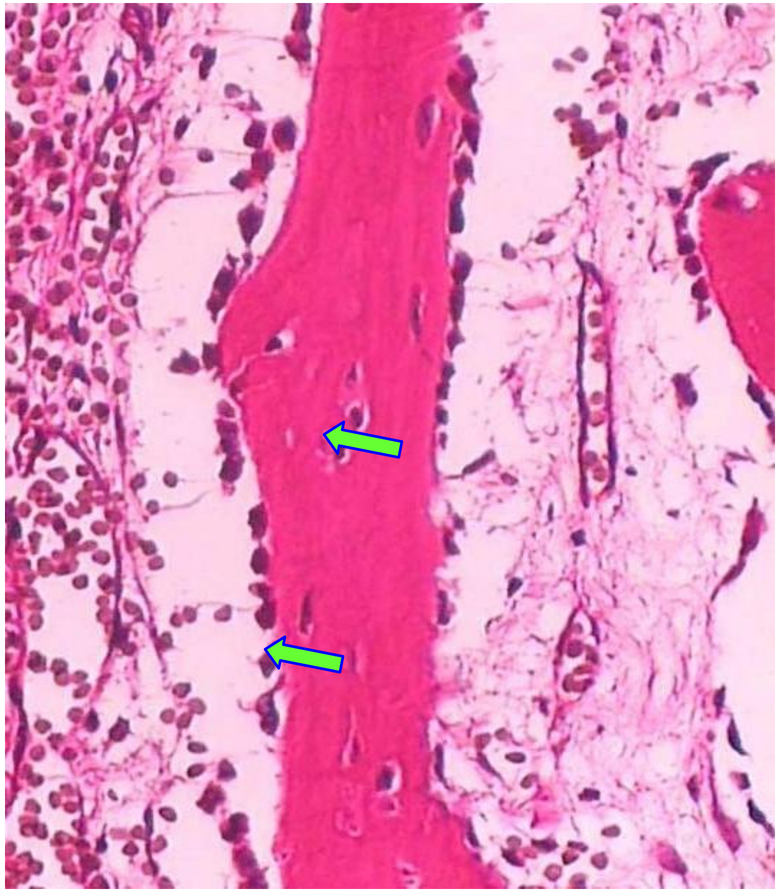


- During their life, they go through phases of activity and rest
  Osteocytes have a long lifespan and do not have the ability to divide.
  Compared to osteblasts, they have weaker organelles

Bone tissue cells - osteocytes

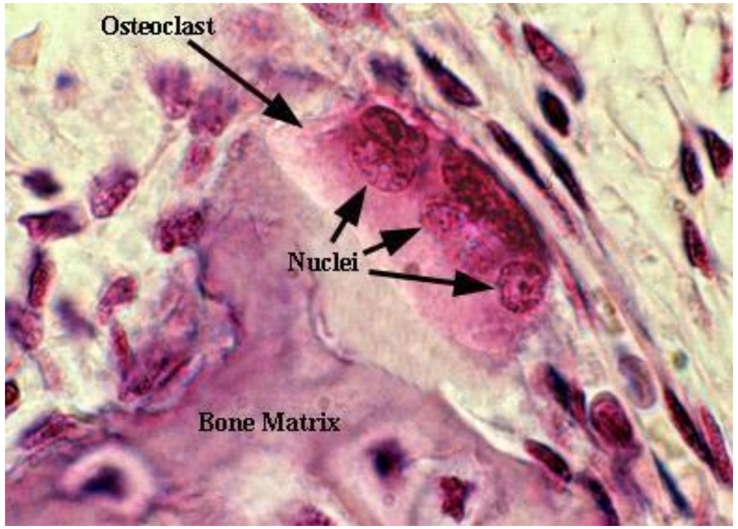
- Numerous thin and long extensions (filopodia) start from their surface and fill the bone canals
- Filopodia of neighboring osteocytes touch, and at the point of contact nexuses are formed

- Through the nexus, nutrients and gases are exchanged between nearby osteocytes (in this way, osteocytes are supplied with necessary substances through each other)
- Their role is to maintain the bone matrix.



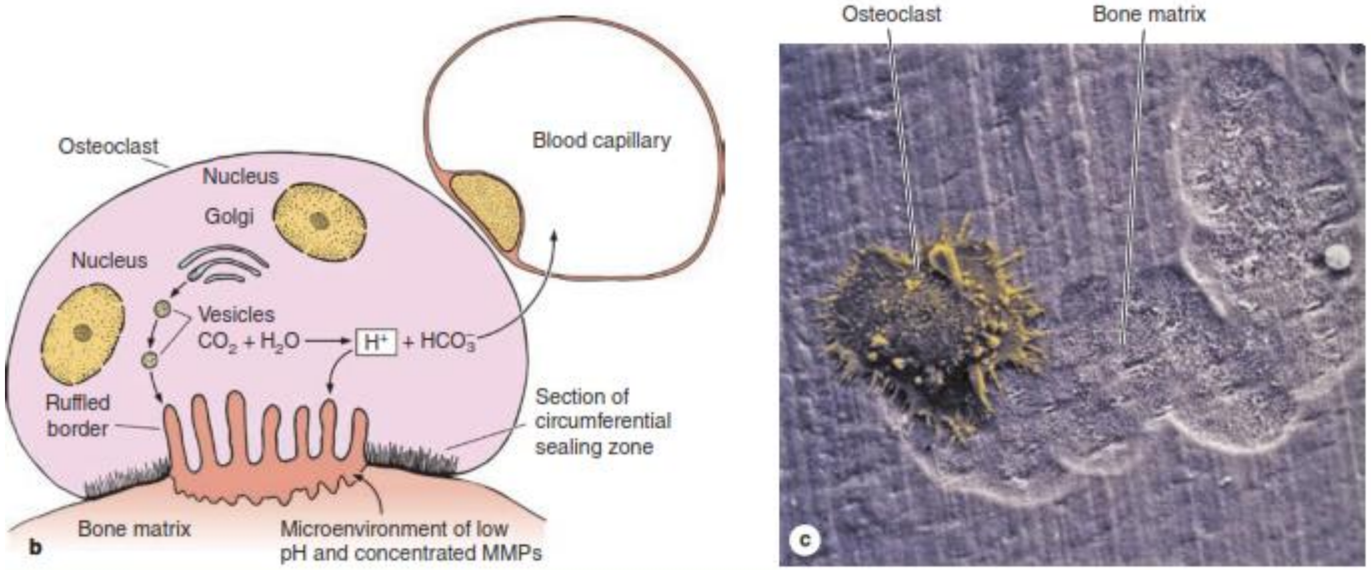
Bone tissue cells - osteoclasts

- Large motile cells that break down bone tissue
- They are formed by the fusion of a large number of monocytes
- They belong to the mononuclear phagocytic system
- They have 2-50 nuclei and well-defined organelles
- They act from the surface of the bone tissue where they make shallow depressions called Hawship's lacunae



Bone tissue cells - osteoclasts

- On the surface facing the bone tissue, osteoclasts have numerous protrusions . That part of the cell is called the ruffled border. The rest part of osteoclast surface is relatively smooth.
- Between the wrinkled edge and the bone there is a narrow subosteoclast space (it is created in it specific acidic microenvironment – catabolic pot



Bone tissue cells - osteoclasts

At the border between the smooth and wrinkled part of the osteoclast surface is located

the so-called bright zone (does not contain organelles and is used by the osteoclast to adhere to the bone)

Bone resorption takes place over the wrinkled edge (matrix demineralization and collagen breakdown) by expelling enzymes into the extracellular space

Cathepsin K i participates in the breakdown of collagen and basic substances

matrix metalloproteinases

HCl secreted by the osteoclast participates in matrix demineralization

* Local and systemic humoral factors regulate osteoclast formation and activity

Systemic factors: parathormone (stimulates), calcitonin (inhibits), corticosteroids, estrogens and androgens

Local factors: RANKL (stimulates), osteoprotegerin (inhibits), interleukins, growth factor

Osteoprogenitor cells

- Resting cells of bone tissue located in periosteum and endosteum
- They have a spindle shape, a flattened core and poorly developed organelles
- They have the ability to divide and differentiate into active bone cells -
- osteoblasts
- They are important for bone growth and fracture healing
- The factor for the activation of these cells is CBFA1 (core binding protein alpha1).

Bone matrix

Organic content:

The largest part of the organic content (about 90%) is collagen type I, and much smaller

part basic substance

The main substance consists of:

Glycoproteins (osteonectin, osteopontin, sialoprotein 1 and 2)

Proteoglycans, which are significantly less in bone than in cartilage

(hyaluronan, chondroitin sulfate and keratan sulfate)

Inorganic content:

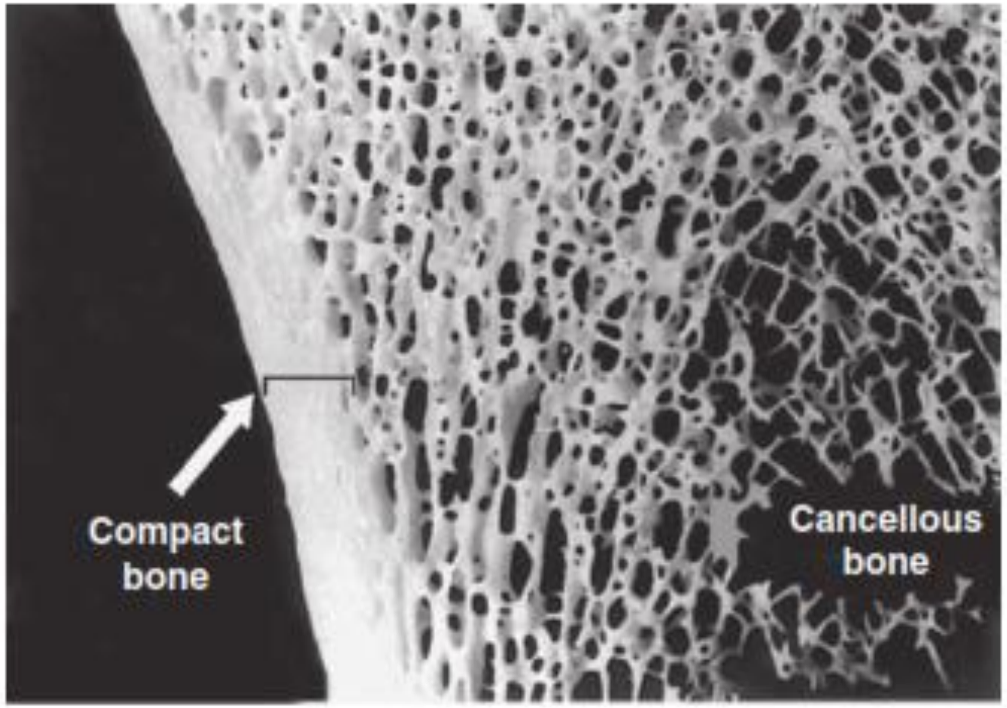
It consists mainly of calcium and phosphorus ions that build hydroxyapatite crystals (they look like needles that dig into collagen fibers).

In addition to calcium and phosphorus, ions are also present in the bone matrix

magnesium, sodium, potassium, bicarbonate, citrate, etc.

Bone structure

- According to the order of occurrence and histologically bone structure can be:
- Primary or immature (formed during embryonic development)
- Secondary or mature (makes the largest part of adult skeleton)



Primary or immature bone

- It is formed during embryonic development or during bone healing
- fracture

- It is temporary in nature and is gradually replaced by mature bone

- It remains permanently only in dental alveoli, auditory ossicles and in
- near the sutures of the flat bones of the skull

- It contains more cells and basic substances and less minerals than mature bone
- Collagen fibers and osteocytes are distributed randomly, without any order or rule

Secondary or mature bone

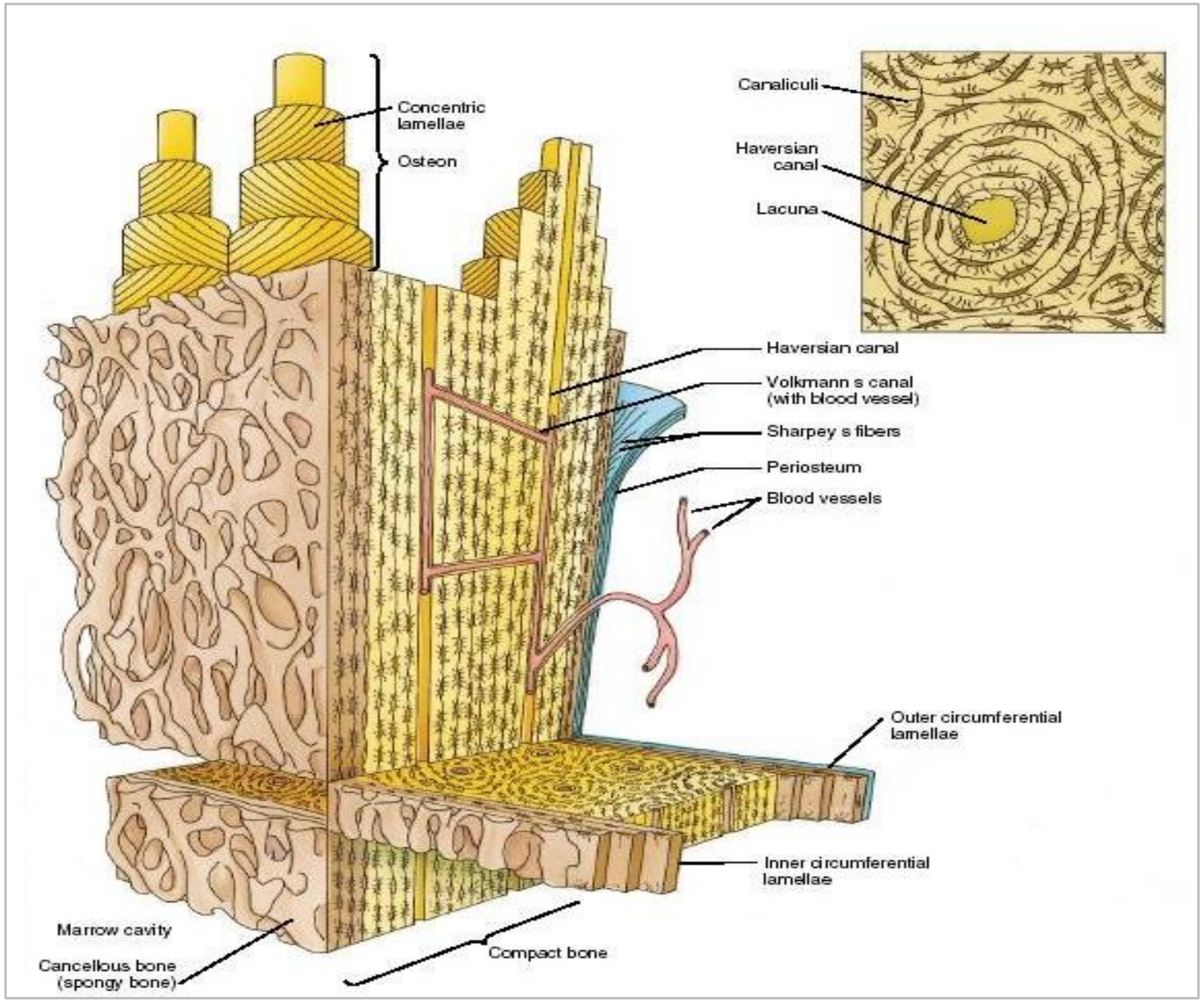
- It makes up the largest part of the skeleton in adults

