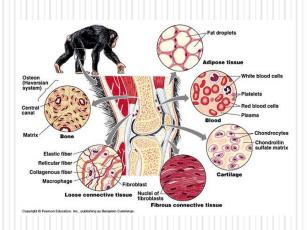
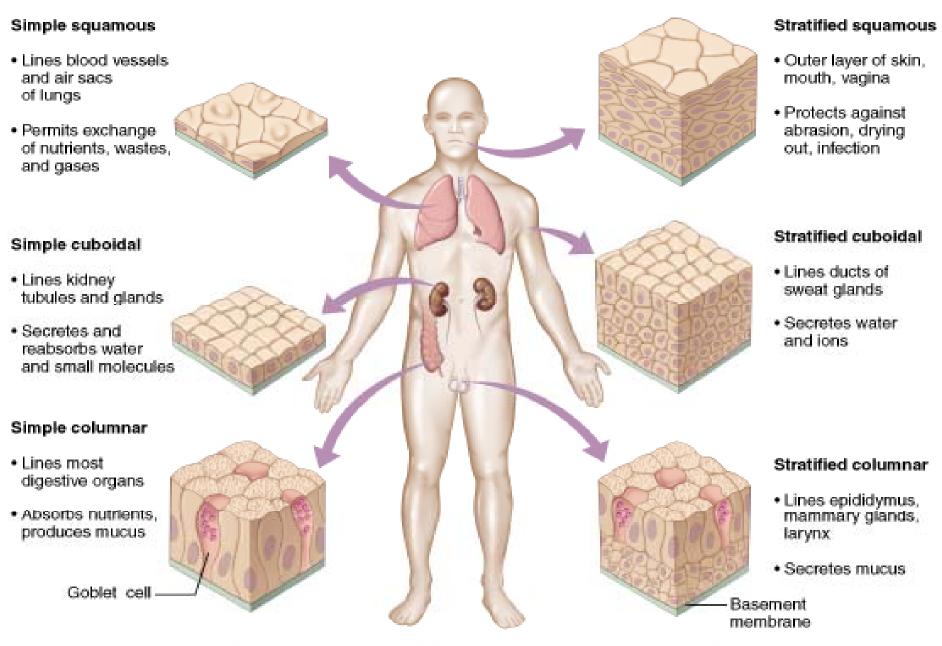
CONNECTIVE TISSUES

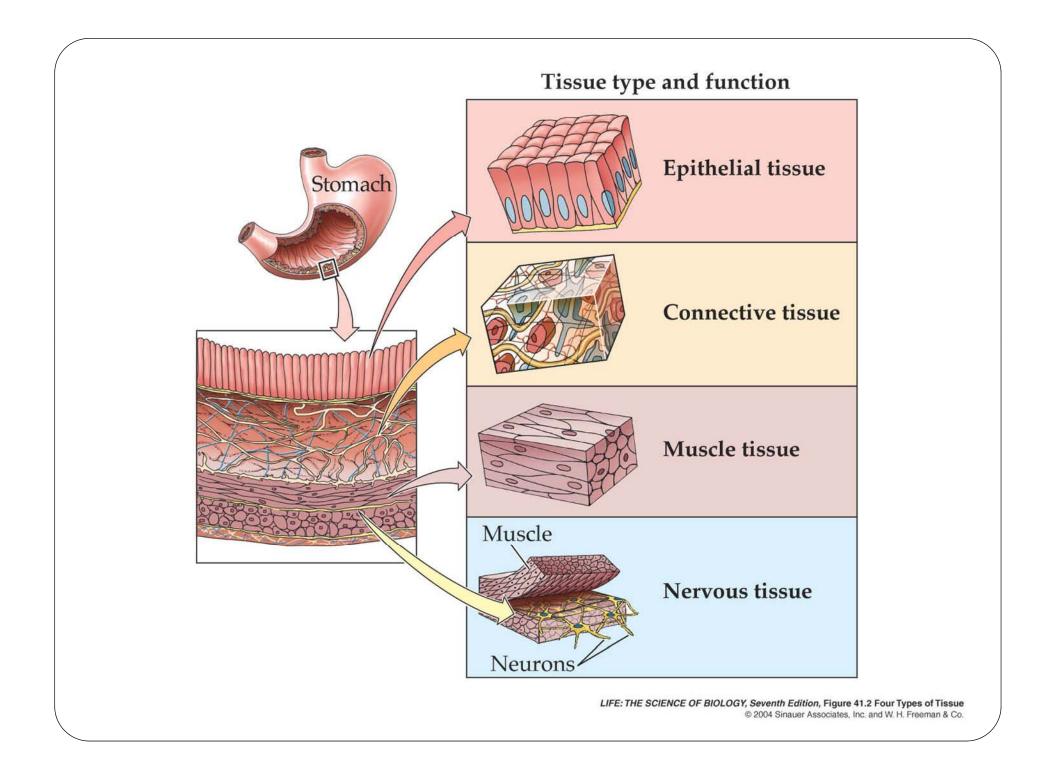


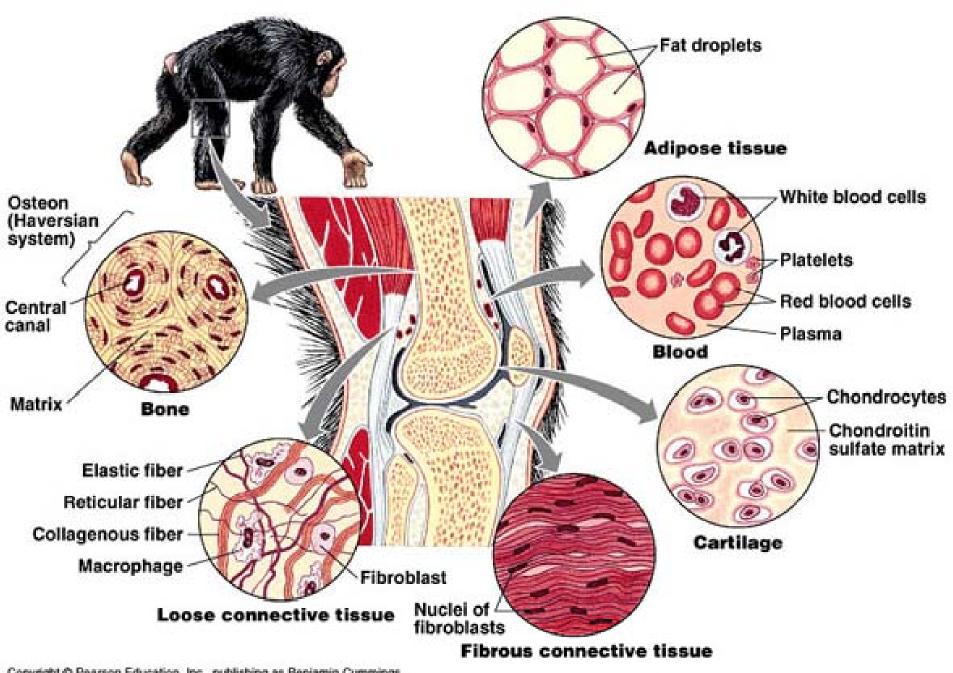




(a) Most epithelial tissues line or cover surfaces or body cavities

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Supporting Connective Tissues

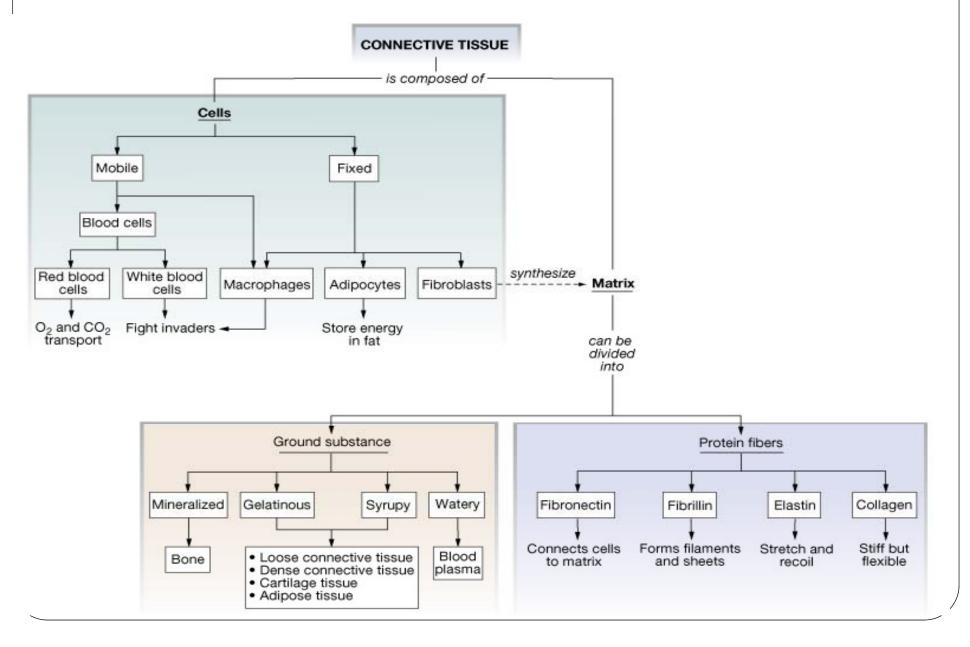


Table 4.8	Connective Tissue Proper			
Туре	Structure	Function	Location	
Loose Connective Tissue	Relatively fewer cells and fibers than in dense connective tissue; fibers are loosely arranged	Cushioning of organs; packing around organs	Surrounding vessels; in spleen and liver; in subcutaneous layer	
Areolar (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	

CONNECTIVE TISSUE

Connective tissues are broadly classified in	Fluid connective tissue types, of which there are only two, are important in transport and body defense	
Connective Tissue Category	Tissue Types	
1. Fluid Connective Tissues	Blood and Lympl	1
2. Connective Tissue Proper	Loose and Dense Tissues	Connective
3. Supportive Connective Tissues	Cartilage and Bo	ne

CONNECTIVE TISSUE

•Connective tissue is responsible for providing structural support for the tissues and organs of the body.

• It is the most diverse tissue.

•Connective Tissue (CT) is found throughout the body.

• In fact the whole framework of the skeleton and the different specialized connective tissues from the crown of the head to the toes determine the form of the body and act as an entity.

•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 •fibers •extracellular matrix.

Structural Elements of Connective Tissue

- Ground substance unstructured material that fills the space between cells
- Fibers collagen, elastic, or reticular
- Cells fibroblasts, chondroblasts, osteoblasts, and hematopoietic stem cells

Fibroblasts are the cells responsible for the production of connective tissue

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

Functions of Connective Tissue

- Binding and support .Connection of body tissues
- Protection
- Insulation, Storage of energy
- Transportation
- Providing structural framework for the body

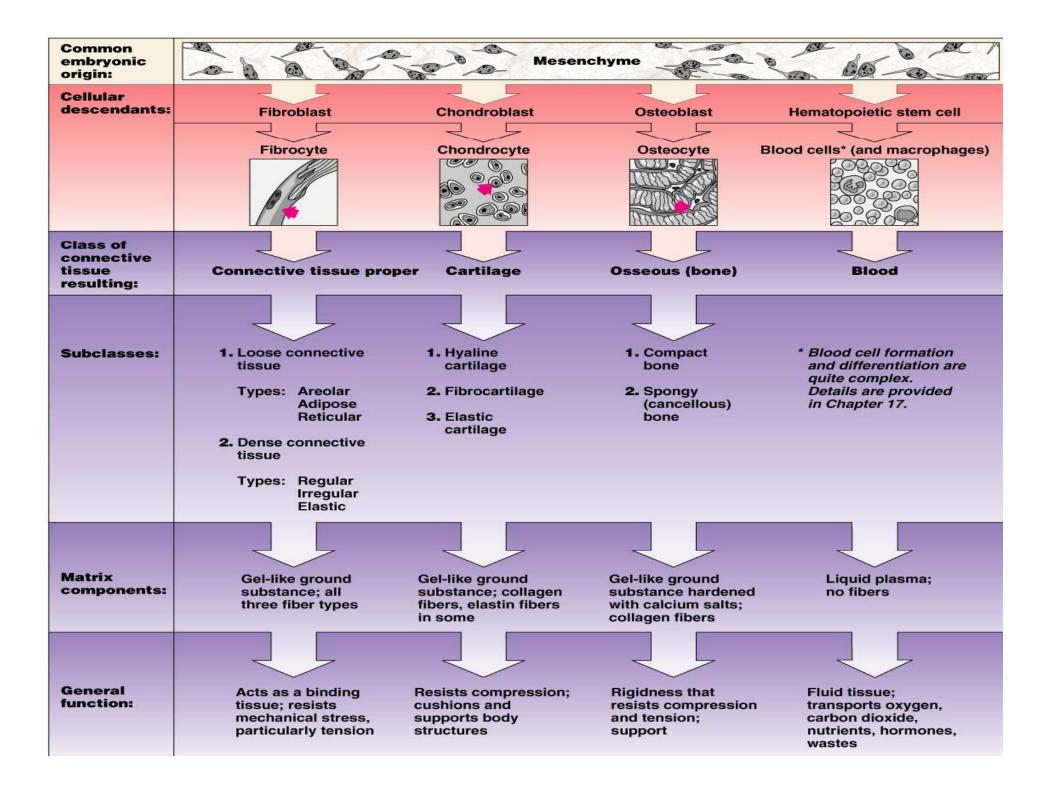
The **extracellular matrix** is composed of :

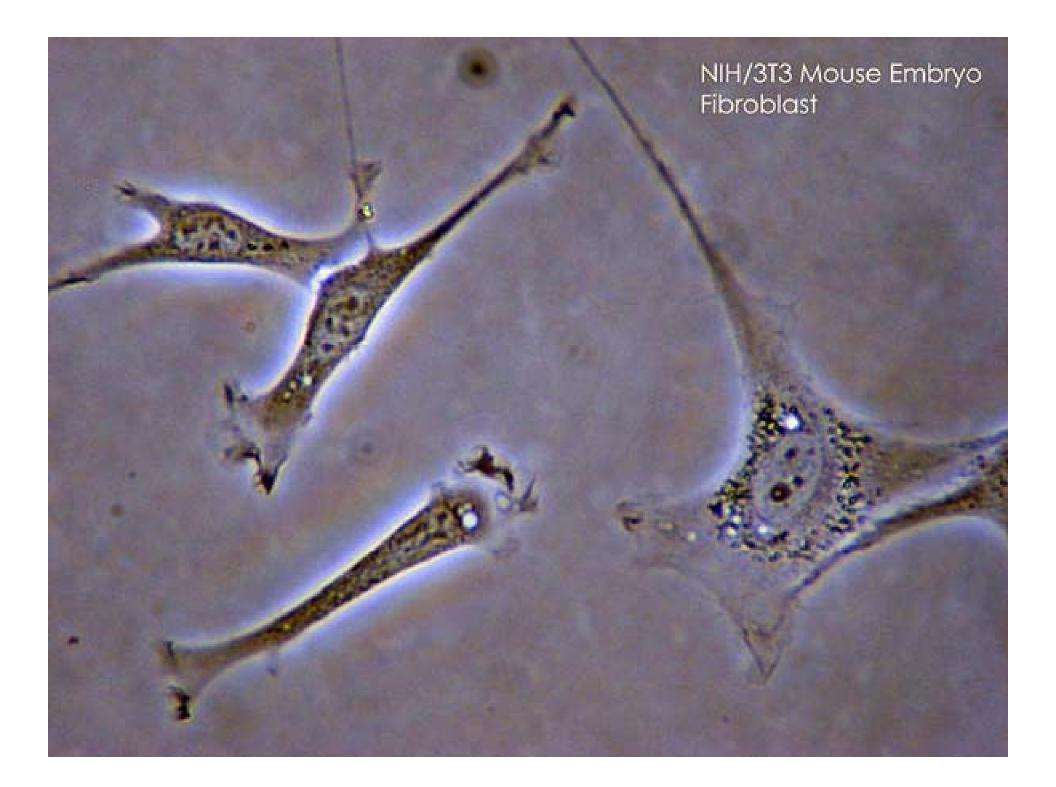
•protein fibers (collagen fibers, reticular fibers, elastic fibers)
•amorphous ground substance
•tissue fluid (not preserved in histological preparations).

