علم الأنسجة العام General Histology

لطلبة السنة الاولى طب بشري

2018 صيف

اعداد أ.د. فرع البسطامي

الجزء الاول

Connective tissue Proper

محتويات

General Histology

1. Epithelium

2. Connective tissue C.T
   - Proper
   - special
     - cartilage
     - bone

3. Nervous tissue

4. Muscular tissue

Recommended book **Junqueira**

(last edition)
(12th ed.)

---

١) يرجى الحضور قبل موعد المحاضرة بخمس دقائق
" " " " الدرس العملي

٢) عدم التحدث مع الزملاء خلال المحاضرة أو الدرس العملي

Connective tissue (23)

All connective tissues are mesenchymal (mesodermal) in origin Except certain parts of the head & neck which develop from neural crest (i.e ectodermal in origin)

↓

Mature connective tissue (C.T)

- Connective tissue proper
  - Cells
    - Fixed → Residents
    - transient → visitents
  - Extracellular matrix (resists compressive & stretching forces)
    - Fibres
      - → collagen
      - → Reticular
      - → Elastic
    - ground substance
      - → glycosaminoglycans
      - → Proteoglycans
- special C.T. (cartilage, bone & blood)

Fixed C.T cells develop & remain within the C.T where they perform their functions

- fibroblasts → most abundant cell
- Adipose cells
- pericytes
- Mast cells
- Macrophages ⊛

Transient C.T cells → free or wandering cells

→ originate mainly in the bone marrow & circulate in the bloodstream → When they receive the proper stimulus, they leave the blood stream → MIGRATE INTO C.T to perform their specific functions

→ Mostly **short-lived**, must be replaced continually

include →
- Plasma cells
- lymphocytes
- Neurophils, basophils, Eosinophils
- Monocytes
- Macrophages ⊛

All contain collagen type I.

Dermis, tendon, ligaments, fibrocartilage

→ Dermatan Sulphate

Protein core

- Keratan Sulphate → Cornea
- Chondroitin Sulphate → predominate in hyaline & elastic cartilage rich in collagen type II
- Heparan Sulphate → associated with Reticular fibres → collagen type III

When **Sulphated glycosaminoglycans (GAGs)** form covalent bonds with **a protein core** they form a family of macromolecules known as **proteoglycans**

Adhesive glycoproteins !! allow cells to bind (adhere) to the components of the intercellular matrix → They can bind cell surface proteins called **integrins** to **collagen fibres** and to **proteoglycans**. Major types of adhesive glycoproteins are **Fibronectin**, **laminin**, **entactin**, **tenascin**.

Fibronectin attaches various extracellular components (collagen, heparan sulphate & hyaluronic acid) to the integrins of cell membrane

Basophilic (Basic stain) → Haematoxylin → H → Nucleus is basophilic → appears blue to violate → Rough endoplasmic reticulum REER associated ribosomes → Basophilic

Acidophilic / Eosinophilic (Acidic stain) → Eosin → E → Most of the cytoplasm is eosinophilic → appears Red to Pink → Smooth endoplasmic reticulum (SER) & mitochondria → Eosinophilic

!!

Metachromatic !! Blue stain → (granules appear) → Red

- PAS stain (Periodic acid schiff) reaction → Stains Carbohydrate violate
- Argyrophilic → stain with silver salts

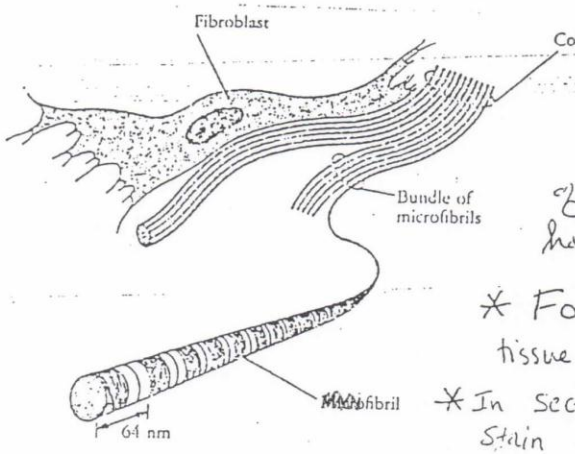
Ground substance → functions as a molecular sieve, facilitating the diffusion of metabolites between the blood and the tissues while at the same time serving as a physical barrier to prevent the spread of large particles such as bacteria & other microorganisms. Aside from water and salts, the ground substance of connective tissue proper is composed of glycosaminoglycans (GAGs) → The most common type is hyaluronic acid → Many pathogenic bacteria such as staphylococcus aureus secrete hyaluronidase, an enzyme that cleaves hyaluronic acid into numerous small fragements thus converting the gel state of the extracellular matrix into a sol state → the consequence of this reaction is to permit the rapid spread of the bacteria through the connective tissue.

