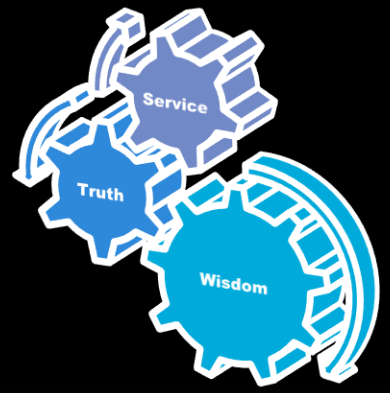
MSK-1 MODULE
Histology of Connective Tissue (LGIS)

By Prof. Dr Saima Naz
Dated: 16th April , 2024

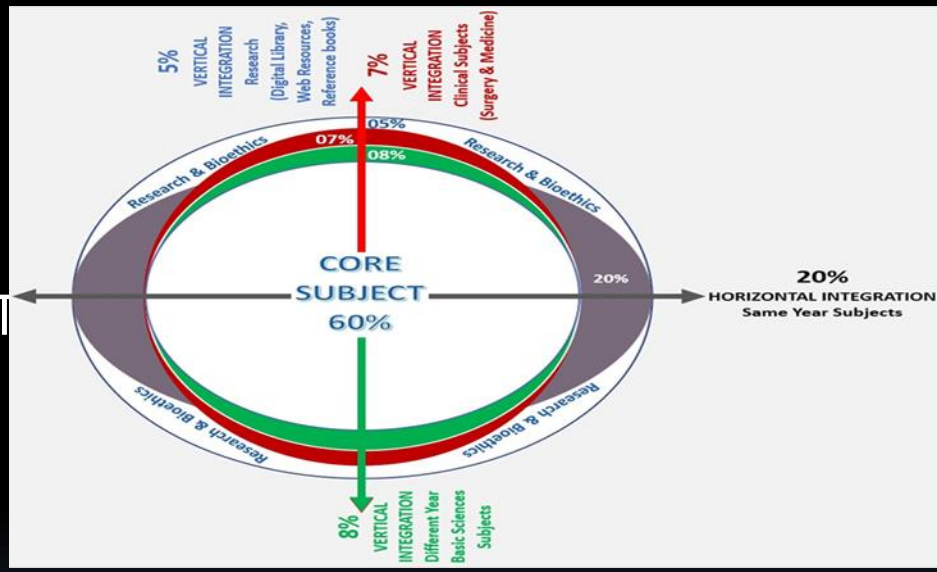
Motto Vision; The Dream/Tomorrow



- To impart evidence-based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

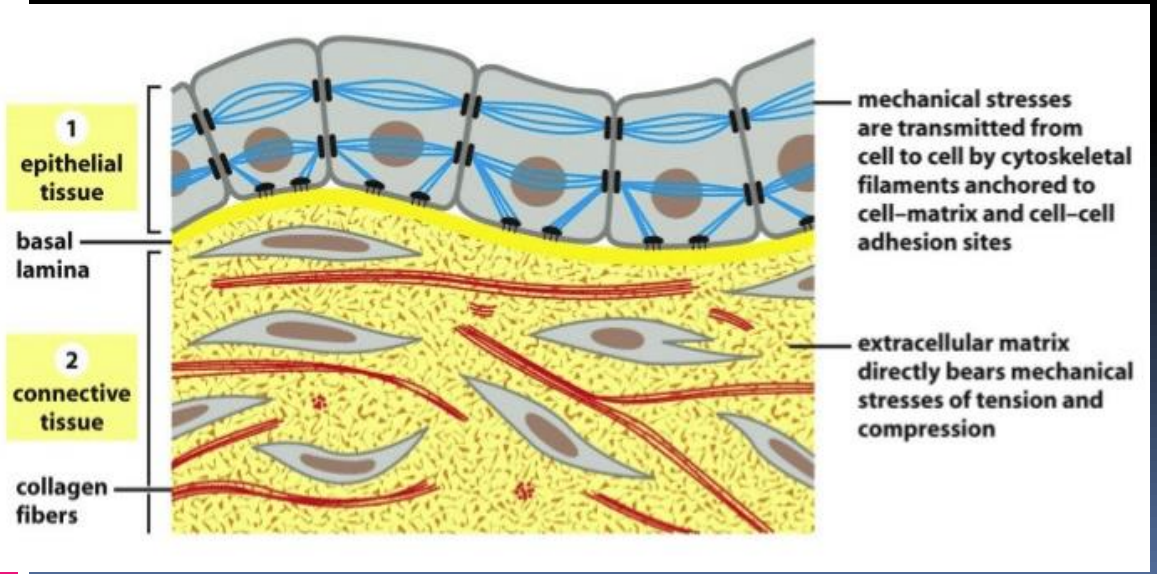
At the end of lecture students will be able to

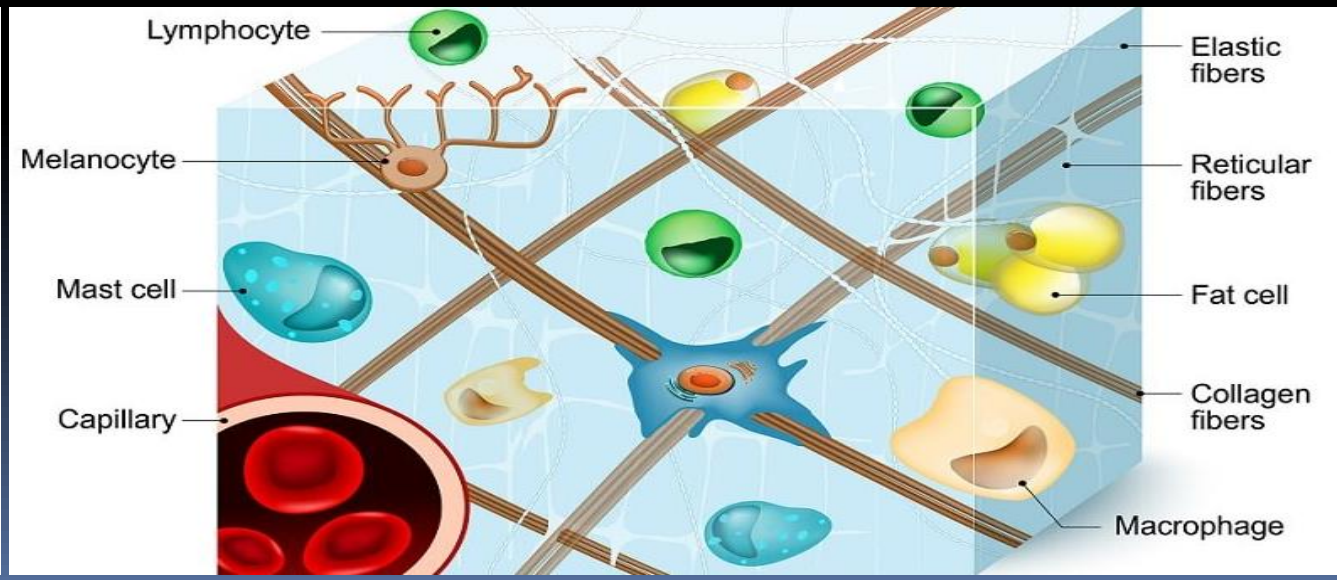
- Review the definition & cells of CT
- Describe the fibers & Ground substance of CT
- Classify CT
- Illustrate histological structure of loose & reticular CT
- Enumerate examples & locations of loose &reticular CT
- Understand the biophysical aspects of CT
- Correlate relevant clinical aspects
- Practice principles of bioethics
- Apply strategic use of AI in health care
- Able to read a relevant research article
- Know to use digital library



Connective Tissue

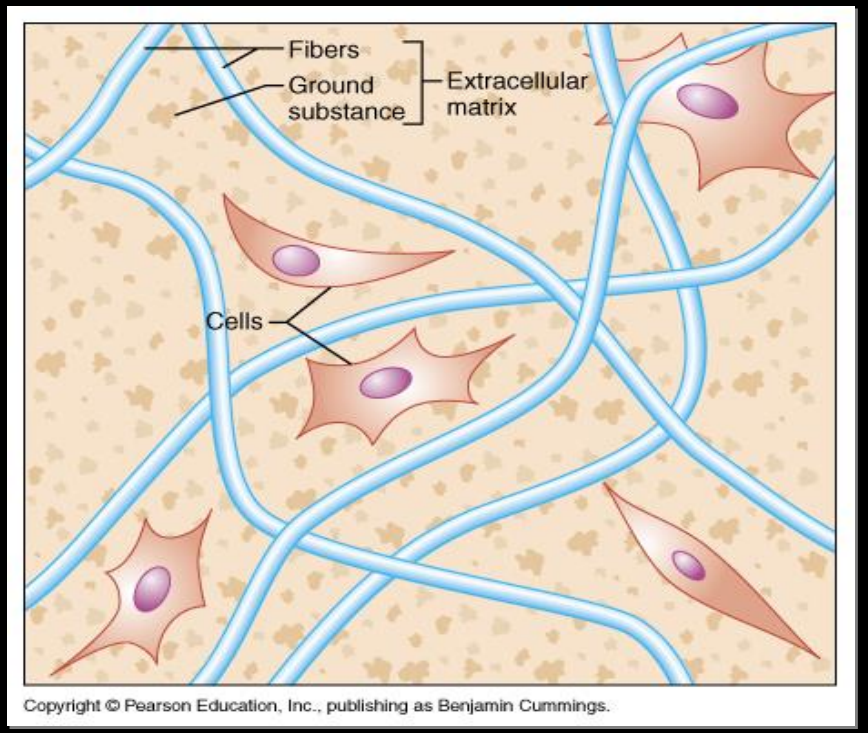
- They are the most abundant and widely distributed tissue type in the body.
- Characterized by fewer cells and large amount of extracellular matrix
- Group of tissues that provide structural support, protect the body ,stores fat, binds tissues and organize them into their shape.





Structural Elements of CT

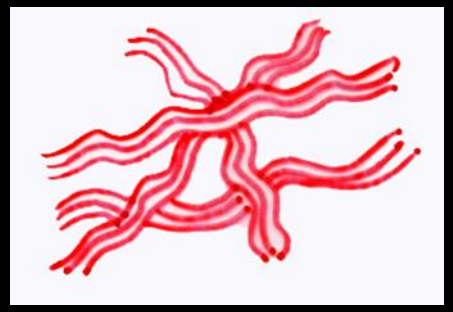
- Cells
- Fibers
- Ground substance

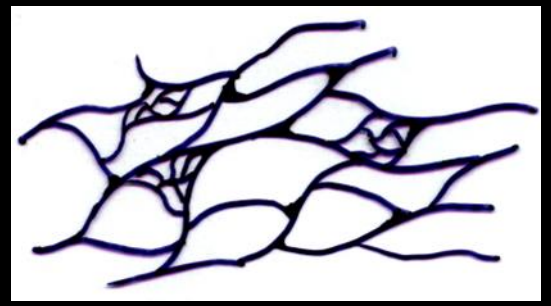


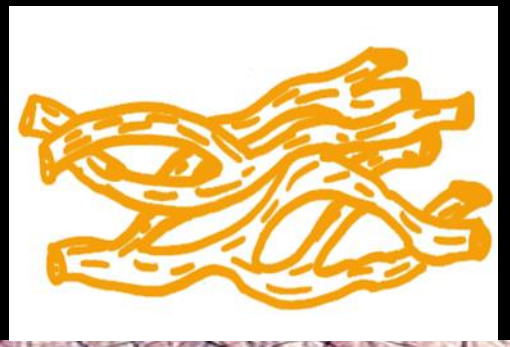
Unlike the tightly packed Epithelial tissues, living cells in connective tissues are separated by a non-living **extracellular matrix** (Ground Substance and Fiber).

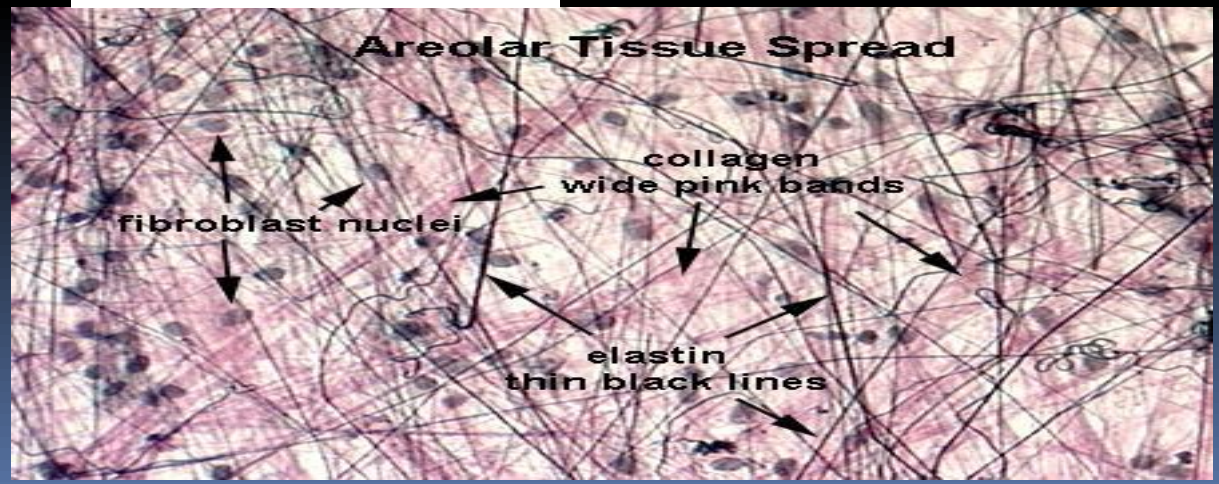
CONNECTIVE TISSUE FIBERS

- Formed by proteins which polymerize into elongated structures
- Specific properties of a CT are largely dependant on the type of fibers present.
- Three types
  - Collagen Fibers
  - Reticular Fibers
  - Elastic Fibers
- Collagen and reticular fibers are formed by the protein collagen, and elastic fibers are composed mainly of the protein elastin