- It can be compact and spongy
- Compact bone - bone tissue dominates, and the tiny canals that cut it lengthwise and crosswise are hard to see with the naked eye.
- Cancellous bone - basically has a spongy appearance because it contains narrow bone beds separated by wide cavities in which the bone marrow is located
- A layer of collagen fibers and a part of the mineralized matrix in which they are embedded form one bone lamella (sheet) - lamellar bone

- Mature bone cells are usually located between adjacent lamellae

Type of Bone	Histological Features	Major Locations	Synonyms
Woven bone, newly calcified	Irregular and random arrangement of cells and collagen; lightly calcified	Developing and growing bones; hard callus of bone fractures	Immature bone; primary bone; bundle bone
Lamellar bone, remodeled from woven bone	Parallel bundles of collagen in thin layers (lamellae), with regularly spaced cells between; heavily calcified	All normal regions of adult bone	Mature bone; secondary bone
Compact bone, ~80% of all lamellar bone	Parallel lamellae or densely packed osteons, with interstitial lamellae	Thick, outer region (beneath periosteum) of bones	Cortical bone
Cancellous bone, ~20% of all lamellar bone	Interconnected thin spicules or trabeculae covered by endosteum	Inner region of bones, adjacent to marrow cavities	Spongy bone; trabecular bone; medullary bone

Secondary or mature bone



Cancellous bone

- It makes up about 10% of the skeleton of an adult

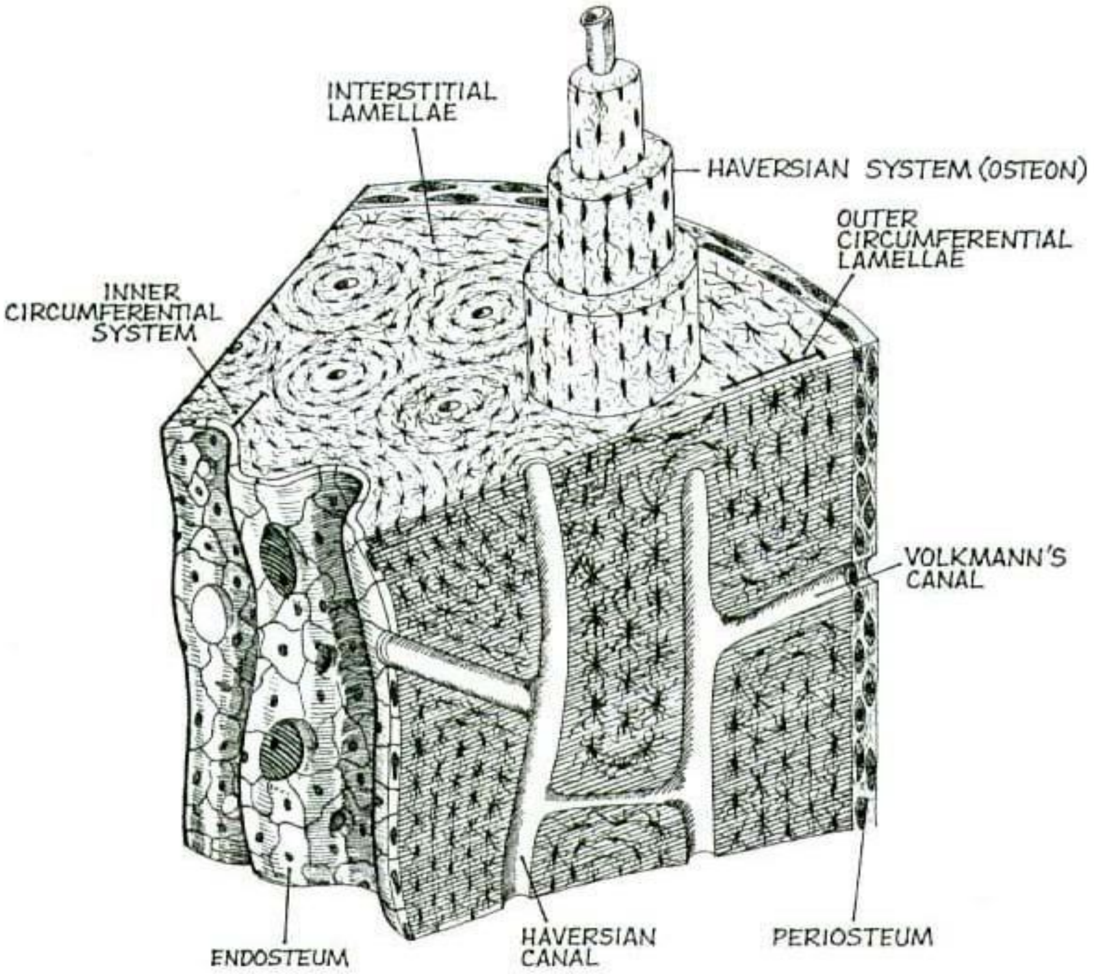
- It consists of bone beds that limit the narrow spaces filled
- bone marrow

- Bone beds are usually thin and do not contain blood vessels, ie
- Haversian and Folkmanian canals

- Osteocytes from cancellous bone are fed by diffusion of substances from
- bone marrow

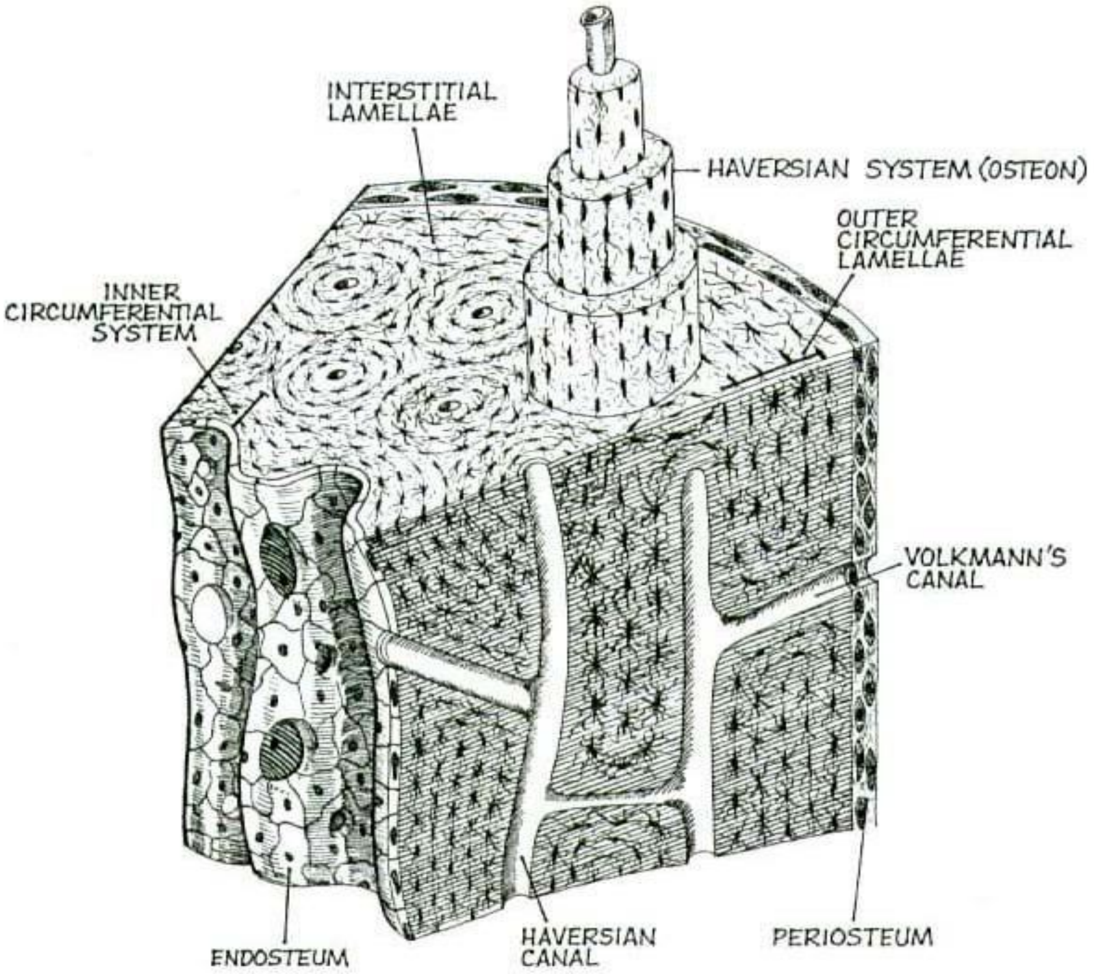
Compact bone

- The basic morphological unit of compact bone is the osteon or Havers system.
- Compact bone contains four types of lamellae, most of which are stacked concentrically, like knots in a tree trunk
- Between the lamellae there are lacunae with osteocytes
- Adjacent lamellae are connected by narrow canals (canaliculi ossei) through which
- osteocytes provide filopodia and establish mutual communication.



Compact bone

- Communication between osteons is carried out through Folkman's channels
- In addition to concentric (Haversian) lamellae, they are described in compact bone
- three more types of lamellae:
- interstitial (transitional) lamellae between osteons
- outer circular lamellae below the periosteum
- internal circular lamellae around the bone marrow cavity



Bone histogenesis

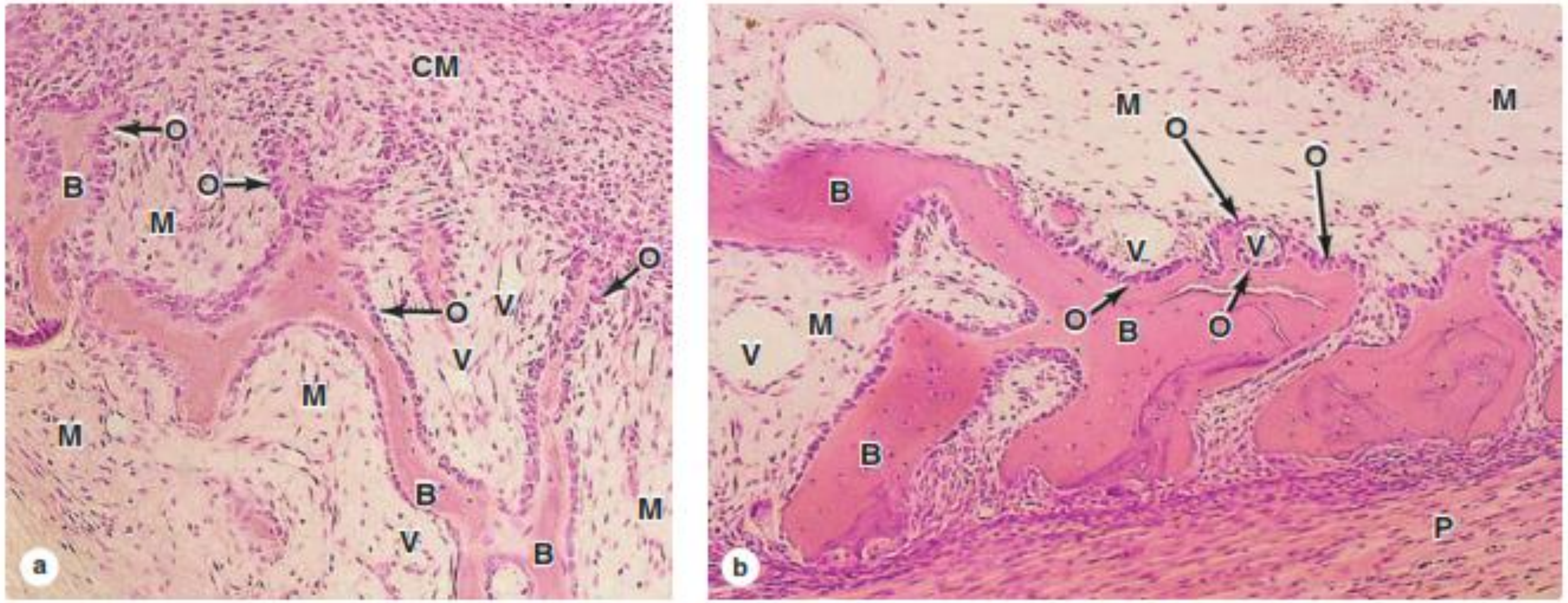
- A smaller part of the skeleton is formed by intramembranous ossification, and a larger part
- by the process of enchondral ossification
- This division indicates only the mechanism of initiation of the ossification process (with intramembranous ossification - directly from the mesenchyme, with enchondral - through the previous cartilaginous model)

- In both cases, primary (immature) bone is formed first, which it later replaces
- secondary (mature) bone

- Even after the cessation of growth in mature bone, two continuous processes take place
- the opposite process - creation of new and breakdown of existing bone tissue (reshaping or remodeling)

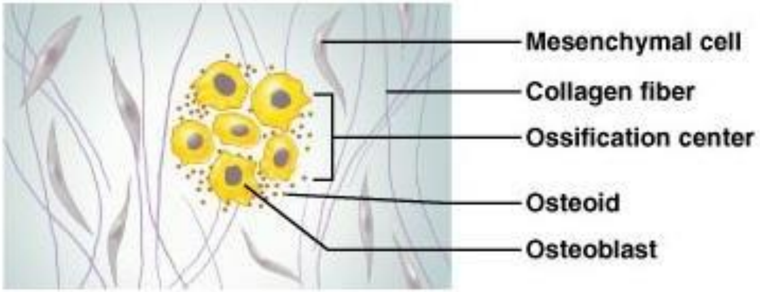
Bone histogenesis

Intramembranous ossification (direct ossification)
This is how most of the flat bones (bones of the roof of the skull, face, clavicle) are formed.
Mesenchymal cells cluster, differentiate into osteoblasts and form
primary ossification center from which the osteoid bands spread radially in the form of beds (trabeculae)
The osteoid is gradually mineralized, and the cells within the trabeculae
transform into osteocytes



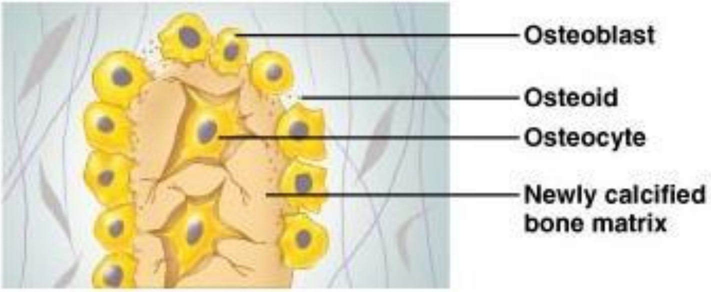
Bone histogenesis

- **Intramembranous ossification (direct ossification)**



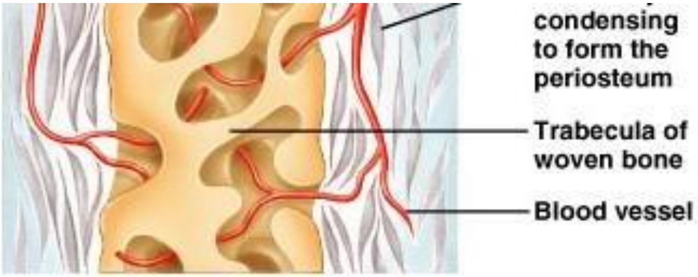
① **An ossification center appears in the fibrous connective tissue membrane.**

- Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.



