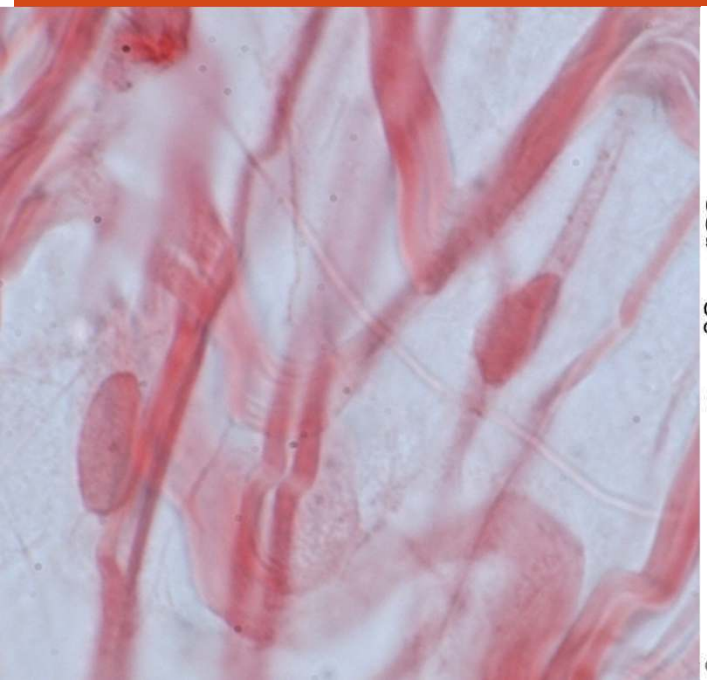
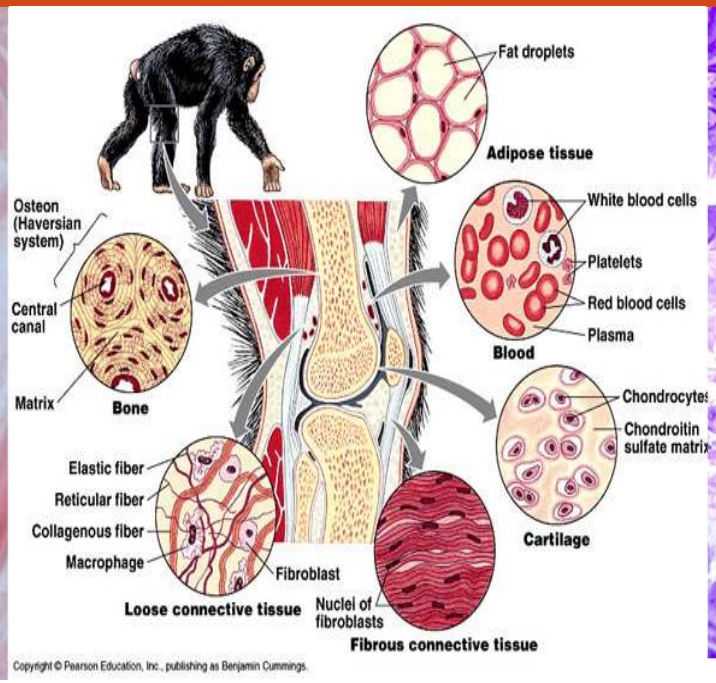
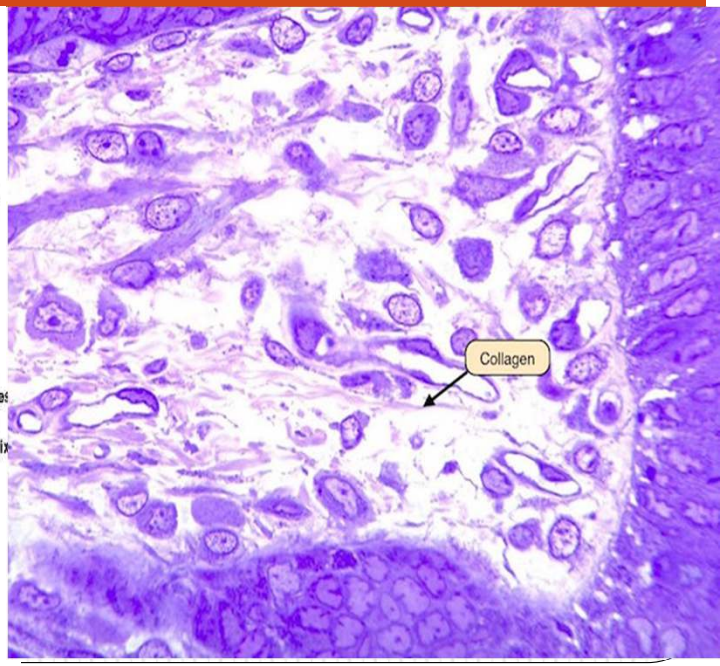
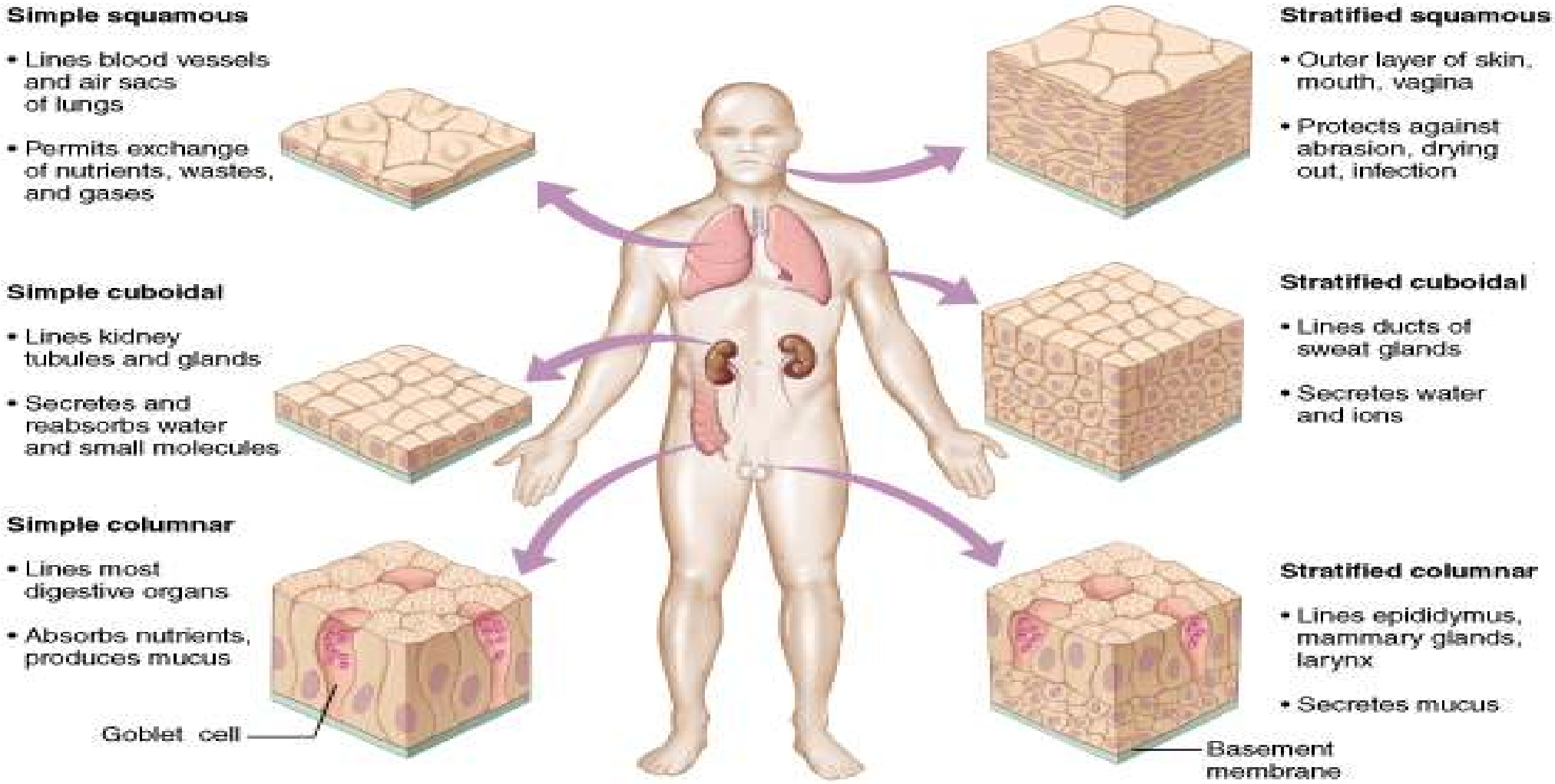
CONNECTIVE TISSUES

DANIL HAMMOUDI. MD

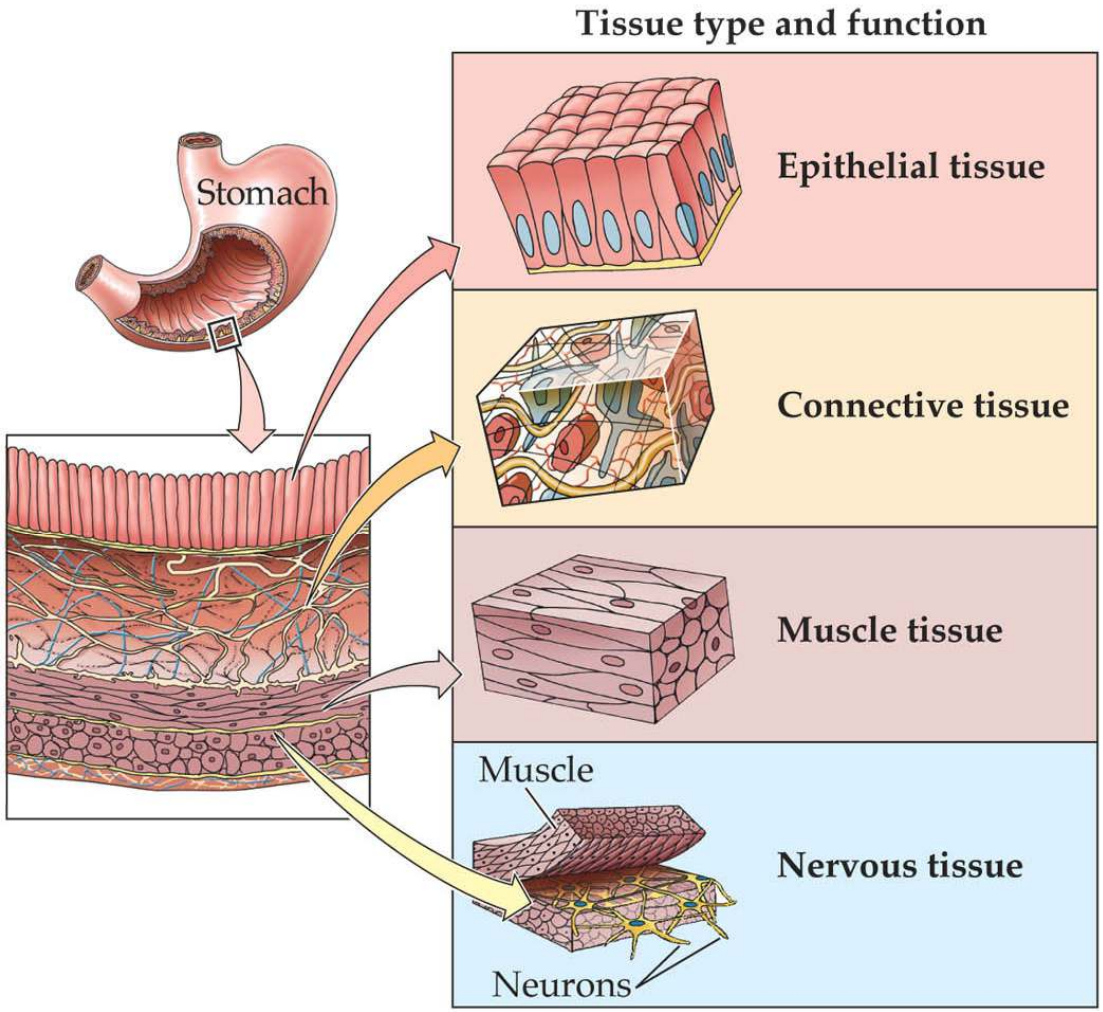








(a) Most epithelial tissues line or cover surfaces or body cavities



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, **Figure 41.2 Four Types of Tissue**

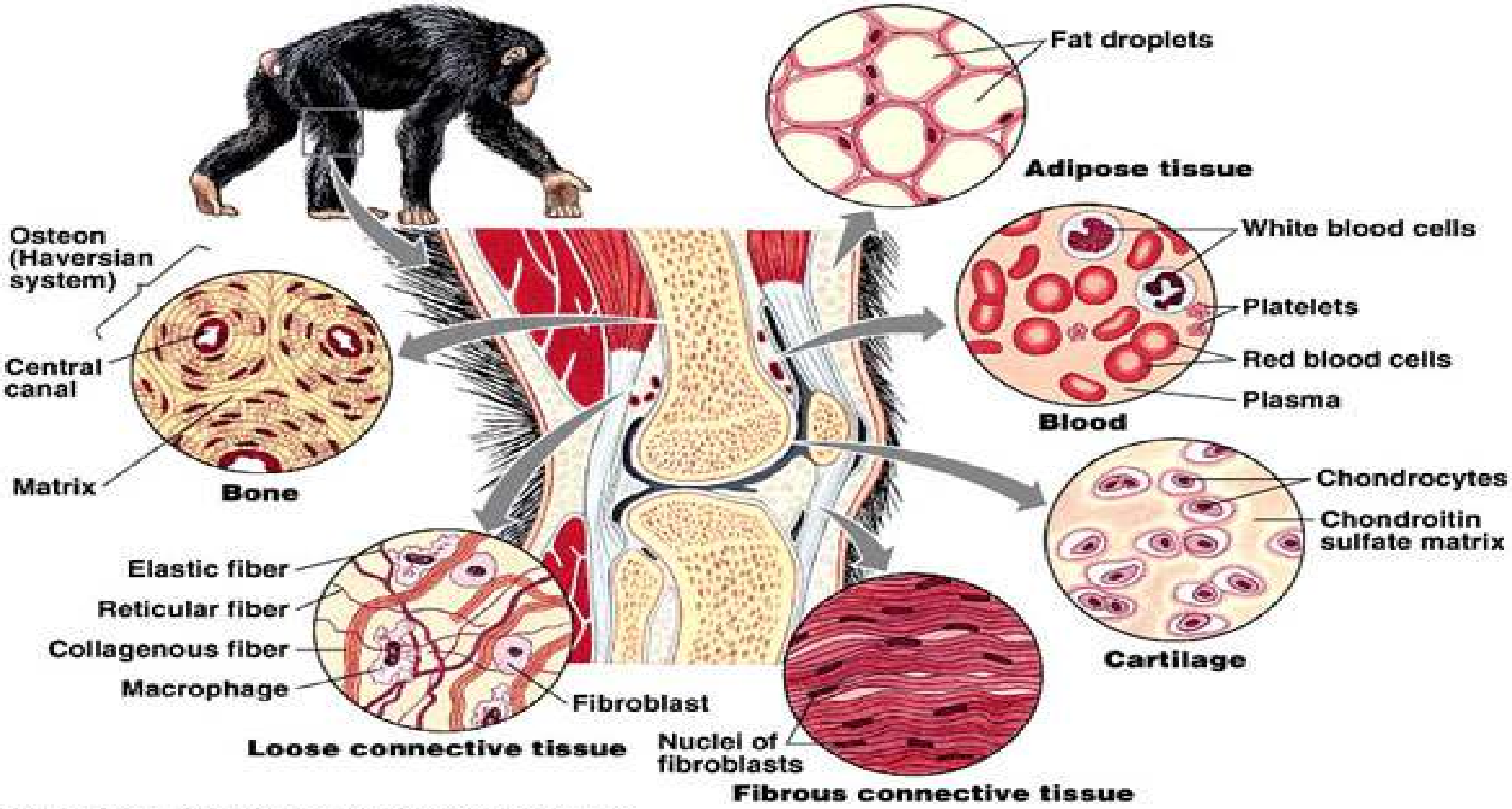
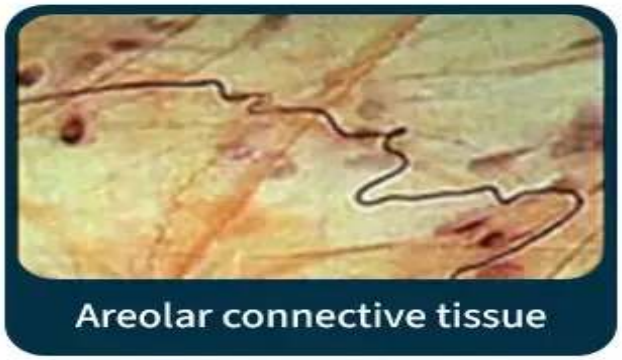
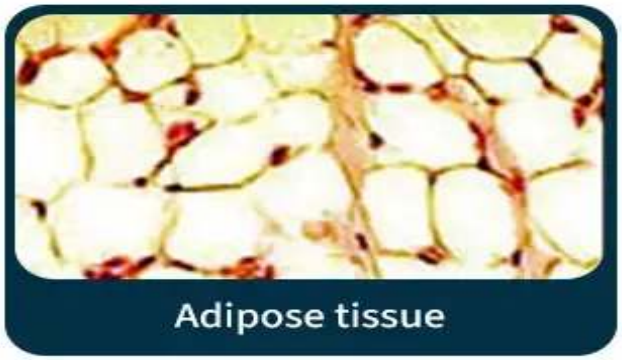
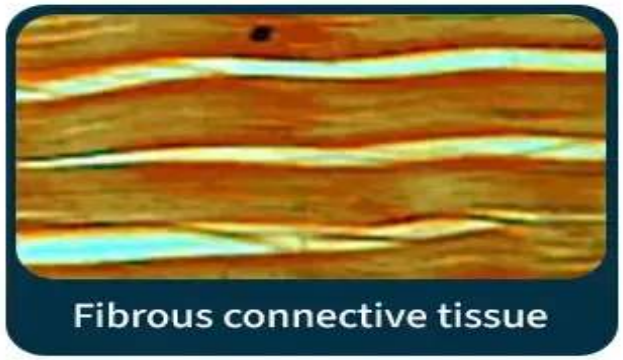


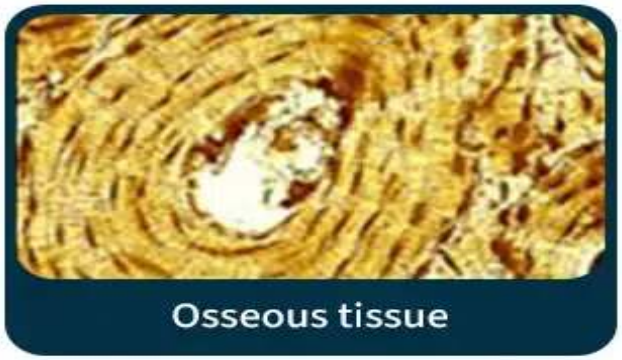
Diagram of Connective Tissue


Areolar connective tissue


Adipose tissue


Fibrous connective tissue


Blood

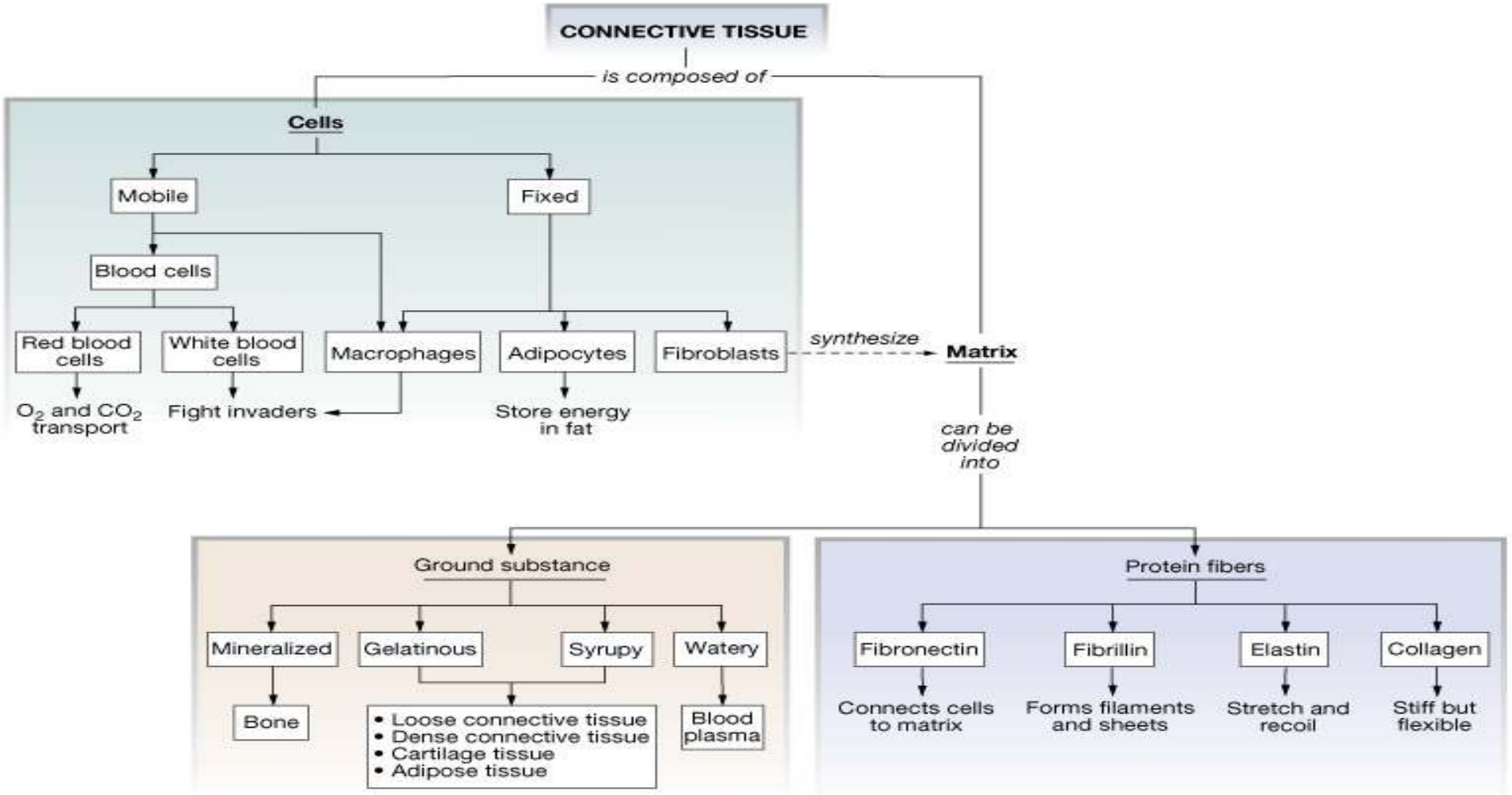

Osseous tissue


Hyaline cartilage

Embryonic Connective Tissue

- All connective tissues derive from the **mesodermal layer of the embryo** .
- The first connective tissue to develop in the embryo is **mesenchyme**, the stem cell line from which all connective tissues are later derived.
- Clusters of mesenchymal cells are scattered throughout adult tissue and supply the cells needed for replacement and repair after a connective tissue injury.
- A second type of embryonic connective **tissue forms in the umbilical cord, called mucous connective tissue or Wharton's jelly.**
- This tissue is no longer present after birth, leaving only scattered mesenchymal cells throughout the body.

Supporting Connective Tissues



Connective Tissue- definition, structure, cells, types, functions, diseases

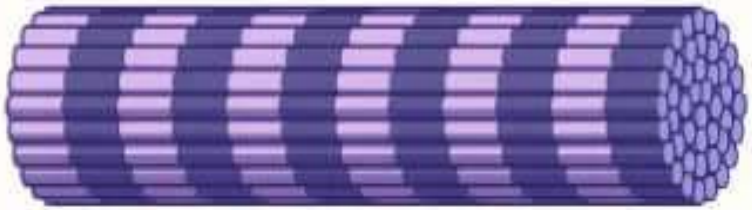


Fig- Collagen fibers

Fibroblasts

Adipocytes

Fig- Elastins

Knee Meniscus

Chondrocyte

Rheumatoid arthritis

Tendons

Osteocyte

Osteoclast

Osteoblast

Osteon

CONNECTIVE TISSUE

- Connective tissue is responsible for providing structural support for the tissues and organs of the body.
- This mechanfunction is important in maintaining the form of the body, organs and tissues.
- The tissue derives its name from its function in connecting or binding cells and tissues.
- Connective tissue is composed of:
  - **cells**
  - **extracellular matrix**.

Structural Elements of Connective Tissue

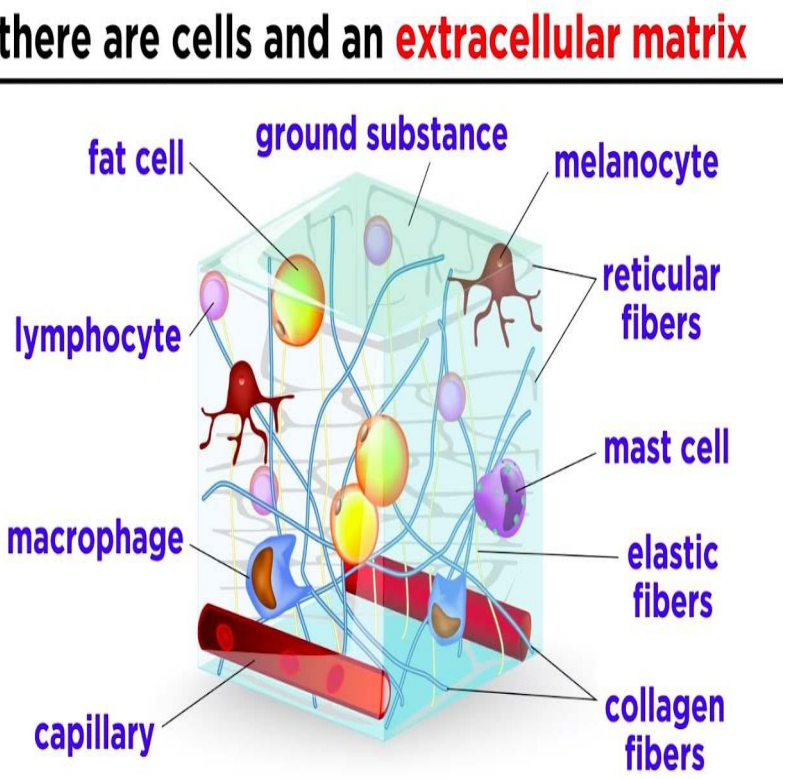
- Ground substance – unstructured material that fills the space between cells.
  - A gel-like substance composed of proteoglycans, glycosaminoglycans (GAGs), and glycoproteins.
  - It fills the spaces between cells and fibers, providing hydration, lubrication, and support.
- Fibers – collagen, elastic, or reticular (provide structural support, elasticity, and resilience to the tissue. Collagen fibers are the most abundant and provide tensile strength.)
- Fluid: Connective tissue contains interstitial fluid, which provides nutrients and oxygen to cells and facilitates waste removal
- Cells –
  - fibroblasts,
  - chondroblasts,
  - osteoblasts,
  - hematopoietic stem cells (red cells, white cells)

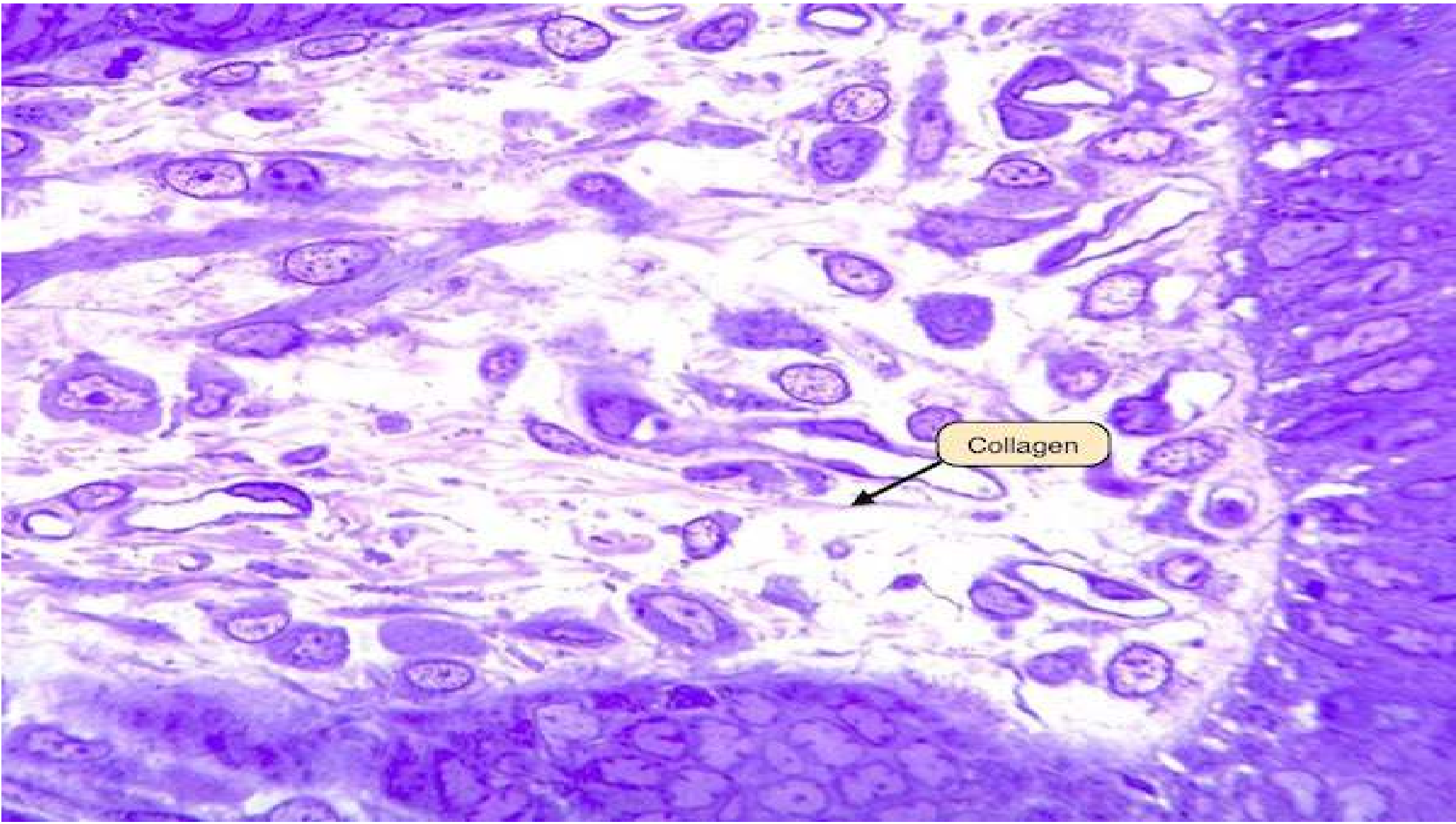
Extracellular Matrix (ECM): The ECM is the non-cellular component of connective tissue and consists of three main elements:

- Fibers:
- Ground substance
- Fluid:

Ground Substance

- **Interstitial (tissue) fluid**
- **Adhesion proteins** – fibronectin and laminin
- **Proteoglycans – glycosaminoglycans (GAGs)**
- Functions: as a molecular sieve through which nutrients diffuse between blood capillaries and cells.
  - Ground substance provides hydration, lubrication, and support to the tissue.




Collagen

Functions of Connective Tissue

- Binding and support
- Protection
- Insulation
- Transportation

functions of connective tissue include:

1.Structural Support: Connective tissue provides structural support to organs, tissues, and the body as a whole. It helps maintain the shape and integrity of organs and supports the weight and tension placed on various body structures.

2.Connection and Binding: Connective tissue connects and binds different tissues and organs together, forming a cohesive framework throughout the body. It creates a network that helps maintain the spatial organization of tissues and organs and allows them to function together as a unit.

3.Protection: Connective tissue provides protection to delicate structures within the body. For example, adipose tissue acts as a cushioning layer around organs, protecting them from mechanical damage. Additionally, certain types of connective tissue, such as dense irregular connective tissue, provide structural support to organs and protect them from external forces.

4.Transportation: Blood, a specialized connective tissue, transports oxygen, nutrients, hormones, and waste products throughout the body. Blood vessels within connective tissue facilitate the distribution of these substances to cells and tissues, ensuring proper function and homeostasis.

5.Immunity: Connective tissue plays a crucial role in the body's immune response. Immune cells, such as macrophages and lymphocytes, are found within connective tissue and help defend against pathogens, foreign particles, and cellular debris. Connective tissue also facilitates the migration of immune cells to sites of infection or injury.

6.Repair and Regeneration: Connective tissue contributes to wound healing and tissue repair processes. Fibroblasts within connective tissue produce extracellular matrix components, such as collagen and elastin, which are essential for tissue remodeling and scar formation. Additionally, connective tissue helps establish a supportive environment for tissue regeneration and recovery.

7.Storage: Adipose tissue, a type of connective tissue, serves as a storage site for energy in the form of triglycerides. It stores excess energy from food intake and releases it when needed for metabolic processes, thermoregulation, and physical activity.

The **extracellular matrix** is composed of :

- **Protein fibers** (collagen fibers, reticular fibers, elastic fibers)
- **Amorphous ground substance**
- **Tissue fluid** (not preserved in histological preparations).

- The amount of tissue fluid is fairly constant and there is an equilibrium between the water entering and leaving the intercellular substance of the connective tissue.

- **In pathological conditions (traumatic injury, inflammation) fluid may accumulate in the connective tissue, a condition known as edema.**

The main components of the extracellular matrix include:

1.Collagen: Collagen is the most abundant protein in the ECM and provides tensile strength and structural integrity to tissues. It forms long, fibrous protein strands that are organized into fibrils and fibers.

- Collagen fibers are essential for maintaining tissue structure and resisting mechanical forces.

2.Elastin: Elastin is a protein that provides elasticity and resilience to tissues, allowing them to stretch and recoil without permanent deformation.

- Elastin fibers are found in tissues that require elasticity, such as skin, blood vessels, and lung tissue.

3.Proteoglycans: Proteoglycans are large molecules composed of a core protein bound to glycosaminoglycan (GAG) chains. They are highly hydrophilic and contribute to the gel-like consistency of the ECM.

- Proteoglycans play a crucial role in retaining water within tissues, providing hydration and lubrication.

4.Glycosaminoglycans (GAGs): GAGs are long, linear polysaccharides composed of repeating disaccharide units.

- They are **highly negatively charged and interact with water molecules**, **contributing to the hydration and viscosity of the ECM.**
- Common GAGs include hyaluronic acid, chondroitin sulfate, and heparan sulfate.

5.Glycoproteins: Glycoproteins are proteins that are covalently bound to carbohydrate chains.

- They serve as adhesive molecules that anchor cells to the ECM and mediate cell-cell and cell-matrix interactions. Examples of glycoproteins in the ECM include fibronectin, laminin, and thrombospondin.

6.Water: Water is an essential component of the ECM, contributing to its hydration and fluidity.

- It fills the spaces between fibers and molecules, providing a medium for cell migration, nutrient transport, and waste removal.

7.Other molecules: The ECM also contains various other molecules, including growth factors, cytokines, and proteases, which regulate cellular behavior and tissue remodeling processes.