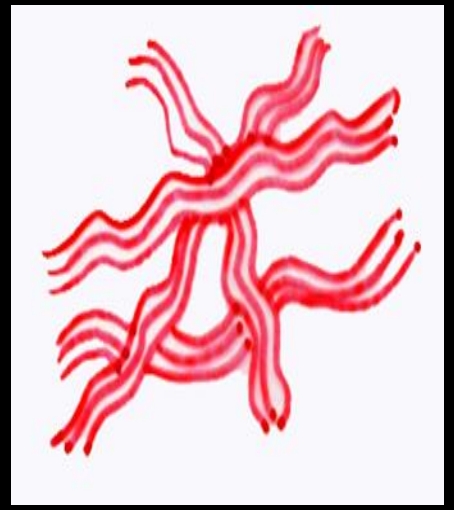


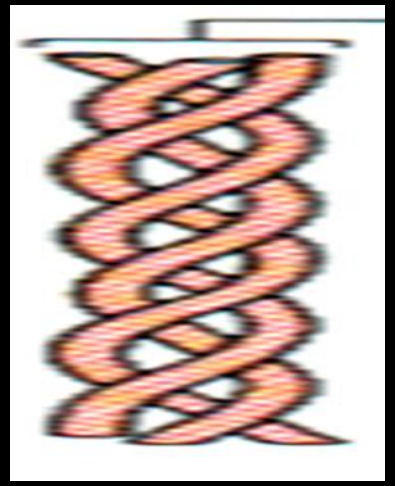






Biophysical Aspect

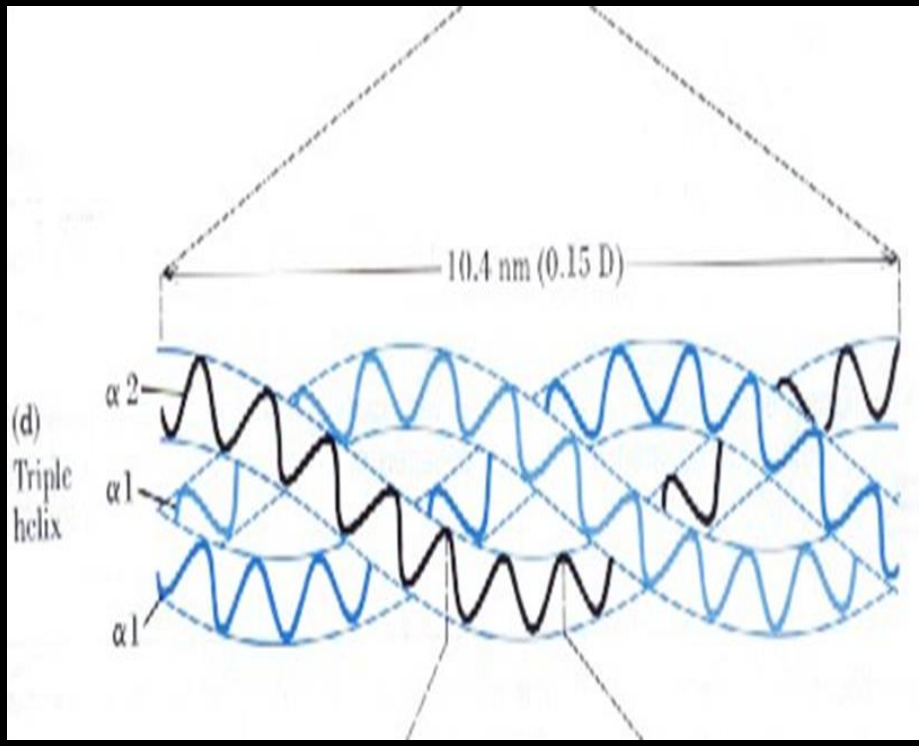


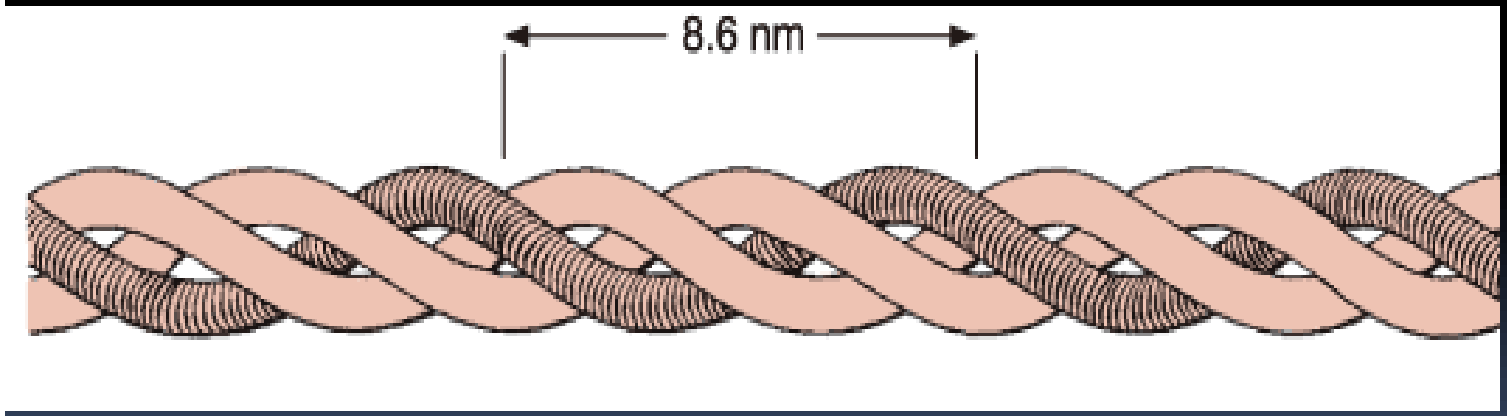


SYNTHESIS AND STRUCTURE OF COLLAGEN

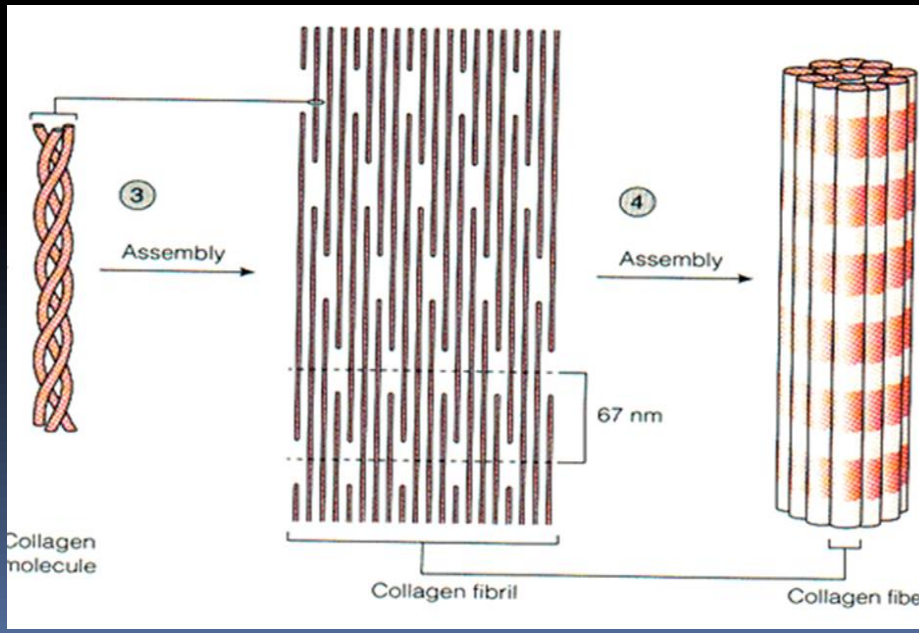
COLLAGEN (Overview)

- Most prominent protein of human body & Extracellular matrix
- Family of closely related proteins
- Collagen consists of amino acids bound together to form a triple helix of elongated fibril
- Three polypeptide chains intertwined together—triple helix (like rope)





Each complete turn of the helix spans a distance of 8.6 nm. The length of each tropocollagen molecule is 280 nm, and its width is 1.5 nm.

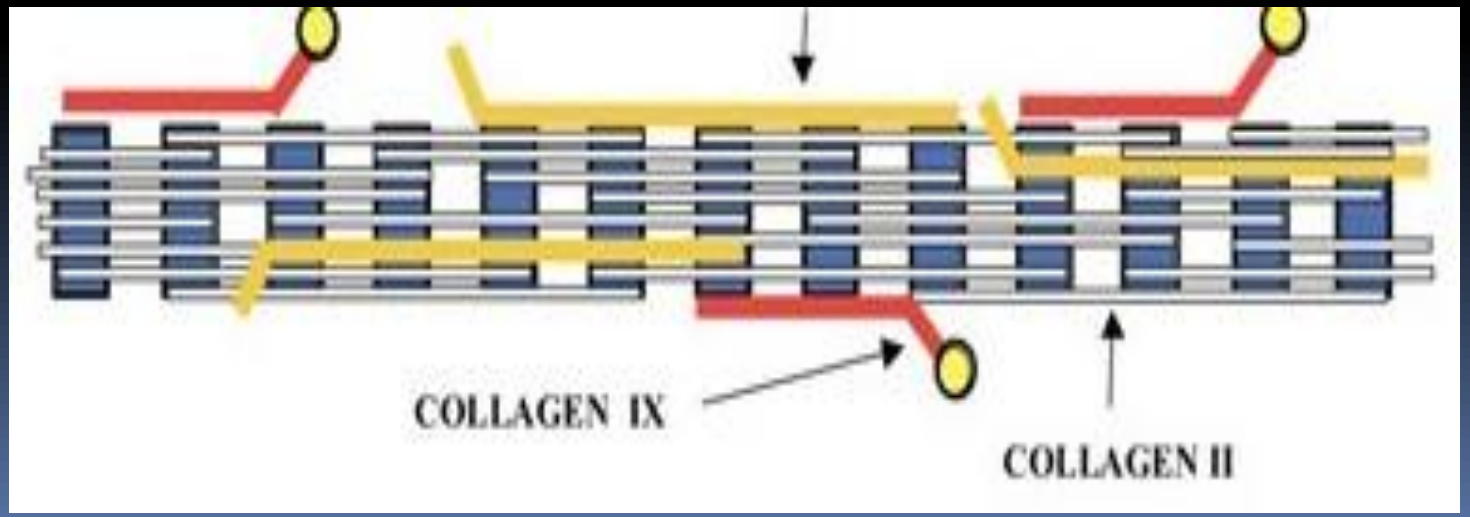


TYPES

- 28 varieties of collagen, type I - type XXVIII collagen
- Most important & best studied are I,II, III, IV &V.
- Depends on length and diameter
- Over 90% of the collagen in the human body is type I co
- **FIBRIL FORMING COLLAGEN**: Long fibril ,

TYPE I, II , III, V ,XI,

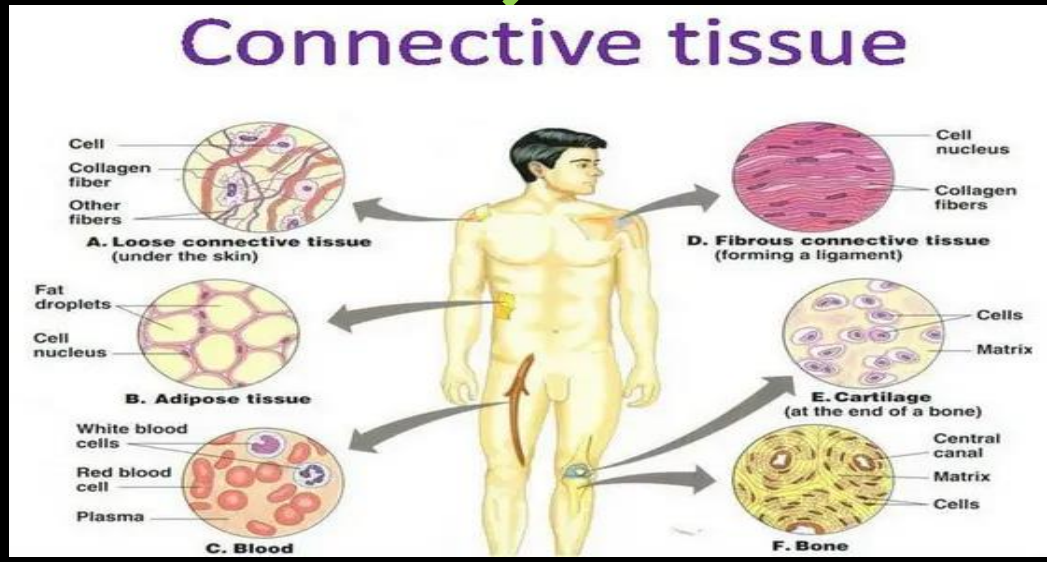
- **Network/sheet forming collagen**: IV , VIII
- **Anchoring fibril forming collagen**: VII, IX, XII , XIV

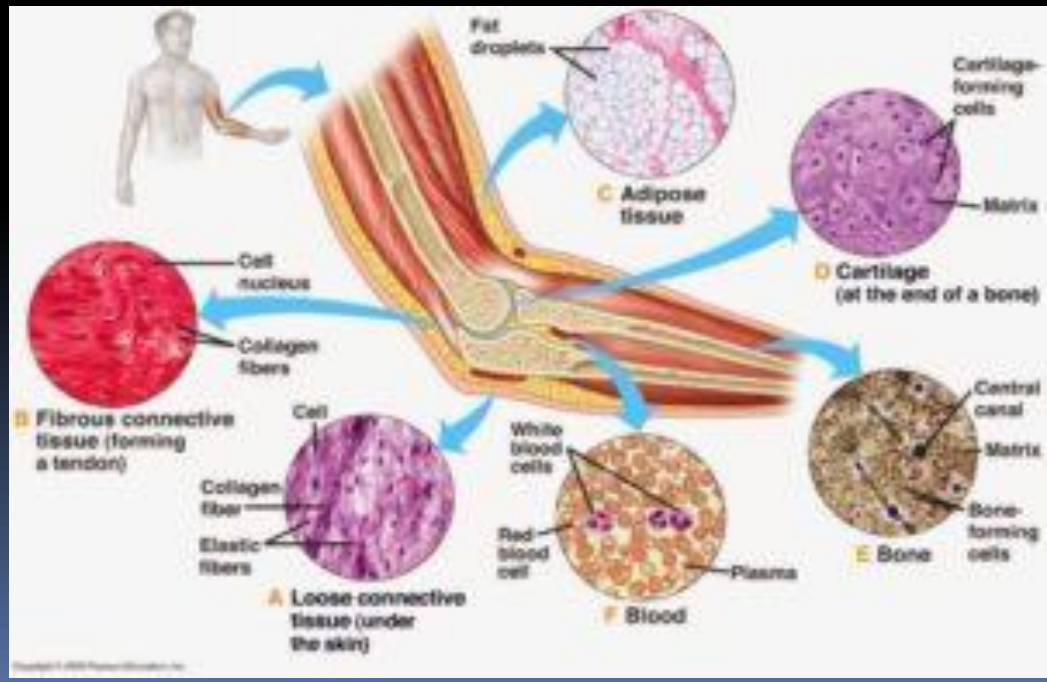


TYPE	TISSUE DISTRIBUTION
	Fibril-forming
I	Skin, bone, tendon, blood vessels, cornea
II	Cartilage, intervertebral disk, vitreous body
III	Blood vessels, skin, muscle
	Network-forming
IV	Basement membrane
VIII	Corneal and vascular endothelium
	Fibril-associated*
IX	Cartilage
XII	Tendon, ligaments, some other tissues

Types (Important to remember)

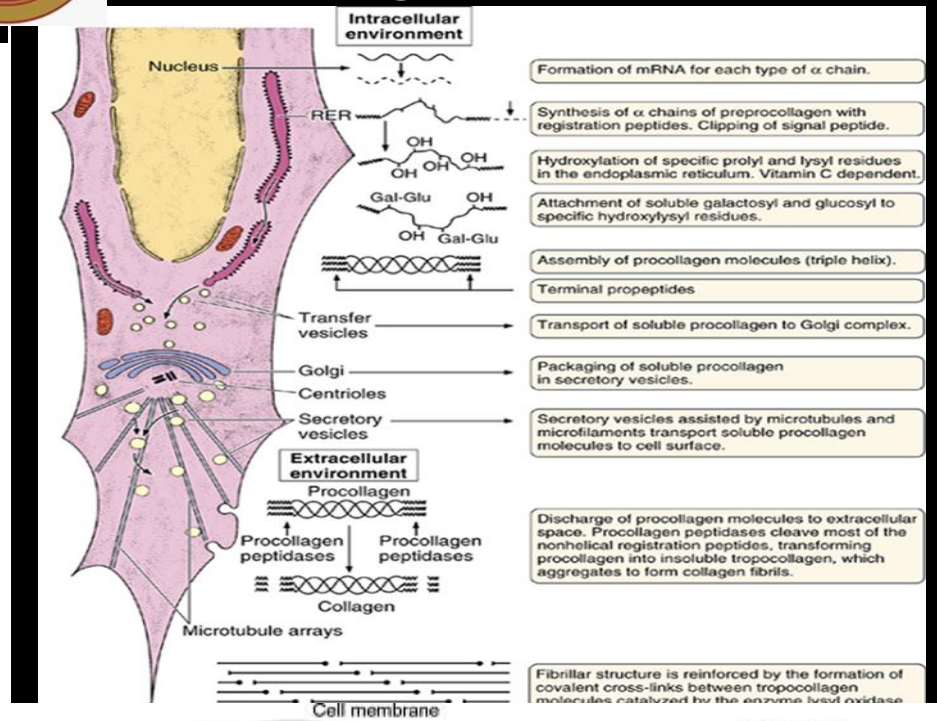
- Type1- 90% of total collagen in the body eg bones ,tendons, dermis etc
- Type2-cartilage
- Type3-reticular fibres
- Type4-basement membrane
- Type5-hair,placenta ,blood vessels