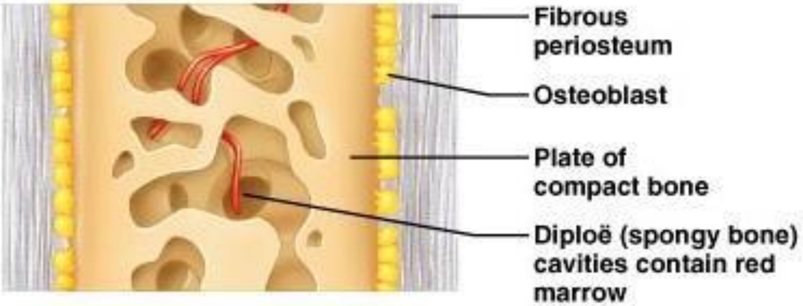
② **Bone matrix (osteoid) is secreted within the fibrous membrane.**

- Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
- Trapped osteoblasts become osteocytes.



③ **Woven bone and periosteum form.**

- Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae.
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.



④ **Bone collar of compact bone forms and red marrow appears.**

- Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.

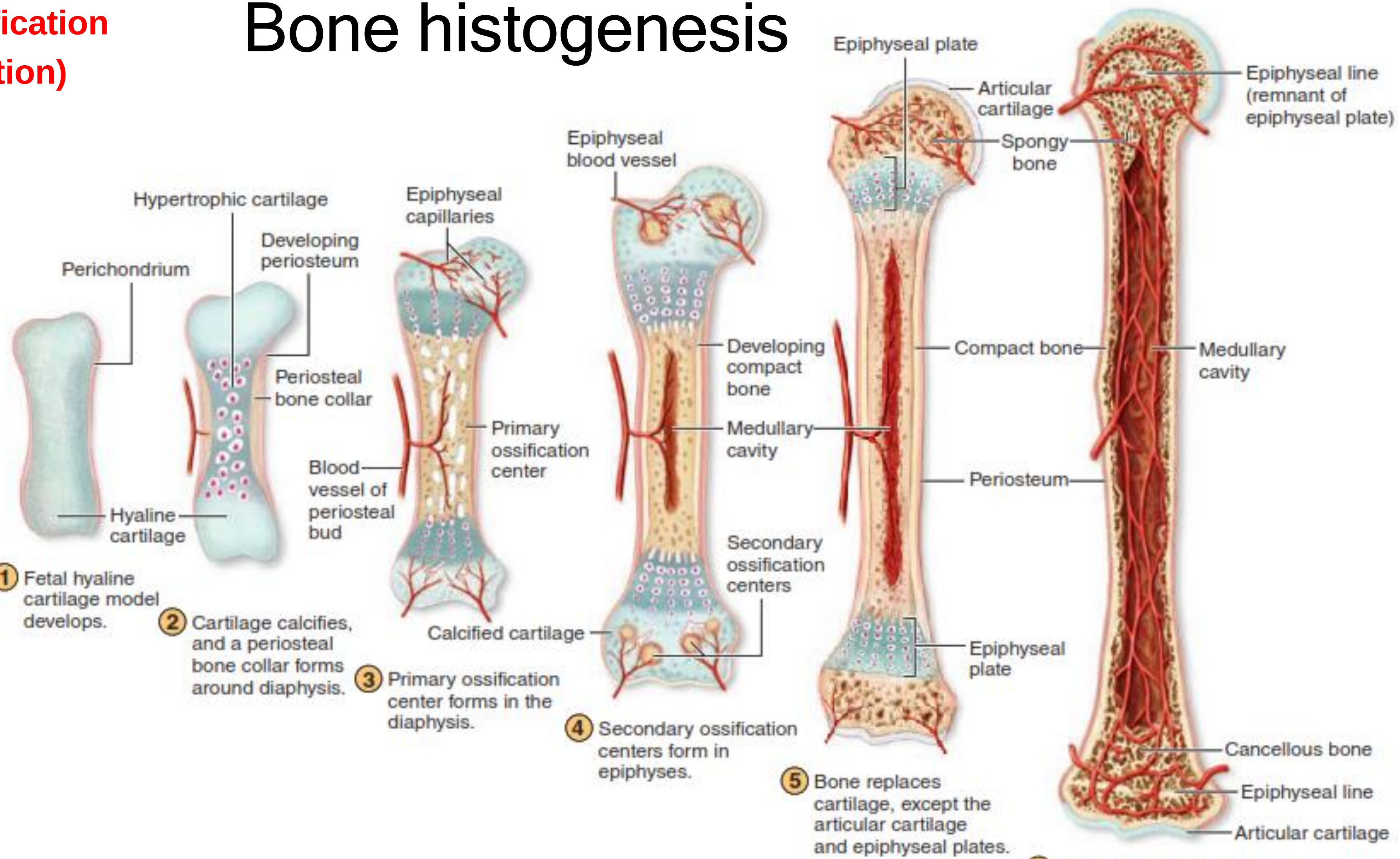
Bone histogenesis

- Enchondral ossification (indirect ossification)
- This is how most of the bones of the human body (the bones of the base of the skull, the spine, the pelvis and the bones of the limbs) are formed.
- The process has two stages, in the first a miniature skeleton is created from hyaline cartilage (cartilaginous model), and in the second bone tissue is deposited in its place
- The cartilaginous model is created by chondroblasts originating from mesenchymal cells and it grows by appositional and interstitial growth

- It begins in the twelfth week of development and lasts as long as a person's growth lasts
- The area in the diaphysis where ossification begins is called the primary (diaphyseal) center of ossification and from there ossification spreads towards both epiphyses

Bone histogenesis

- **Enchondral ossification (indirect ossification)**

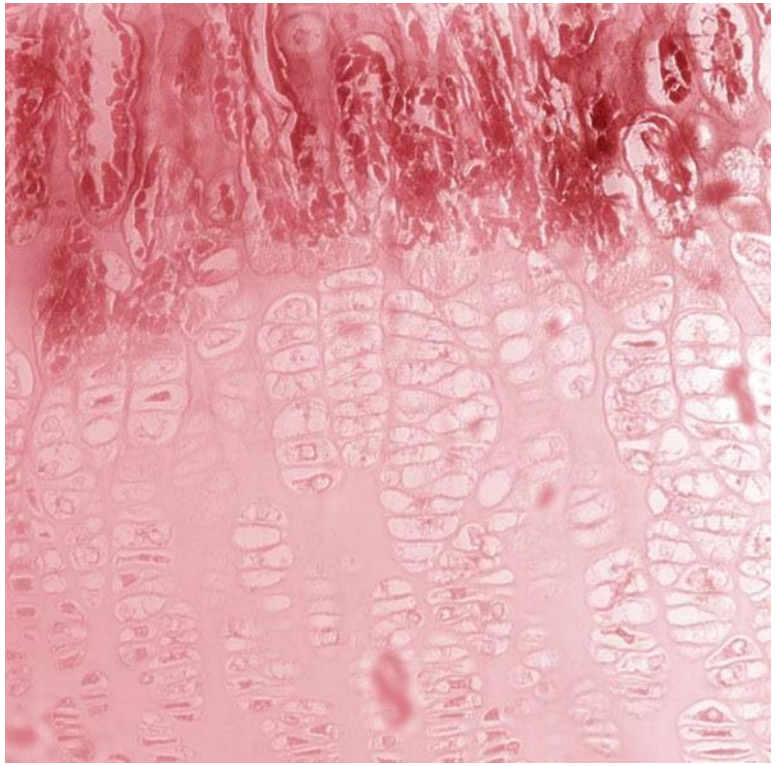


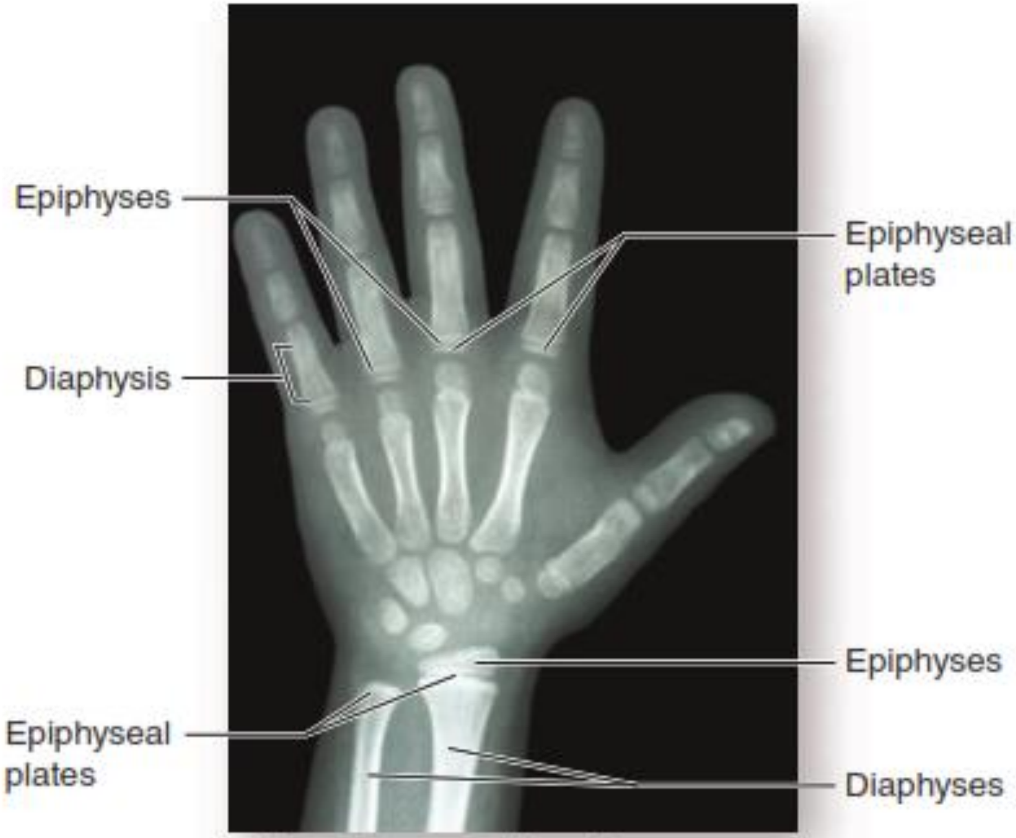
1. Fetal hyaline cartilage model develops.
2. Cartilage calcifies, and a periosteal bone collar forms around diaphysis.
3. Primary ossification center forms in the diaphysis.
4. Secondary ossification centers form in epiphyses.
5. Bone replaces cartilage, except the articular cartilage and epiphyseal plates.
6. Epiphyseal plates ossify and form epiphyseal lines.