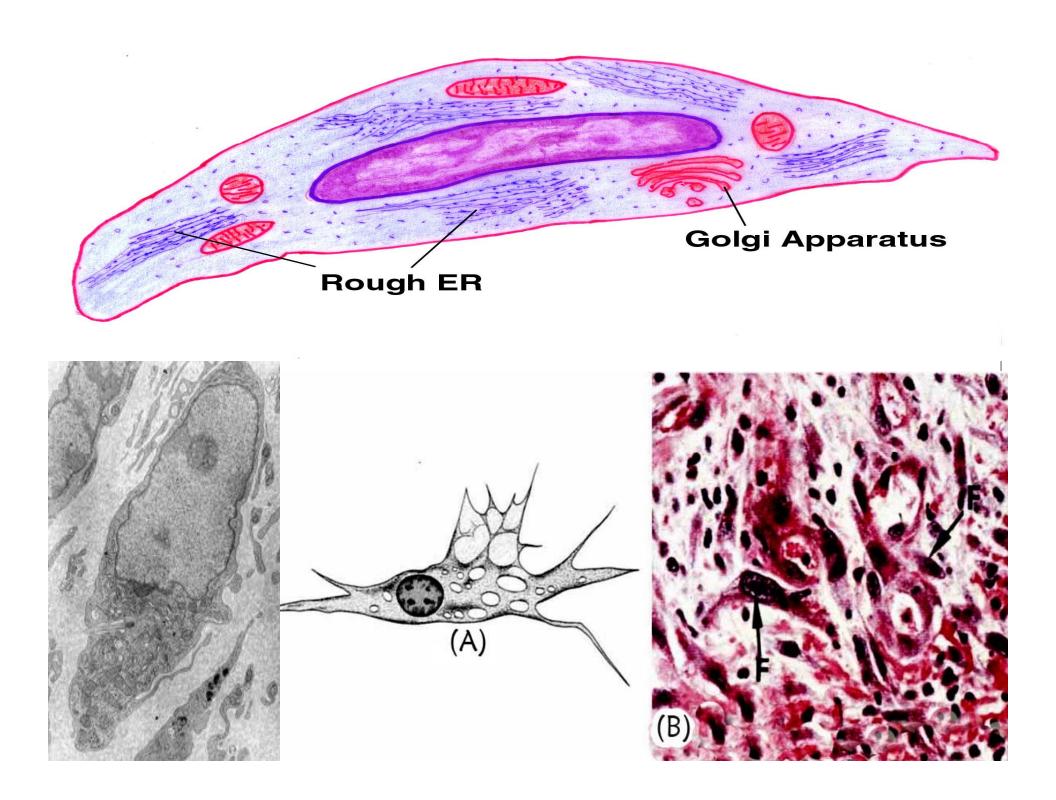
•The amount of tissue fluid is fairly constant and there is an equilibrium between the water entering and leaving the intercellular substance of the connective tissue.

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

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





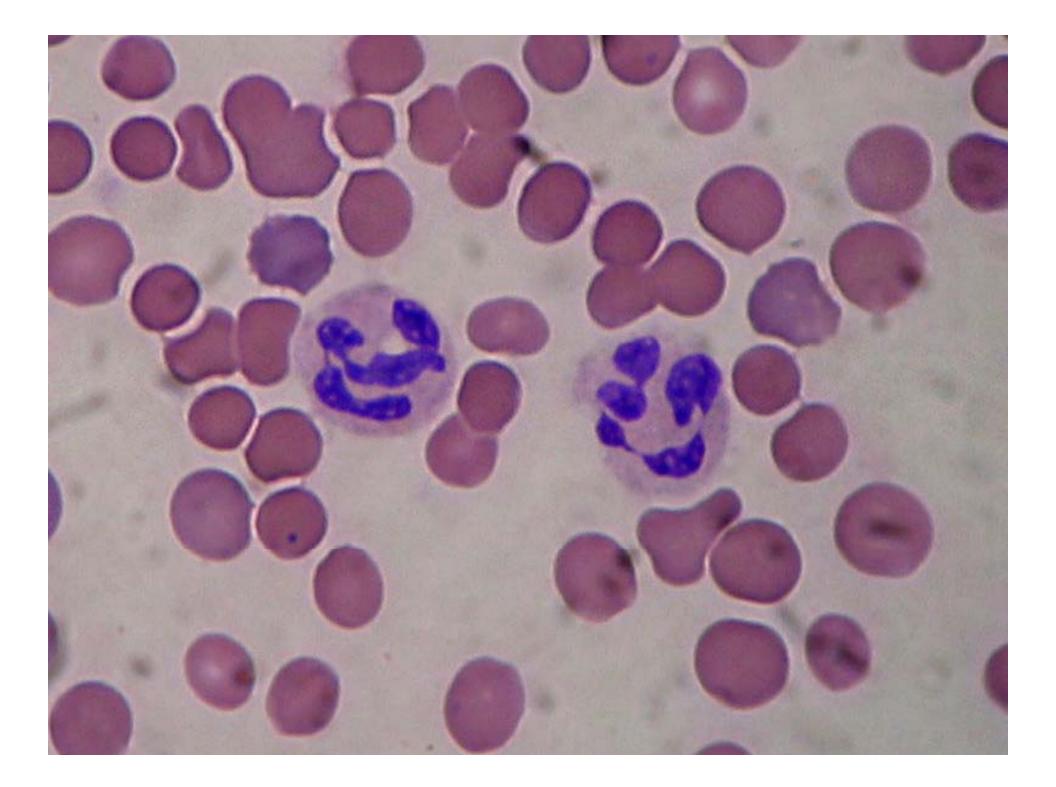


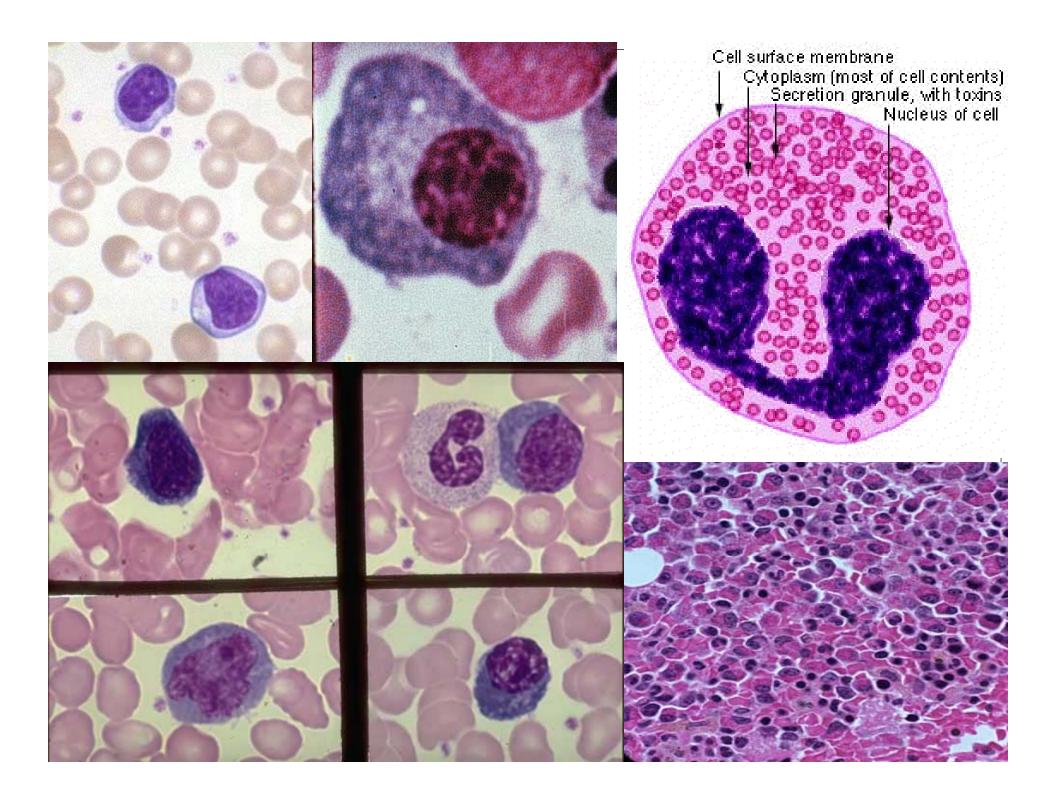
Leucocytes in situ

Neutrophils : rare; multilobed nuclei poorly stained cytoplasm
Eosinophils : abundant in loose ct; bilobed nuclei strongly eosinophilic cytoplasmic granules

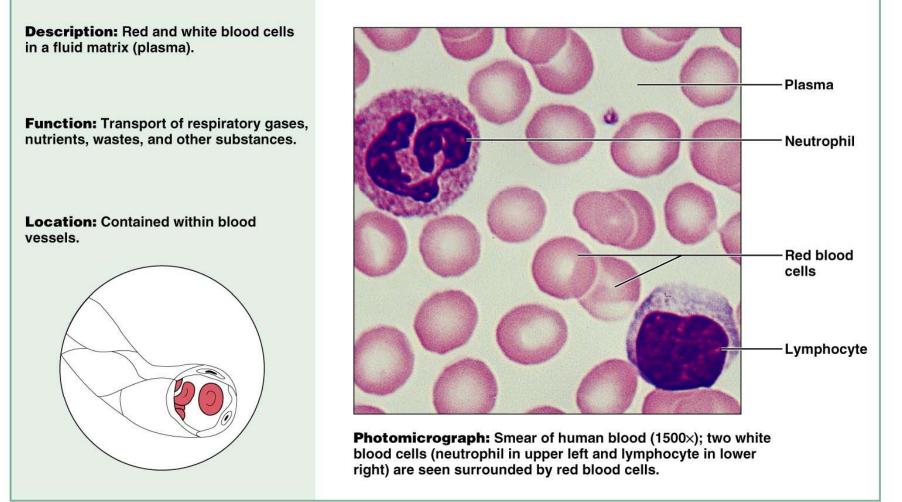
•Basophils : resemble mast cells; poorly stained in H&E

Macrophages

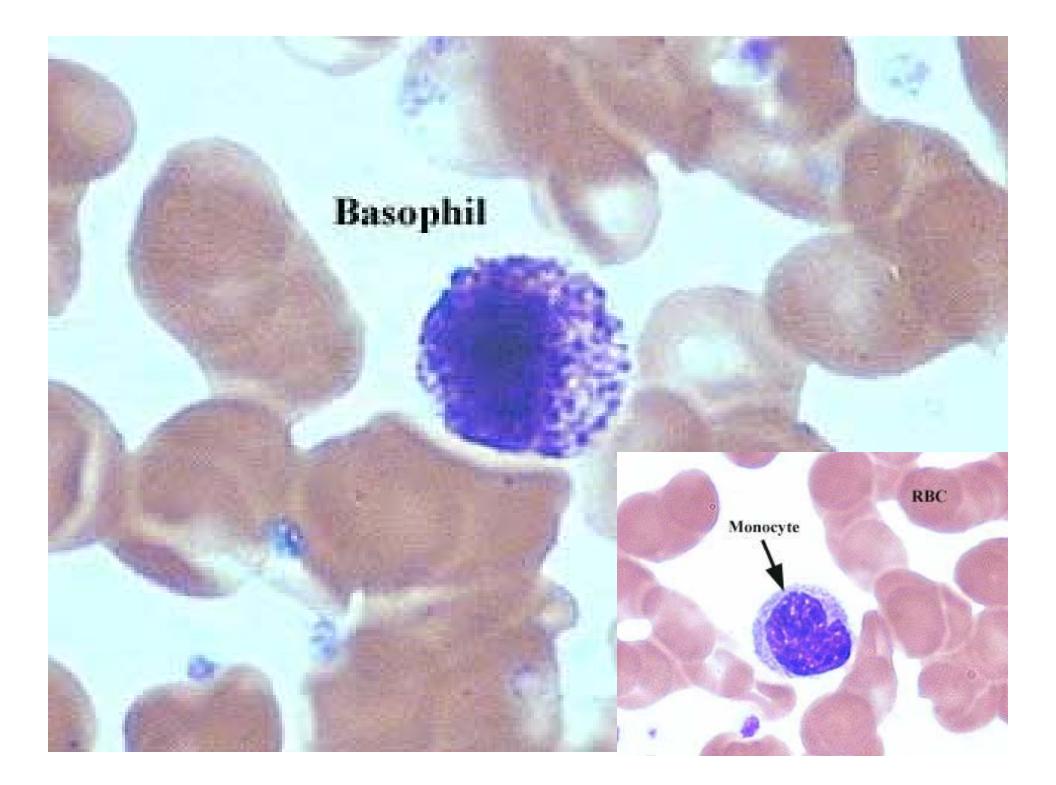




(j) Others: blood



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Macrophages

•Macrophages show pronounced phagocytotic activity.

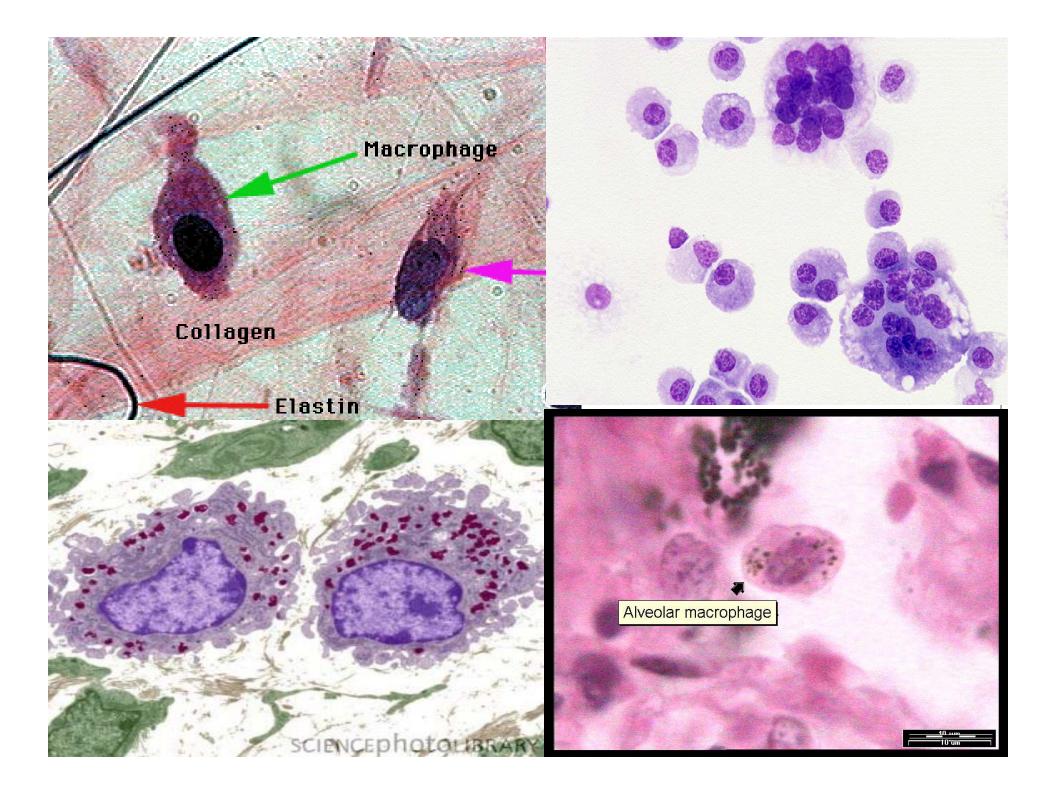
•Macrophages originate from monocytes (from precursor cells in bone marrow), which migrate to connective tissue and differentiate into tissue macrophages.

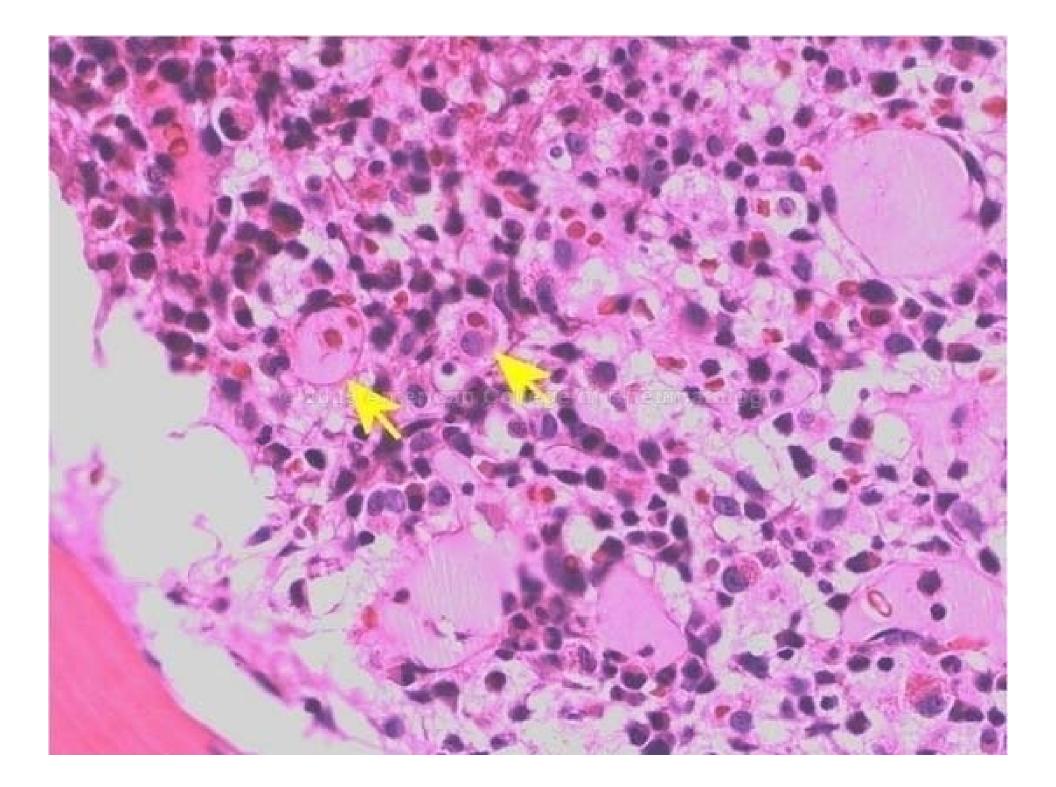
•Today the various macrophages of the body are grouped in a common system called the **Mononuclear Phagocyte System** (MPS).

