Connective and supportive tissue

- have great
  morphologic,
  topographic
  structural diversity.

function

- Structural support
- Metabolic functions
- Defensive functions

CT proper is formed of

cells
fibers
matrix

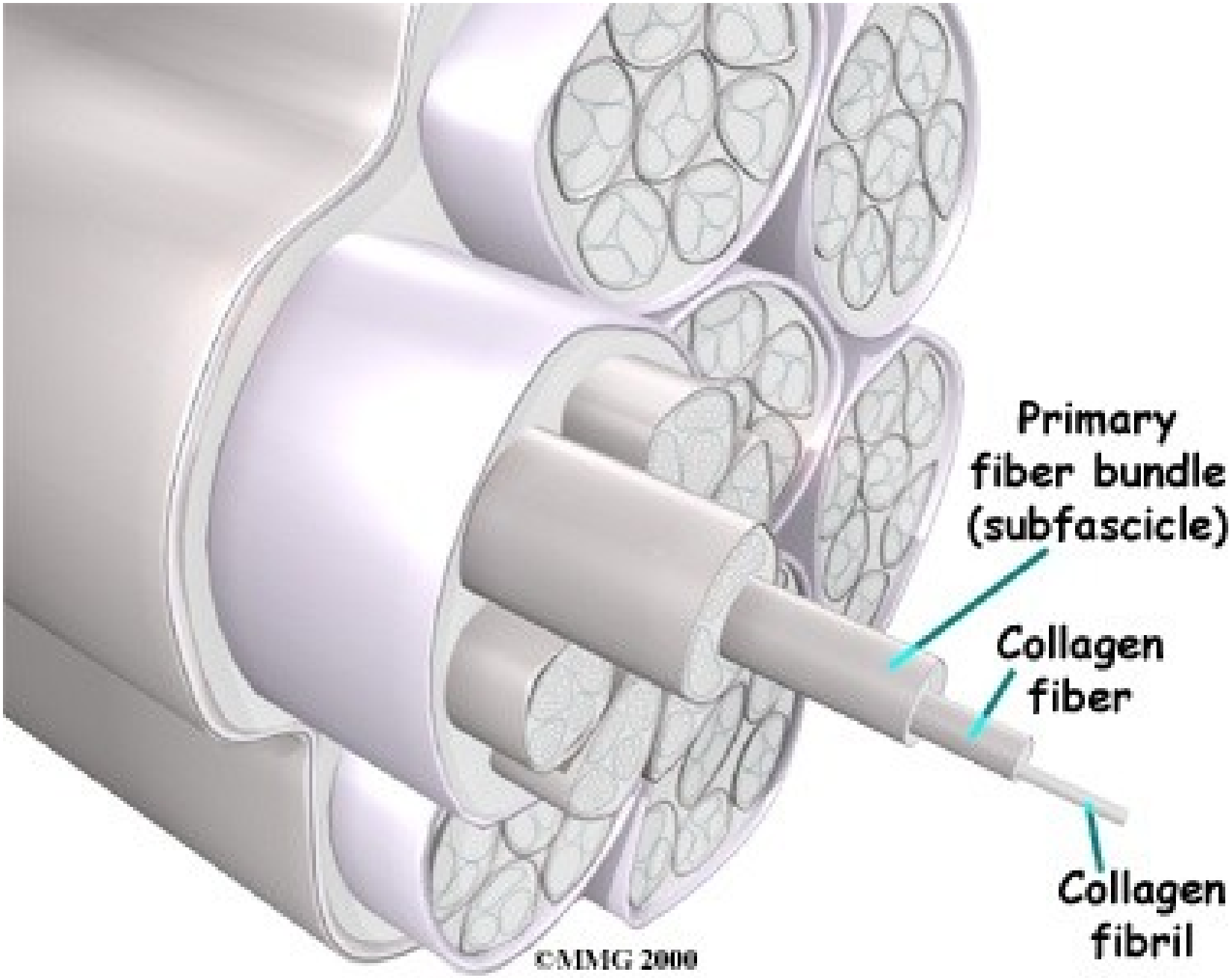
A. Connective tissue fibers

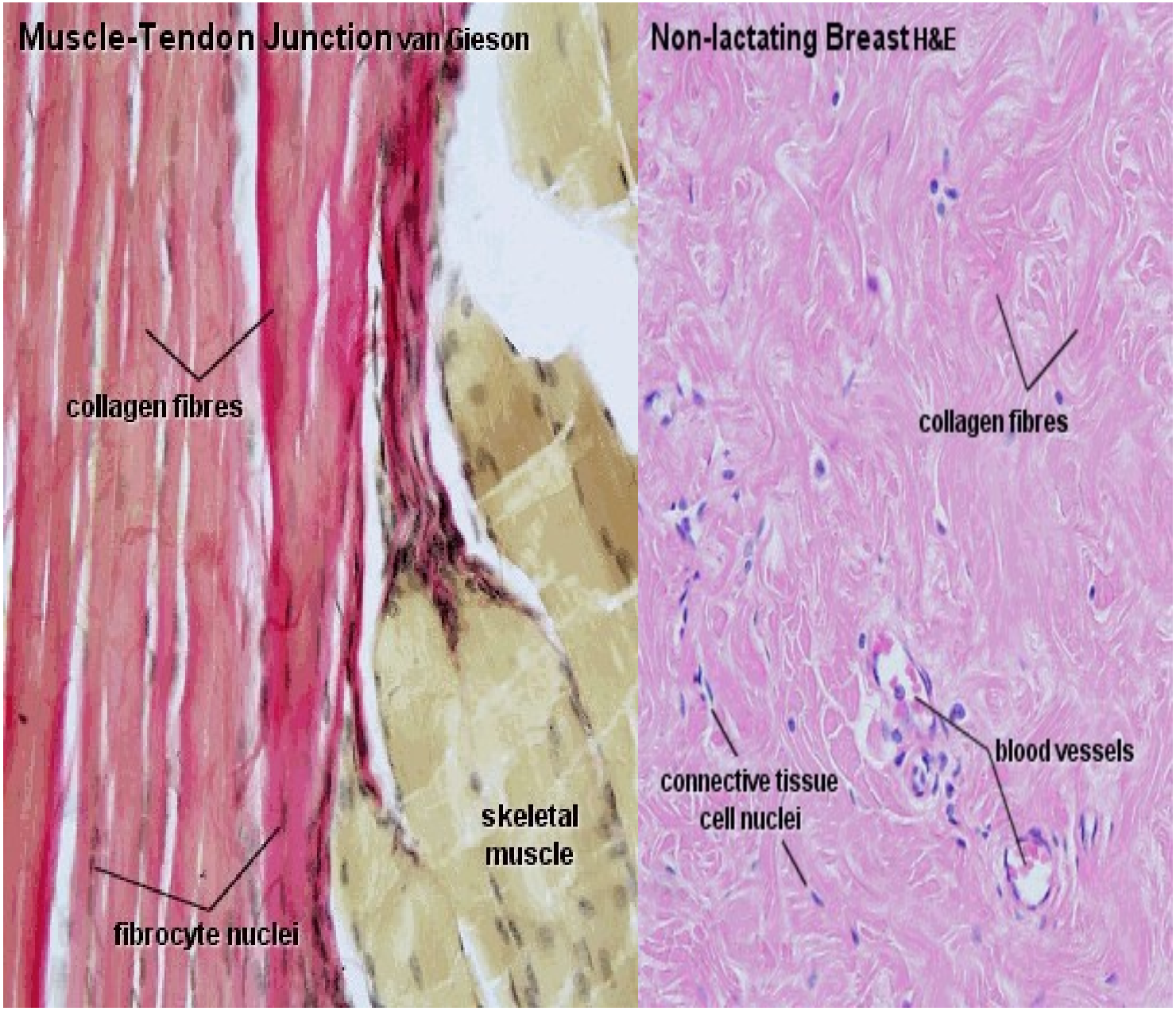
- **are found out side CT cells**
- **the fibers largely vary only in quantity and arrangement.**
- **CT fibers are composed of structural proteins.**
- **three main types of fibers**
  - **collagen fibers**
  - **reticular fibers**
  - **elastic fibers**

1.Collagen fibers

- Composed of several sub unit-collagen fibrils
- The basic unit of collagen bundles are formed of tropocollagen molecules.
- Tropocollagen _ fibrils - fibers - collagen bundles
- Collagen fibers consist of closely packed orderly fibrils and when seen in bundles appear white
- after staining they are acidophilic.

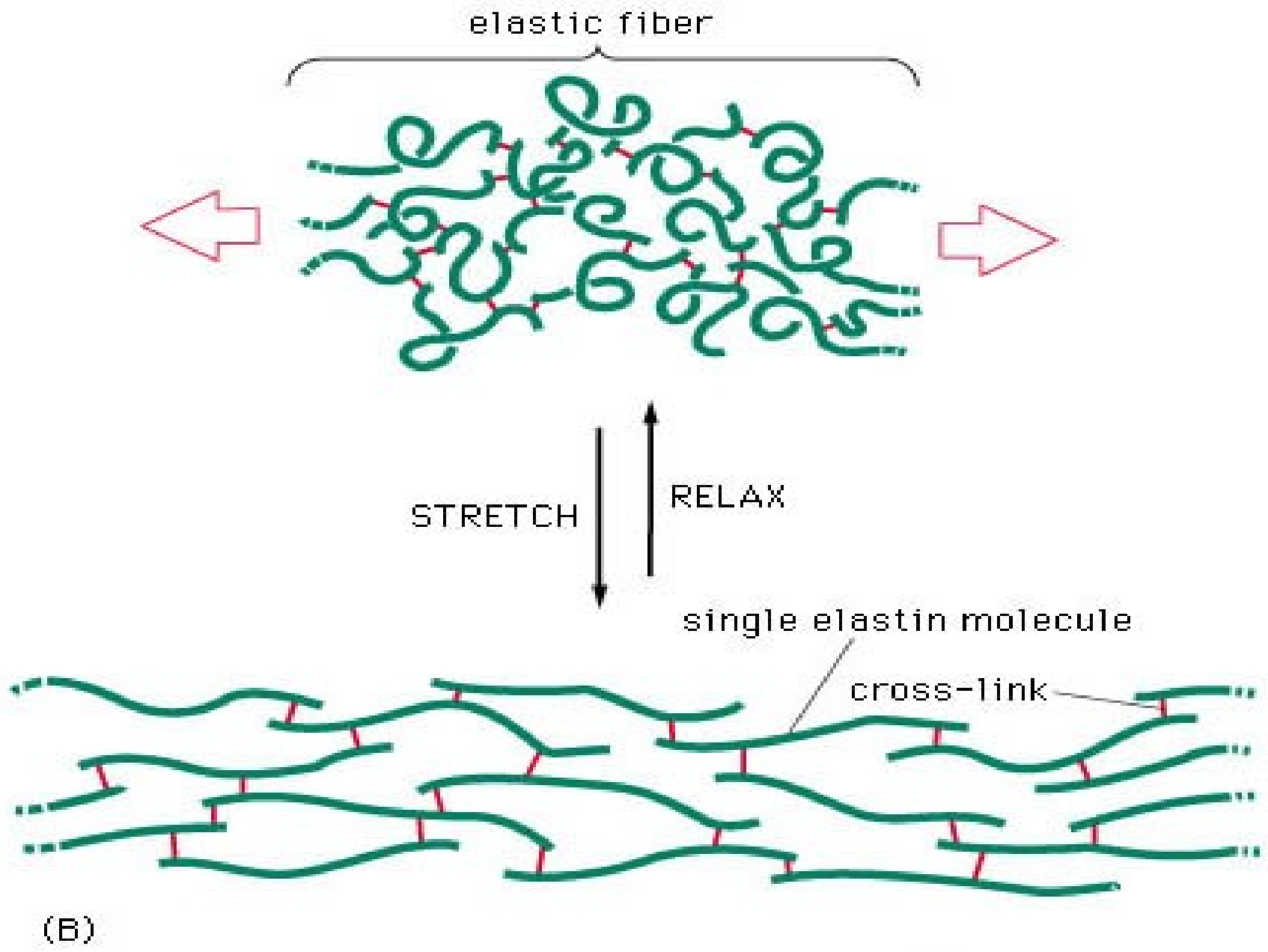
- CF formed by chondroblasts and osteoblasts,
- but mainly by fibroblasts.


