

Connective tissue

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Supporting tissues

Characteristics: cells are dispersed, the tissues are dominated by an intercellular substance produced by the cells (**extracellularis matrix, ECM**), The ECM is composed of fibers and a macromolecular network.

Functions: mainly determined by th ECM, primarily mechanical, supporting. They form the skeletal system of the body.

Supporting tissues

Connective tissue

Cartilage tissue

Bone tissue

Connective tissues (used in the English textbooks)

Connective tissue proper

Adipose tissue,

Cartilage tissue,

Bone tissue,

Blood and hemopoetic tissue,

Lymphatic tissue

The connective tissue proper

(presented on the example of the loose connective tissue)

1. Connective tissue cells

A.) Fixed cells

Fibroblast, fibrocyte
Fat cell
(Melanocyte)

B.) Mobile (free) cells

Macrophage
Mast cell
Lymphocyte
Plasma cell
Neutrophilic granulocyte
Eosinophilic granulocyte

2. Intercellular substance (extracellular matrix, ECM)

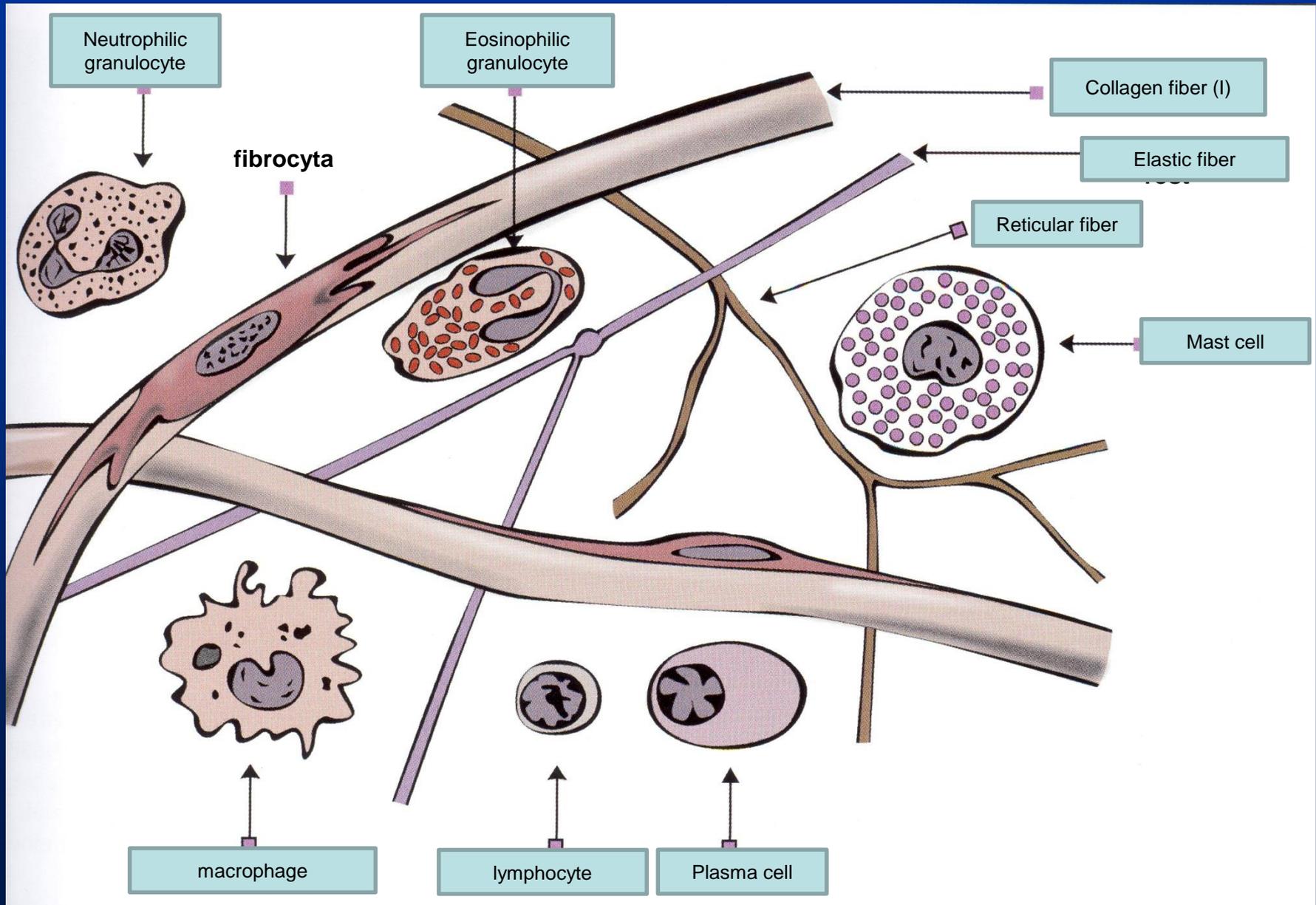
A.) Connective tissue fibers

Collagen fibers
Elastic fibers
Reticular fibers
Fibrillin

B.) Amorphous ground substance

Glucosaminoglycans (GAG)
Proteoglycans (PG)
Adhesion glycoproteins

Components of the loose connective tissue

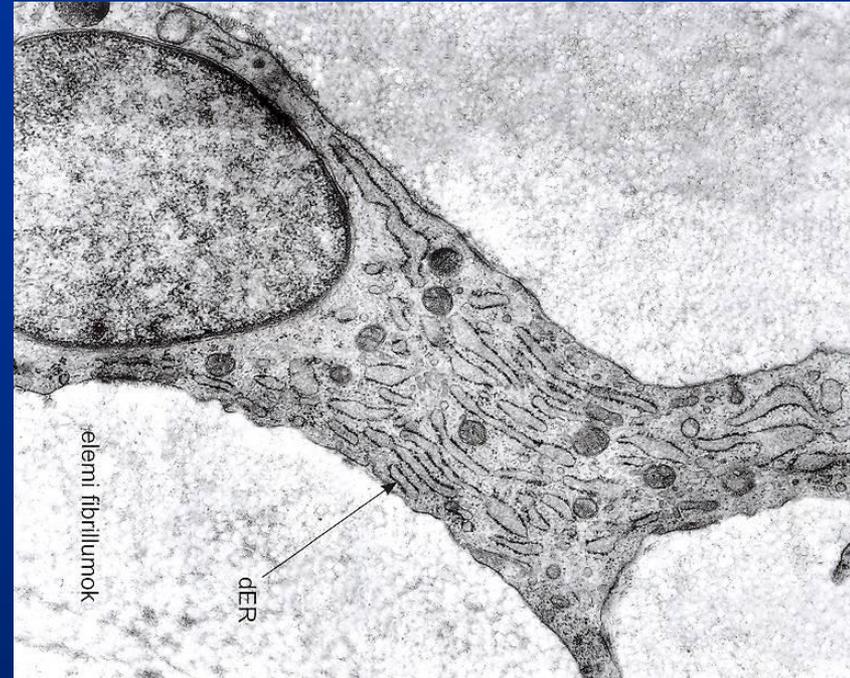


1. *Connective tissue cells*

Fibrocyte, fibroblast

Fibroblast. Connective tissue cell producing substance of the fibers and amorphous ground substance. Due to the intensive protein synthesis and presence of high number of ribosomes cytoplasm has a **basophilic** staining. EM: well developed **rough ER and Golgi apparatus, secretion vacuoles.**

Present during development of the connective tissue, regeneration of the c.t. during wound healing, ...

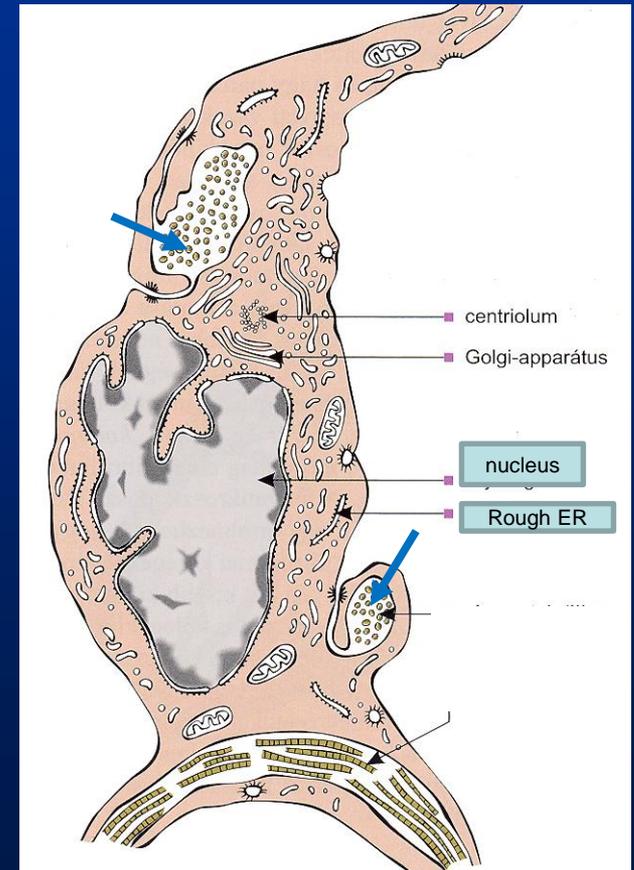
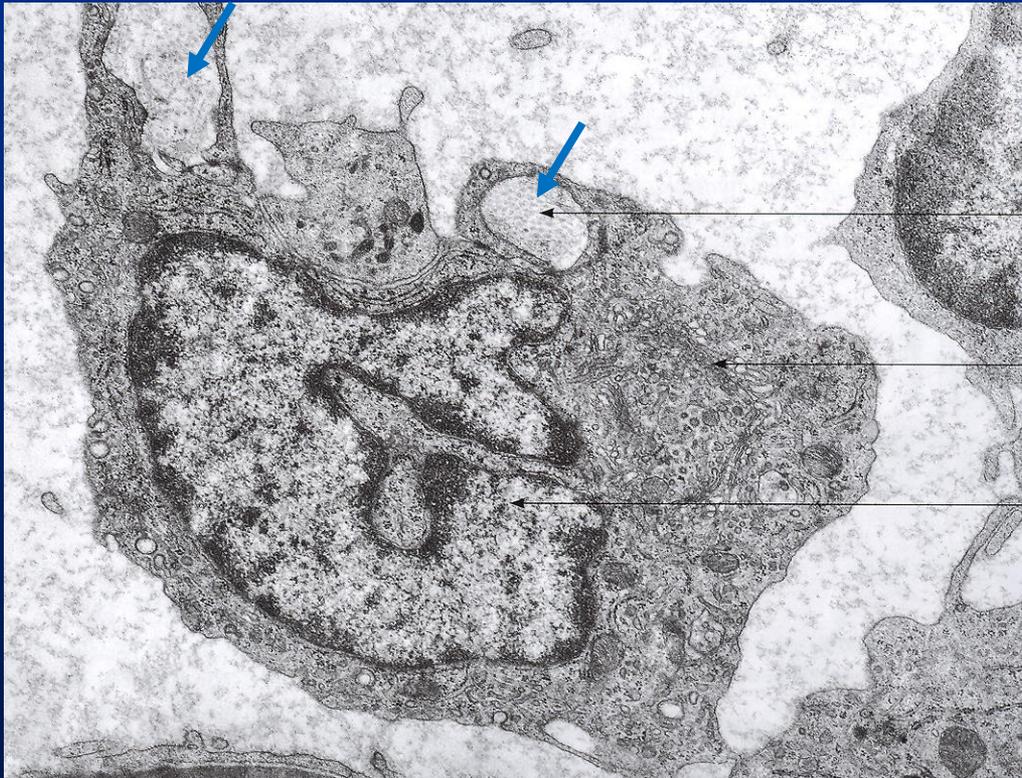