Bone histogenesis

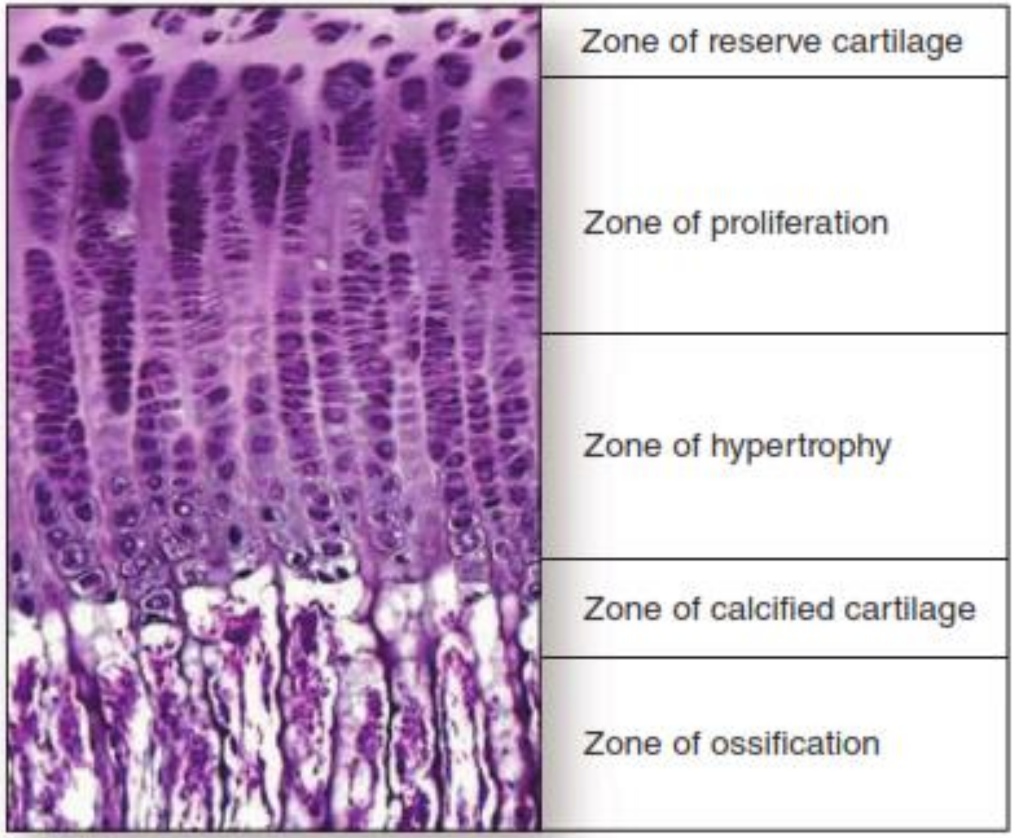
- At the border between the epiphysis and the diaphysis, a band of cartilaginous tissue remains, called the epiphyseal cartilage or epiphyseal plate.
- (growth plate)

- In the epiphyseal plate it can be separated
- five zones:
- resting zone
- proliferation zone
- zone of hypertrophy
- zone of calcification
- ossification zone

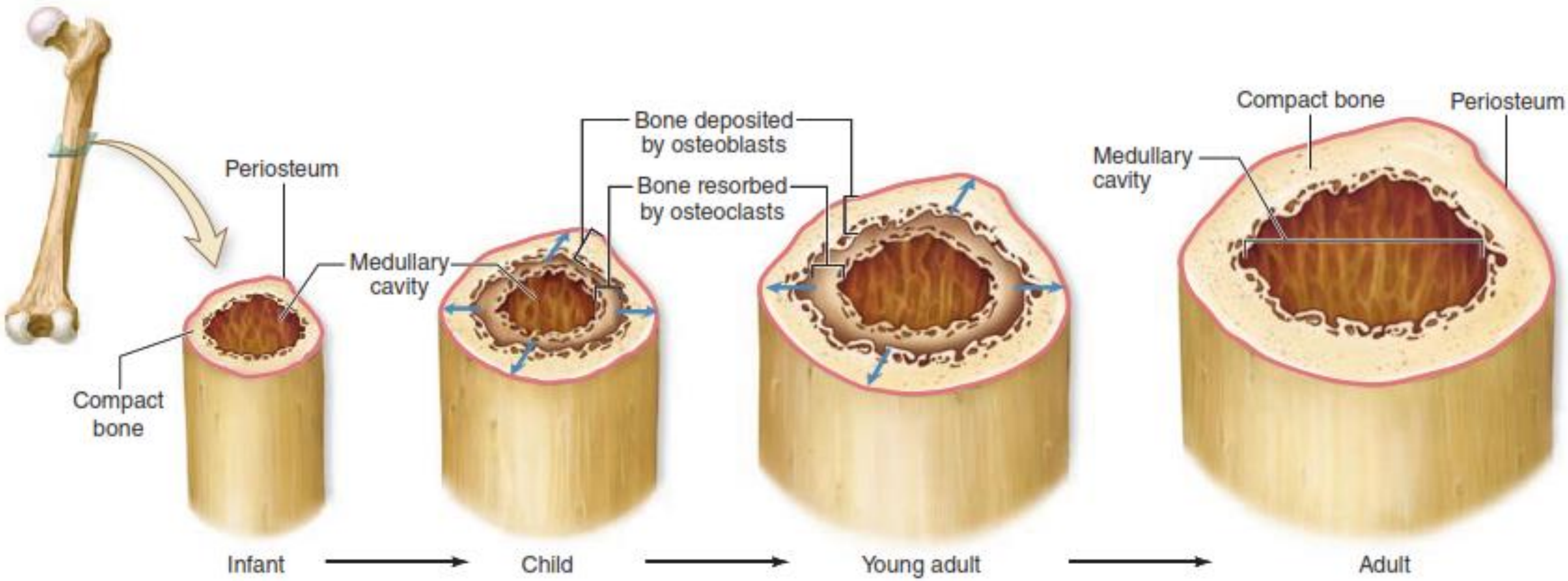




a X-ray of a normal hand



b Epiphyseal plate



Bones increase in diameter as new bone tissue is added beneath the periosteum in a process of appositional growth. Also called radial bone growth, such growth in long bones begins with formation of the bone collar early in endochondral ossification. During radial bone growth, formation of new bone at the periosteal surface occurs concurrently with bone removal at the endosteal surface around the large medullary, enlarging this marrow-filled region and not greatly increasing the bone's weight.

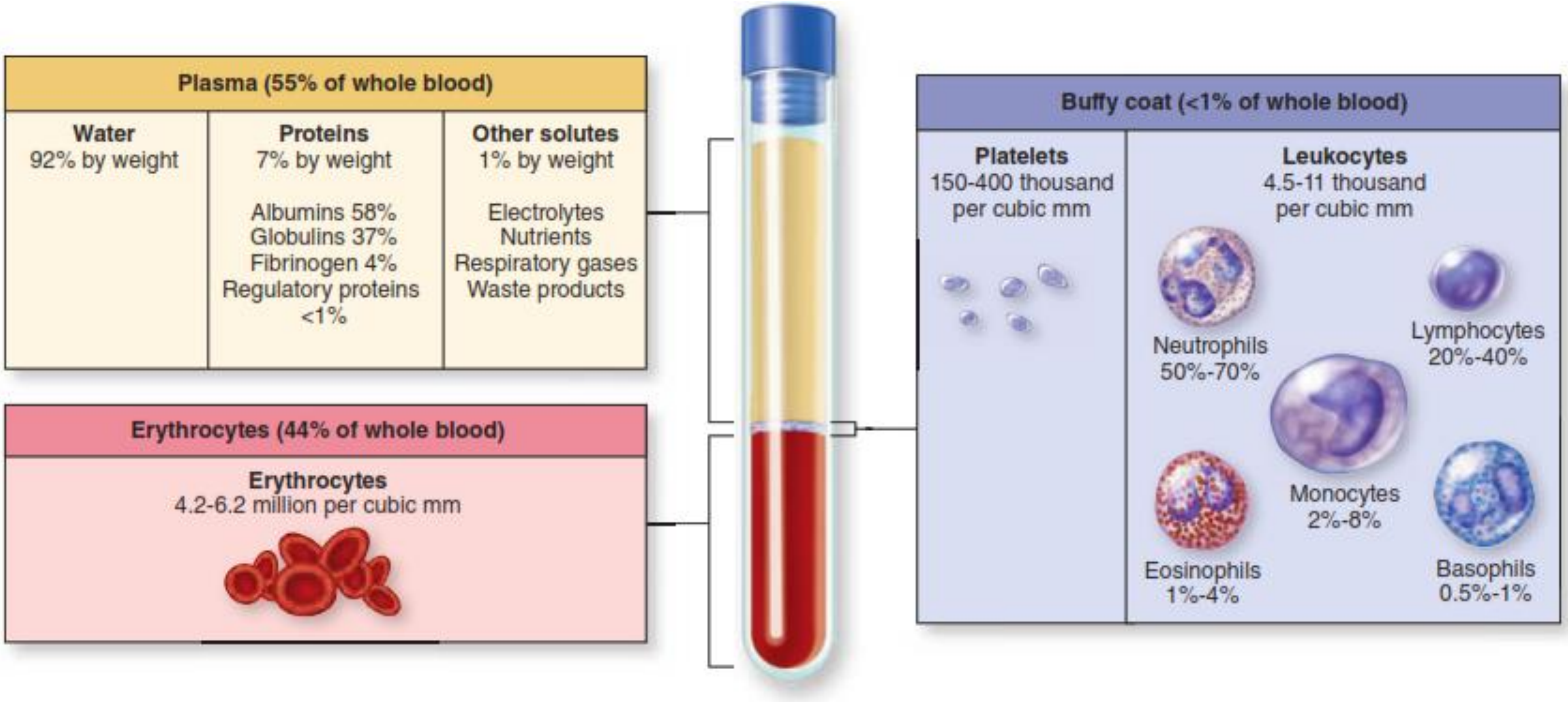
- Factors that regulate bone growth
- Vitamin D: increases the absorption of Ca from the intestine
- Parathyroid hormone (PTH): increases the level of calcium in the blood
- Calcitonin: reduces the level of calcium in the blood
- Growth hormone: causes bone growth through the growth of the epiphyseal plate
- Sex hormones: closure of the epiphyses of the bone
- IGF, TNF, TGF beta, BMP (bone morphogenic protein), IL1, IL6......

Blood

- Specialized connective tissue, which does not have fibers, and the cells do not have a fixed position.
- Basic roles of blood:
- Transport of oxygen and nutrients,
- Transport of carbon dioxide and metabolic products,
- Maintaining homeostasis, osmotic pressure and acid-base balance,
- Dissemination of hormones and regulators,
- Regulation of body temperature,
- Transport of immunoglobulins and lymphocytes.

Blood composition

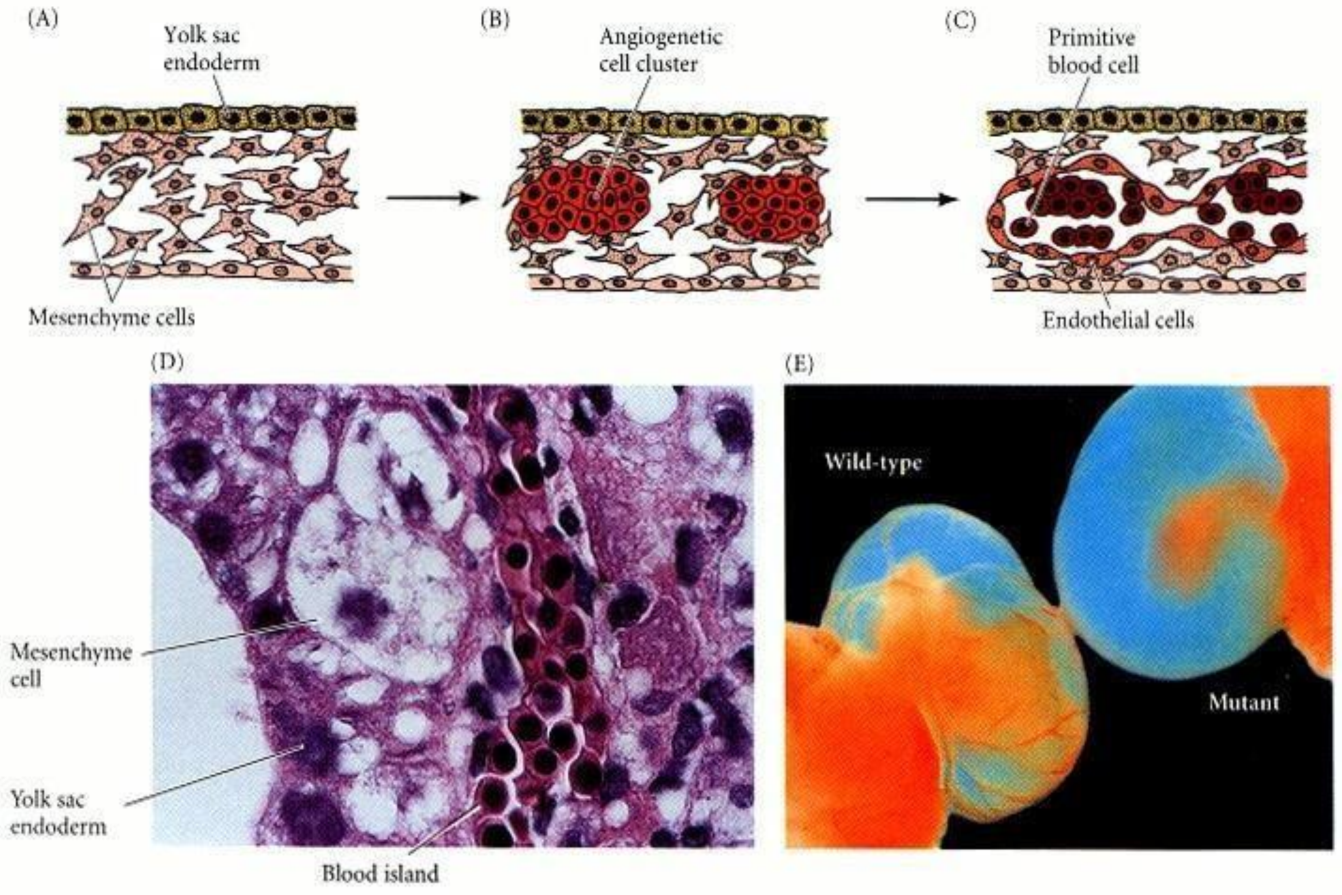
- By centrifuging the blood, the precipitate is separated, which consists of 45% blood cells, and 55% liquid intercellular substance - blood plasma.
- Blood plasma consists in the largest percentage of water (91-92%) in which proteins, ions, glucose, vitamins, lipids, amino acids, hormones and enzymes are dissolved.
- Plasma proteins (7-8%) consist of albumins (responsible for osmotic pressure), globulins (immunoglobulins), and fibrinogen (responsible for blood clotting).
- The blood cells in the largest number are erythrocytes 45%, and the rest 1% are leukocytes and thrombocytes.