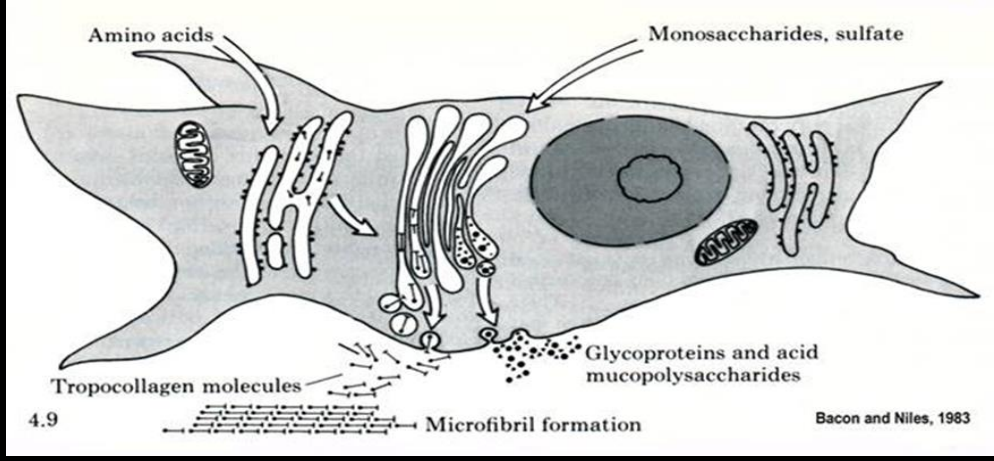


HORIZONTAL INTEGRATION

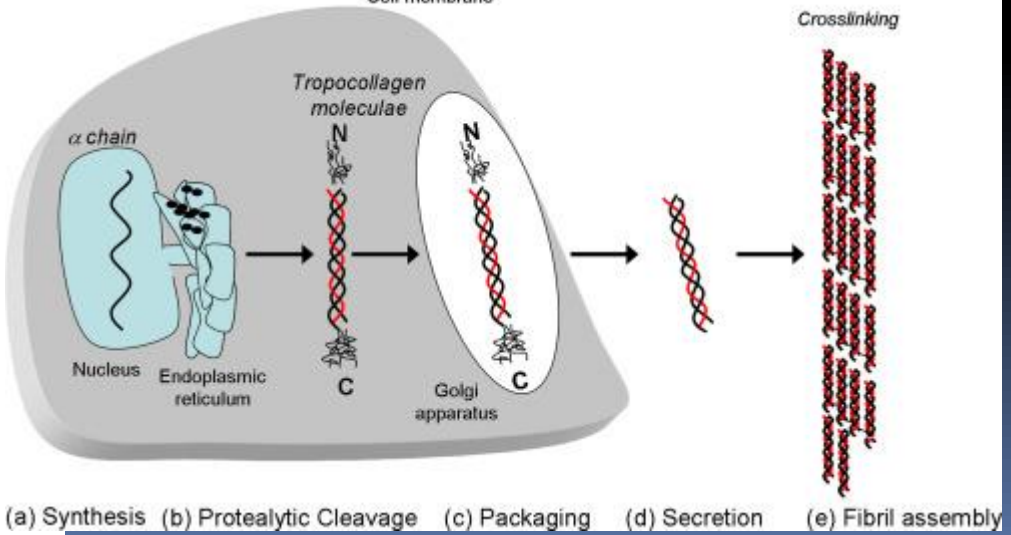
Synthesis



- Amino acids
- Procollagen
- Three chains
- Tropocollagen
- Collagen

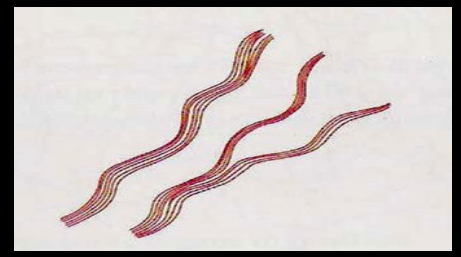


- Tropocollagen is synthesized by fibroblasts and released into extracellular space where they get polymerized to form collagen fibrils
- Collagen fiber formation involves events that occur both within and outside the fibroblast
- Collagen on boiling gives gelatin

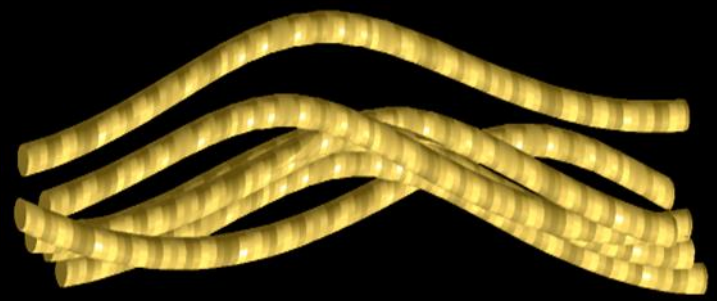


CONNECTIVE TISSUE FIBERS

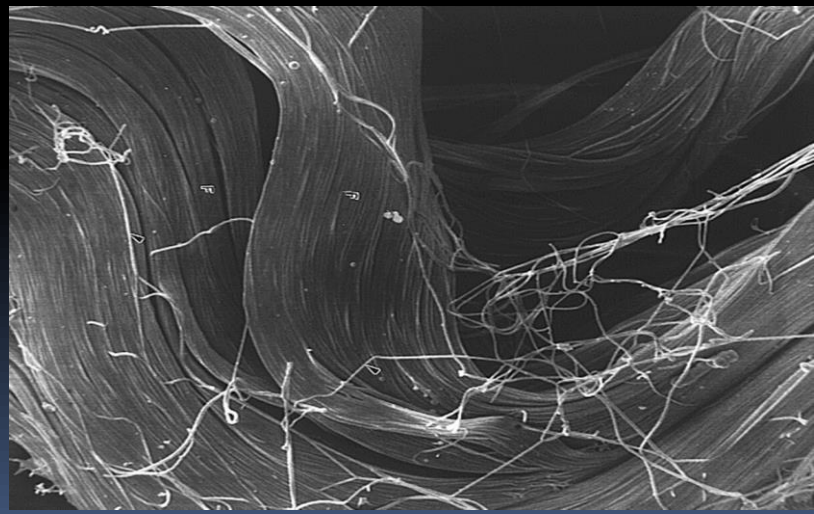
1. Collagen Fibre



- ***Collagen protein*** forms Fibres
- ***White*** colour when fresh



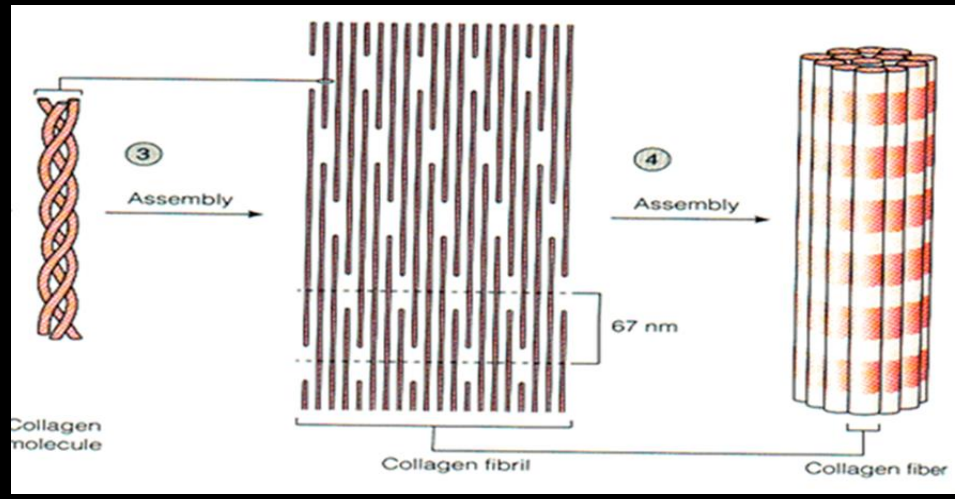
- Most abundant and commonest type of C.T fibers (35% of the protein in the body is collagen)
- Made up of protein collagen type I
- Do not branch,wavy
- Indefinite length
- Run randomly in various directions
- In many parts, collagen fibers lie parallel to each other forming bundles of various sizes
- Flexible but inelastic (non-extensible

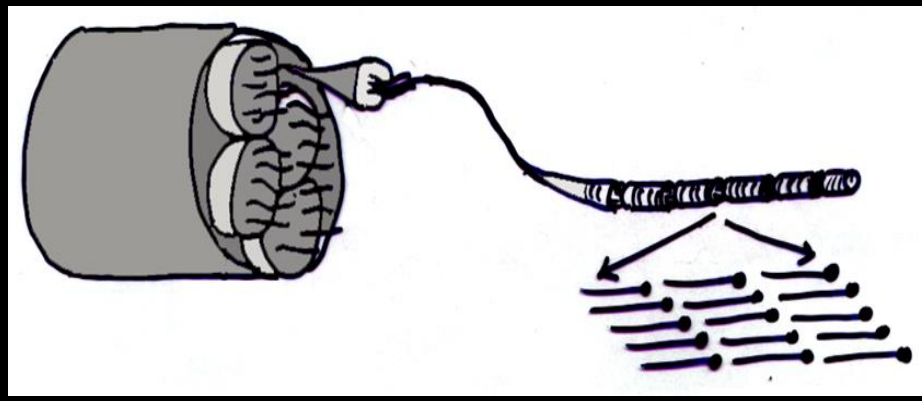


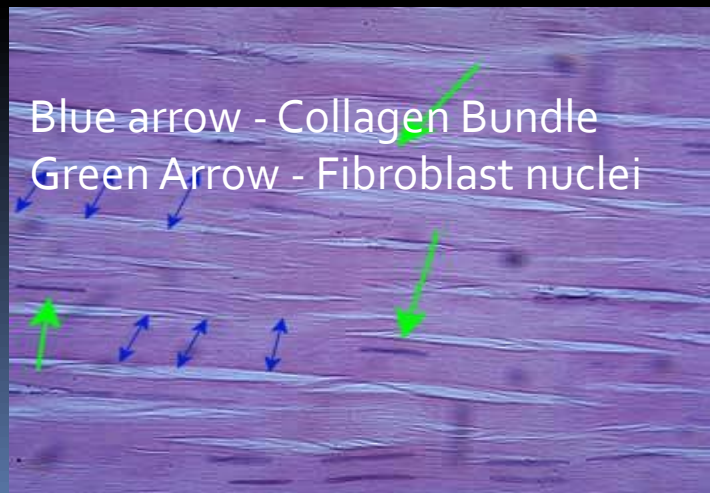
SCANNING EM OF COLLAGEN FIBER BUNDLES

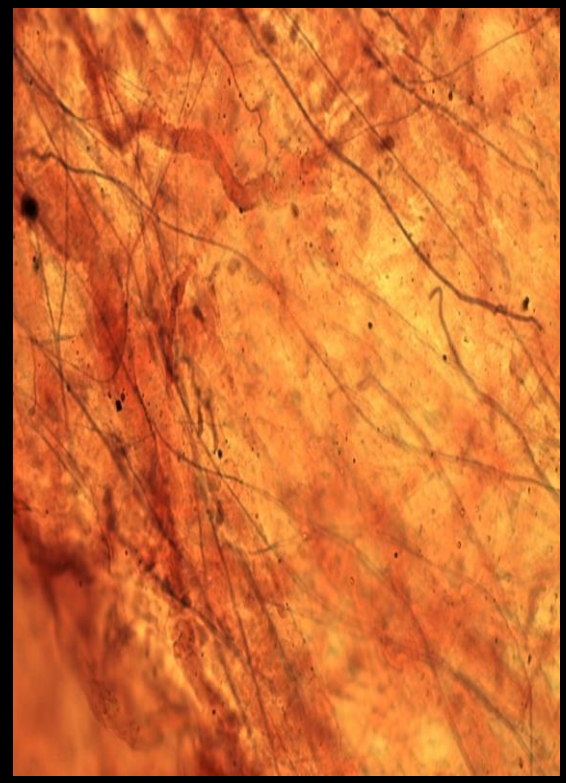
Collagen fibers

- In bundle forms, thickness 10-100 micrometer,
- Individual fiber Dm is 2-10 micrometer,
- Fibres composed of fibril made of microfibrils
- Fibril 0.2- 0.5 mm thick
- E/M has shown that each fibril consists of microfibrils (unit fibers of collagen) having diameter 40 to 100 nm
- Micro fibrils made up Each microfibril is made up of long polypeptide chains that consist of tropocollagen-striations







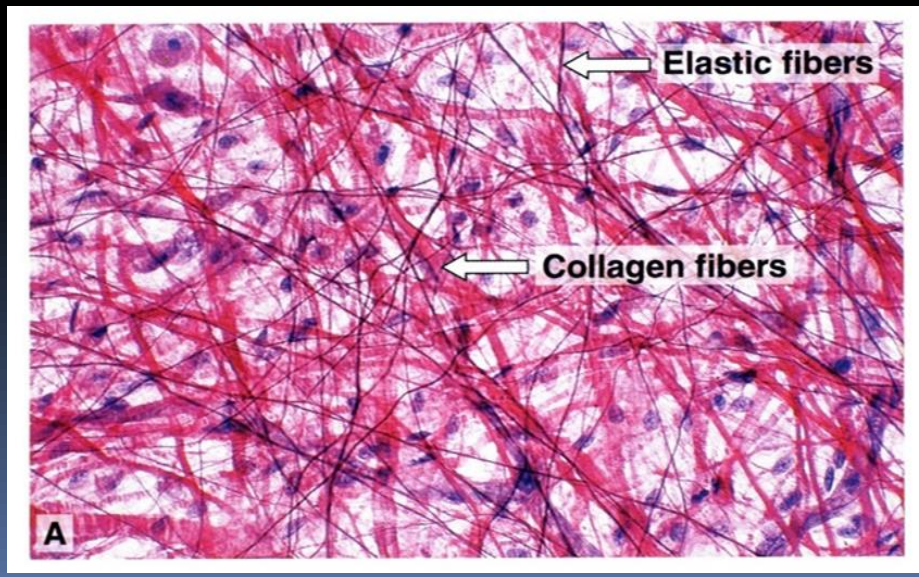


- Bundles branch but individual fibers donot branch
- Cross striations in collagen fibrils are due to

1.Staggered arrangement of collagen molecules

2.Presence of intermolecular gaps(20nm)

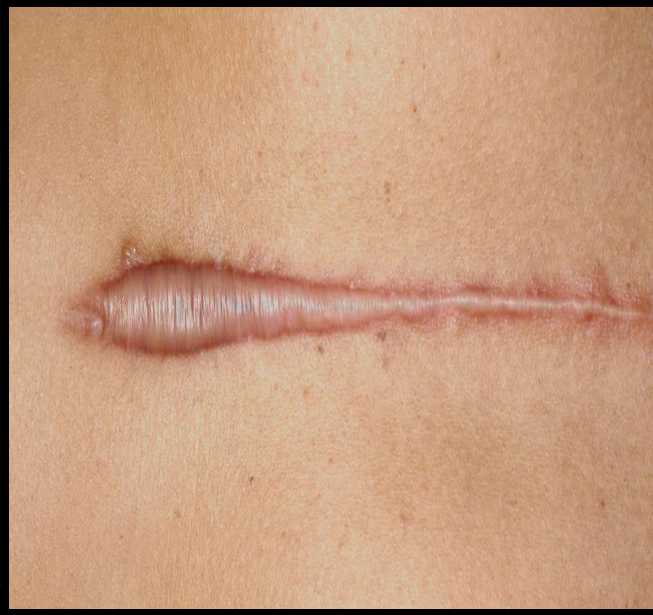
- In tissue sections fibers are colored pink to red by H.E., more specifically they are stained by acid fuchsin (red) and anilin blue