Fibrocyte. Inactive form of the fibroblast. Elongated cell with fine processes at the two ends. EM: Few cell organelles. Bundles of microfilaments (together with myosin) in the cytoplasm (stress fibers).

Myofibroblast. Numerous contractile microfilament bundles containing actin and myosin. Intermediate form between fibroblast and smooth muscle cell. Contractile, fibroblast-like cell, occurring during wound healing and around tubules of testis.

Reticulum cell

A special type of fibroblast (fibrocyte) in the reticular connective tissue. Produces the extracellular matrix (reticular fibers and ground substance). Usually situated at branching points of the reticular fibers and ensheathes them with lamellar cell processes (arrows ←).



Macrophage

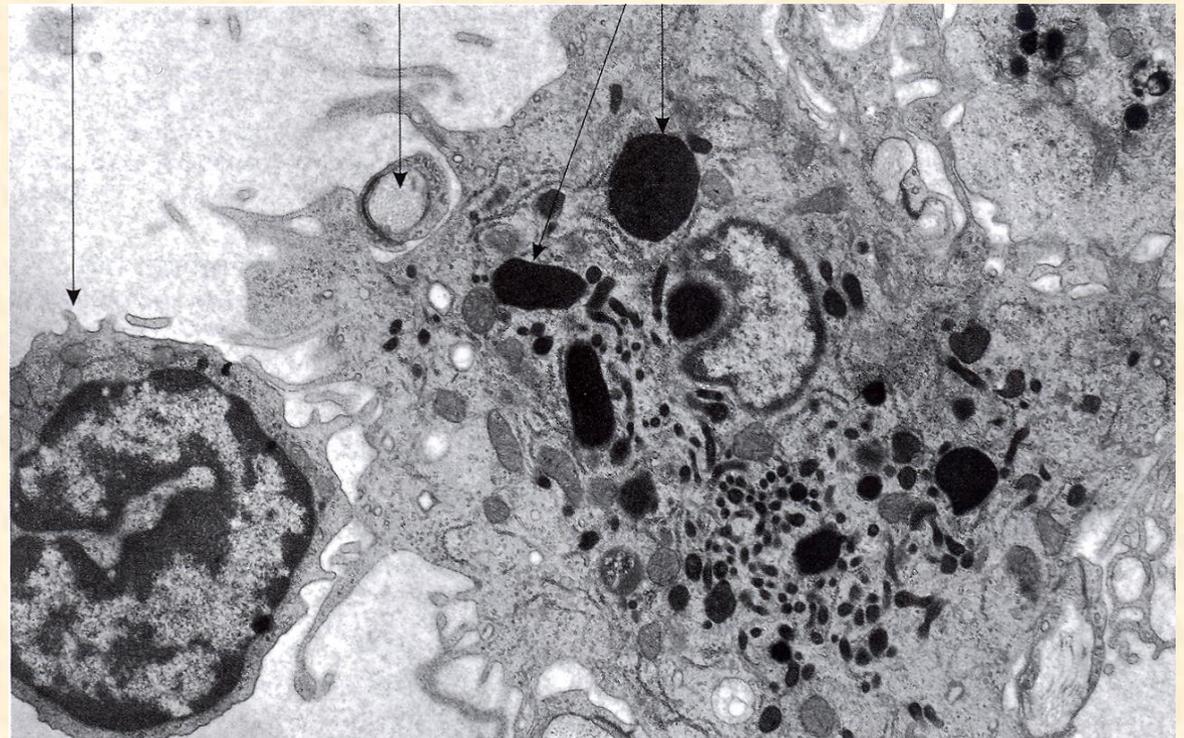
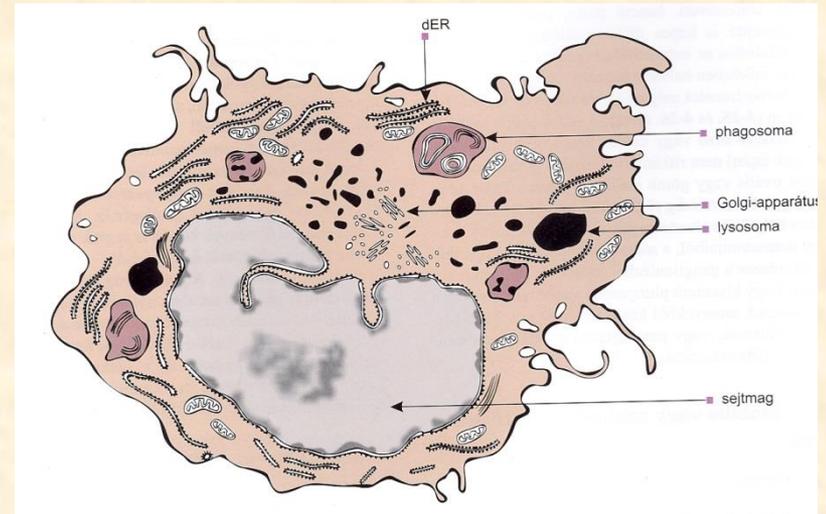
Mobile cell type specialized for phagocytosis.

LM: Round cell with labyrinthic cell surface, irregularly shaped cell nucleus, granules, phagocytosed bodies in the cytoplasm.

EM: Phagosomes, lysosomes, rough ER.

Originates from blood monocytes emigrating through the vessel wall.

Member of the **mononuclear phagocytic system (MPS)**.



Functions:

- **Non-specific defense against bacteria and foreign particles..** Phagocytosis and intracellular digestion of these particles with lysosomal enzymes.
- **Cleaning of tissue spaces** with phagocytosis of dead cells or cell debris.
- **Synthesis and secretion of growth factors** (IL1, IL6, PDGF, FGF, TGF beta, TNF, GM-CSF, ...)

Mast cell

Round or oval cell filled with basophilic granules.

Most important components of the membrane-limited granules are: **heparin** (a glucosaminoglycan with many negative charges), **protein** and **histamine**. Further components: SRS-A, ECF-A,.