Primary
fiber bundle
(subfascicle)
Collagen
fiber
Collagen
fibril
©MMG 2000


Muscle-Tendon Junction van Gieson
collagen fibres
skeletal muscle
fibrocyte nuclei
Non-lactating Breast H&E
collagen fibres
blood vessels
connective tissue cell nuclei

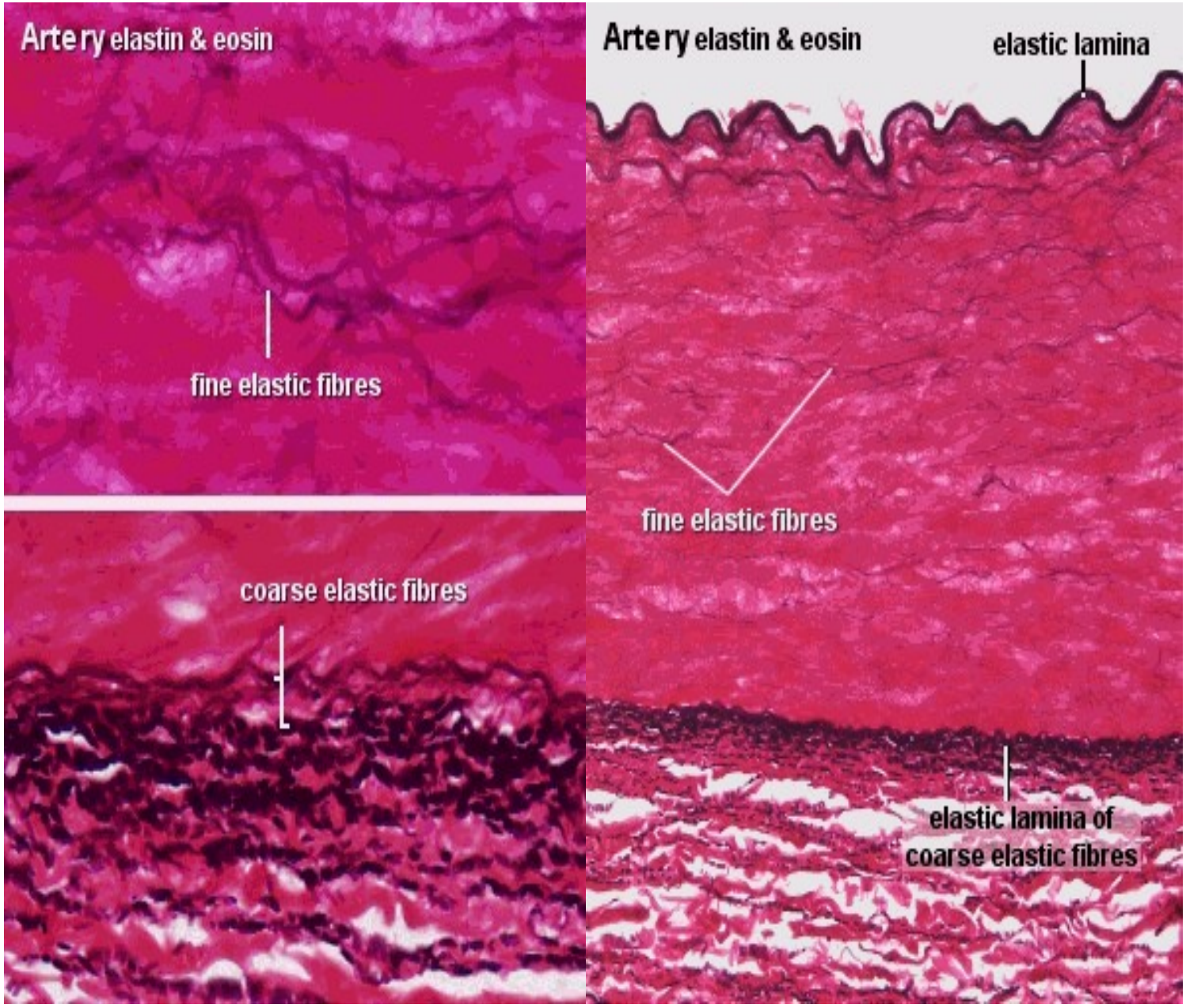
2.Elastic fibers

- highly elastic and stretch in response to tension.
- formed by fibroblasts and smooth muscles cells
- run singly, not in bundles
- are stretchable and branching(anastomosing)
- Primarily formed of elastin and micro fibril
- elastin is somewhat amorphous in structure
- Its molecules is coiled and joined together by stable covalent cross links.
- Micro fibrils is made of protein and glycogen
- It covers the periphery of elastic fibers


elastic fiber
STRETCH
RELAX
single elastin molecule
cross-link
(B)

cont…

- Site: **aorta and elastic ligaments, lung, external** ear, vocal chords, trachea, arteries and skin


Artery elastin & eosin
fine elastic fibres
coarse elastic fibres
Artery elastin & eosin
elastic lamina
fine elastic fibres
elastic lamina of
coarse elastic fibres

3.Reticular fibers

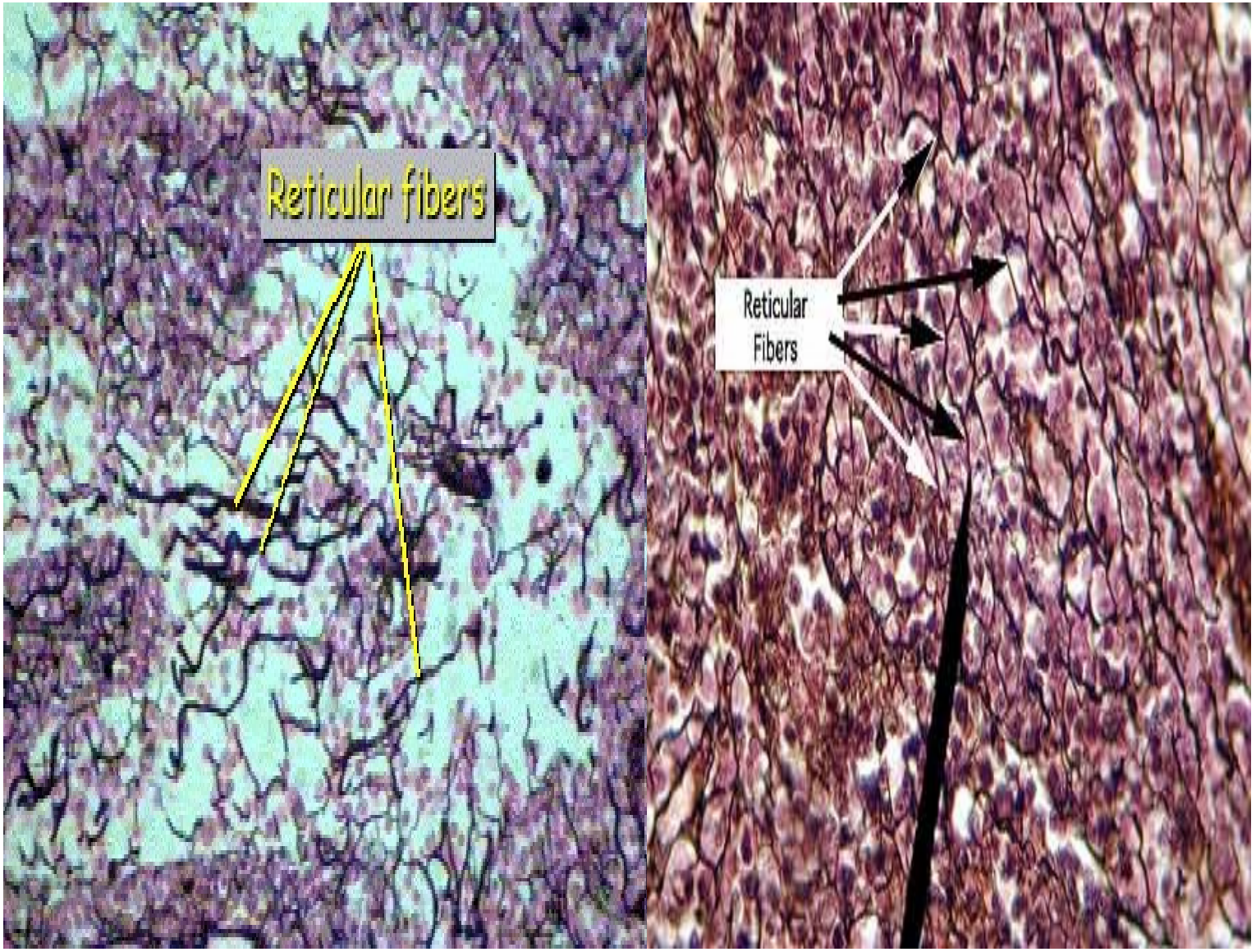
- **are actually individual collagen fibers coated by proteoglycans and glycoprotein.**
- **short, branching and anostomising fibers forming a network (or a meshwork)**
- **form delicate, flexible networks around capillaries, muscle fibers, adipose cells and hepatocytes.**
- **also serves as a scaffolding to support cells**

of endocrine, lymphatic and blood forming organs.

- **They are integral part of basement membrane of capillaries**

conti

- **prominent in loose CT and**
- **in structures that are subject to periodic changes in size and volume**
- **or are exposed to physical stresses requiring some degree of flexibility (e.g., dermis of skin and wall of intestines).**
- **-Molecular structure is collagen type III**
- **Not visible in routine histological preparations**
- **Argrophil (silver stain) gives brownish black**


Reticular fibers
Reticular
Fibers

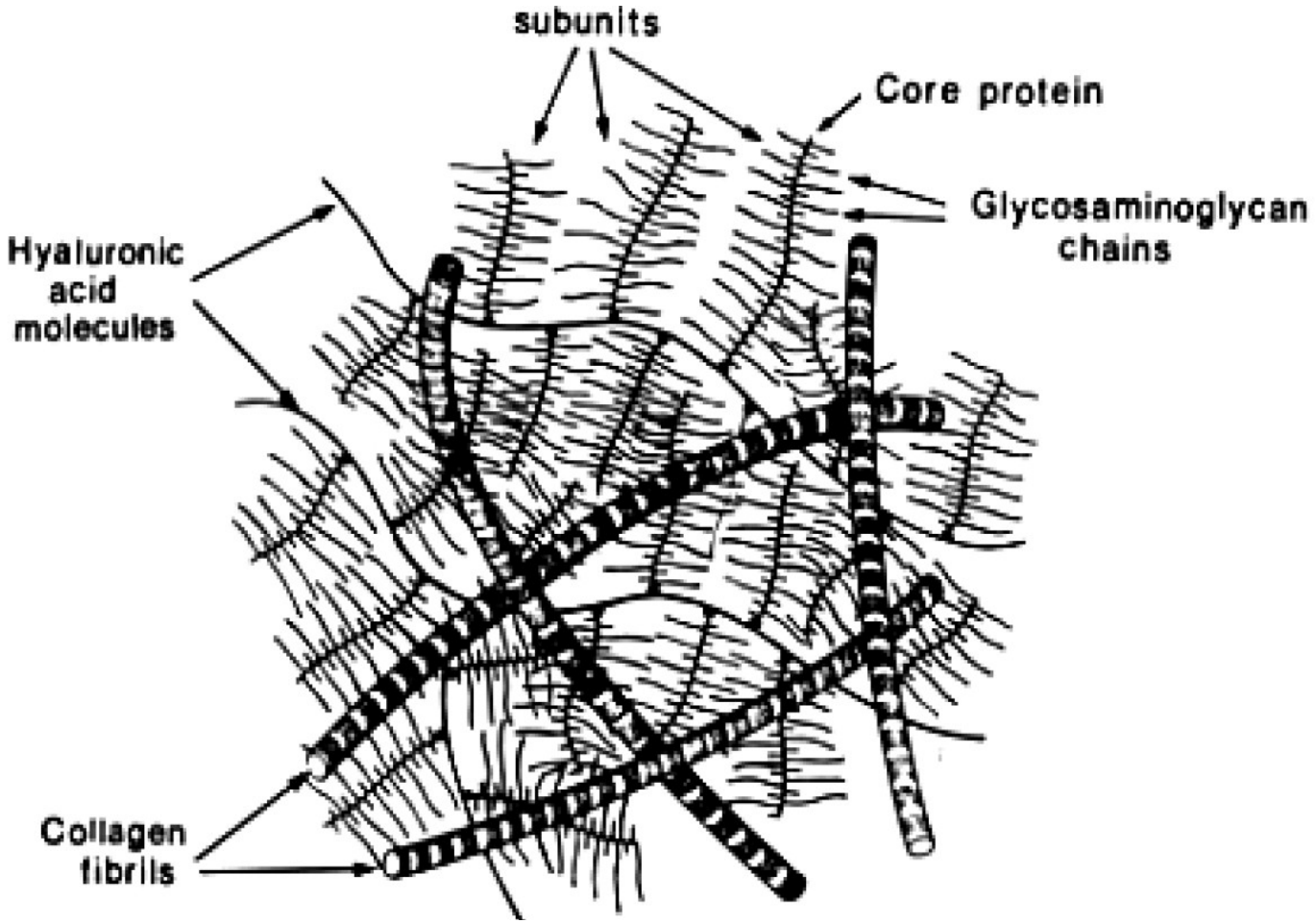
2.Matrix (ground substance)

- The intercellular ground substance is an amorphous, transparent with a fairly high water content.
- they are produced by connective tissue cells(fibroblasts)
- connective tissue cells and fibers are embedded in AGS
- All substances passing to and from cells must pass through the ground substance.
- jelly mass predominantly composed of **proteoglycans**

Conti

- seven specific GAGs found include
  - hyaluronic acid,
  - chondroitin-4 and 6-sulfate(2)
  - dermatin sulfate
  - keratan sulfate,
  - heparan sulfate
  - heparin

Conti..


subunits
Core protein
Glycosaminoglycan chains
Hyaluronic acid molecules
Collagen fibrils

Conti’..

- The proportion of these all AGS determine the morphological appearance and the functional properties of CT.
- Ground substance may be highly modified in the special forms of CT
- In blood, the ground substance lacks stabilizing molecules.

Cont…

- Hence- free-flowing ground substance ***plasma***.
- In skeletal tissue, the ground substance may become mineralized by deposition of calcium salts.
- We call this rigid ground substance ***bone***.
- In cartilage, the ground substance is much more solid than in ordinary connective tissue but still retains more resiliency than bone.