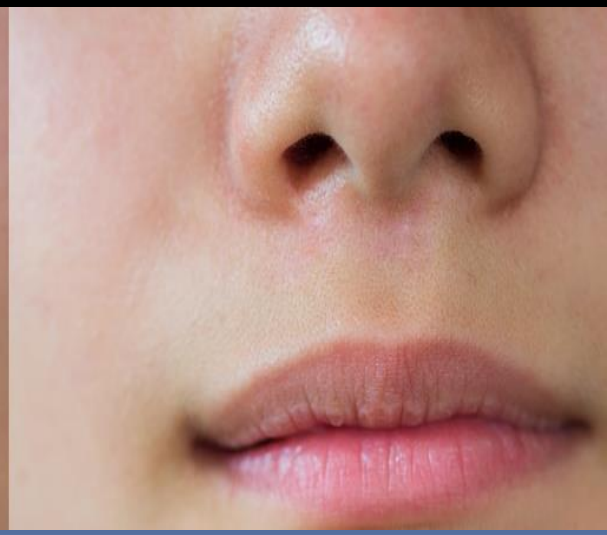


VERTICAL INTEGRATION

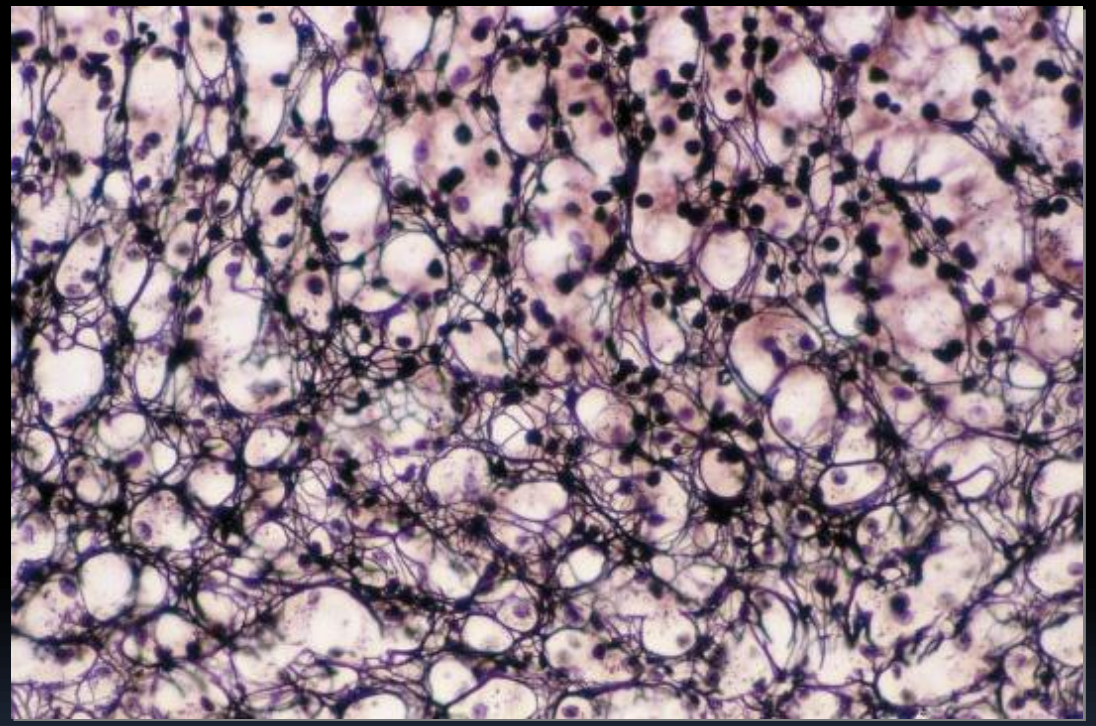
CLINICAL APPLICATION

- A keloid is a local swelling caused by abnormally large amounts of collagen that form in scars of the skin.
- It can happen if you have too much of a substance called collagen in your skin.
- It can happen after any sort of injury or damage to your skin such as a cut, burn, surgery, acne or a body piercing.



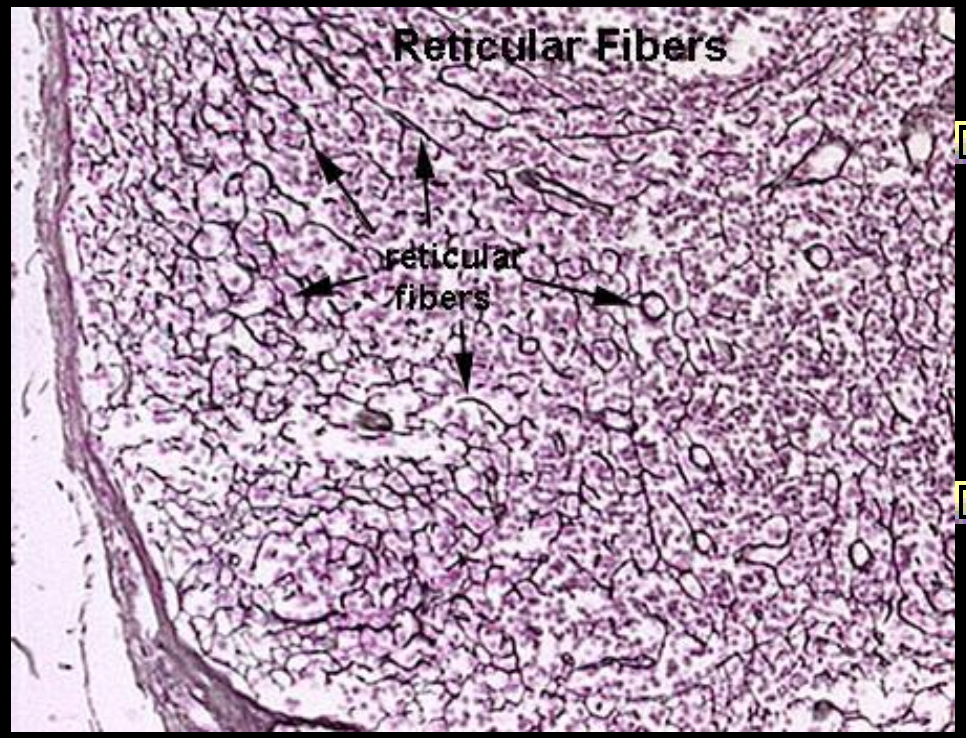


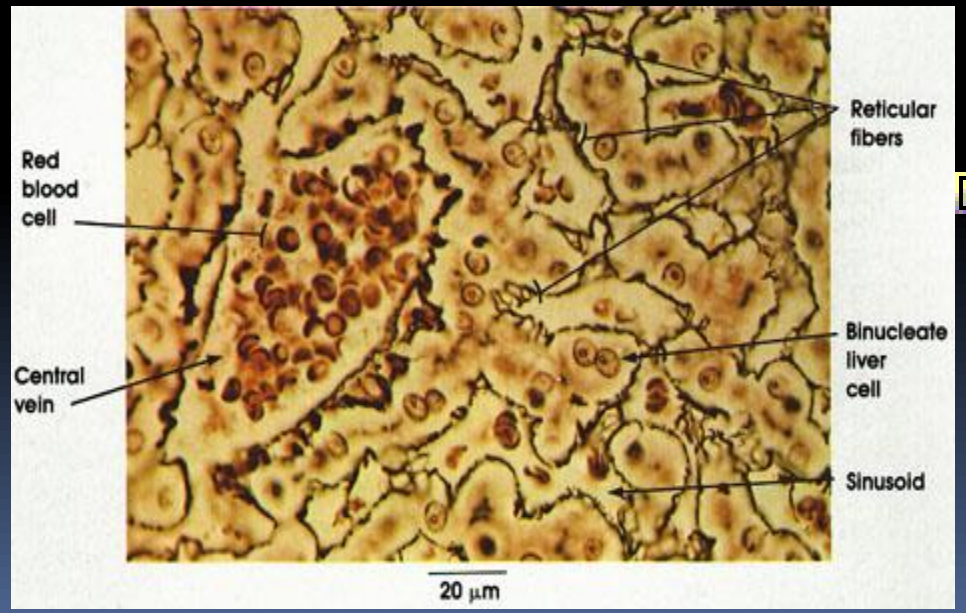
2.RETICULAR FIBERS



Section of an adrenal cortex, silver stained to show reticular fibers. Nuclei are black, and cytoplasm is unstained.

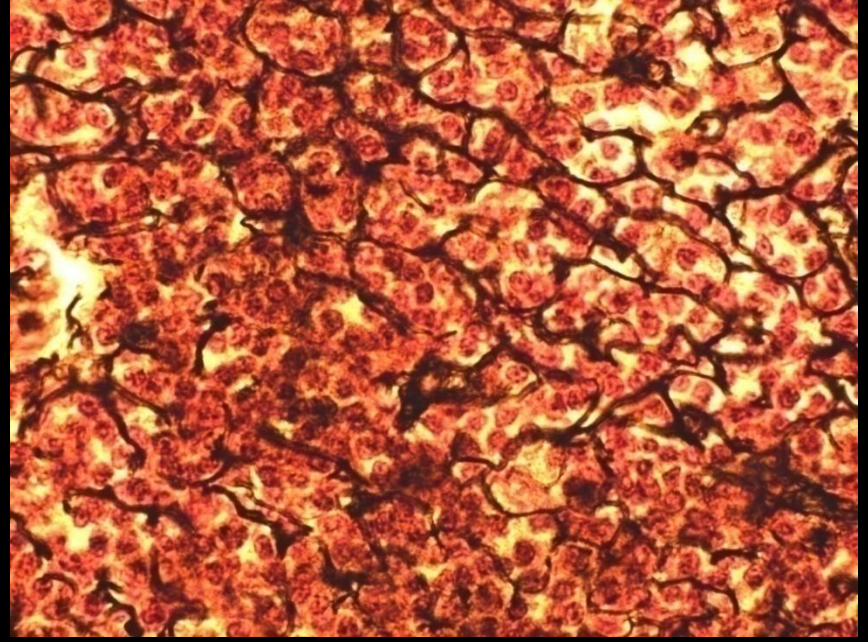
- Extremely thin fibers (diameter 0.5-2 μm)
- Mainly consist of type iii collagen
- Reticular fibers are named for their arrangement in a mesh-like pattern or extensive network (Latin ; Rete=net)
- They have a spider web appearance and appear black under stain.
- Branch





- Not distinguishable in ordinary H&E staining due to their thinness.
- Can be visualized with PAS staining (periodic acid schiff), seen as red strands by due to presence of carbohydrates
- Called argyrophilic fibers because of their high affinity for silver salts.

- Produced by fibroblasts & reticular cells.
- Found in CT throughout the body
- Abundant in CT surrounding the muscle fibers, nerve fibers, acini of glands, lymphoid organs & bone marrow
- Also form supporting framework of lymphoid organs and bone marrow



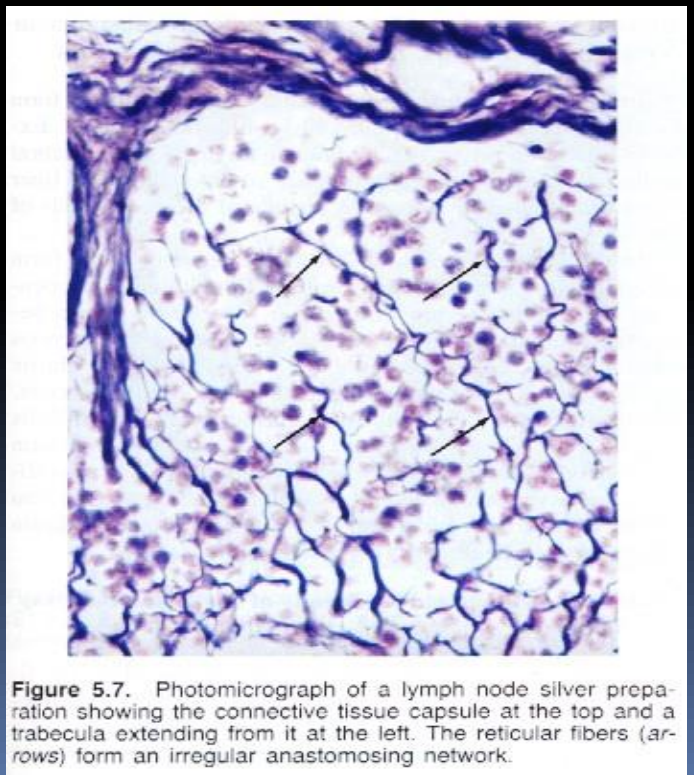
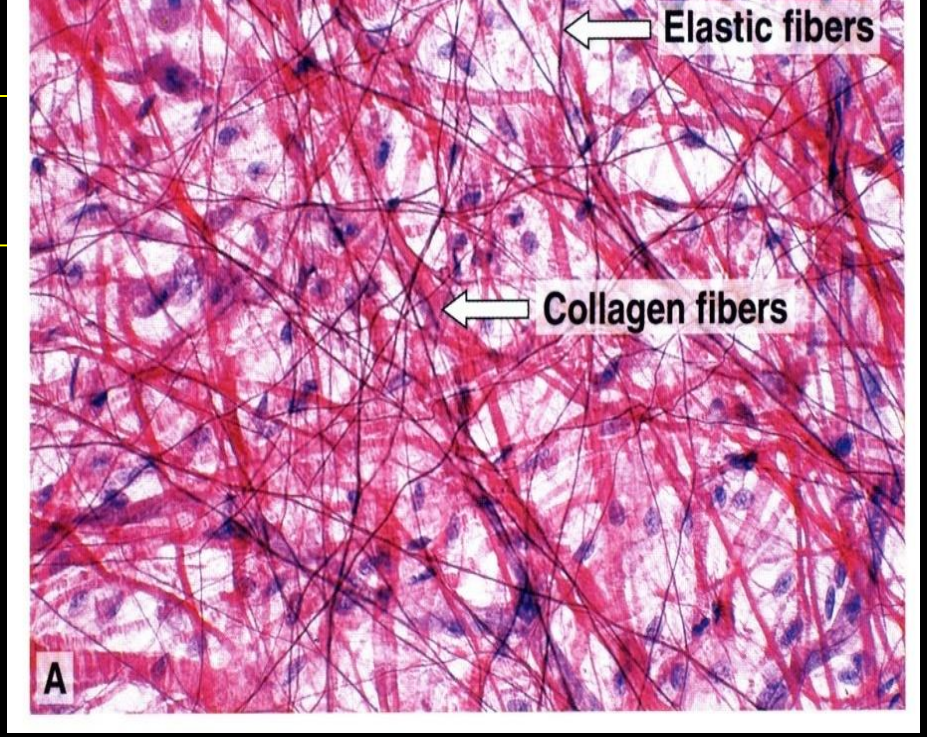
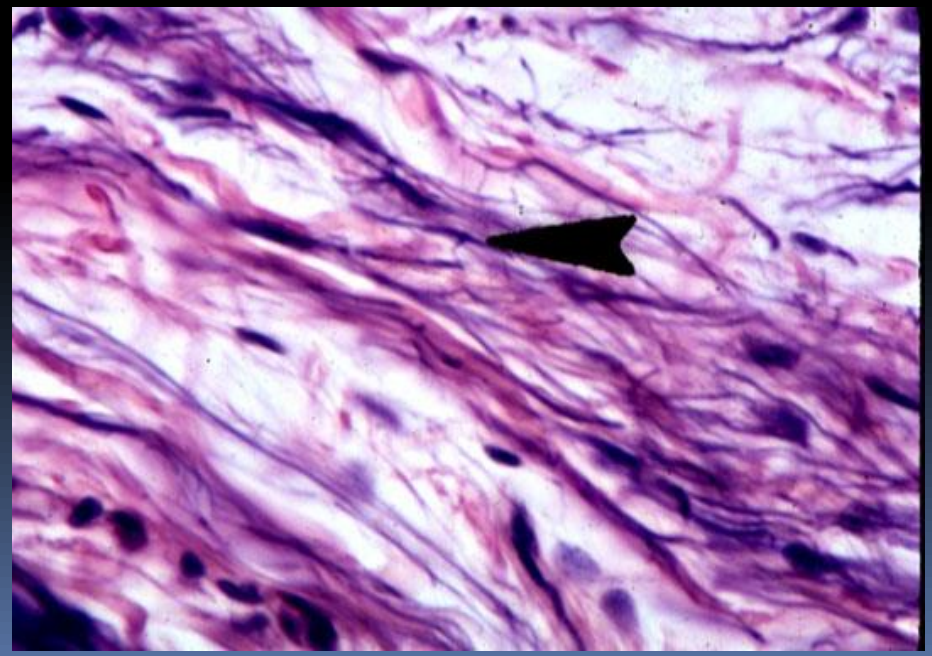


Figure 5.7. Photomicrograph of a lymph node silver preparation showing the connective tissue capsule at the top and a trabecula extending from it at the left. The reticular fibers (*arrows*) form an irregular anastomosing network.