Electron micrograph of a mast cell in a connective tissue



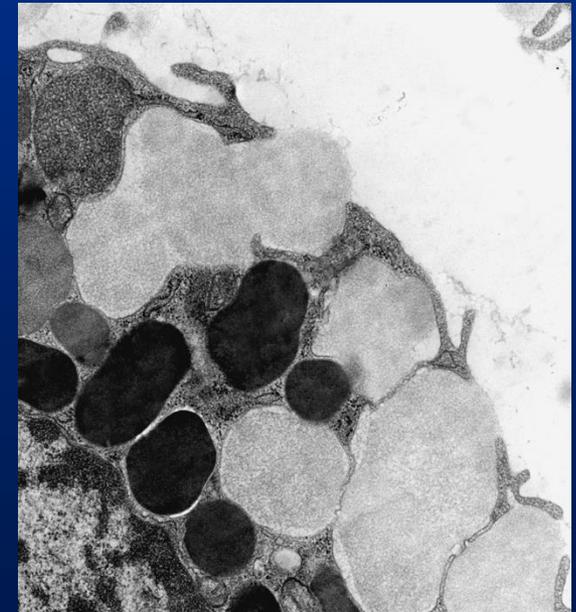
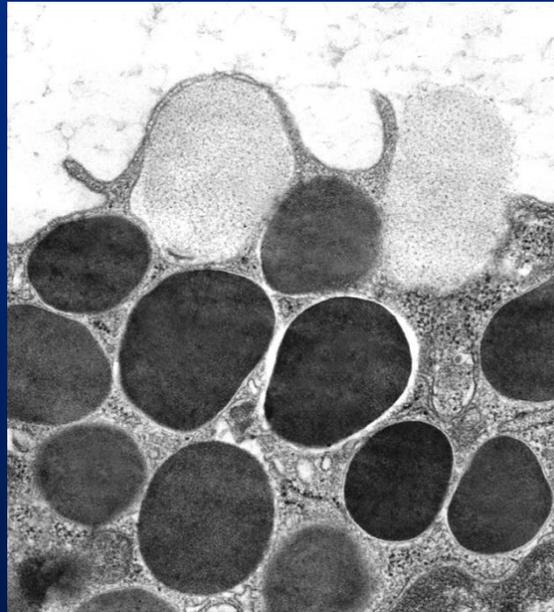
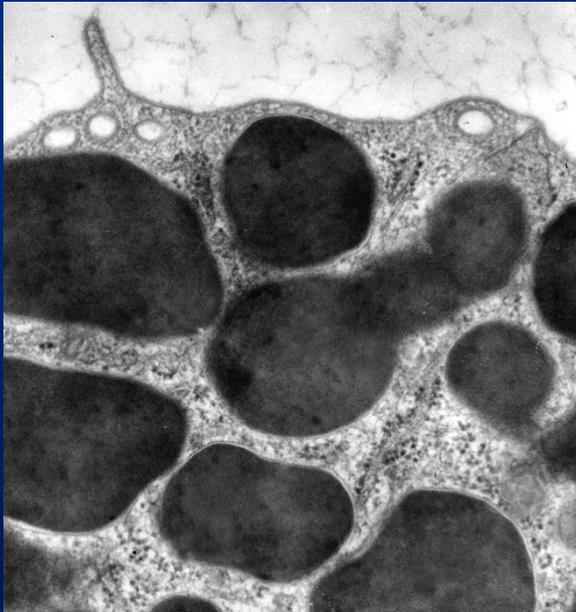
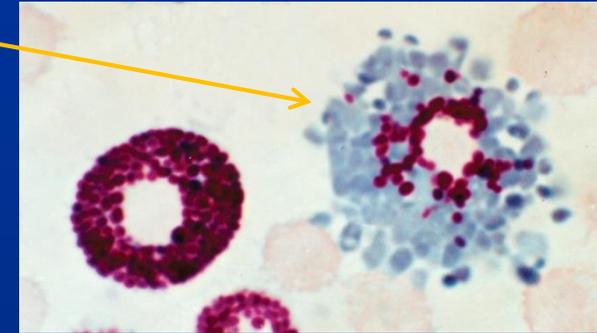
Metachromatic staining: When the mast cells are stained with the basophilic dye toluidine blue, the granules appear in a reddish-violet color (due to the many negative charges of heparin).

Mast cell degranulation

In response to an adequate stimulus the cell releases the contents of its granules: **degranulation**.

A resting and a degranulating mast cell are seen on the picture. Exocytosed granules are seen in blue color. (Alcian blue – safranin staining).

Granules of the mast cell contain the bioactive agent histamine in high concentration. **Mast cells are therefore the largest histamine store of the organism.**



Substance of the granules is released by subsequent exocytoses of the granules: **sequential exocytosis**.
Electron micrographs.

Mast cell sensitization

1. **IgE-receptors** are present in the cell membrane of mast cells.
2. The immune system (plasma cells) produces against a foreign antigen (allergen) **IgE-type antibodies**.
3. The **IgE molecules are bound to IgE-receptors** in the cell membrane, thereby sensitizing the mast cell against the allergen („sensitized mast cell”).
4. When the allergen newly appears at a later time, it binds to the specific IgE molecules on the surface of the mast cell .
5. This binding induces **exocytosis of the mast cell granules** (degranulation) through a signal transduction.
6. **Histamine is released** quickly from the exocytosed granules. Histamine acts on the surrounding blood vessels (vessels are dilated, become more permeable for fluid and proteins, „sterile inflammation”), and smooth muscle cells. „Allergic reaction”

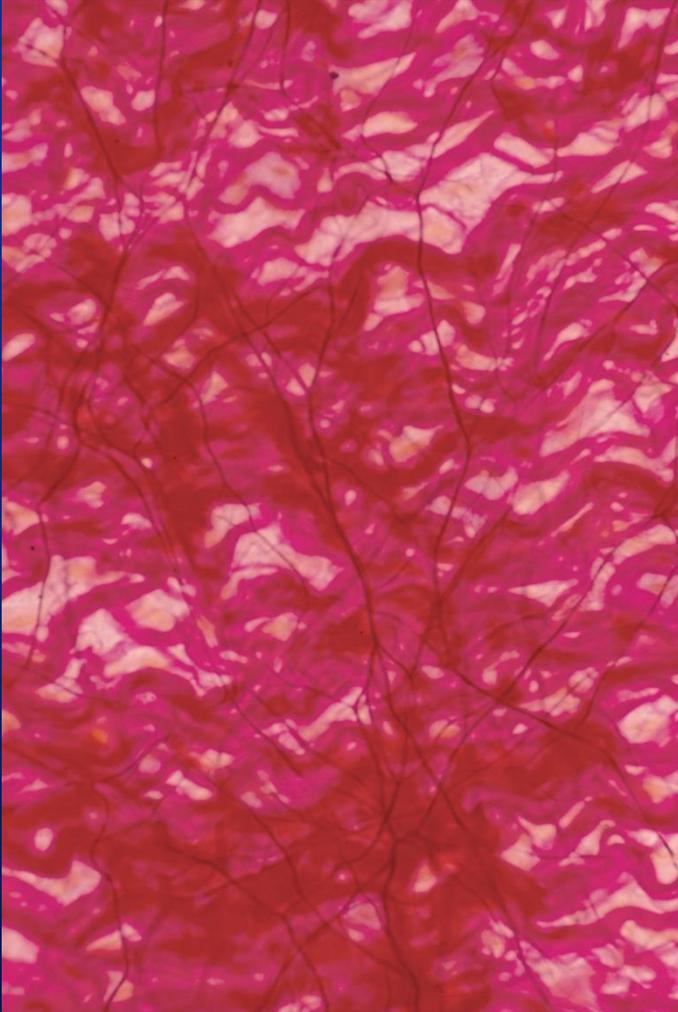
Degranulation of mast cells can be also induced by other substances in a non-allergic pathway. Example: bee venom.

2. Extracellular matrix (ECM)

A. Connective tissue fibers

1. Collagen fibers
2. Reticular fibers
3. Elastic fibers

Collagen fibers



The most frequent connective tissue fibers.

Wavy appearance, various fiber thickness (2-20 μm), fibers can be dissolved in acid or basic solutions.

Very **resistant against pull**, a fiber having a cross sectional area of 1 mm^2 can hold a weight of 6 kg!

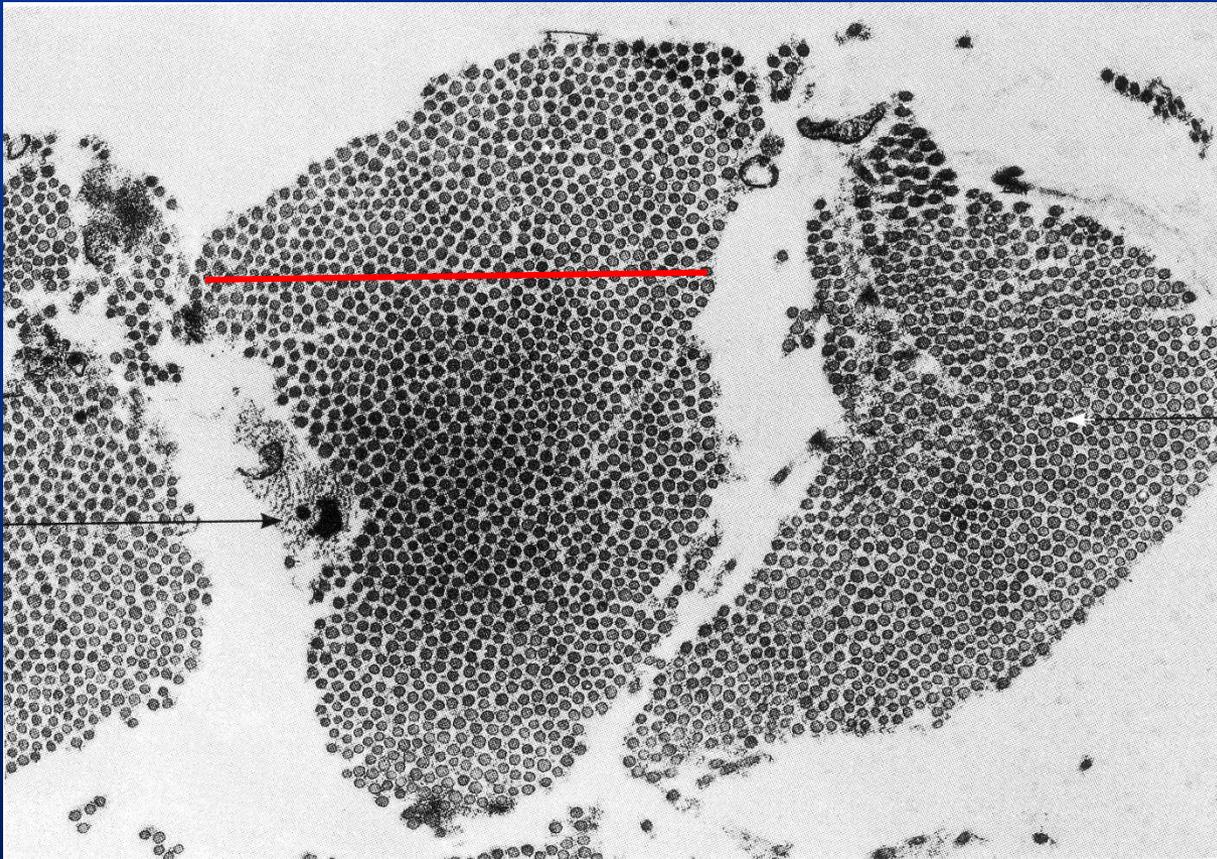
Most important constituent of tendons, ligaments, aponeuroses, ...