Plasma (55% of whole blood)
Water
92% by weight
Proteins
7% by weight
Albumins 58%
Globulins 37%
Fibrinogen 4%
Regulatory proteins
<1%
Other solutes
1% by weight
Electrolytes
Nutrients
Respiratory gases
Waste products
Erythrocytes (44% of whole blood)
Erythrocytes
4.2-6.2 million per cubic mm
Buffy coat (<1% of whole blood)
Platelets
150-400 thousand
per cubic mm
Leukocytes
4.5-11 thousand
per cubic mm
Neutrophils
50%-70%
Lymphocytes
20%-40%
Monocytes
2%-8%
Eosinophils
1%-4%
Basophils
0.5%-1%

Hemopoiesis

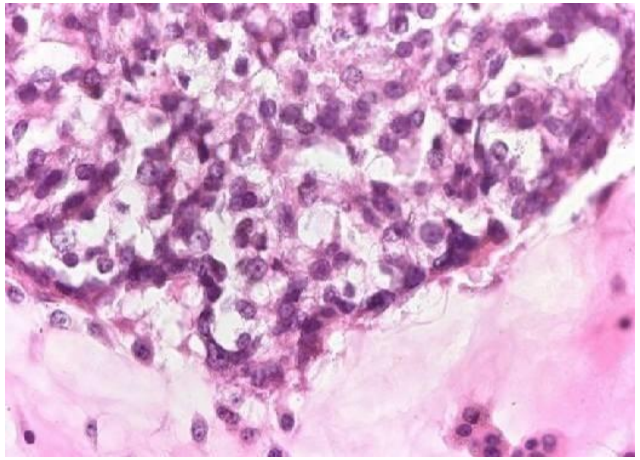
- It represents the process of creation and maturation of mature blood elements.
- It begins in the third week of embryonic development and lasts until the end of life.
- It is divided into prenatal and postnatal hematopoiesis

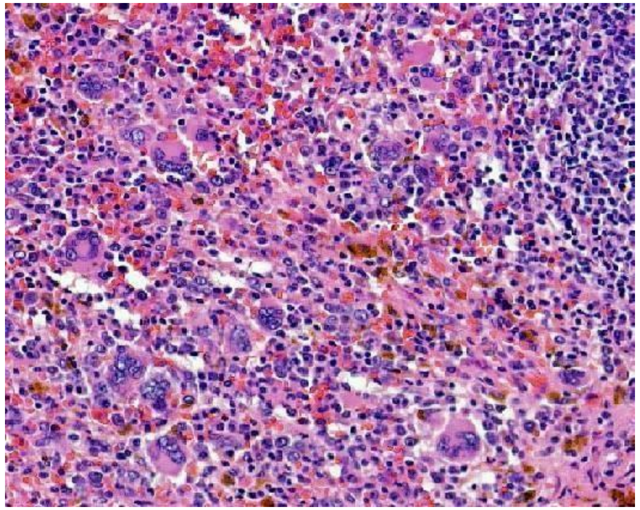


Prenatal hematopoiesis

- It begins with the formation of large embryoblast (megaloblast) cells in the wall of the yolk sac in the third week of embryonic development.
- Megaloblasts then mature into primitive erythrocytes.
- In the sixth week of gestation, the focus of hematopoiesis is moved to the liver where
- the formation of leukocytes and trobocytes begins.
- In the seventh week, hematopoiesis takes place in the spleen.

- From the sixth month of intrauterine development
- the main hematopoietic organ becomes bone core

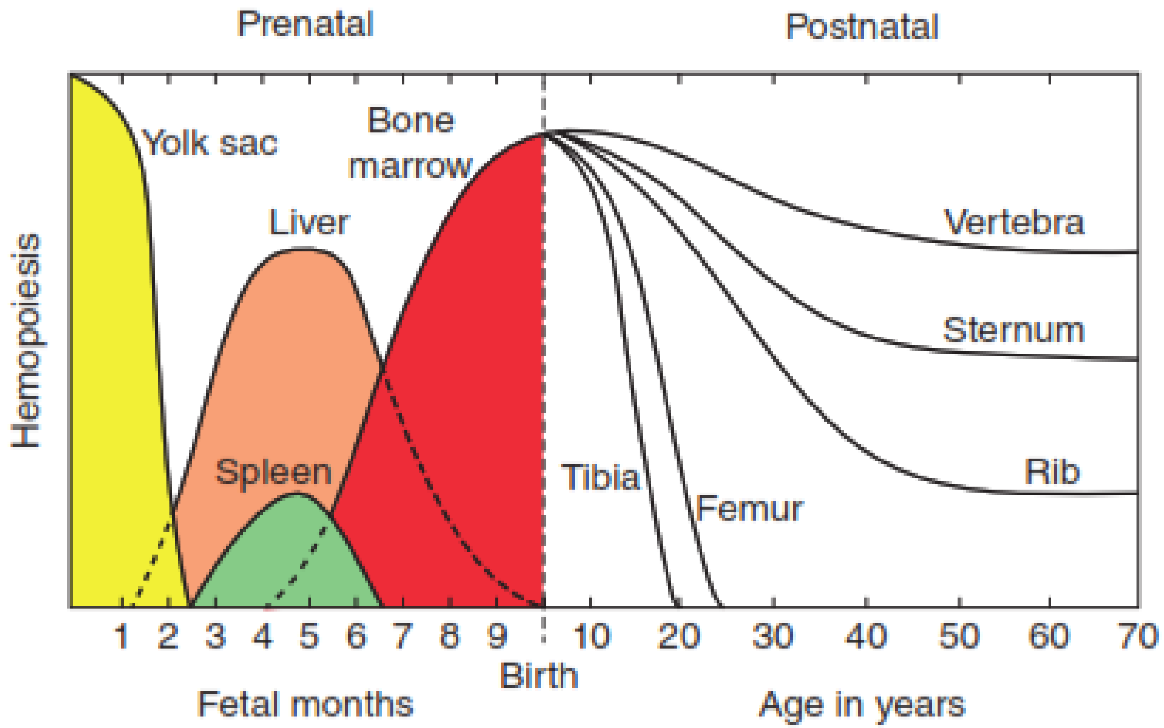




Postnatal hematopoiesis

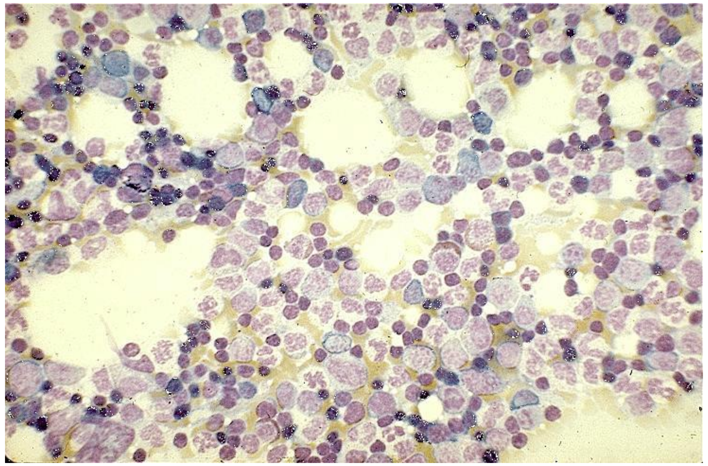
- It takes place in hematopoietic tissue
- red bone marrow.

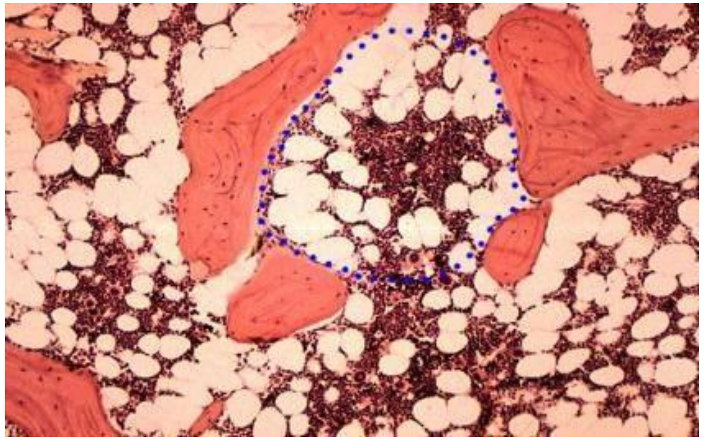
- Liver and spleen in the postnatal period
- period, they do not participate in hematopoiesis, except in certain pathological conditions.
- In normal physiological conditions, only mature cellular elements go into the circulation, the exception being lymphocytes whose maturation and
- functional activation ends in
- lymphatic organs.



Bone marrow

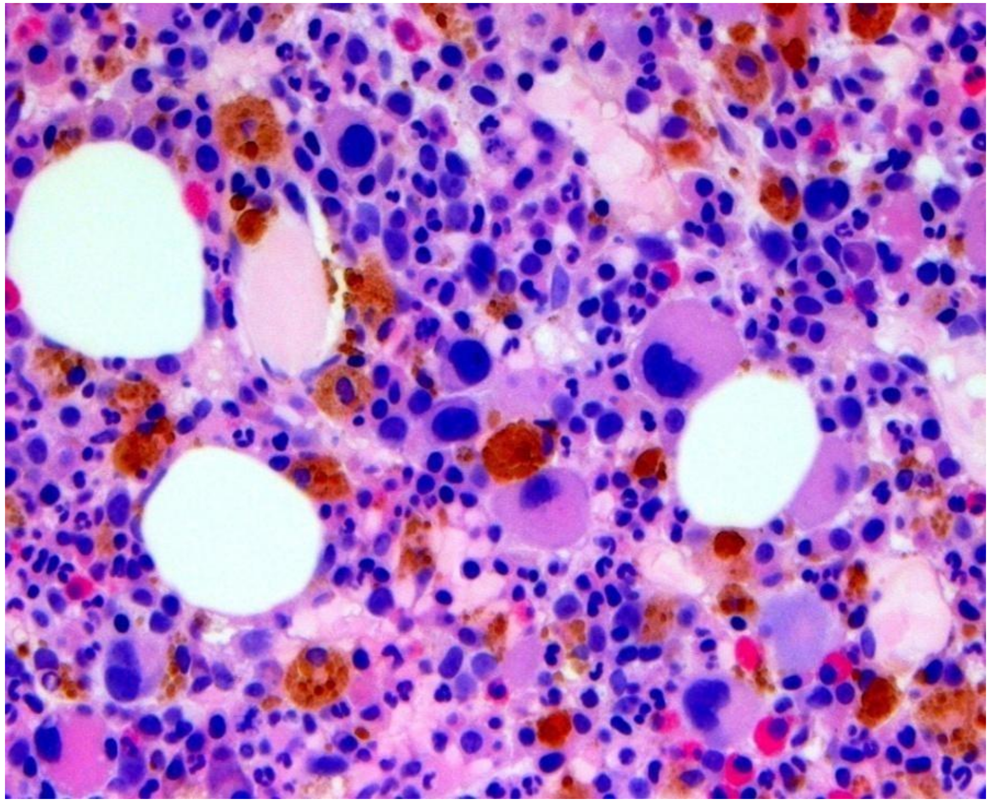
- It represents a specialized well-vascularized reticular connective tissue in which hematopoiesis takes place.
- In newborns, all bone cavities are filled with active bone marrow called red bone marrow.
- From the age of five, the process of infiltration by fat cells begins, so that in adults, the red bone marrow lags behind only in flat bones, while the rest are filled with yellow (fatty) bone marrow.
- One of the most important characteristics of bone marrow is cellularity.





Bone marrow

- Stroma
  - Reticular connective tissue
  - Fat cells, macrophages and etc.
- Vascular compartment
  - Sinusoidal capillaries
  - Hematopoietic strips



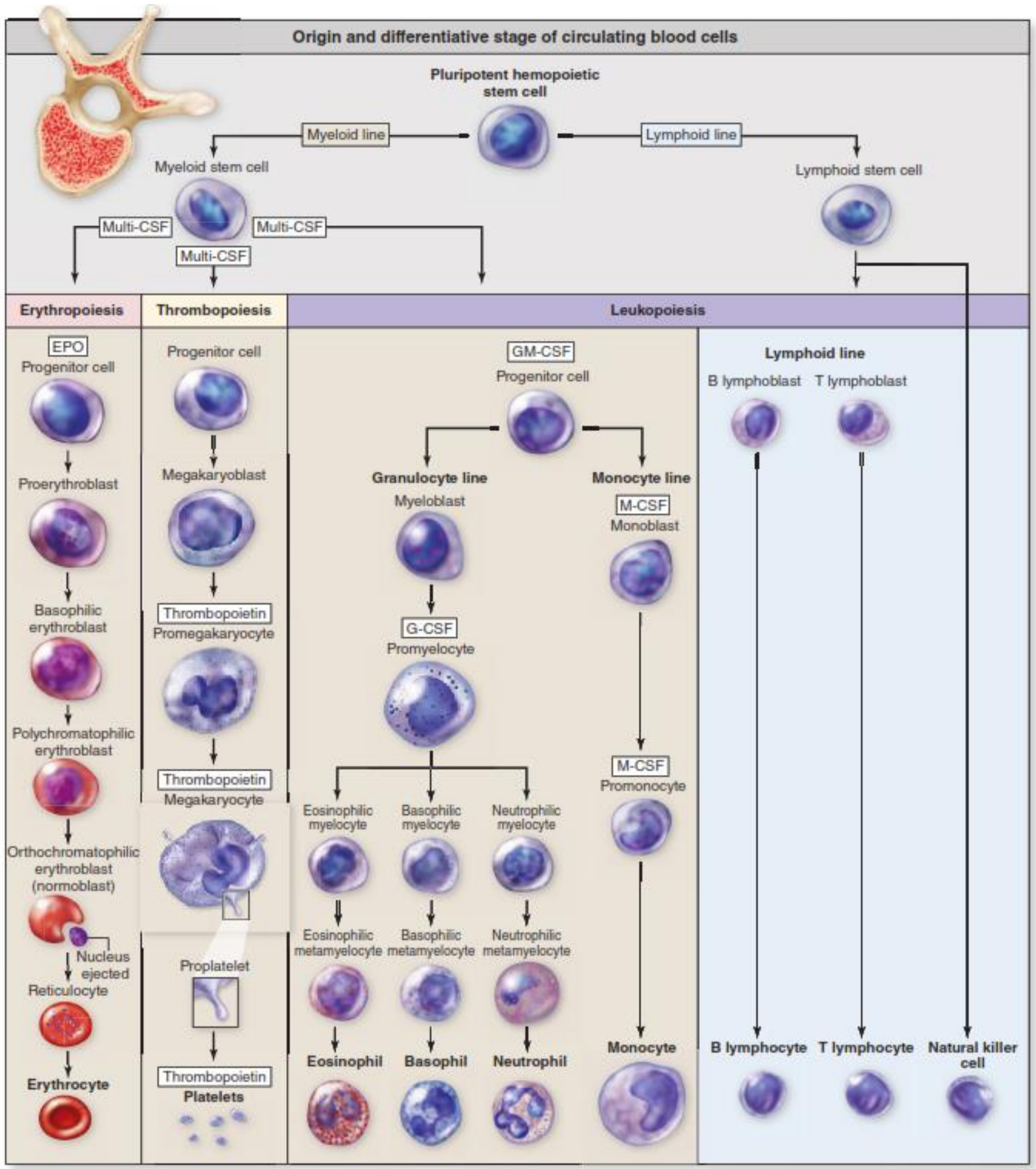
Stem, progenitor and precursor cells

- Cells of all blood lineages arise from a common pluripotent stem cell in the bone marrow.
- The basic characteristics of the stem cell are the impossibility of morphological identification, self-renewal, orientation, determinism.