CONNECTIVE TISSUES

Types

- ***Loose CT***:
  - biological packing material;
  - supports epithelia lining gut,
  - respiratory & urinary tracts, etc.;
  - open = areolar.
- ***Dense CT***: physical support,
- ***Regular*** : ligaments, tendons and caps
- ***irregular*** : dermis
- ***Adipose tissue*** (adipocytes)

  Brown: multilocular
  White: unilocular
- ***Cartilage***
  - Hyaline
    Elastic
    Fibroelastic
- ***Bone***

Table 4.8	Connective Tissue Proper		
Type	**Structure**	**Function**	**Location**
Loose Connective Tissue	Relatively fewer cells and fibers than in dense connective tissue; fibers are loosely arranged	Cushioning of organs; packing around organs	Surrounding vessels; in spleen and liver; in subcutaneous layer
Areolar (loose) connective tissue	Fibroblasts; lesser amounts of collagen and elastic fibers; viscous ground substance	Binds and packs around organs	Surrounding nerves, vessels; forming subcutaneous layer
Adipose tissue	Adipocytes	Protects; stores fat; insulates	Subcutaneous layer; surrounding kidney and selected other organs
Reticular connective tissue	Stroma of reticular fibers	Forms stroma of lymphatic organs	Stroma of spleen, liver, lymph nodes, bone marrow
Dense Connective Tissue	Higher proportion of fibers to ground substance; protein fibers densely packed together	Provides strength and support	Fibrous capsules; tendons, ligaments, dermis
Dense regular connective tissue	Densely packed collagen fibers are parallel to direction of stress	Provides strength and flexibility	Tendons and ligaments
Dense irregular connective tissue	Densely packed collagen fibers are interwoven; fibers are irregularly clumped together	Provides tensile strength in all directions	Dermis; capsules of organs
Elastic connective tissue	Elastic and collagen fibers are arranged irregularly	Provides framework and supports organs	Walls of large arteries

TABLE 5-4 Characteristics of Connective Tissue

Tissue Type	Function	Location and Cellular Description
Adipose connective tissue	Protects and insulates, stores fat	Beneath skin, around kidneys, behind eyes, on surface of heart; cells in fluid-gel matrix
Areolar connective tissue	Binds organs	Beneath skin, surrounding organs; cells in fluid-gel matrix
Blood	Transports gases, defends against disease, acts in clotting	Throughout the body in close system of blood vessels and heart chambers; cells and platelets in fluid matrix
Bone	Supports and protects, provides framework	Bones of skeleton and in middle ear; cells in solid matrix
Cartilage Elastic cartilage Fibrocartilage Hyaline cartilage	Supports and protects (provides flexible framework) (absorbs shock) (provides framework)	Cells in solid-gel matrix External ears, part of larynx Between bony parts of spinal column, parts of pelvic girdle, and knee Ends of bones, nose, and rings in respiratory passage walls
Dense irregular connective tissue	Sustains tissue tension	Dermis; cells in fluid-gel matrix
Dense regular connective tissue	Binds body parts	Tendons, ligaments; cells in fluid-gel matrix
Elastic connective tissue	Provides elasticity	Connects parts of spinal column, also in walls of arteries and airways; cells in fluid-gel matrix
Reticular connective tissue	Provides support	Walls of liver and spleen; cells in fluid-gel matrix

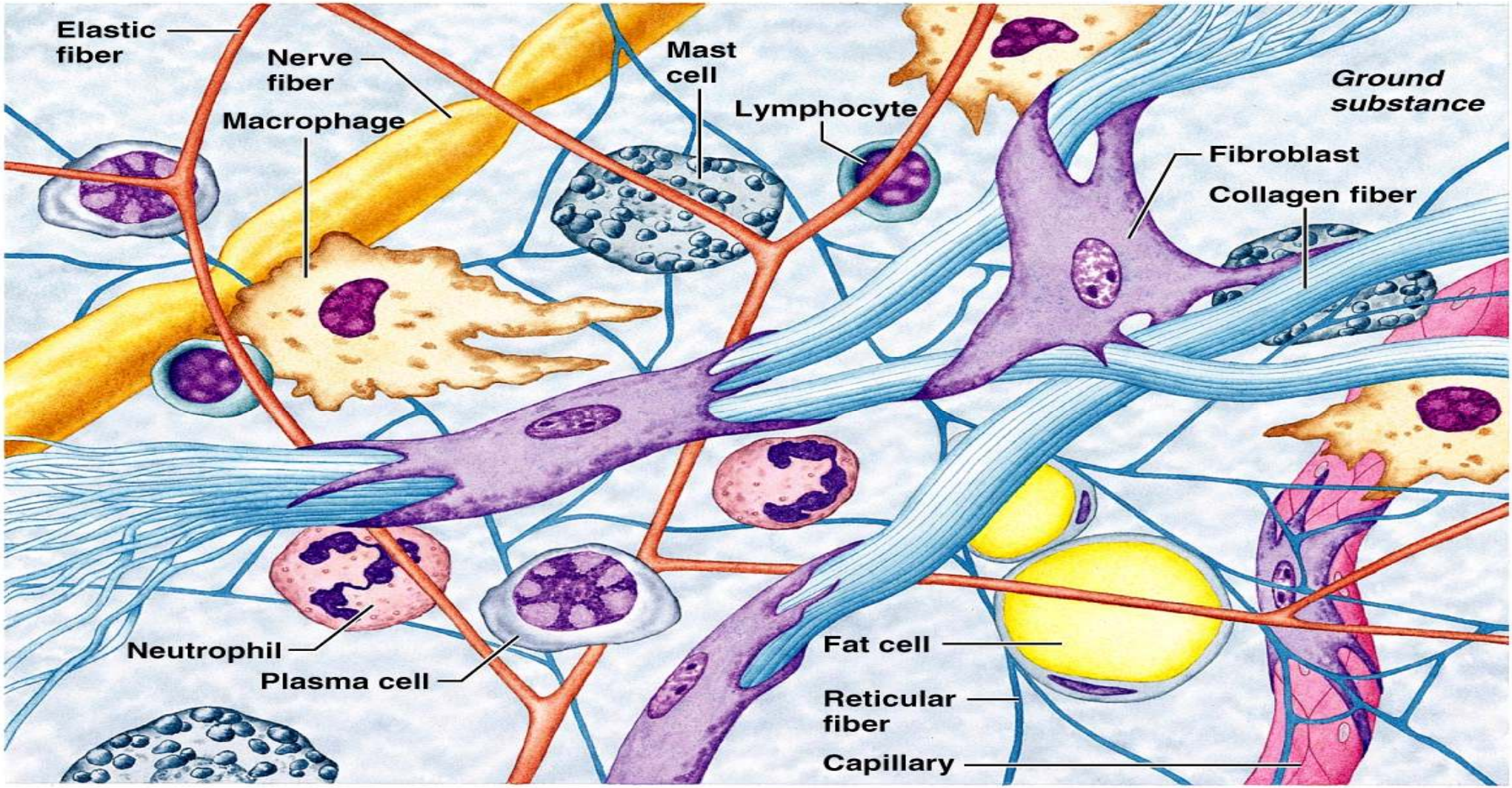
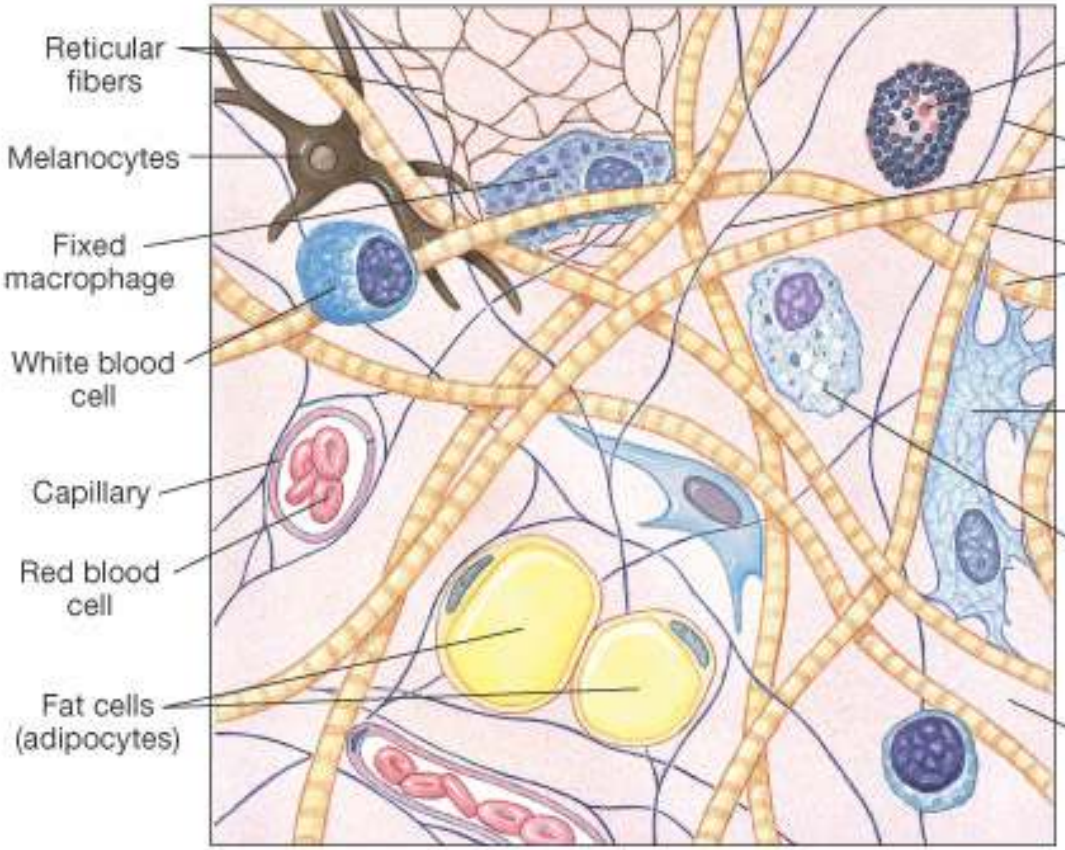
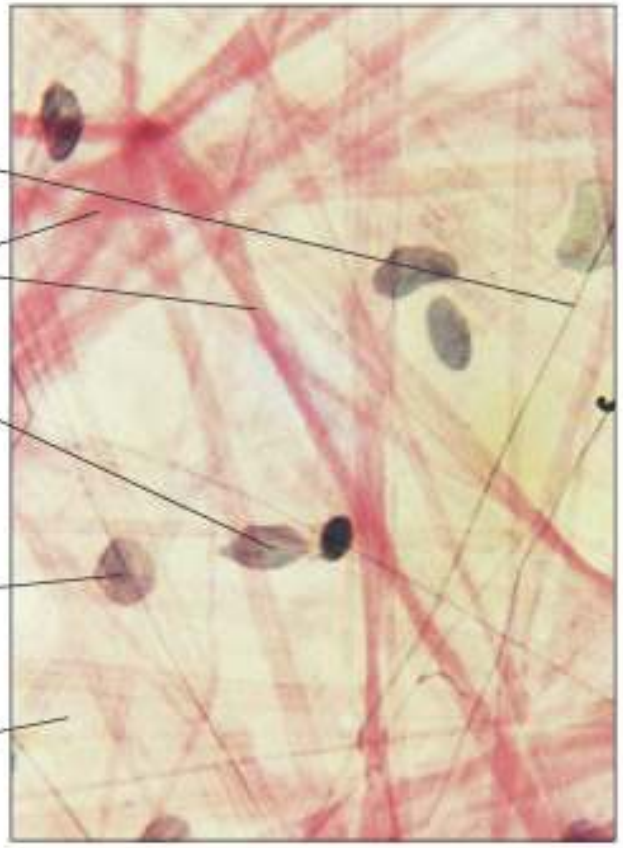


Figure 4.8

Connective Tissues (CT)



Loose connective tissue



Light micrograph of loose connective tissue

CLASSIFICATION OF CONNECTIVE TISSUE

The two main categories of connective tissue are:

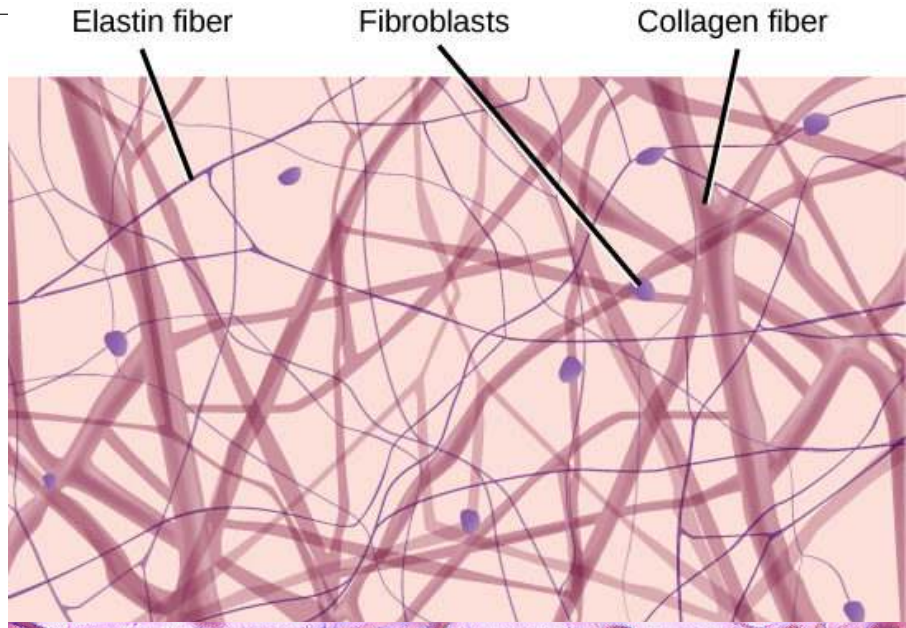
- **Loose Connective Tissue**
- **Dense Connective Tissue**

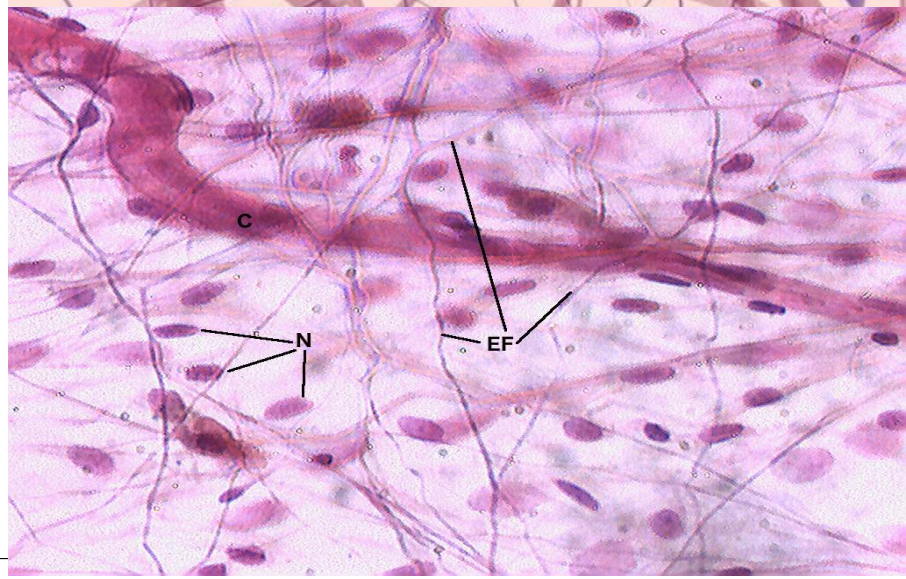
Types of connective tissue proper						
	Loose connective tissue proper			Dense connective tissue proper		
Constituents	**Areolar connective tissue**	**Reticular connective tissue**	**Adipose**	**Regular dense connective tissue**	**Irregular dense connective tissue**	**Elastic dense connective tissue**
Cells	Fibroblasts, w/some macrophages, other white blood cells	Fibroblasts, w/many white blood cells	Adipocytes, w/some macrophages, other white blood cells.	Fibroblasts, w/ some macrophages, other white blood cells	Fibroblasts, w/ some macrophages, other white blood cells	Fibroblasts, w/ some macrophages, other white blood cells
Protein fibers	Collagen, elastic	Reticular	Collagen, some reticular	Thick collagen fibers, in parallel	Thick collagen fibers, no consistent arrangement	Elastic mainly, some collagen
Ground substance	Jelly-like, abundant	Jelly-like abundant	Smaller amounts due to abundant cells	Smaller amounts due to abundant fibers	Smaller amounts due to abundant fibers	Smaller amounts due to abundant fibers
Locations	Under epithelia of skin, mucous membranes, capillaries, organs	Spleen, lymph nodes, bone marrow	Under skin, surrounding organs, between muscle fibers, in pericardium.	Tendons, ligaments, aponeuroses	Capsules around joints and organs, dermis of skin	Walls of large arteries, walls of bronchial tubes, vertebral ligaments

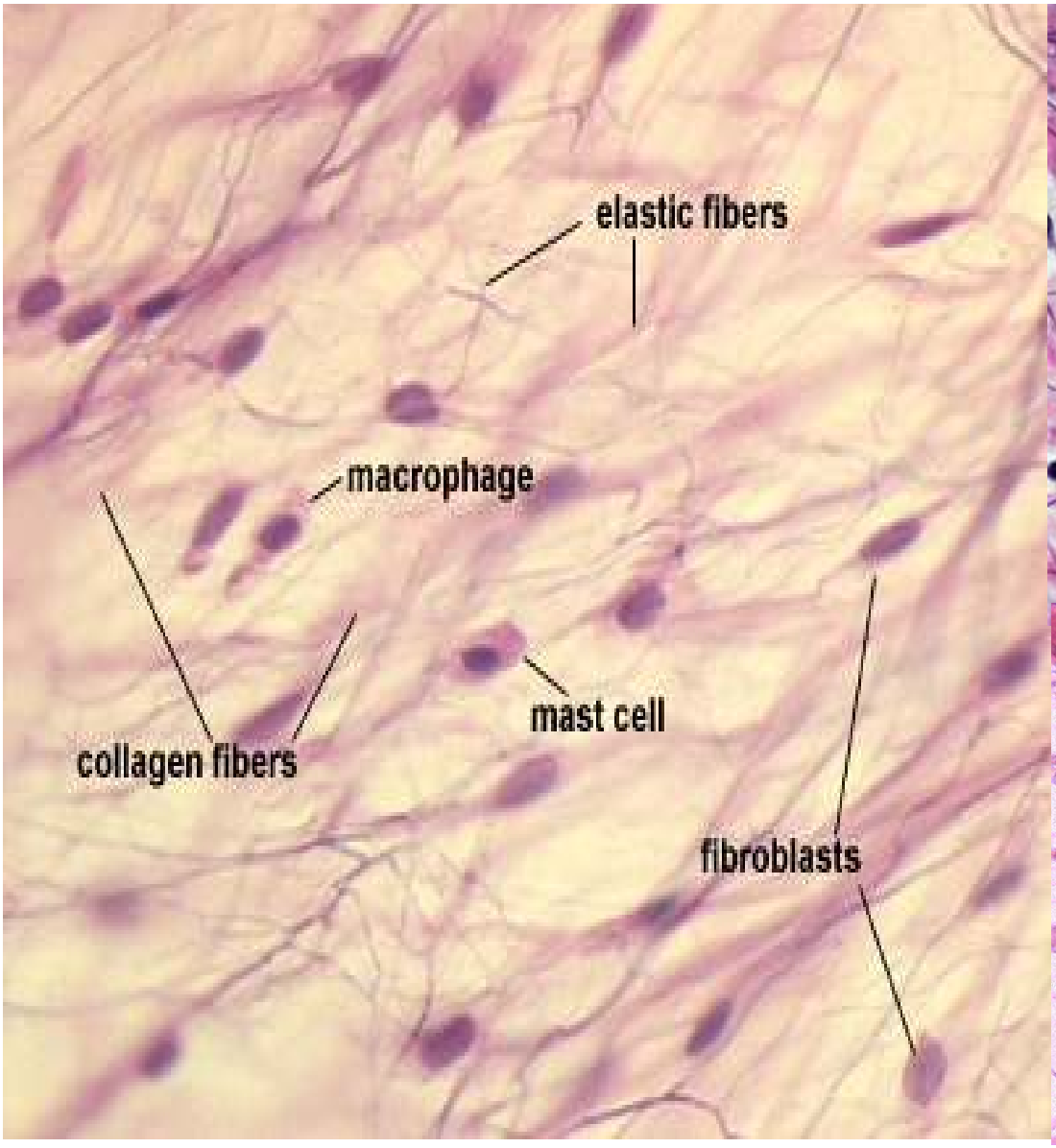
Loose Connective Tissue or areolar connective tissue

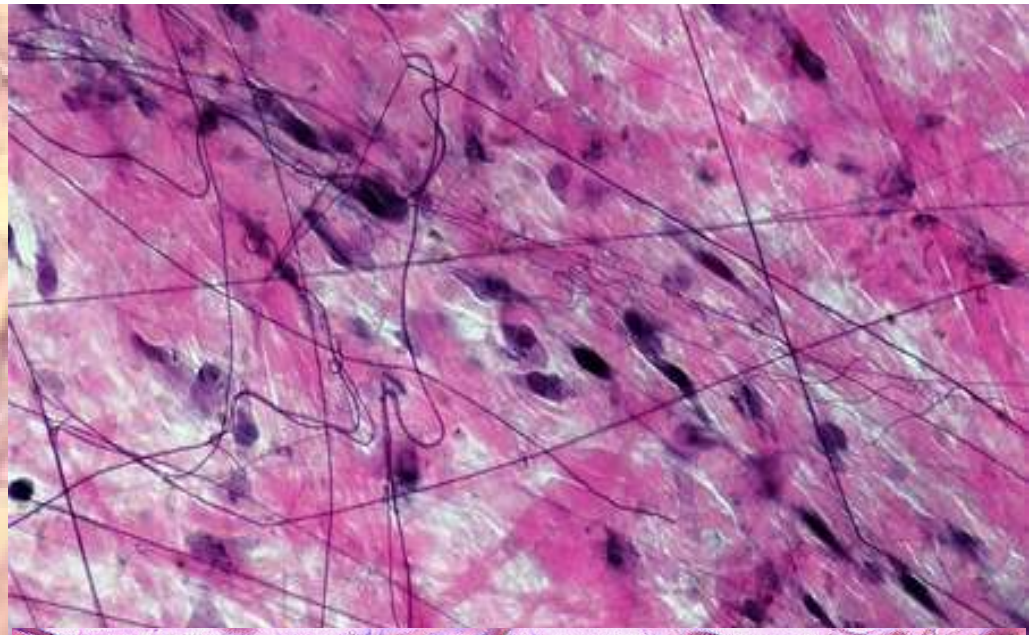
- Loose connective tissue (**areolar tissue**) is the more common type.

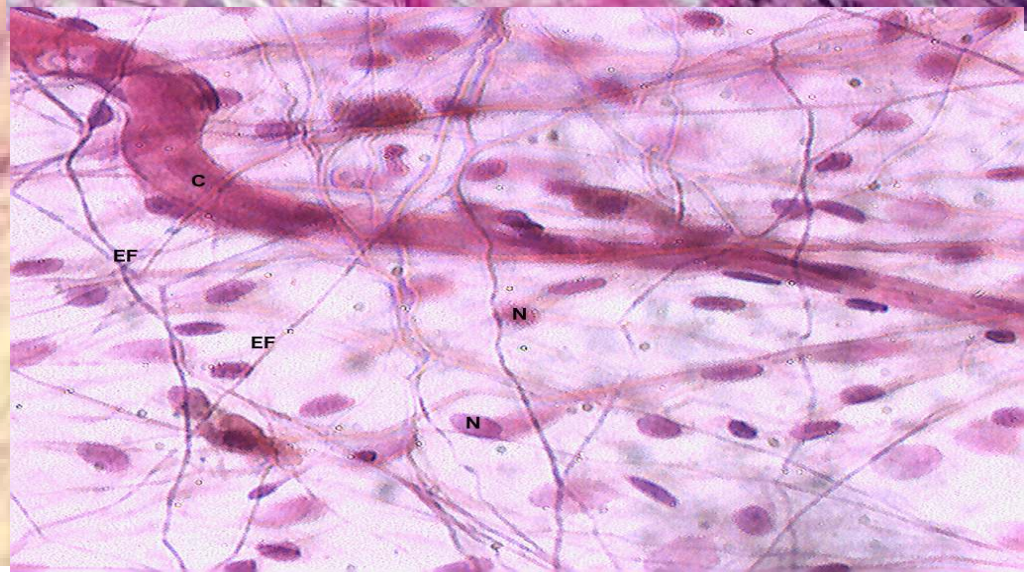
- It fills the spaces between
  - **muscle fibers,**
  - **surrounds blood and lymph vessels,**
  - **is present in the serosal lining membranes (of the peritoneal, pleural and cardiac cavities),**
  - **in the papillary layer of the dermis and in the lamina propria of the intestinal and respiratory tracts etc.**






elastic fibers
macrophage
mast cell
collagen fibers
fibroblasts

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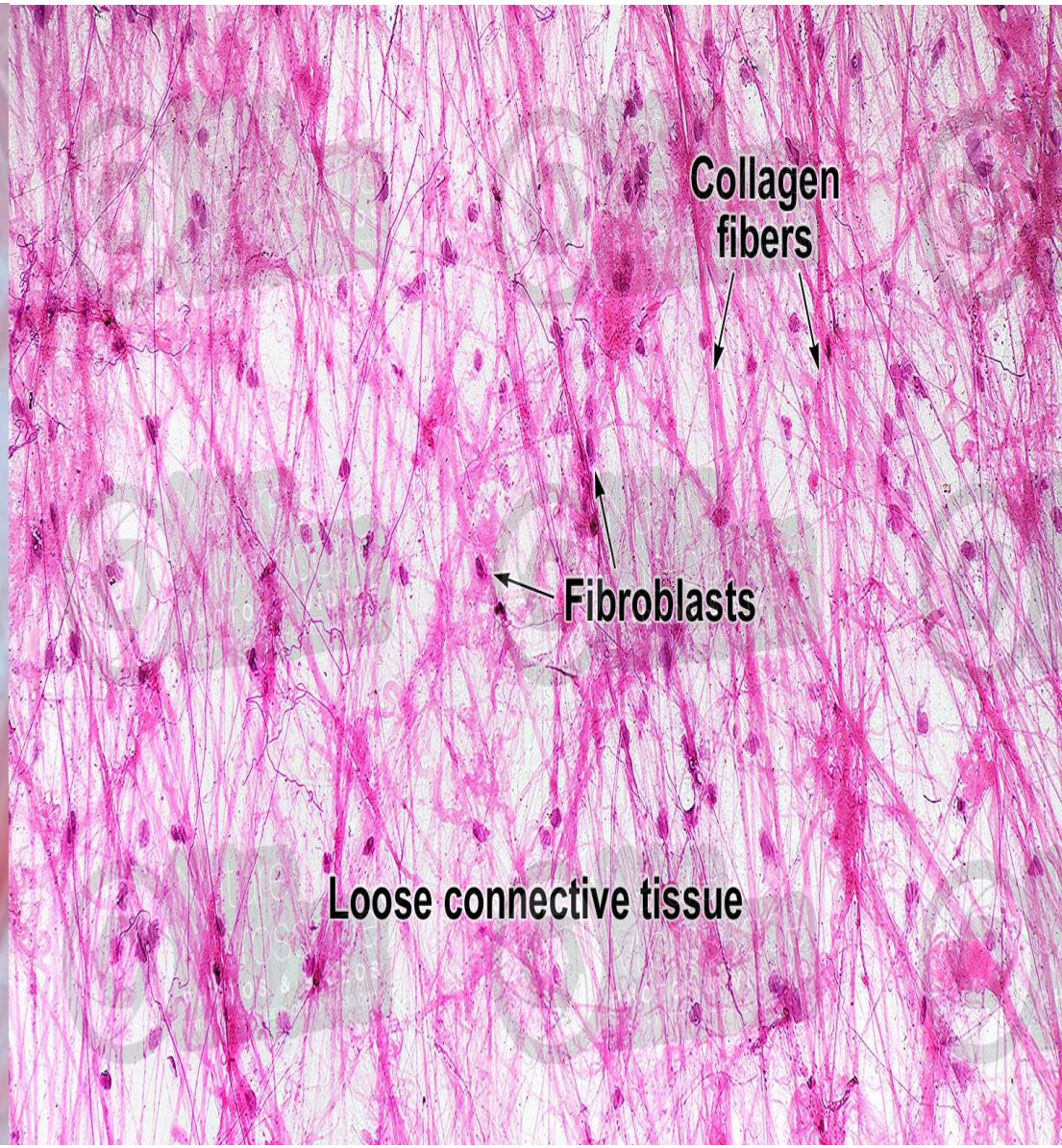

Collagen fibers
Fibroblasts
Loose connective tissue

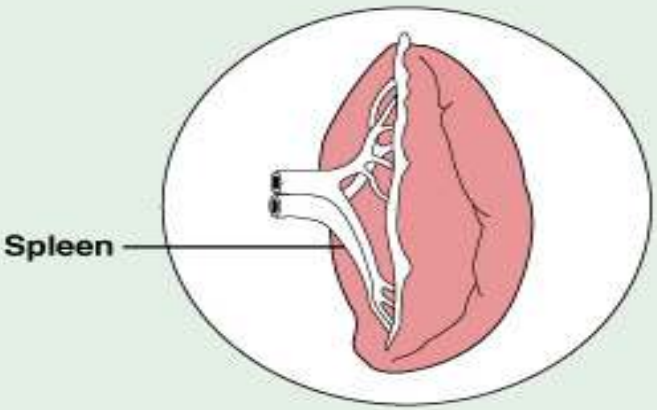
Connective Tissue Proper: Loose

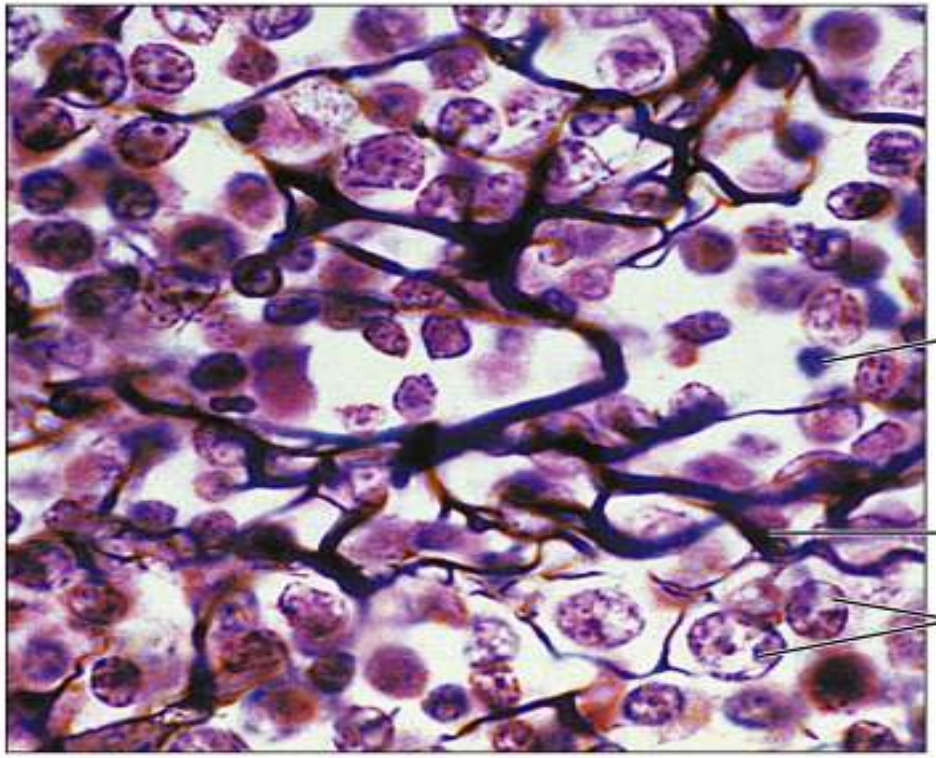
(d) Connective tissue proper: loose connective tissue, reticular

Description: Network of reticular fibers in a typical loose ground substance; reticular cells lie on the network.

Function: Fibers form a soft internal skeleton (stroma) that supports other cell types including white blood cells, mast cells, and macrophages.

Location: Lymphoid organs (lymph nodes, bone marrow, and spleen).





Photomicrograph: Dark-staining network of reticular connective tissue fibers forming the internal skeleton of the spleen (350×).

Dense Connective Tissue

Dense connective tissue is divided into two sub-categories:

- **dense irregular connective tissue**
- **dense regular connective tissue**

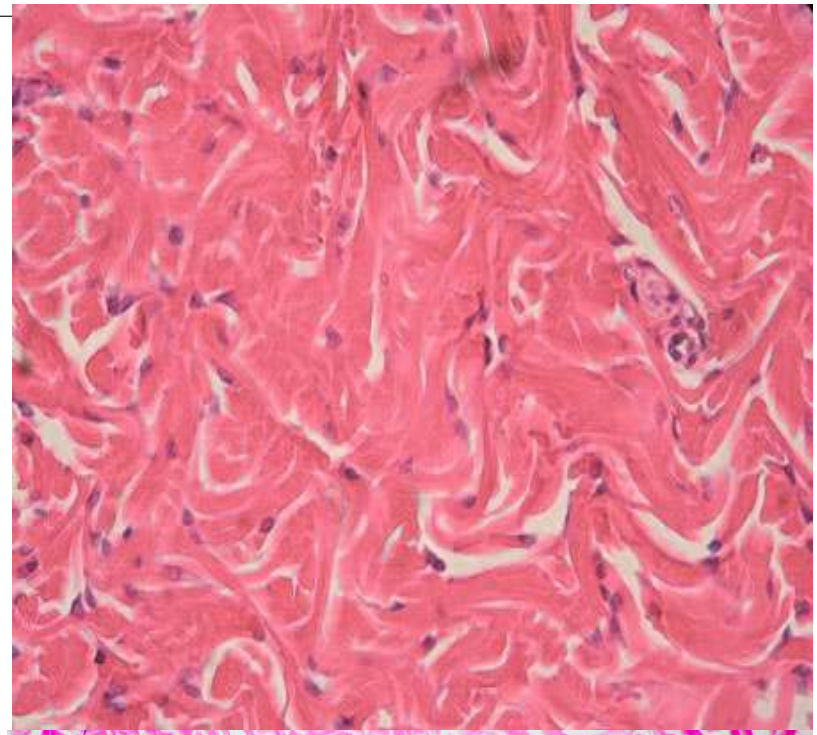
Dense connective tissue contains relatively few cells with much greater numbers of collagen fibers.

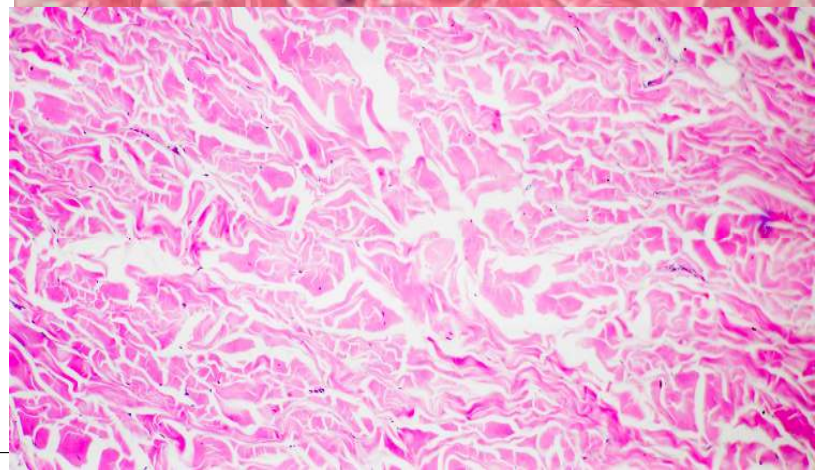
Dense irregular connective tissue has bundles of collagen fibers that appear to be fairly randomly orientated (as in the dermis).

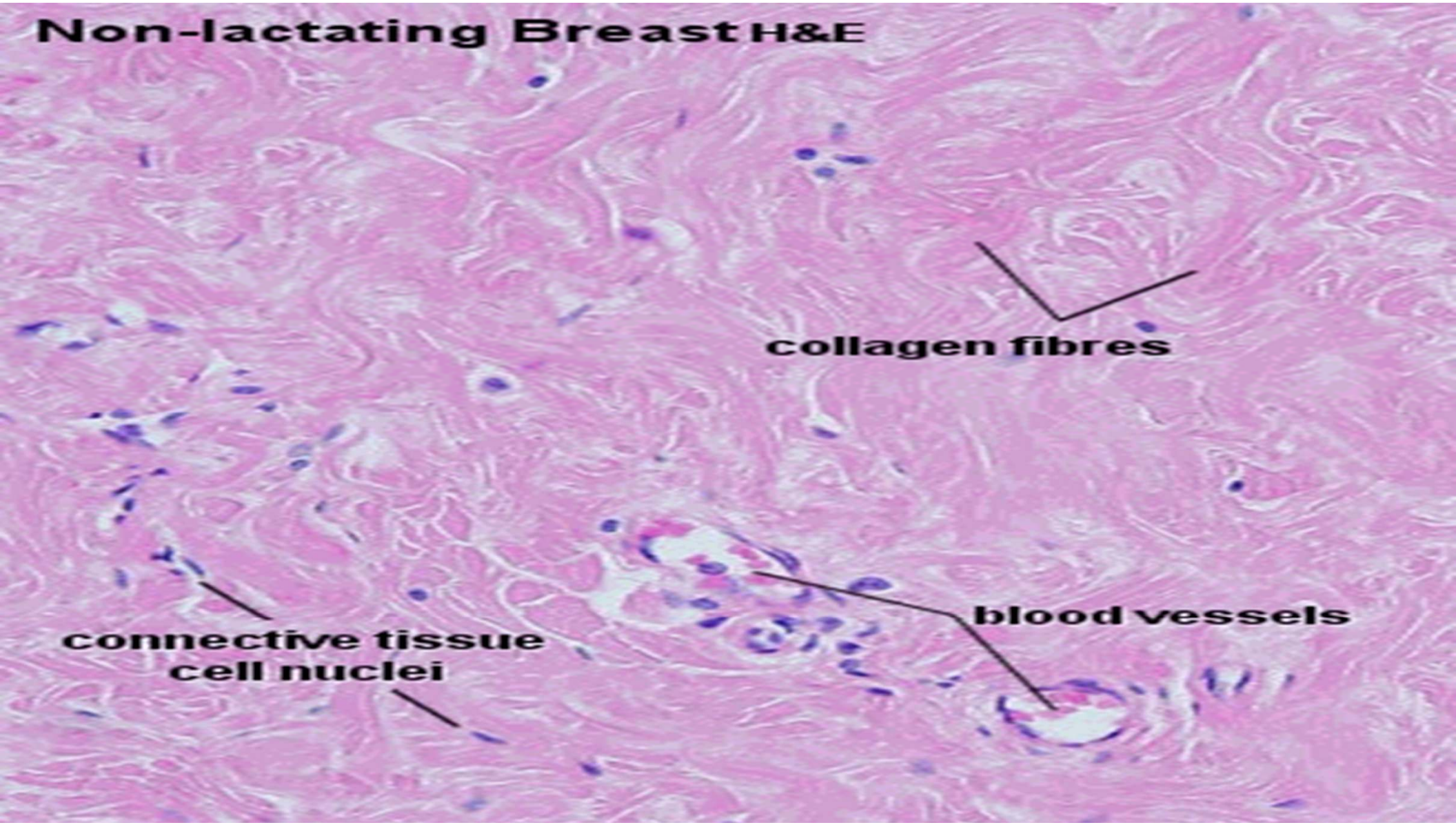
Dense regular connective tissue has closely-packed densely-arranged fiber bundles with clear orientation (such as in tendons) and relatively few cells.