Solid form of certain organs (eye bulb, penis) depends on collagen fibers: a fibrous capsule is formed by collagen fibers and is „inflated” by a fluid.

EM: a fiber consists of collagen microfibrils of 50-90nm diameter. The thickness of collagen fibers depends on the number of these microfibrils.

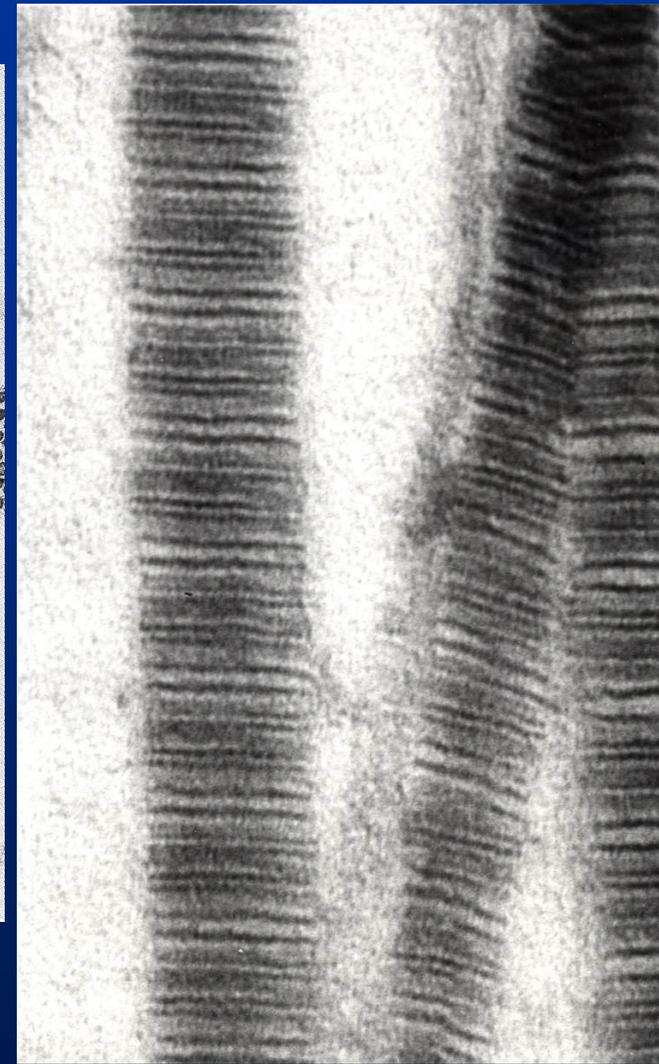
Collagen and reticular fibers

Collagen microfibrils on EM pictures



Two collagen fibers in cross section

Several hundreds of microfibrils form a collagen fiber observed in the light microscope

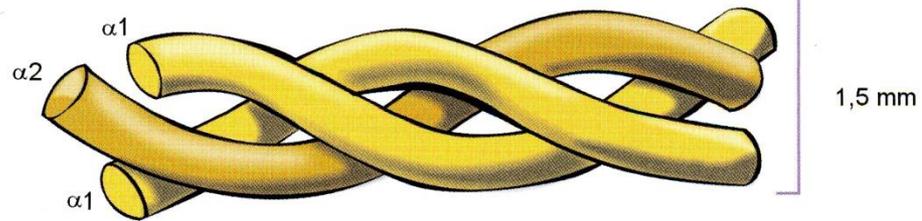


Microfibrils in longitudinal section

High EM magnification

Molecular structure of collagen

Trimer (triple helix)



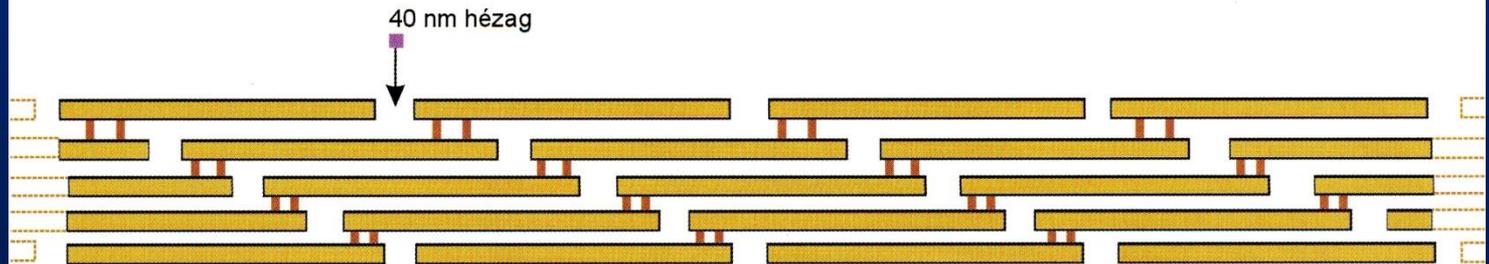
Three polypeptide chains wound around each other

Tropocollagen molecule



Dimensions of a tropocollagen molecule

Microfibril



Tropocollagen molecules are connected laterally by covalent bonds

Protein family of collagens

1. Fibrillar collagens

- **Collagen I** (most frequently occurring (90%), e.g. connective tissue, bone, dentin, ...)
- **Collagen II** (fine fibrils in cartilage)
- **Collagen III** (reticular fibers, form delicate network)
- **Collagen V**

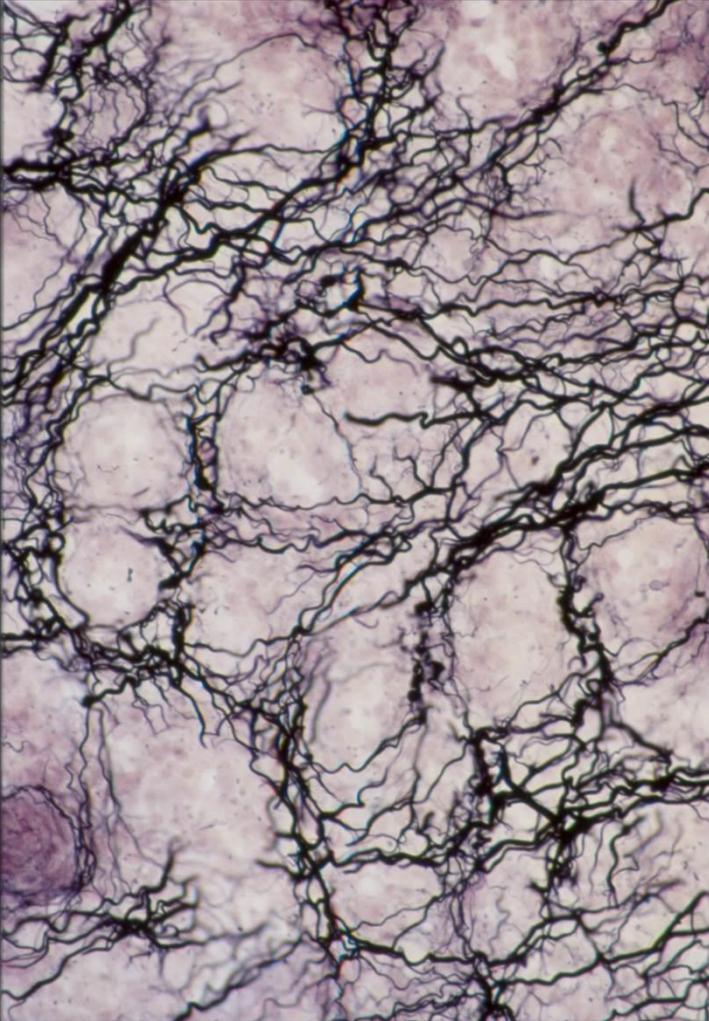
2. Fiber-associated collagens

- **Collagen IX** (associated to type II collagen in cartilage)
- **Collagen XII** (bound to type I collagen)

3. Network-producing collagens

- **Collagen IV** (basal lamina)
- **Collagen VII** (short collagens associated with basal lamina)
- **Collagen VIII** (component of the Descemet-membrane in the cornea)

Reticular fibers



Fine branching fibers, form a 3D network.

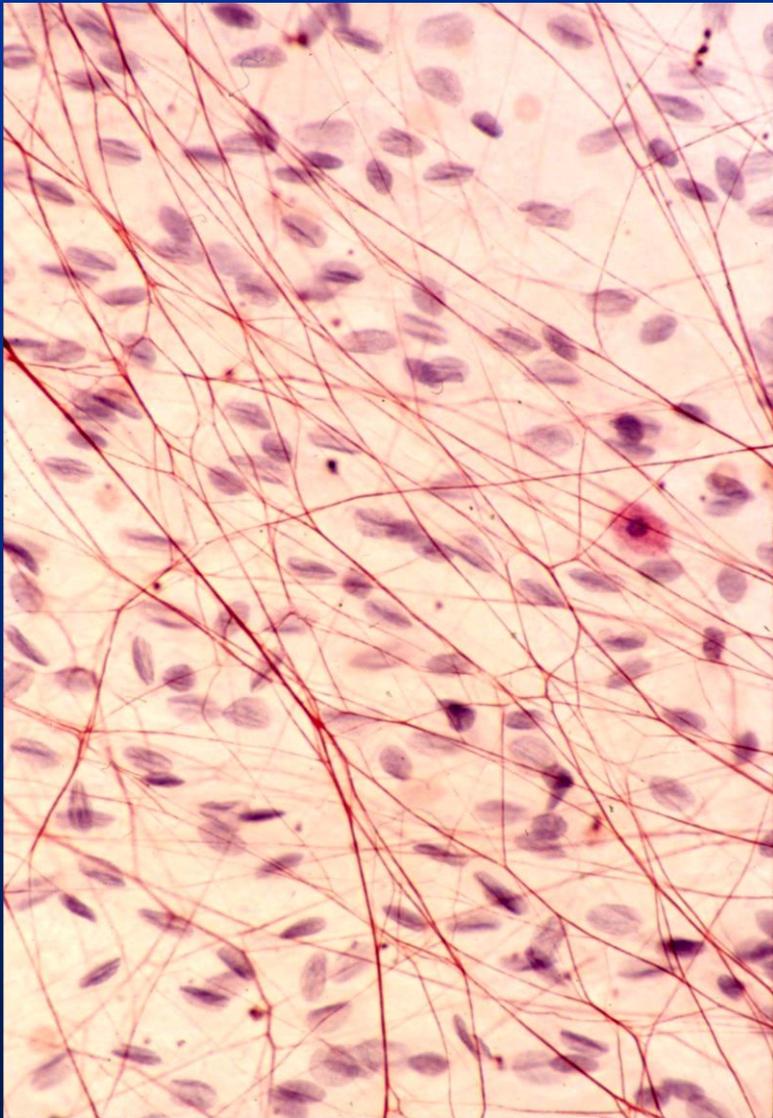
Histological detection: silver staining, PAS reaction.