Connective tissue (FIBERS)

→ Provide GENERAL SUPPORT for other tissue
→ they form a dense framework in the dermis
→ they form STROMA for Parenchymal organs e.g glands
→ support individual cells < muscle, fat cells
→ Form < tendons (bind muscle to bone)
< ligaments (" bone to bone)
→ Hollow organs & blood vessels < expand & contract
contain C.T fibres that provide flexibility

Fibres of connective tissue { collagenous, elastic, reticular }

Dr Mustafa



Collagenous fibres

* The MOST NUMEROUS of connective tissue fibres and have the greatest tensile strength
* Found in all types of connective tissue Except blood and lymph.
* In sections stained with H&E → they Stain weakly pink with eosin
* they stain red with Van Gieson's stain and green with Masson's trichrome stain. The fibres measure 1–10 µm in thickness.
* Each collagen fibre is composed of parallel fibrils. In turn each fibril is composed of bundles of parallel microfibrils (cold view)
* The fibrils can be seen only with the electron microscope and measure between 20 and 100 nm diameter → They show characteristic major cross banding with a periodicity of 64 nm.
* Each fibril is composed Chemically of molecules of Tropocollagen each of which is about 260 nm long and 1.5 nm thick. The tropocollagen molecules lie parallel to each other and overlap by about one-quarter of their lengths (the overlapping is responsible for the banding pattern).
* Each molecule of tropocollagen consists of 3 polypeptide chains called α-units arranged in a helix and link by hydrogen bonds
* The polypeptides are rich in glycine and Proline and also contains hydroxyProline and hydroxylysine.

* The amount of collagen in a tissue can be determined by measuring the hydroxyproline level

↓

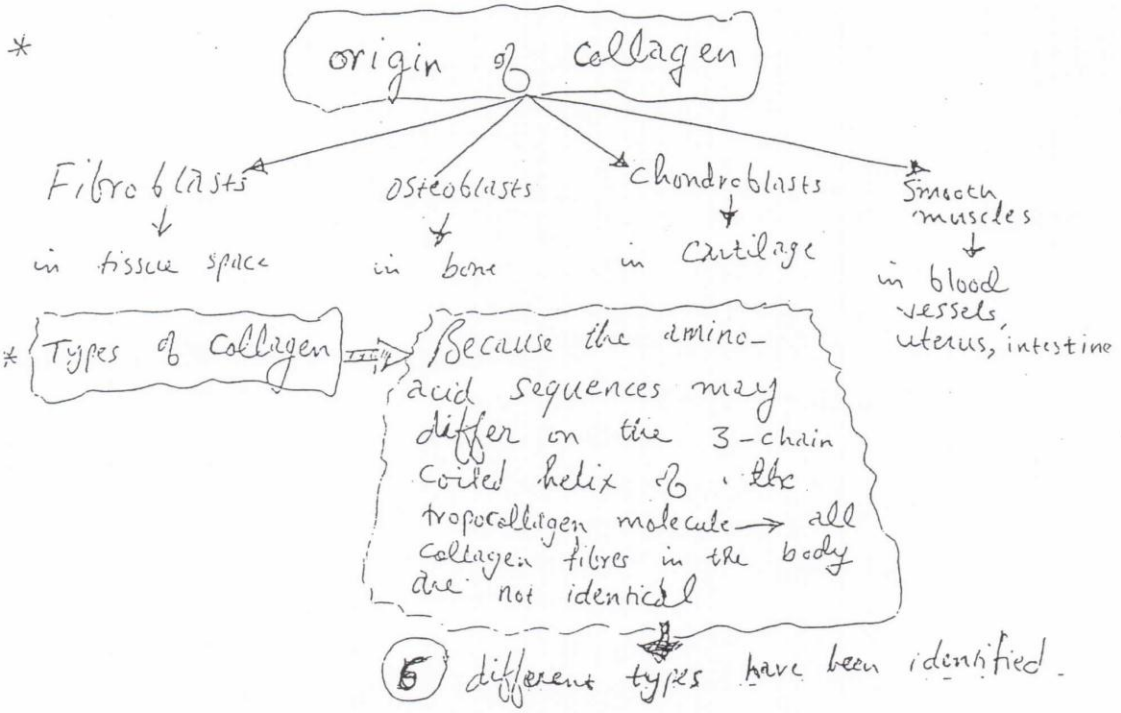
Ascorbic acid (Vit.C) is essential for the conversion of Proline to hydroxyProline