- The division of these cells results in two types of multipotent stem cells:

- cells of the myeloid lineage

- cells of the lymphocyte lineage

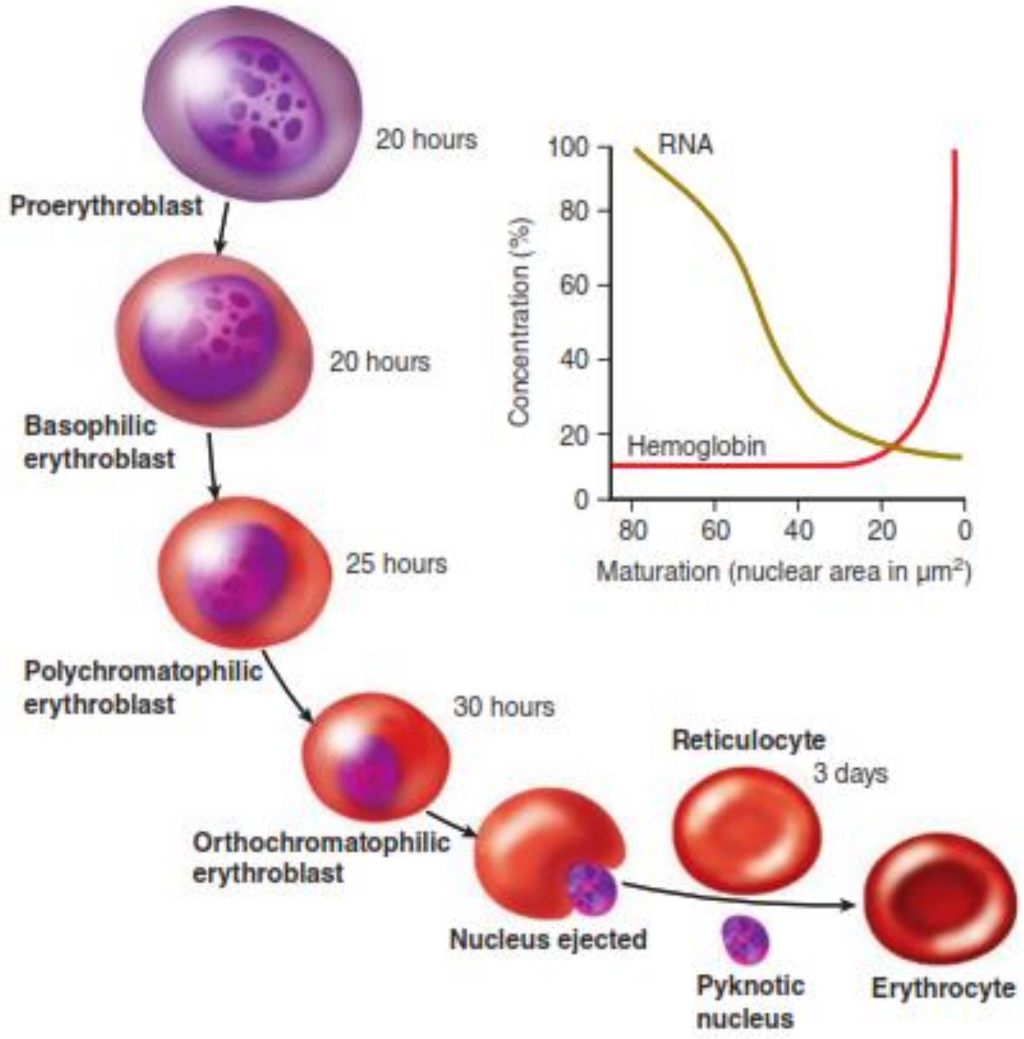


Stem, progenitor and precursor cells

*The division of the multipotent stem cell for the formation of the myeloid lineage produces five types of progenitor cells for the formation of erythrocytes, eosinophilic granulocytes, basophilic granulocytes, trobocytes and a common progenitor cell for the formation of neutrophil granulocytes and monocytes.
*The division of the multipotent stem cell of the lymphocyte lineage results in two
*cell types of progenitor cells, one for the formation of T lymphocytes, a
*other B lymphocytes.
*Proliferation and differentiation of progenitor cells give rise to the first morphologically differentiated cells called precursor cells.
*Further differentiation of precursor cells leads to the formation of a mature cell.

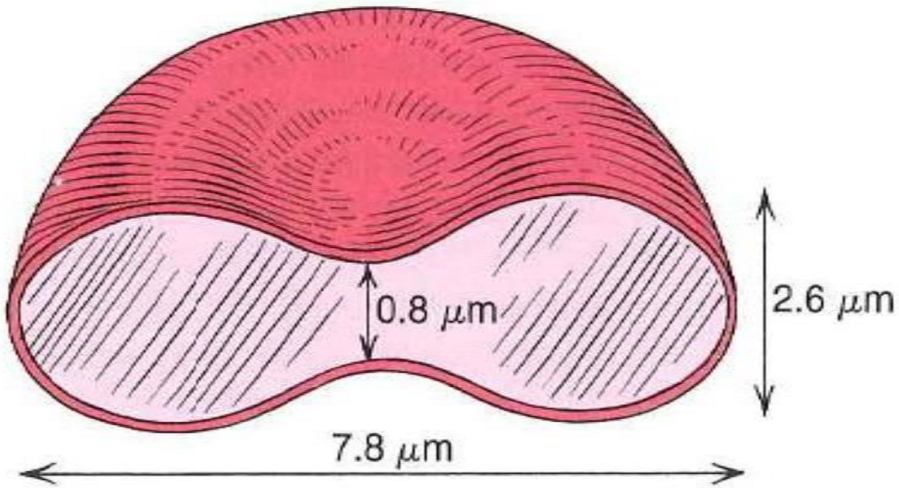
Erythrocyte maturation

- The process of formation and maturation of erythrocytes.
- Erythropoiesis is regulated by various factors, the most important of which is the hormone erythropoietin.
- Stages of erythrocyte development:
  - Proerythroblast
  - Basophilic erythroblast
  - Polychromatophilic erythroblast
  - Acidophilic erythroblast - (nucleus expulsion)
  - Reticulocyte (contains mitochondria, ribosomes, Golgi apparatus)
  - Erythrocyte
- The process of differentiation and maturation of erythrocytes is characterized by:
- Reduction in cell size,
- gradual loss of cytoplasmic basophilia,
- organelle reduction,
- increase in hemoglobin synthesis and
- reducing the size of the sail until its complete disappearance.

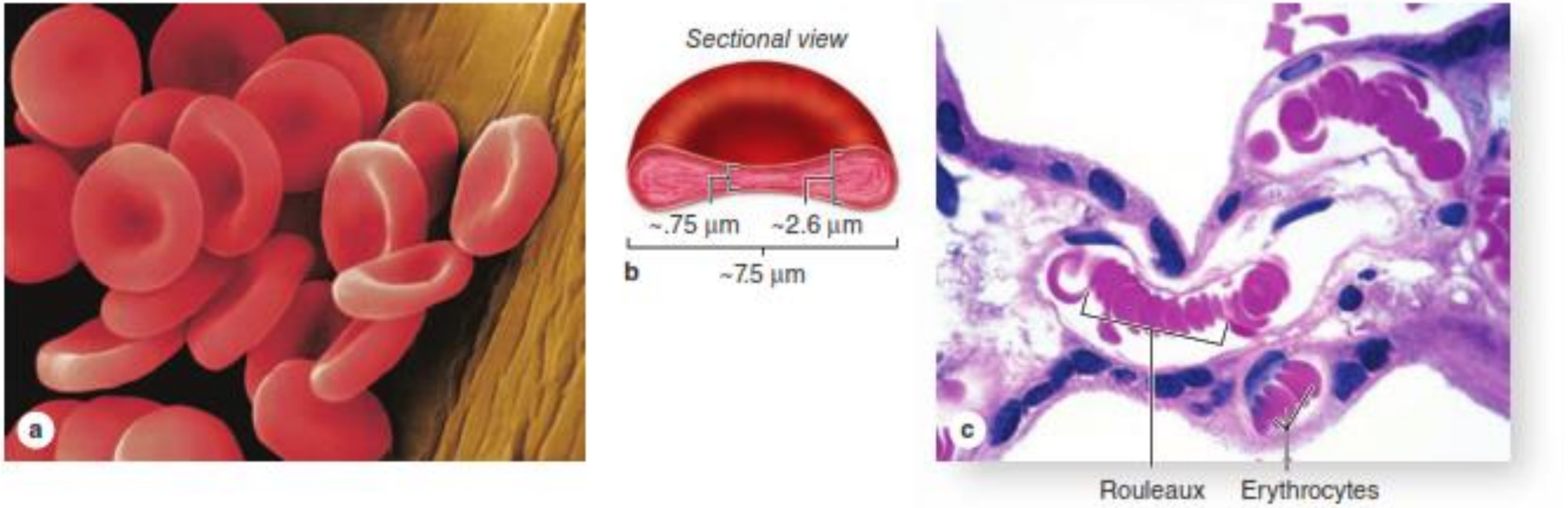


Erythrocytes

* Erythrocytes are in charge of transporting oxygen and
* removal of carbon dioxide from all cells in the body.
* Mature erythrocytes have the appearance of a biconcave disk with a diameter of 7.5 x 2.6 μm
* An erythrocyte is a cell without a nucleus and mitochondria
* whose shape and elasticity it enables
* spectrin membrane skeleton
* Normal number of erythrocytes
* for men it is 4.3-5.7 million, and for women
* 3.9-5.0 million.



* The lifespan is 120 days, after which the aged cells are broken down in the spleen, bone marrow and liver. The main component of erythrocytes is hemoglobin, which transports oxygen from the lungs to the tissues and carbon dioxide in the reverse direction
* *It is synthesized during the development of the erythrocyte lineage and consists of a protein part - globin and a functional group - heme, which contains an iron ion in the central part.

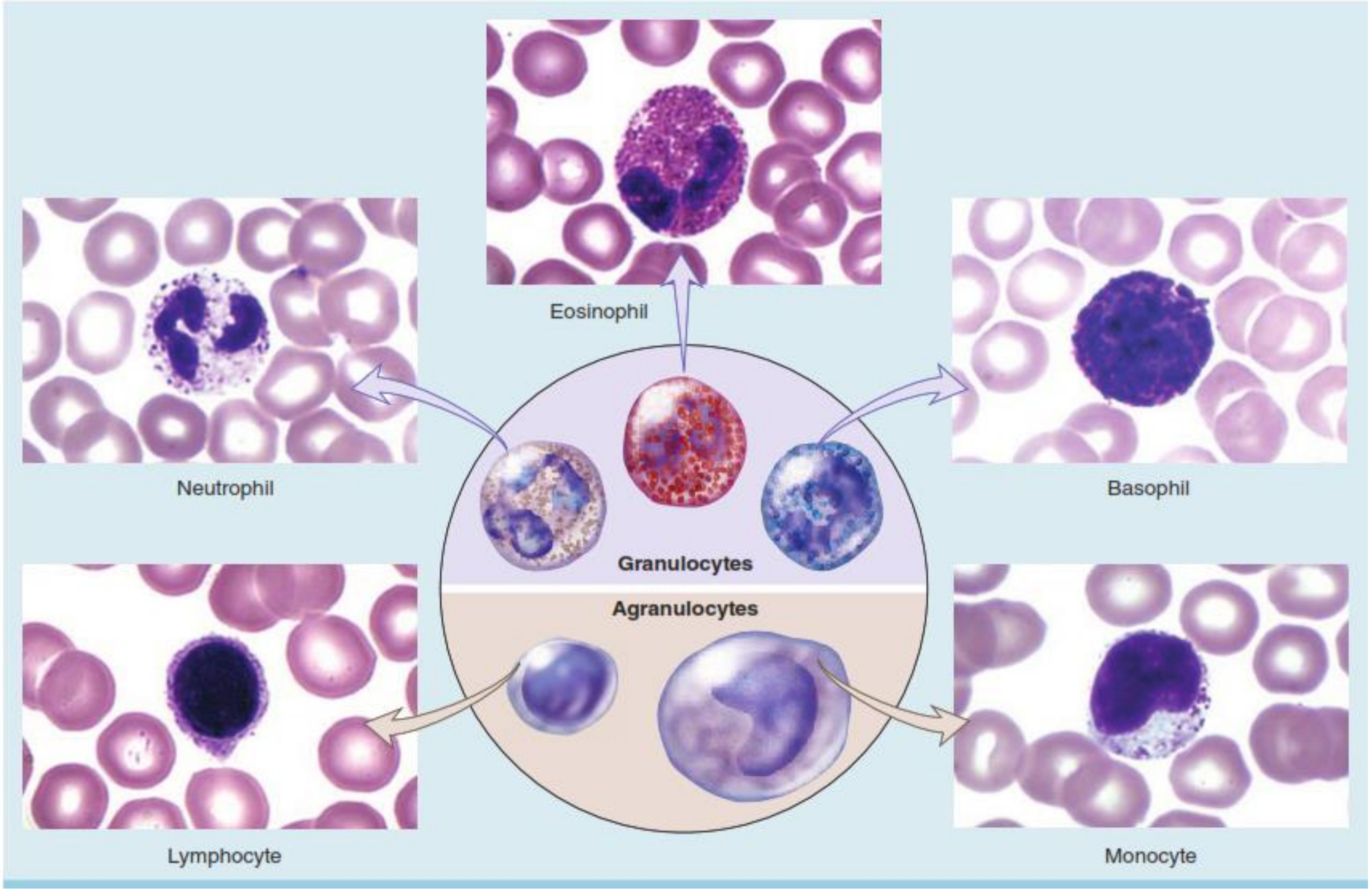

a
Sectional view
~.75 µm
~2.6 µm
b
~7.5 µm
c
Rouleaux
Erythrocytes

Leukocytes

*Leukocytes are divided into granulocytes, which include neutrophils, eosinophils and basophilic granulocytes, and agranulocytes, which include lymphocytes and monocytes.
*They have a role in defense and immune reactions.
*Unlike erythrocytes, they have a nucleus, cell organelles and granules.
*Normal values of leukocytes range from 5000 to 9000.