Occurrence: in lymphatic and hemopoetic organs, around smooth muscle cells, fat cells, small blood vessels, under the basal lamina, in parenchymatous organs, ...

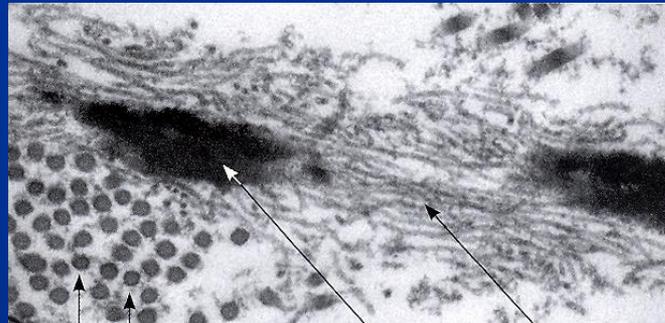
Type III collagen, consists of 20 nm thick microfibrils.

Reticular fibers in the spleen.

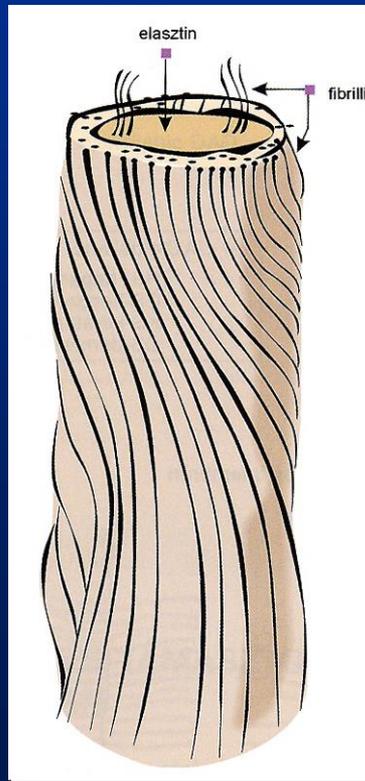
Elastic fibers



Elastic fibers, orcein staining



Longitudinal section,
EM picture



Thin, straight fibers, occasionally branched. Can be pulled out up to 50% of their length.

Histology: orcein (brown color), rezorcin-fuchsin (violet),

EM: dark, homogeneous internal substance (elastic protein: elastin), surrounded by 8-10 nm fibrillin fibers.

Cells producing elastic fibers: fibroblasts, smooth muscle cells.

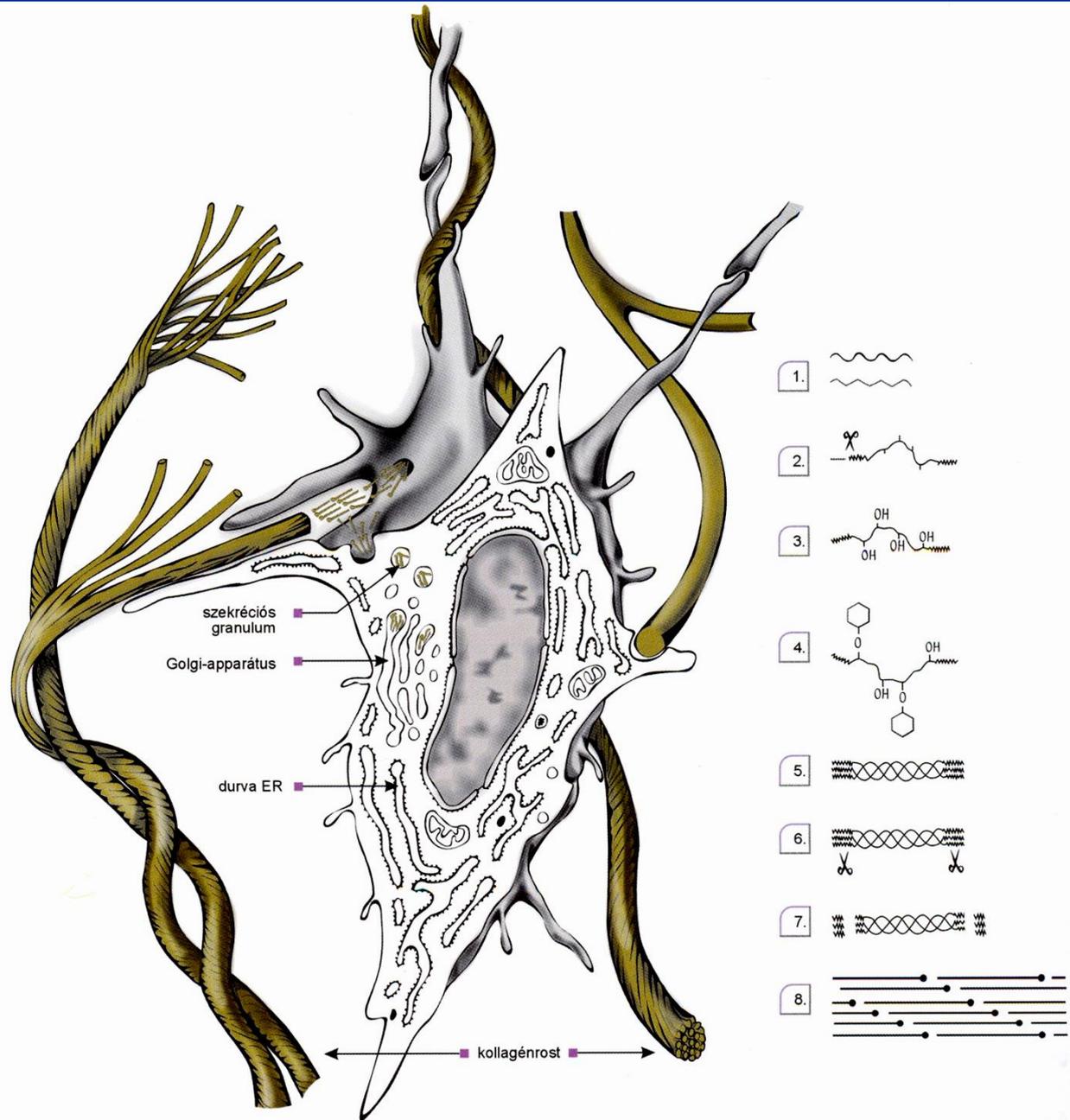
Molecular structure:

Elastin protein consists of polypeptide chains with many loops with hydrophobic amino acids. The loops can be deformed by pull and regain their original structure on relaxation.

Fibrillin filaments are at the periphery and have a spiral course. Resistant against overpulling.

Fibrillogenesis

(formation of collagen fibers)



2. Extracellular matrix

B. Amorphous ground substance

Glucosaminoglycans (GAG)

Repeating disaccharide units, different in various GAGs

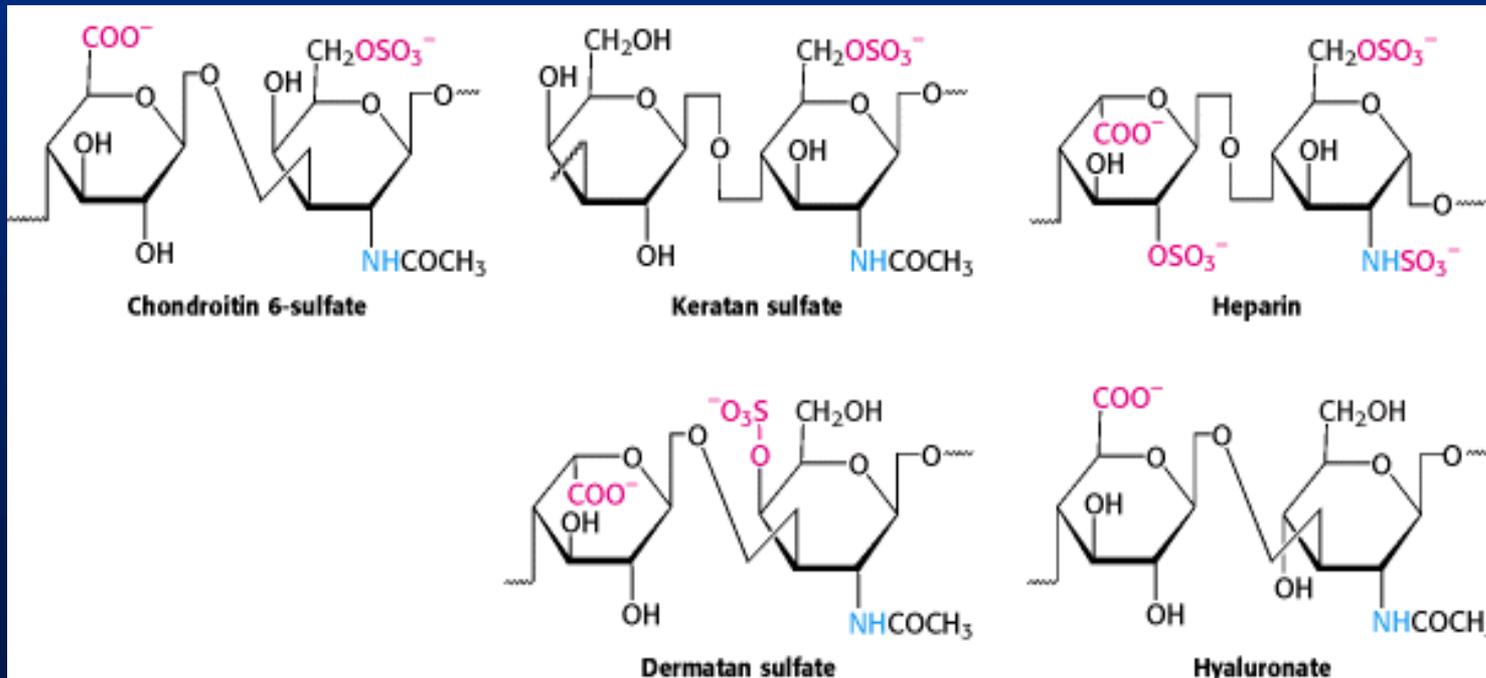
Long, non-branching carbohydrate chains. **Consist of many (often hundreds of) disaccharide units.**