Bustami

↓

In the absence of Vit.C, as in Scurvy, this Conversion does not occur and WOUND HEALING does NOT take place

*



① Type I → in connective tissue proper, bone, dentine
② Type II → in hyaline & elastic cartilages
③ Type III → reticular fibres
④ Type IV → lamina densa of basal lamina (not assembled into fibres)
⑤ Type V → associated with type I collagen and in the placenta
⑥ Type VII → attaching the basal lamina to the lamina reticularis

Biosynthesis of Collagen type I

Polypeptide α chains are assembled on polyribosomes bound to rough endoplasmic reticulum and injected into the cisternae as PREPROCOLLAGEN (i.e α-chains possessing additional amino acid sequence known as **propeptide**) at the amino & carboxyl ends

(Registration peptides) → {Keeps procollagen molecule soluble & Prevent collagen fibre formation within the cell}

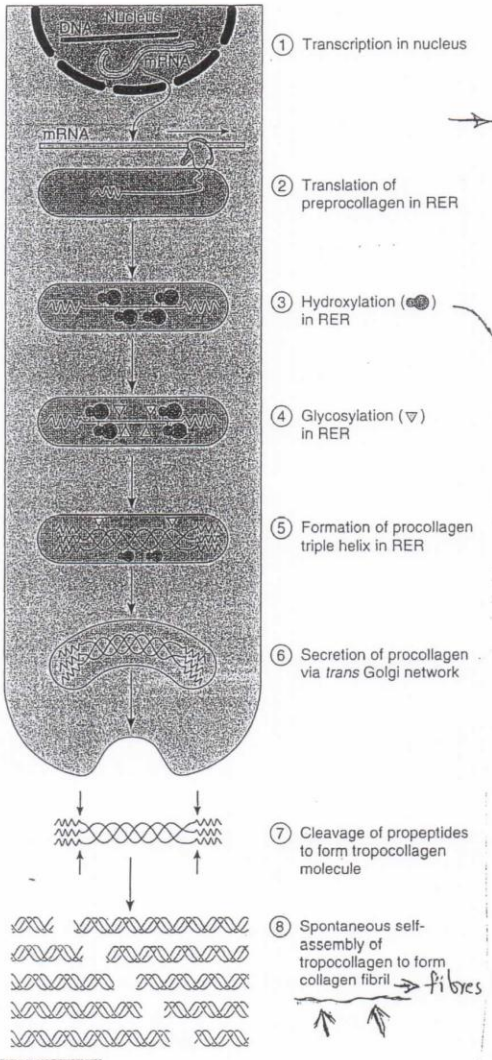


Figure 4–7 Schematic diagram of the sequence of events in the synthesis of type I collagen.

→ Formation of mRNA for each type of alpha chain

- Principle amino acids that make up collagen are glycine 33.5%. proline 12%. hydroxyproline 10%.
⊕ hydroxyproline ⊕ hydroxylysine

Hydroxylation of Proline requires Vit. C → In Scurvey (vit. C deficiency) → tropocollagen molecules are unable to form fibrils → Bleeding gums & loose teeth

The formation & maintenance of the fibrillar structure is augmented by covalent bonds formed between lysine & hydroxylysine of adjacent tropocollagen molecules

collagen that **forms fibrils** → I, II, III, V, XI

collagen that **forms network** → IV

⊛ {Fibrillar structure is absent in type III collagen because the propeptides are not removed from the procollagen molecules}

Ibrahim

CLINICAL CORRELATIONS

At the end of surgery, the cut surfaces of skin are carefully sutured; usually, a week later the sutures are removed. The tensile strength of the dermis at that point is only about 10% that of normal skin. Within the next 4 weeks, the tensile strength increases to about 80% of normal, but in many cases it never reaches 100%. The initial weakness is attributed to the formation of type III collagen during early wound healing, whereas the later improvement in tensile strength is due to scar maturation, when type III collagen is replaced by type I collagen.

Some individuals, especially blacks, are predisposed to an excessive accumulation of collagen during wound healing. In these patients, the scar forms an elevated growth known as a **keloid.**

Fibrillar structure is reinforced by the formation of covalent cross-links between tropocollagen molecules. This process is catalyzed by the action of the enzyme **lysyl oxidase,** which also acts in the extracellular space.