3.CONNECTIVE TISSUE CELLS

- Connective tissue cells can be **branched** or

unbranched

Branched cells:

- **Undifferentiated mesenchemal cells (UMCs)- the mother (stem cells)**
- **Fibroblast and fibrocyte**
- **Melanophores (pigment cells)**
- **Pericyte**
- **Macrophages**

- **Non- branched cells**
  - Plasma cell
  - Mast cell
  - Fat cell
  - Extra vascular leukocytes
- Connective tissue cells can be fixed or free.
- fixed cell -are steady, or move slowly

frequently encountered in proper CT

includes :

Adipocytes(which store fat)

Fibroblasts (which secrete the fibers and ECM)

Cont’..

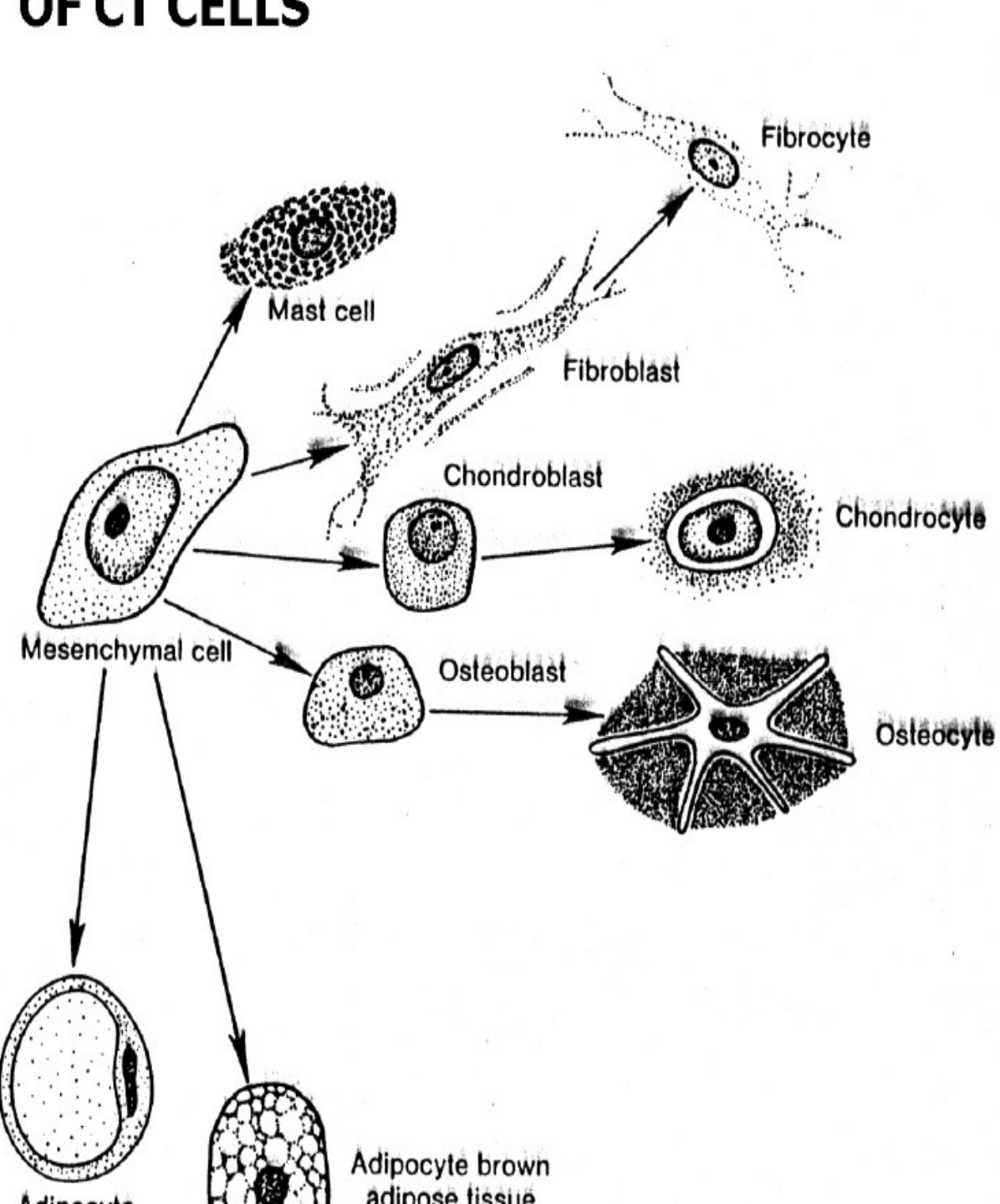
- **Immigrant(free) cells** - motile cell
- includes
  - mast cell
  - plasma cell
  - **monocytes** and **neutrophils**

Branched cells

1. **Undifferentiated mesenchemal cells (UNMCs)**

- **UNMCs are embryonic cells present mainly in the connective tissue of embryo**
- **Can be differentiated to give many other connective tissue cells - hence(mother cell)**
- **Can also differentiate into smooth muscle**

ORIGINS



- Nearly all CT cells have common stem
- Some variant of the fibroblast is always present

Cont'…

2.Pericyte

- **mesenchyme-like cells persist in adult connective tissue.**

similar to UMCs

- can give rise to smooth muscle cells and fibroblasts.
- is branched but fixed
- ***Site:*** it is present along blood capillaries (b/n their BM and endothelial cells)

Cont…

3. Fibroblast and fibrocyte

Fibroblast

- **are the most common cell type found in CT.**
- **Abundant rough endoplasmic reticulum**
- **active Golgi bodies are found in the cytoplasm**
- **Oval and central nucleus**
- **Well defined borders**
- **bigger than UMCs**

Cont…

Fibrocyte

- **ill-defined borders (less branching)**
- **less rER**
- **pale(yekesa, yegereta) cytoplasm**
- **aged cell, less active than the fibroblast**

Origin: undifferentiated mesenchymal cells and pericyte

4. Pigment cells

- branched cells found in skin and iris of the eye
- origin from umcs
- with round and central nucleus
- melanophores (chromophores) b/cs they contain melanin pigments
- *Function*: pigmentation (giving colour)

5. Macrophage

- is branched phagocytic cell
- originate from monocytes which come from UMCs
- Contain numerous lysosomes which are used for breaking down of ingested material.
- nucleus is kidney shaped, dark and eccentric.

LM -large cell with multiple processes

EM. rich in lysosomes and rER, Golgi apparatus

Cont…

- Function: defense mechanism

  Phagocytosis(pinocytosis)

  Secretion of interleukins (cytokines ….broad and loss category of small protein important in cell signaling)

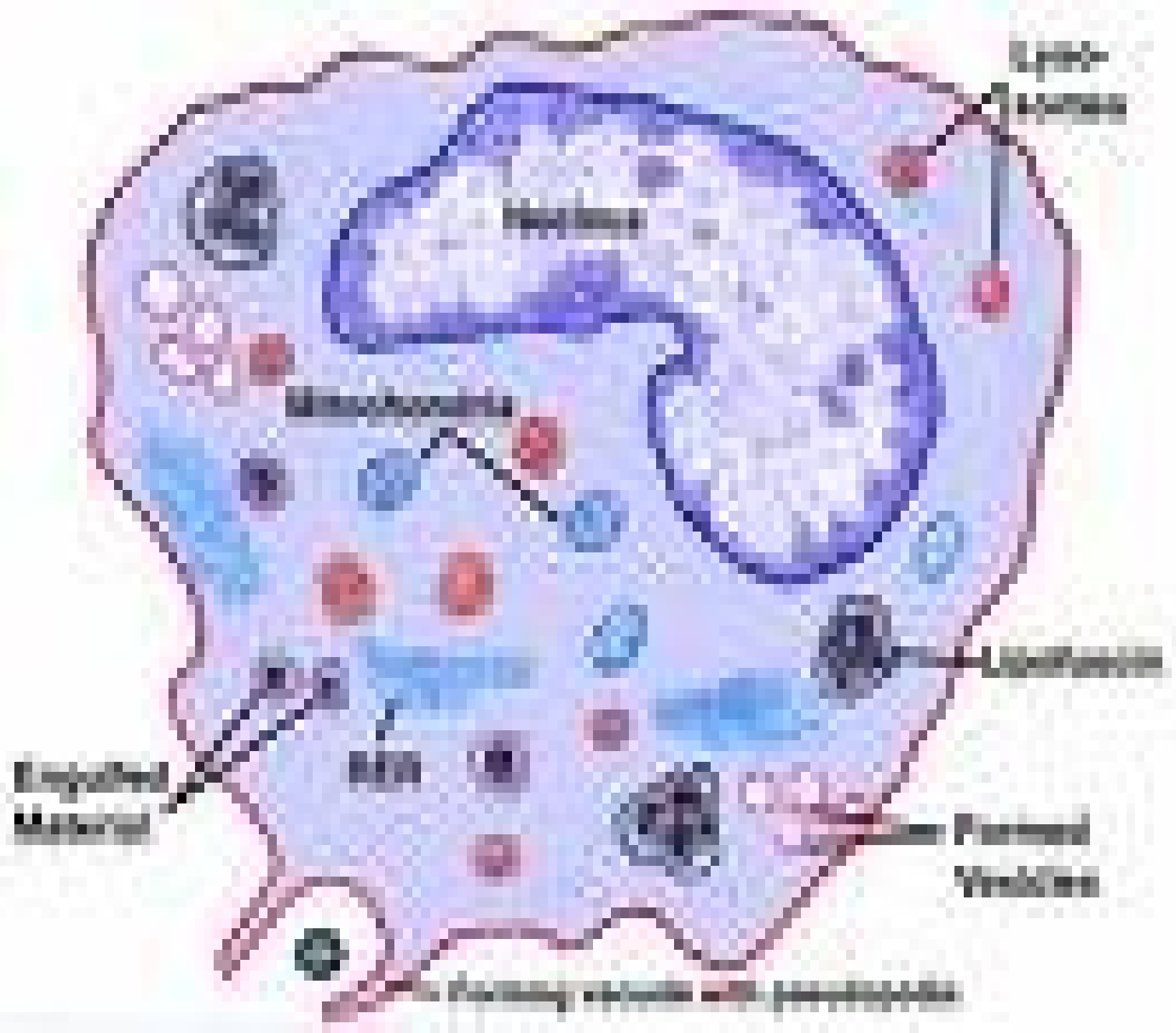
  Cytocidal(killing or tending to kill individual cells) and bacteriocidal(asubstance that kills bacteria) substances

Cont’..

- present antigens to lymphocytes
- Activating humoral and cell-mediated immunity
- **Intracellular digestion** occurs as a result of fusion of **lysosomes** with the **phagosome.**
- Macrophages can gather and fuse into **giant cells** at sites of damage or foreign material.

Cont…

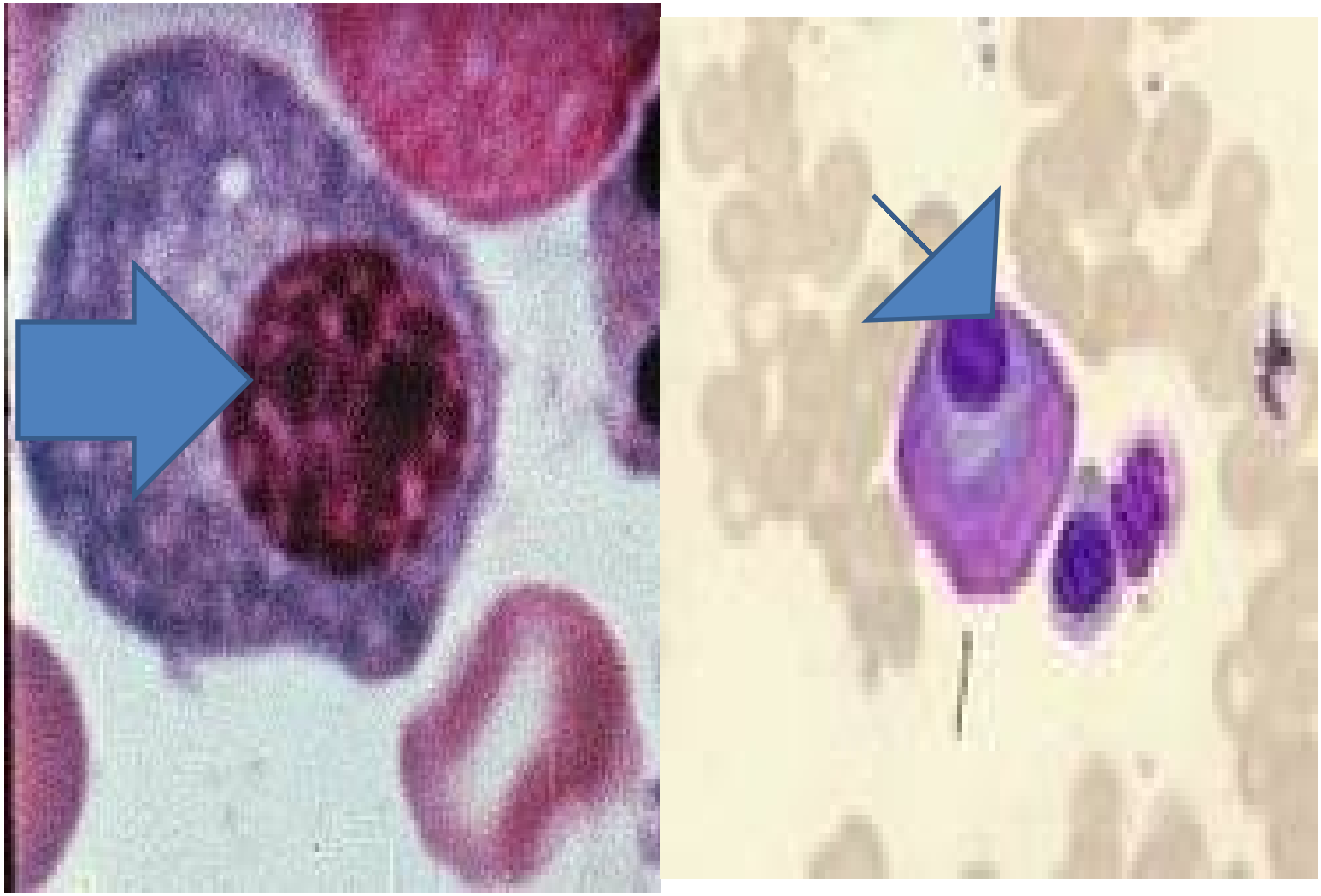
- Have a variety of names depending on the tissue
  - Histiocytes (lungs)
  - Kupffer cells (liver)
  - Langerhan's cells (skin)
  - Microglia (nervous tissue).