In the disaccharide unit one component carries a **COOH**-group, while the other one has an **amino**-group (to which usually an **acetate** group is bound).

Most GAGs contain in their disaccharide units 1-3 **sulfate** groups..

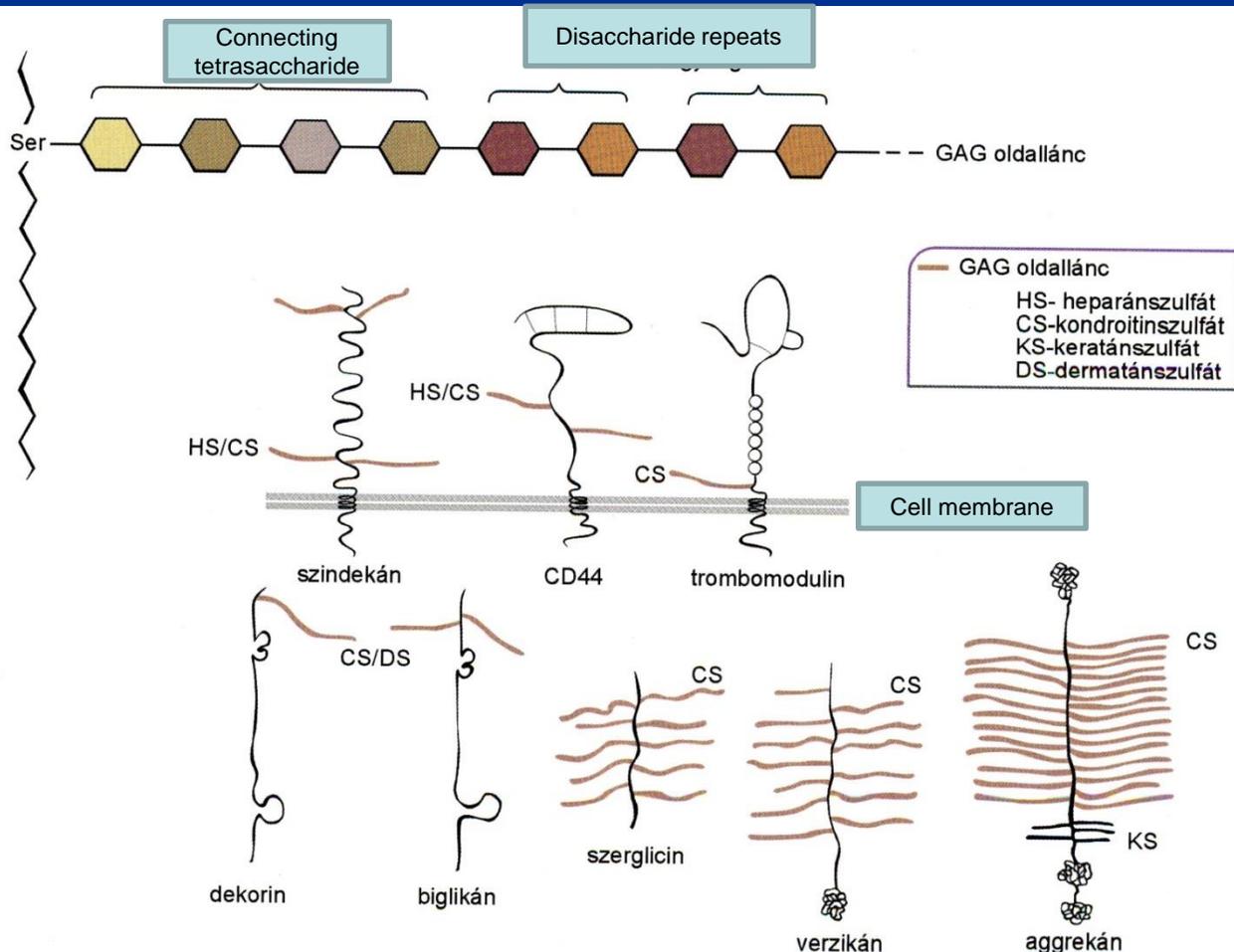
Due to their carboxyl and sulfate groups, GAGs are **strongly negatively charged**.

The negative electrical charges attract Na ions and water molecules. GAGs are **highly hydrated** molecules.



Proteoglycans

Two types of components: core protein and GAGs.

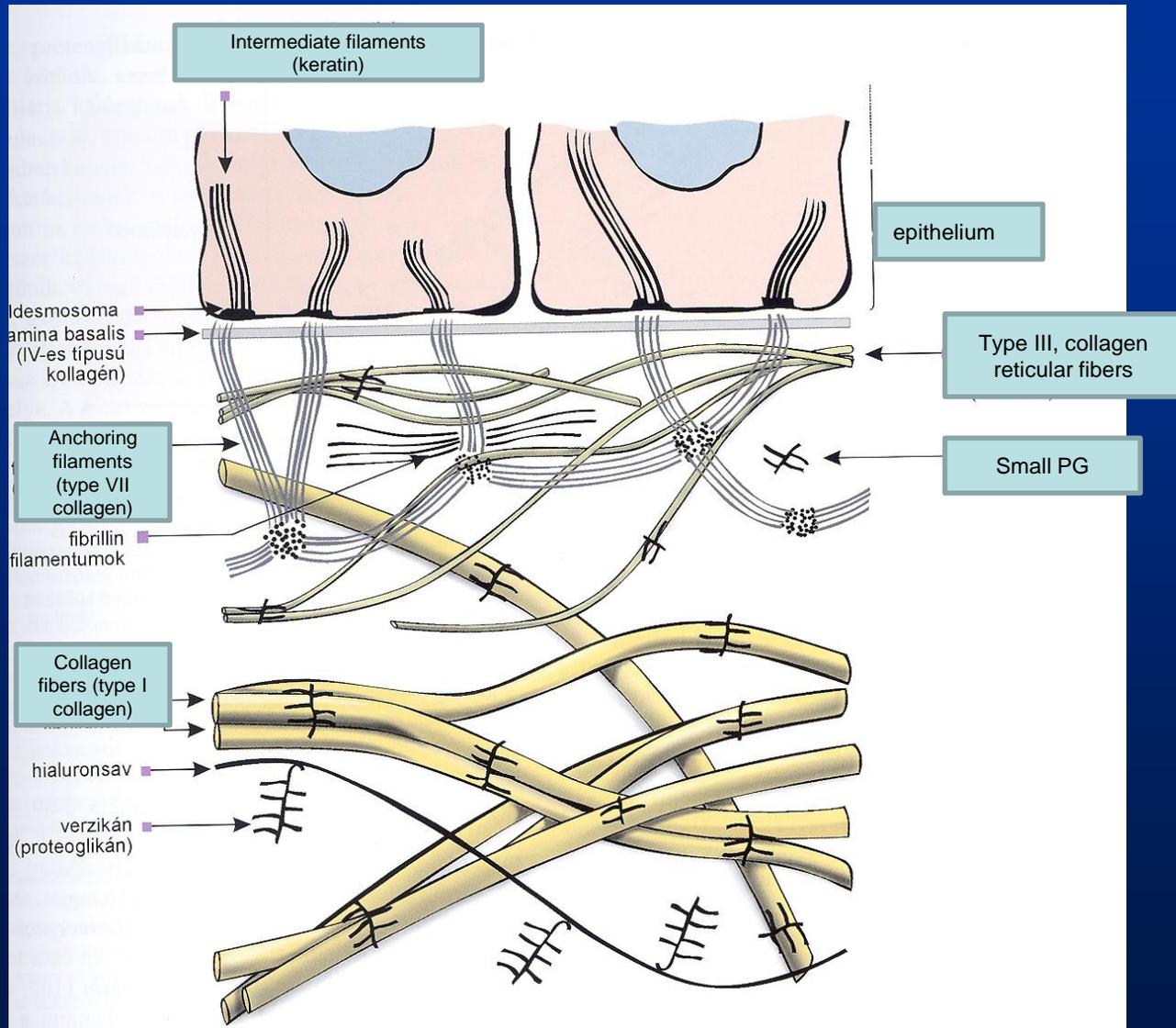


High amount of water bound (PGs are resistant to pressure: turgor). A jelly-like substance.