3. ELASTIC FIBERS

- Typically ***thinner*** than collagen fibers
- Arranged in ***branching pattern*** to form a three dimensional network
- Interwoven with collagen fibers
- Rare but important
- Imparts yellow colour





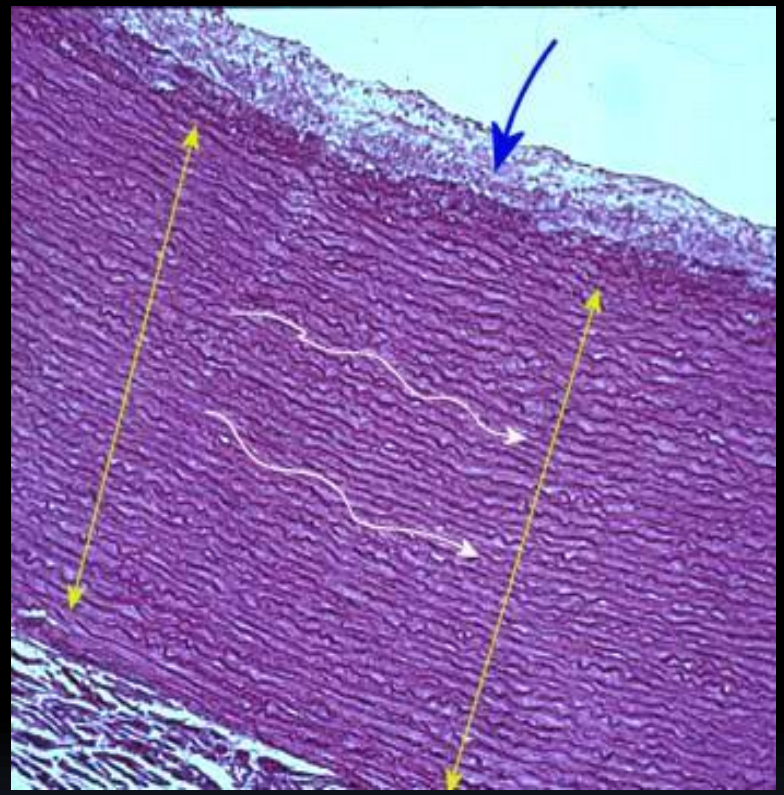
Elastic fibers

- Composed of elastin protein
- Singly present
- Branched and anastomose forming a network
- Synthesized by fibroblast and smooth muscle cells in blood vessels
- Highly elastic can stretch one and half time their original length
- Diameter (0.2 to 1.0 mic.m)
- Found in lungs, large arteries, ligamenta flava (connecting laminae of successive vertebrae)

Elastic fibers

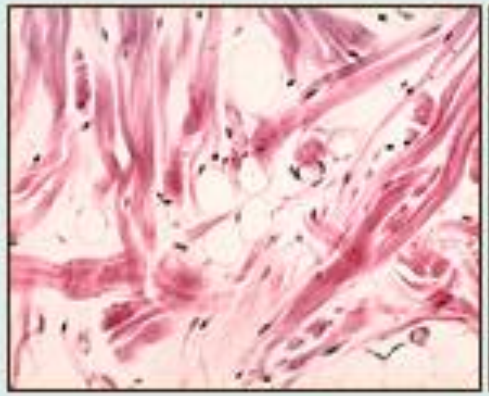
- They are thin flexible fibers made from the protein elastin, that generally stain black.

- Composed of two ***structural components***
  - Elastin
  - Fibrillin 1

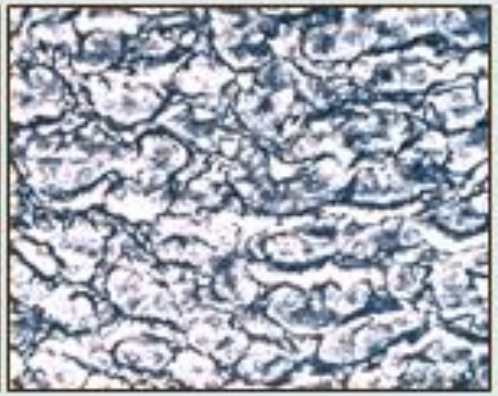


Elastic fibers are composed of the protein elastin. These fibers stretch easily and appear wavy, curly, and black.

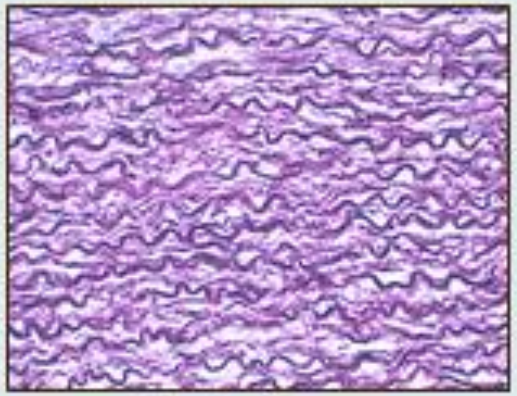
Note: each connective tissue fiber type requires different staining method!



collagen fibres
(HE)

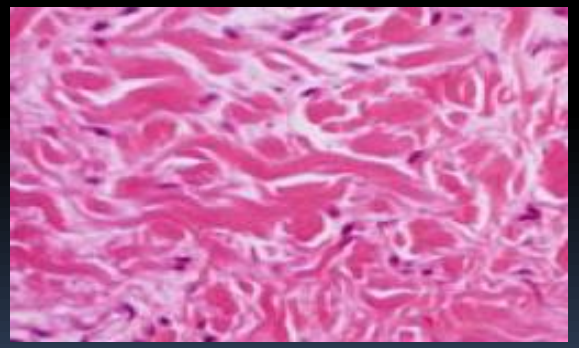
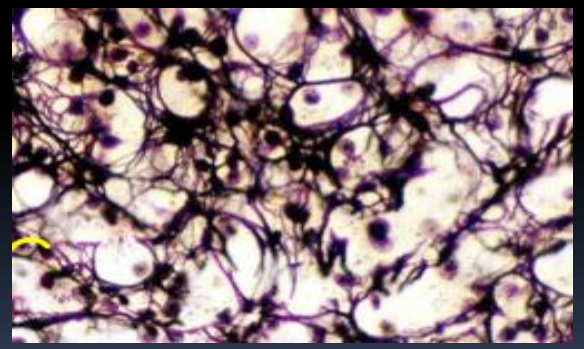
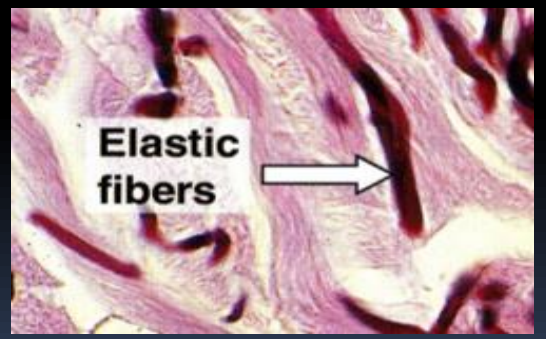


reticular fibres
(silver-impregnation)



elastic fibres
(resorcin-fuchsin)

❑ Fibers (Review)

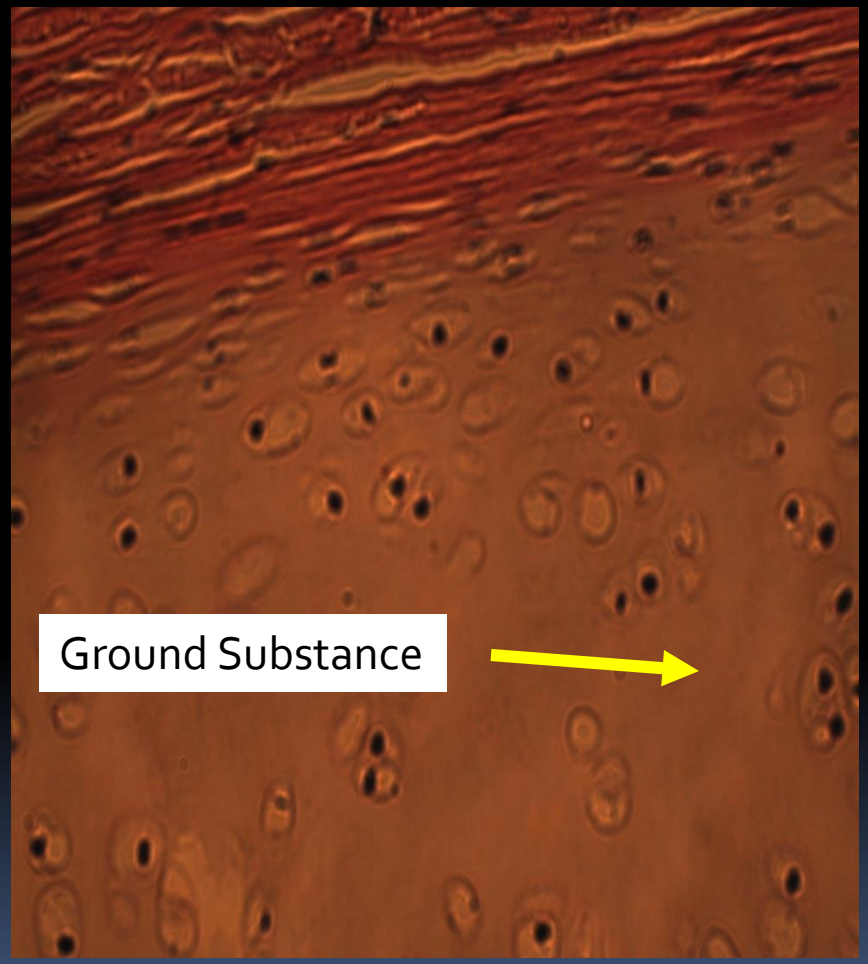
1) Collagen Fibers	2) Reticular Fibers	3) Elastic Fibers
• Made of **collagen type I**	• Made of **collagen type III**	• Made of **elastin**
• Non-branched fiber , arranged in bundles *bundles form the branch.	• Branch and form a network	• Branched
• Acidophilic	• Stained black with silver	• Stained brown with orcein
		

➢**Other important types of collagen include:**

1- type II (in cartilage). 2- type IV (in basement membranes)

GROUND SUBSTANCE

Ground Substance



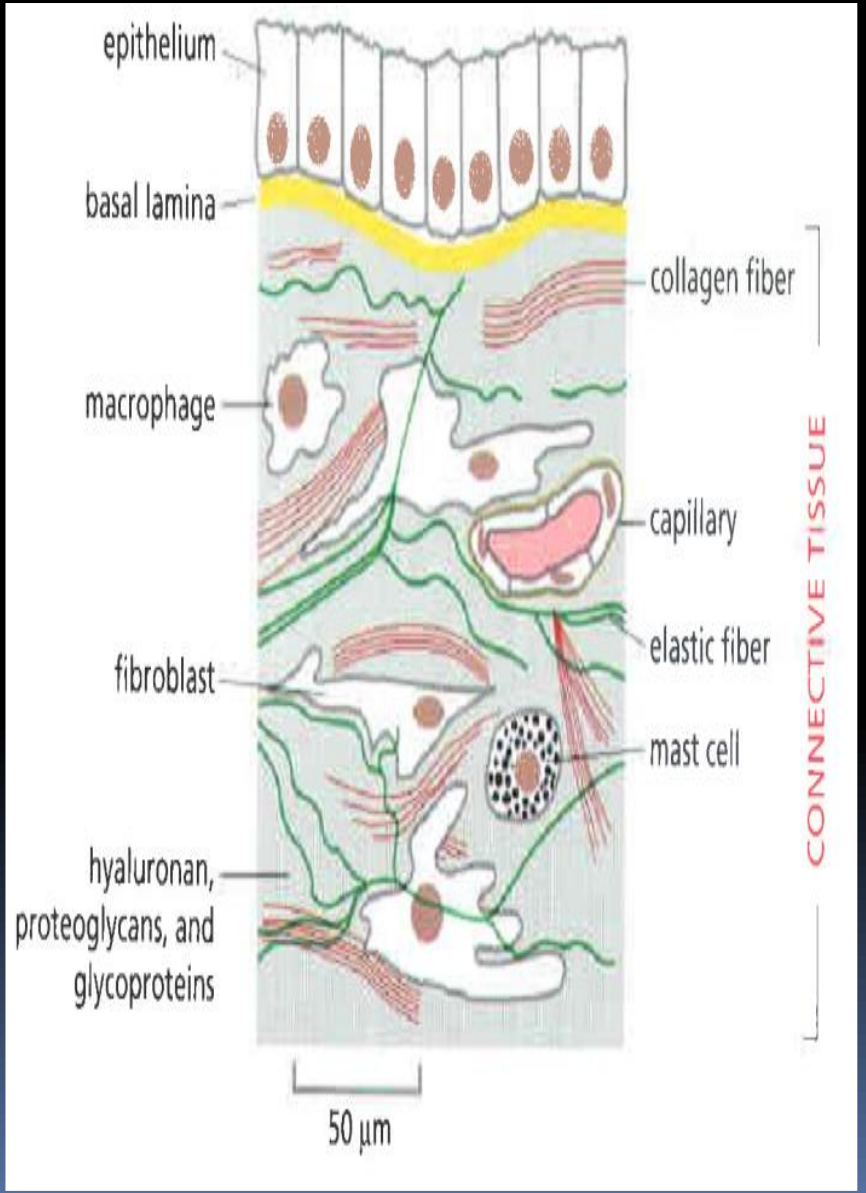
- Cells and fibers are embedded in an amorphous back ground material called ground substance.
- Gel like material with high water content
- Fills the space between cells & fibers of CT
- Highly hydrated, colorless & transparent
- The ground substance holds large amounts of fluid and serves as a medium through which nutrients and other substances can diffuse between blood vessels and the cells.

EXTRA-CELLULAR MATRIX

- **Ground Substance**

Composition:

- Mucopolysaccharides/Glycosaminoglycans
- Structural Glycoproteins &Proteoglycans
- Water & Electrolytes

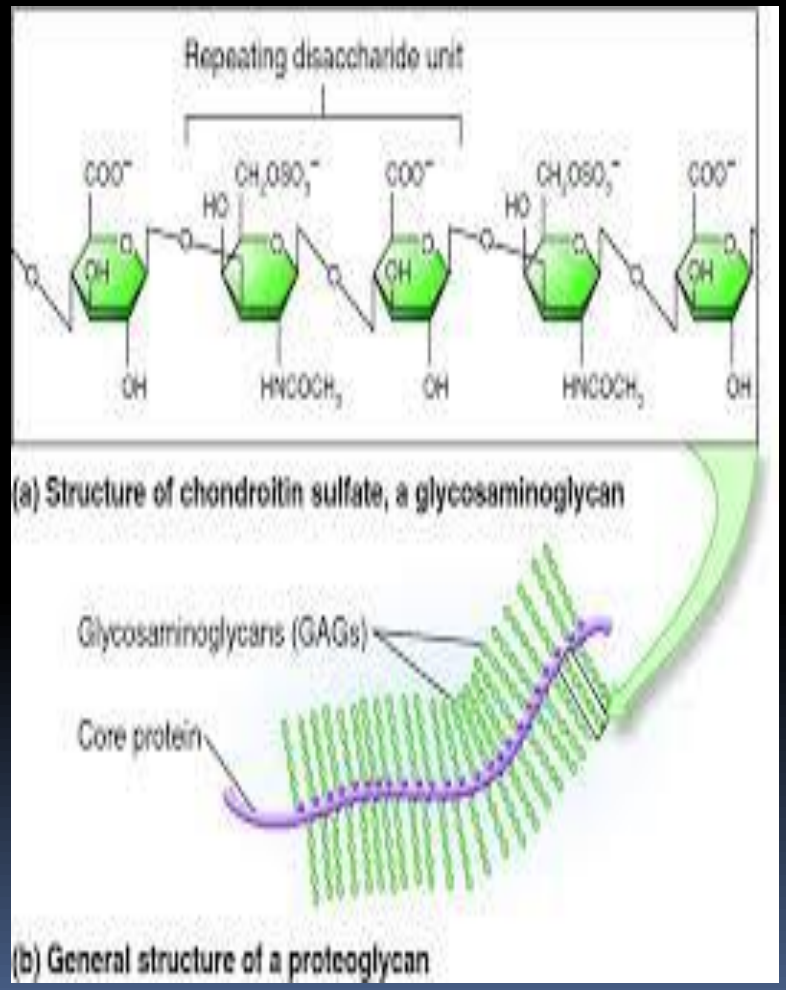


1. GLYCOSAMINGLYCANS

- Long chain polysaccharides composed of repeating diasaccharide units.