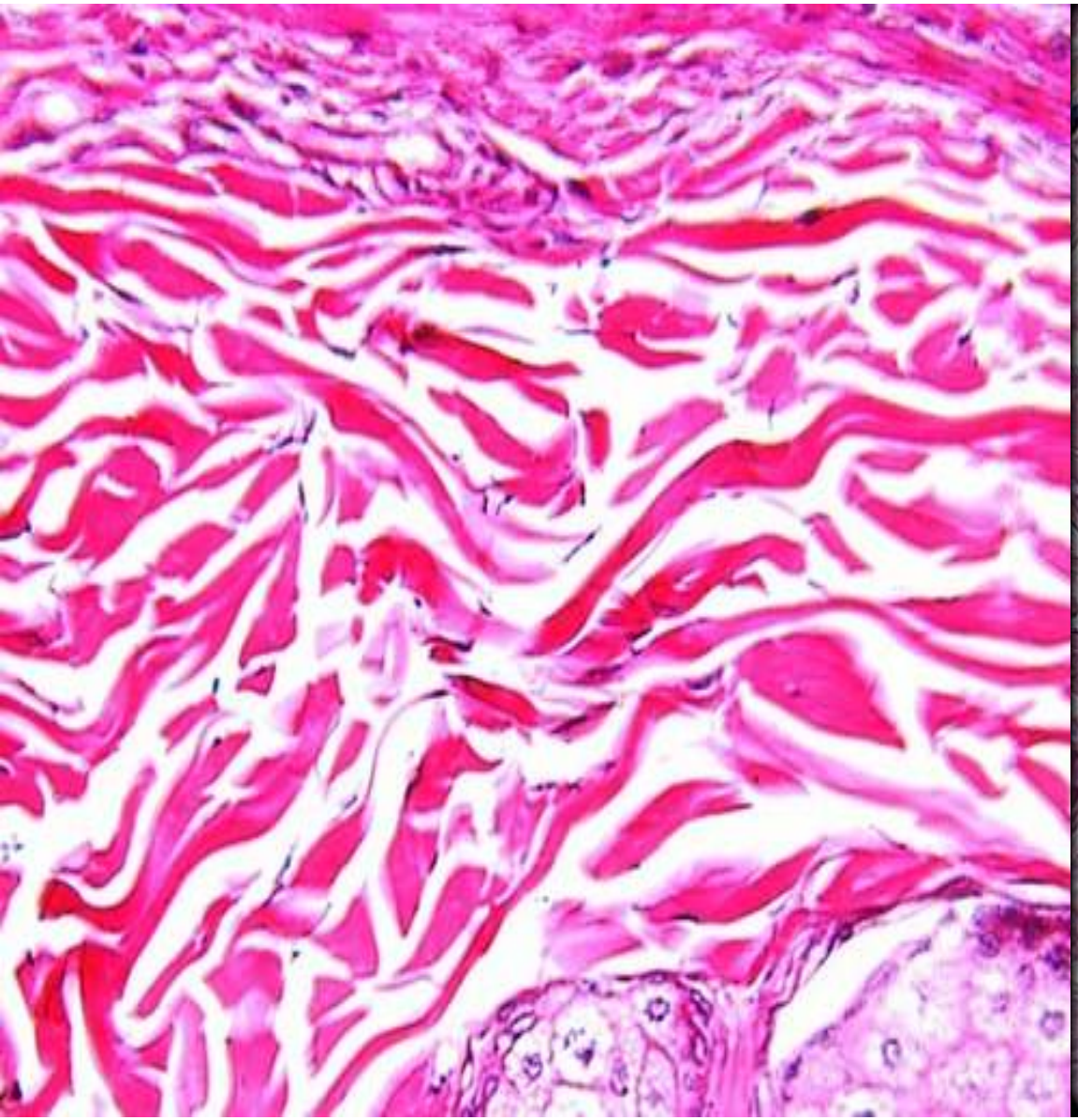
Dense Irregular Connective Tissue:

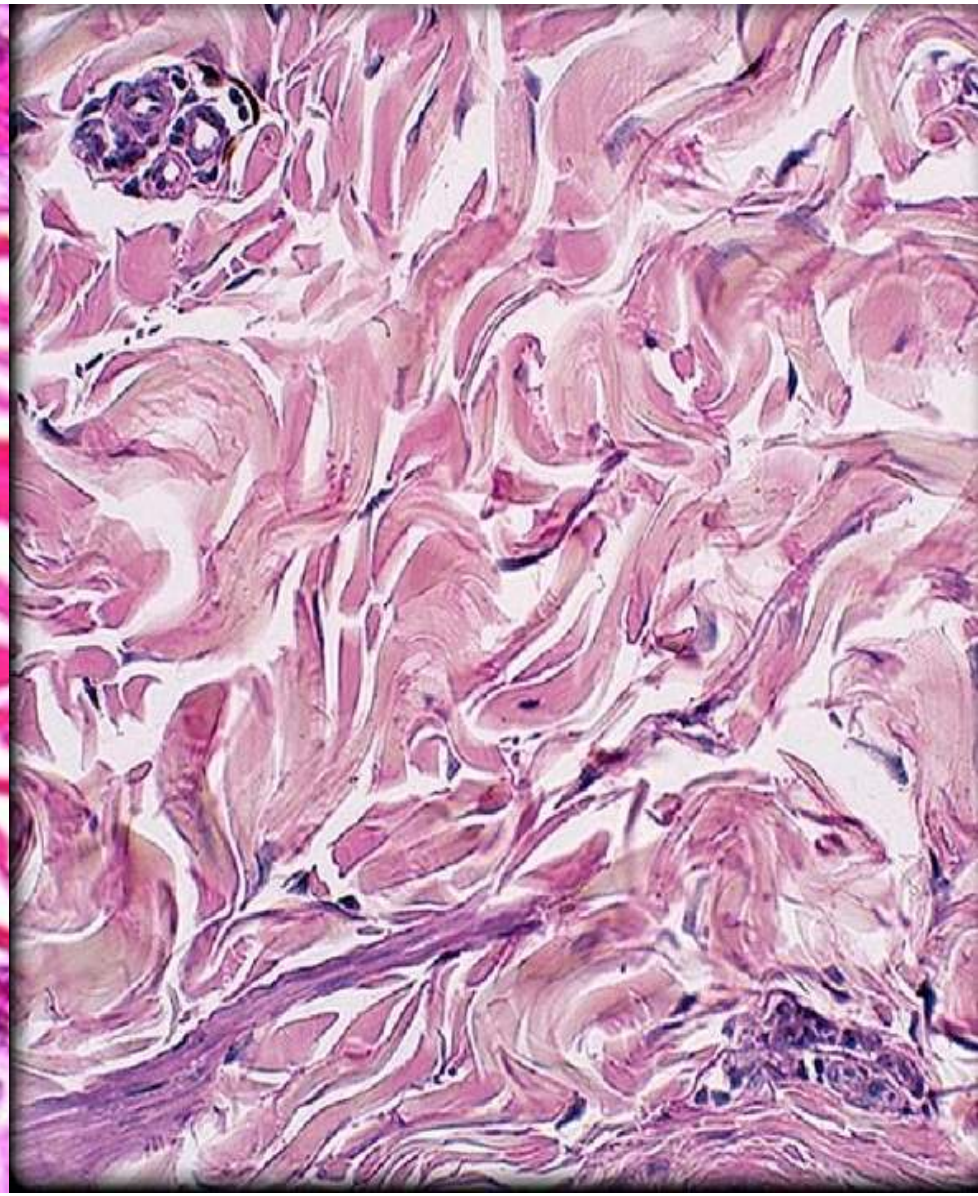
- Dense irregular connective tissue is characterized by **densely packed collagen fibers arranged in a random, irregular pattern.**
- Unlike dense regular connective tissue, the collagen fibers in **dense irregular connective tissue are not oriented in a specific direction**, allowing it to resist forces applied from multiple directions.
- Fibroblasts are interspersed among the collagen fibers and produce the extracellular matrix.
- Dense irregular connective tissue is found in structures such as
  - the dermis of the skin,
  - the capsules surrounding organs,
  - the fibrous coverings of nerves and blood vessels, where it provides strength, support, and protection.



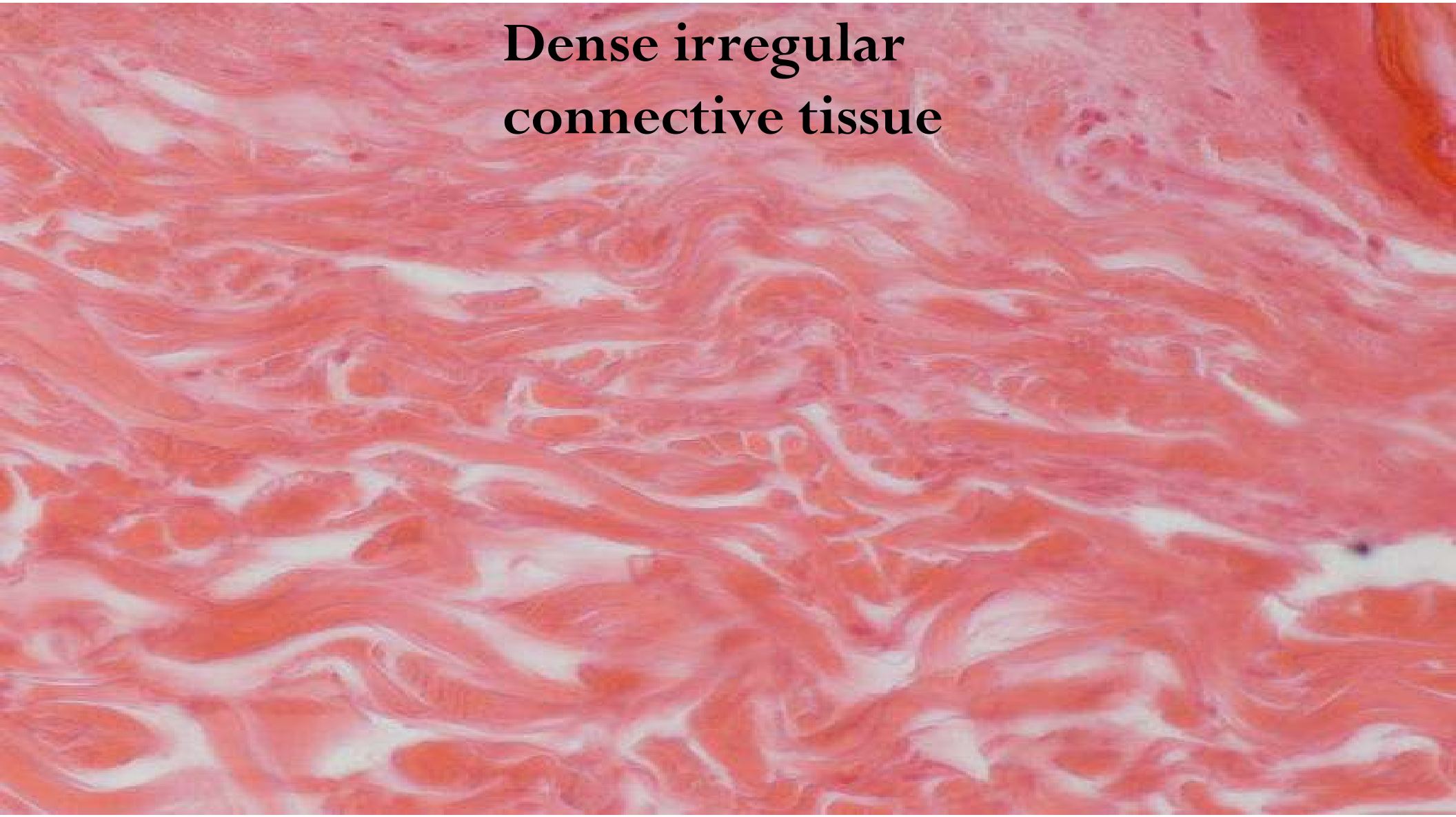



Non-lactating Breast H&E
collagen fibres
blood vessels
connective tissue
cell nuclei





Dense irregular connective tissue

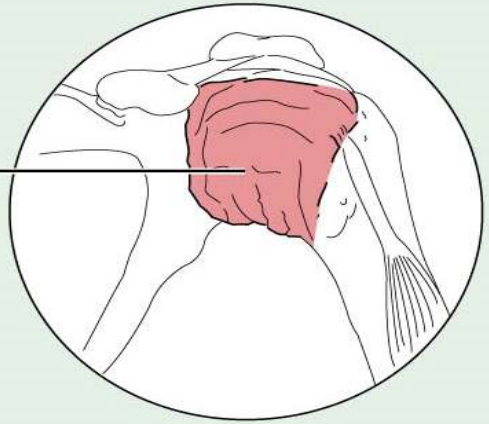


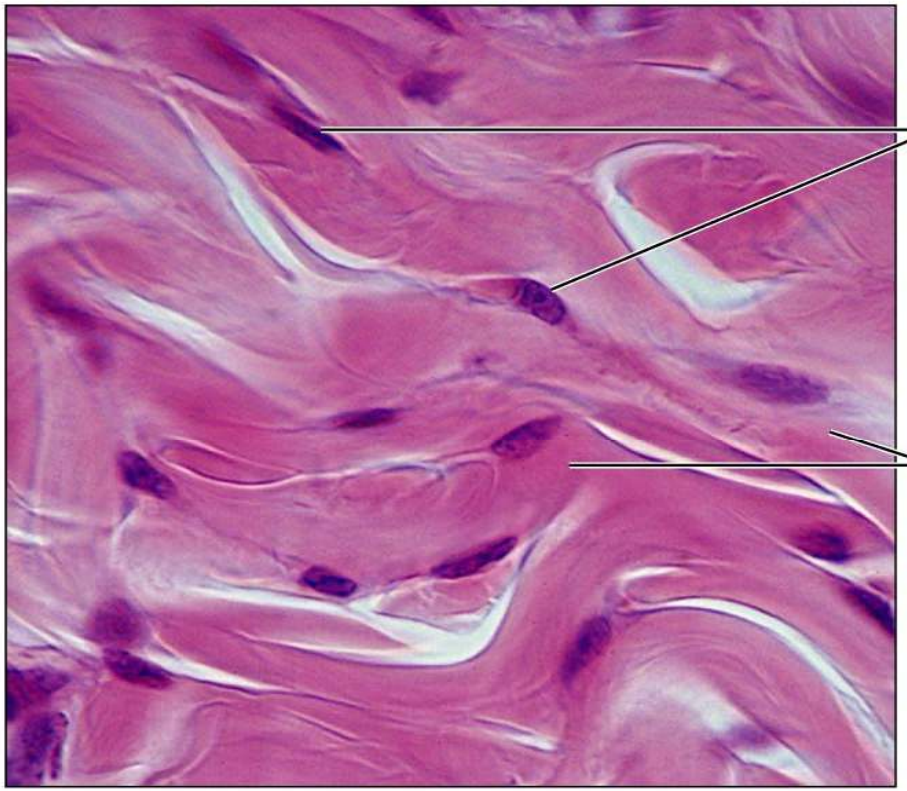
(e) Connective tissue proper: dense connective tissue, dense irregular

Description: Primarily irregularly arranged collagen fibers; some elastic fibers; major cell type is the fibroblast.

Function: Able to withstand tension exerted in many directions; provides structural strength.

Location: Dermis of the skin; submucosa of digestive tract; fibrous capsules of organs and of joints.





Photomicrograph: Dense irregular connective tissue from the dermis of the skin (400×).

Figure 4.9e

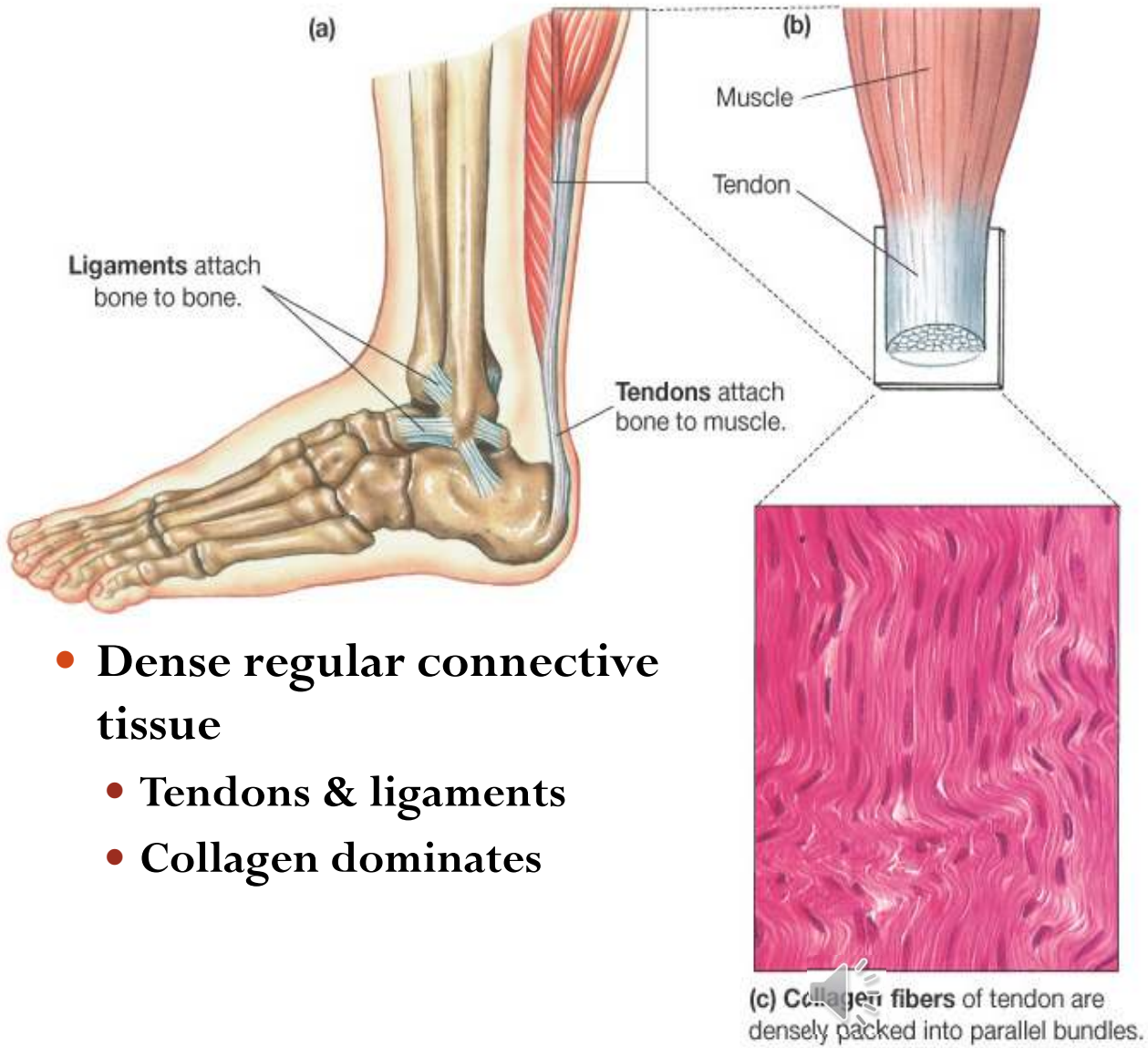
Connective Tissues

Dense Regular Connective Tissue:

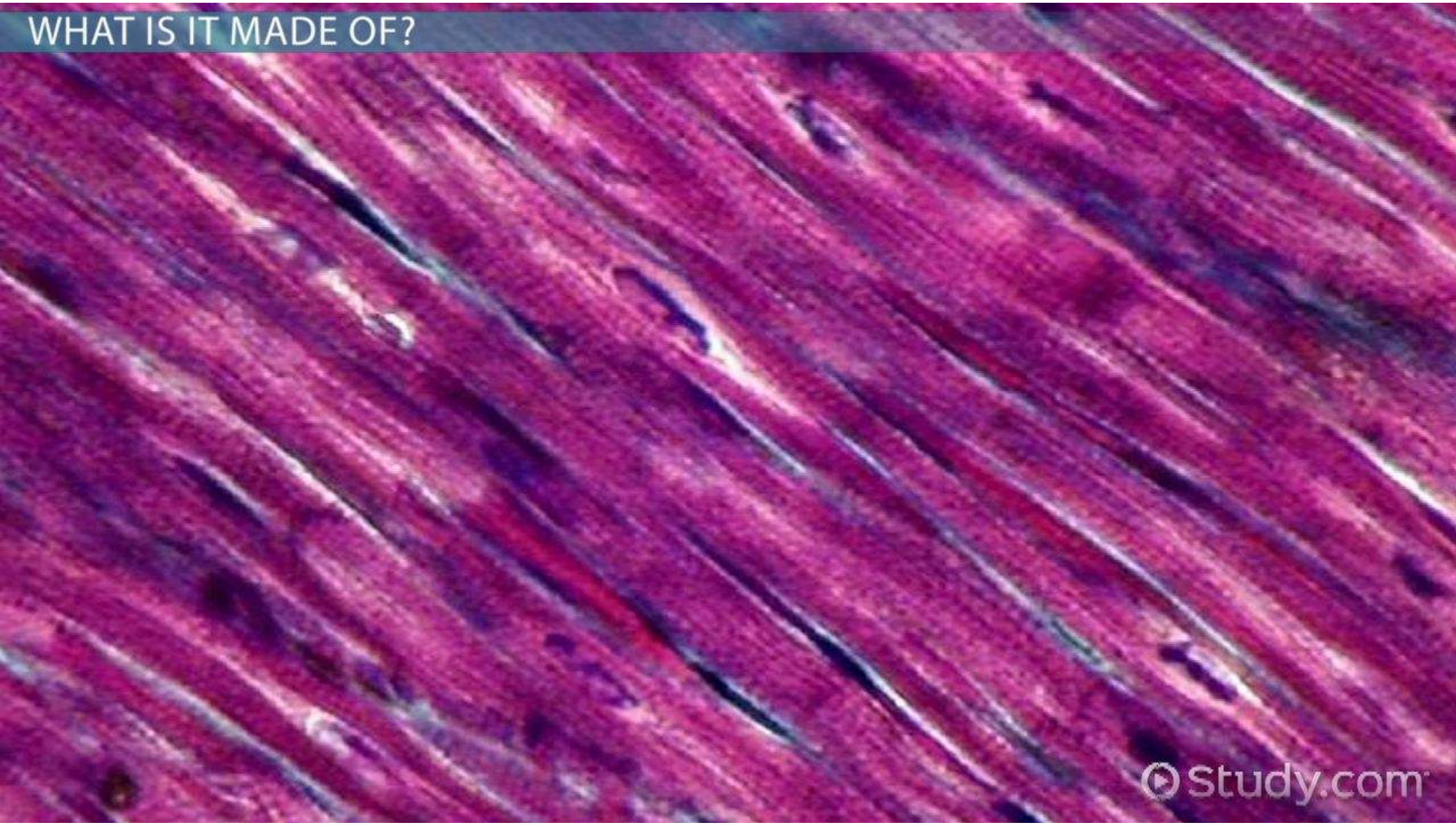
- In dense regular connective tissue, **collagen fibers are densely packed and arranged parallel to each other, providing strength and resistance to forces applied in a single direction.**

- Fibroblasts, the primary cell type responsible for producing collagen fibers, are elongated and aligned along the direction of the fibers.

- Dense regular connective tissue is found in structures such as
  - tendons (which attach muscles to bones)
  - ligaments (which connect bones to other bones), where it provides strong attachment and stability.



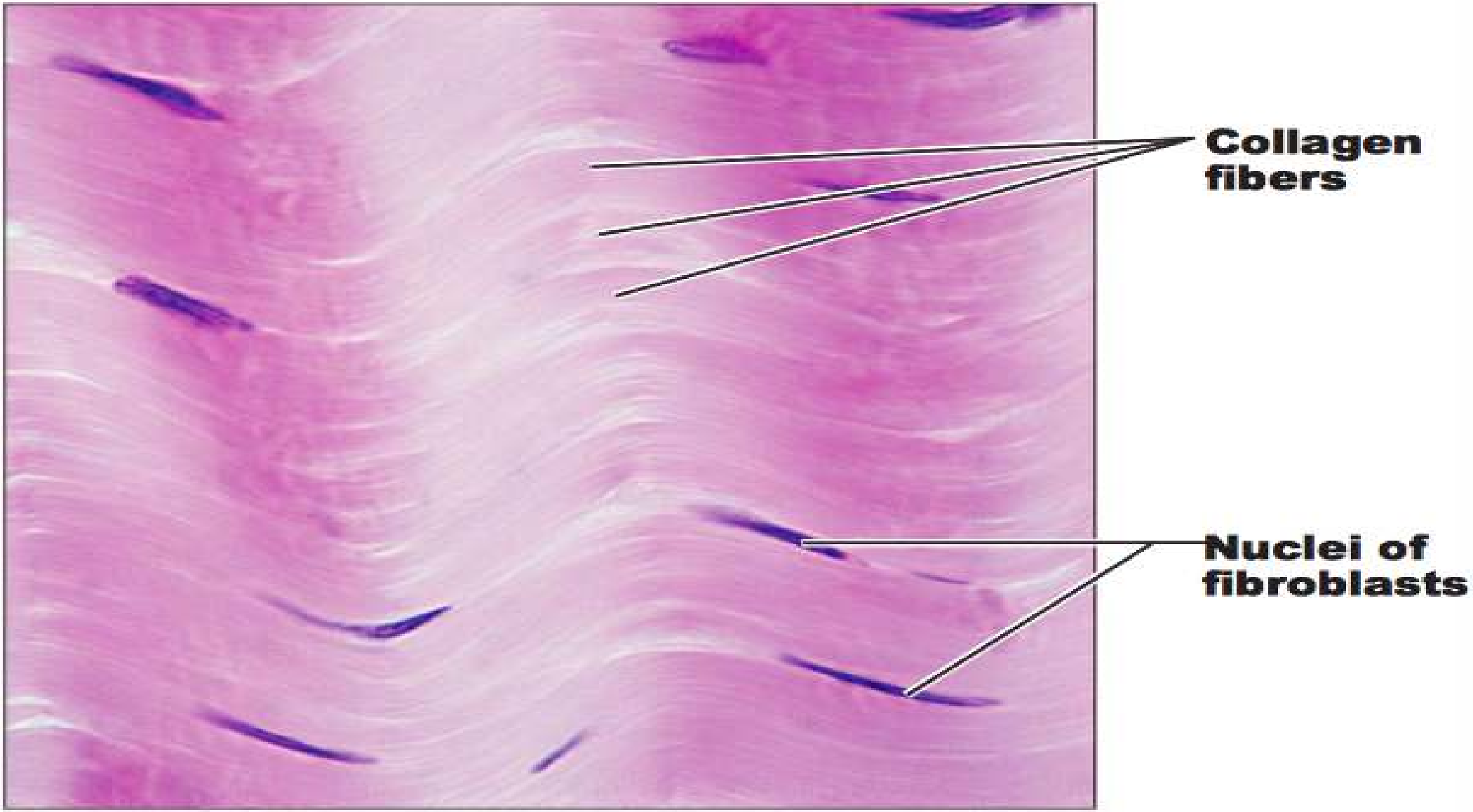
- **Dense regular connective tissue**
  - **Tendons & ligaments**
  - **Collagen dominates**


WHAT IS IT MADE OF?
Study.com

Dense regular connective tissue

Dense regular connective tissue is a dense connective tissue characterized by extracellular fibers (collagen fibers) arranged in parallel bundles.

COLLAGEN

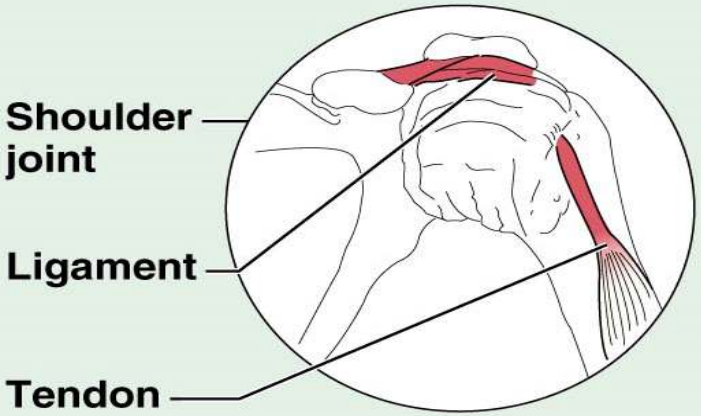

Collagen fibers
Nuclei of fibroblasts

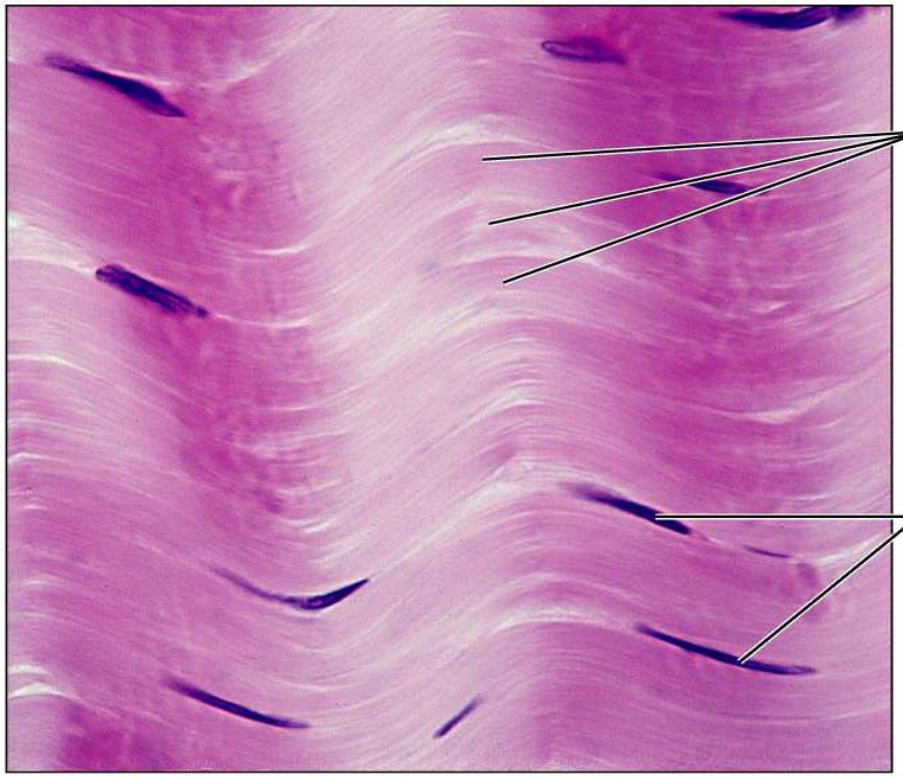
(d) Connective tissue proper: dense connective tissue, dense regular

Description: Primarily parallel collagen fibers; a few elastin fibers; major cell type is the fibroblast.

Function: Attaches muscles to bones or to muscles; attaches bones to bones; withstands great tensile stress when pulling force is applied in one direction.

Location: Tendons, most ligaments, aponeuroses.





Photomicrograph: Dense regular connective tissue from a tendon (1000×).

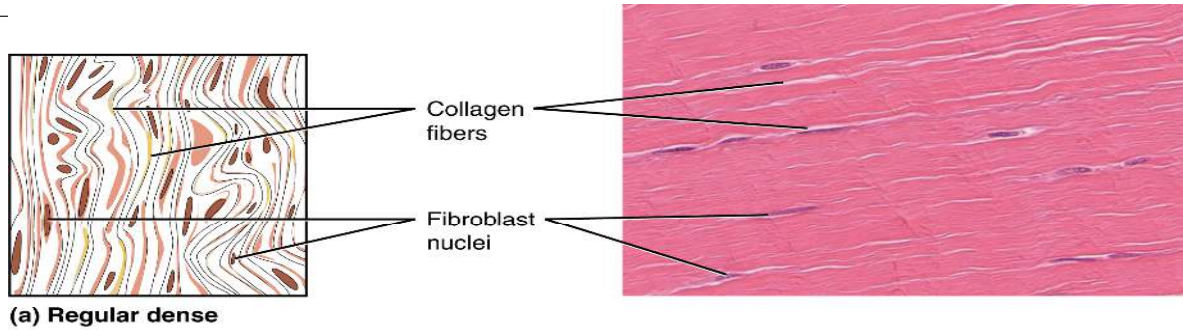
Figure 4.9d

CONNECTIVE TISSUE FIBERS

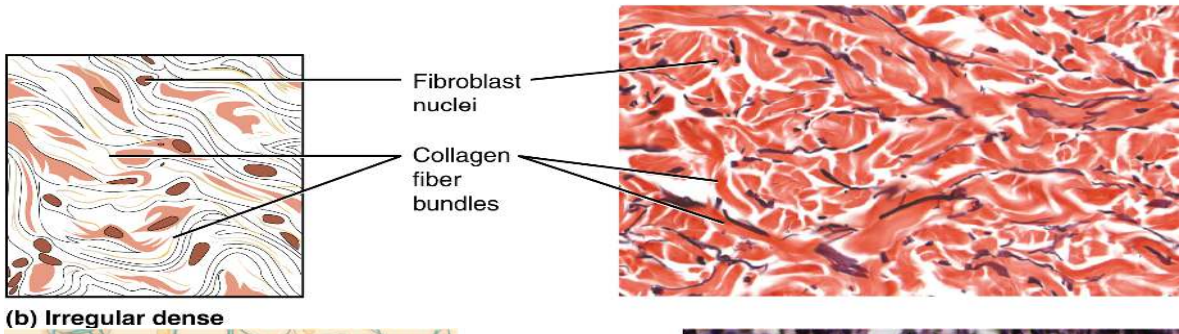
Connective tissue fibers are composed of structural proteins. These fibers are **produced by fibroblasts**

The three main types of fibers are:

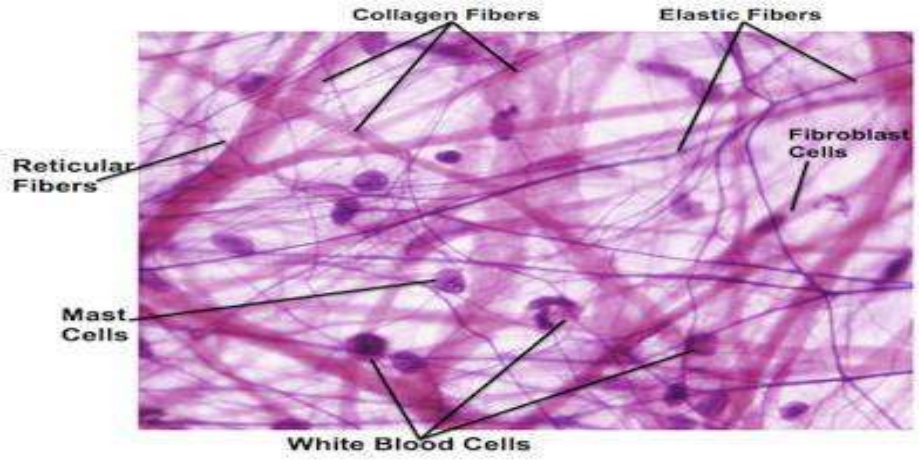
- **collagen fibers**
- **reticular fibers**
- **elastic fibers**

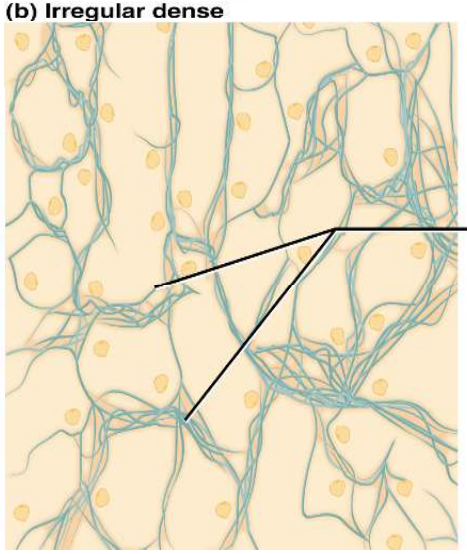


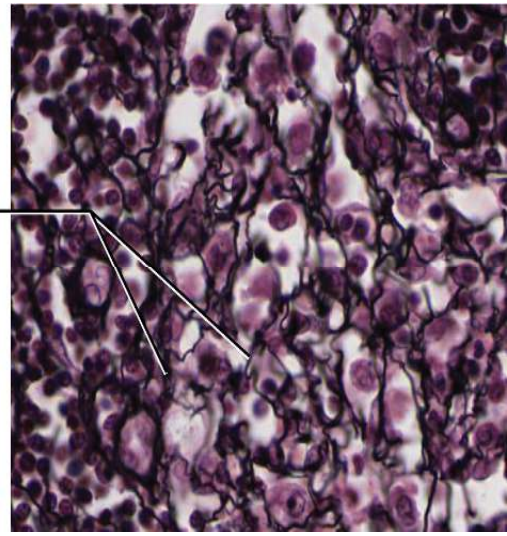
(a) Regular dense



(b) Irregular dense







Fibers

- **Collagen** – tough; provides high tensile strength, **secreted as tropocollagen**
- **Elastic** – long, thin fibers that allow for stretch, secreted as tropoelastin;
- **Reticular** – branched collagenous fibers that form delicate networks

Collagen fibers

- Collagen is the most abundant protein in the human body
- is a major component of the extracellular matrix (ECM) found in various tissues and organs.
- It provides structural support, strength, and resilience to tissues, contributing to their integrity and function.
- Collagen is a fibrous protein that forms long, triple-stranded helical structures composed of repeating amino acid sequences, primarily glycine, proline, and hydroxyproline

Functions of collagen include:

1.Structural Support: Collagen fibers form a network within the ECM that provides **structural support to tissues, organs, and structures such as skin, bones, tendons, ligaments, cartilage, and blood vessels.**

- It gives tissues their tensile strength and resistance to mechanical stress.

2.Tissue Integrity and Organization: Collagen helps maintain the integrity and organization of tissues **by forming a scaffold** that supports and organizes other cellular and matrix components.

- It plays a crucial role in tissue development, organization, and architecture during embryonic development and throughout life.

3.Wound Healing and Tissue Repair: Collagen is involved in the process of wound healing and tissue repair.

- During tissue injury or damage, collagen synthesis increases, leading to the formation of new collagen fibers that help repair the damaged tissue and restore its structure and function.
- Collagen also promotes cell migration, proliferation, and differentiation during the healing process.

4.Skin Elasticity and Strength: In the skin, collagen fibers provide elasticity, resilience, and strength, giving the skin its structural integrity and firmness.