Non- branched connective tissue cells

- **1. Plasma cell**
- **derived from B Lymphocyte**
- Oval or rounded cell with rounded, eccentric nucleus
- **LM:** presence of golgi apparatus
- -Basophilic cytoplasm
- -Acidophilic granules are found in old (elderly) plasma cells.
- **EM:** presence of rER (main), golgi apparatus, mitochondria etc.

Plasma cell



CONT,...

2. Mast cell:

- Originates from UMCs
- **LM:** it is rounded or oval cell with large, rounded and peripheral nucleus
- Cytoplasm has many basophilic granules called ***histamines***
- *Staining*: by toluidne blue (metachromasia) changed to purple
- *Site*: along blood vessel (ex. in mesenteric blood vessel) such as that of stomach
- **EM:** nucleus may be obscured(not clear)(not apparent) due to the many granules
- It is rich in mitochondria and free ribosomes

Diagram

3. Fat cell (adipocyte)

- Originates from UMCs

Two types are present

unilocular fat cell

- large and oval cell
- flat and eccentric nucleus
- big fat globule (only one)
- present in white fat

Cont…

multilocular fat cell

- small and round cell
- round and peripheral nucleus
- multiple small fat globule
- present in brown fat

• *staining*

- Sudan III (IV)- orange red
- Sudan black- black
- Hematoxylin eosin-signet ring appearance of unilocular fat cell

Diagram

4. EXTRA VASCULAR leukocytes

can be **granular or agranular**

Granular leukocytes:

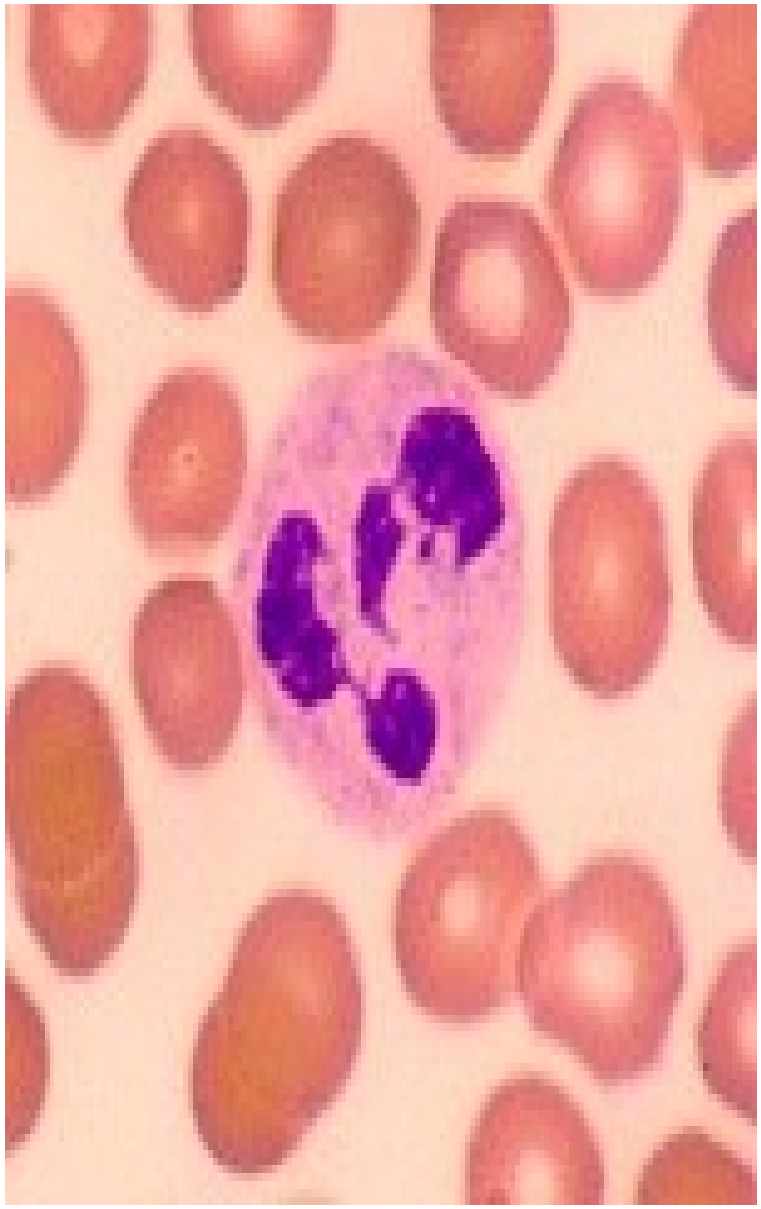
A)Neutrophils

- Multi lobed nucleus
- Migrate to connective tissue

  the first WBC to enter the tissue during acute inflammation.

❖ The cytoplasm contains many lysosomal granules.

neutrophil

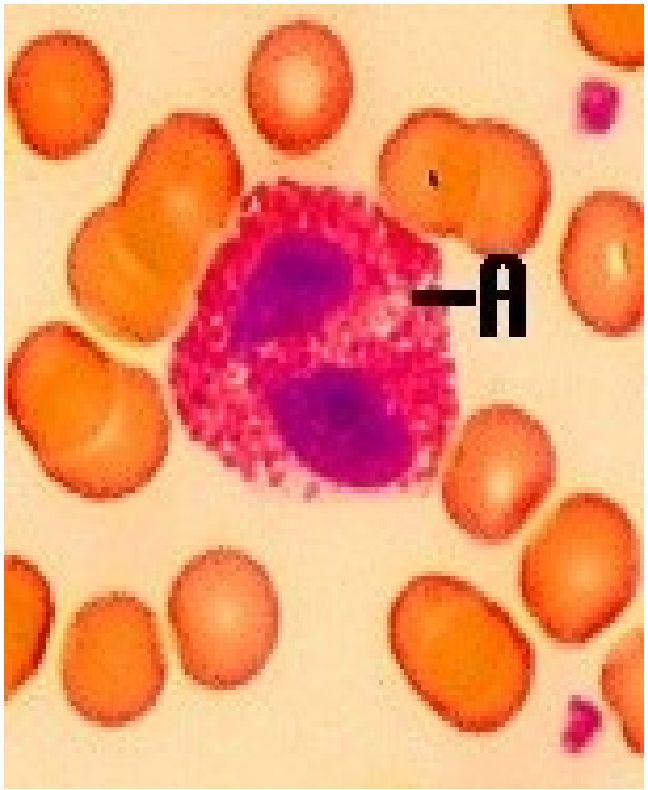


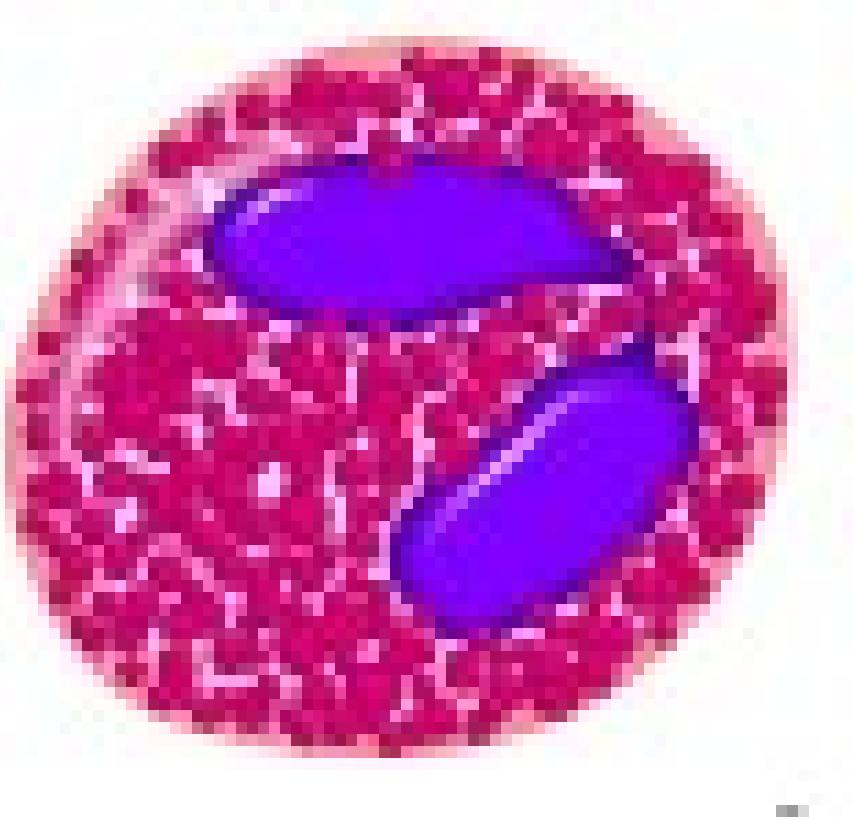
B)Eosinophils

- Bilobed nucleus

  release cytotoxins to kill parasites

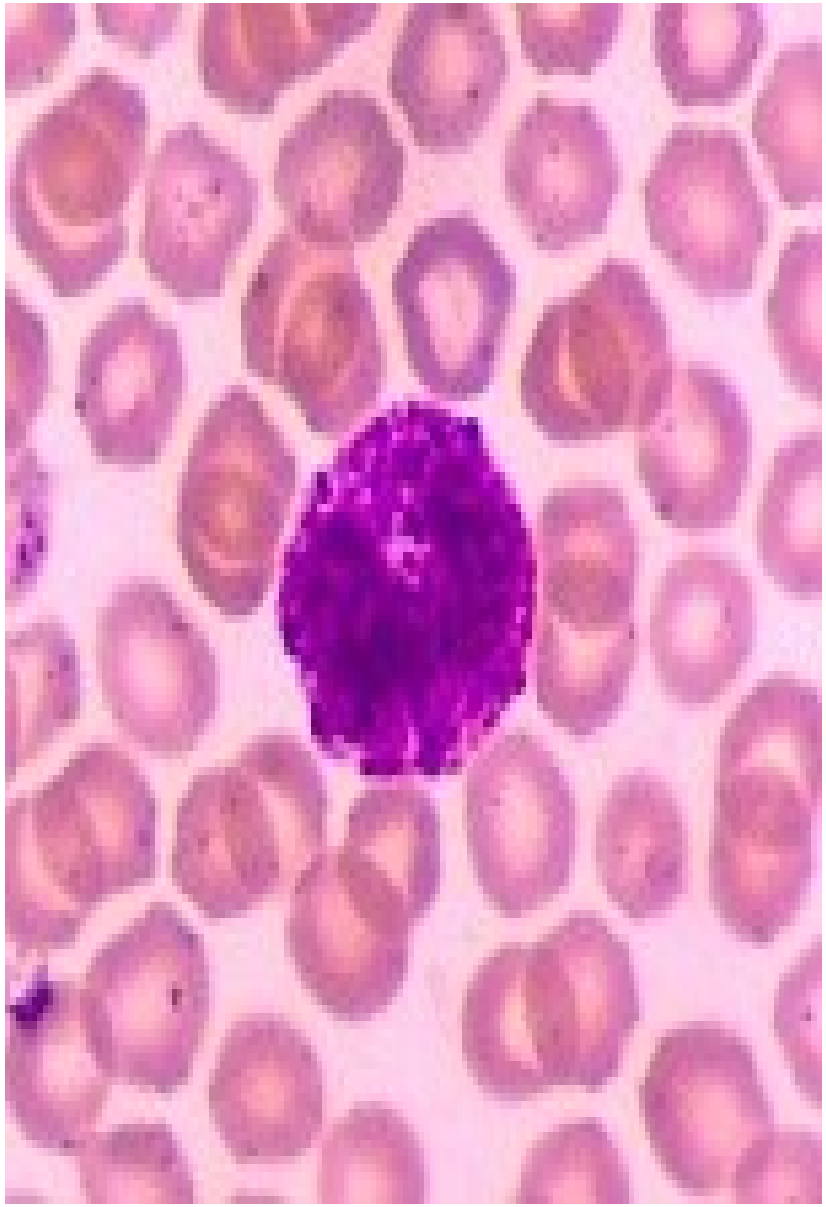
The cytoplasm is full of granules which assume a characteristic pink-orange color with eosin stain.