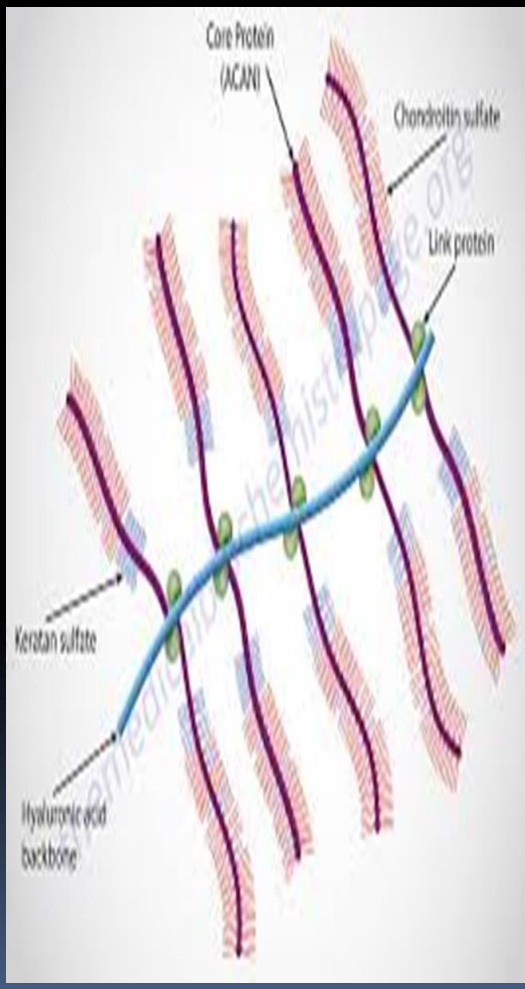
- There are at least seven glycosaminoglycans (GAGs), Hyaluronic acid, Keratin sulfate and chondroitan sulfate I and II, heparin, heparan sulfate and dermatan sulfate.

- Largest is hyaluronic acid



2. PROTEOGLYCANS

- Core protein to which sulfated gags attached
- They are synthesized on RER, mature in the Golgi, where the GAG side chains are added, and secreted from cells by exocytosis
- Structurally, proteoglycans resemble bottlebrushes, the protein core being the stem and the radiating glycosaminoglycan chains the bristles.
- Negative charge of GAGs attract sodium which attract water thus matrix is hydrated



3. GLYCOPROTEINS (adhesive)

- Binding sites for collagen, proteoglycans, gags
- Fasten various components of connective tissue with each other

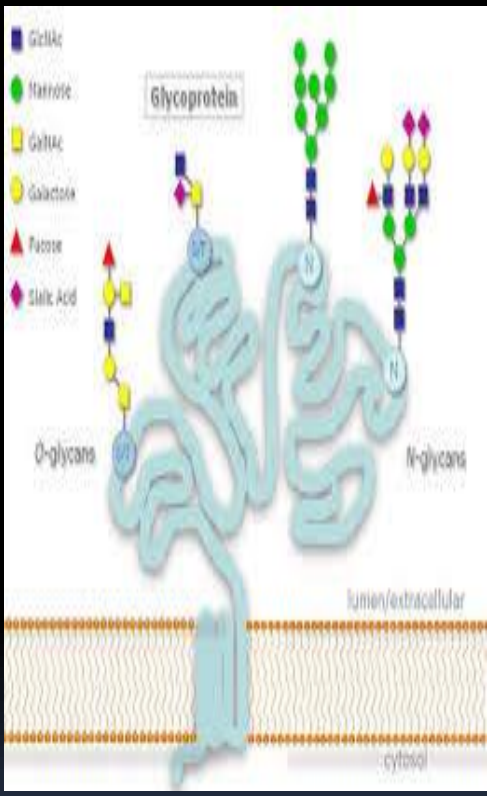
Types

Fibronectin, Laminin,Chondronectin, Osteonectin

Functions:

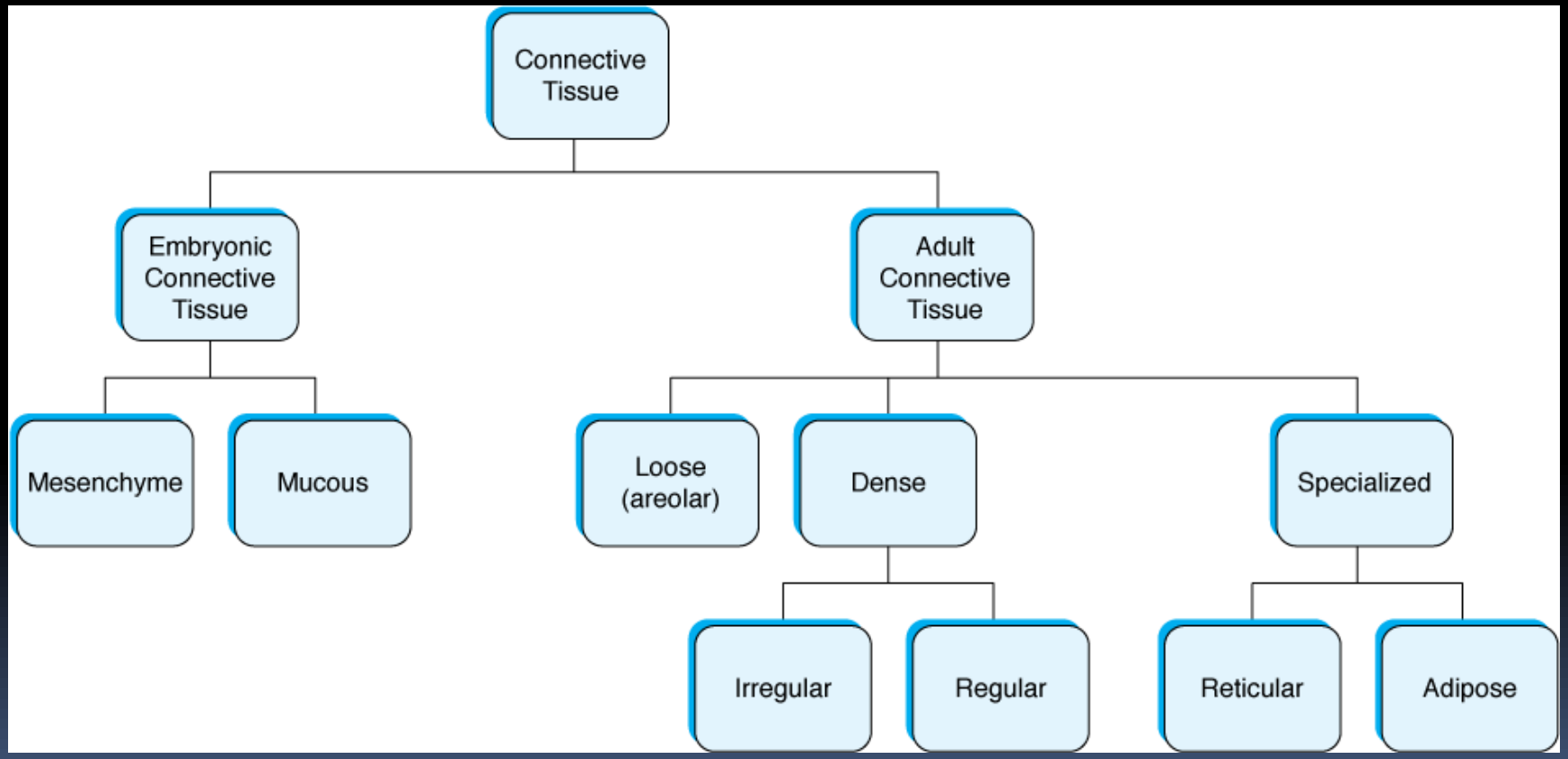
1.They have (fironectin and laminin) have binding sites for collagens and for integrin proteins in cell membranes, thus allowing temporary attachments between cells and the ECM ; required for cell migration and positioning.

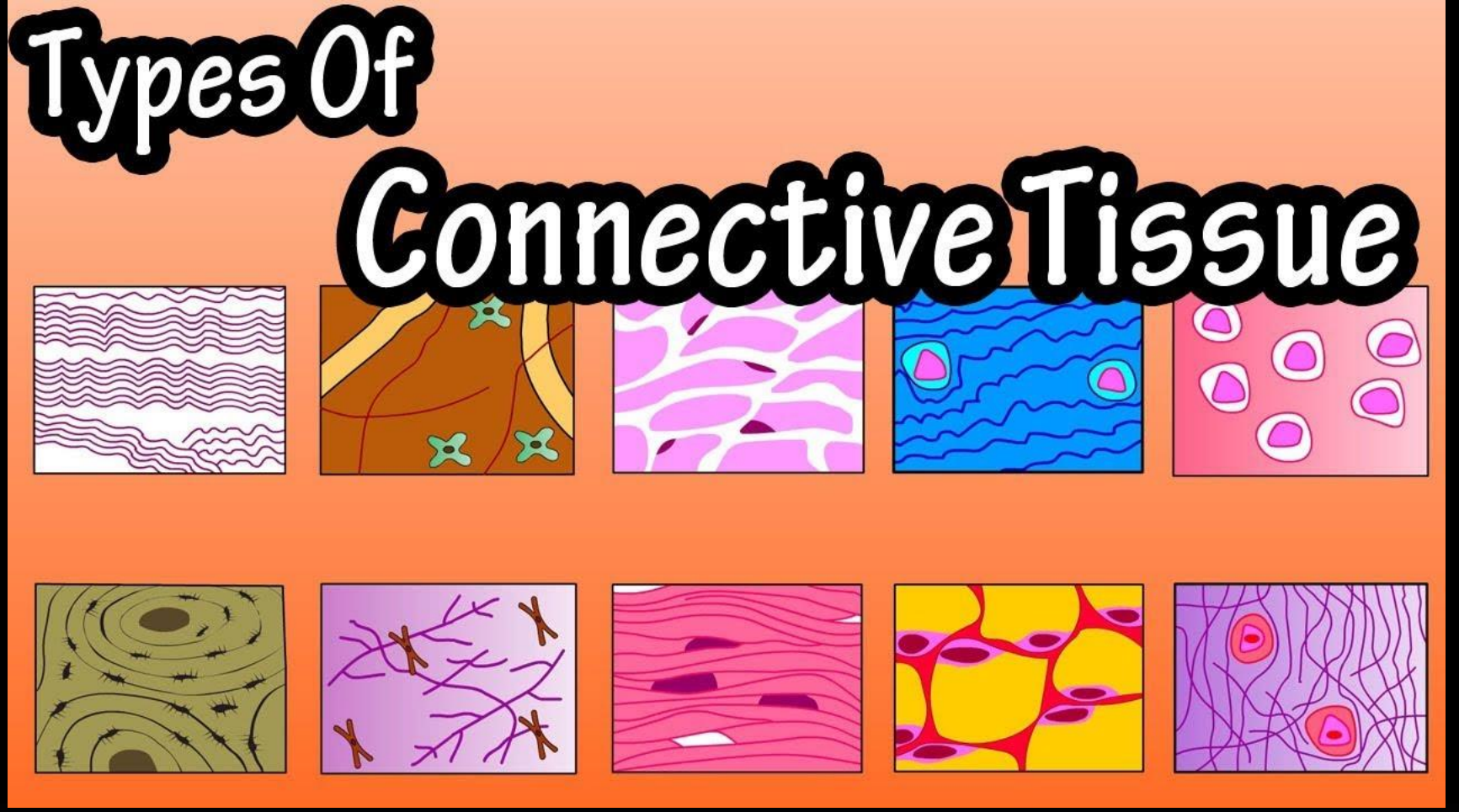
2.They bind to receptor proteins called integrins ie located on plasmalemma of cell



(Glycoproteins are proteins to which carbohydrates are covalently linked through glycosidic bonds. Proteoglycans are a subclass of glycoproteins with distinctive features of carbohydrate structure)

Classification of Connective Tissue





Connective Tissue Proper

Loose/Areolar Connective Tissue

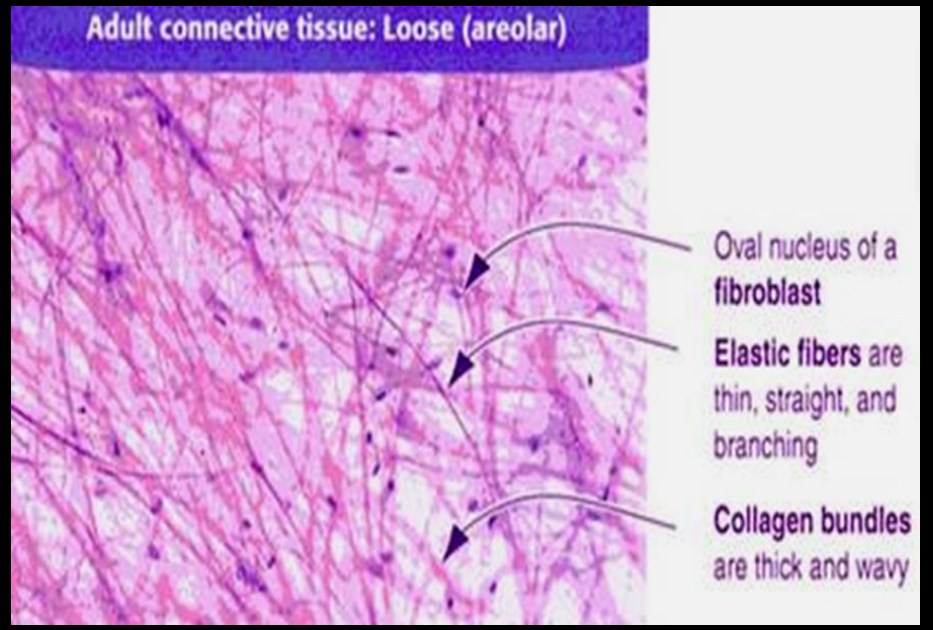
- Widely distributed in the body
- Highly vascular
- More flexible & offers less resistance to stresses.

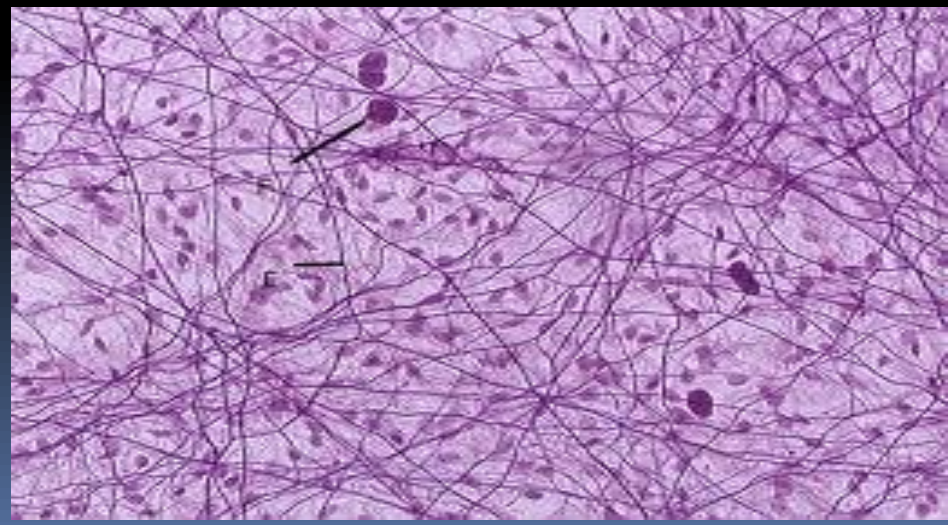
Cell component.