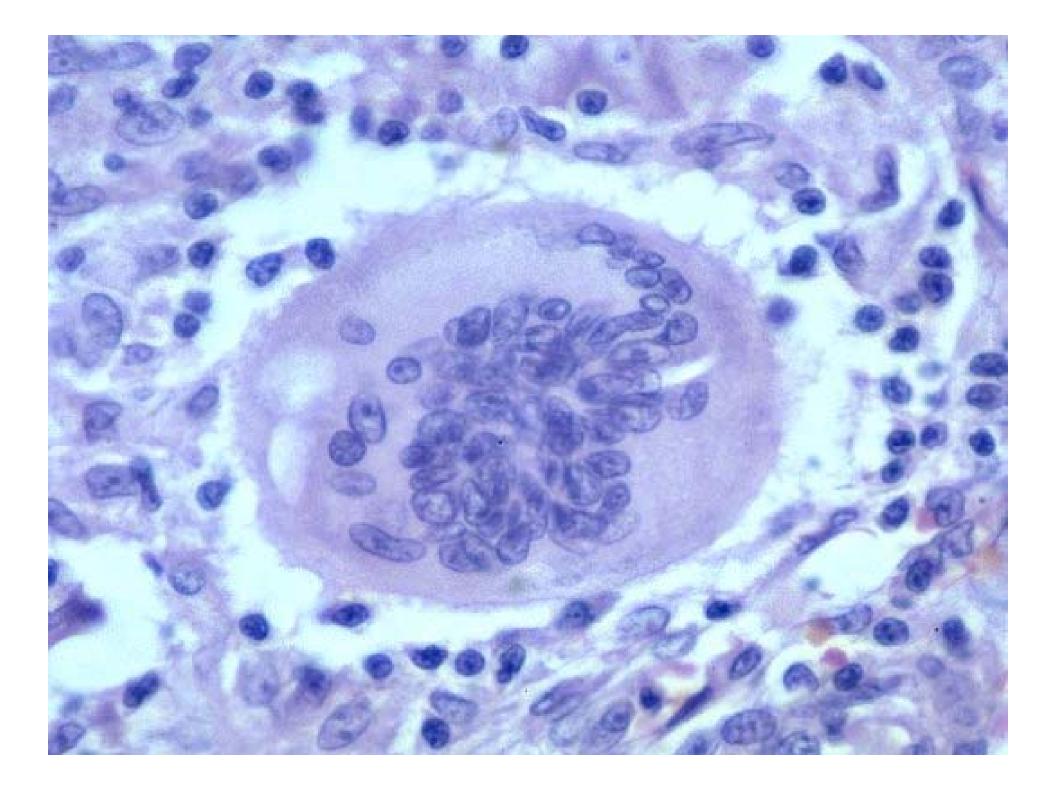
• Today a wide range of macrophages are included in the MPS and include : **Kupffer** cells of the liver, alveolar macrophages of the lung, osteoclasts, microglia etc.

•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.







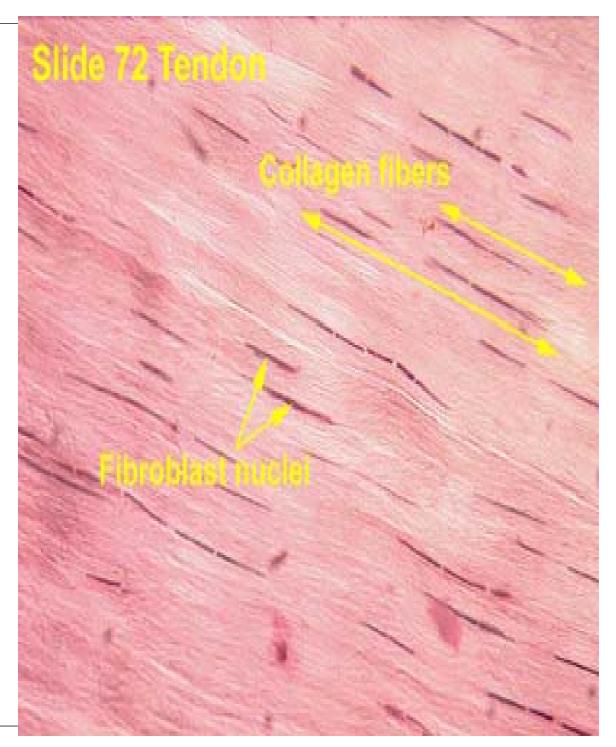
CONNECTIVE TISSUE FIBERS

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

Types of fibers:

Tissue	Components	Location
Collagenous fibers	Alpha polypeptide chains	 •tendon, •ligament, •skin, •cornea, •cartilage, •bone, •blood vessels, •gut, •intervertebral disc.
Elastic fibers	elastic microfibrill & elastin	•extracellular matrix
Reticular fibers	_	•liver,•bone marrow,• lymphatic organs

Collagen fibers



<u>Collagen Types</u> :	
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)

So far, 28 types of collagen have been identified and described. The five most common types are:

•Collagen I: skin, tendon, vascular ligature, organs, bone (main component of the organic part of bone)

•Collagen II: cartilage (main component of cartilage)

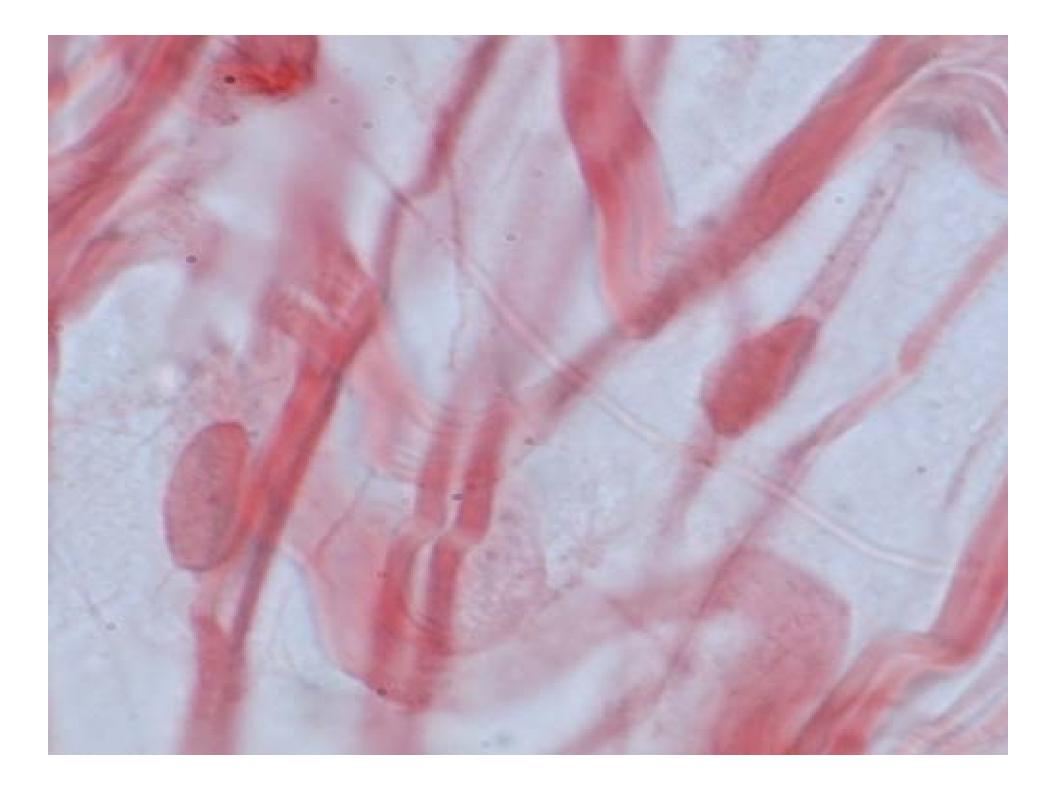
•Collagen III: reticulate (main component of reticular fibers), commonly found alongside type I.

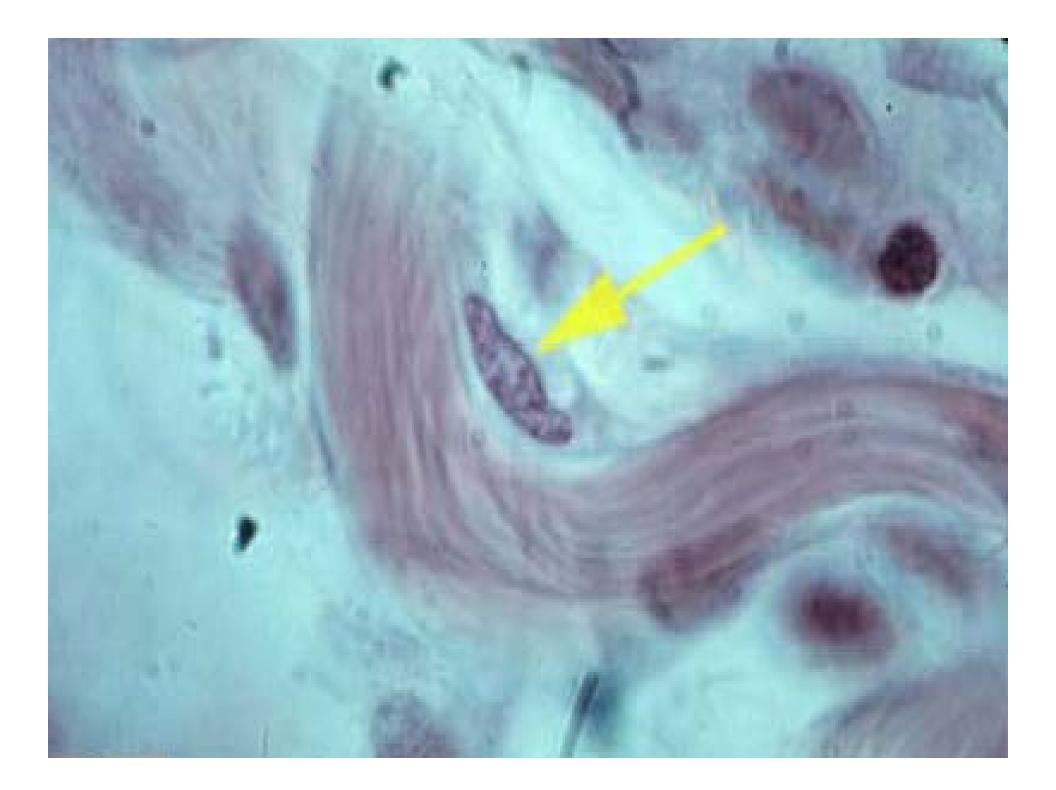
•Collagen IV: forms bases of cell basement membrane

•Collagen V: cell surfaces, hair and placenta

Extracellular matrix comprised of proteins

Collagen (25% total body protein)Elastin (wrinkles with aging)





Muscle-Tendon Junction van Gieson

collagen fibres

skeletal muscle

fibrocyte nuclei

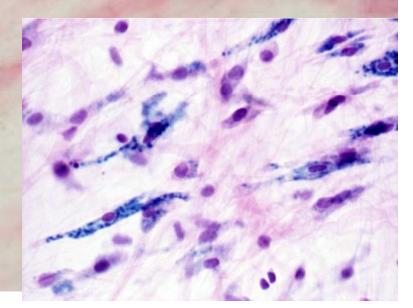
Non-lactating Breast H&E

collagen fibres

connective tissue cell nuclei blood vessels



fibroblast



COLLAGEN RELATED DISORDERS •Ehlers-Danlos Syndromes: Hyperextensibility of •skin and joints.





•Osteogenesis Imperfecta



•Scurvy:Vitamin-C deficiency leads to malfunctioning •prolyl hydroxylase



Recessive Dystrophic Epidermolysis Bullosa:

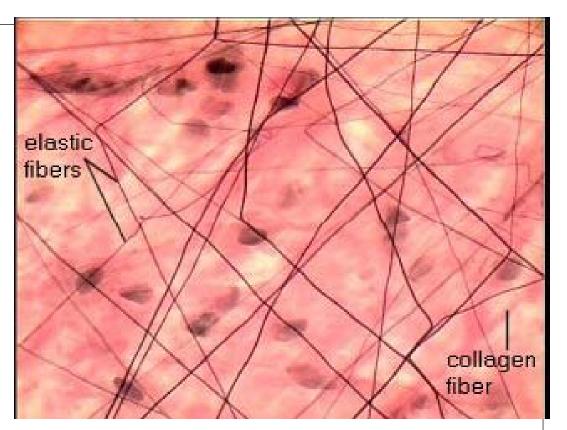
Too much collagenase



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Elastic fibers



Elastic fibers (or **yellow fibers**) are bundles of proteins (elastin) found in <u>extracellular matrix</u>

Produced by fibroblasts and smooth muscle cells in arteries

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:.

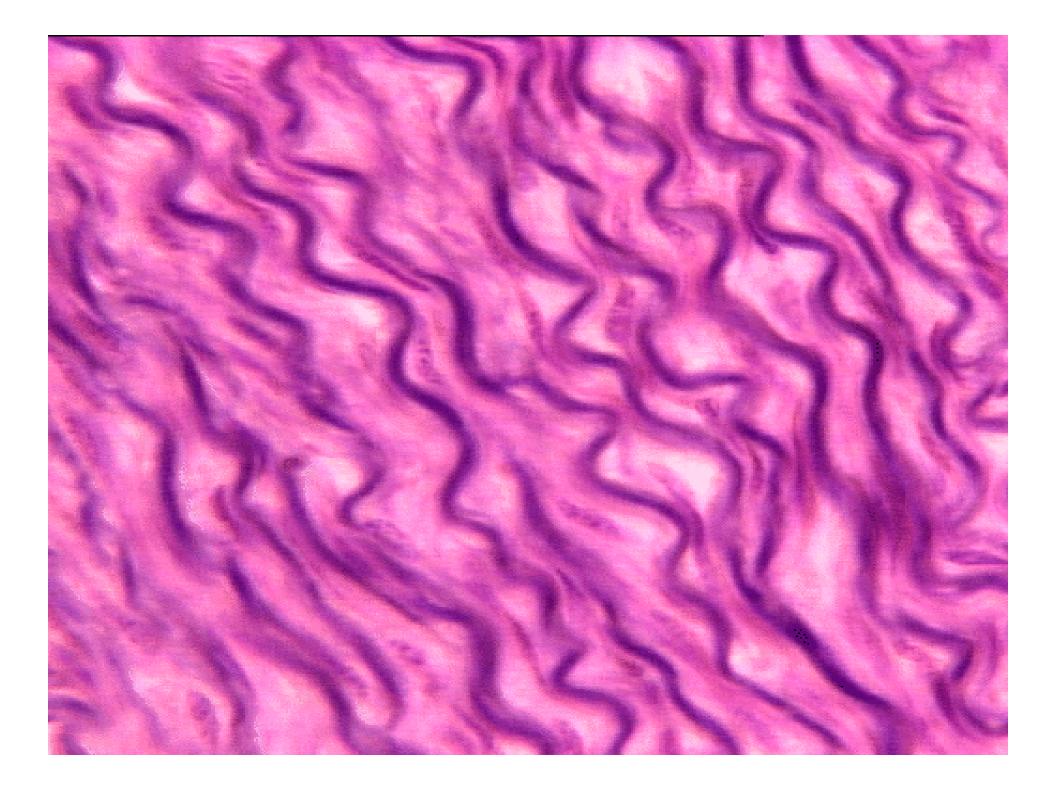
Elaunin and oxytalan

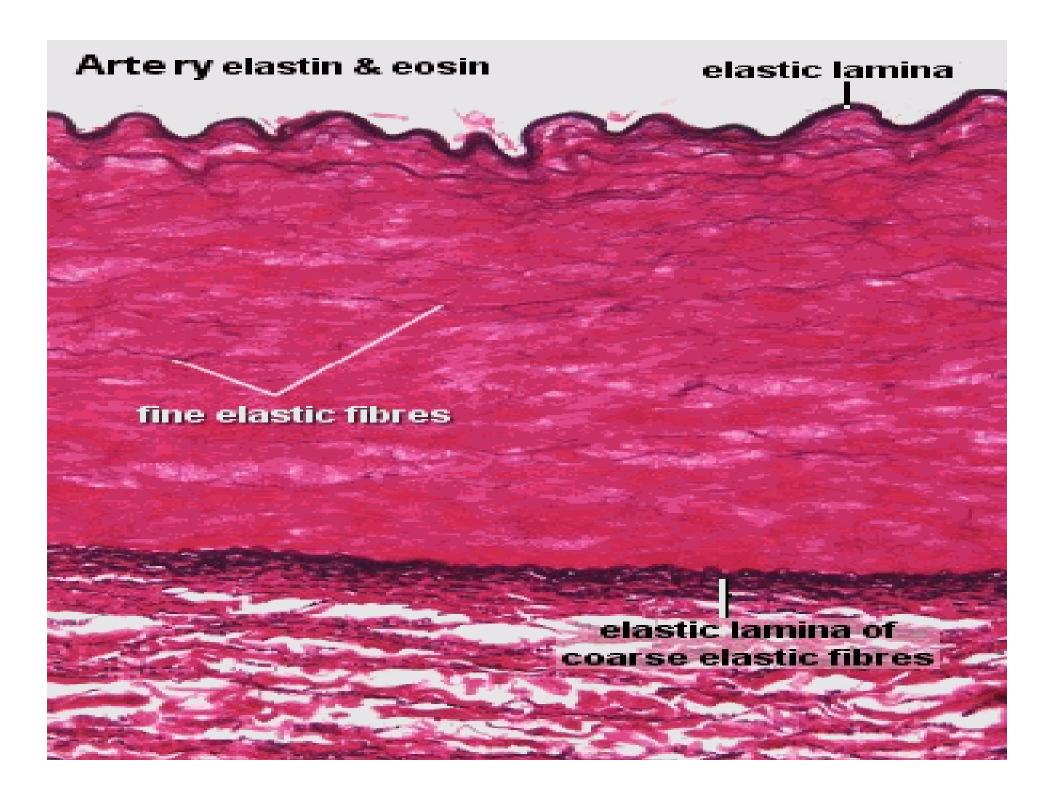
•AGING: Wrinkles occur as microfibrillar structure is lost
•Emphysema: Loss of elasticity in lung. Rare form = congenital malfunction of elastase in lung.