28/2

Deficiency of the enzyme **lysyl hydroxylase,** a genetic disorder known as **Ehlers-Danlos syndrome,** results in abnormal cross-links among tropocollagen molecules. Individuals afflicted with this anomalous condition possess abnormal collagen fibers that result in hypermobile joints and hyperextensive skin. In many instances, the skin of affected patients is readily traumatized and the patient is subject to dislocation of the affected joints.

Dr Mustafa

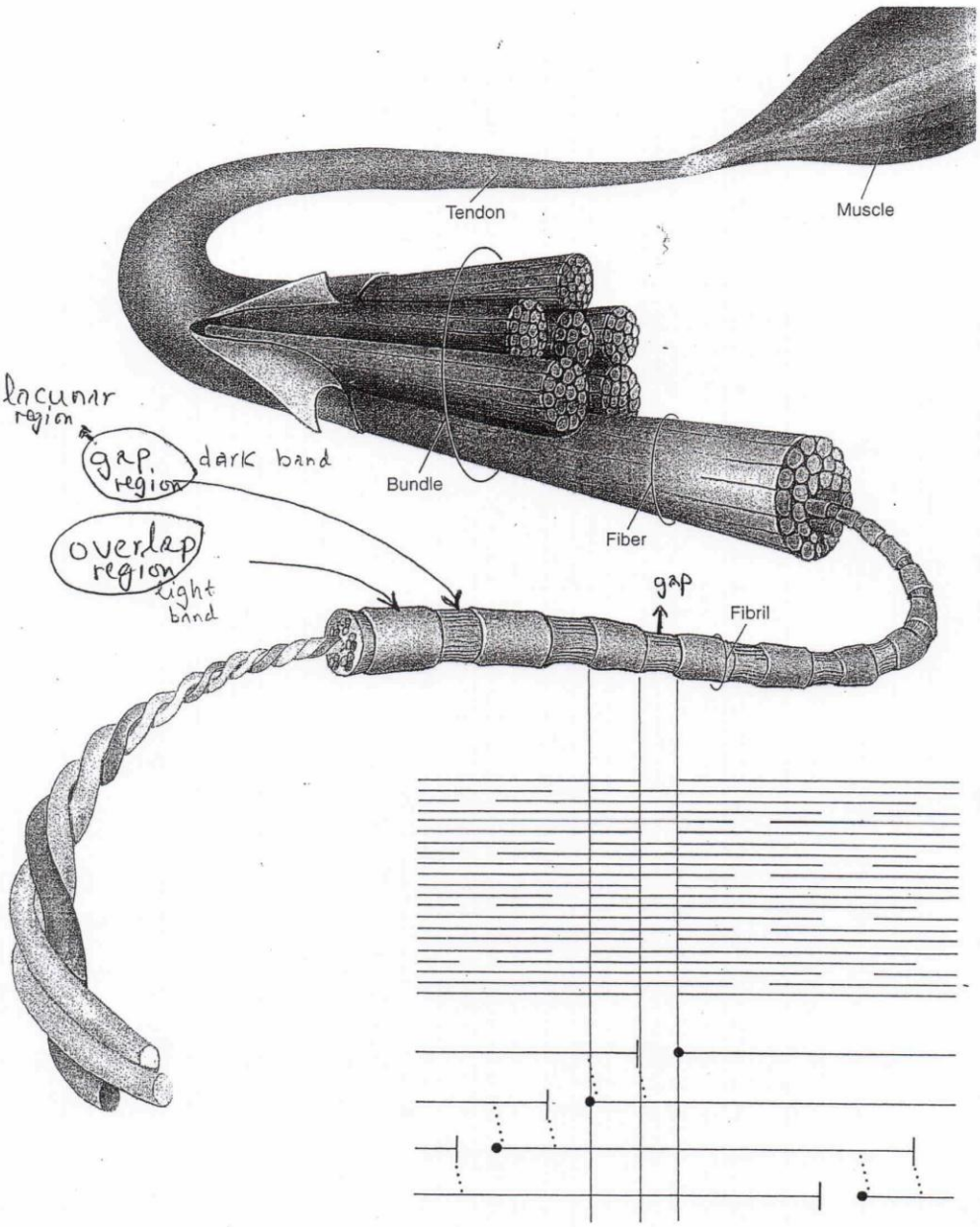
- **Type I collagen,** the most common type, forms thick fibers and is present in connective tissue proper, bone, dentin, and cementum (Fig. 4–6).
  - Resists tension
  - Produced by fibroblasts, osteoblast, odontoblast
- **Type II collagen** forms slender fibers and is almost exclusively found in the matrices of hyaline and elastic cartilage.
  - Resists Pressure
  - Produced by chondroblasts
- **Type III collagen** is also referred to as **reticular fiber** because it had been thought to differ from collagen. It is now known that reticular fiber is a type of collagen that becomes highly glycosylated and forms thin fibers 0.5 to 2.0 μm in diameter. Because of the rich coating of sugar groups, type III collagen fibers are preferentially stained by silver salts or by the periodic acid–Schiff (PAS) reaction.
  - Forms structural framework of Spleen liver lymph node Smooth muscle & adipose tissue
  - Produced by fibroblast, reticular cell smooth muscle cell Hepatocytes
- **Type IV collagen** does not form fibers and does not display the 67-nm periodicity. Instead, it forms a meshwork of **procollagen** molecules matted together to form a supporting carpet of basal lamina.
  - Forms lamina densa of the basal lamina
  - Produced by epithelial cell muscle cell
- **Type V collagen** forms very thin fibrils, possesses a 67-nm periodicity, and is found in association with type I collagen.
  - forms Dermis, tendon, ligament ------etc,
  - Produced by fibroblasts & mesenchymal cell
- **Type VII collagen** forms small aggregates, known as **anchoring fibrils,** that secure the basal lamina to the underlying type I and type III collagen fiber bundles.
  - produced by epidermal cells
  - present at the junction of dermis & epidermis