- Has cells ,fibers and ground substance in equal parts
- Fibroblast and macrophages abundant.
- Mast cells and adipocytes also present

Fibrous component

- Collagen fibers abundant
- Elastic fibers and few reticular fibers.





Loose/Areolar CT

Found in:

superficial & deep fascia ,Omentum, mesentry, pleural membrane.

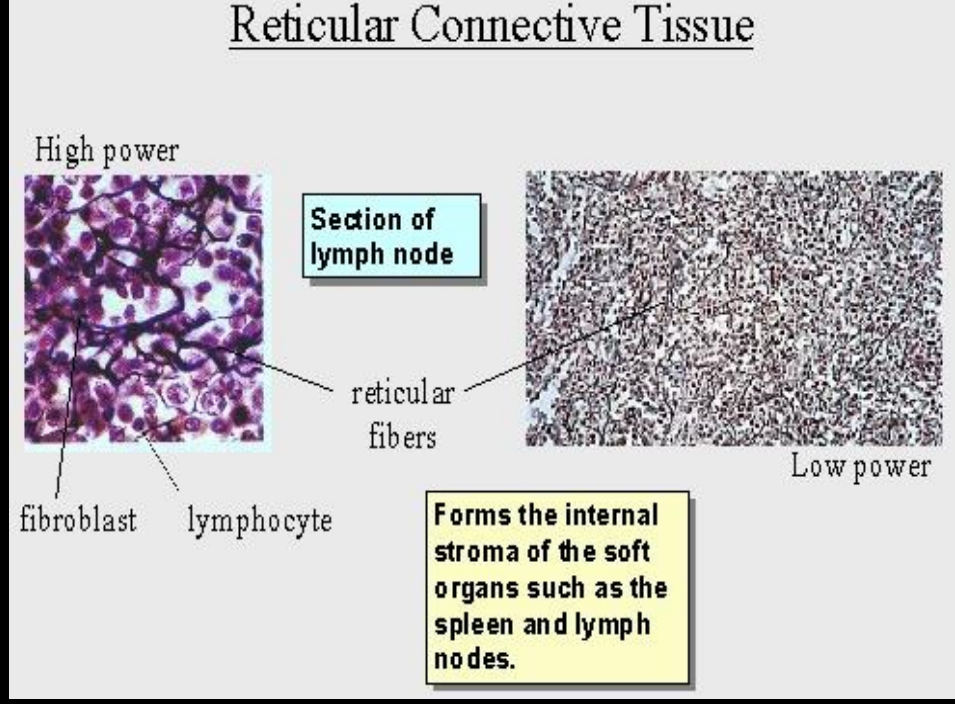
Functions:

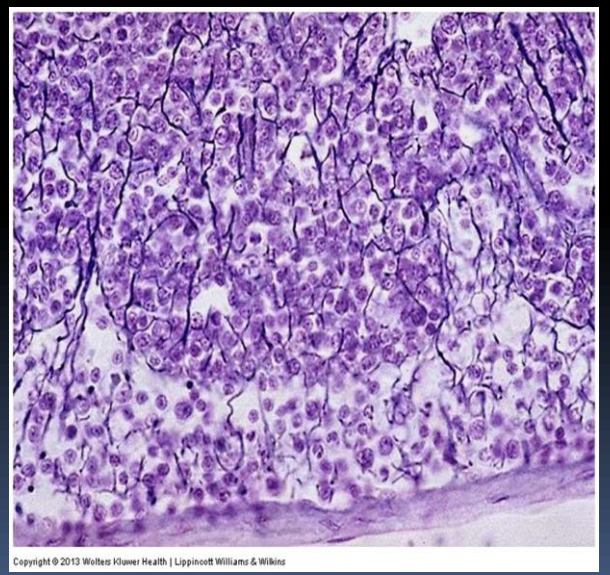
- Helps to form the subcutaneous layer
- Serves to support most epithelium
- Fills spaces between organs & supports epithelium
- Forms a layer that separates skin from deeper structures like muscles
- Wraps and cushions organs "packing material"
- Macrophages phagocytize bacteria
- Holds and conveys tissue fluid.
- Highly vascularized, shots given in this tissue for quick transport of drugs

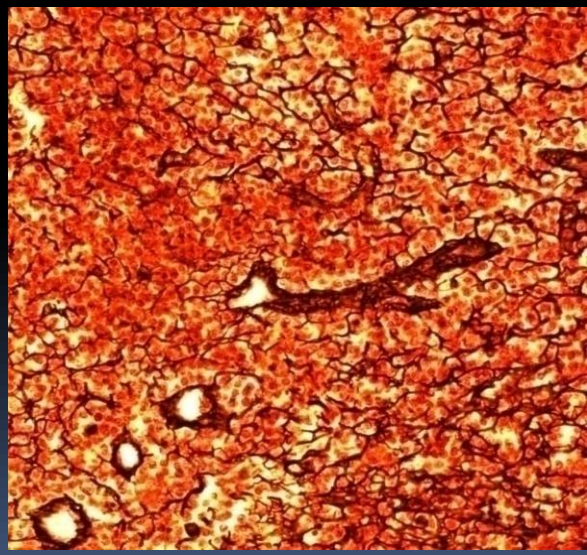
Reticular Tissue

Structure –

- A network of reticular fibers with macrophages interspersed.
  - Reticular Connective Tissue – made of interlacing reticular fibers and reticular cells that connect to each other to form a network.
    - Used to bind together smooth muscle cells and to filter out worn out blood cells and bacteria
    - Thus cells and fibers form spongy network

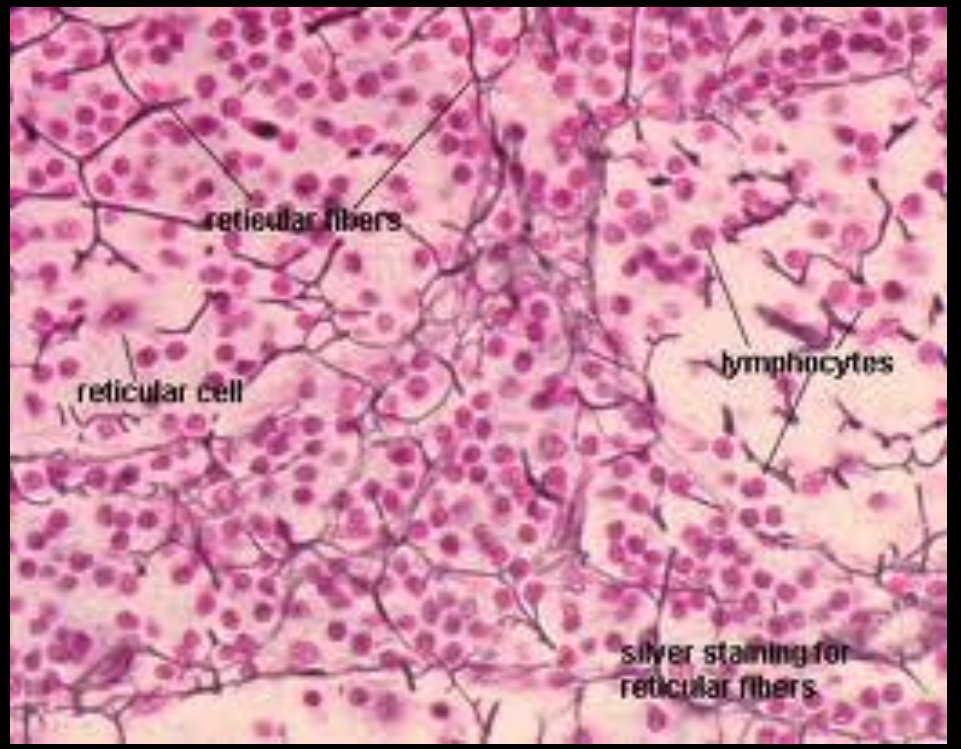






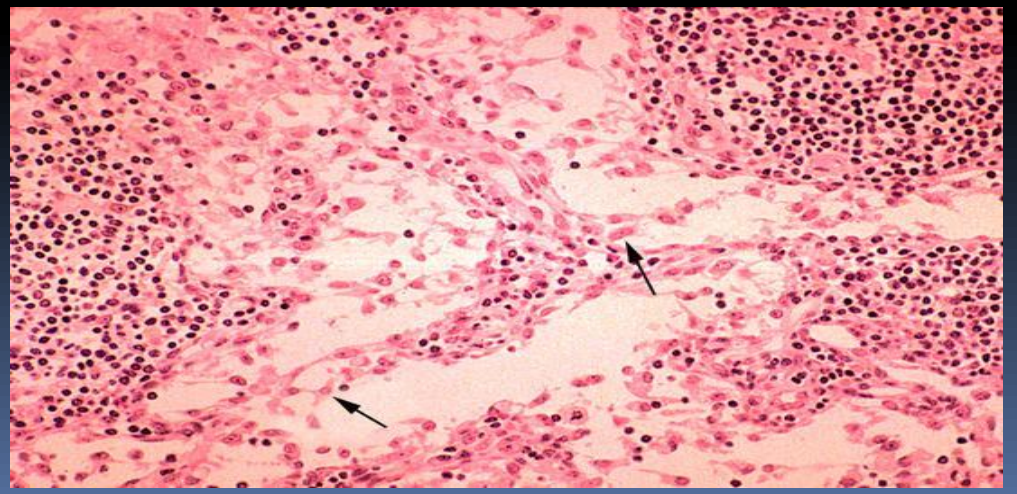
Reticular Connective Tissue

- **Consists of fine interlacing reticular fibers:**
- collagen type lll
- Arranged in mesh like network



Reticular Cells—

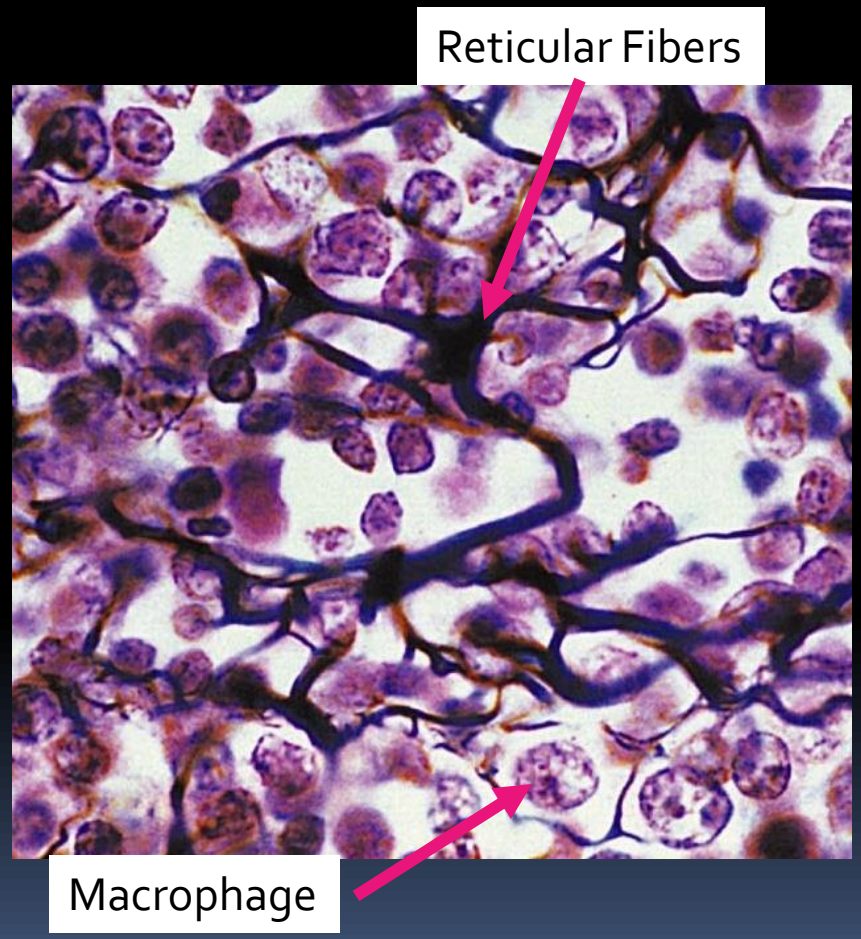
- Special variety of fibroblast
- Satellite shape & have long processes.



Reticular Tissue

Location –

- Spleen
- Lymph nodes
- Liver
- Found in Bone marrow, lymph node & spleen

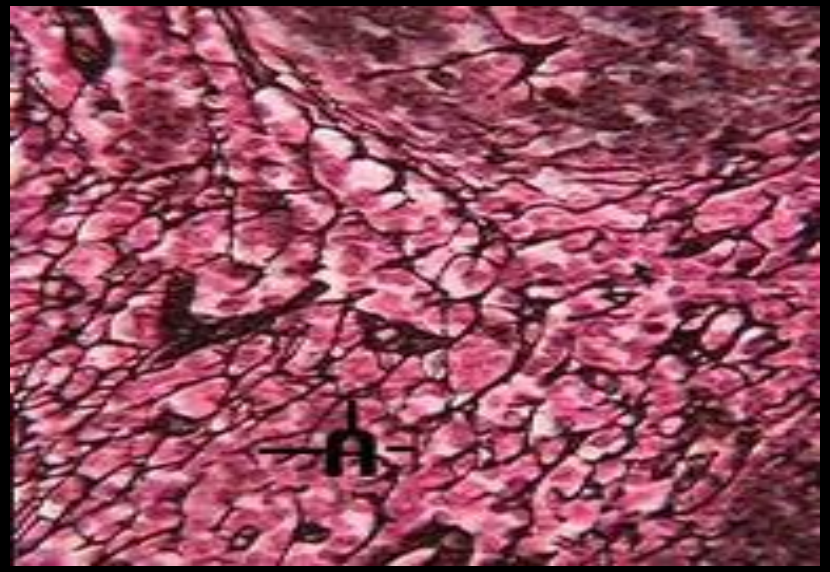


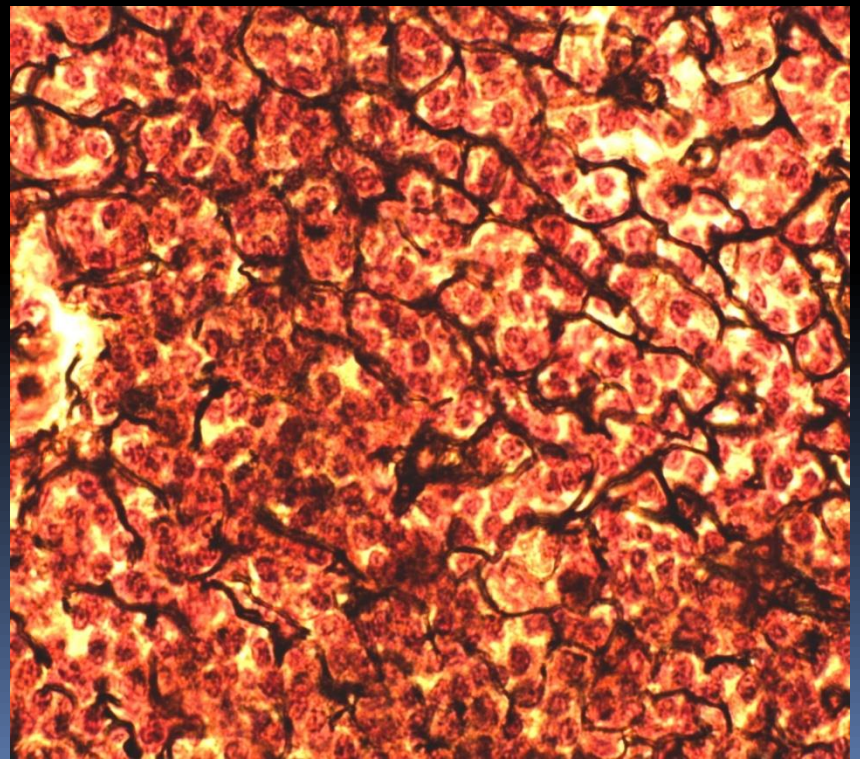
Reticular Tissue

Functions:

Forms the framework (stroma) of organs and binds together smooth muscle tissue cells. Processes of reticular cells make contact with each other and with reticular fibers.