Elastic fibers are found in

- The skin,
- Lungs,
- •Arteries,
- •Veins,
- •Connective tissue proper,
- Elastic cartilage,
- Periodontal ligament,
- •Fetal tissue







Artery elastin & eosin

fine elastic fibres

coarse elastic fibres

Reticular fibers = reticulin

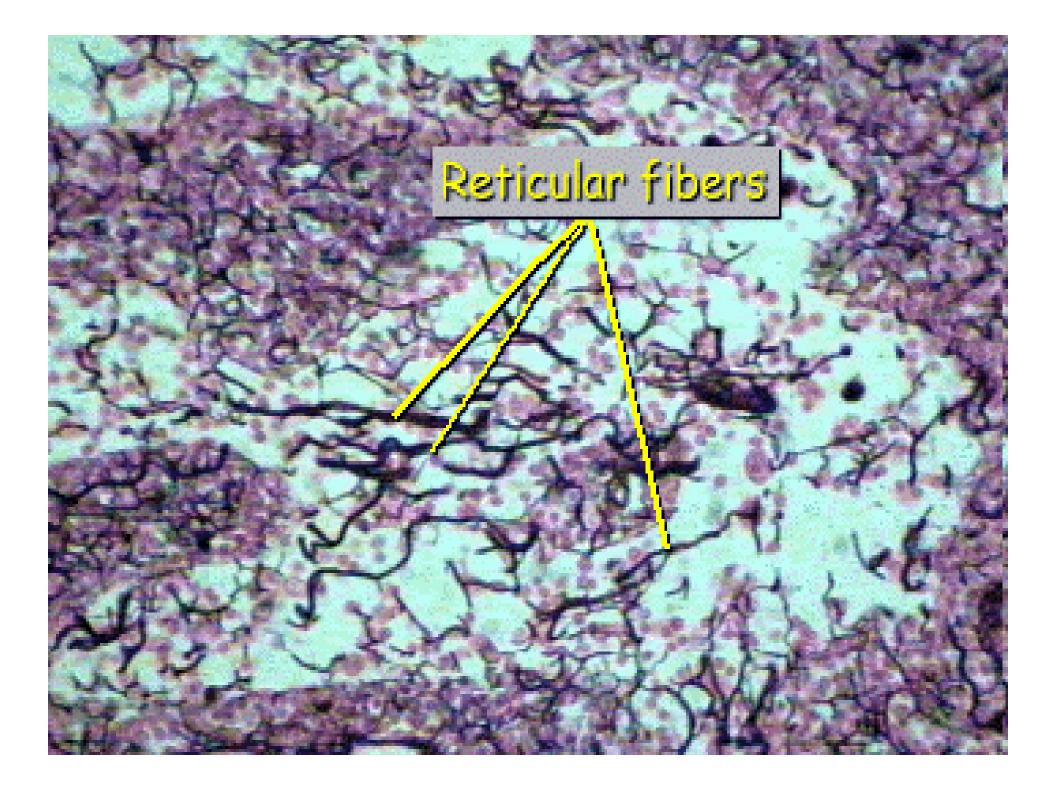
Composed of type III collagen.

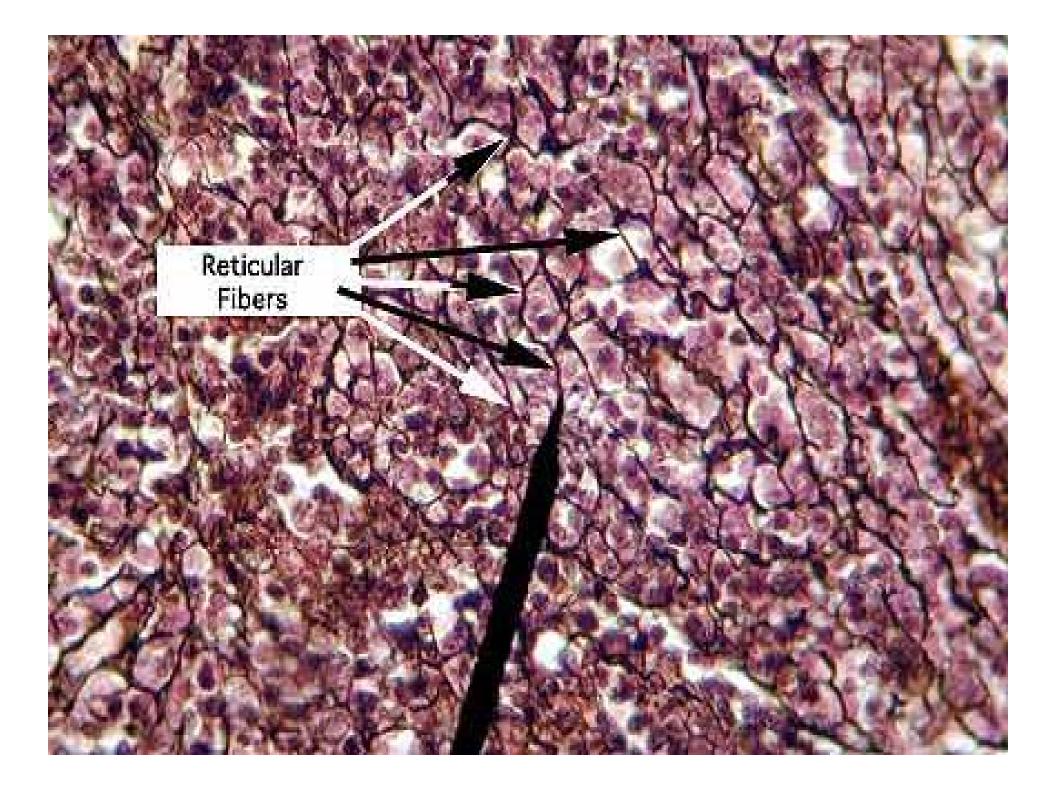
Reticular fibers crosslink to form a fine meshwork (reticulin).

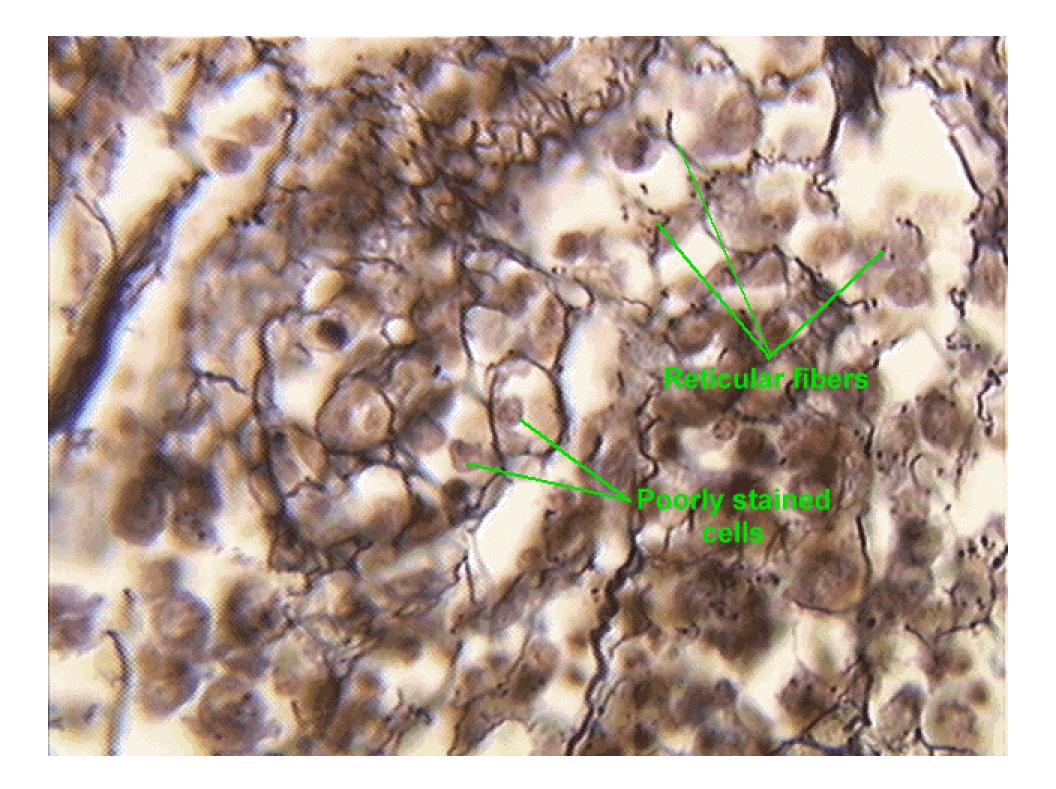
This network acts as a supporting mesh in soft tissues such as

- liver,
- bone marrow,

•and the tissues and organs of the lymphatic system [spleen, lymph nodes]







reticular fibers

reticular cell

lymphocytes

silver staining for reticular fibers

<u>Types</u>

- <u>Loose CT</u>:
 - biological packing material;
 - supports epithelia lining gut,
 - respiratory & urinary tracts, etc.;
 - open = areolar.

<u>Dense CT</u>: physical support,

• <u>regular</u>: ligaments, tendons and caps

irregular: dermis

- <u>Adipose tissue</u> (adipocytes) Brown: multilocular White: unilocular
- <u>Cartilage</u>
- Hyaline Elastic Fibroelastic

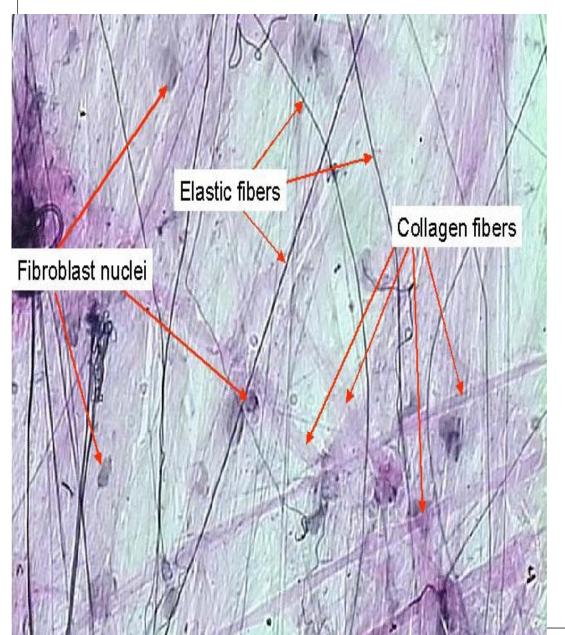
• <u>Bone</u>

CLASSIFICATION OF CONNECTIVE TISSUE

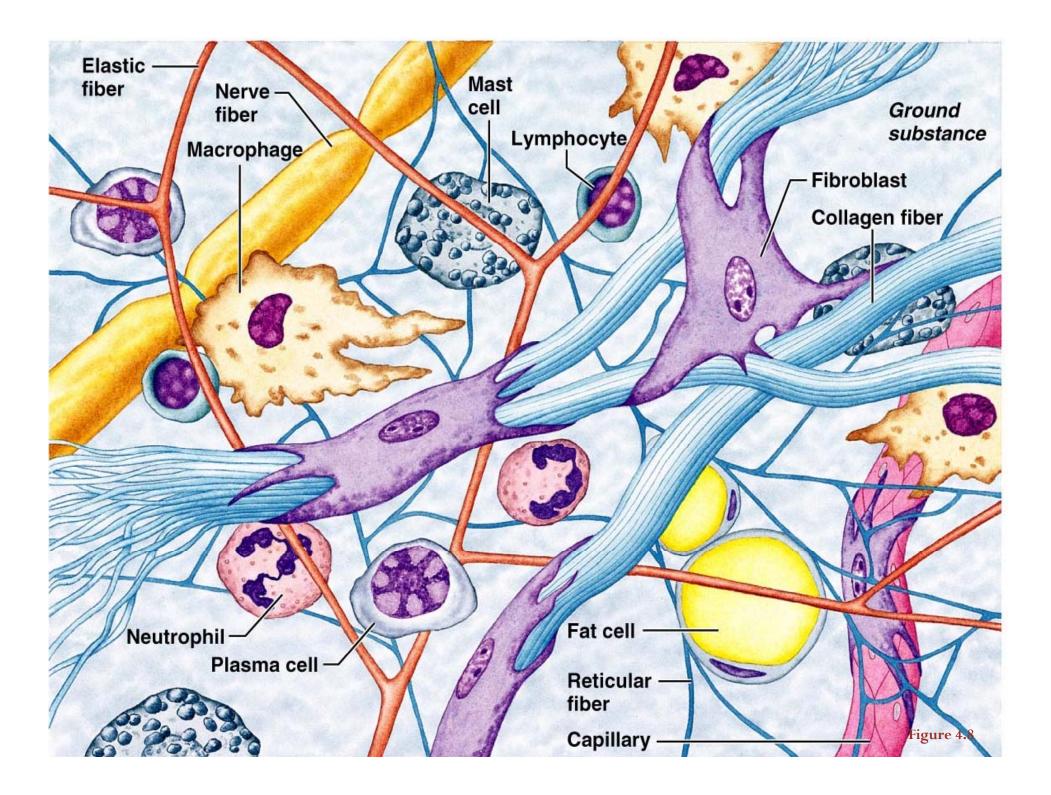
The two main categories of connective tissue are:

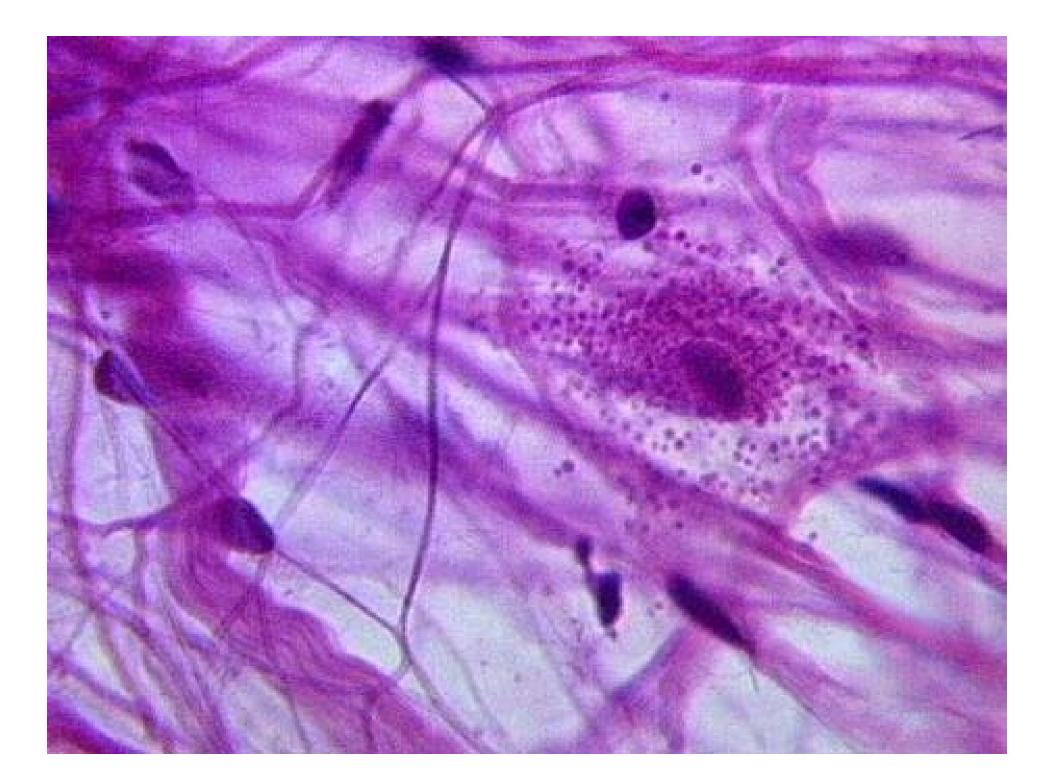
Loose Connective TissueDense Connective Tissue