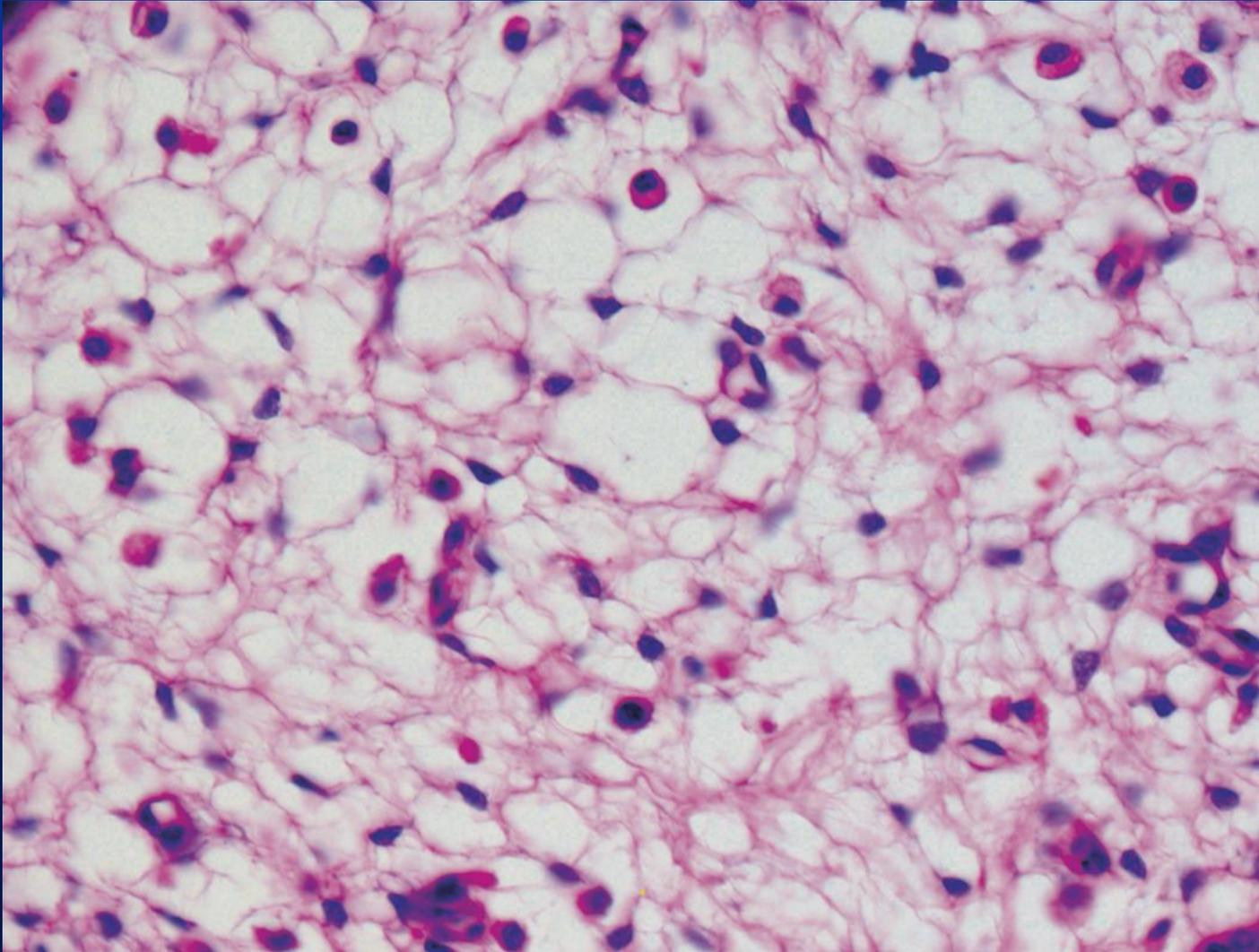
PGs can store signal molecules (FGF, TGF),

PGs are often bound to connective tissue fibers and cells.

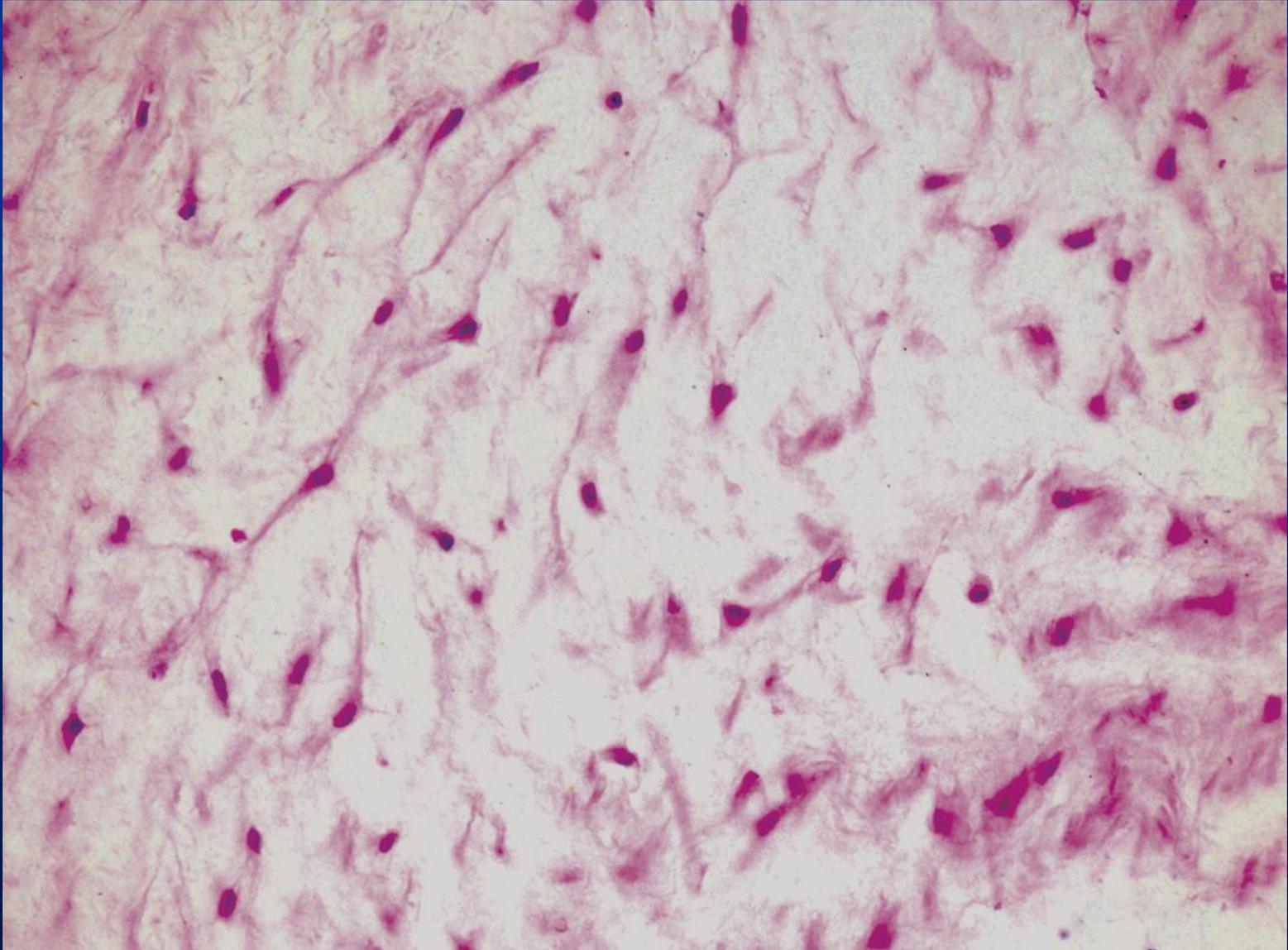
Connection of epithelium and connective tissue



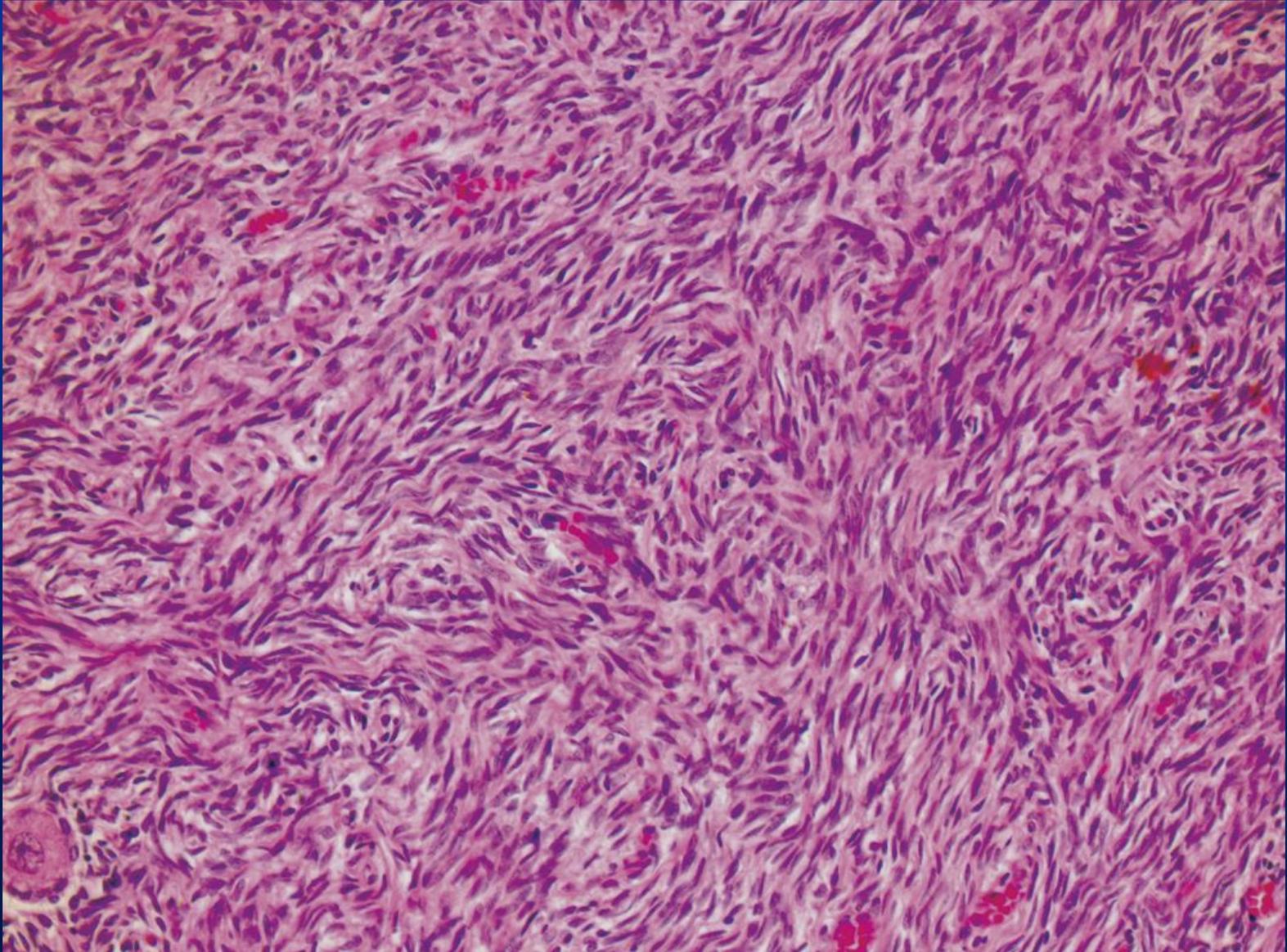
Mesenchyme (embryonic connective tissue)