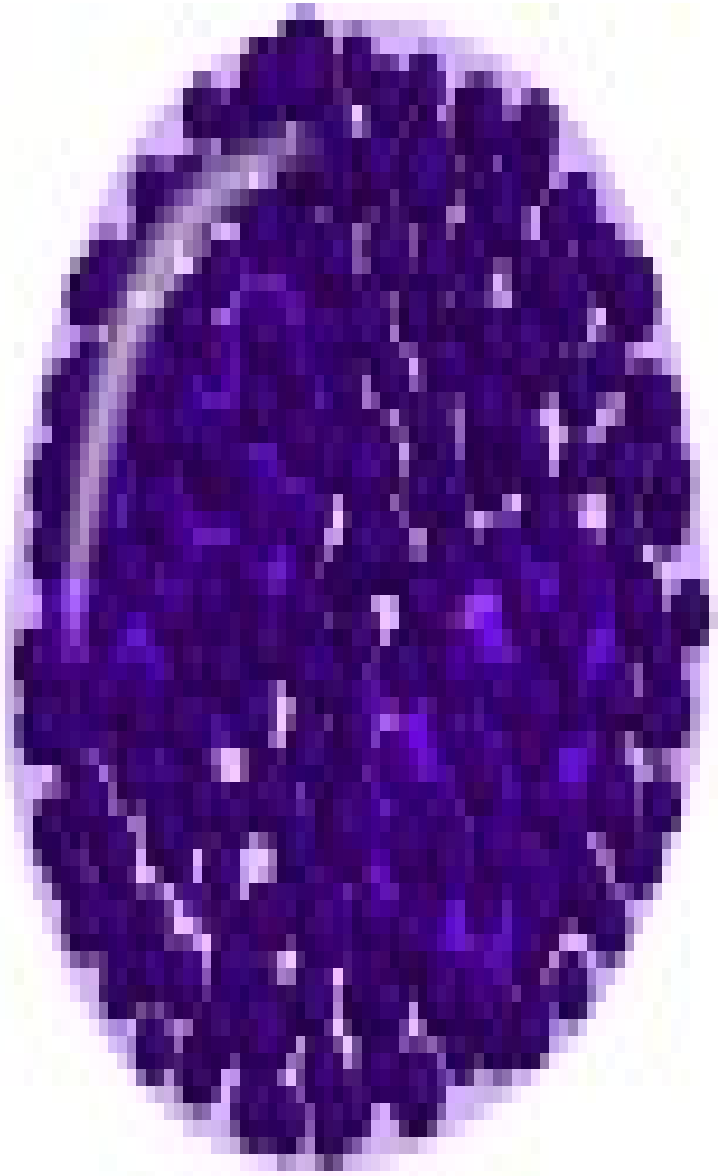




C) Basophils

Responsible for allergic
The nucleus is bi- or tri-lobed,
Hard to see because of the number of coarse granules which hide it.
They are characterized by their large blue granules.
stained with basic stains.

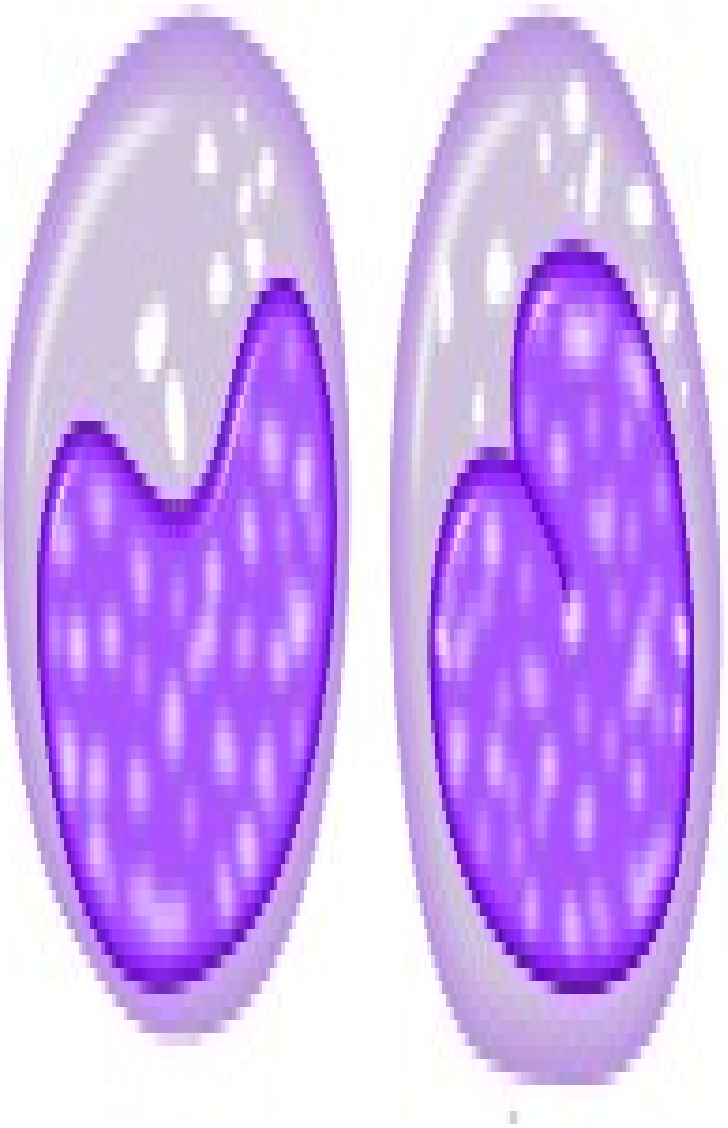




Agranular leukocyte

A) Monocyte

- They have the kidney shaped nucleus and are typically agranulated.
- They also possess abundant cytoplasm
- migrate from the bloodstream to other tissues and differentiate into tissue resident macrophages or dendritic cell



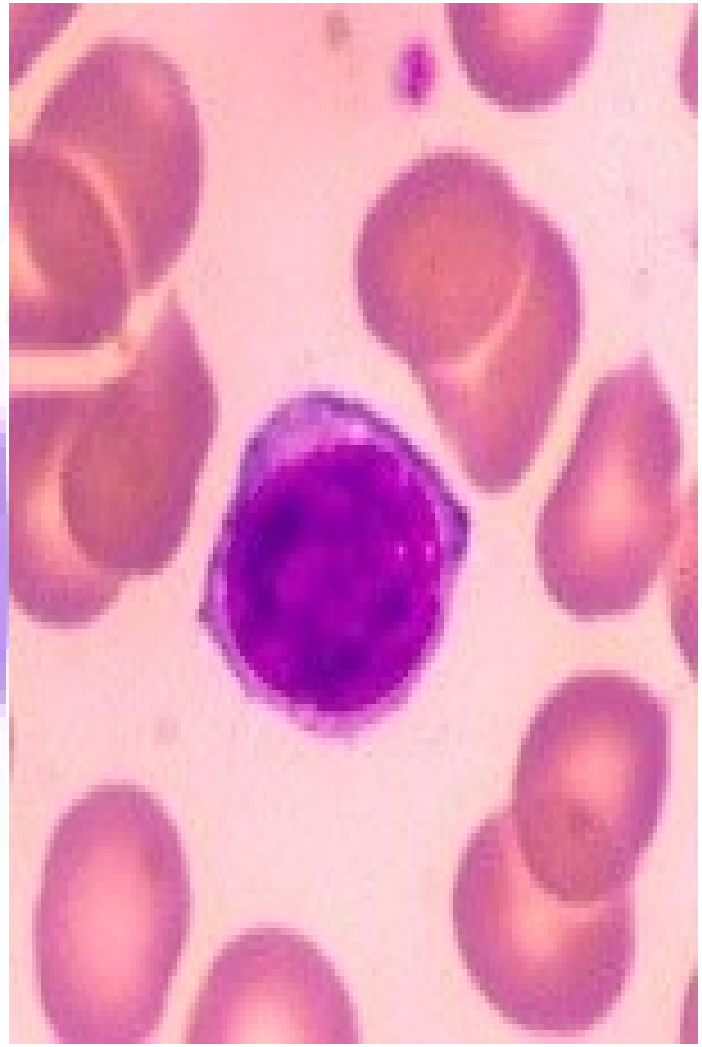
B)Lymphocyte

agranular cell with very clear cytoplasm which stains pale blue.

Its nucleus is very large for the size of the cell and stains dark purple.

The nucleus almost fills the cell leaving a very thin rim of cytoplasm.

lymphocyte



Types of connective tissue proper

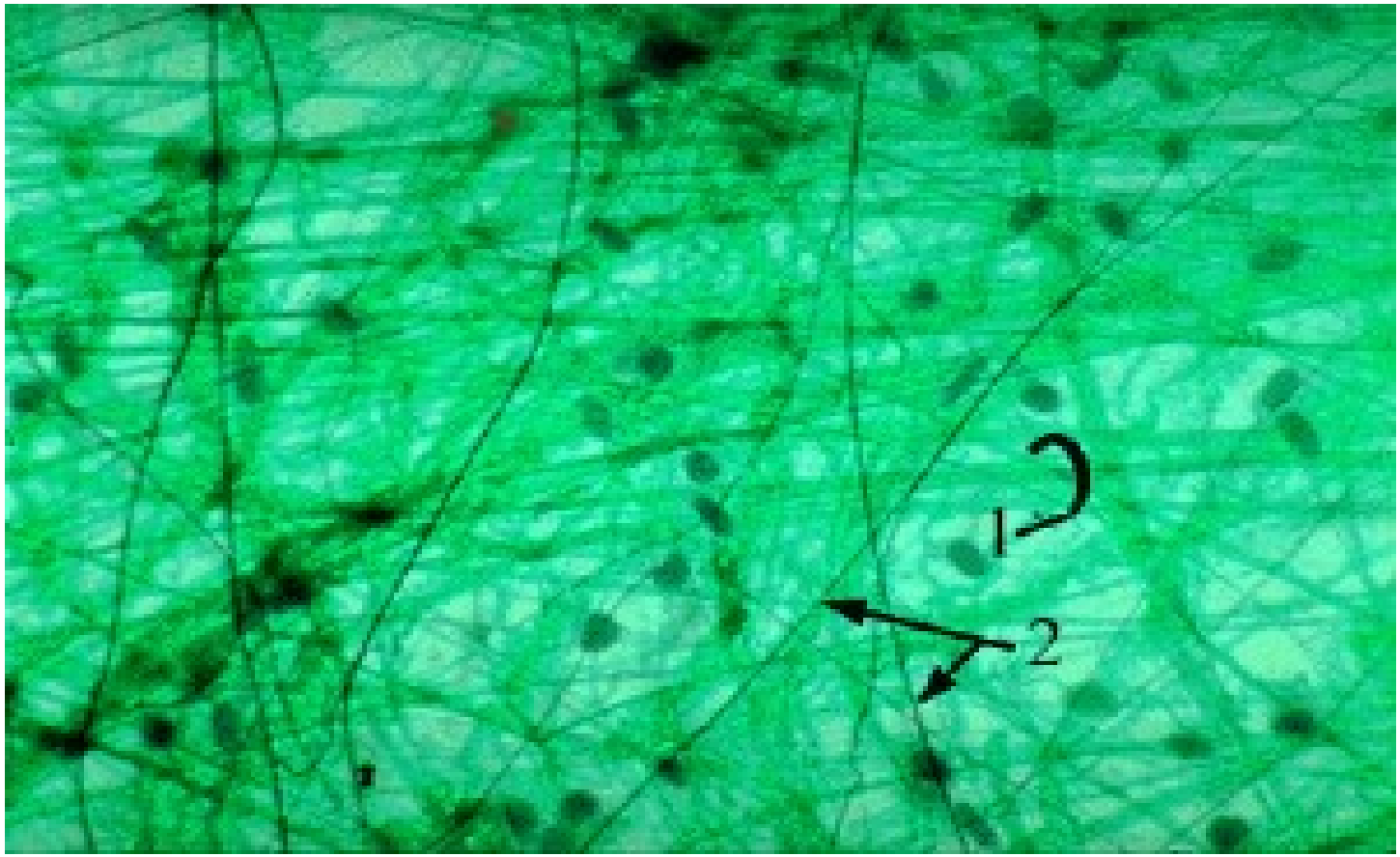
- **A. Loose Connective Tissue/ Areolar CT**
- **areolar" refers to the many small spaces (filled with ground substance.**
- **Characterized by abundant amount of AGS and high population of CT cells**
- **Contains all connective tissue fibers arranged in loose**
- lacks the massive fibrous reinforcement that characterizes dense connective tissue.
- Nevertheless, the same types of fibers are still found,

Function

Areolar connective tissue holds organs in place and

- attaches epithelial tissue to other underlying tissues.
- It also serves as a reservoir of water and salts for surrounding tissues.
- Almost all cells obtain their nutrients from and release their wastes into areolar connective tissue.

Conti..