Connective Tissue Proper: Loose



- Reticular connective tissue
 - Loose ground substance with reticular fibers
 - Reticular cells lie in a fiber network
 - Forms a soft internal skeleton, or stroma, that supports other cell types
 - Found in <u>lymph nodes</u>, <u>bone marrow</u>, and the <u>spleen</u>





Loose Connective Tissue

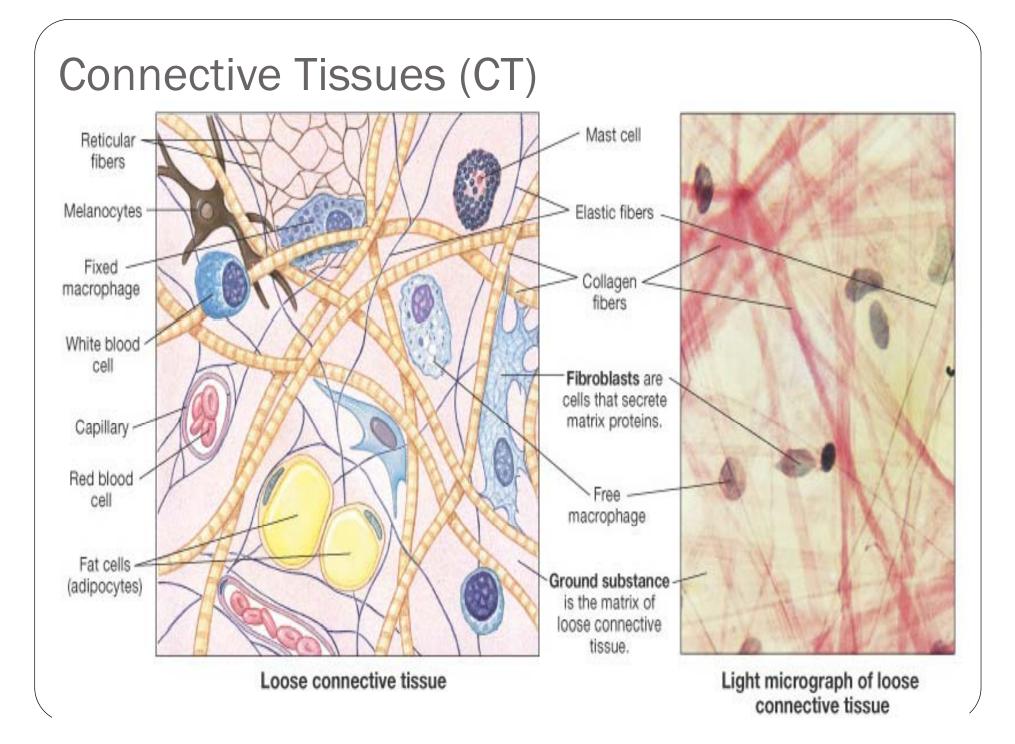
Loose connective tissue (areolar tissue) is the more common type.

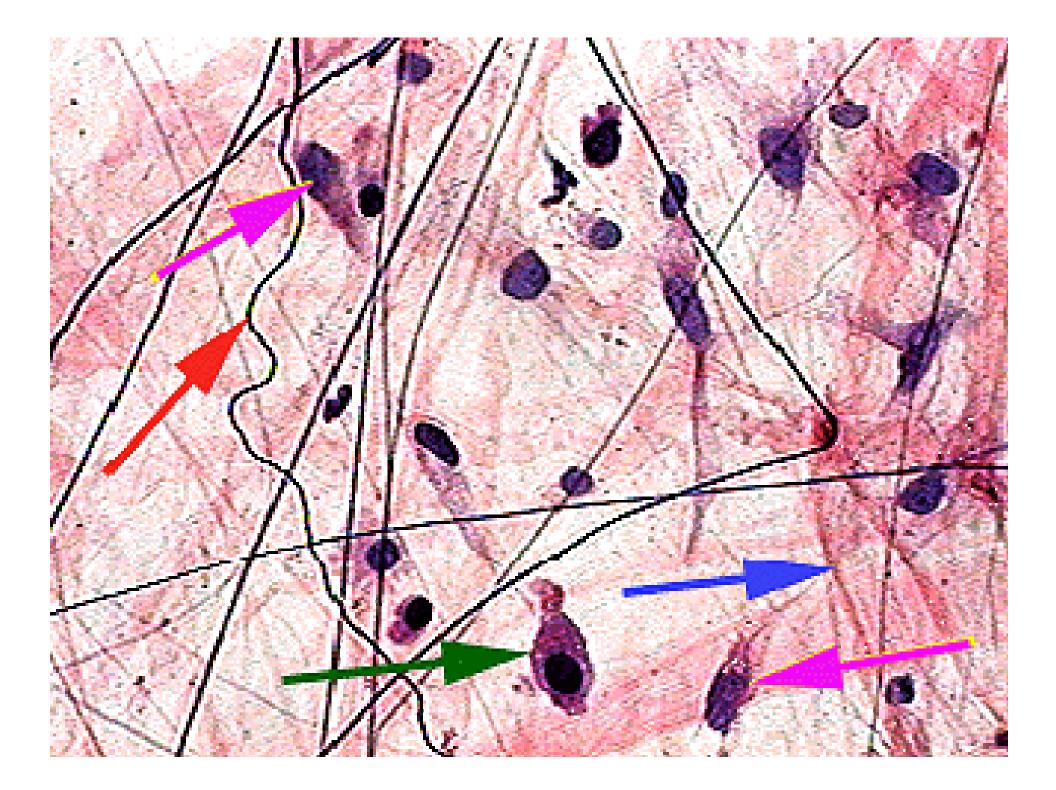
It fills the spaces between

•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

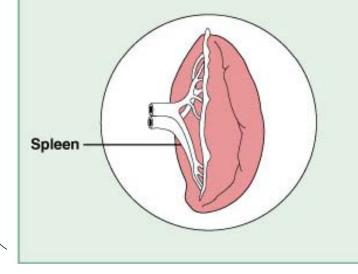
Connective Tissue Proper: Loose

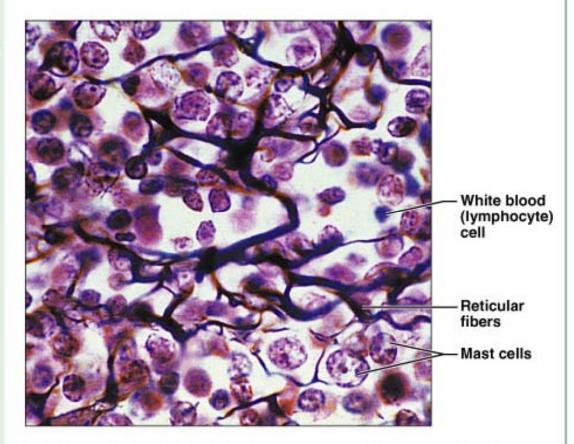
(d) Connective tissue proper: loose connective tissue, reticular

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 co the spleen (350×).

Dense Connective Tissue

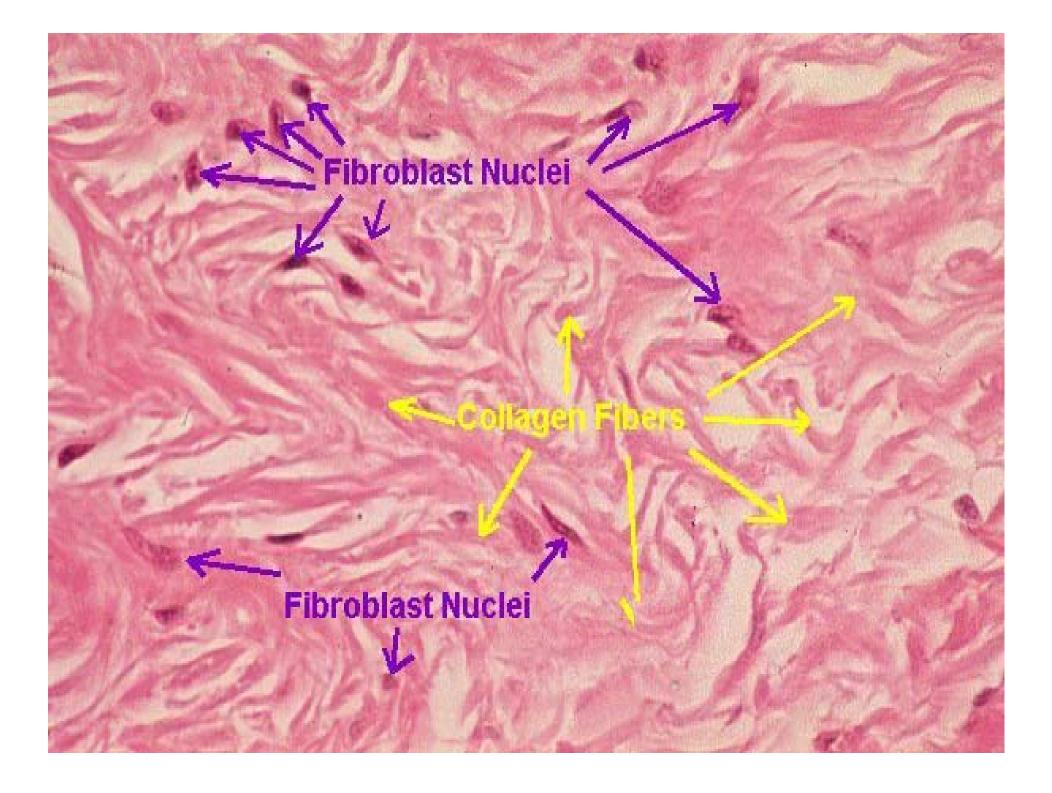
Dense connective tissue is divided into two sub-categories: •dense irregular connective tissue •dense regular connective tissue

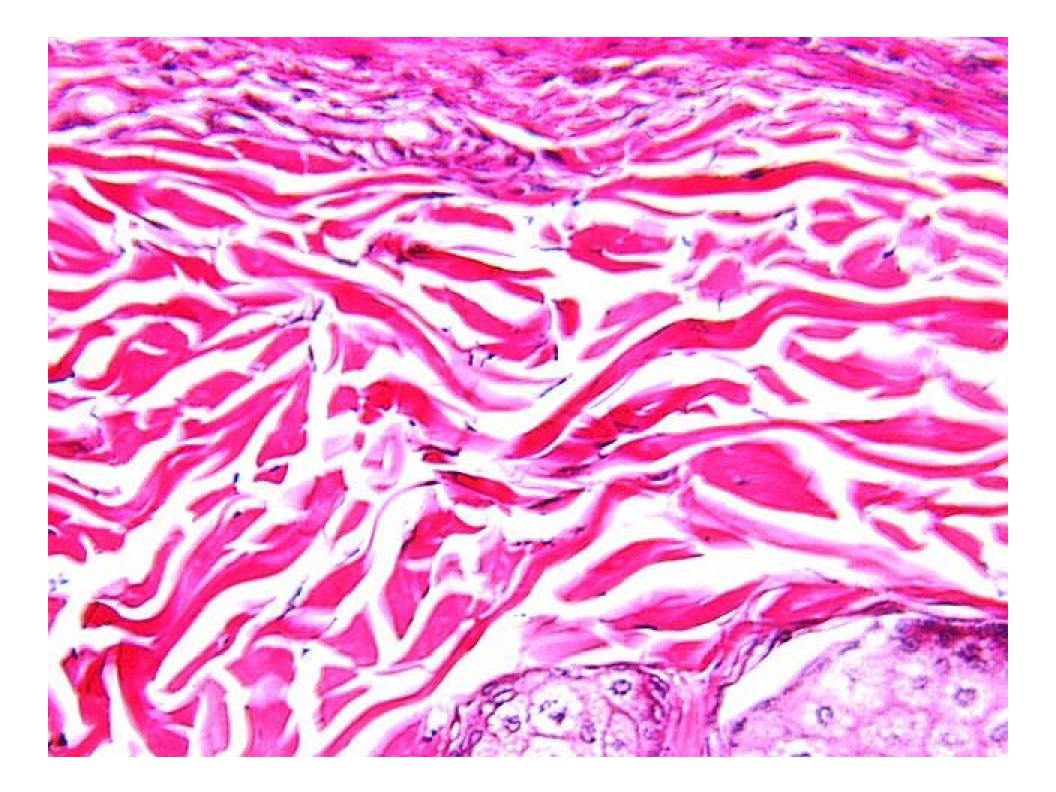
<u>Dense connective tissue</u> contains relatively few cells with much greater numbers of collagen fibers.

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

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

Dense irregular connective tissue

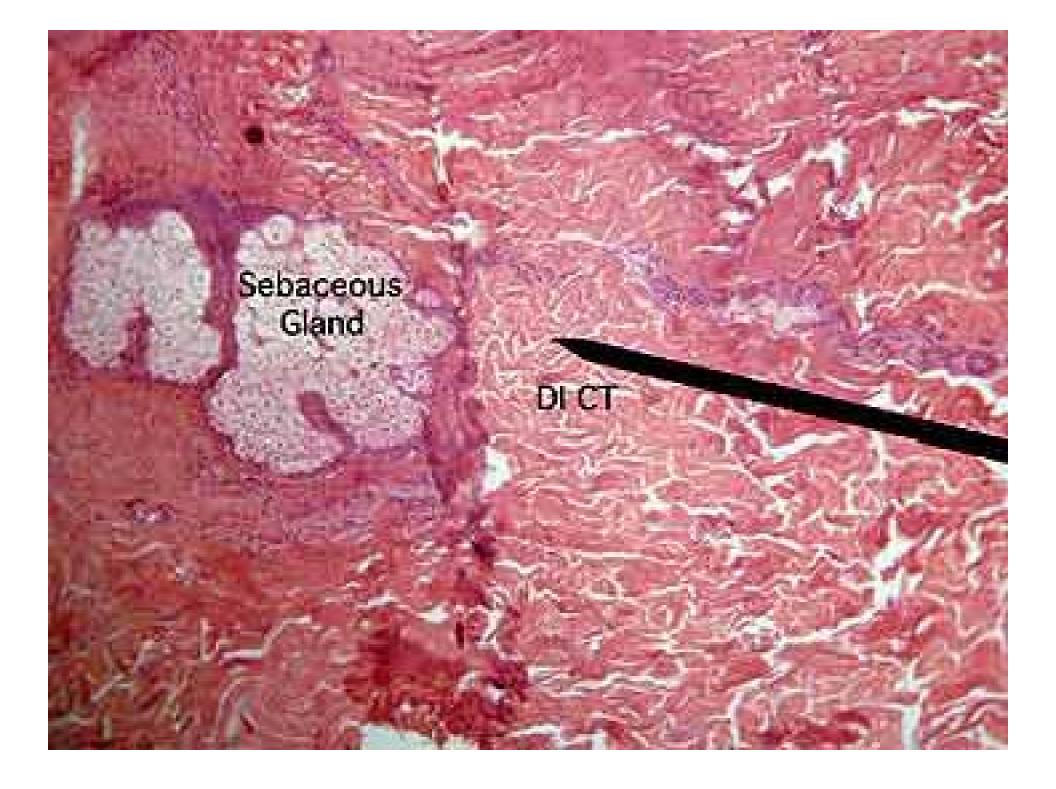




Non-lactating Breast H&E

collagen fibres

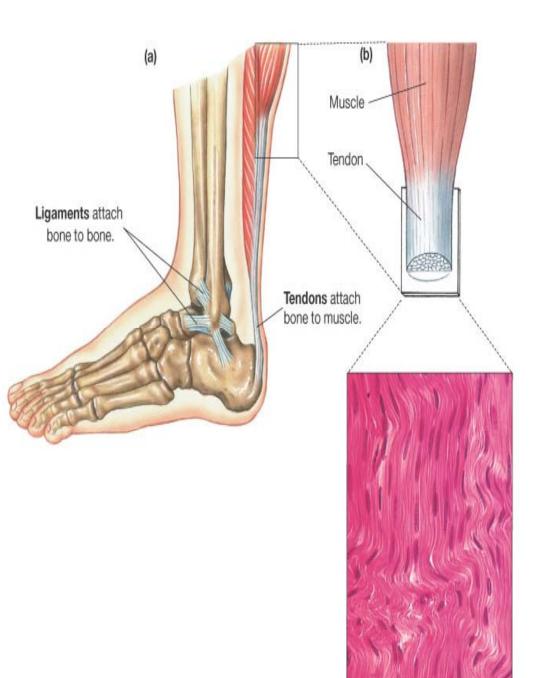
connective tissue cell nuclei blood vessels