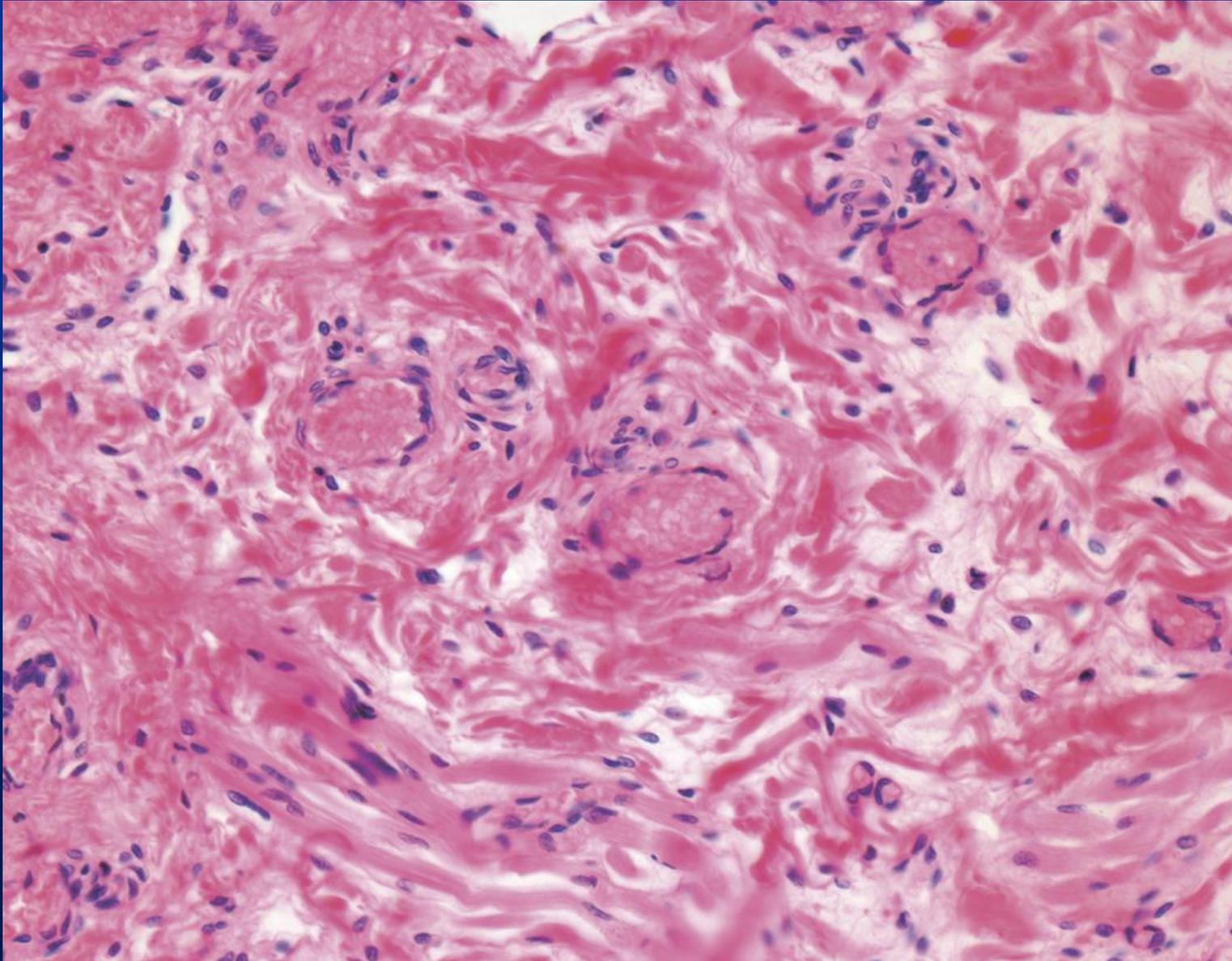
Wharton jelly (from umbilical cord)



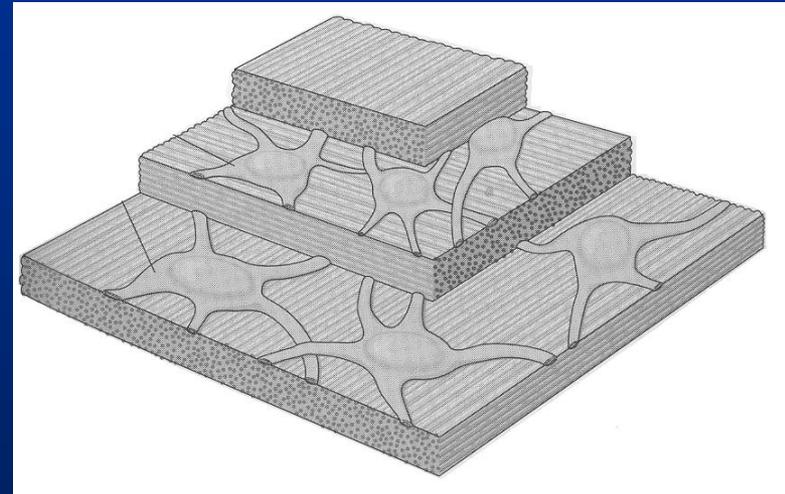
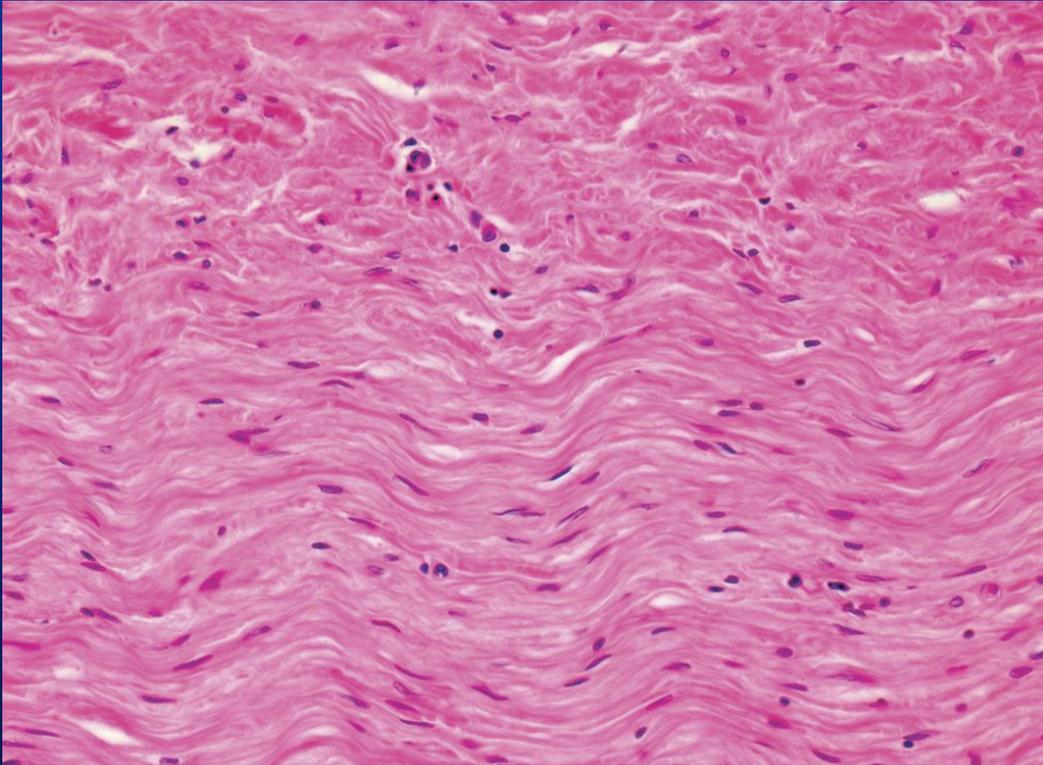
Spinocellular connective tissue (ovarium)



Loose connective tissue



Lamellar connective tissue



Dense connective tissue (tendon)