B.Dense Connective Tissue

Have more CT fibers and

- **less amount of AGS and CT cells.**
- ***Dense connective tissue contains relatively few cells.***
- **with much greater numbers of collagen fibers.**
- **Collage nous fibers are characteristic of dense white CT.**

whereas elastic fibers are characteristic of dense yellow CT

- **The fibers may be either regularly or irregularly arranged.**

Dense connective tissue is divided into two sub-categories:

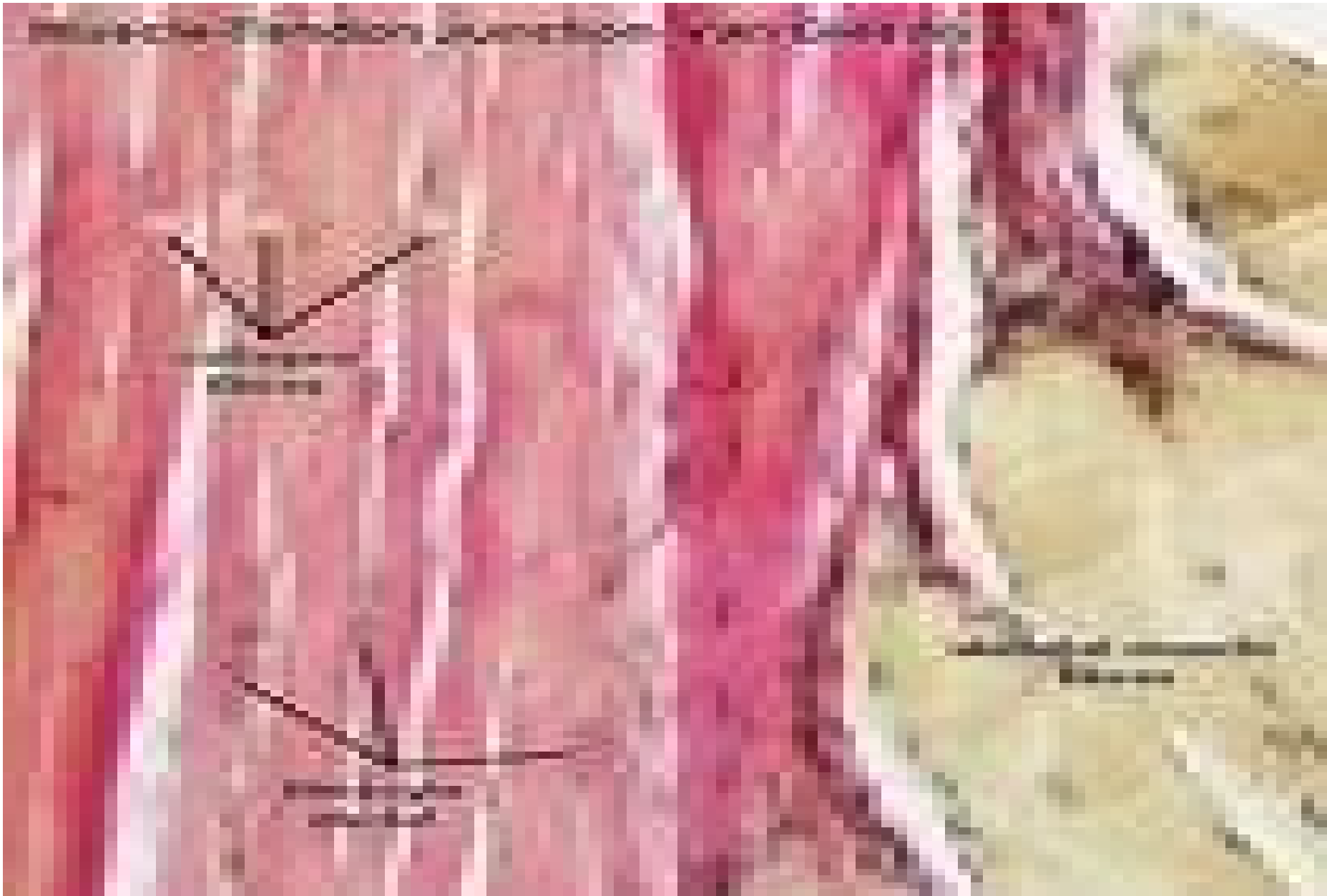
1. Dense irregular connective tissue

- has bundles of collagen fibers that appear to be fairly randomly oriented (as in the dermis
- the fibers are arranged randomly in all directions

2.Dense regular connective tissue

- Has closely-packed ,densely-arranged fiber bundles
- with clear orientation (such as in tendons) and few cells.
- the fibers are all aligned in a single direction and same plane.
- **A.Tendons**
- **B.Ligaments**

Dense regular



Dense irregular

Summary

- **Fiber orientation**
  - Regular or irregular
- **Fiber packing**
  - **Loose or dense**
- **Fiber type**
  - **Collagen**
  - **Elastic**
  - **Reticular**

Supportive tissue

1.**cartilage**

- Is special connective tissue used for supportive role.
- Composed of cells(**chondrocytes),** fibers and matrix
- Covered by dense irregular CT-perichonderium
- Collagen and elastic fibers form a dense network that firmly embed the AGS

This arrangement confers tensile strength

- Collagen and elastic fibers form a structure known as osteon
- Chondrocytes occur within in a space called lacunae

Cont’..

- ❖ Avascular
- ❖ Devoid of nerve and lymph supply
- ❖ Permeable
- conducts nutrients and water
- ❖ Flexible but Weight-Bearing
- resistance to compression
- ❖ Elasticity and Resiliency
- Resistance to Shear Forces
- ❖ Slippery
- low friction at articular joints
- ❖ Poor Regenerative Capacity

CONT’..

- ***Cartilage cells***:

Chondroblasts: come from pericytes or UMCs
Function: mature to give chondrocytes
Chondrocytes:
round cells with central nucleus

Types of cartilage..

- Based on structural characteristics of ct fibers and AGS

❖ ***1.Hyaline cartilage:***

❖ Surface tip of nose, fetal skeleton, costal cartilage, trachea and bronchi, articular surfaces (soft and gliding surfaces)

❖ In articular spaces there is no perichondorium

❖ Much more common in the embryo, where it plays an important role in long bone development.

2.ELASTIC CARTILAGE

The same structure as hyaline cartilage, perichondorium and cells are found

- **yellow elastic fibers** are found in it.
- Has large quantities of elastic fibers in the matrix
- x-zed by great flexibility and elasticity

Sites: External ear ,External auditory canal , Epiglottis of the larynx

3.FIBROCARTILAGE

- Found in areas of the body subjected to high mechanical stress or weight bearing.
- It lacks the flexibility of the other cartilage types
- No perichonderium
- Chondrocytes are arranged in rows or columns
- Matrix is full of collagen fibers, which are dense (type I)
- These collagen fibers are the dominant feature of the matrix and with relatively **little AGs**
- The matrix appearing acidophilic H&E
- Sites: intervertebral discs, symphisis pubis, and shoulder joint (around glenoid cavity)

Bones

- supportive tissue or specialized connective tissue
- with cells and fibers embedded in a hard unbending substance
- well suited for supportive and protective functions.
- It is a dynamic tissue
- Renewed and remodeled through the life of all animal especially man.
- It is solid and on bending it is fractured

Constituents are:

a.Periostum: outer covering of a bone

b.Endosteum: inner lining of the bone cavities

c.Matrix: very solid, calcified or ossified tissue

d.bone cells

BONE CELLS

- Classified in to two main types:
- **Bone forming cells** are Osteogenic cell, Osteoblast and Osteocyte
- **Bone eating**, resorbing or destroying cells are Osteoclast
- **1.Osteogenic cell**: is a flat cell with flat nucleus.
- Site: under periosteum, lining endosteum
- Origin:_from pericytes or UMCs
- EM: rich in rER, mitochondria, golgi apparatus
- Function: can give osteoblast by maturation

Cont’..

2.Osteoblasts:

- found in relation to surface of bone
- Origin: from osteogenic cell
- LM: - is branching cell, i.e minute processes are found
- -round eccentric vesicular nucleus, with prominent nucleolus
-
- It has well developed golgi apparatus beside the nucleus
- -fine granules present in cytoplasm which contain alkaline phosphatase
- Biochemical aspect: rich in enzymes alkaline phosphatase, which precipitates calcium salts (direct)

Cont…

- Orthopyrophosphatase, inhibits calcium salts inhibitors, it also helps precipitation of calcium (in direct)
- EM: rER, golgi apparatus, mitochondria, lysosomes etc.
- Sites: - mainly under periosteum
- -some times in endosteum
- Function: -formation of matrix and also collagen fibers
- -calcification of bone by two enzymes
- Fate: matures to osteocytes

3.Osteocyte

mature bone forming cell

- Origin: from osteoblast
- Sites: matrix of bone (sometimes in periosteum and endoestium), their secretory product in a place called lacunae
- LM: -oval cell with oval central nucleus
- -branching cell with long processes
- -surrounded by lacunae
- -Processes are found in canals-canaliculi (which are extensions of the lacunae to cover the long processes).
- Through this process they supply their nutrients.
-

Cont’…

- – lacunae is irregular oval space in which one or more osteocytes are situated.
- - Processes of different osteocytes are
- a. present in canaliculi
- b. connected to each other by gap junction (2nm)
- -rich in alkaline phosphatase and orthopyrophosphatase enzymes

function: -bone formation by helping the process of calcification

- -formation of matrix
- **Bone vesicles**: - are membranous vesicles that originate from osteoblasts and osteocytes_
- - present in matrix of bones
- - contain enzymes (AP) for Ca++ precipitation

Bone eating cell

Osteoclasts: - is bone resorbing (destroying) cell

- is macrophage cell (phagocytic cell)

Origin: from blood monocytes

LM: - giant (large) cell having brush border (at one side)

- - Multinucleated (>6)
- - Acidpohilic cytoplasm
- -Surrounded by lacunae (towards the brush border only) on one side called Howship’s lacuna

EM:

a. ruffled border zone- brush border formed of ruffled microvilli

b.Clear zone: with less amounts of organoids

c. Vesicular zone: contains mitochondria, organoids and basal infoldings of microvilli

d. basal zone: contains nuclei and some **organoids**

Function: -dissolution of bone from inside (endosteum)

Mechanism:

Secretion of $CO_2 + H_2O$ H_2CO_3 which gives acidic resorbing and destroying medium

Layers of bone

- 1.Periosteum:
- is outer covering of the bone
  formed of two layers
- Outer fibrous layers: tough

Inner osteogenic layer: located below outer fibrous layer
and it is rich in osteogenic cells and osteoblasts.

Function: supportive, origin and insertion of muscles, nutritive or vascular supply

Cont’..

2.Endosteum: - inner lining of bone marrow cavities

- lined by vascular tissue (blood vessels), osteogenic cell, osteoblast and Osteoclast
- The periosteum and endosteum contain **osteoprogenitor cells**
- are also involved in bone repair after injury.
- their blood vessels are involved in supply of nutrition.

Matrix of bone:consists of organic and *inorganic* substances..

organic matrix

is composed of **type I collagen fiber (10%**

- embedded in an AGs
- consisting of:

  sulfated glycosaminoglycans
- various **bone proteins** (bone sialoprotein, osteocalcin).

account for minimal amount of tissue fluid and 1/3 of weight of bone

Cont’..

inorganic matrix formed of in organic substance

- calcium phosphate,
- calcium citrate, and
- calcium carbonate and other elements like
- Na, Mg and Fe

➢ responsible for hardness and rigidity of bone

➢ account for2/3 of weight of bone

Microscopic architecture of the bone

Haversian system - (osteon) entire complex, functional unit of bone

Haversian canal - Carries blood vessel through center of osteon

Lamellae - "little layer" of matrix between concentric rings of osteocytes

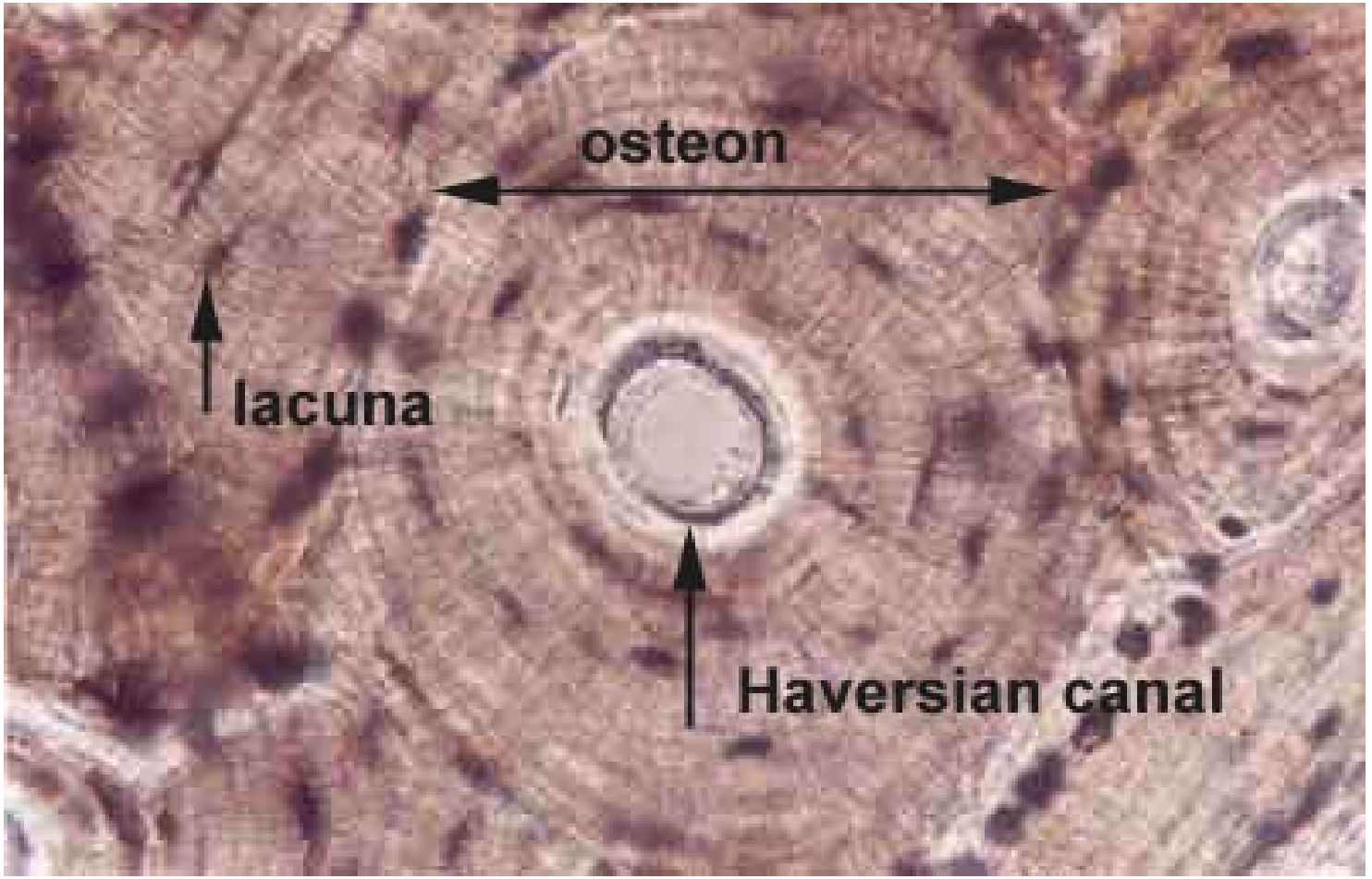
Lacunae - "pools" which house osteocytes