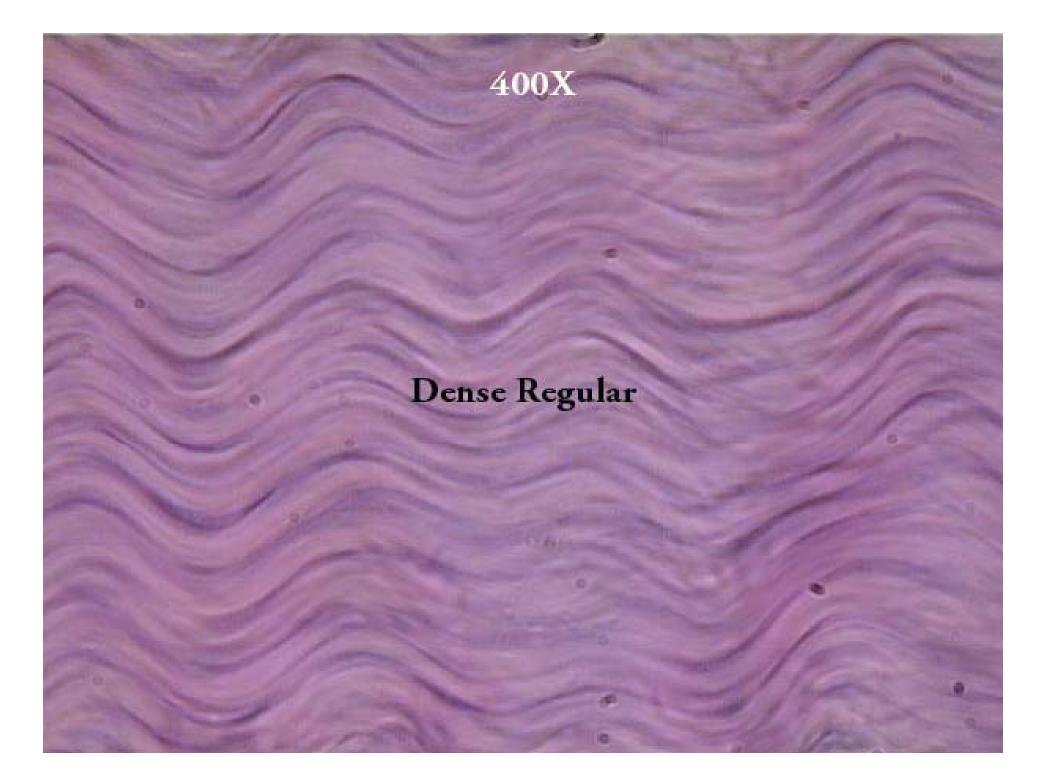
More Connective Tissues

Dense connective tissue

- Tendons & ligaments
- Collagen dominates

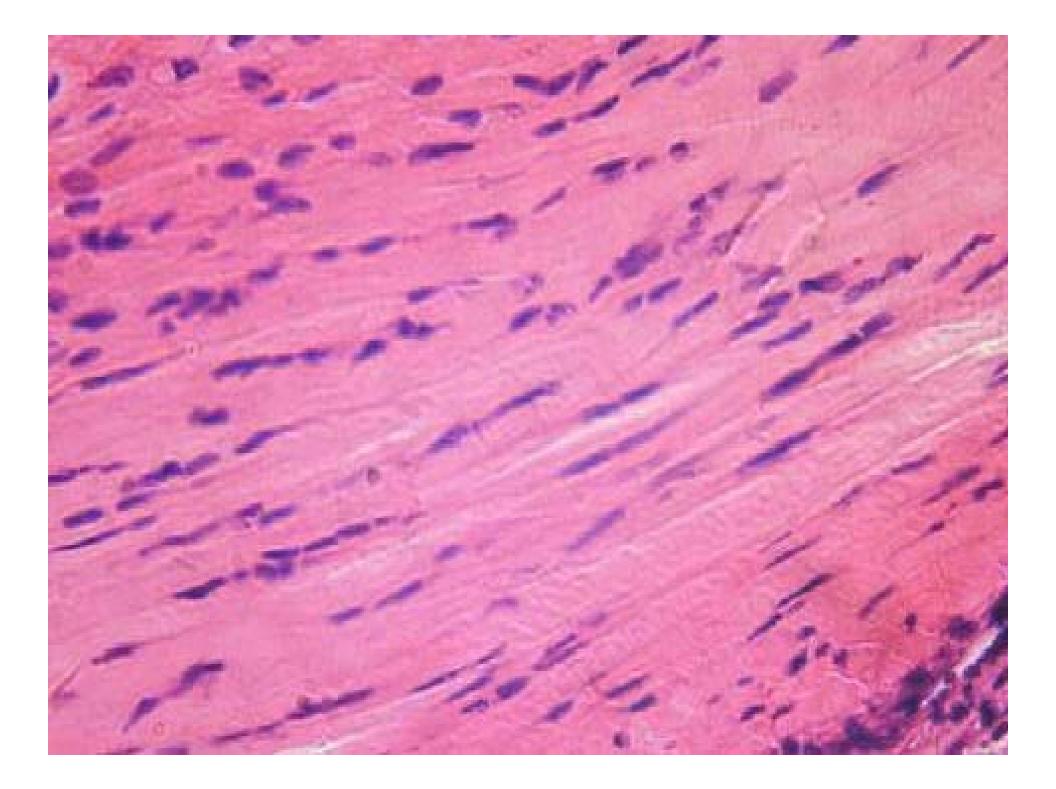


(c) Collagen fibers of tendon are densely packed into parallel bundles.



fibroblasts

collagen fibers

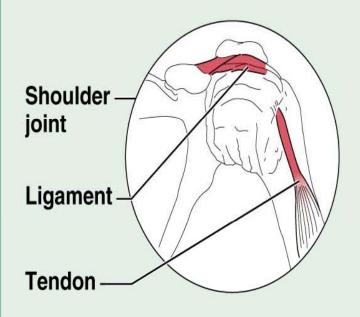


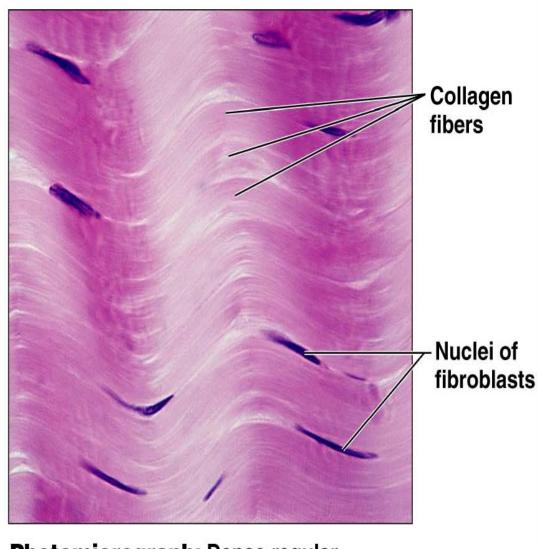
(d) Connective tissue proper: dense connective tissue, dense regular

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.

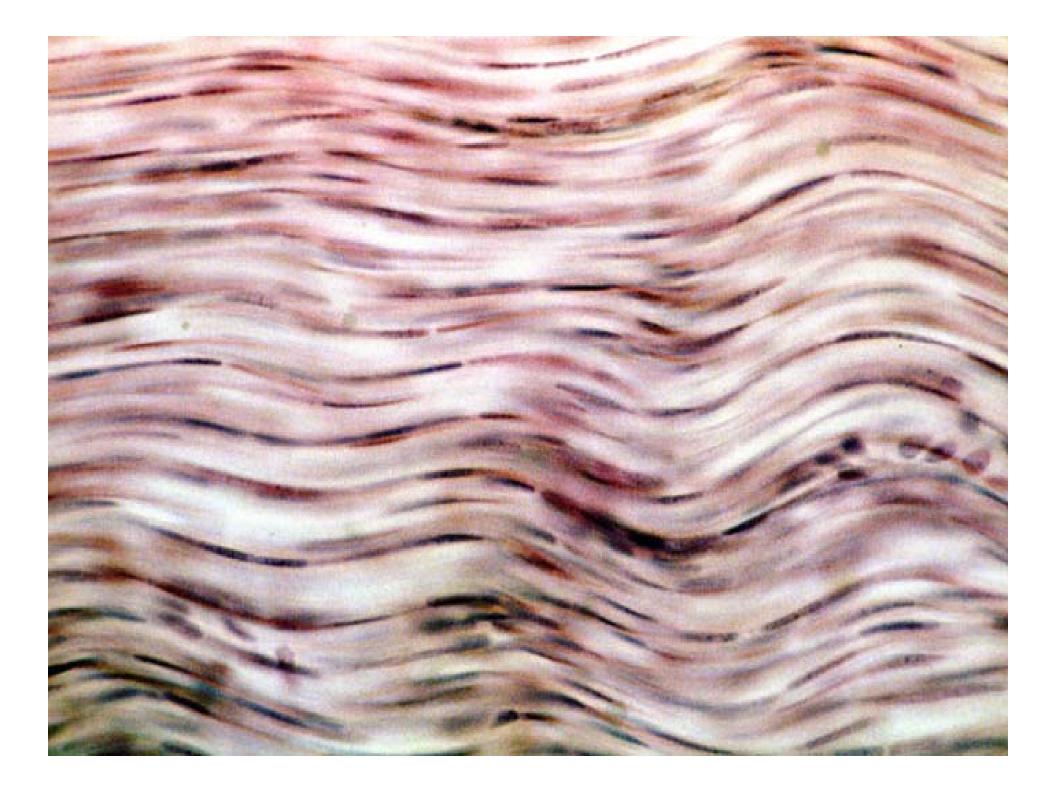
Location: Tendons, most ligaments, aponeuroses.





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

Figure 4.9d

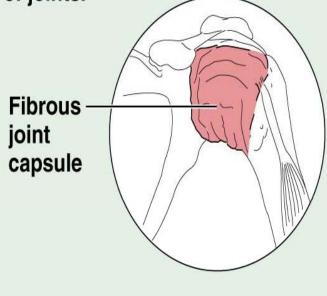


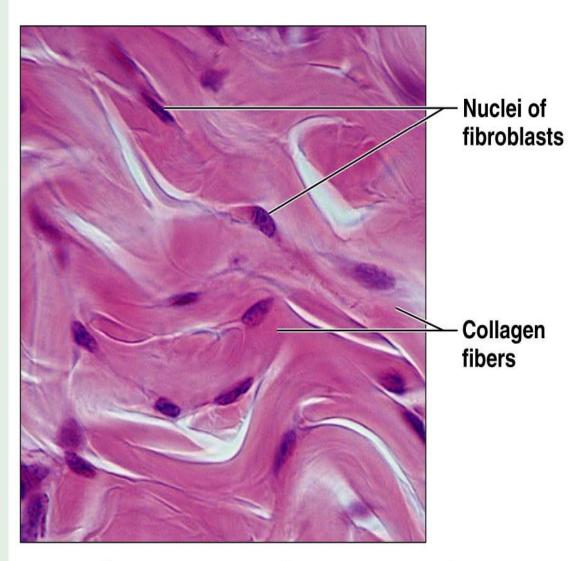
(e) Connective tissue proper: dense connective tissue, dense irregular

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.

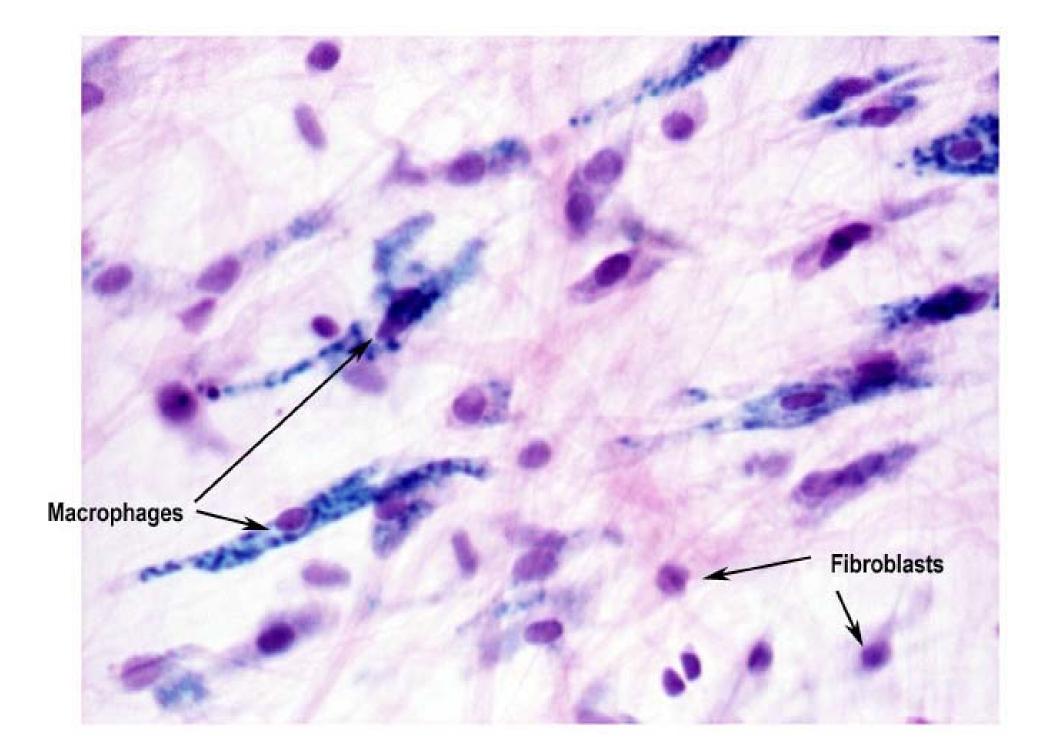
Location: Dermis of the skin; submucosa of digestive tract; fibrous capsules of organs and of joints.

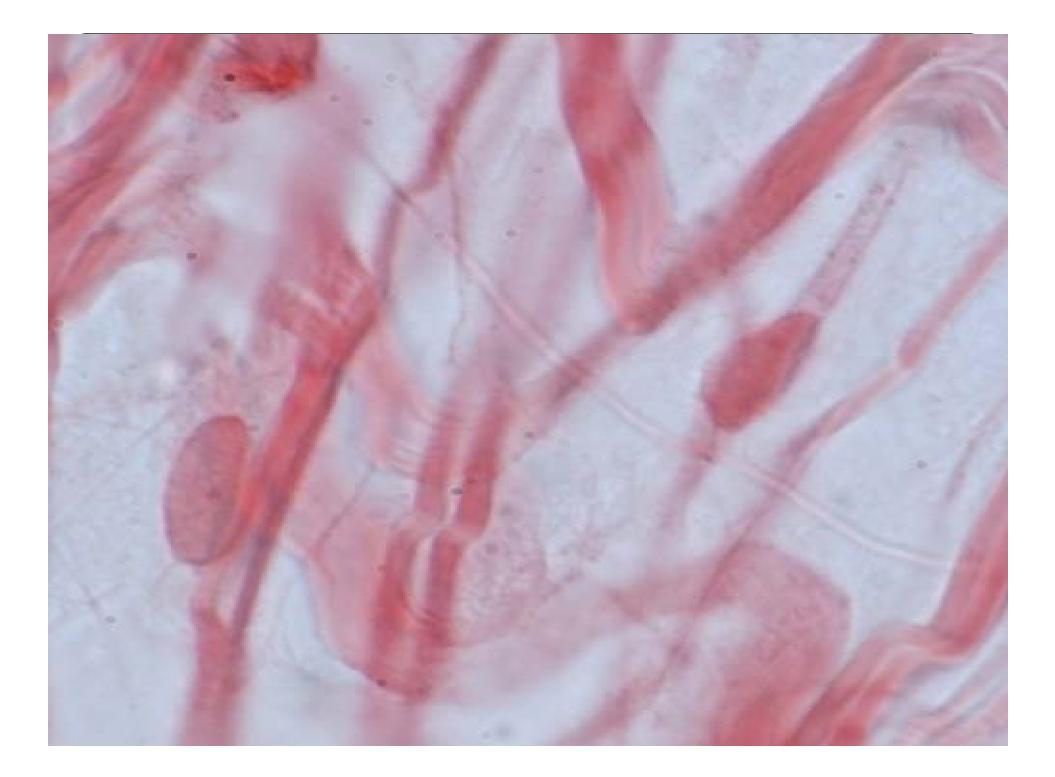


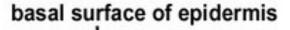


Photomicrograph: Dense irregular connective tissue from the dermis of the skin (400×).