- **Collagen helps maintain skin elasticity and prevents sagging, wrinkles, and fine lines associated with aging and skin damage.**

5.Bone and Cartilage Formation: Collagen is a major component of bone and cartilage tissues, where it provides the framework for mineralization and tissue growth. In bone, collagen fibers form the organic matrix that mineralizes to create strong and rigid bone tissue.

- In cartilage, collagen fibers contribute to the tensile strength and flexibility of the tissue.

6.Organ and Blood Vessel Function: Collagen fibers contribute to the structure and function of organs such as the liver, lungs, and kidneys, providing support and maintaining tissue architecture.

- In blood vessels, collagen helps maintain vessel integrity, elasticity, and resistance to blood pressure changes.

Collagen Types some types:

Collagen I:	**Skin + Bone** (tendon, fascia, dentin,cornea, late wound)
Collagen II: Cartilage	(incld. Hyaline/Elastic C.),vitreus, nucleus pulposus
Collagen III: Aorta (Reticular Fibers)	fetal tissue, granulation tss. These are also associated with **elastic fibers** A silver stain will only stain reticular fibers.
Collagen IV:	**Basement Membrane** or basal lamina of smooth muscle & blood vessle Basement membranes retain the registration peptide. As a result they don't form fibers but instead form sheets. (cf. Collagen Type X : Epiphyseal plate)

locations where collagen is abundant include:

1.Skin: Collagen is the main structural protein in the skin and is found in the dermis layer. It forms a dense network of fibers that provides tensile strength, elasticity, and firmness to the skin, helping to maintain its structural integrity and prevent sagging and wrinkles.

2.Bone: Collagen is a major component of bone tissue, where it forms the organic matrix that provides the framework for mineralization. Collagen fibers in bone provide strength, flexibility, and resilience, helping to support and protect the skeletal system.

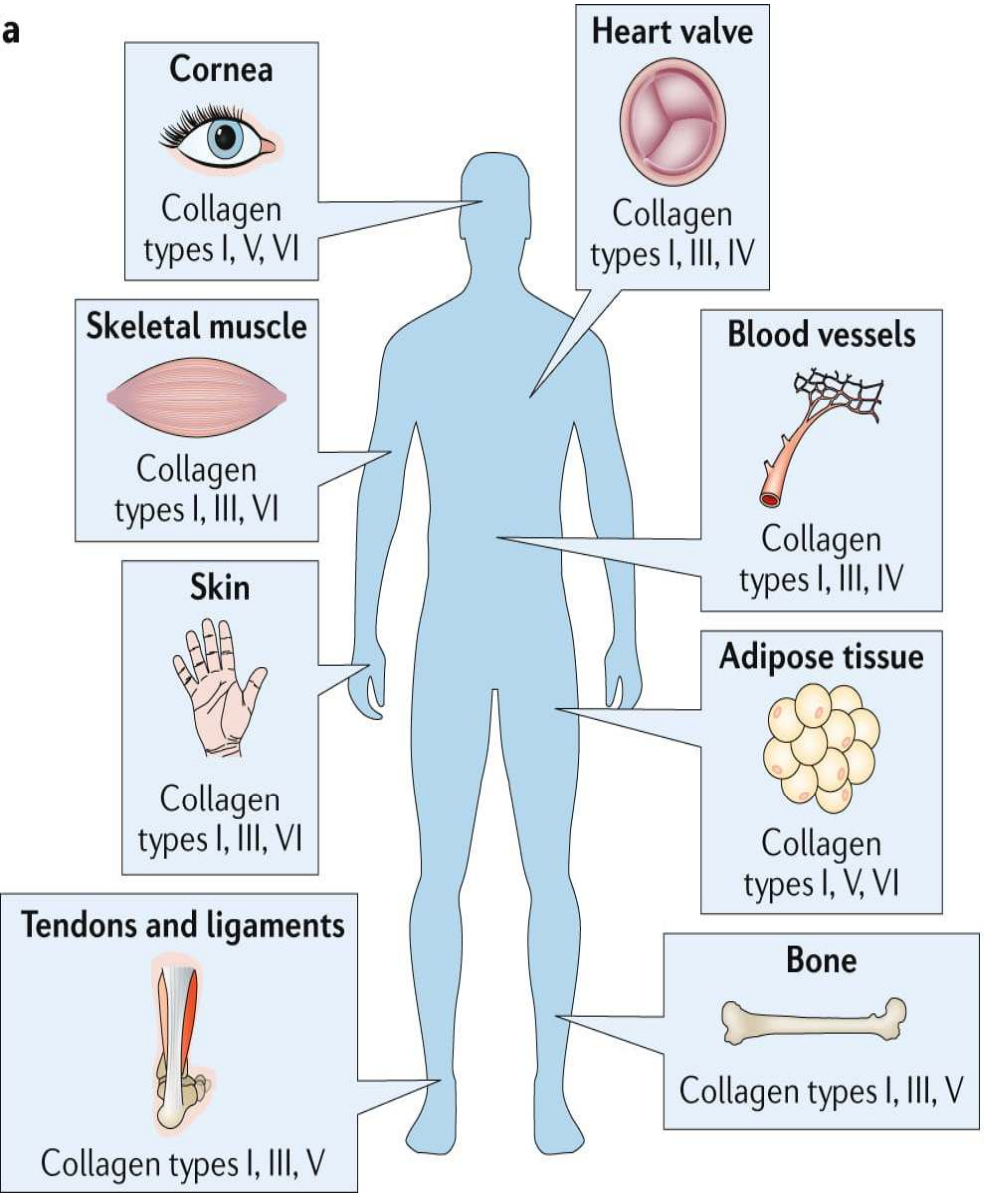
3.Tendons and Ligaments: Tendons and ligaments are connective tissues that attach muscles to bones (tendons) and bones to other bones (ligaments). Collagen fibers in tendons and ligaments provide strength and stability, allowing for movement and providing support to joints and the musculoskeletal system.

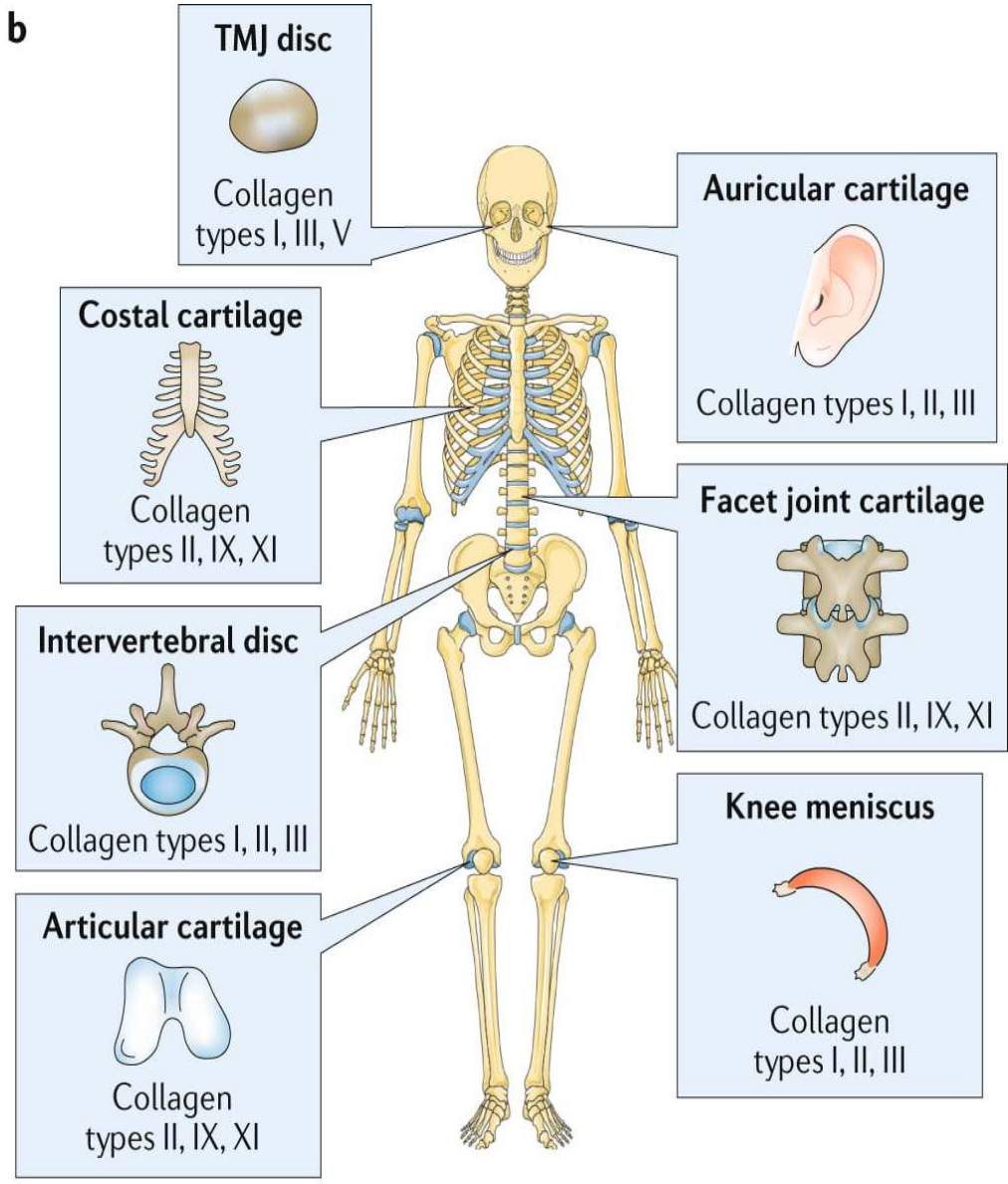
4.Cartilage: Collagen is a major component of cartilage tissue, where it forms a dense network of fibers that provide structural support and resilience. Collagen fibers in cartilage help maintain the elasticity and flexibility of the tissue, allowing for smooth joint movement and shock absorption.

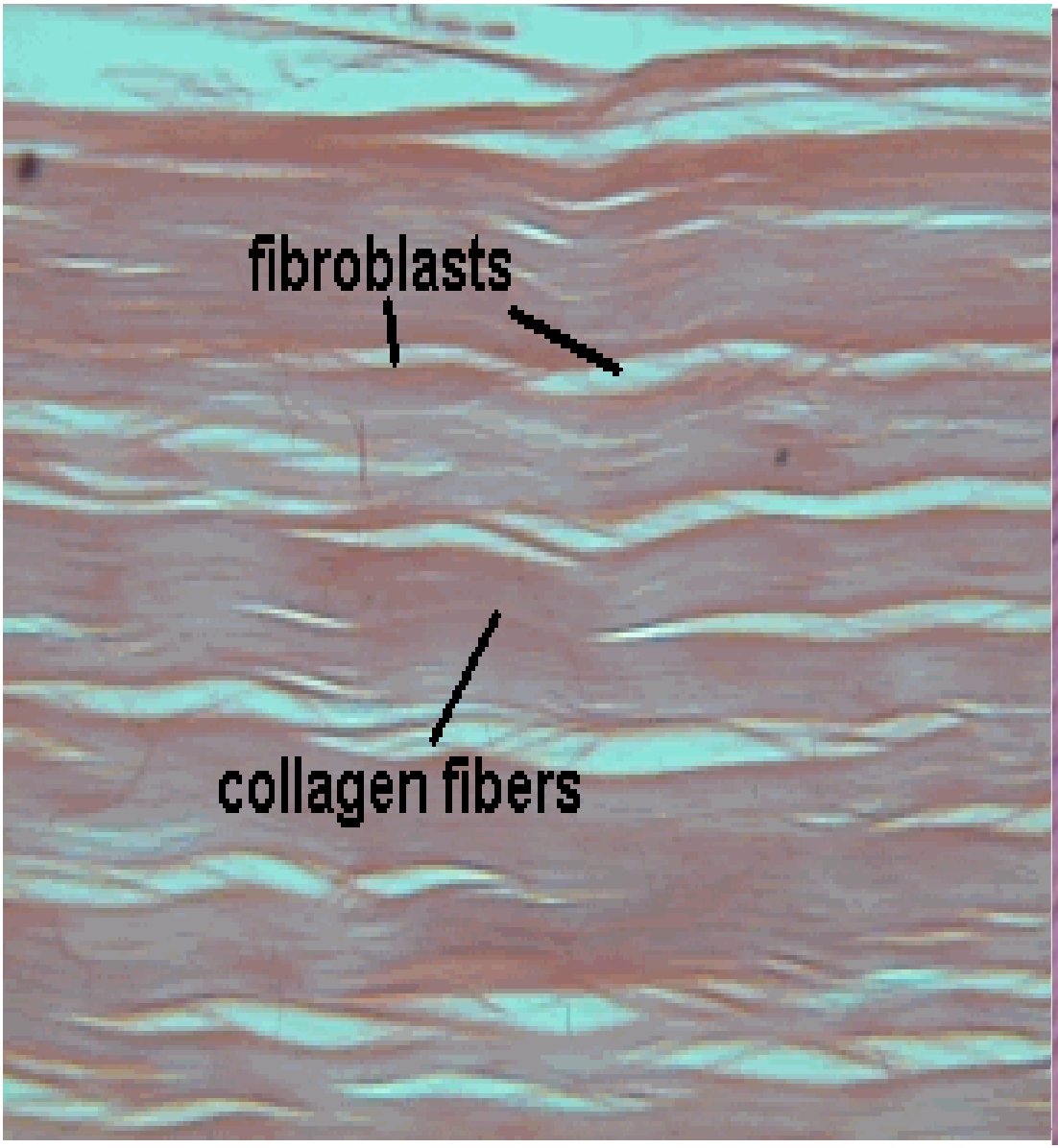
5.Blood Vessels: Collagen is present in the walls of blood vessels, where it provides structural support and helps maintain vessel integrity and elasticity. Collagen fibers in blood vessels contribute to the strength and resilience of the vessel walls, helping to withstand changes in blood pressure and flow.

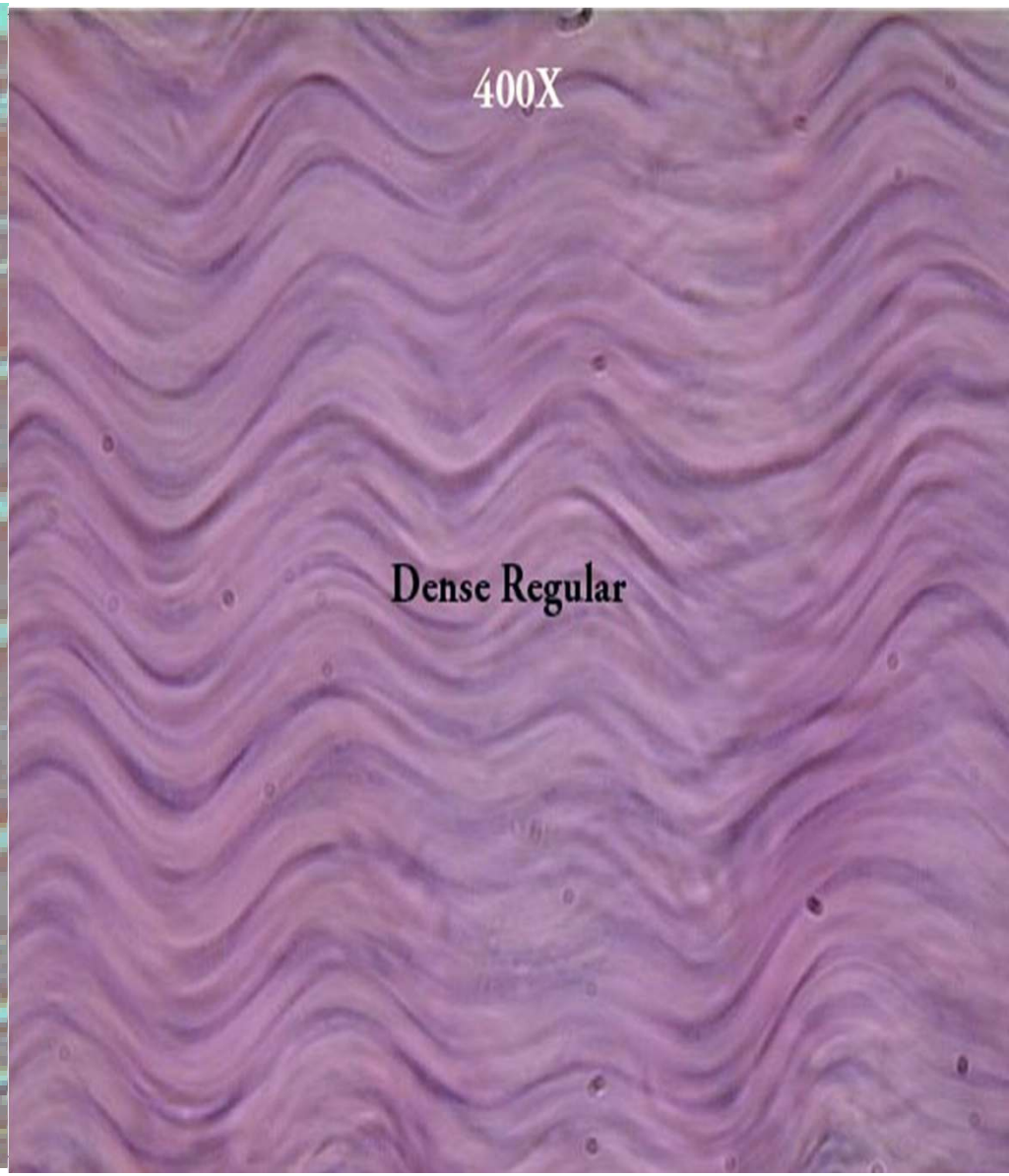
6.Cornea: Collagen is a key component of the cornea, the transparent outer layer of the eye. Collagen fibers in the cornea provide strength, transparency, and shape to the structure, allowing light to pass through and focusing on the retina.

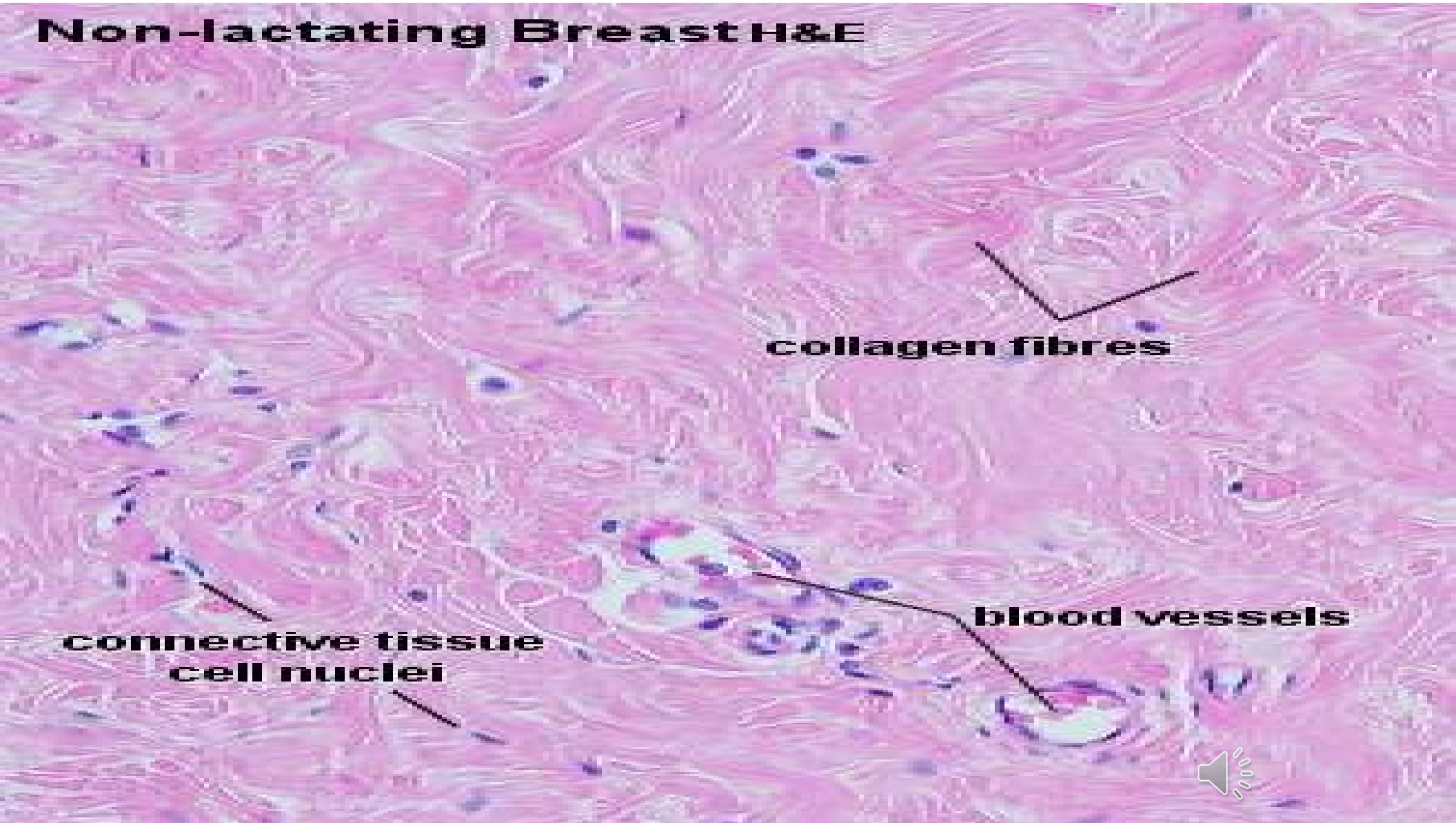
7.Organs and Tissues: Collagen is also found in various organs and tissues throughout the body, including the liver, lungs, kidneys, heart, and gastrointestinal tract. In these locations, collagen provides structural support, maintains tissue integrity, and contributes to organ function.


a
Cornea
Collagen types I, V, VI
Heart valve
Collagen types I, III, IV
Skeletal muscle
Collagen types I, III, VI
Blood vessels
Collagen types I, III, IV
Skin
Collagen types I, III, VI
Adipose tissue
Collagen types I, V, VI
Tendons and ligaments
Collagen types I, III, V
Bone
Collagen types I, III, V


b
TMJ disc
Collagen types I, III, V
Auricular cartilage
Collagen types I, II, III
Costal cartilage
Collagen types II, IX, XI
Facet joint cartilage
Collagen types II, IX, XI
Intervertebral disc
Collagen types I, II, III
Knee meniscus
Collagen types I, II, III
Articular cartilage
Collagen types II, IX, XI


fibroblasts
collagen fibers


400X
Dense Regular


Non-lactating Breast H&E
collagen fibres
blood vessels
connective tissue
cell nuclei

Elastic fibers

- Elastic fibers are a type of connective tissue component that provides elasticity and resilience to tissues in the body.
- These fibers are composed primarily of the protein elastin, along with other proteins such as fibrillin.

- Elastic fibers are found in various tissues and organs throughout the body and play a crucial role in maintaining tissue structure and function.

characteristics and functions of elastic fibers include:

1.Elasticity: Elastic fibers **are highly flexible** and stretchable, allowing tissues to **stretch and recoil** without permanent deformation.

- **This elasticity is essential for tissues subjected to mechanical stress and movement, such as the skin, lungs, and blood vessels.**

2.Resilience: Elastic fibers provide resilience to tissues, allowing them to return to their original shape and size after being stretched or compressed.

- This property helps maintain tissue integrity and function, particularly in structures that undergo repeated stretching and relaxation.

3.Tissue Structure: Elastic fibers contribute to the structural integrity of tissues by forming a network or framework within the extracellular matrix (ECM).

- **They interact with other matrix components, such as collagen and proteoglycans, to provide support and stability to tissues.**

4.Skin Elasticity: In the skin, elastic fibers are abundant in the dermis layer and provide elasticity, firmness, and flexibility.

- They allow the skin to stretch and recoil in response to movements and changes in body shape, helping to maintain skin integrity and prevent sagging and wrinkles.

1.Blood Vessel Function: Elastic fibers are present in the walls of blood vessels, particularly in arteries and arterioles.

- They contribute to the elasticity of blood vessel walls, allowing them to expand and contract in response to changes in blood pressure and flow.
- This elasticity helps regulate blood pressure and ensures efficient blood circulation.

2.Lung Function: In the lungs, elastic fibers are found in the walls of alveoli and bronchioles.

- They facilitate lung expansion during inhalation and recoil during exhalation, promoting efficient gas exchange and respiratory function.

locations where elastic fibers are abundant include:

1.Skin: Elastic fibers are present in the dermis layer of the skin, where they contribute to skin elasticity, firmness, and flexibility. They allow the skin to stretch and recoil in response to movement and changes in body shape, helping to maintain skin integrity and prevent sagging and wrinkles.

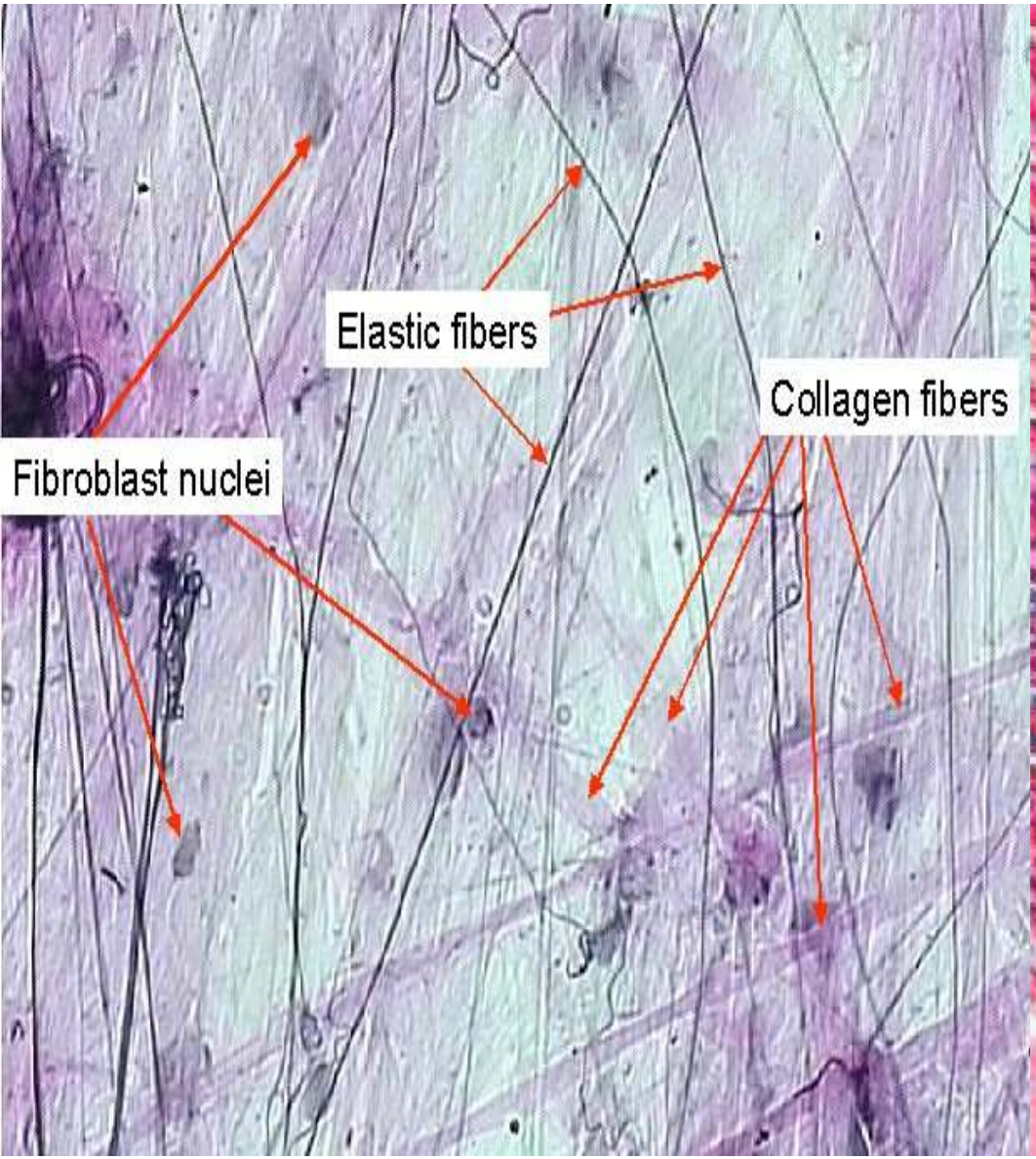
2.Lungs: Elastic fibers are abundant in the walls of the alveoli (air sacs) and bronchioles of the lungs. They facilitate lung expansion during inhalation and recoil during exhalation, promoting efficient gas exchange and respiratory function. Elastic fibers help maintain the structural integrity of lung tissue and prevent collapse of the airways.

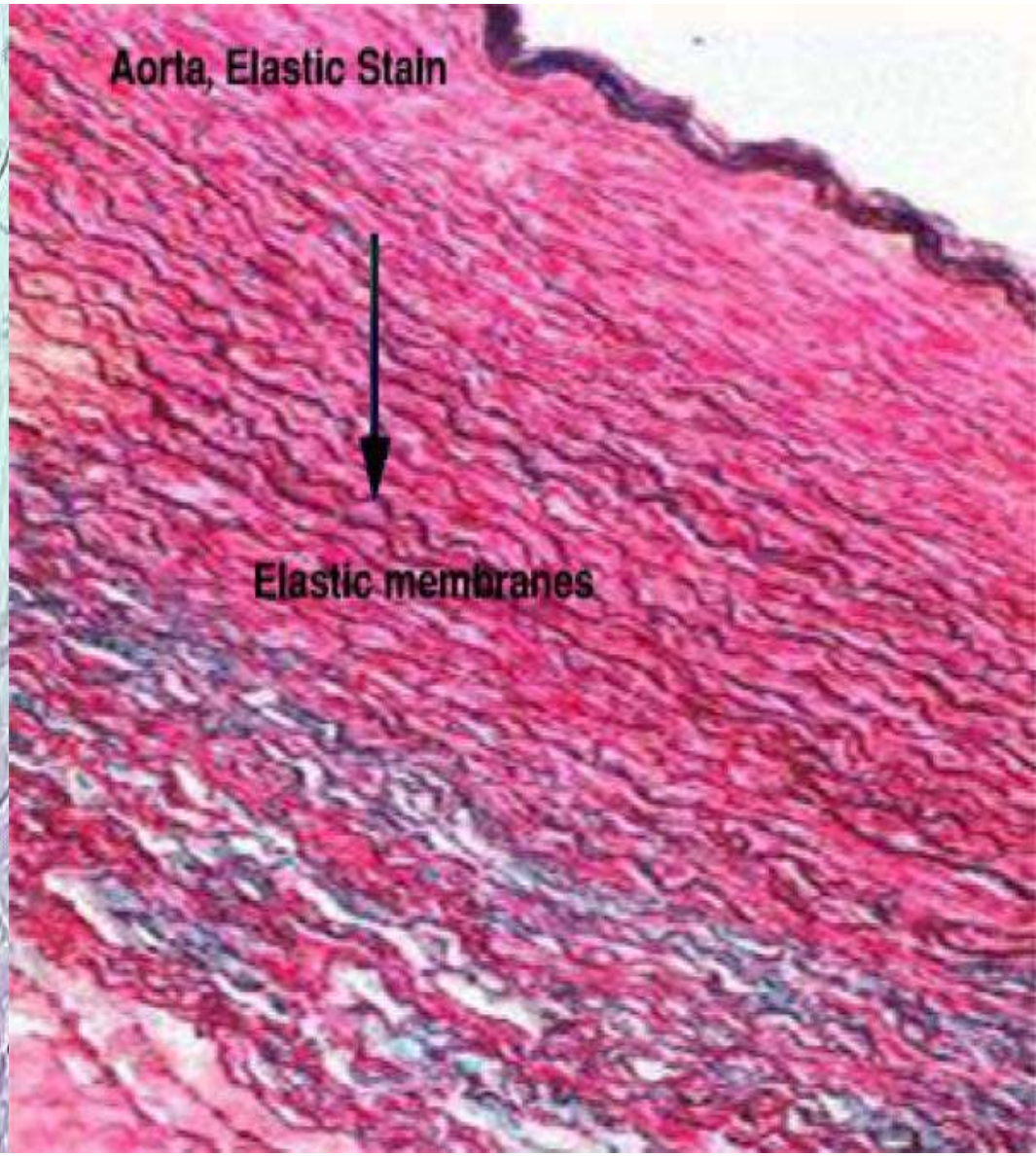
3.Blood Vessels: Elastic fibers are found in the walls of arteries, arterioles, and some larger veins. They contribute to the elasticity of blood vessel walls, allowing them to expand and contract in response to changes in blood pressure and flow. This elasticity helps regulate blood pressure and ensures efficient blood circulation.

4.Heart: Elastic fibers are present in the walls of the heart, particularly in the myocardium (heart muscle) and the connective tissue of the heart valves. They provide elasticity and resilience to heart tissue, allowing the heart to expand and contract rhythmically during the cardiac cycle.

5.Elastic Cartilage: In some tissues, such as elastic cartilage, elastic fibers are a major structural component. Elastic cartilage is found in the external ear (pinna), epiglottis, and auditory (Eustachian) tube. Elastic fibers in elastic cartilage provide flexibility and maintain the shape of these structures.

6.Connective Tissue: Elastic fibers are also present in various types of connective tissue, including **loose connective tissue, dense connective tissue, and elastic connective tissue.** In these tissues, elastic fibers contribute to the overall structure, elasticity, and resilience of the tissue.


Elastic fibers
Collagen fibers
Fibroblast nuclei


Aorta, Elastic Stain
Elastic membranes

ELASTIC FIBERS:

Arrangements of elastic fibers: They can be arranged in 3 different ways

- **Fibers / Fiber Bundles** -- as in skin
- **Lamellae (sheets)** -- as in vasculature
- **Fine Networks** -- as in the lung

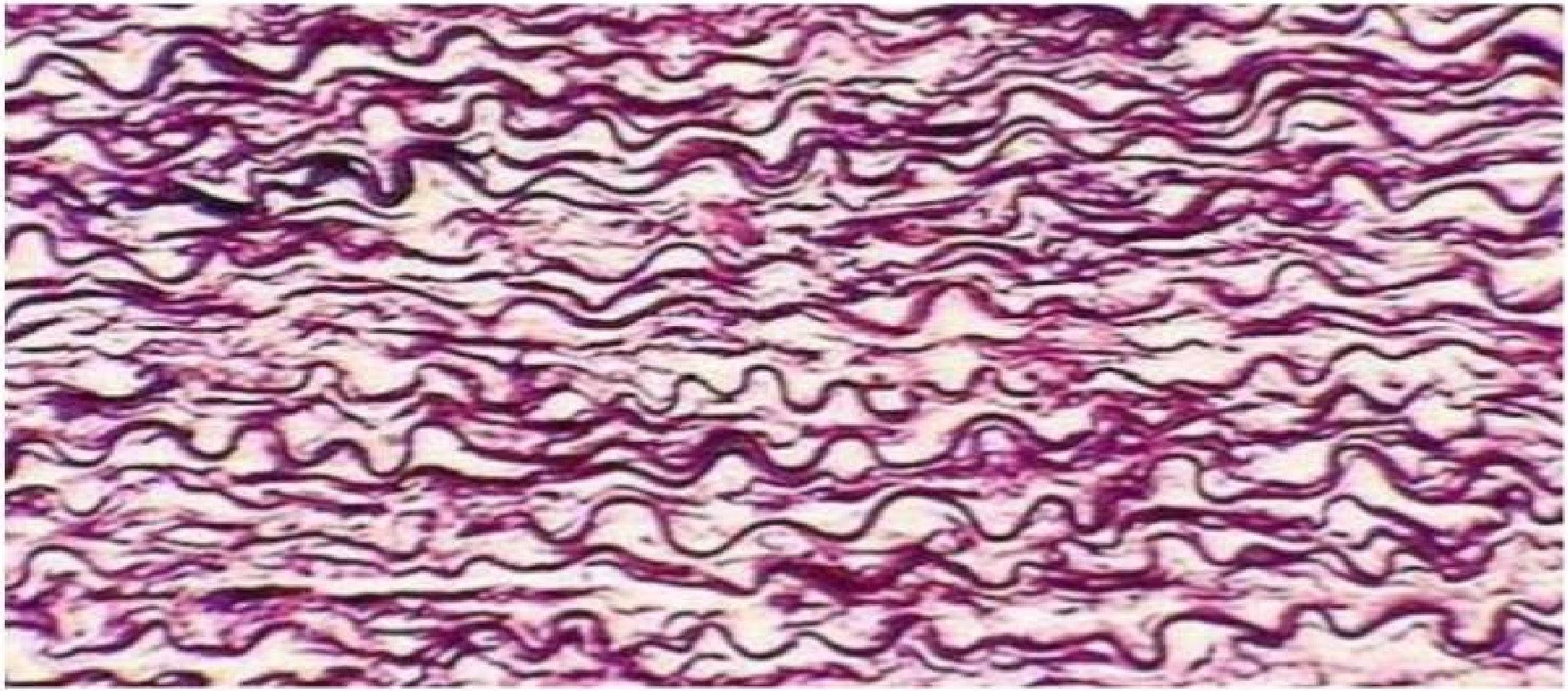
Protein Composition:

- **Microfibrillar Protein:**
- **Elastin:**.
  - Elastin is resistant to degradation, except by **elastase**.
- **Desmosine & Isodesmosine**:.