- In Lymph Nodes – macrophages devour bacteria, viruses and cancer cells.
- In Spleen – macrophages break down dying RBC's.
- In Liver – macrophages (Kupffer cells) devour bacteria.
- This tissue forms a soft internal skeleton that supports other cell types.



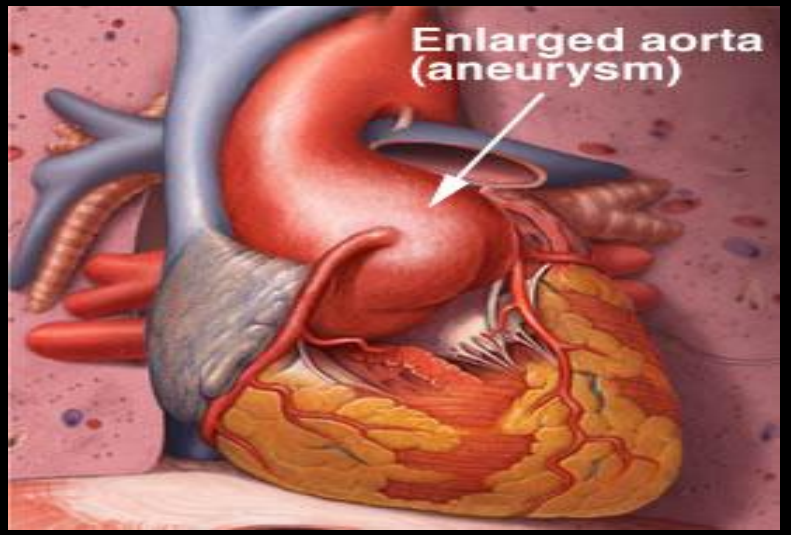


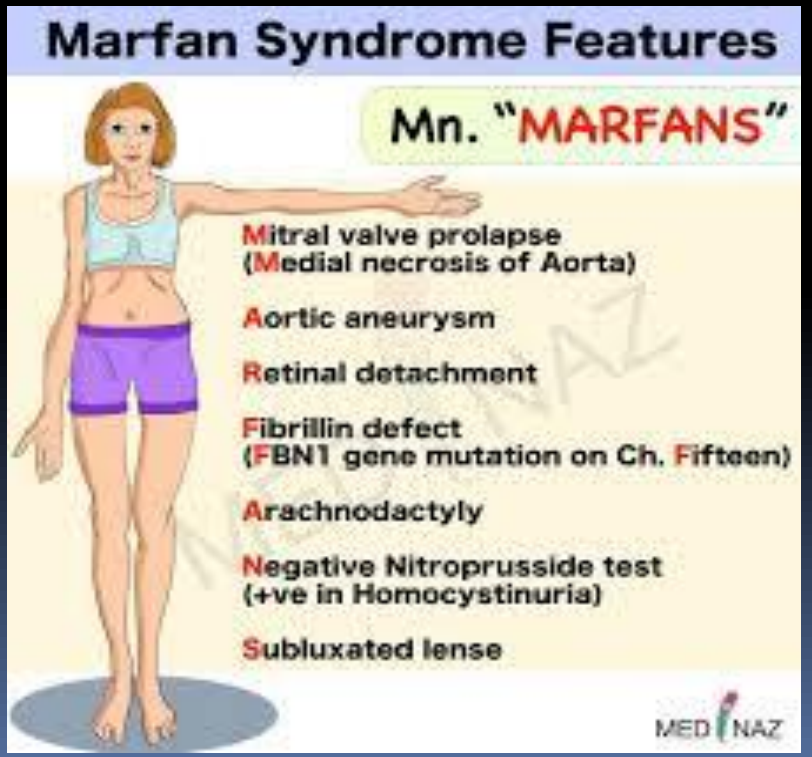
Disorders of connective tissue

VERICAL INTERGATION

Marfan Syndrome

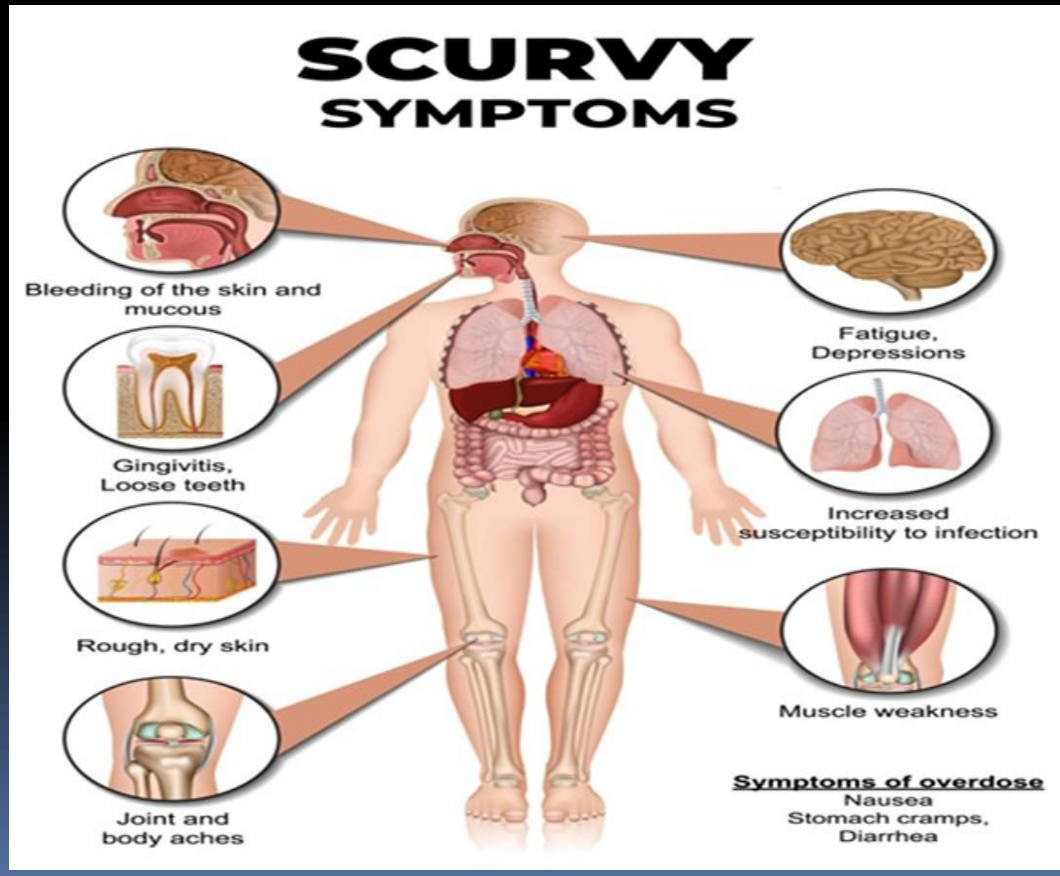
- Genetic disorder that effects the production of connective tissue /causing abnormal fibrillin
- Defective elastic fibers
  - Effects just about every system in the body
  - Especially dangerous for blood vessels: collapse and/or bursting of aorta
  - Spontaneous pneumothorax – collapsed lungs, believed to be related to subtle abnormalities in connective tissue





SCURVY

Scurvy - dietary deficiency in Vit.C leading to abnormal collagen.



Ehlers-danlos syndrome

- A genetic disease causing progressive deterioration of collagens affecting different sites in the body such as joints, heart valves & arterial walls

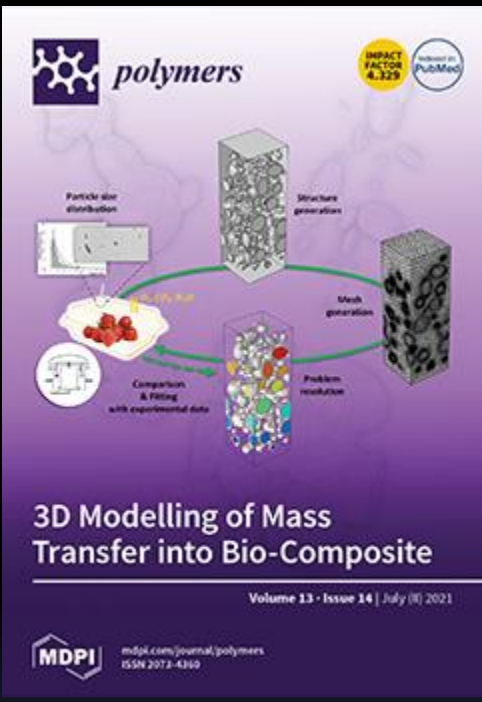
TAKE HOME MESSAGE

- **Core Bioethical Principles:**
  The first 2 can be traced back to the time of Hippocrates "to help and do no harm," while the latter 2 evolved later.
  "Every human being has a right to determine what shall be done with his own body"
  According to Aristotle "giving to each that which is his due".
  Everyone should qualify for equal treatment

Title: A Review of the Effects of Collagen Treatment in Clinical Studies

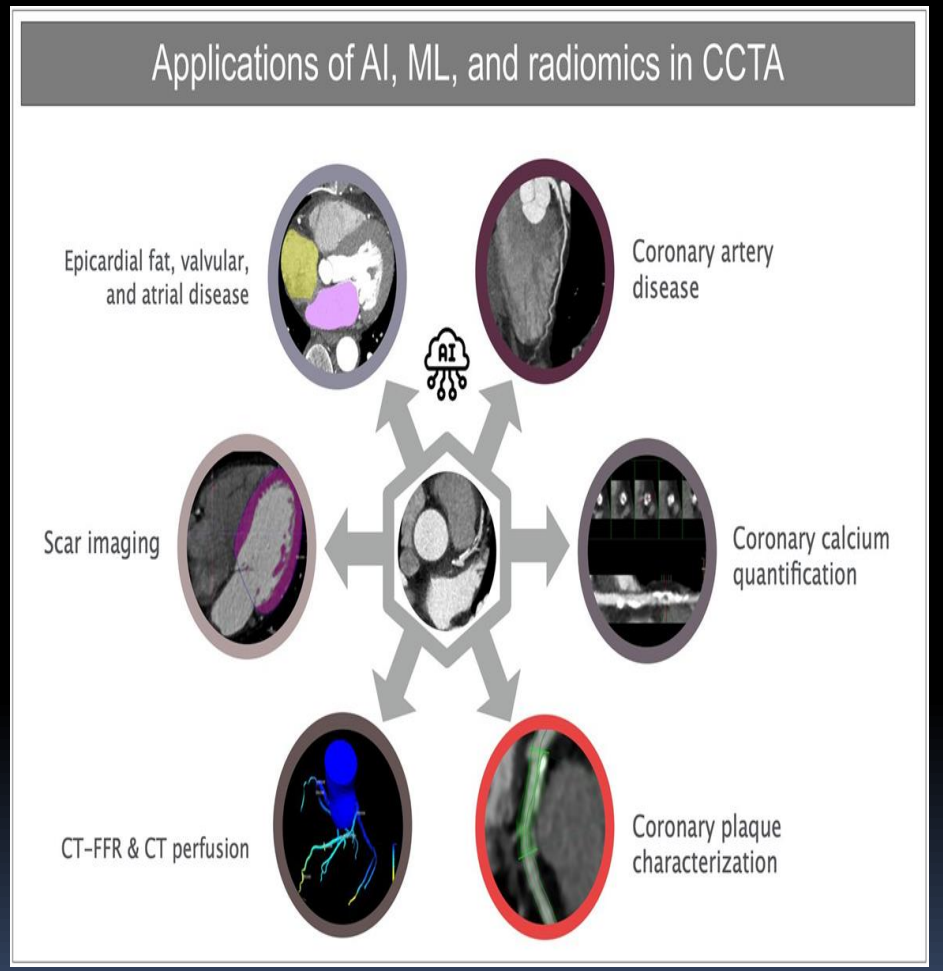
Cite:Wang H. A Review of the Effects of Collagen Treatment in Clinical Studies. Polymers (Basel). 2021 Nov 9;13(22):3868. doi: 10.3390/polym13223868. PMID: 34833168; PMCID: PMC8620403.Abstract

Abstract: Collagen, an abundant extracellular matrix protein, has been found to have a lot of pharmaceuticals, medicine, food, and cosmetics applications. Increased knowledge of collagen sources, extraction techniques, structure, and properties in the last decades has helped develop more collagen-based products and tissue engineering biomaterials. Collagen products have been playing an important role in benefiting the health of the human body, especially for aging people. In this paper, the effects of collagen treatment in different clinical studies including skin regeneration, bone defects, sarcopenia, wound healing, dental therapy, gastroesophageal reflux, osteoarthritis, and rheumatoid arthritis have been reviewed. The collagen treatments were significant in these clinical studies.....



Role Of Artificial Intelligence

- Early Detection and Diagnosis: AI algorithms can analyze medical imaging such as echocardiograms, MRI scans, and CT scans to detect signs of Marfan's disease at an early stage.
- These algorithms can identify subtle abnormalities in the heart, blood vessels, and other affected organs, helping physicians make accurate diagnoses sooner.



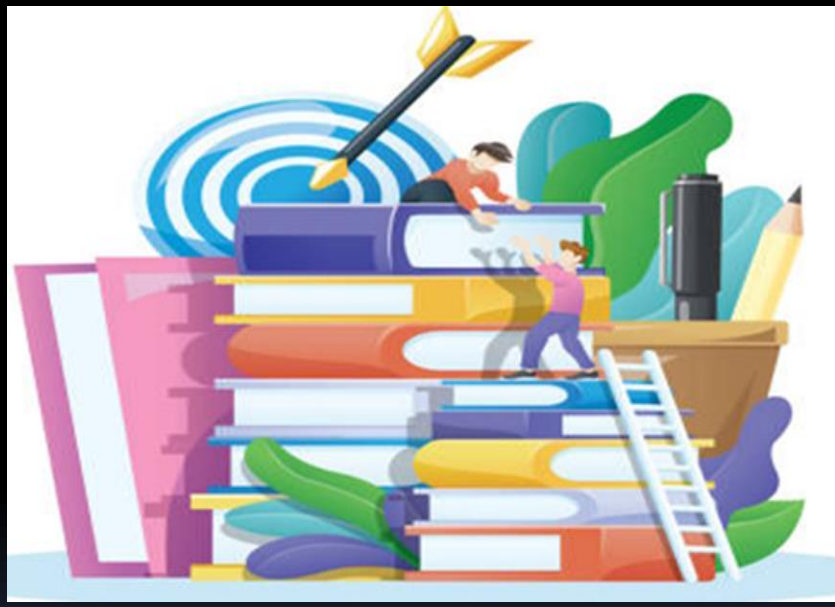
How to use the digital library

Steps to Access HEC Digital Library

- Go to the website of **HEC National Digital Library**.
- On Home Page, click on the **INSTITUTES**.
- A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library (HNDL).
- Select your desired Institute.
- A page will appear showing the resources of the institution
- Journals and Researches will appear
- You can find a Journal by clicking on **JOURNALS AND DATABASE** and enter a keyword to search for your desired journal.

Learning Resources

- Junqueira's Basic Histology 12th Edition
- Histology , A text and Atlas by Michael H.Ross
- Histology by Liaq Hussain
- Google scholar
- Google images



BY Prof Dr. SAIMA NAZ