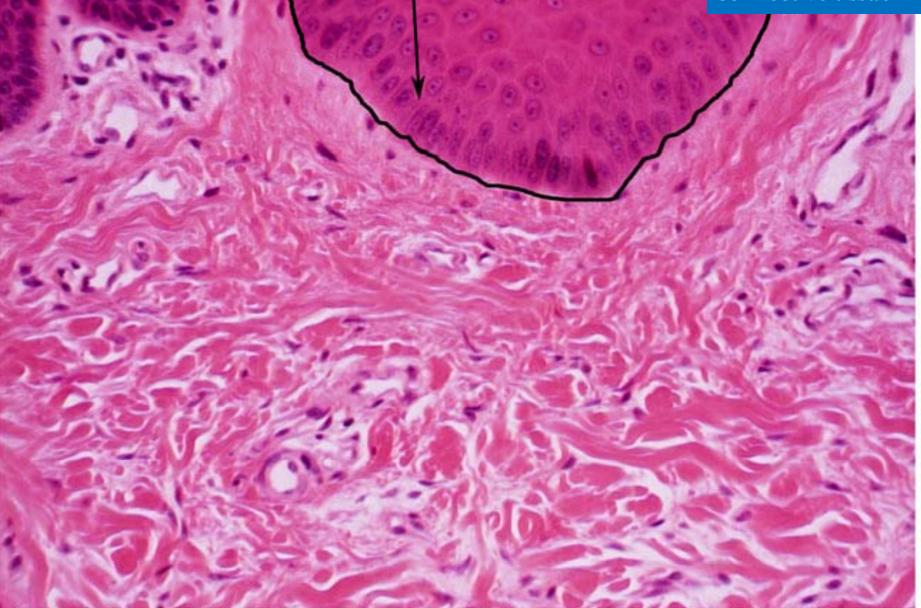
Figure 4.9e



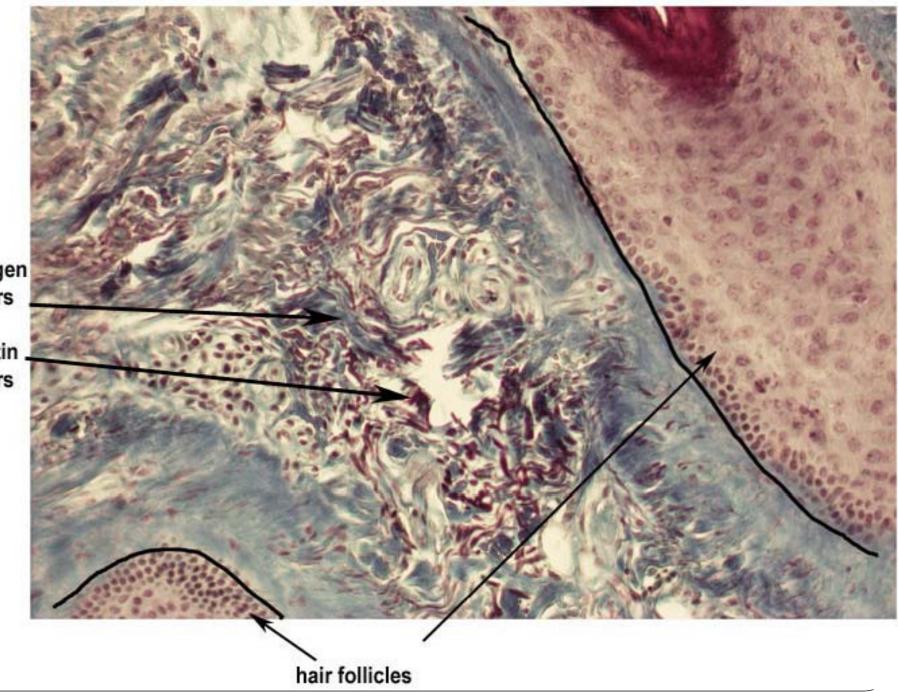




Dense irregular connective tissue

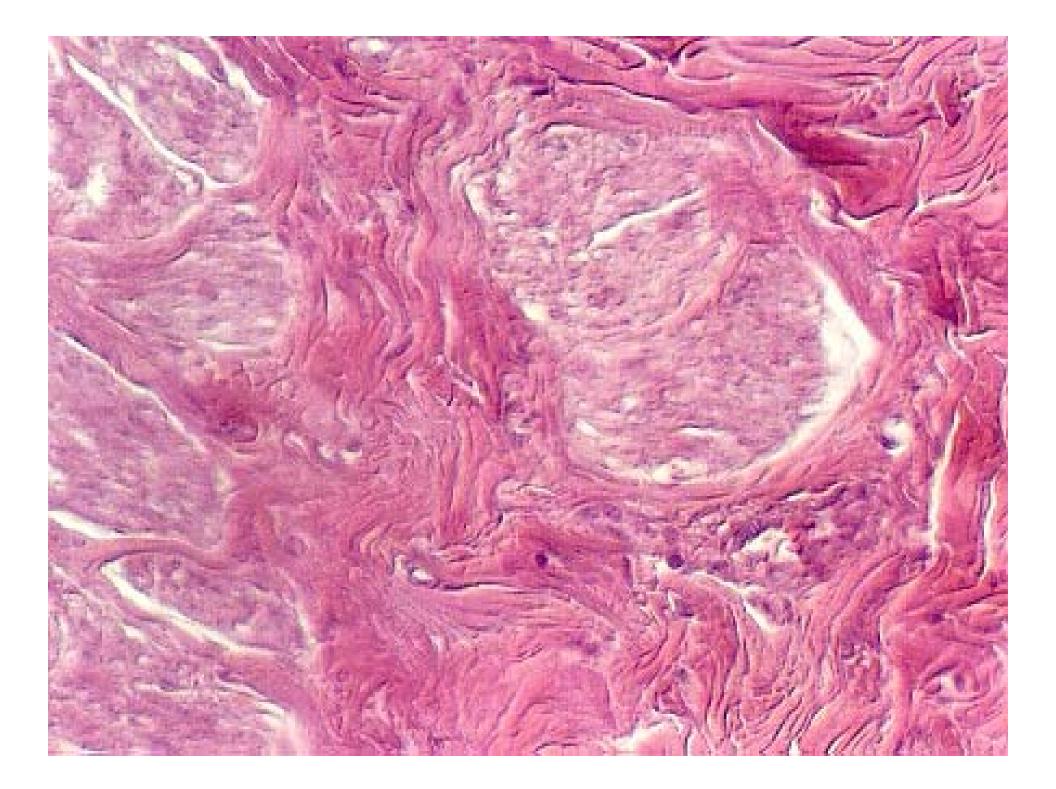


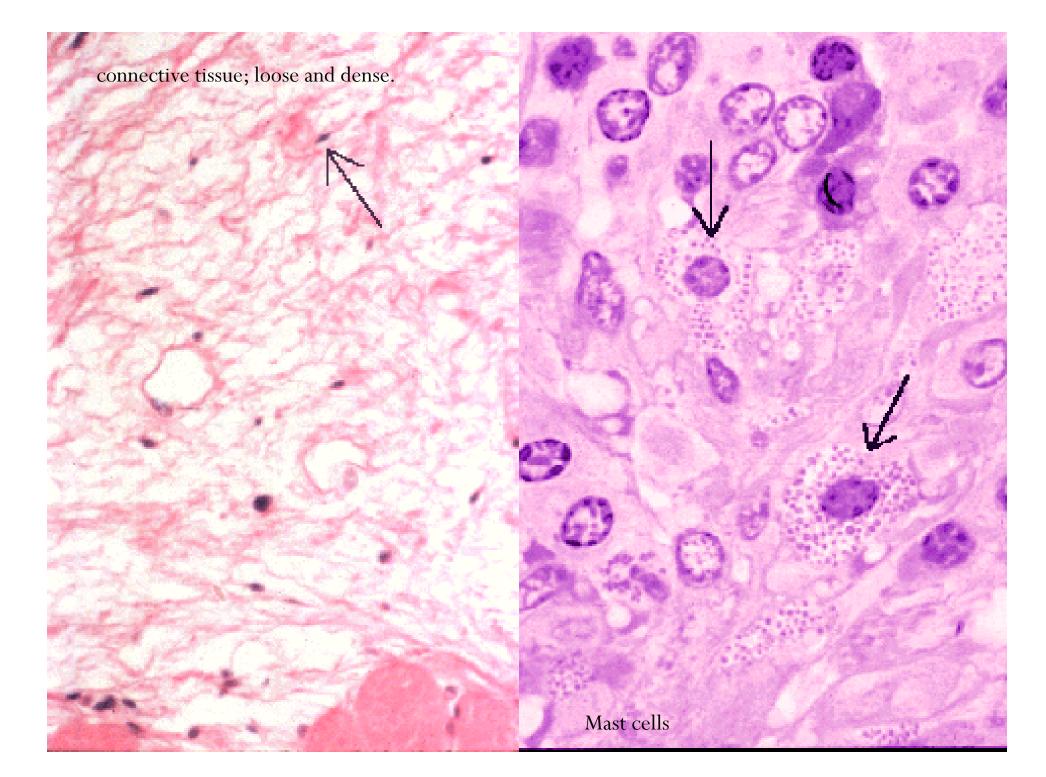
Note that the connective tissue found beneath the basal surface of the epidermis is randomly oriented.



collagen fibers

elastin . fibers





Loose Connective Tissue Mesentery, total preparation C=blood capillary

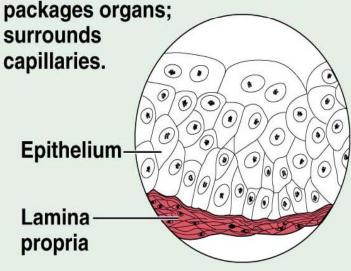
500 m

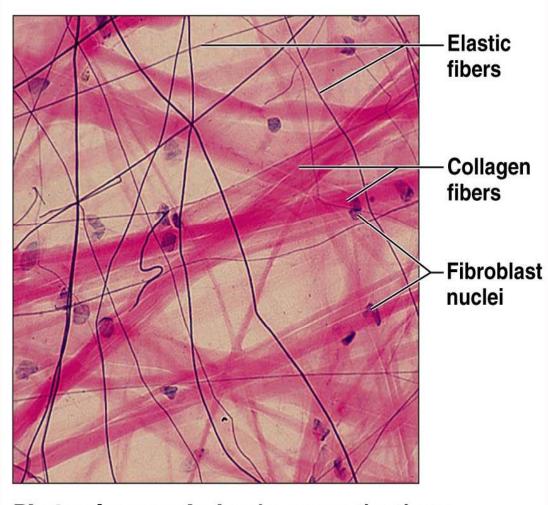
(a) Connective tissue proper: loose connective tissue, areolar

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;





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

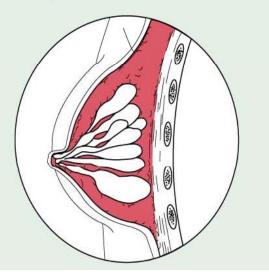
Adipose tissue

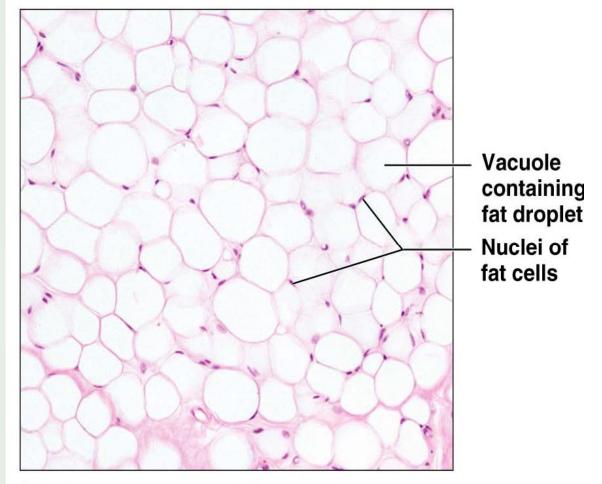
(b) Connective tissue proper: loose connective tissue, adipose

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

Adipose tissue

•Loose connective tissue composed of adipocytes.

It is technically composed of roughly only 80% fat;
fat in its solitary state exists in the liver and muscles.

•Adipose tissue is derived from lipoblasts.

•Its main role is to store energy in the form oflipids, although it also cushions and insulates the body.

•Major endocrineorgan, as it produces hormones such as :

•leptin,

•estrogen,

- resistin,
- the cytokine TNFα.

•Moreover, adipose tissue can affect other organ systems of the body and may lead to disease.

• The two types of adipose tissue are white adipose tissue (WAT) and brown adipose tissue (BAT).



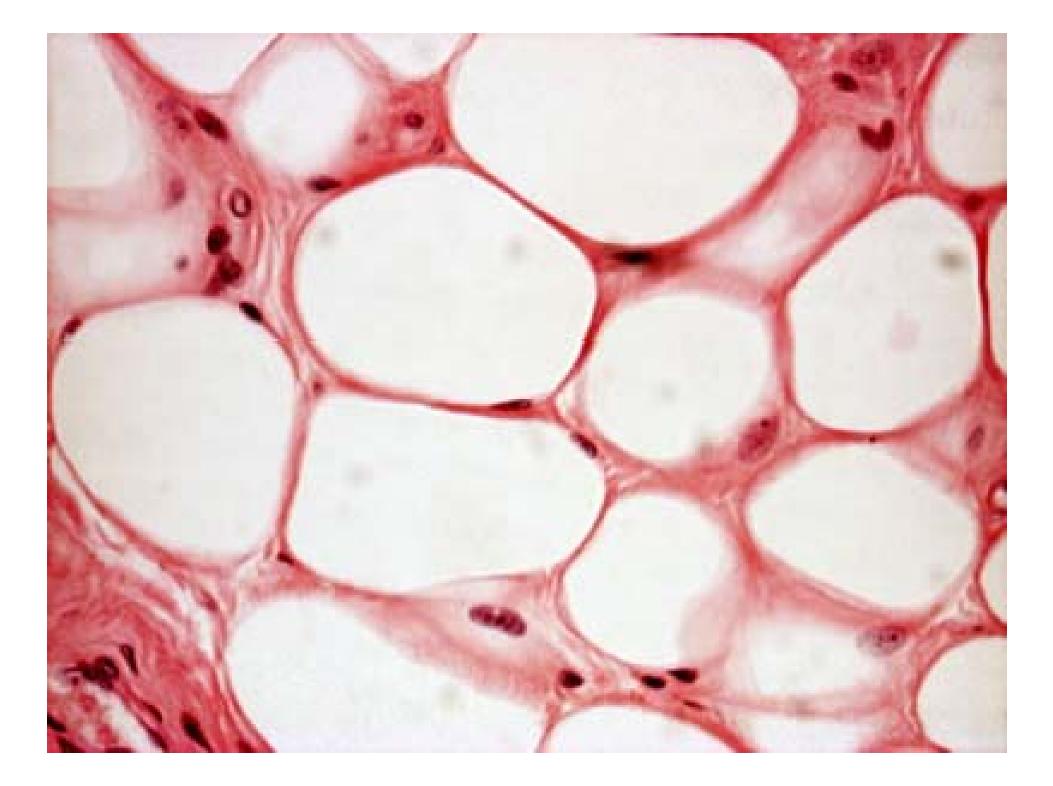
White adipose tissue

•Normal body fat

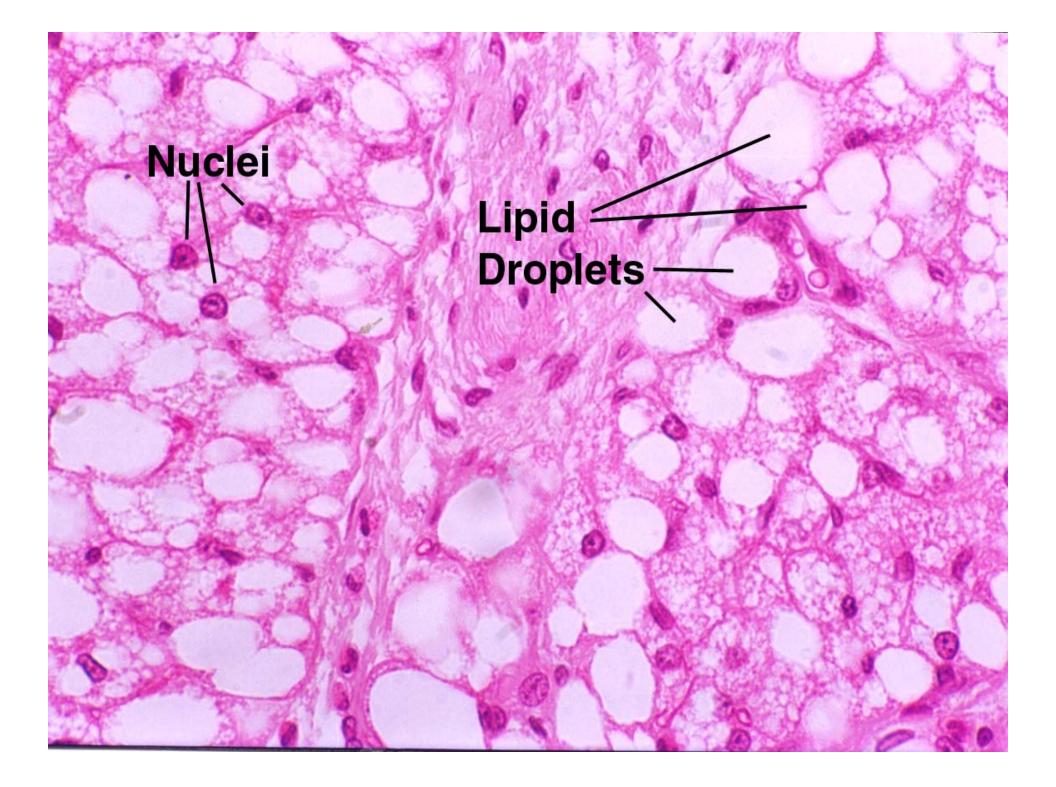
- •Very large spherical cells which may become polyhedral due to deformation
- •Contain single fat droplet with cytoplasm reduced to thin rim net to plasma membrane
- •Nucleus displayed to one side of cell and flattened by accumulated fat
- •Routine histological techniques extract the fat, leaving a 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



Adipose Tissue, Brown Multilocular fat cells



Adipose tissue

Adipose tissue is located :

beneath the skin (subcutaneous fat),
around internal organs (visceral fat),

- in bone marrow (yellow bone marrow)
- in breast tissue.