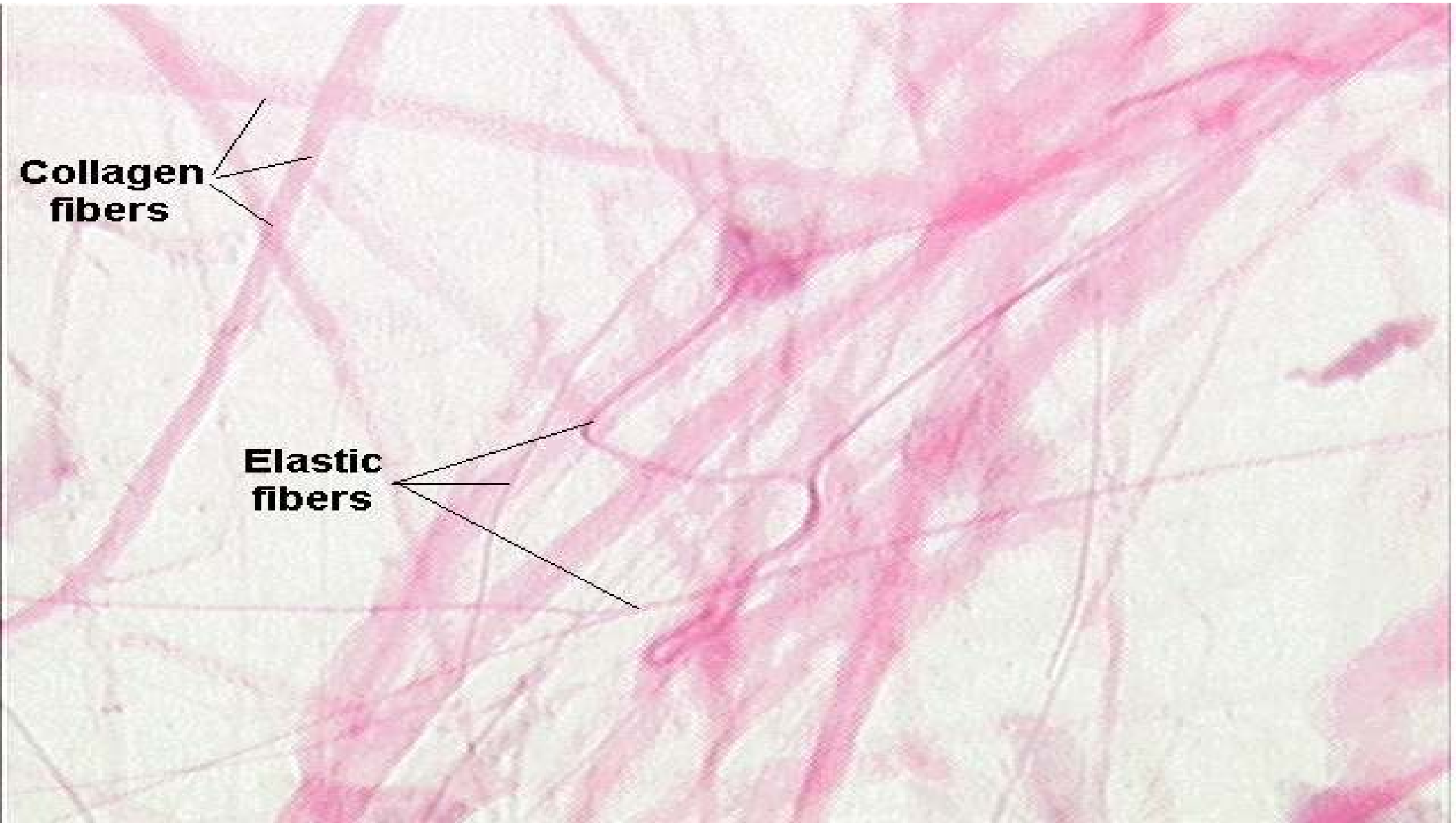
- AGING: Wrinkles occur as microfibrillar structure is lost

- **Emphysema:** Loss of elasticity in lung. Rare form = congenital malfunction of elastase in lung.

Elastic Connective Tissue (Dense Connective Tissue)



Hint: note the wave-like, rubber-band structure of elastic fibers and relate it to their flexibility

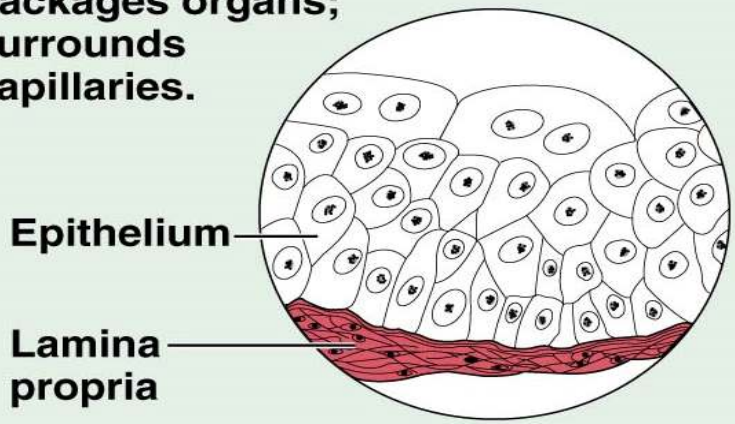

Collagen fibers
Elastic fibers

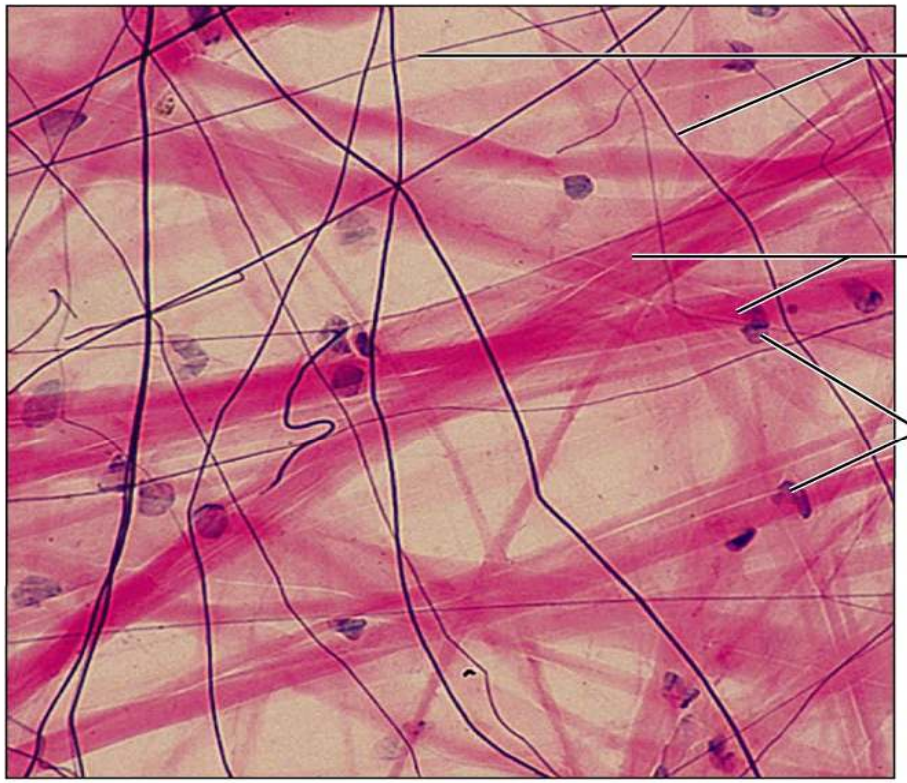
(a) Connective tissue proper: loose connective tissue, areolar

Description: Gel-like matrix with all three fiber types; cells: fibroblasts, macrophages, mast cells, and some white blood cells.

Function: Wraps and cushions organs; its macrophages phagocytize bacteria; plays important role in inflammation; holds and conveys tissue fluid.

Location: Widely distributed under epithelia of body, e.g., forms lamina propria of mucous membranes; packages organs; surrounds capillaries.





Photomicrograph: Areolar connective tissue, a soft packaging tissue of the body (400×).

Figure 4.9a

Reticulin fibers

- Reticulin fibers, also known as reticular fibers, are a type of fibrous protein found in the extracellular matrix (ECM) of various tissues and organs throughout the body.
-
- These fibers are **composed primarily of type III collagen**, along **with glycoproteins and proteoglycans.**

- Reticulin fibers are thinner and more delicate than collagen fibers and form a network or mesh-like structure that ***provides support and scaffolding for cells and other matrix components.***

Think Lymph nodes and spleen

functions of reticulin fibers include:

1.Supportive Framework: Reticulin fibers form a supportive framework or scaffold within the extracellular matrix of tissues and organs.

- They create a network of interconnected fibers that supports and organizes other cellular and matrix components, such as cells, collagen fibers, and blood vessels.

2.Tissue Architecture: Reticulin fibers help maintain the architecture and organization of tissues by providing structural support and stability.

- They contribute to the three-dimensional structure of tissues and organs, helping to maintain their shape and integrity.

3.Cellular Attachment: Reticulin fibers serve as attachment sites for cells, allowing them to adhere to the ECM and interact with neighboring cells and matrix components.

- Cell adhesion to reticulin fibers is important for cell migration, proliferation, and differentiation during tissue development, repair, and remodeling.

4.Barrier Function: Reticulin fibers can act as a barrier or boundary within tissues, helping to compartmentalize different cellular and matrix components.

- They create physical barriers that separate and define tissue compartments, such as the reticular lamina in basement membranes.

5. **Support for Blood Vessels and Organs**: Reticulin fibers provide structural support for
    - blood vessels, particularly small capillaries and sinusoids,
    - as well as for certain organs and tissues.
    - In **the liver**, for example, reticulin fibers form the reticular framework of the hepatic sinusoids, supporting liver cells (hepatocytes) and facilitating the exchange of nutrients and waste products.

6.Stromal Function: Reticulin fibers are a key component of the stroma, the supportive tissue framework of organs and tissues.

- They contribute to the stromal architecture and play a role in maintaining tissue homeostasis, function, and mechanical properties.

locations where reticular fibers are abundant include:

1.Lymphoid Organs: Reticular fibers form the structural framework of lymphoid organs such as **lymph nodes, spleen, and bone marrow.**

- In these organs, reticular fibers create a network **or scaffold that supports immune** cells (such as lymphocytes) and facilitates the movement and interaction of cells within the lymphoid tissue.

2.Bone Marrow: Reticular fibers provide structural support within the bone marrow, particularly in the stroma or reticular tissue.

- **They form a network that supports hematopoietic stem cells and blood cell precursors, as well as stromal cells that produce extracellular matrix components**.

3.Liver: In the liver, reticular fibers form the reticular framework of the hepatic sinusoids, which are specialized blood vessels that allow for the exchange of substances between blood and liver cells (hepatocytes).

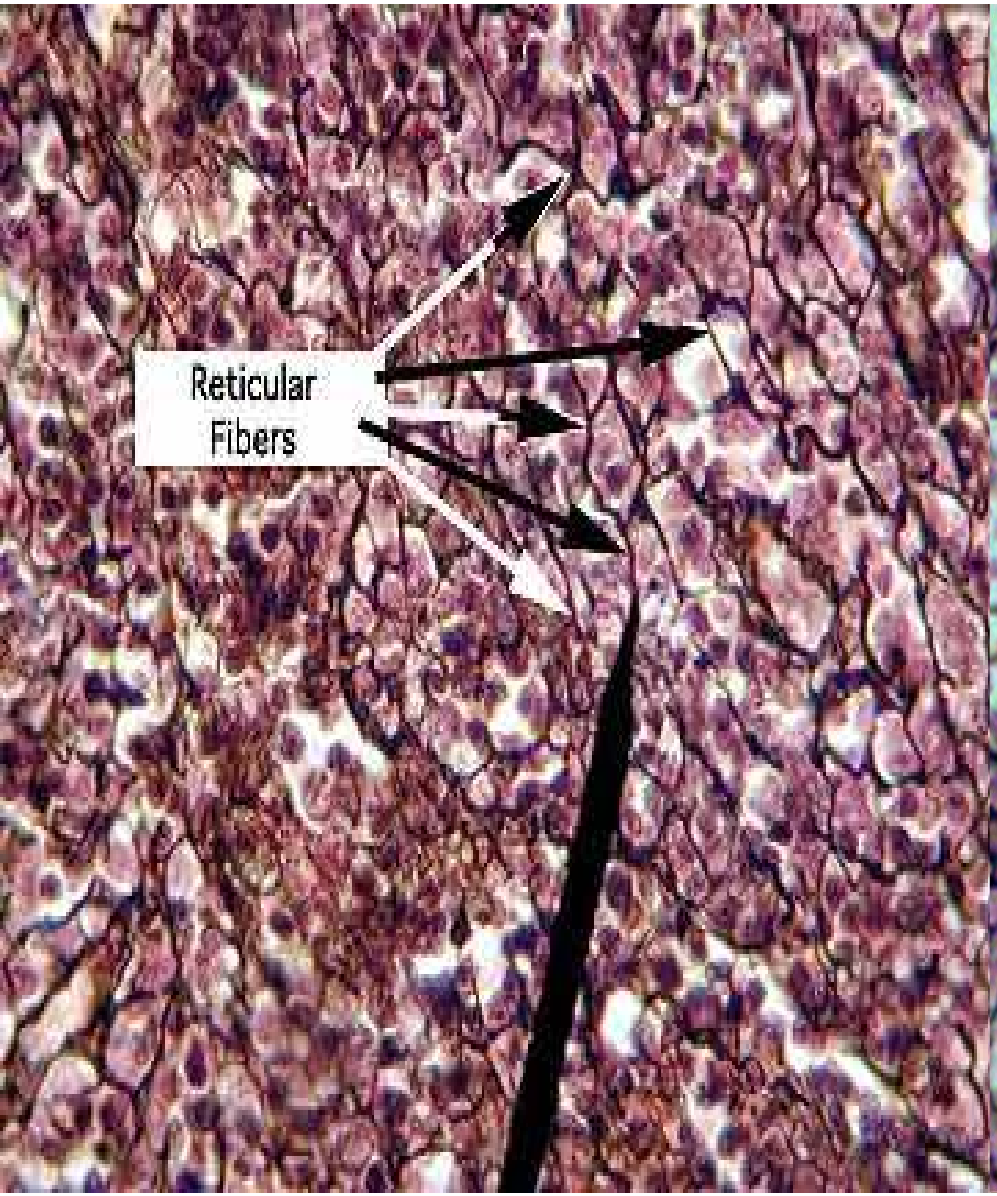
- Reticular fibers **support the sinusoidal endothelial cells and Kupffer cells (macrophages) within the liver tissue**.

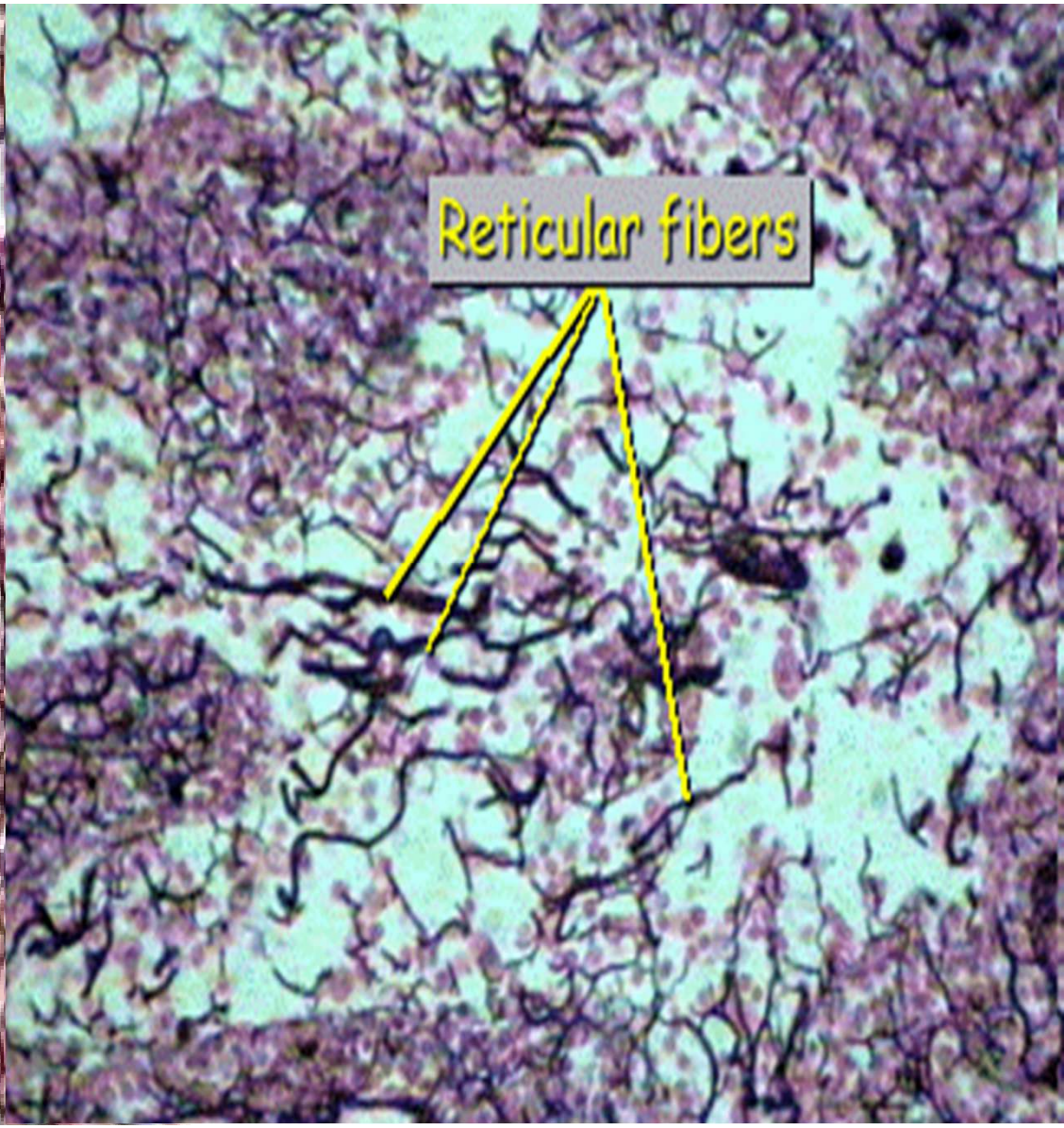
4.Spleen: Reticular fibers are abundant in the red pulp of the spleen, where they form a network that supports blood vessels and red blood cells.

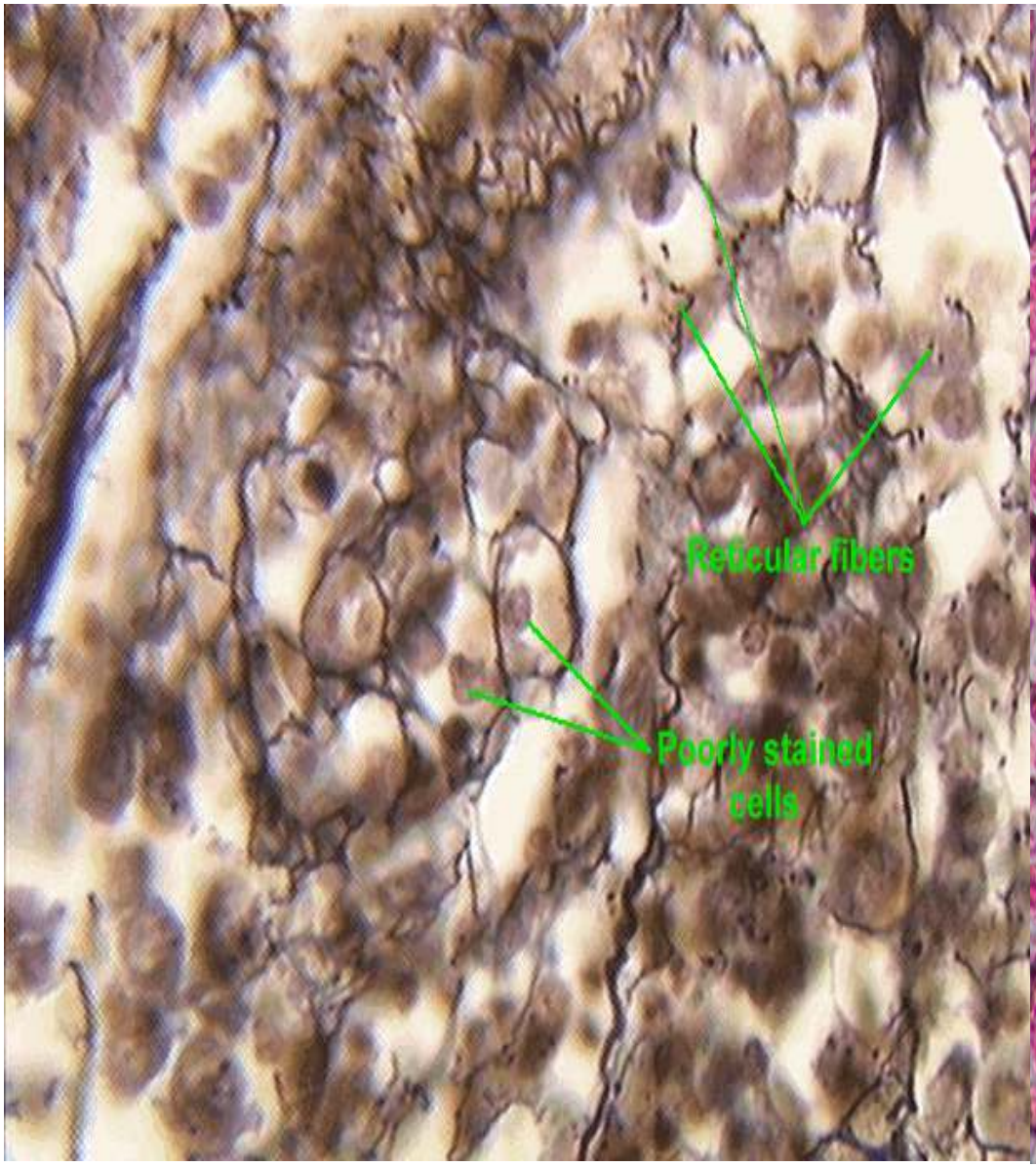
- They provide structural integrity to the splenic cords and facilitate the movement of blood cells within the spleen.

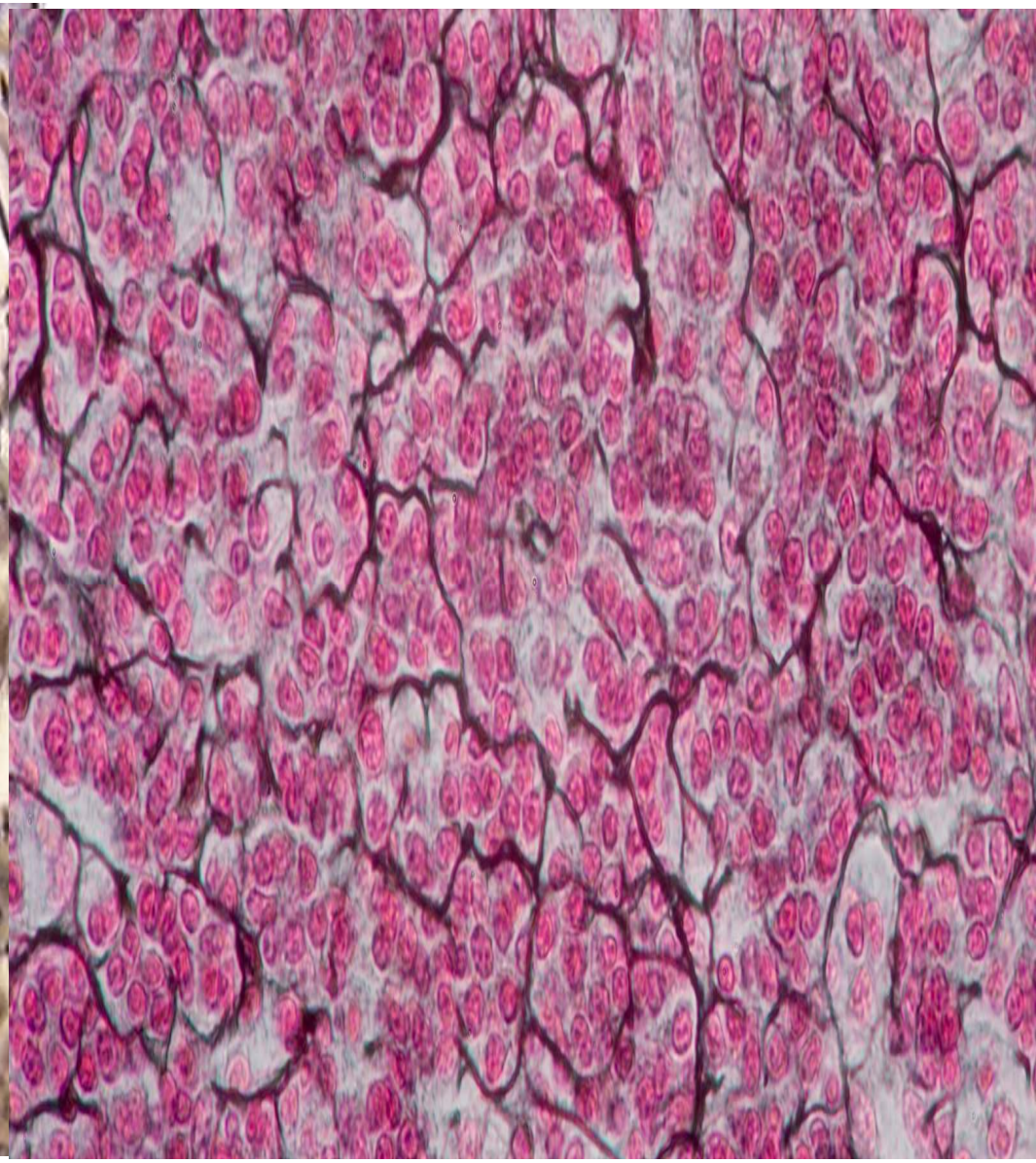
5. **Endocrine Organs**: Reticular fibers are present in endocrine glands such as the
    - adrenal gland
    - thyroid gland
    - pituitary gland.
- They provide structural support and organization to the glandular tissue, helping to maintain the architecture of the gland and support the function of hormone-secreting cells.

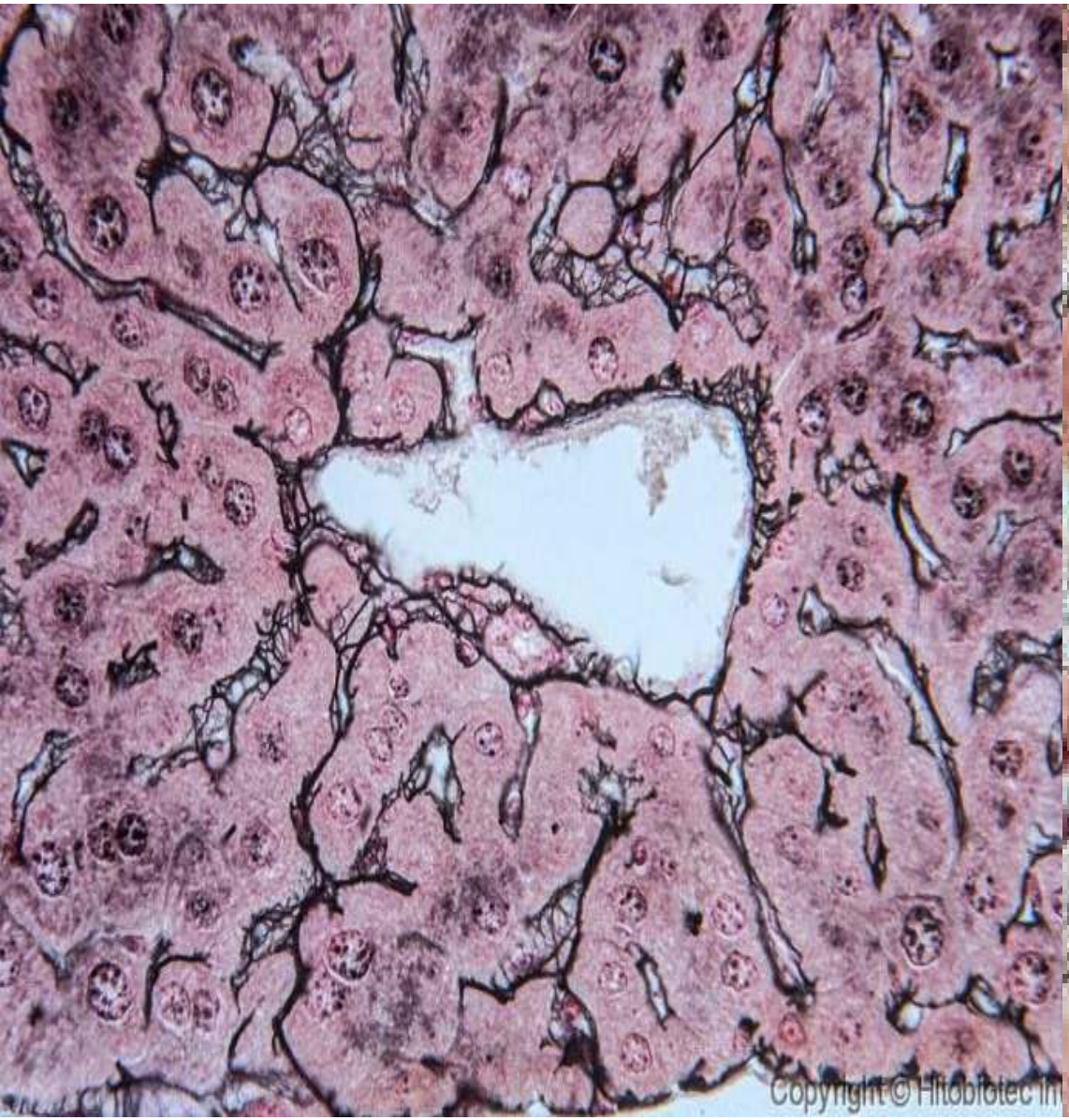
6.Stromal Tissue: Reticular fibers are also found in the stromal tissue of various organs and tissues, including
    - adipose tissue,
    - smooth muscle tissue,
    - peripheral nerves.
- They contribute to the structural framework of these tissues and provide support to surrounding cells and structures.


Reticular
Fibers


Reticular fibers


Reticular fibers
Poorly stained cells




Copyright © Histobiotec In


Liver reticulin
reticular fibres
hepatocyte nuclei

Cell type	Chief function
Mesenchyme	Embryonic source of all connective tissue cells
Fibroblasts **Chondroblasts** **Osteoblasts**	Structural support
• **Plasma cells** **Lymphocytes** **Neutrophils** **Eosinophils** **Basophils** **Mast cells** **Macrophages**	Defense and immune
Adipocytes	Metabolic Energy storage Thermal insulation

Common embryonic origin:	**Mesenchyme**			
Cellular descendants:	**Fibroblast**	**Chondroblast**	**Osteoblast**	**Hematopoietic stem cell**
	Fibrocyte 	**Chondrocyte** 	**Osteocyte** 	**Blood cells* (and macrophages)** 
Class of connective tissue resulting:	**Connective tissue proper**	**Cartilage**	**Osseous (bone)**	**Blood**
Subclasses:	**1.** Loose connective tissue Types: Areolar, Adipose, Reticular **2.** Dense connective tissue Types: Regular, Irregular, Elastic	**1.** Hyaline cartilage **2.** Fibrocartilage **3.** Elastic cartilage	**1.** Compact bone **2.** Spongy (cancellous) bone	* *Blood cell formation and differentiation are quite complex. Details are provided in Chapter 17.*
Matrix components:	Gel-like ground substance; all three fiber types	Gel-like ground substance; collagen fibers, elastin fibers in some	Gel-like ground substance hardened with calcium salts; collagen fibers	Liquid plasma; no fibers
General function:	Acts as a binding tissue; resists mechanical stress, particularly tension	Resists compression; cushions and supports body structures	Rigidness that resists compression and tension; support	Fluid tissue; transports oxygen, carbon dioxide, nutrients, hormones, wastes

Cells: (fusiform (spindle); stellate (star))

- ***fibroblasts***
  - nuclei condensed and elongated in direction of collagen fibers; cytoplasm reduced
  - essential for the maintenance of connective tissue integrity and function.
- ***Adipocytes***

- ***tissue macrophages, mast cells, leucocytes (formerly reticular endothelial system)***

- **Reticular cells** (lymph nodes and hematopoietic cords of bone marrow) synthesize reticulum; may exhibit phagocytic activity; collagen type III

- **Mast cells:** resemble basophils; long lived; can proliferate *in situ; degranulation* results in release of histamine and other vasoactive mediators; metachromatic; lack glycogen

- leucocytes *in situ*

Functions of fibroblasts include:

1.Synthesis of Collagen: Fibroblasts are primarily responsible for synthesizing collagen, the main structural protein in the extracellular matrix.

- Collagen provides tensile strength and structural support to tissues, allowing them to withstand mechanical stress.

2.Production of Elastin: Fibroblasts also produce elastin, a protein that provides elasticity and resilience to tissues, allowing them to stretch and recoil without permanent deformation.

- Elastin is particularly important in tissues that require elasticity, such as skin and blood vessels.

3.Secretion of Ground Substance: Fibroblasts secrete ground substance, a gel-like material that fills the spaces between cells and fibers in the extracellular matrix.

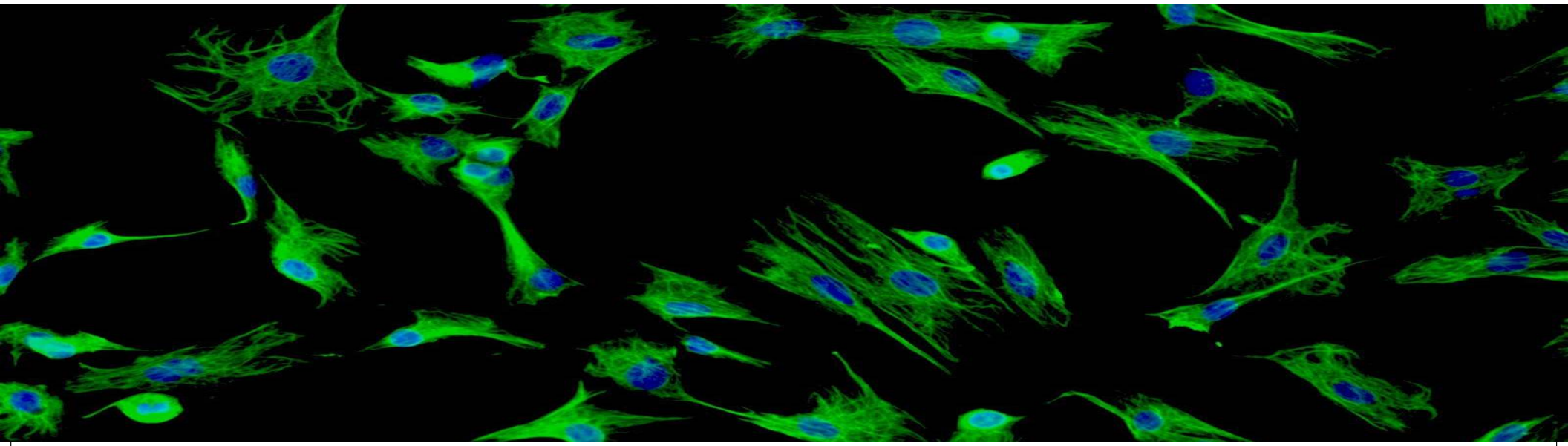
- Ground substance consists of water, glycosaminoglycans (GAGs), proteoglycans, and glycoproteins, and provides hydration, lubrication, and support to the tissue.

4.Remodeling of ECM: Fibroblasts are involved in the remodeling and turnover of the extracellular matrix, which is necessary for tissue repair, wound healing, and adaptation to changing physiological conditions.

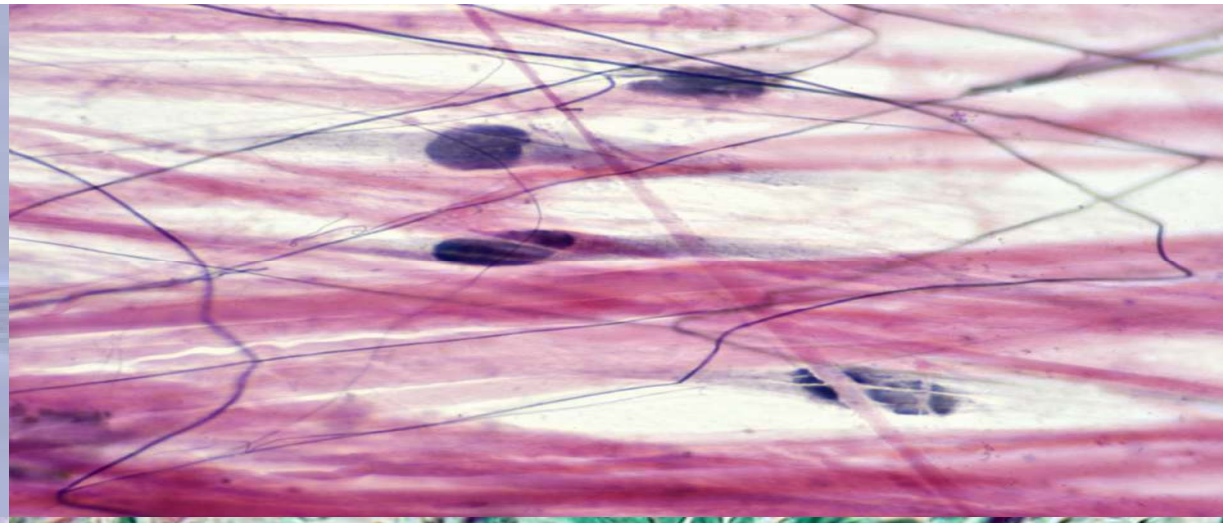
- They can degrade old or damaged ECM components and synthesize new ones to maintain tissue homeostasis.