Osteocytes - "bone cells" which maintain bone

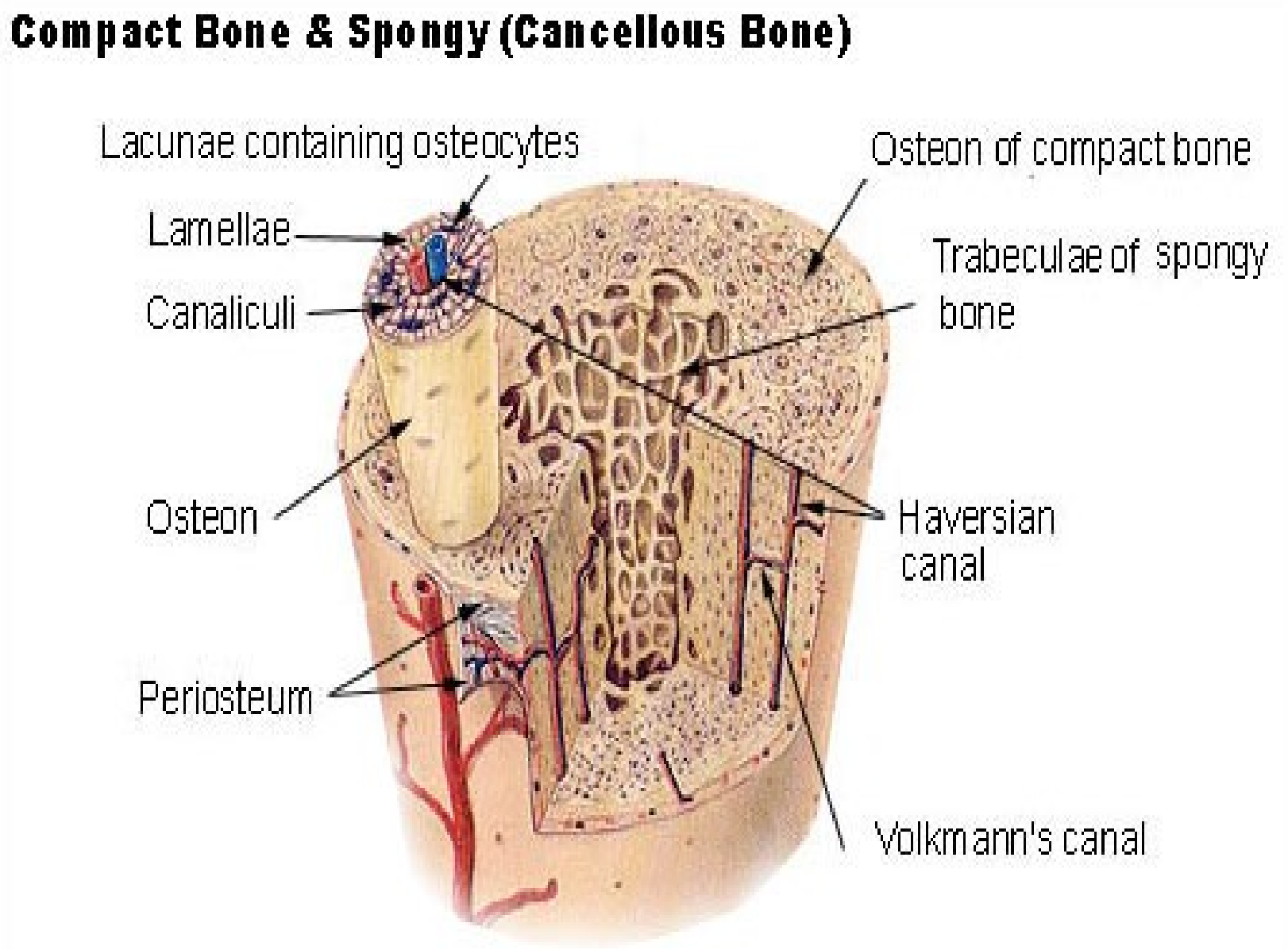
Volkmann's canal - feeder cross connecting vessel for blood supply

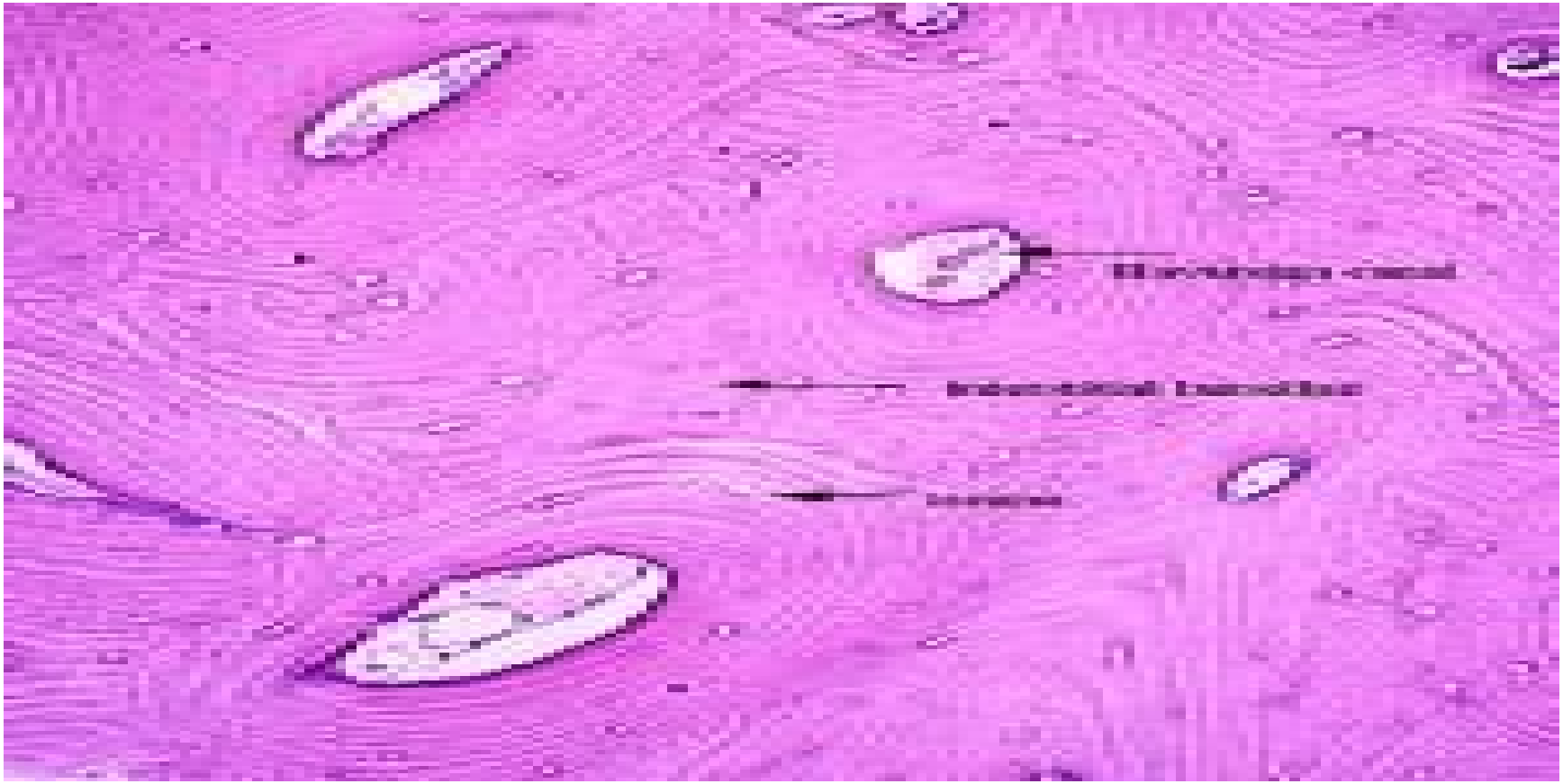
canaliculi - protoplasmic extensions from osteocytes

Bone histology

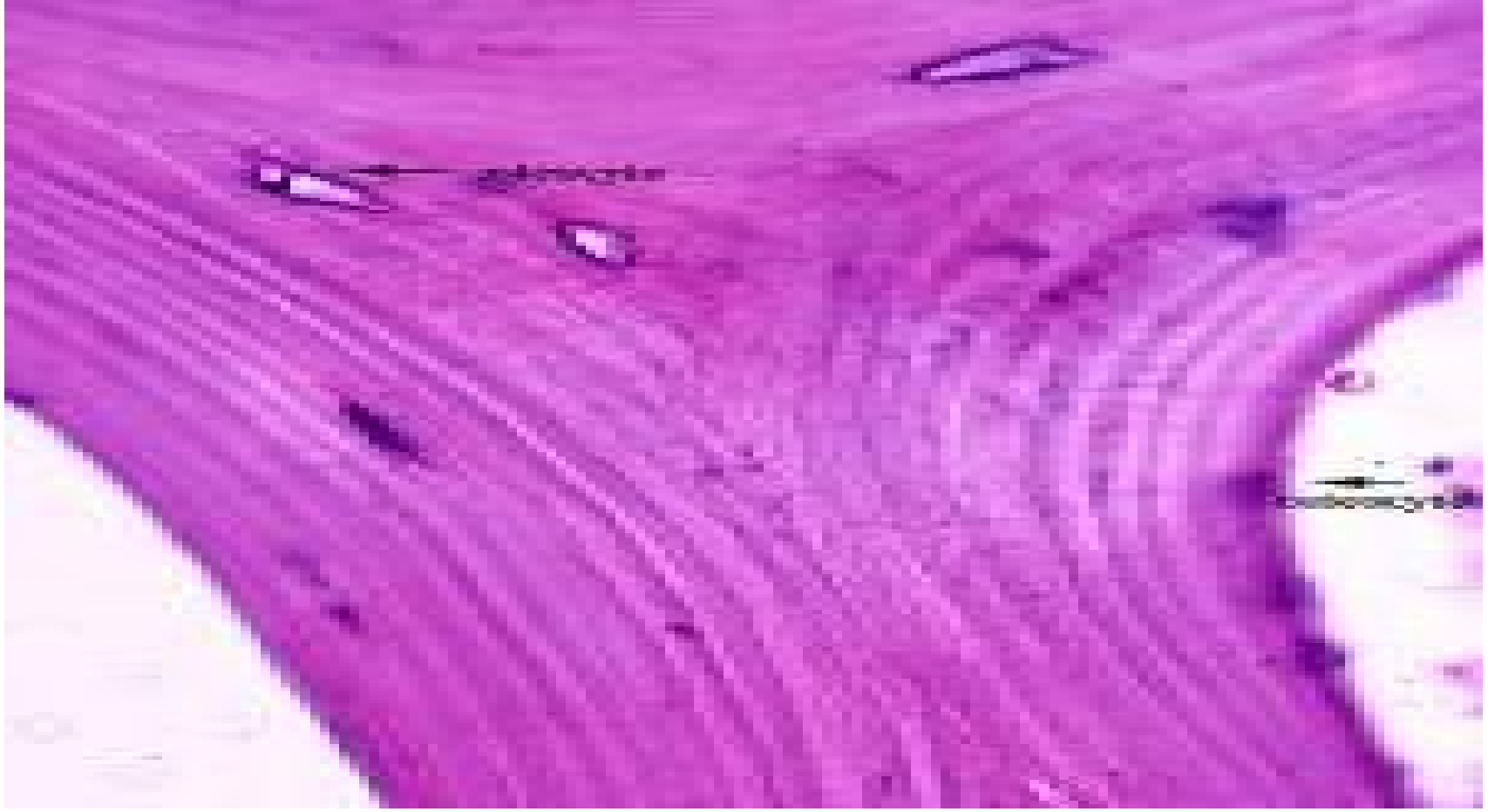


Diagram


Compact Bone & Spongy (Cancellous Bone)
Lacunae containing osteocytes
Lamellae
Canaliculi
Osteon
Periosteum
Osteon of compact bone
Trabeculae of spongy bone
Haversian canal
Volkmann's canal



Cortical bone is composed of haversian systems (osteons). Each osteon has a central haversian canal and peripheral concentric layers of lamellae.