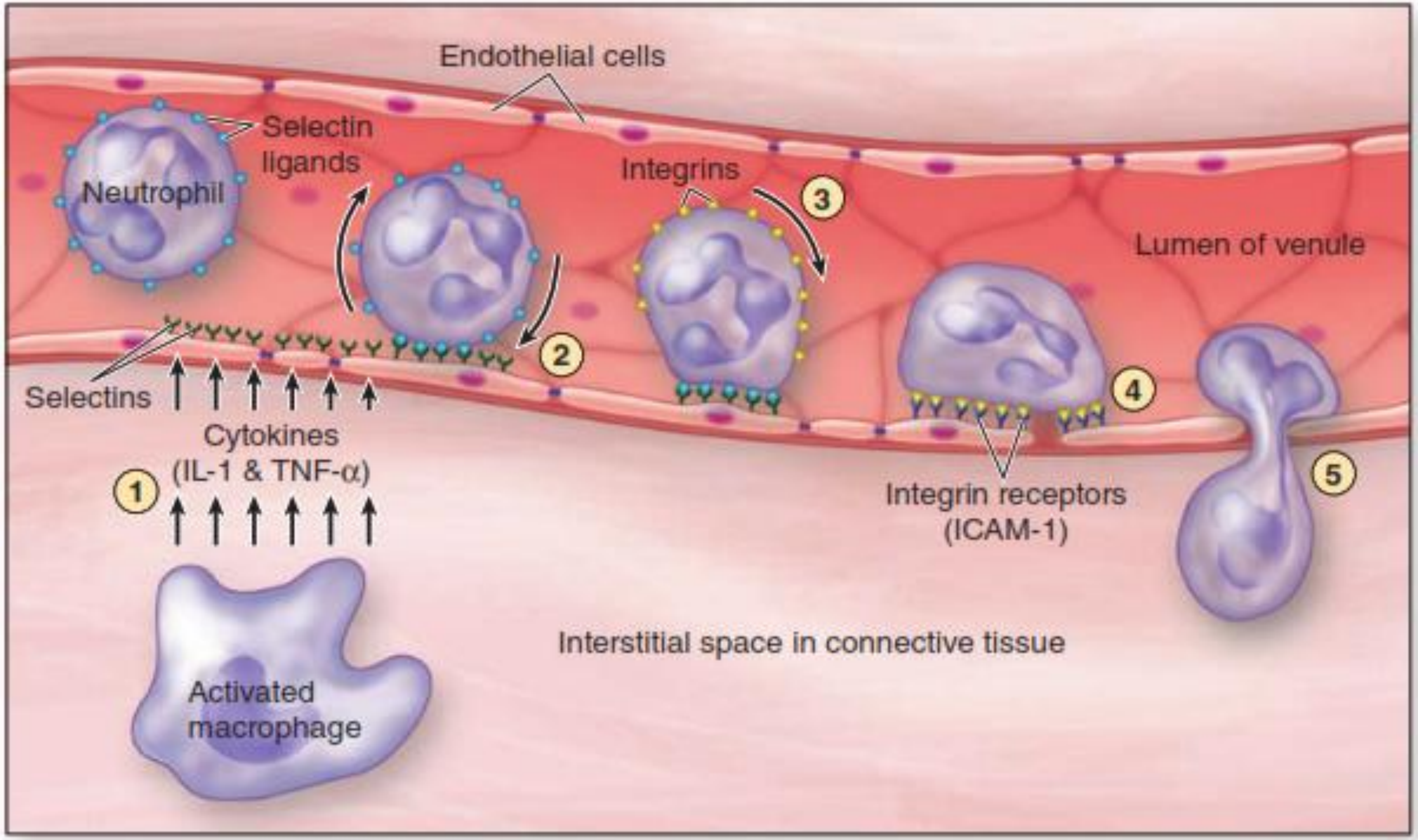
*Leukocyte formula:

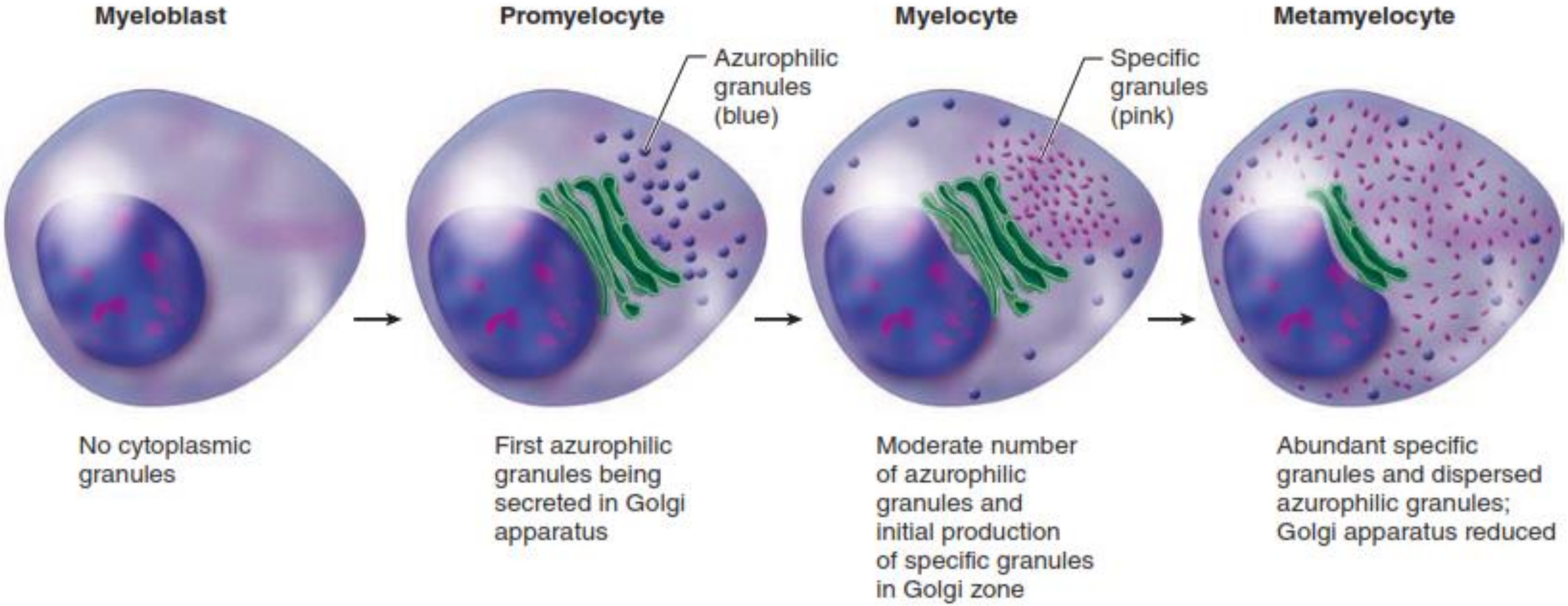
*neutrophils 50-70%
*basophils 0.5-1%
*eosinophils 1-4%
*lymphocytes 20-30%
*monocytes 3-8%



Eosinophil
Neutrophil
Basophil
Granulocytes
Agranulocytes
Lymphocyte
Monocyte

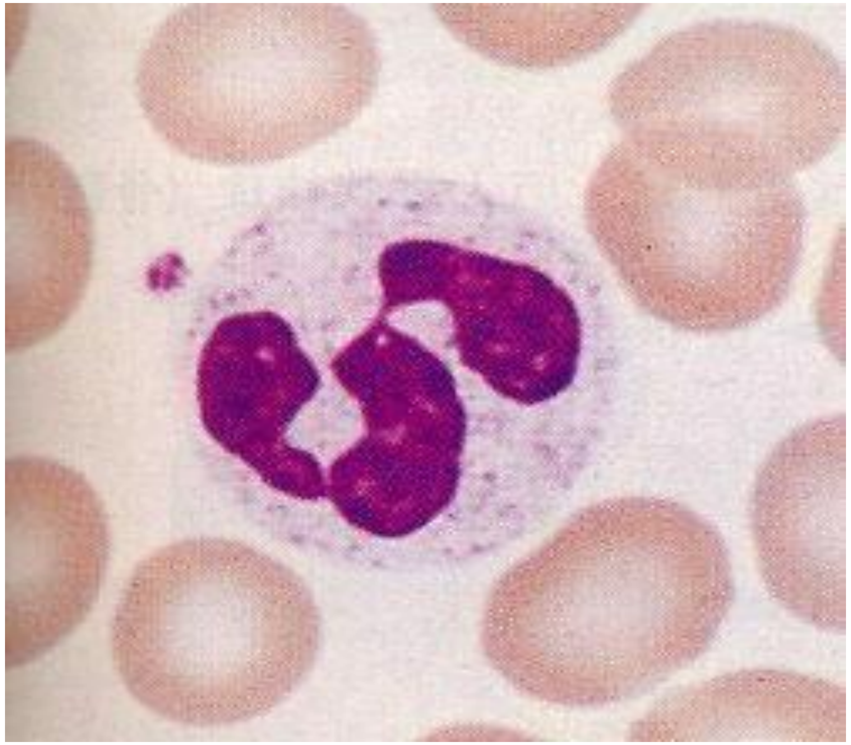
Type	Nucleus	Specific Granules[a]	Differential Count[b] (%)	Life Span Outside the Blood	Major Functions
Granulocytes					
Neutrophils	3-5 lobes	Faint/light pink	50-70	1-4 d	Kill and phagocytose bacteria
Eosinophils	Bilobed	Red/dark pink	1-4	1-2 wk	Kill helminthic and other parasites; modulate local inflammation
Basophils	Bilobed or S-shaped	Dark blue/purple	0.5-1	1-3 d	Modulate inflammation, release histamine during allergy
Agranulocytes					
Lymphocytes	Rather spherical	(none)	20-40	Hours to many years	Effector and regulatory cells for adaptive immunity
Monocytes	Indented or C-shaped	(none)	2-8	Hours to years	Precursors of macrophages and other mononuclear phagocytic cells


Endothelial cells
Selectin
ligands
Neutrophil
Integrins
3
Lumen of venule
2
Selectins
Cytokines
(IL-1 & TNF-α)
1
4
Integrin receptors
(ICAM-1)
5
Interstitial space in connective tissue
Activated
macrophage


Myeloblast
Promyelocyte
Myelocyte
Metamyelocyte
Azurophilic granules (blue)
Specific granules (pink)
No cytoplasmic granules
First azurophilic granules being secreted in Golgi apparatus
Moderate number of azurophilic granules and initial production of specific granules in Golgi zone
Abundant specific granules and dispersed azurophilic granules; Golgi apparatus reduced

Neutrophils

* Neutrophils make up 50% to 70%
* from the total population of leukocytes,
* They have dimensions of 10-12 µm,
* Lifetime 3-4 days,
* The sail has 3 to 5 segments,
* They are located in the cytoplasm
* specific and azurophilic granules.



*They have microvilli on the surface, and when they enter tissues, they move using pseudopodia, performing phagocytosis. This is why they are called microphages.

*They represent the body's first line of defense, mainly against bacterial infections.

*They produce mediators of inflammatory reactions.

Basophils

*Basophils have the smallest diameter of all granulocytes (9-11 μm),

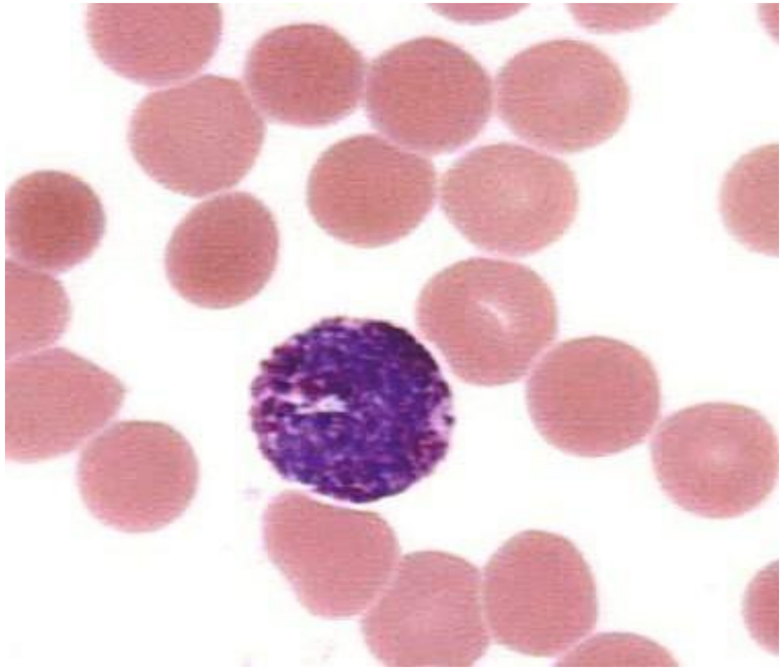
*They make up 0.5% to 1% of total leukocytes,

*They have a bilobed core that is masked by a large number of granules:

*specific granules (heparin, histamine and leukotrienes)

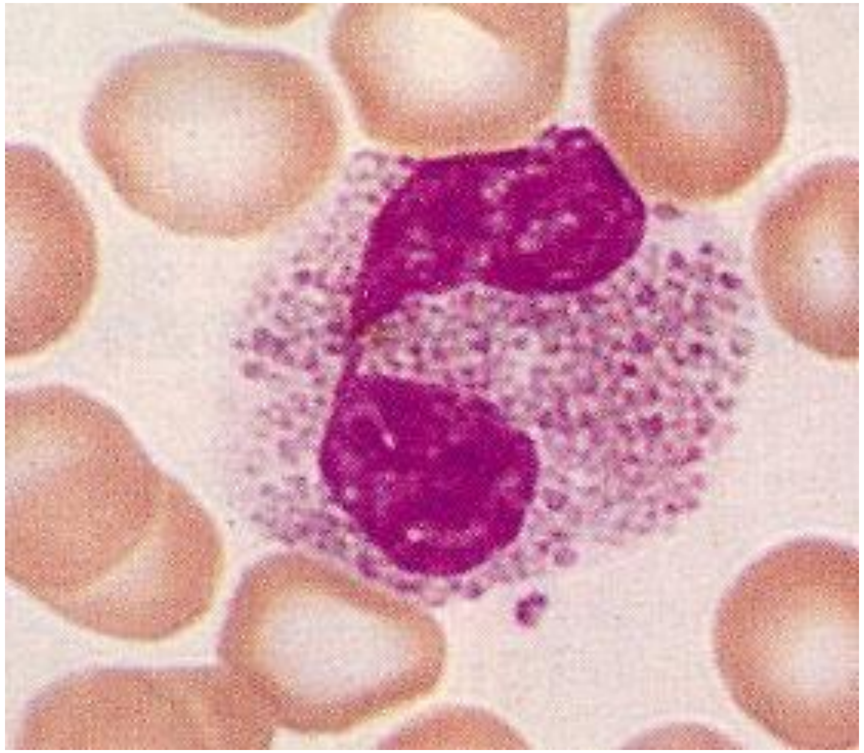
*azurophilic granules (myeloperoxidase)