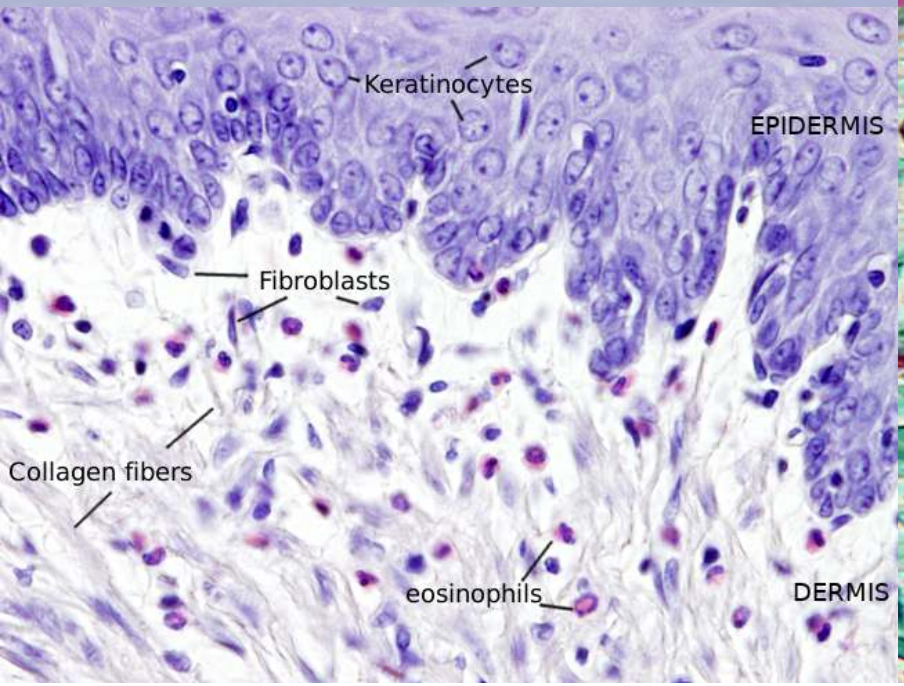
5.Response to Injury and Inflammation: Fibroblasts play a role in the inflammatory response to injury by secreting cytokines, growth factors, and other signaling molecules that attract immune cells and promote tissue repair.

- They can proliferate and differentiate into myofibroblasts, specialized cells involved in wound contraction and scar formation.



- Fibroblasts are a type of cell found in connective tissue that plays a key role in the synthesis and maintenance of the extracellular matrix (ECM).
- They are the most abundant cell type in connective tissue and are responsible for producing and secreting the structural proteins and other components that make up the ECM, including collagen, elastin, and glycosaminoglycans (GAGs).




Keratinocytes
EPIDERMIS
Fibroblasts
Collagen fibers
eosinophils
DERMIS


Collagen
FIBROBLASTS

Leucocytes in situ

- neutrophils: rare; multilobed nuclei poorly stained cytoplasm
- eosinophils: abundant in loose ct; bilobed nuclei strongly eosinophilic cytoplasmic granules
- basophils: resemble mast cells; poorly stained in H&E
- monocytes = phagocytes = macrophages, fixed macrophages, histiocytes
    - nuclei irregular; heterochromatin clumped around envelope.
    residual bodies may be exocytized or sequestered
    antigen presenting cells (APC) also called dendritic cells
    combined or coated with antibodies and complement: opsonins; opsonization: enhancement of phagocytosis
    - lymphokines: act to increase metabolic and phagocytic activity.
- lymphocytes: small, densely-stained nuclei
- plasma cells: synthesize antibodies; **clockface (cartwheel) nuclei; negatively stained golgi apparatus** (paranuclear); extensive basophilic cytoplasm
- Macrophages

Macrophages

•Macrophages show pronounced **phagocytotic activity**.

•Macrophages originate from monocytes (from precursor cells in bone marrow), which migrate to connective tissue and differentiate into tissue macrophages.

•Today the various macrophages of the body are grouped in a common system called the **Mononuclear Phagocyte System** (MPS).

• Today a wide range of macrophages are included in the MPS and include : **Kupffer cells** of the liver, **alveolar macrophages** of the lung, **osteoclasts**, **microglia** etc.

•The main functions of macrophages are ingestion by **phagocytosis** of microorganisms (bacteria, viruses, fungi), parasites, particulate matter such as dust, and they also participate in the breakdown of aged cells including erythrocytes. The **intracellular digestion** occurs as a result of fusion of **lysosomes** with the **phagosome** (ingested body).

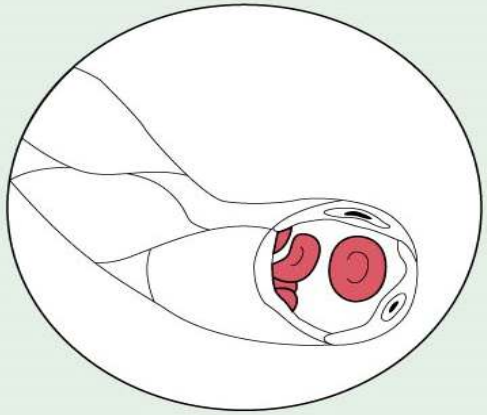
•Macrophages are normally long-lived and survive in the tissues for several months. In some cases where a foreign body (such as a small splinter) has penetrated the inner tissues of the body, several macrophages may fuse together to form multinuclear **foreign body giant cells**. These large cells accumulate at sites of invasion of the foreign body and sites of inflammation.

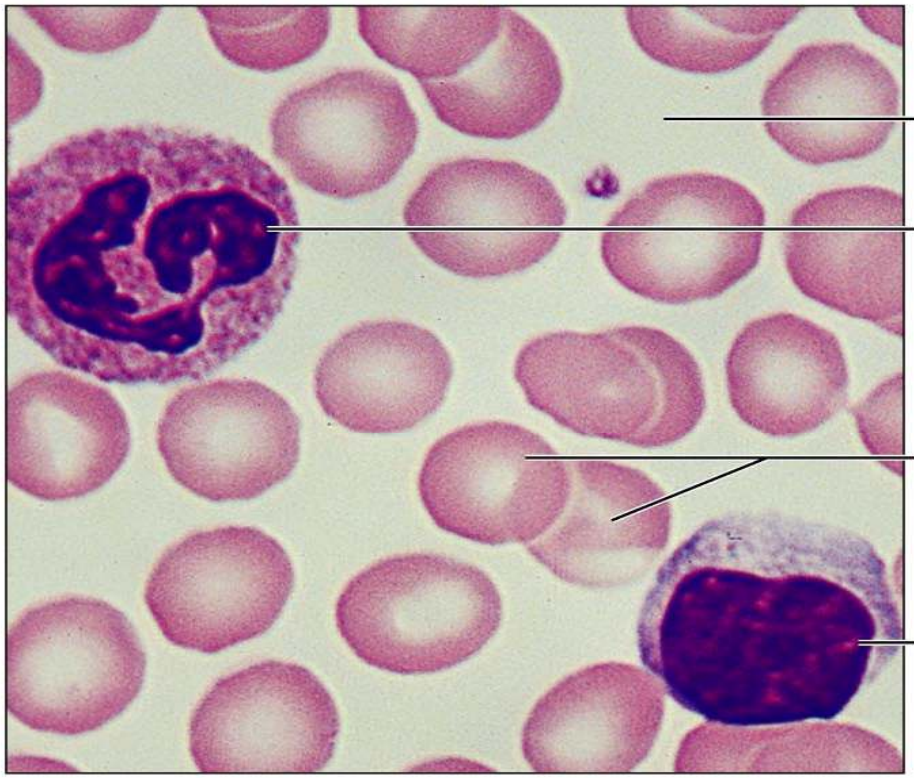
(j) Others: blood

Description: Red and white blood cells in a fluid matrix (plasma).

Function: Transport of respiratory gases, nutrients, wastes, and other substances.

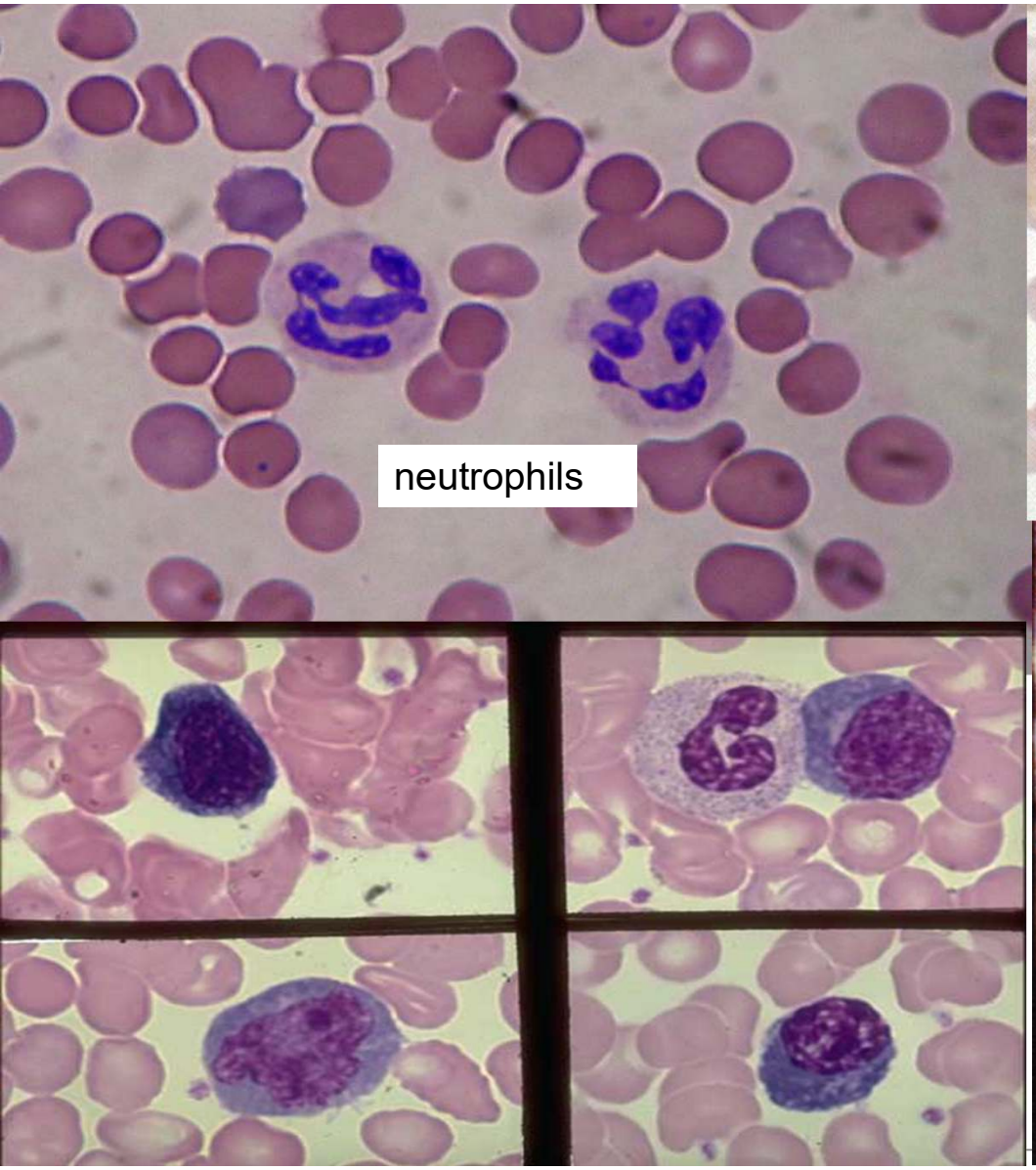
Location: Contained within blood vessels.

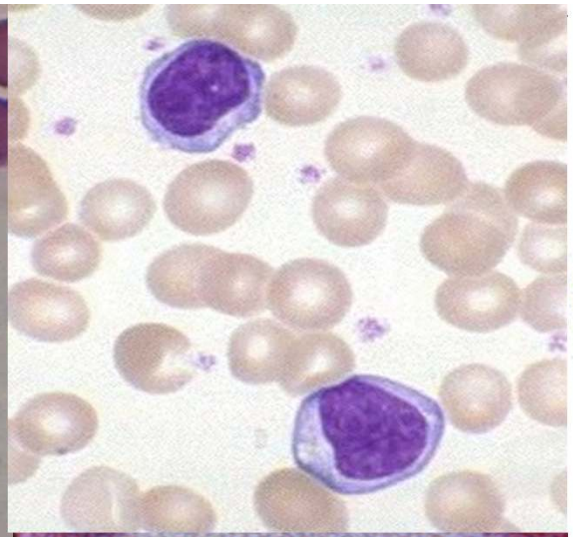


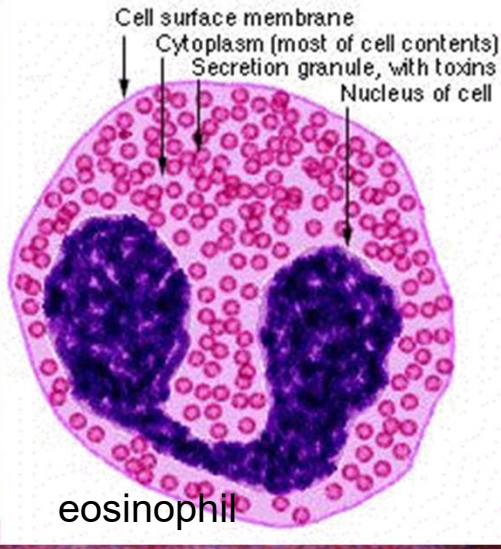


Photomicrograph: Smear of human blood (1500×); two white blood cells (neutrophil in upper left and lymphocyte in lower right) are seen surrounded by red blood cells.

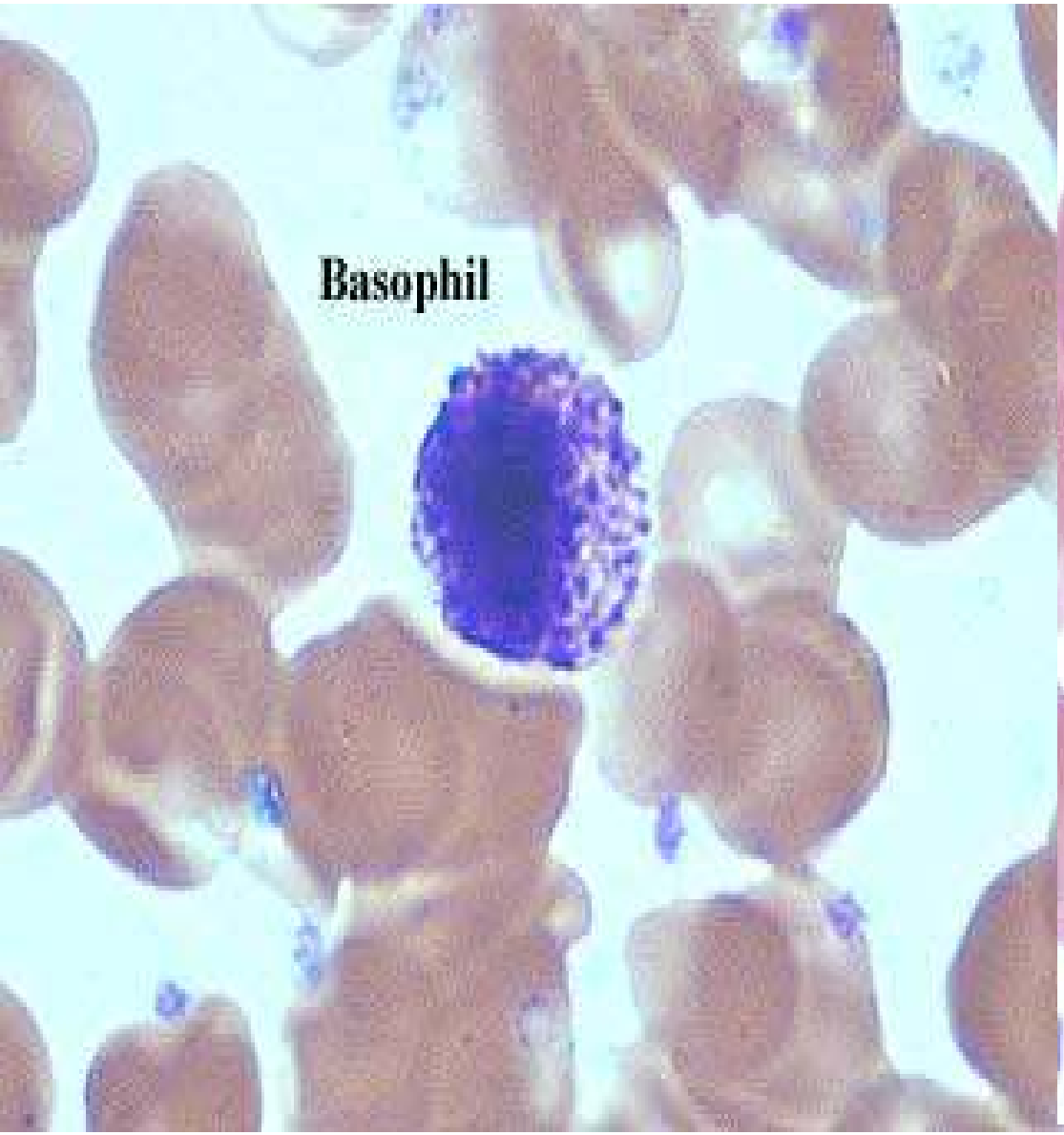
Figure 4.9j

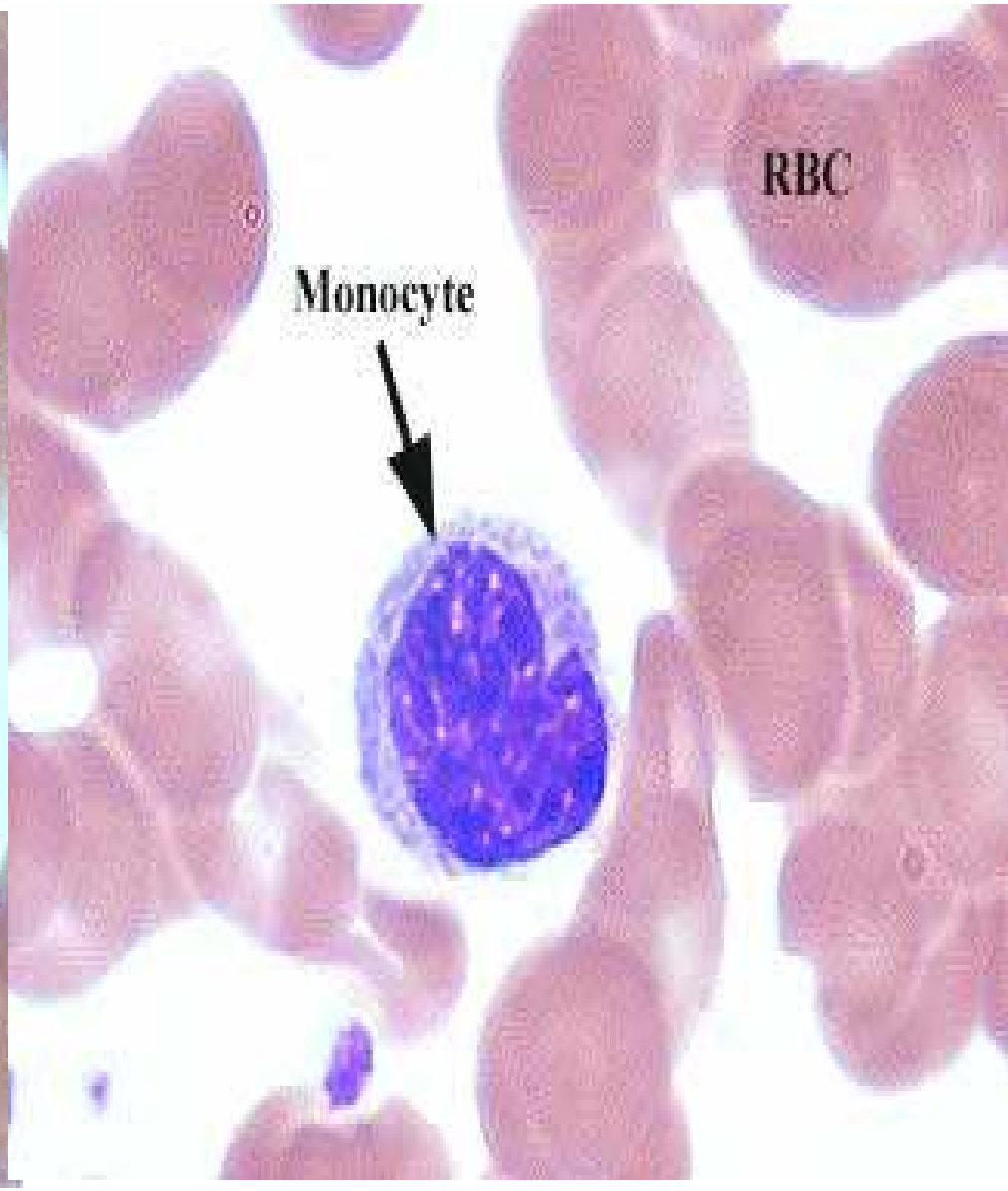

neutrophils

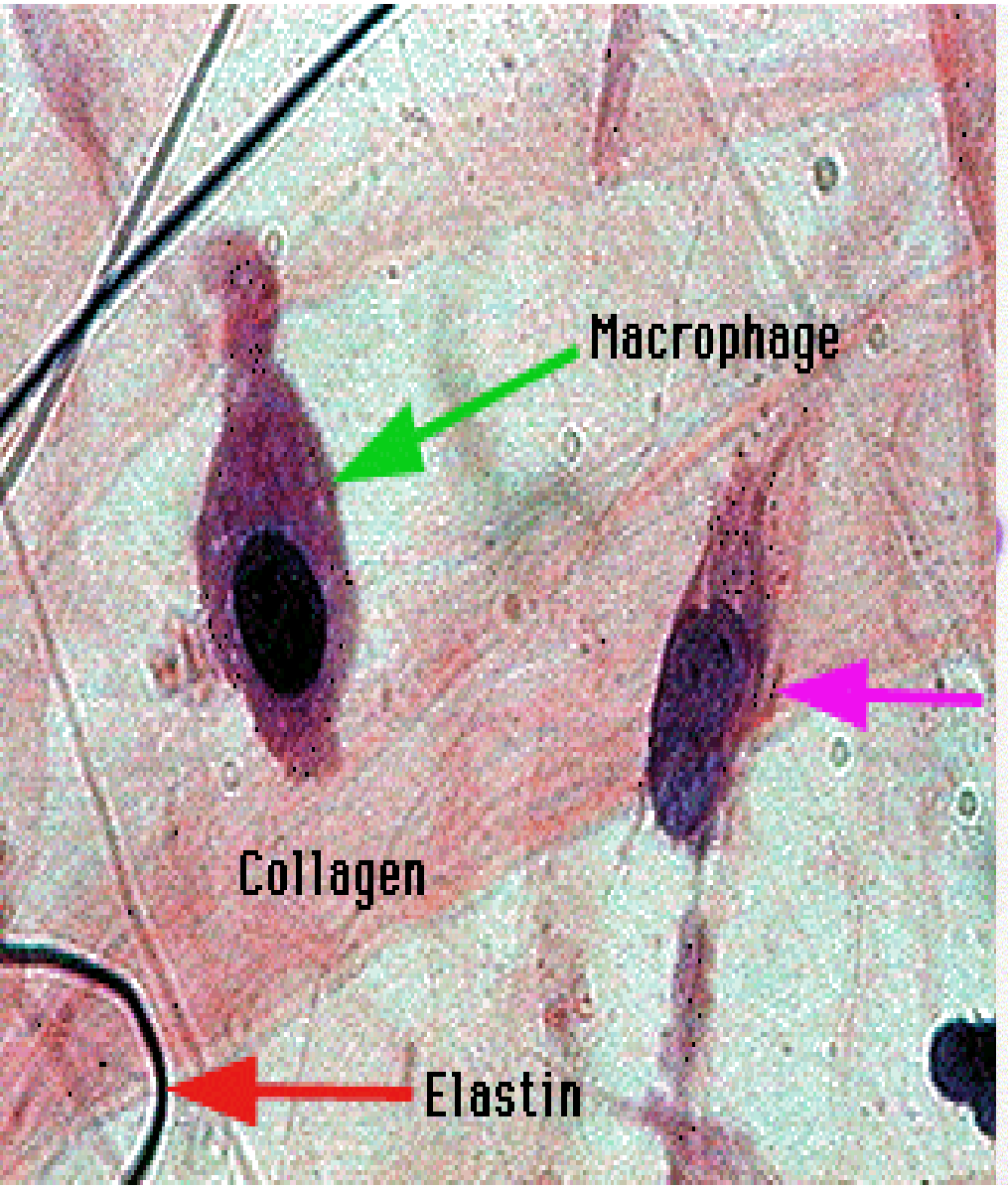


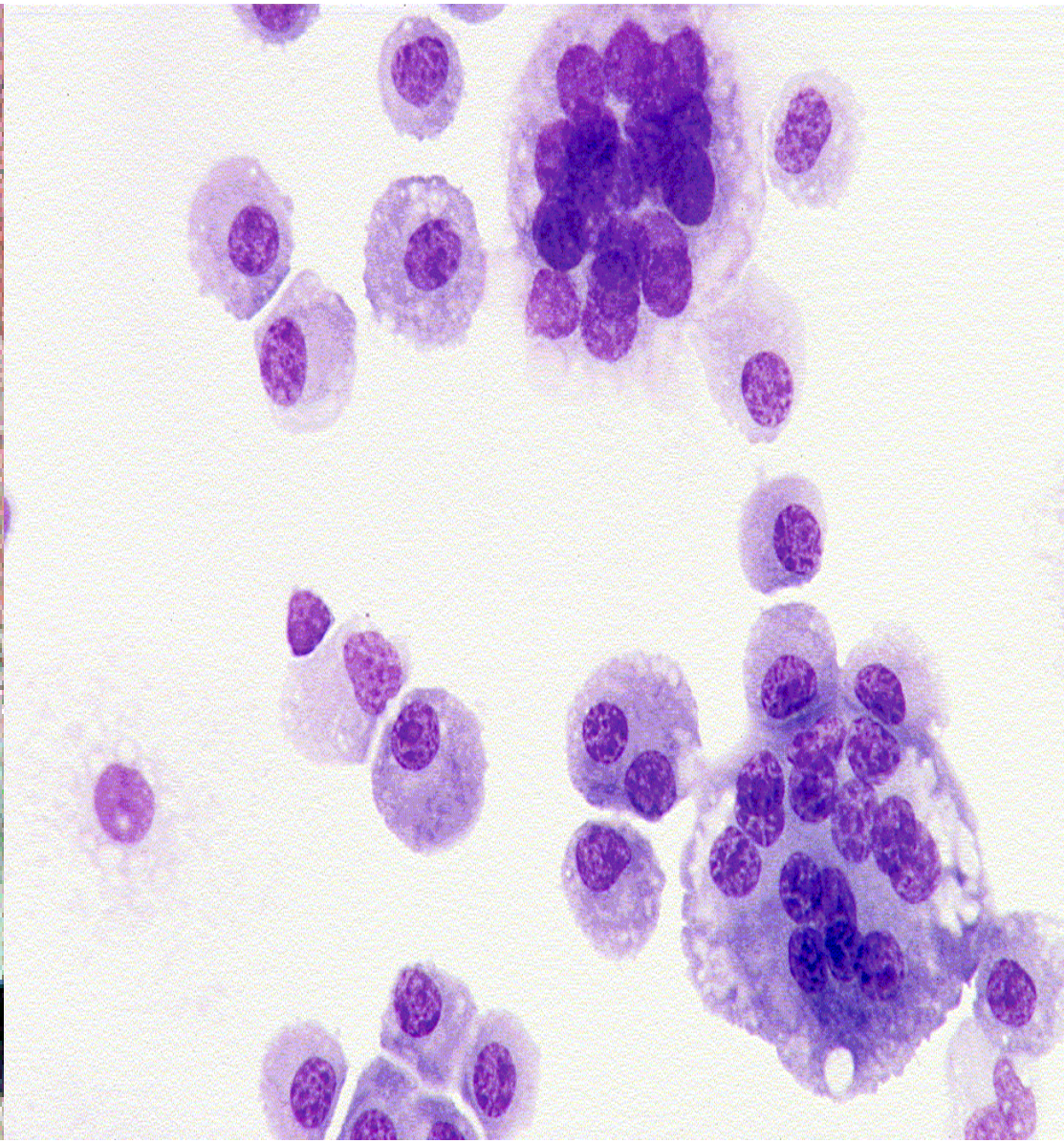

Cell surface membrane
Cytoplasm (most of cell contents)
Secretion granule, with toxins
Nucleus of cell
eosinophil


Plasma cell


Basophil


RBC
Monocyte


Macrophage
Collagen
Elastin



White adipose tissue

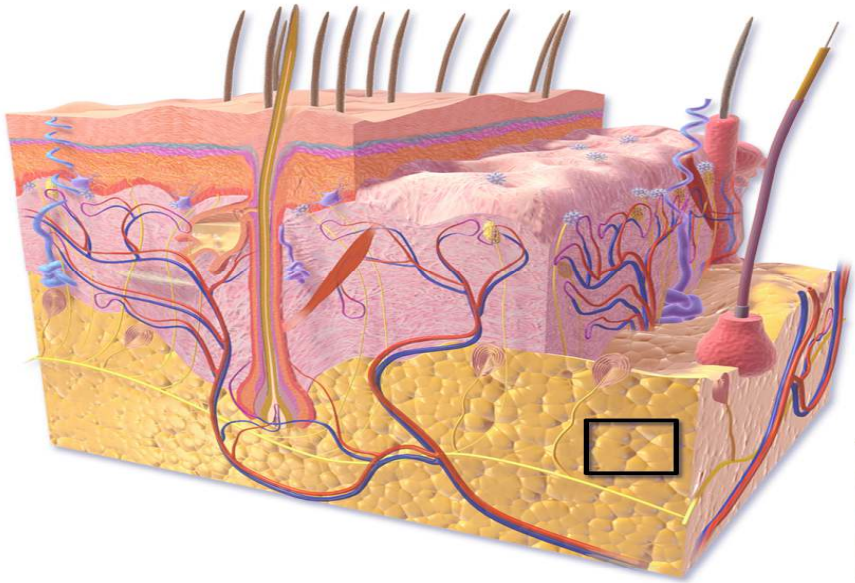
- **Normal body fat**
- Very large spherical cells which may become polyhedral due to deformation
- Contain single fat droplet with cytoplasm reduced to thin rim net to plasma membrane
- Nucleus displayed to one side of cell and flattened by accumulated fat
- Routine histological techniques extract the fat, leaving a large unstained space
- Adipose tissue may be portioned by connective tissue septa visible to the naked eye

Brown adipose tissue

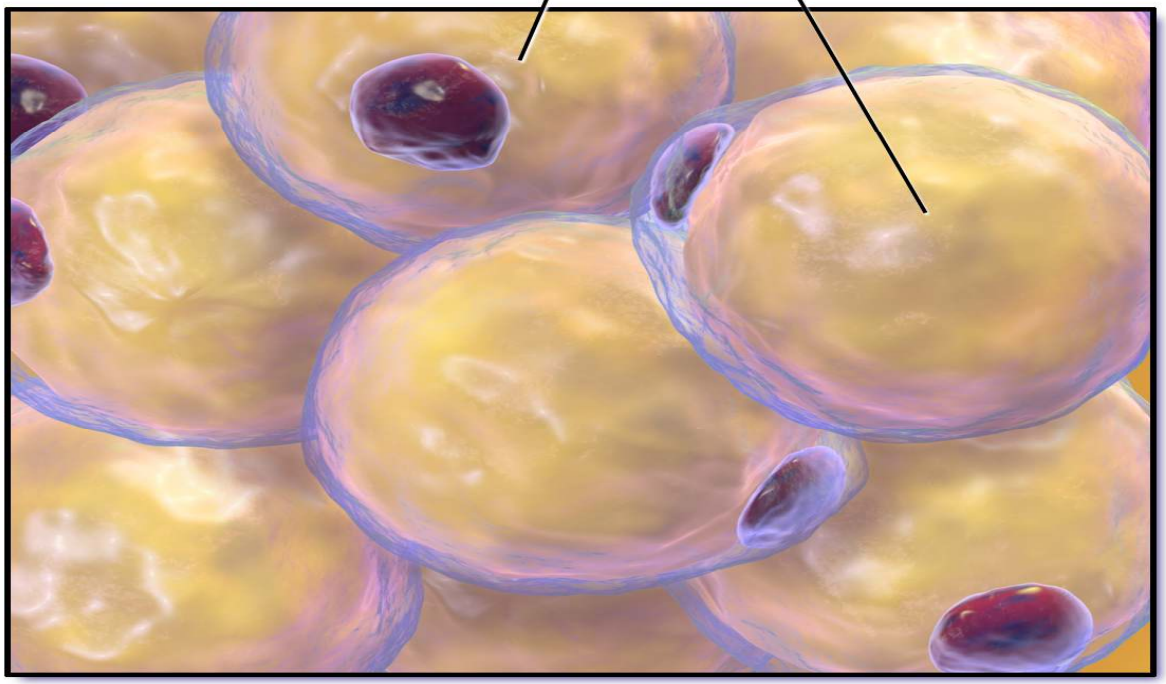
- Prominent in newborn of all mammals
- In adults most conspicuous in species which hibernate
- Present in man throughout life
- Cells are smaller than those of white adipose tissue
- Cytoplasm relative abundant and contains lipid droplets of varying size
- Cytoplasm contains extraordinary large number of mitochondria
- Brown fat has a lobular organization
- Highly vascular with blood vessel distribution similar to that of a gland
- Numerous small unmyelinated nerves with axons ending on cell surface

Dynamic Regulation:

- Adipocytes are dynamic cells that respond to changes in
  - **nutritional status,**
  - **hormonal signals**
  - **environmental cues.**
- They can undergo
    - **hypertrophy (increase in size)**
    - **hyperplasia (increase in number)**
  - in response to excess energy intake or depletion, leading to changes in adipose tissue mass and distribution.

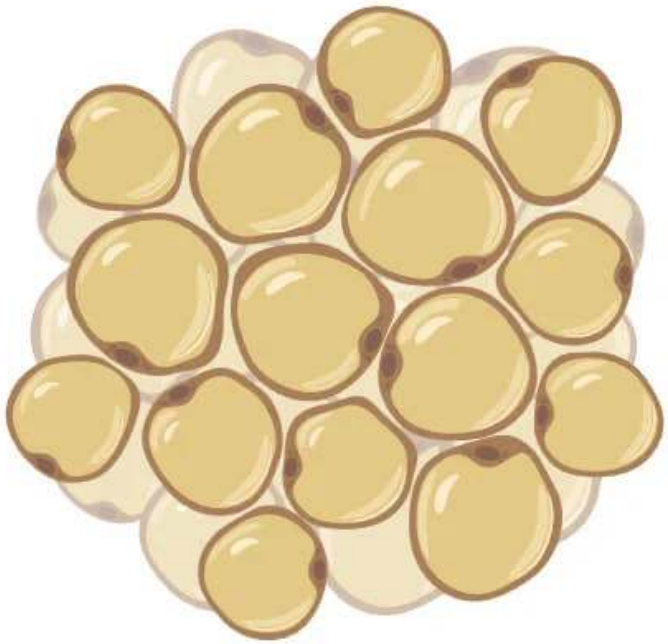


Adipocytes
(white adipose cells)



Adipose Tissue

Fat Cells (Adipocytes or Adipose Cells)



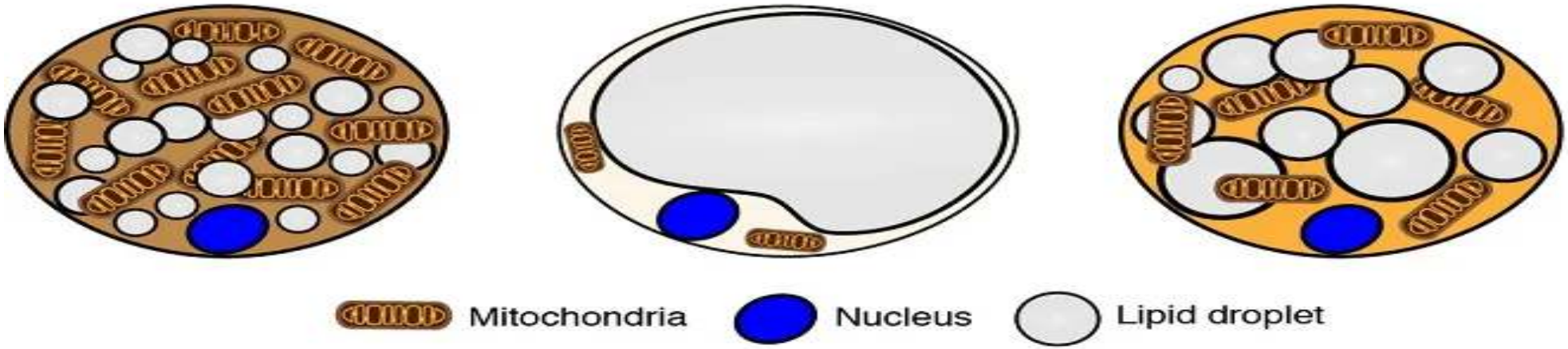
Adipose Tissue

Adipocyte (White)

Adipocyte (Brown)

Adipocyte (Beige)

Brown Adipocyte **White Adipocyte** **Brite (or Beige) Adipocyte**



	Brown	***White***	***Brite/beige***
UCP1 Expression	Positive	Negative	Positive
Mitochondrial Density	High	Low	Medium
LD Morphology	Multi-locular	Uni-locular	Multi-locular
Primary Function	Thermogenesis Endocrine	Energy storage Endocrine	Thermogenesis? Endocrine?