Mature trabecular bone exhibits lamellae and osteocytes between the lamellae

Osteocytes are present in lacunae; their cytoplasmic processes contact each other through the canaliculi

Blood histology

Blood is considered a connective tissue for two basic reasons:

(1)embryologically, it has the same origin (mesodermal) as do the other connective tissue types

(2)blood connects the body systems together bringing the needed oxygen, nutrients, hormones and other signaling molecules, and removing the wastes.

Conti..

In circulating blood two different cell types are found:

enucleated erythrocytes or red blood cells nucleated leukocytes or white blood cells.

Erythrocytes (red blood cells)

RBCs are small (7 um) cells lacking a nucleus.

They stain red with eosin and due to their concave shape have a lighter staining center.

Hemopoiesis

Hemopoiesis is the continual production of new blood cells. There are two kinds of hemopoietic tissue:

(1)myeloid tissue or bone marrow where RBCs, granular WBCs, platelets, monocytes are produced and

(2)lymphoid tissue - thymus, spleen, lymph nodes, where lymphocytes are made.

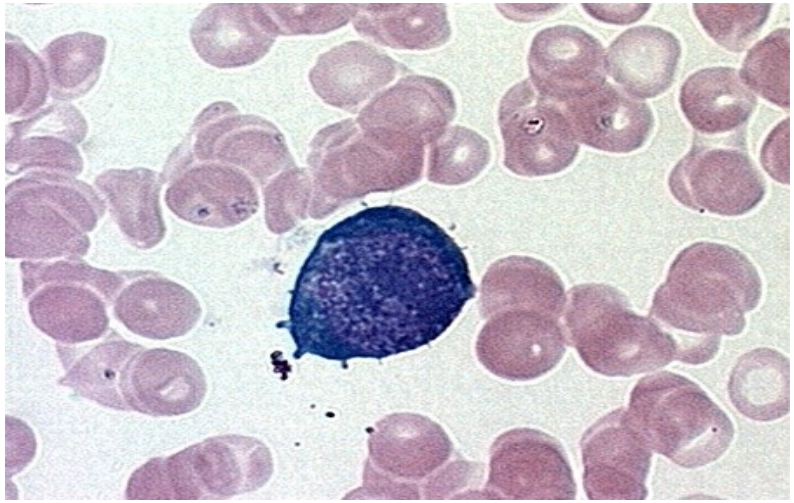
Erythropoiesis -

All blood cells have a common pluripotent stem cell which develops into each type in clonal units will result in a recognizable morphological stages.

During erythropoiesis, the large stem cells first accumulated ribosomes and then decrease in size, condensing their nuclei and synthesizing hemoglobin.

Basophilic erythroblasts

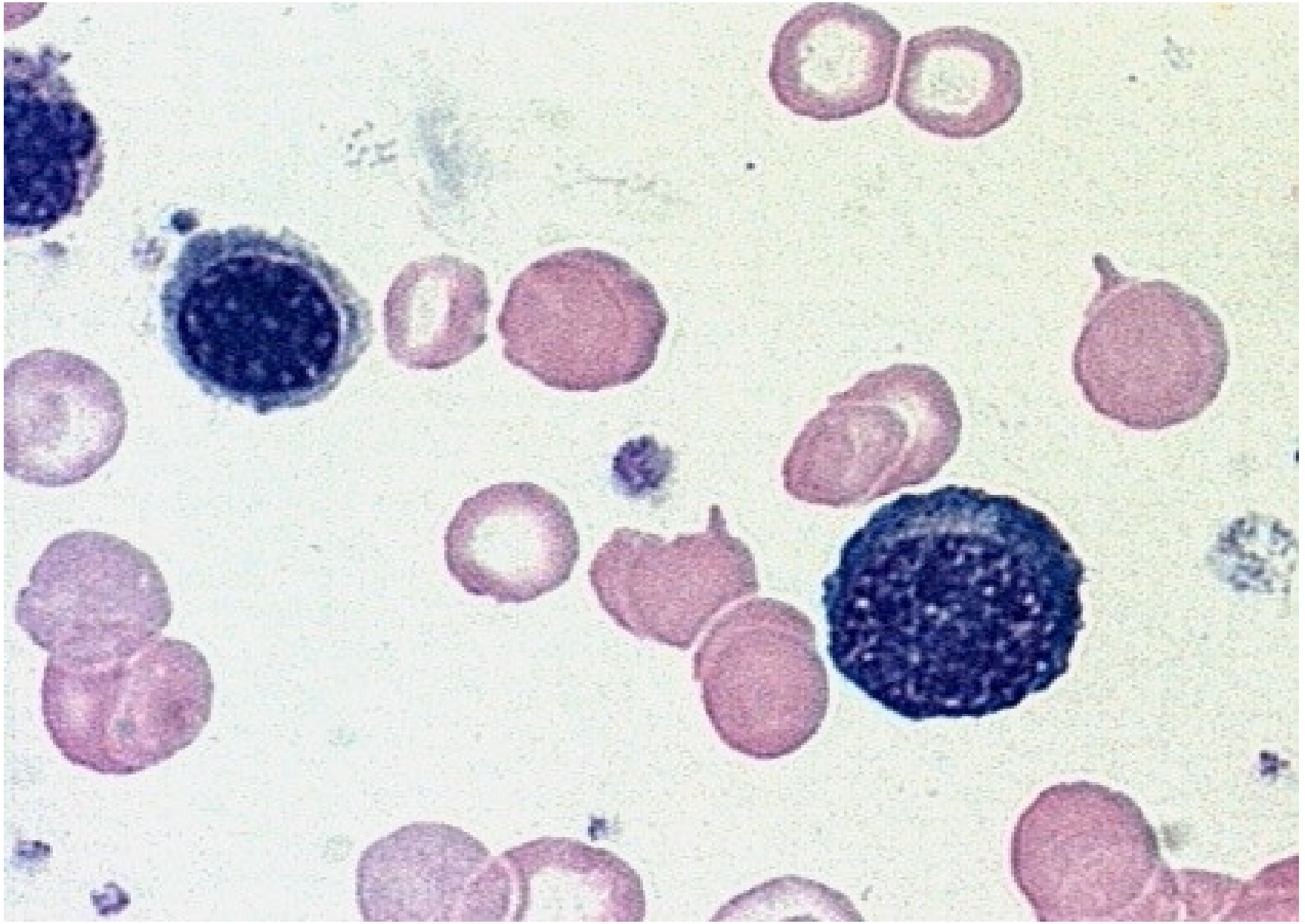
Basophilic erythroblasts are large cells (12-15 um) with a large nucleus beginning to condense. The cytoplasm, full of free ribosomes, stains intensely ba



Polychromatophilic erythroblasts

Polychromatophilic erythroblasts are formed as the nucleus becomes more condensed (a soccer ball-like morphology) and hemoglobin begins to accumulate in the cytoplasm.

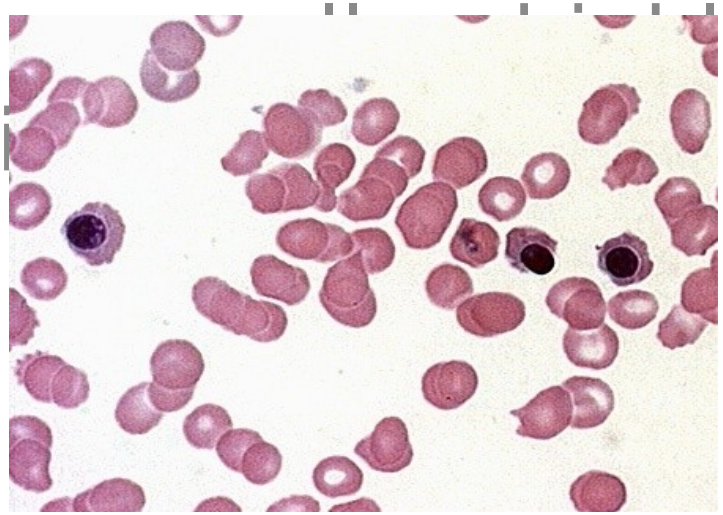
The combined staining of the basophilic ribosomes and acidophilic hemoglobin give these cells a grayish cytoplasm



Normoblasts

Normoblasts are approximately the size of mature RBCs and stain almost the same since most ribosomes have been lost as more hemoglobin accumulates.

They retain a [illegible] condensed (pycnoti[illegible]



Polychromatophilic erythrocytes or reticulocytes

Polychromatophilic erythrocytes or reticulocytes are formed when a normoblast loses its nucleus.

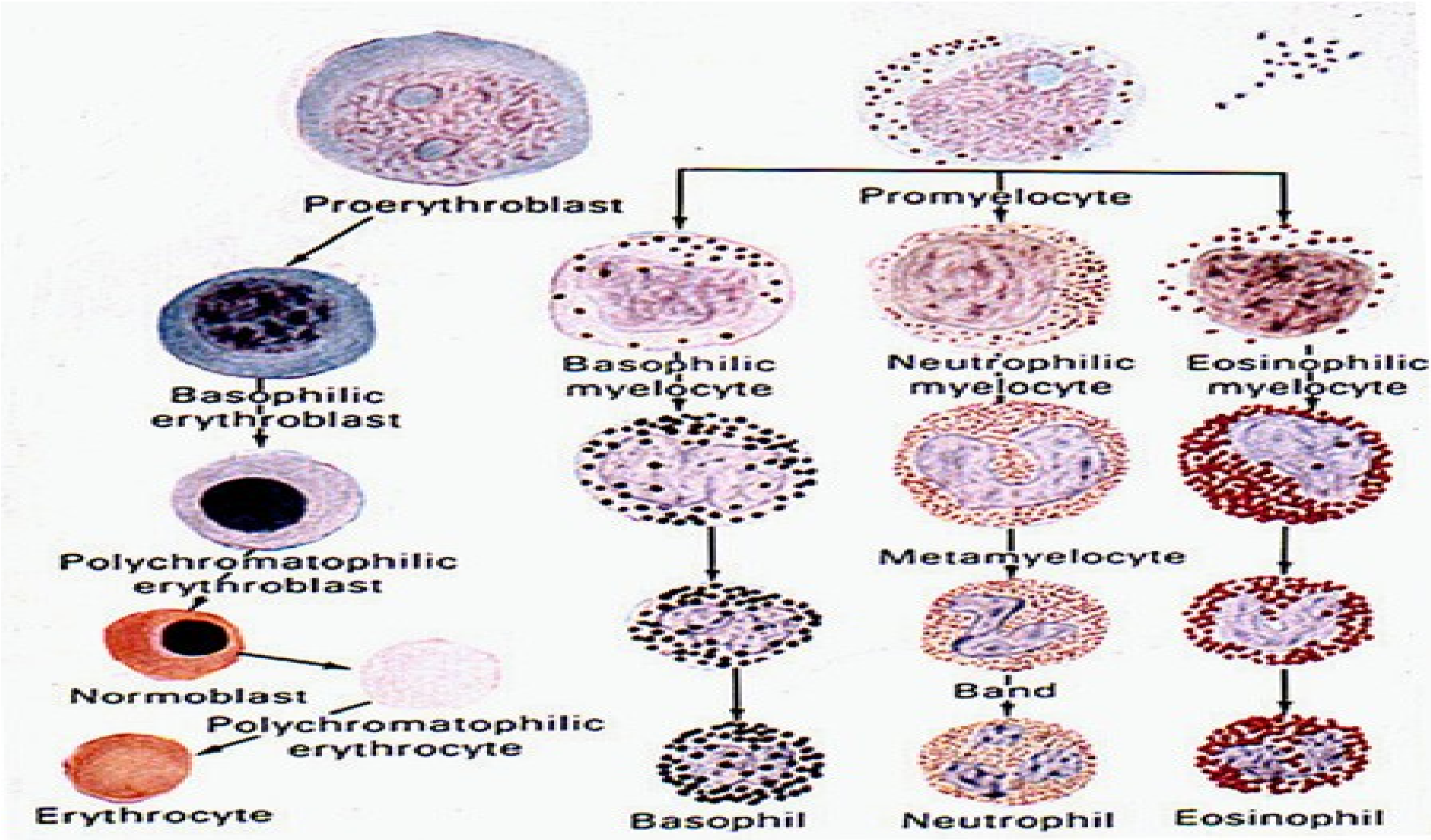
However, these cells still retain some ribosomes and combined with the hemoglobin, some polychromatic staining (pink-blue cytoplasm) is observed .

Granulopoiesis

This process occurs in bone marrow along side erythropoiesis with each type (eosinophil, basophil, neutrophil) going through its own pathway.

Two processes take place simultaneously:

(1)nuclei condense to adult form (bi-lobed, multi-lobed, etc) and

(2)the cell begins to synthesize and collect its specific granule population.

A summary of the developmental stages are found in this diagram