** Basophils are activated in allergic reactions.



Eosinophils

* They have the same shape as neutrophils,
* but they are somewhat larger (up to 14 μm),
* They make up 1-4% of the total number of leukocytes,
* The sail consists of two segments
* There are two types of granules in the cytoplasm:
* specific granules - which have a high affinity for acid dyes,
* azurophilic granules



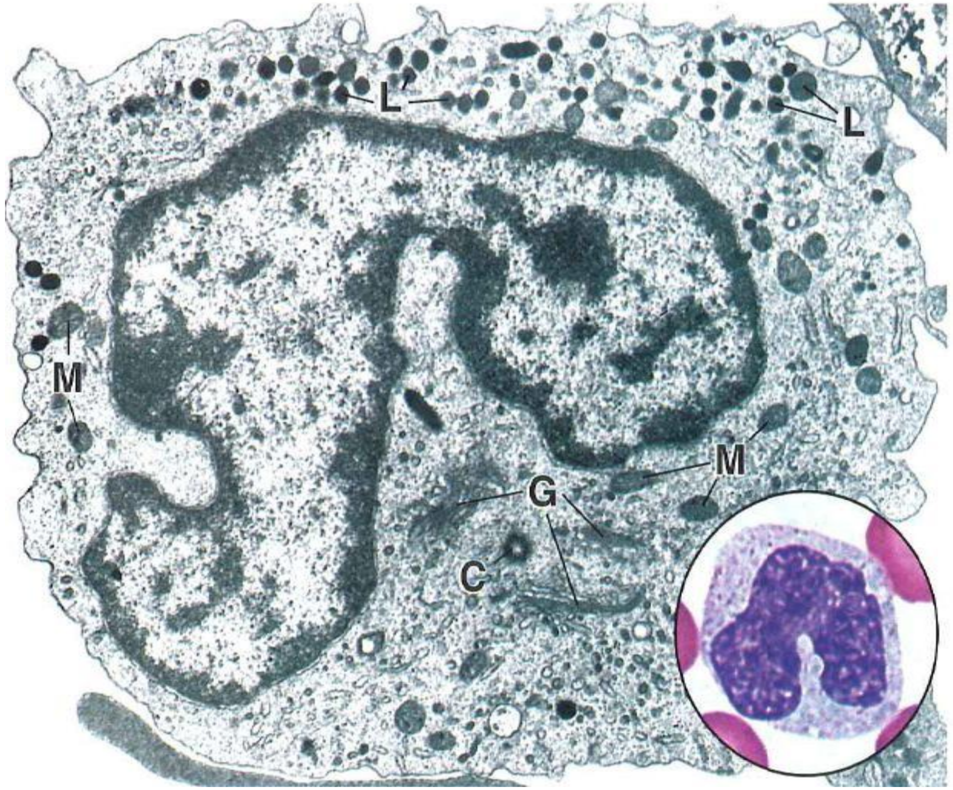
* In allergic and parasitic diseases, their number increases, and they destroy the parasites by pushing out the contents of the granules.

Monocytes

- Monocytes are the largest blood cells with dimensions of 12-20 µm, round shape and a large, oval, eccentric core.

- They are present in the cytoplasm
- mitochondria, ribosomes, Golgi
- apparatus and cisterns of the endoplasmic reticulum and azurophilic granules.

- By moving into the connective tissue
- monocytes are subject to phenotypic
- modifications and increased macrophages responsible for phagocytosis.



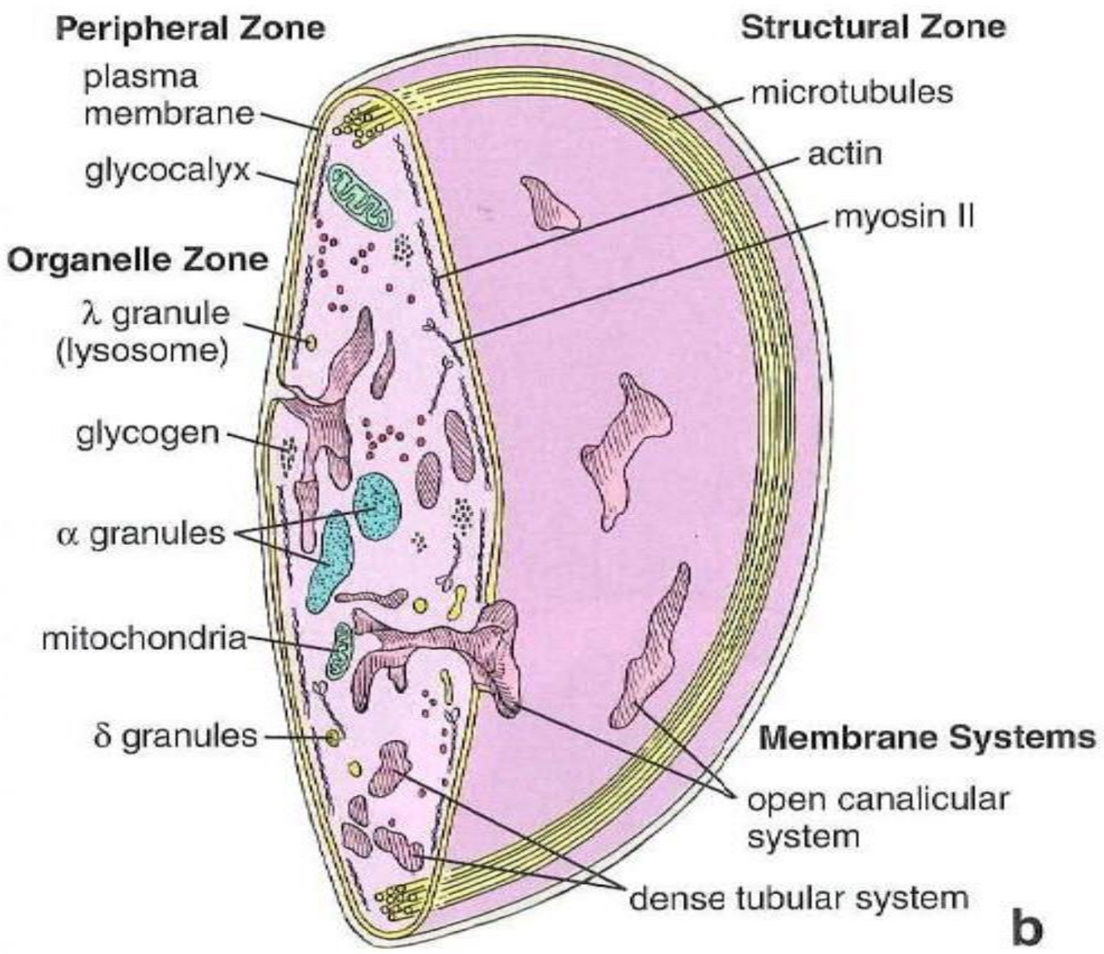
Thrombocytopoiesis

*Throbocyte development begins with a progenitor cell for megakaryocytes, which divides to form a megakaryoblast.
*Megakaryoblast, through nuclear division without cell division, first forms a diploid, then a tetrapoid nucleus, and in the maturation phase it can reach
*polyploid form with 64 nuclei. With these divisions, the sail becomes
*lobed, and azurophilic granules appear in the cytoplasm, and the cell at that stage is called a promegakaryocyte.

*Further differentiation of the promegakaryocyte results in a megakaryocyte.
*The megakaryocyte does not enter the circulation, but remains attached to the wall of the sinusoidal capillaries extending its extensions into the lumen.
*Platelets break off from the extensions under the pressure of the blood currents and enter the circulation.

*Thrombocytopoiesis is regulated by the glycoprotein thrombopoietin.

Platelets

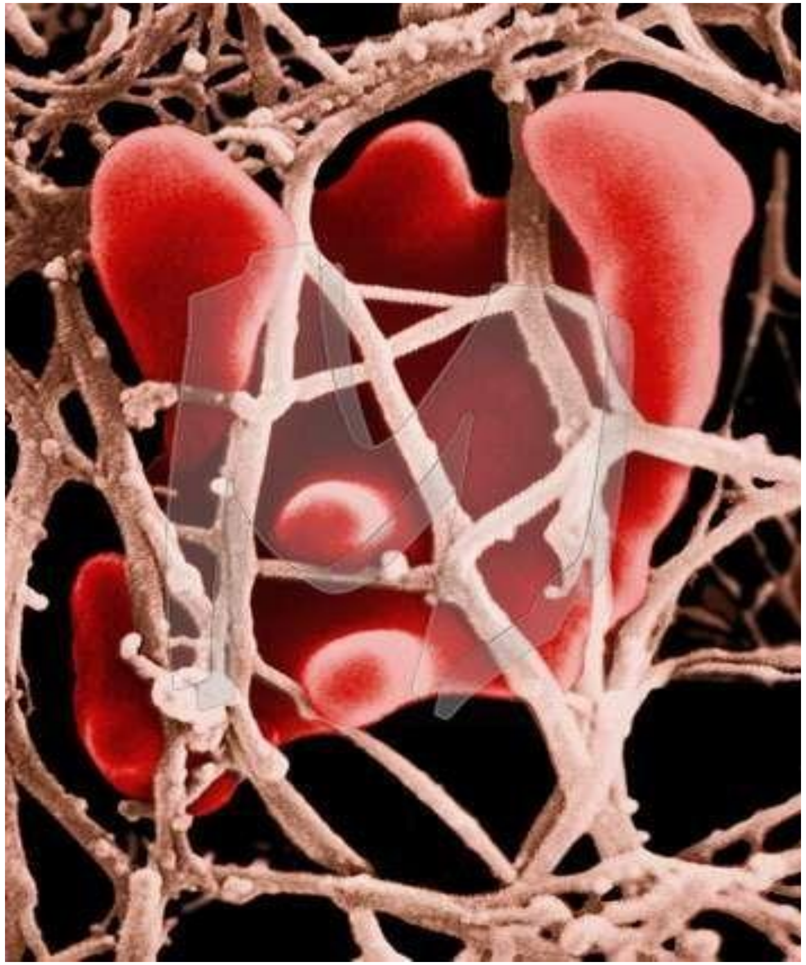


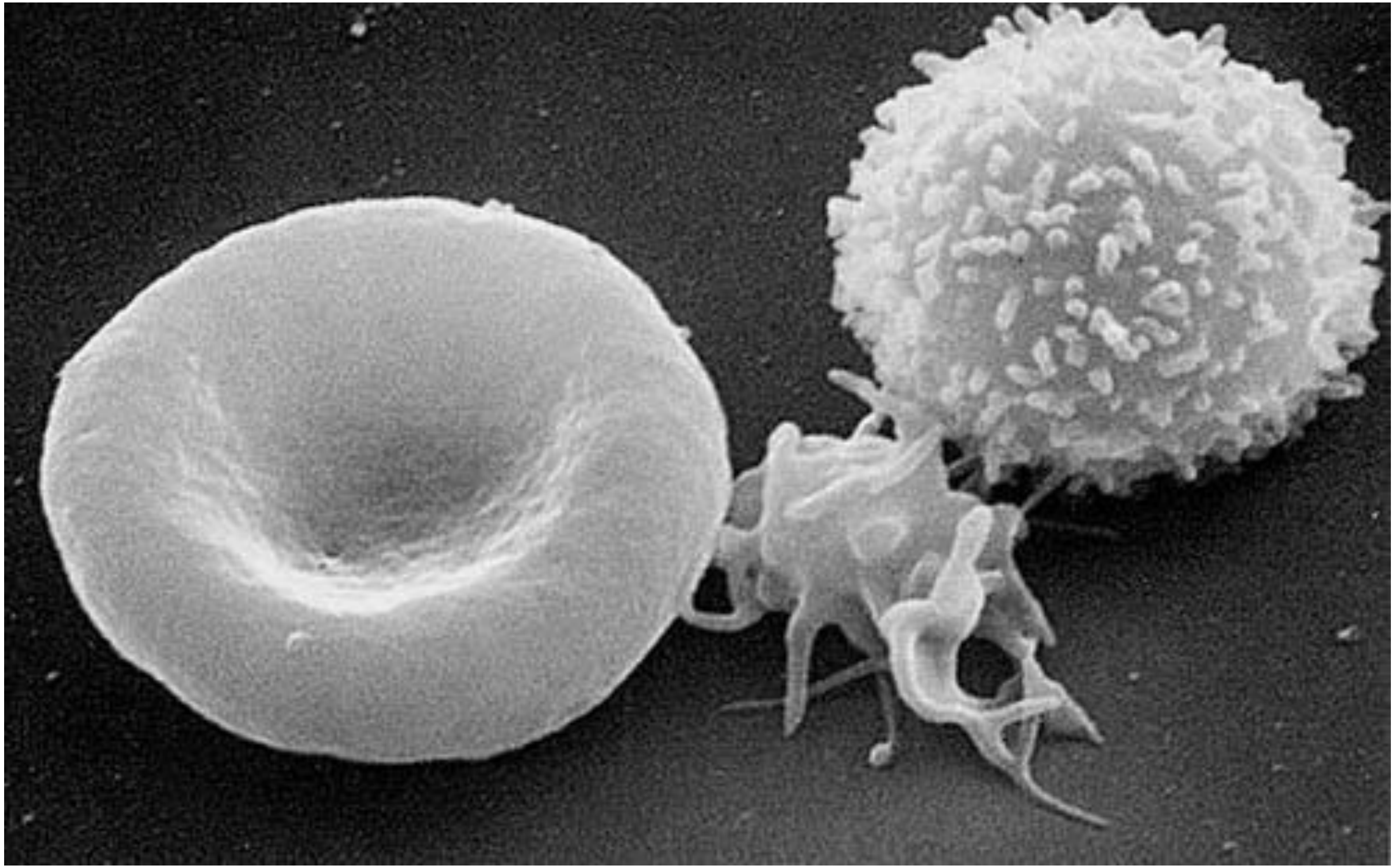
*Granulomer - the central part of the platelet in which there are:
*alpha granules (von Willebrand's
*factors, factor VIII, platelet factor IV),
*delta granules (serotonin, pyrophosphate, ATP, ADP)
*lambda granules (lysosomes with hydrolase
*enzymes)
*Hyalomere - the peripheral part of platelets, does not contain organelles, but only elements of the cytoskeleton

*marginal bundle of microtubules (8- 24)
*actin and myosin

Platelets

- Platelets play a key role in the processes of hemostasis and clot formation at the site of blood vessel damage.
- The normal number of platelets is 150,000-400,000 per cubic
- millimeter of blood.





erythrocyte, blood platelet and lymphocyte