1.Energy Storage: The main function of adipocytes **is to store energy in the form of triglycerides, which are synthesized from dietary fats and carbohydrates.**

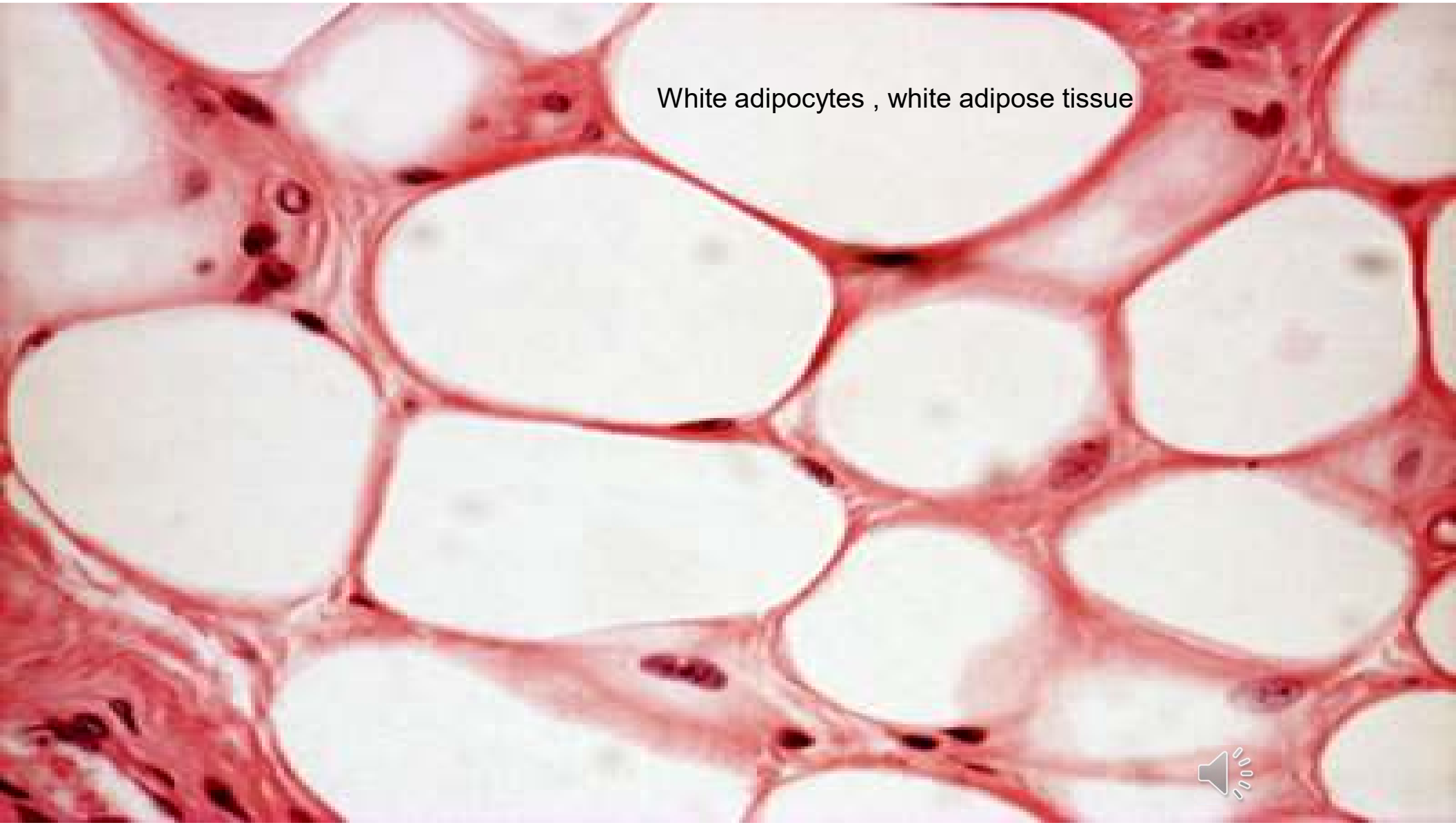
- Adipose tissue serves as **a reservoir for excess energy**, allowing the body to store surplus calories during times of abundance and mobilize them when energy is needed.

2.Insulation: Adipose tissue provides insulation to the body by forming a layer beneath the skin (**subcutaneous fat)** and **around internal organs (visceral fat).**

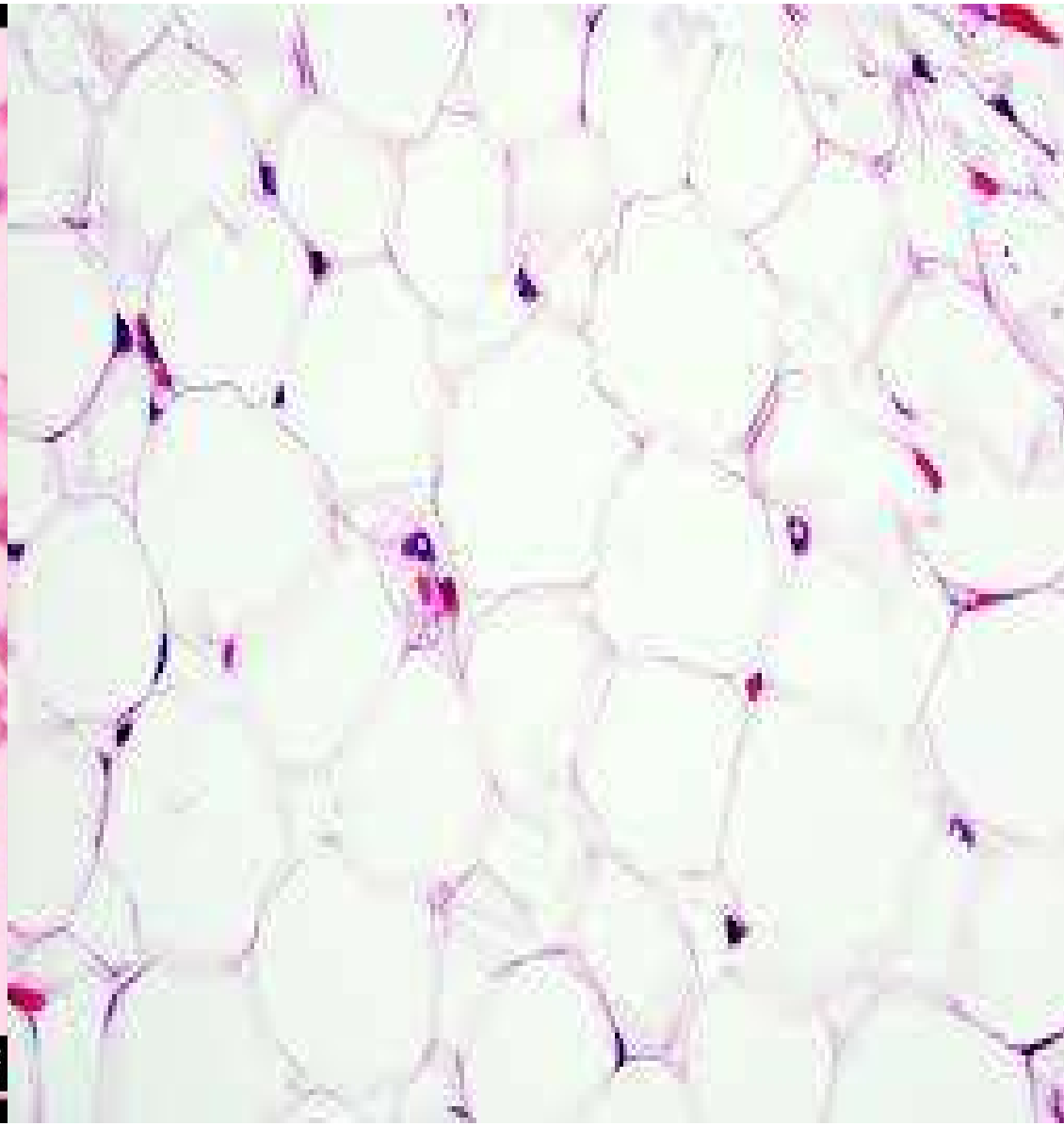
- This adipose layer helps to **regulate body temperature by reducing heat loss and providing thermal insulation.**

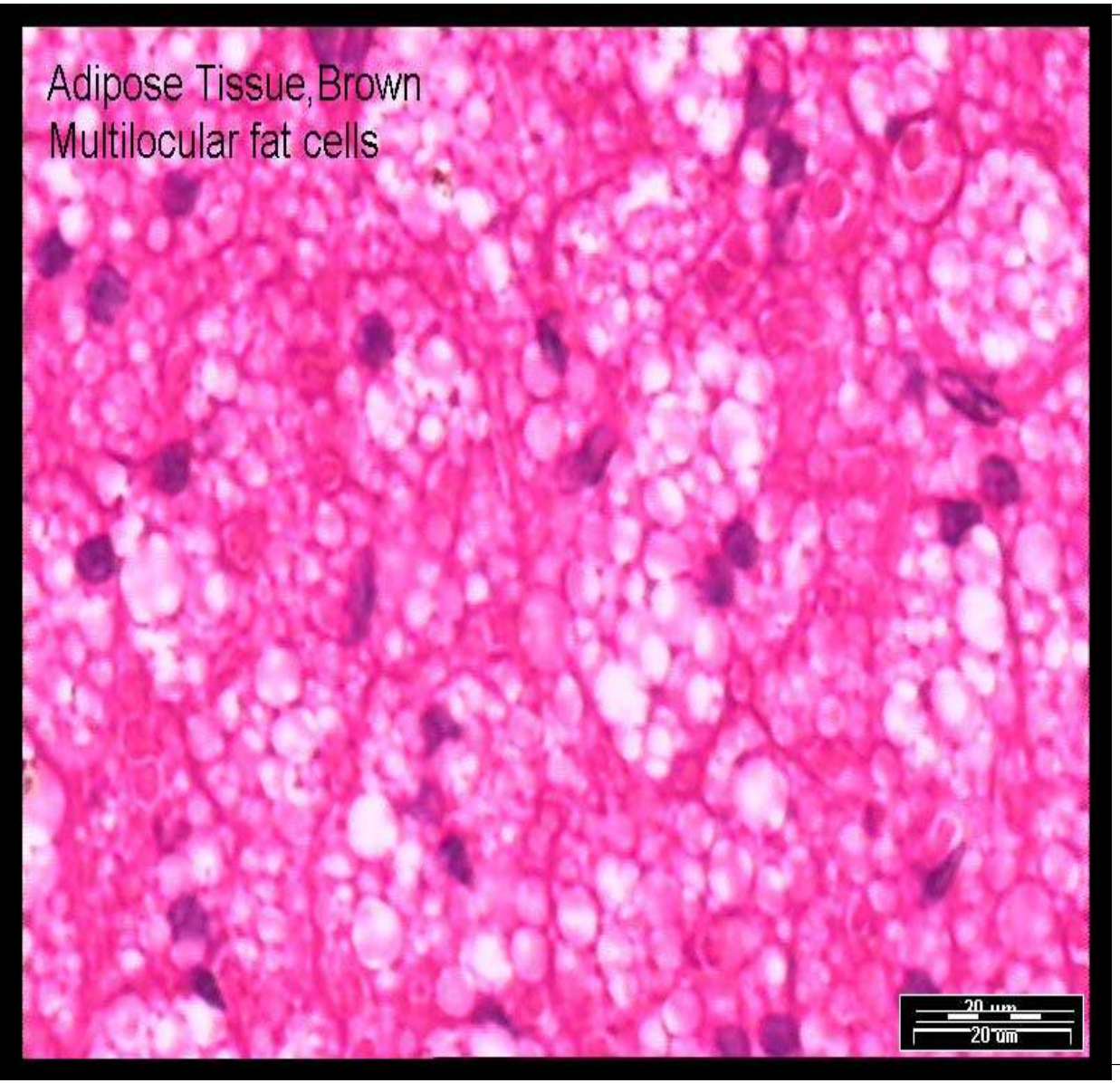
3.Endocrine Function: Adipocytes secrete various hormones and signaling molecules collectively referred to as **adipokines**.

- These include
  - adiponectin,
  - leptin,
  - resistin,
- among others, which regulate
  - metabolic processes,
  - appetite,
  - inflammation,
  - insulin sensitivity.
- Adipokines play a role in systemic metabolism, energy balance, and the regulation of body weight.


White adipocytes , white adipose tissue

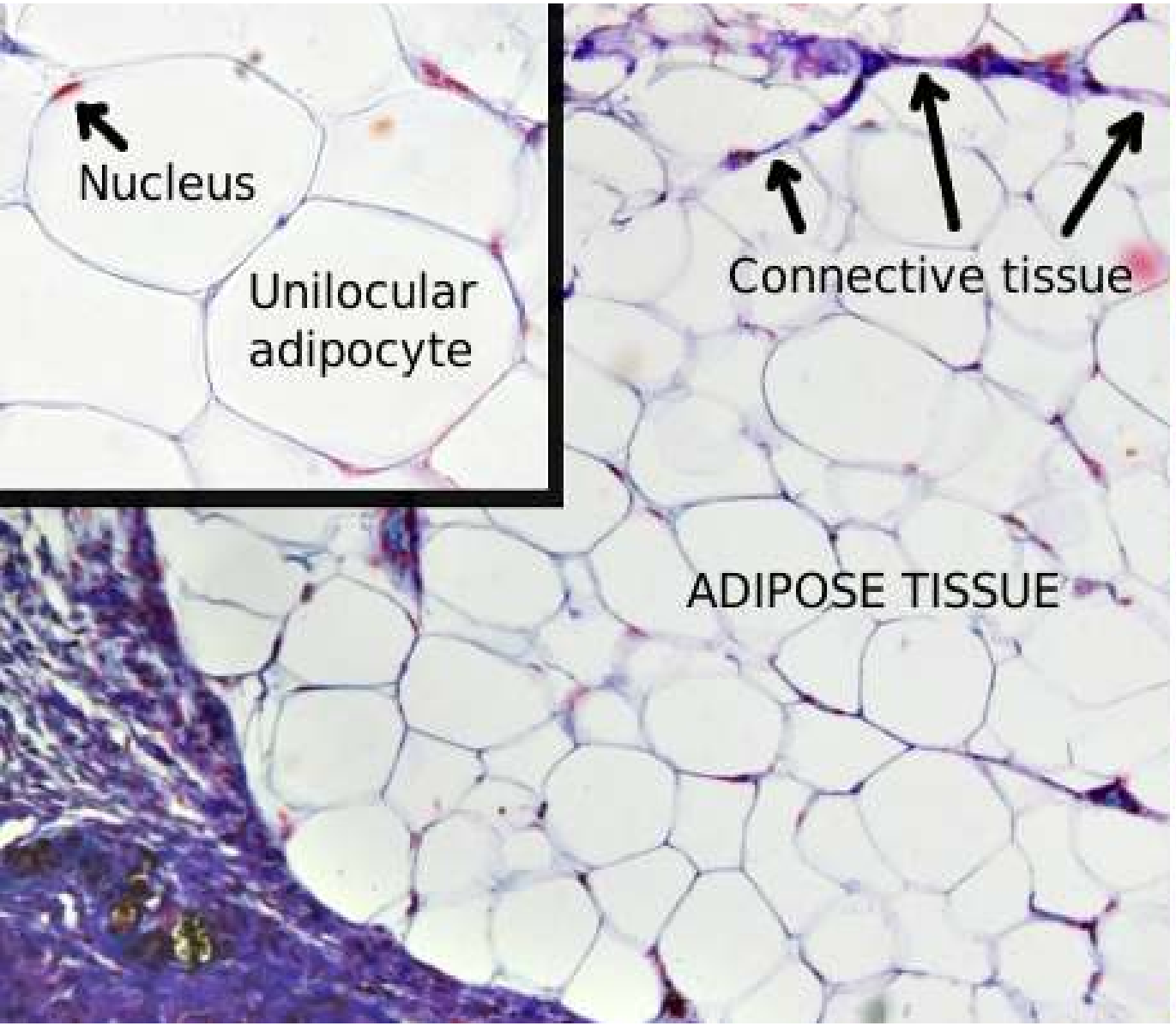

Adipose Tissue, White
50 um

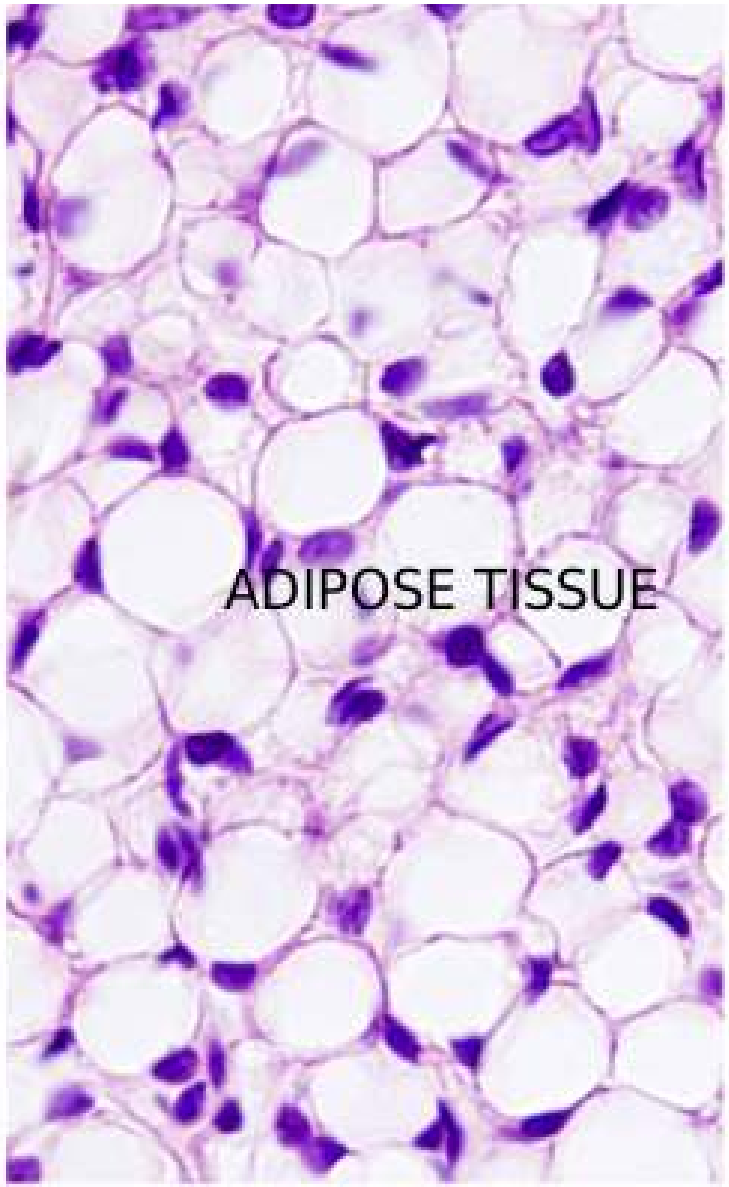




Locations:Neck:

- Around the supraclavicular area (above the collarbones)
- Upper Chest: Behind the breastbone (mediastinum)
- Kidneys: Surrounding the kidneys (perirenal)
- Spinal Cord: Along the spine (paravertebral)


Nucleus
Unilocular adipocyte
Connective tissue
ADIPOSE TISSUE

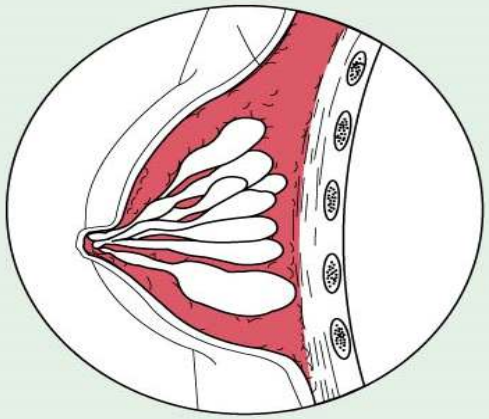

ADIPOSE TISSUE

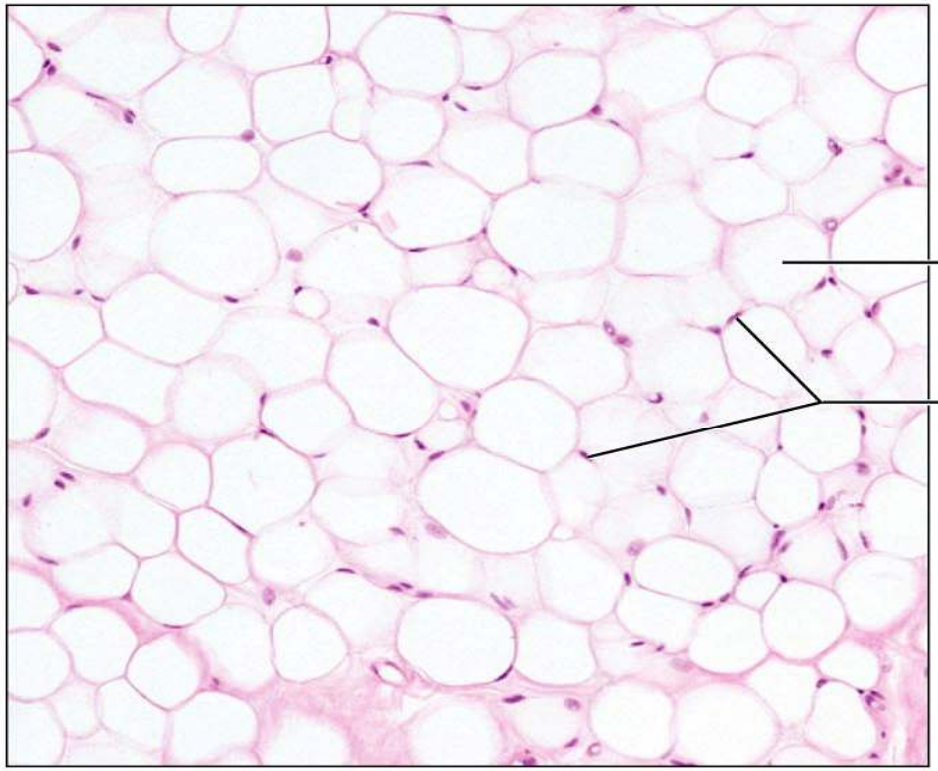
(b) Connective tissue proper: loose connective tissue, adipose

Description: Matrix as in areolar, but very sparse; closely packed adipocytes, or fat cells, have nucleus pushed to the side by large fat droplet.

Function: Provides reserve food fuel; insulates against heat loss; supports and protects organs.

Location: Under skin; around kidneys and eyeballs; within abdomen; in breasts.





Photomicrograph: Adipose tissue from the subcutaneous layer under the skin (450×).

Figure 4.9b

Hormones of the adipose tissue

These hormones, collectively called adipokines, significantly influence energy metabolism, insulin sensitivity, and other physiological functions. Here's a breakdown of the key hormones produced by adipose tissue:

1. Leptin:

•**Function:** Often referred to as the "satiety hormone," leptin signals satiety (feeling full) to the brain, regulating appetite and food intake.

•**Mechanism:** Leptin levels rise proportionally with increased fat stores.

- The hypothalamus, a region in the brain that regulates hunger and satiety, detects leptin and reduces appetite, promoting a decrease in food intake and body weight.

•**Importance:** Leptin deficiency or leptin resistance (inability of the body to respond to leptin) can contribute to obesity.

Adiponectin:

•**Function:** Adiponectin acts as an insulin sensitizer, promoting the body's ability to utilize glucose for energy. It also has anti-inflammatory properties.

•**Mechanism:** Adiponectin levels are generally lower in obese individuals. It enhances insulin signaling in target tissues like muscle and liver, leading to improved glucose uptake and lower blood sugar levels.

•**Importance:** Low adiponectin levels are associated with increased risk of insulin resistance and type 2 diabetes.

3. Resistin:

•**Function:** The role of resistin is still under investigation, but it might be involved in promoting insulin resistance.

•**Mechanism:** Resistin levels tend to be higher in individuals with obesity and type 2 diabetes.

- The exact mechanism by which it affects insulin sensitivity is not fully understood.

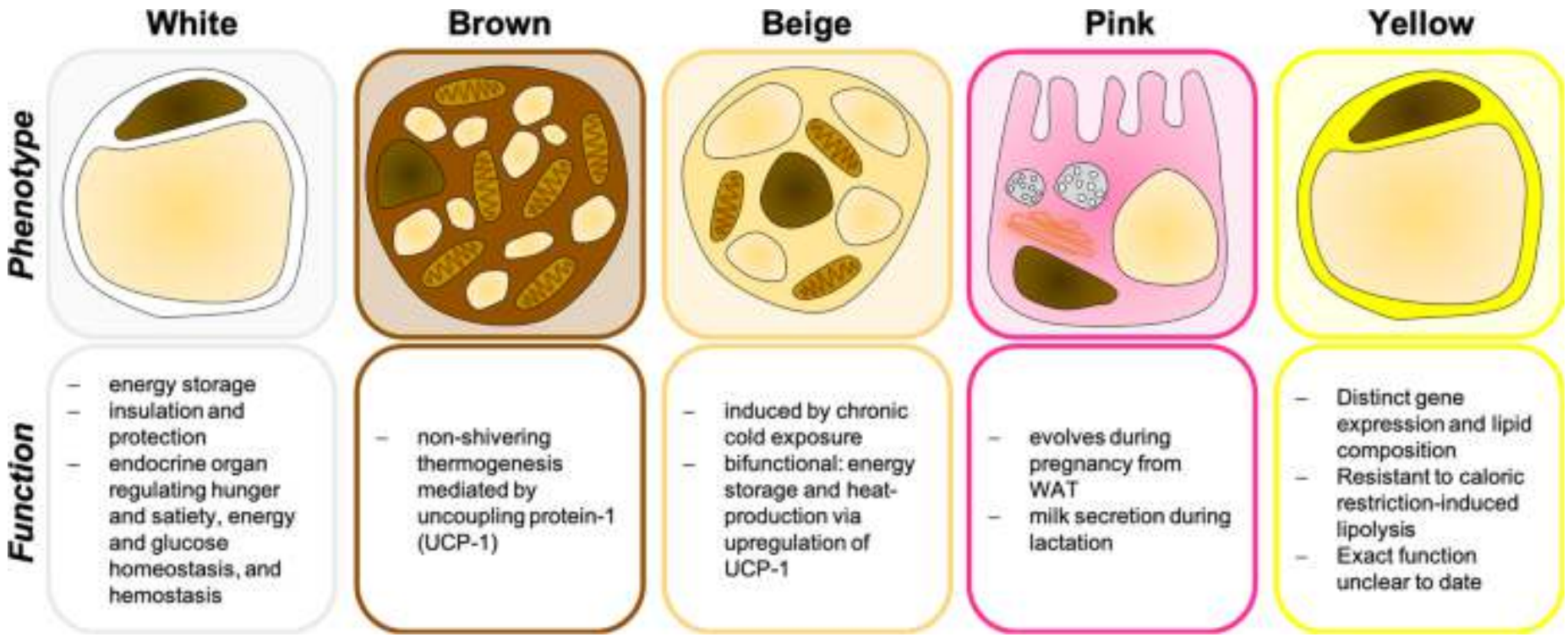
•**Importance:** Further research is needed to clarify the specific role of resistin in metabolic regulation.

Other Adipokines:

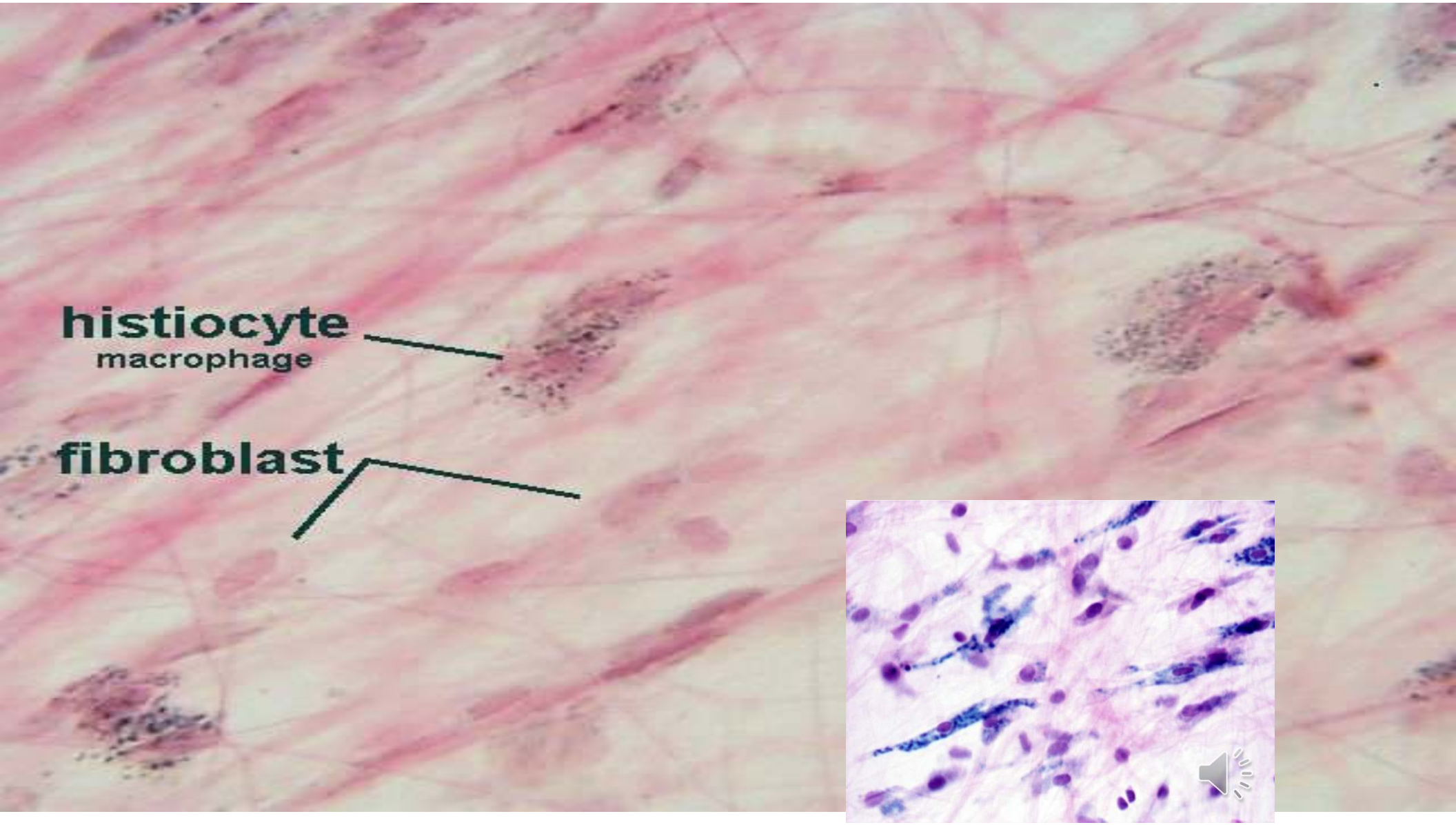
•Adipose tissue also produces other hormones like:

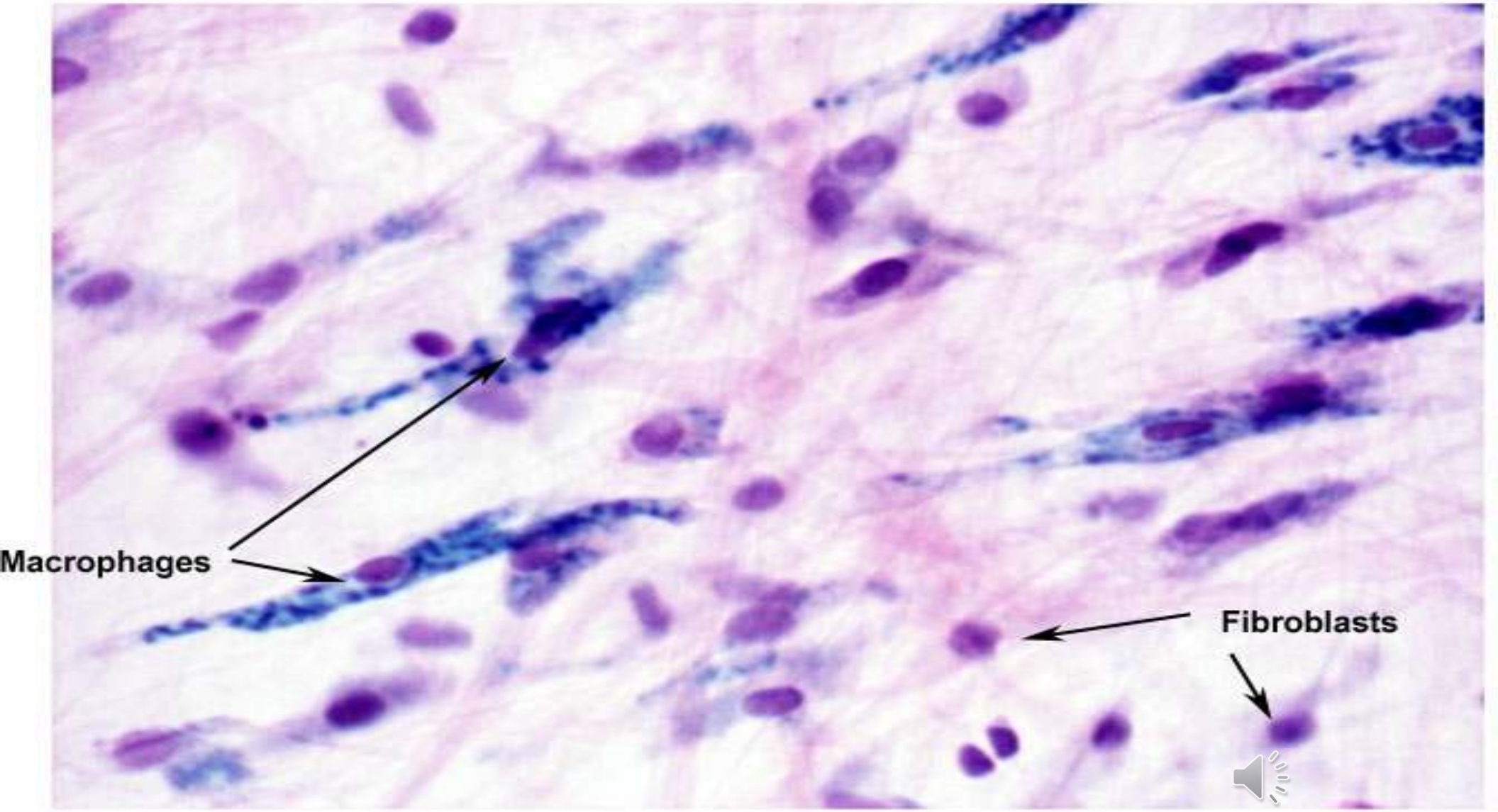
- **Visfatin:** May have roles in inflammation and insulin sensitivity.
- **Chemerin:** Might be involved in regulating appetite and fat metabolism.
- **Wnt proteins:** Signaling molecules with diverse functions, including adipogenesis (fat cell formation) and insulin sensitivity.