Adipose tissue

Adipose tissue contains several cell types, with the highest percentage of cells being :

- •Adipocytes, which contain fat droplets.
- Fibroblasts,
- Macrophages,
- Endothelial cells
- •Stem cells

excess adipose tissue hanging downward from the abdomen is referred to as a panniculus (or pannus). A panniculus complicates surgery of the morbidly obese.

Adipose tissue is the greatest peripheral source of aromatase in both males and females, contributing to the production of estradiol.

Adipose derived hormones include:

- Adiponectin
- Resistin
- •Plasminogen activator inhibitor-1 (PAI-1)
- •TNFα
- •IL-6
- •Leptin
- •Estradiol (E2)

Adipose tissues also secrete a type of cytokines (cell-to-cell signalling proteins) called adipokines (adipocytokines), which play a role in obesity-associated complications.

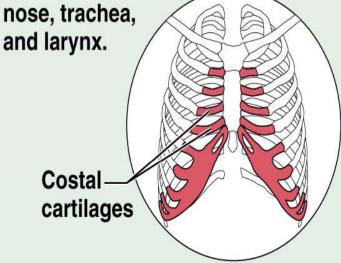
Other that will be studied in the mutual section

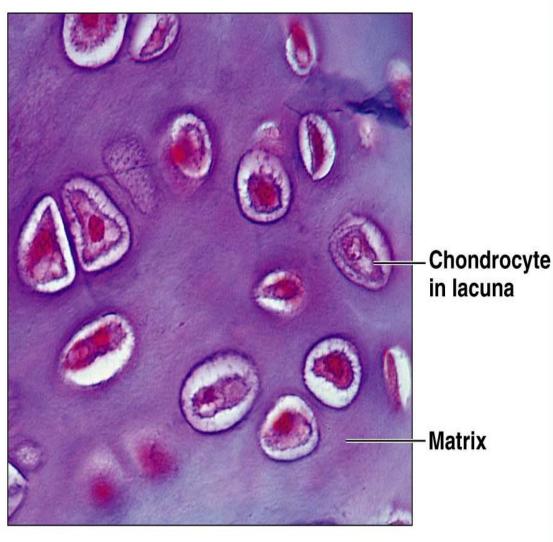
(f) Cartilage: hyaline

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





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

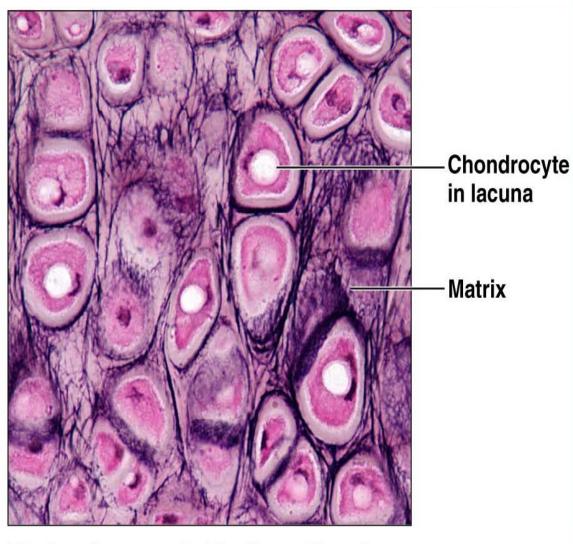
(g) Cartilage: elastic

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×).

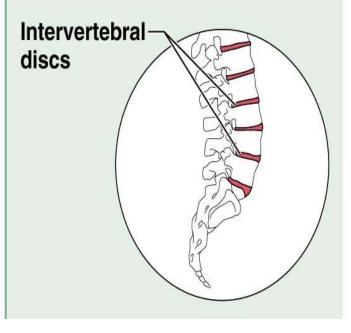
Figure 4.9g

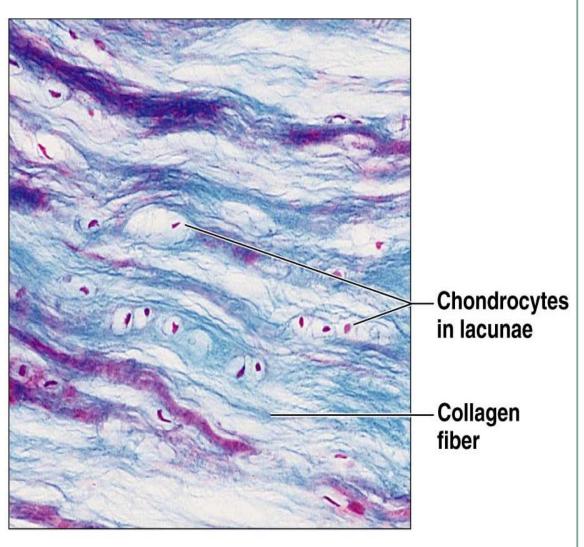
(h) Cartilage: fibrocartilage

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.

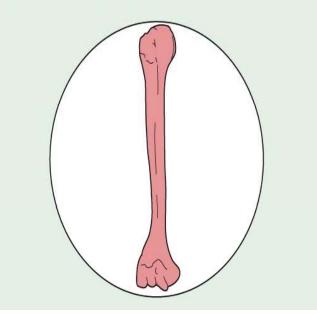
Figure 4.9h

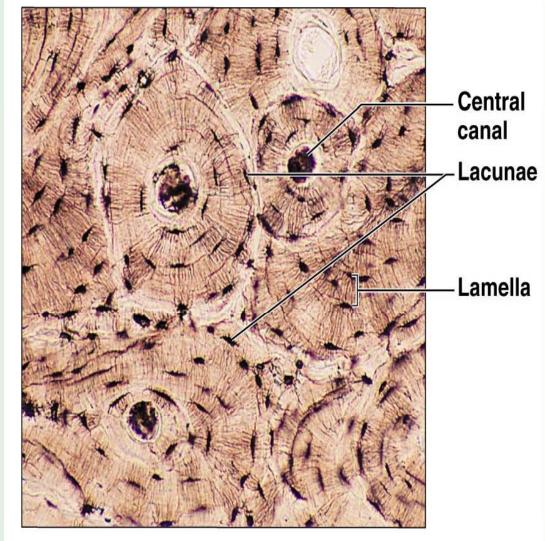
(i) Others: bone (osseous tissue)

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



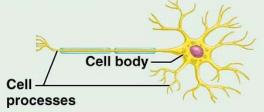


Photomicrograph: Cross-sectional view of bone (70×).

Figure 4.9i

Nervous tissue

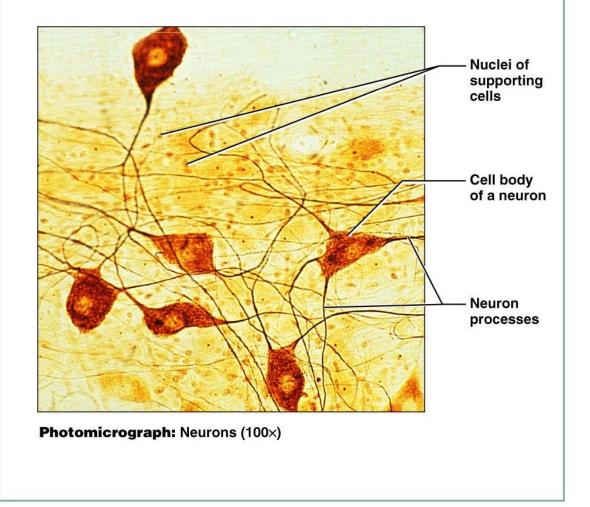
Description: Neurons are branching cells; cell processes that may be quite long extend from the nucleus-containing cell body; also contributing to nervous tissue are nonirritable supporting cells (not illustrated).



Function: Transmit electrical signals from sensory receptors and to effectors (muscles and glands) which control their activity.

Location: Brain, spinal cord, and nerves.





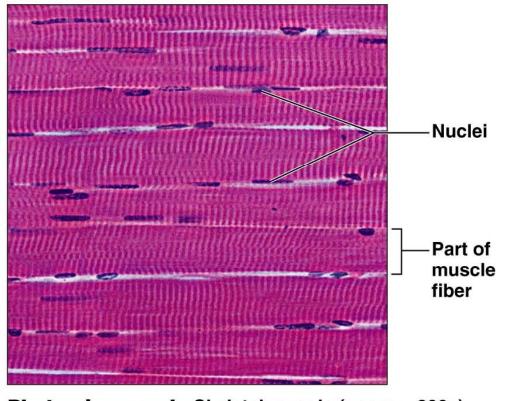
(a) Skeletal muscle

Description: Long, cylindrical, multinucleate cells; obvious striations.

Function: Voluntary movement; locomotion; manipulation of the environment; facial expression; voluntary control.

Location: In skeletal muscles attached to bones or occasionally to skin.





Photomicrograph: Skeletal muscle (approx. 300×). Notice the obvious banding pattern and the fact that these large cells are multinucleate.

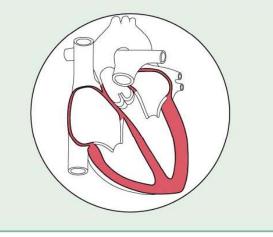
(b) Cardiac muscle

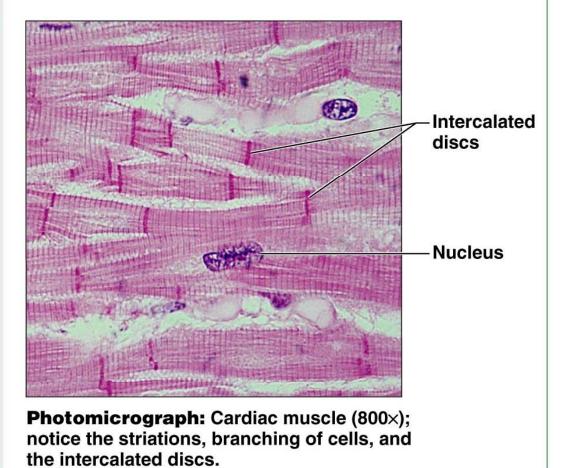
Description: Branching, striated, generally uninucleate cells that interdigitate at specialized junctions (intercalated discs).



Function: As it contracts, it propels blood into the circulation; involuntary control.

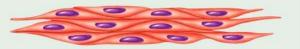
Location: The walls of the heart.





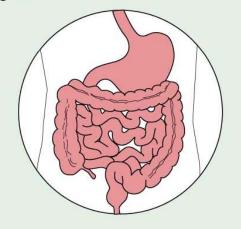
(c) Smooth muscle

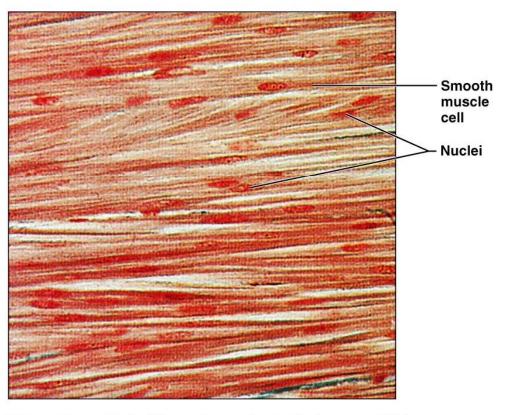
Description: Spindle-shaped cells with central nuclei; no striations; cells arranged closely to form sheets.



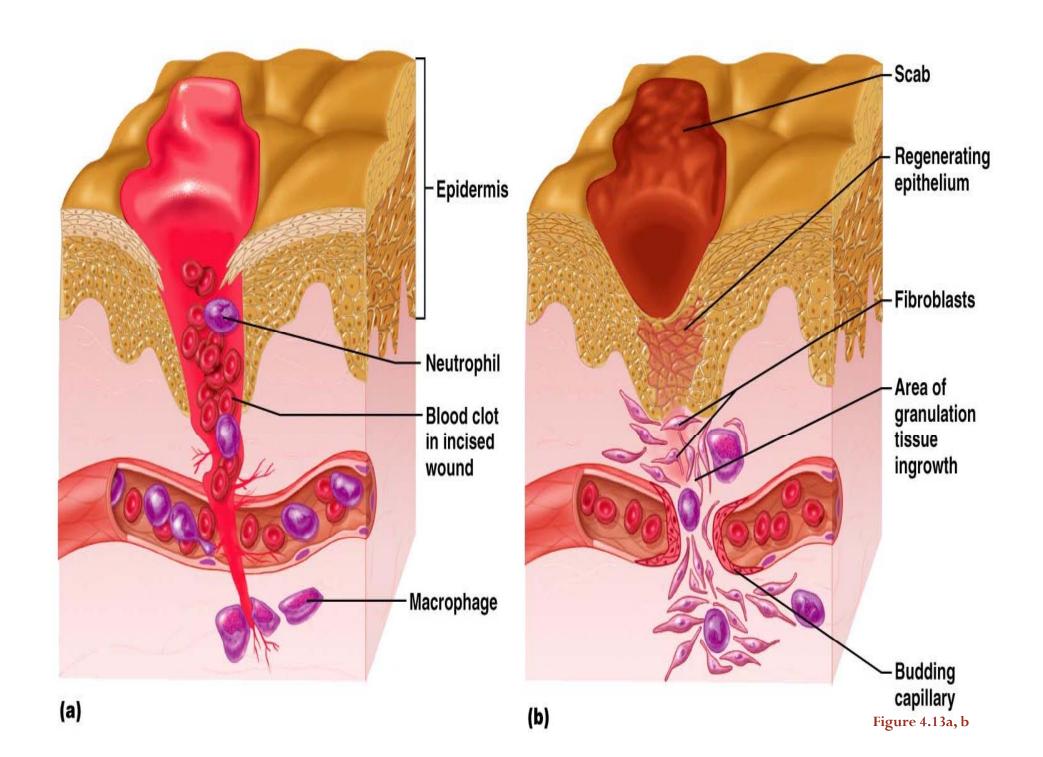
Function: Propels substances or objects (foodstuffs, urine, a baby) along internal passageways; involuntary control.

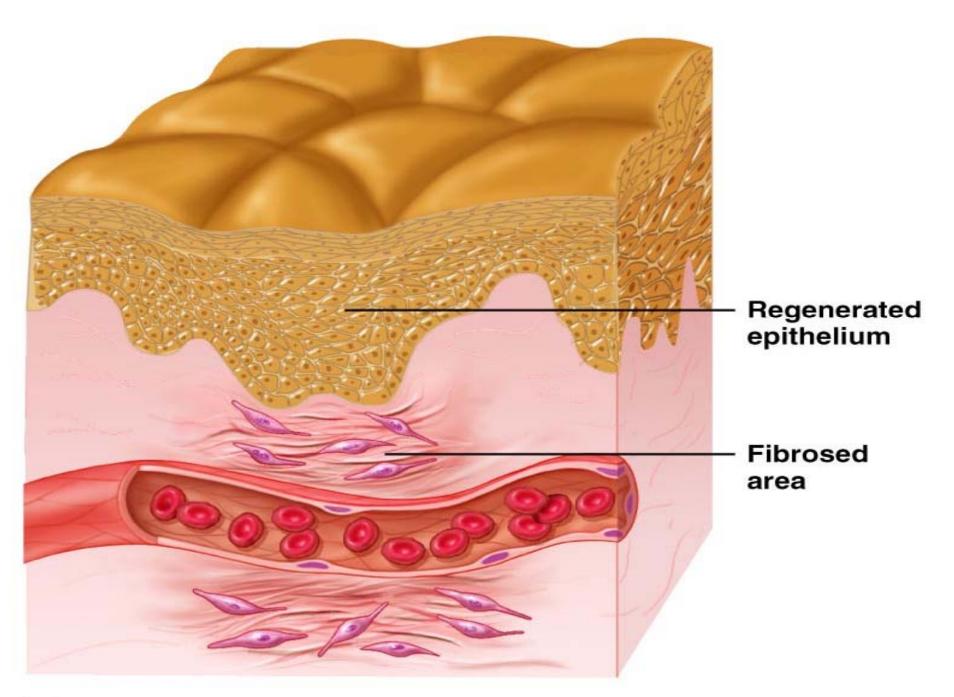
Location: Mostly in the walls of hollow organs.





Photomicrograph: Sheet of smooth muscle (approx. 600×).





Connective Tissue Diseases

Disease

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

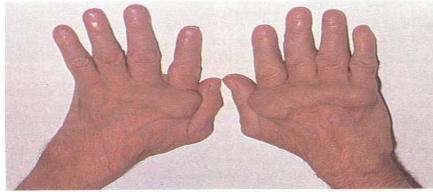
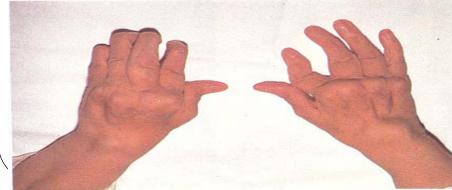


Fig. 4 RA at later stage. Considerable MCP joint thickening, subluxation and ulnar deviation.





Sjogren Syndrome