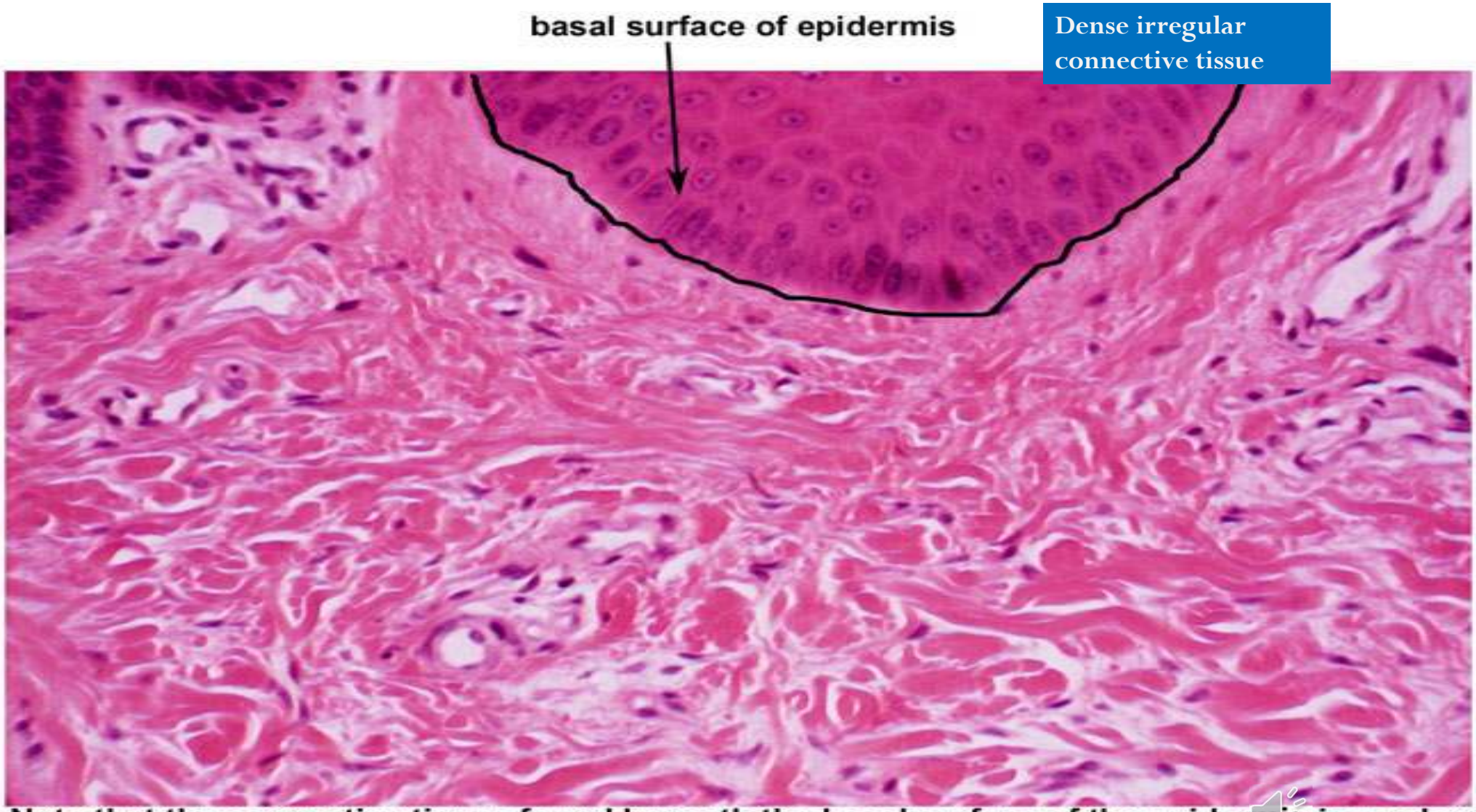
The reality


White
Brown
Beige
Pink
Yellow
Phenotype
Function
– energy storage
– insulation and protection
– endocrine organ regulating hunger and satiety, energy and glucose homeostasis, and hemostasis
– non-shivering thermogenesis mediated by uncoupling protein-1 (UCP-1)
– induced by chronic cold exposure
– bifunctional: energy storage and heat-production via upregulation of UCP-1
– evolves during pregnancy from WAT
– milk secretion during lactation
– Distinct gene expression and lipid composition
– Resistant to caloric restriction-induced lipolysis
– Exact function unclear to date

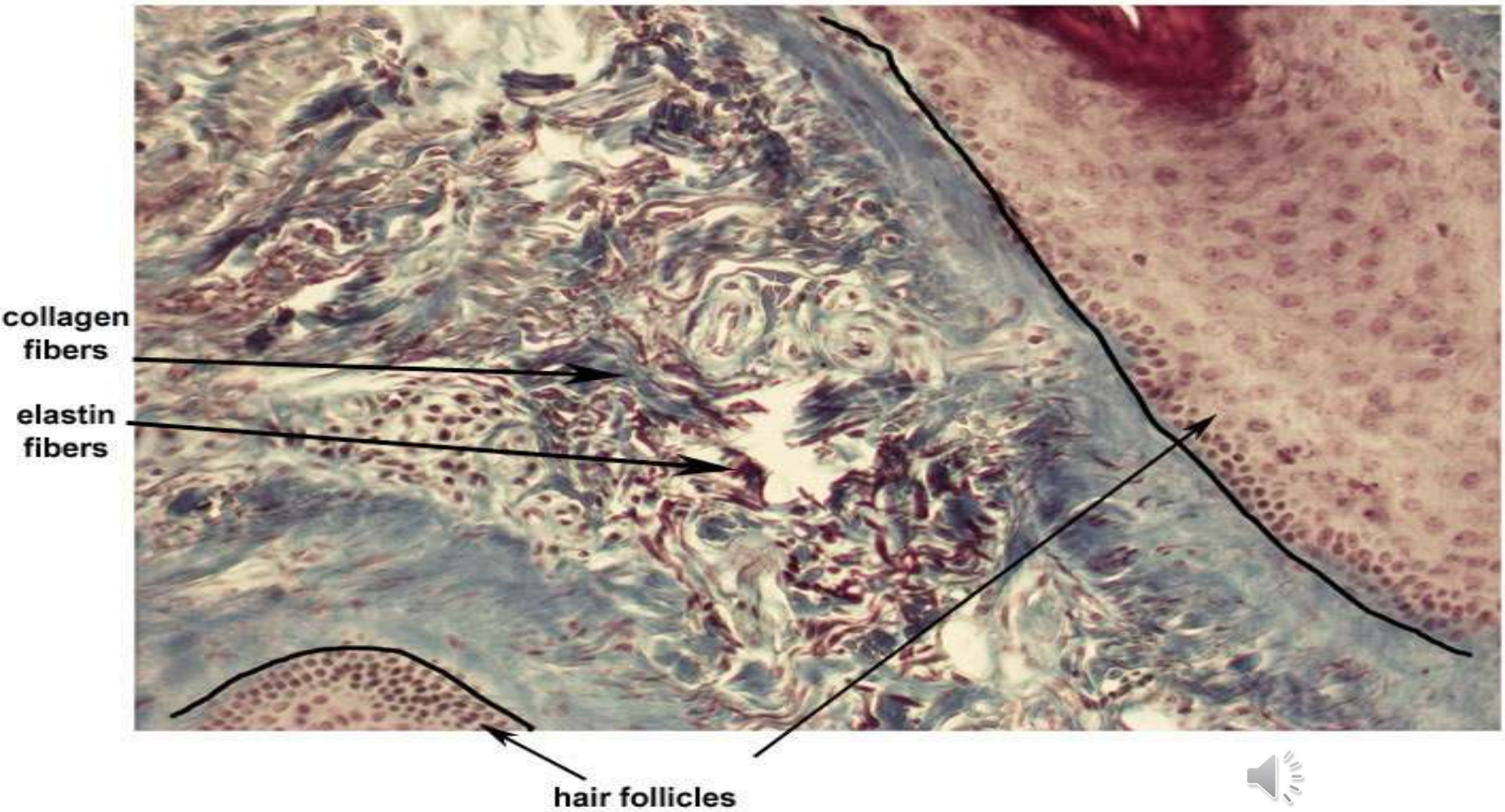
Slides review

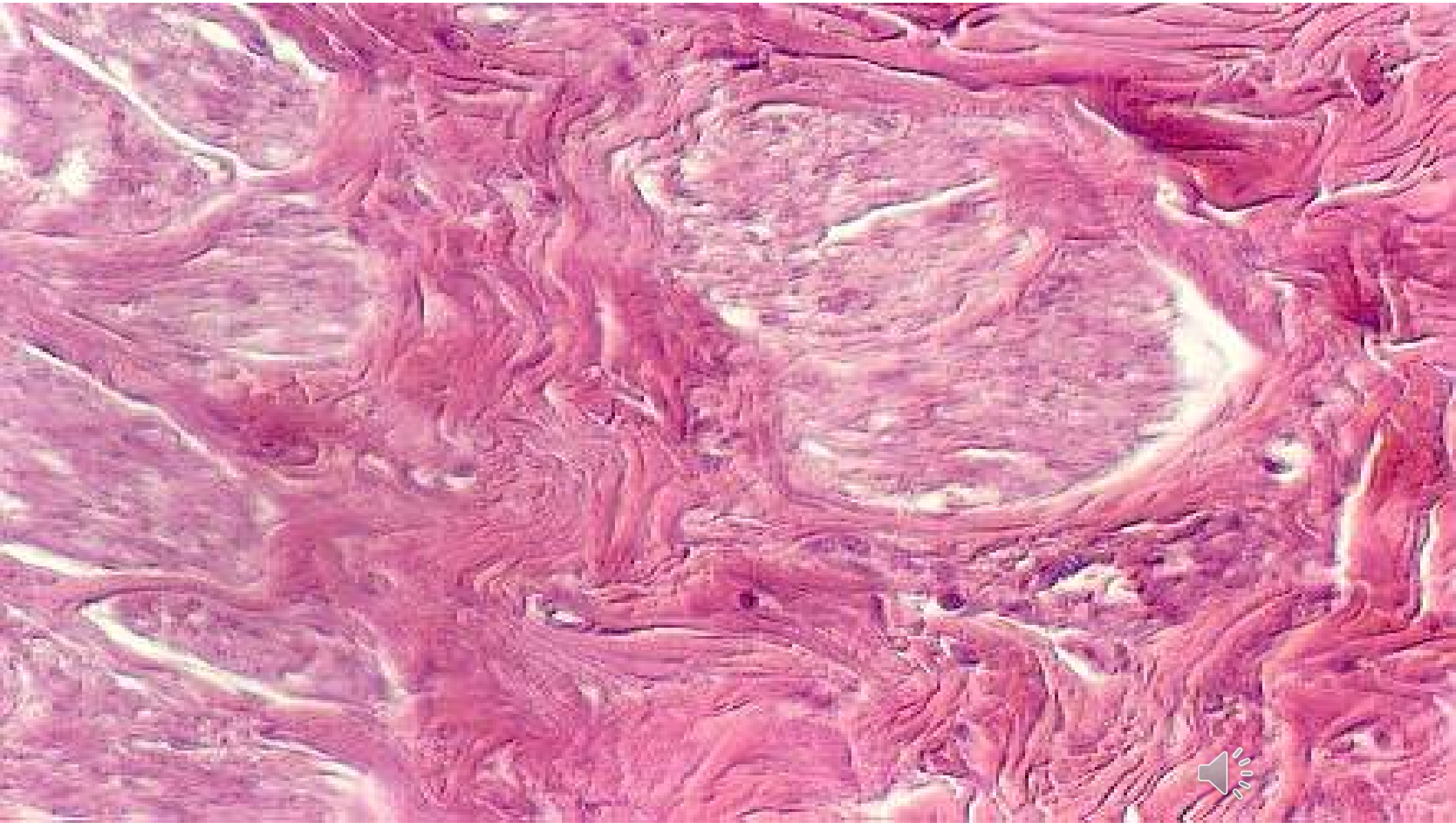

histiocyte
macrophage
fibroblast

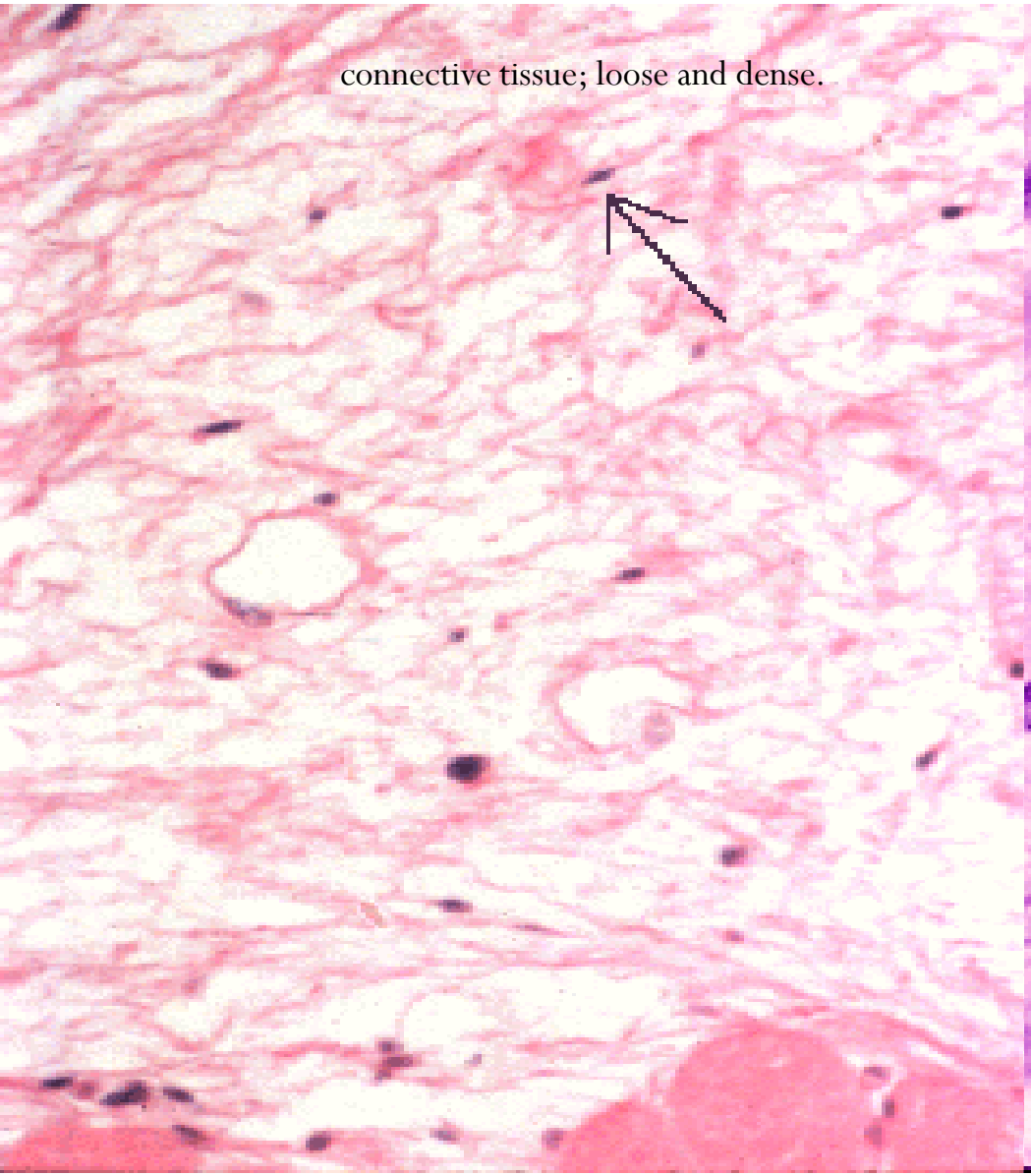

Macrophages
Fibroblasts

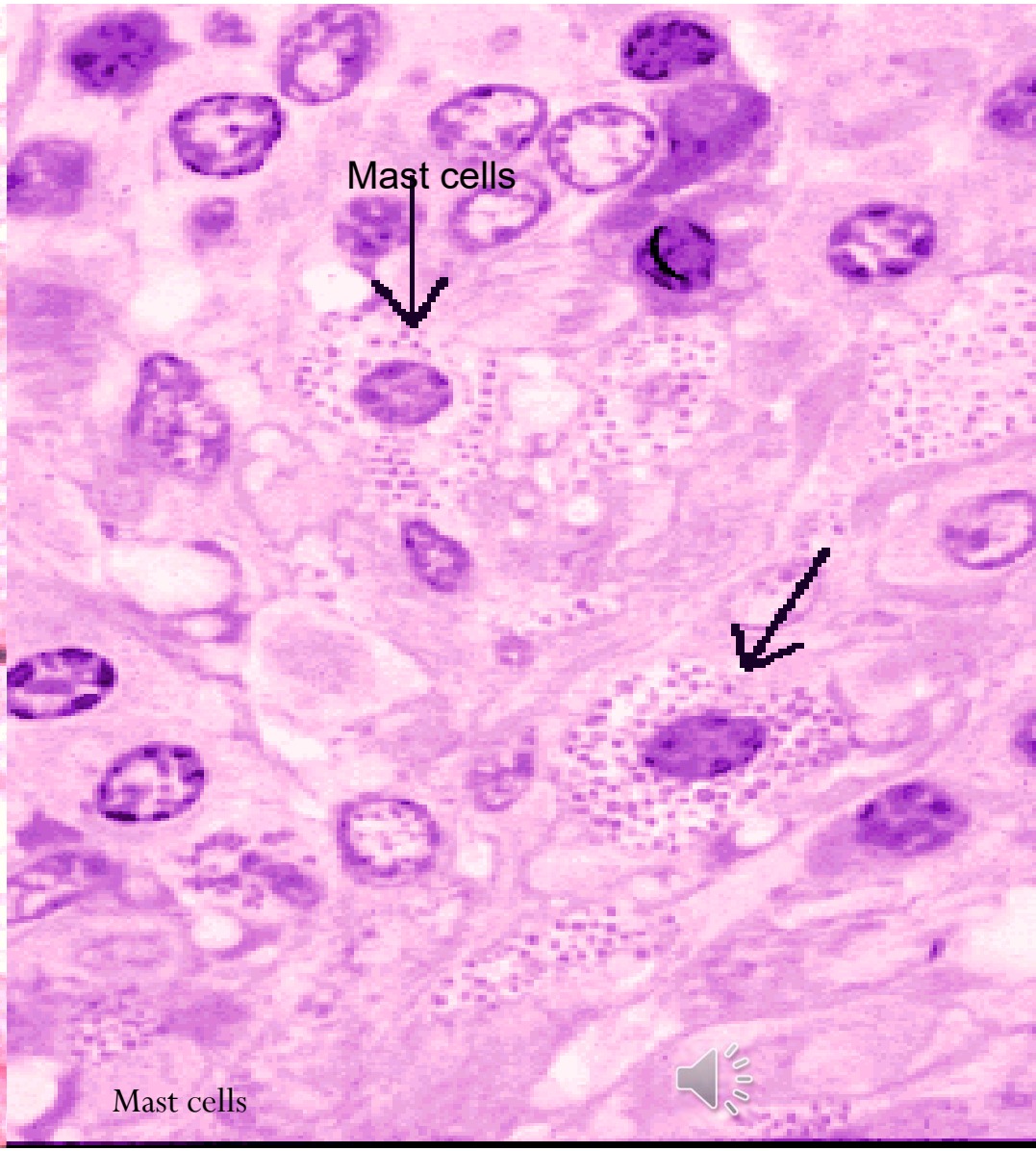


Note that the connective tissue found beneath the basal surface of the epidermis is randomly oriented.


collagen fibers
elastin fibers
hair follicles




connective tissue; loose and dense.


Mast cells
Mast cells


Loose Connective Tissue
Mesentery, total preparation
C=blood capillary
C
C
C
50 um
50 um

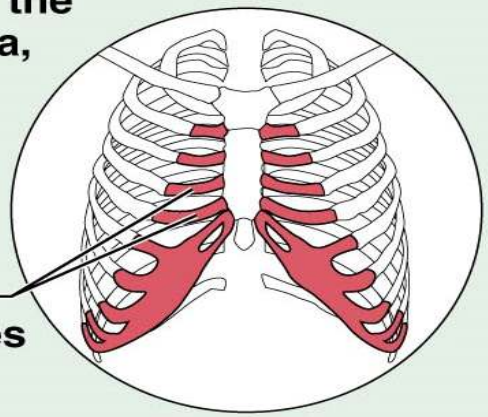
We will cover the following connective tissue in bone

(f) Cartilage: hyaline

Description: Amorphous but firm matrix; collagen fibers form an imperceptible network; chondroblasts produce the matrix and when mature (chondrocytes) lie in lacunae.

Function: Supports and reinforces; has resilient cushioning properties; resists compressive stress.

Location: Forms most of the embryonic skeleton; covers the ends of long bones in joint cavities; forms costal cartilages of the ribs; cartilages of the nose, trachea, and larynx.



Photomicrograph: Hyaline cartilage from the trachea (300×).

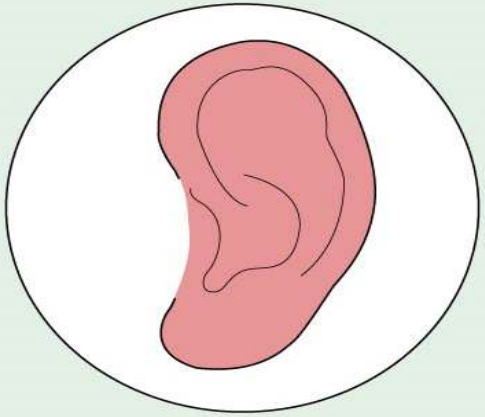
Figure 4.9f

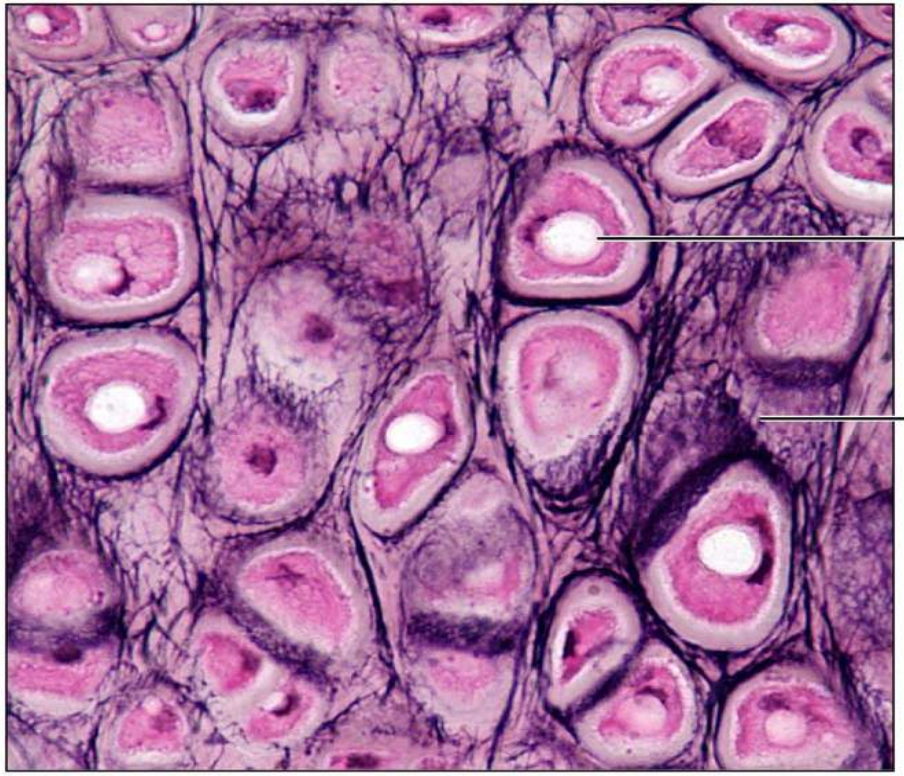
(g) Cartilage: elastic

Description: Similar to hyaline cartilage, but more elastic fibers in matrix.

Function: Maintains the shape of a structure while allowing great flexibility.

Location: Supports the external ear (pinna); epiglottis.





Photomicrograph: Elastic cartilage from the human ear pinna; forms the flexible skeleton of the ear (640×).

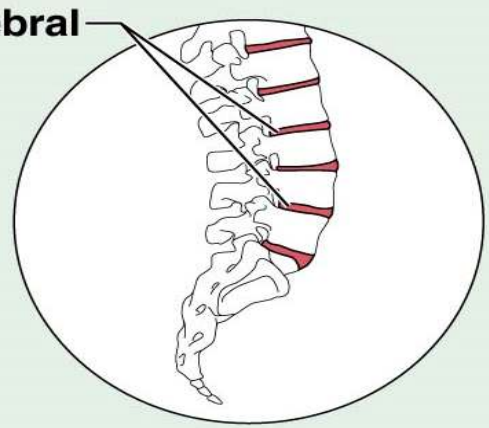
Figure 4.9g

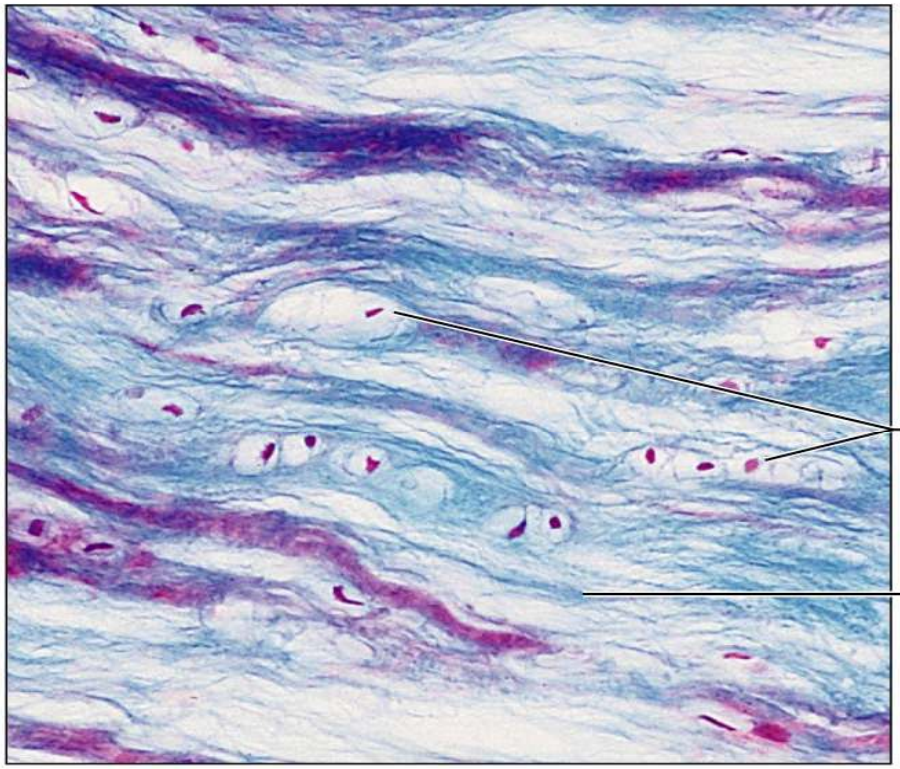
(h) Cartilage: fibrocartilage

Description: Matrix similar to but less firm than that in hyaline cartilage; thick collagen fibers predominate.

Function: Tensile strength with the ability to absorb compressive shock.

Location: Intervertebral discs; pubic symphysis; discs of knee joint.





Photomicrograph: Fibrocartilage of an intervertebral disc (200×). Special staining produced the blue color seen.

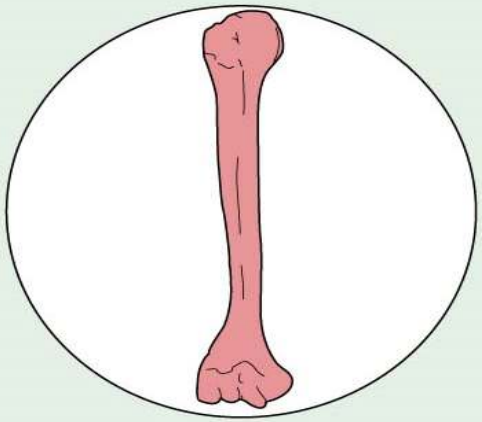
Figure 4.9h

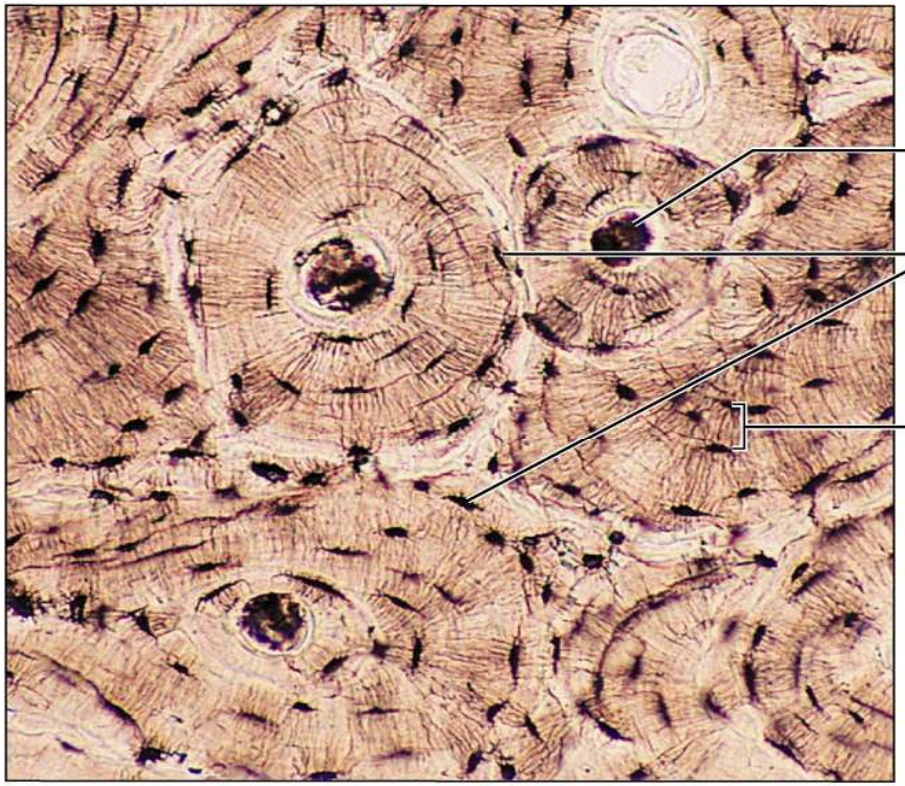
(i) Others: bone (osseous tissue)

Description: Hard, calcified matrix containing many collagen fibers; osteocytes lie in lacunae. Very well vascularized.

Function: Bone supports and protects (by enclosing); provides levers for the muscles to act on; stores calcium and other minerals and fat; marrow inside bones is the site for blood cell formation (hematopoiesis).

Location: Bones





Photomicrograph: Cross-sectional view of bone (70×).

Figure 4.9i

Healing process in resume

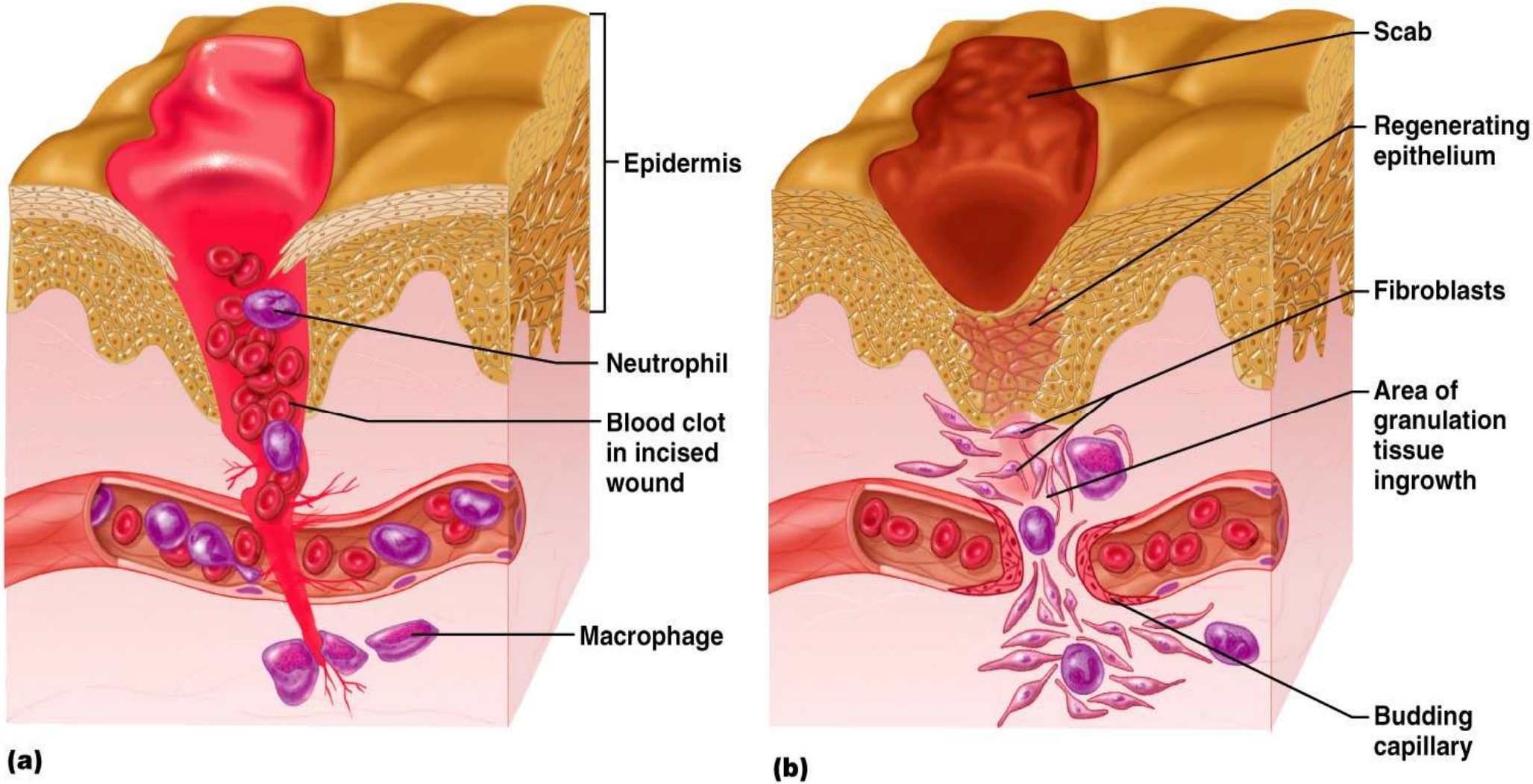
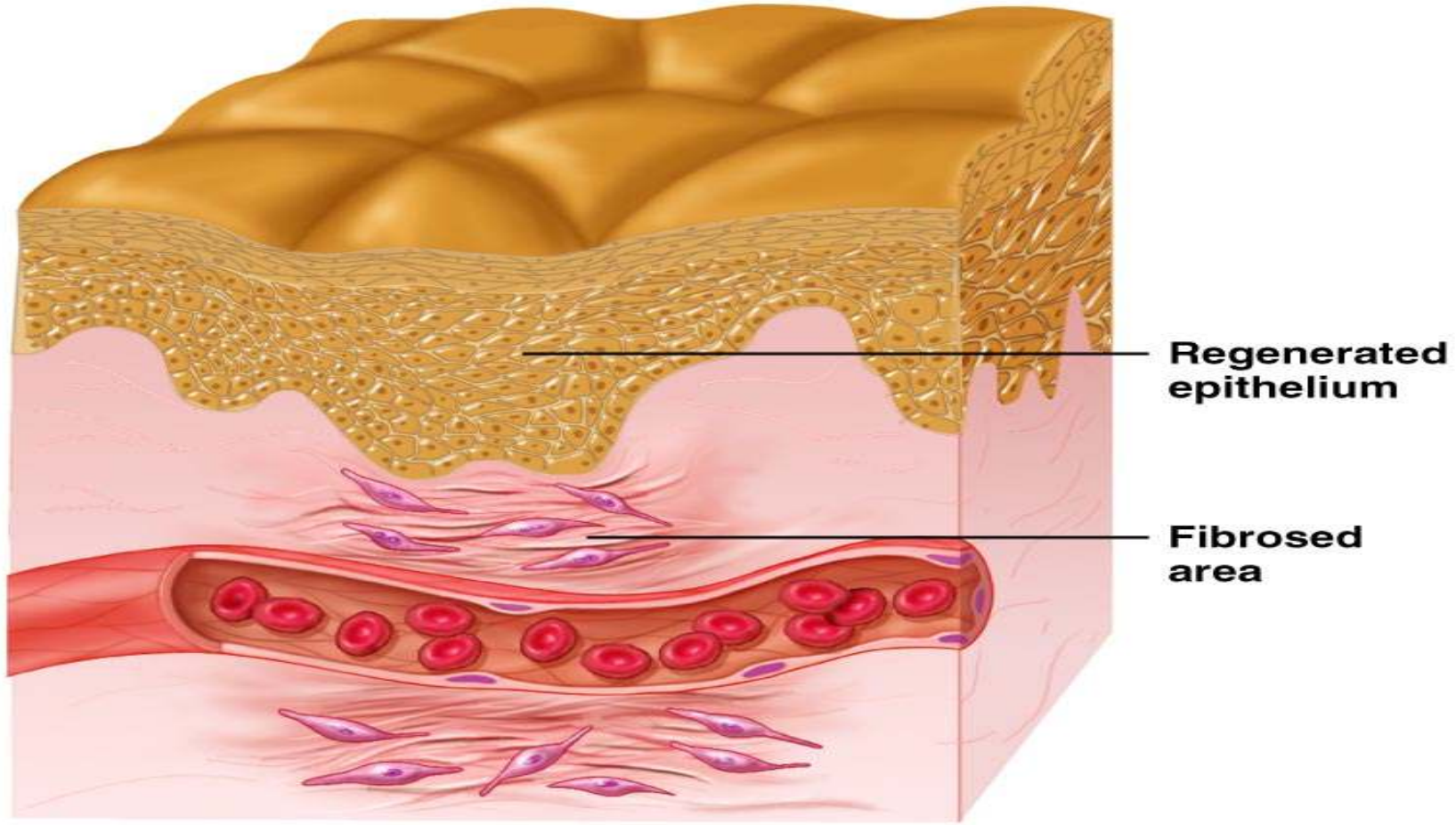


Figure 4.13a, b



(c)

Figure 4.13c

Some diseases

Connective Tissue Diseases

Disease	Autoantibody
Systemic Lupus Erythematosus	Anti-dsDNA, Anti-SM
Rheumatoid Arthritis	RF, Anti-RA33
Sjogrens Syndrome	Anti-Ro(SS-A), Anti-La(SS-B)
Systemic Sclerosis	Anti-Scl-70, Anti-centromere
Polymyositis/Dermatomyositis	Anti-Jo-1
Mixed Connective Tissue Disease	Anti-U1-RNP
Wegener's Granulomatosus	c-ANCA

Systemic Lupus Erythematosus

- Discoid Lupus: Cutaneous manifestations
- Scar upon healing

Rheumatoid Arthritis

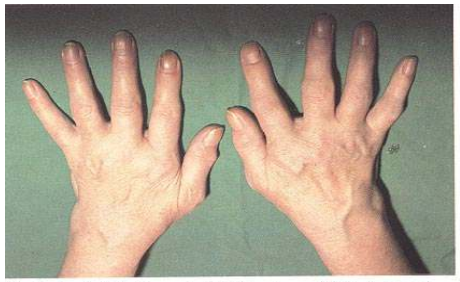


Fig. 3 Early RA. Synovial thickening of PIP joints and wrists. Deformity minimal.

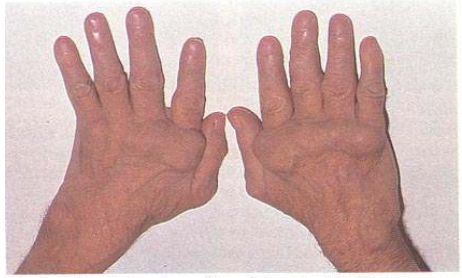
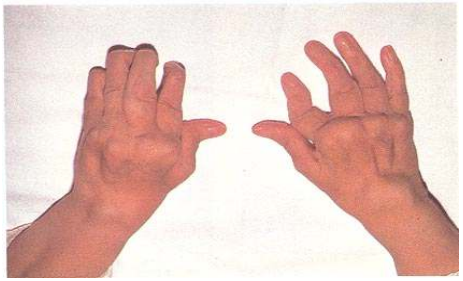


Fig. 4 RA at later stage. Considerable MCP joint thickening, subluxation and ulnar deviation.



Sjogren Syndrome

Scleroderma

COLLAGEN RELATED DISORDERS

- **Ehlers-Danlos Syndromes**:
  - Hyperextensibility of
  - skin and joints.

- **Osteogenesis Imperfecta**

- **Recessive Dystrophic Epidermolysis Bullosa:**
- Too much collagenase.

- **Scurvy**:
  - Vitamin-C deficiency leads to malfunctioning
  - prolyl hydroxylase.

Keloid

https://www.pearson.com/channels/anp/learn/bruce/tissues-and-histology/connective-tissue-proper-loose-connective-tissue