Major types & characteristics of Collagen

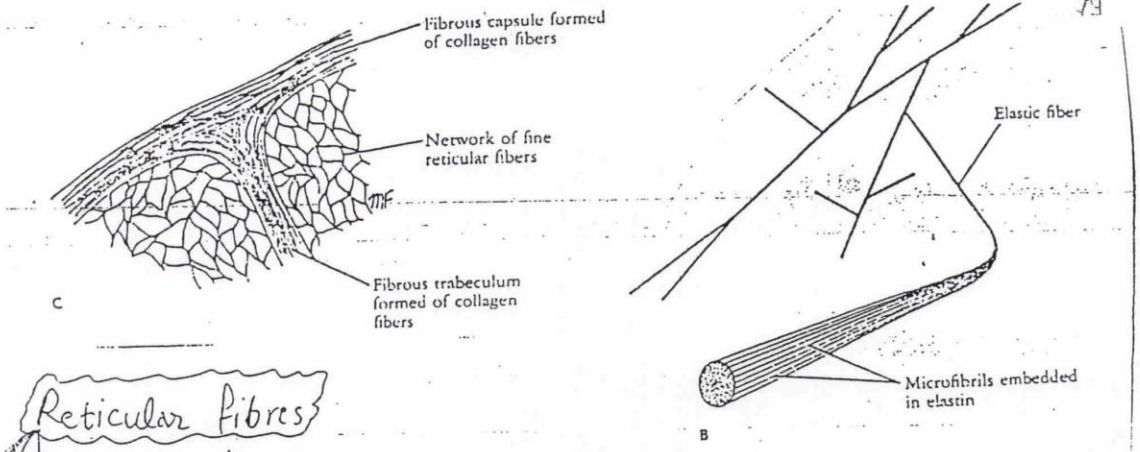
Remember type IV → does not form fibres !! Why ?

Dr Mustafa

GRAPHIC 3-1. Collagen



Each collagen fiber bundle is composed of smaller fibrils, which in turn consist of aggregates of **tropocollagen molecules.** Tropocollagen molecules self-assemble in the extracellular environment in such a fashion that there is a gap between the tail of the one and the head of the succeeding molecule of a single row. As fibrils are formed, tails of tropocollagen molecules overlap the heads of tropocollagen molecules in adjacent rows. Additionally, the **gaps** and **overlaps** are arranged so that they are in register with those of neighboring (but not adjacent) rows of tropocollagen molecules. When stained with a heavy metal, such as osmium, the stain preferentially precipitates in the gap regions, resulting in the repeating **light** and **dark banding** of collagen.



Reticular fibres

- do not form bundles as collagen fibres
- tend to be present in delicate networks
- not apparent in H&E preparations, but can be demonstrated with silver salts (argyrophilic) and PAS (reacts with a mucopolysaccharide coat of the fibres).
- are sparse in loose connective tissue but plentiful as the STROMA of lymphoid and myeloid tissue, glandular structures and in sheaths around blood vessels muscles and nerves.
- In electron micrographs ⇒ reticular fibres show the same banding pattern and consists of the same unit fibrils as collagen III ⇒ they differ mainly in the number and arrangement of the unit fibrils rather than in their chemistry.

Elastic fibres

- appear as thin strands which are smaller and of more uniform size than collagen fibres
- they cannot be distinguished in routine H&E preparations and require special stains to make them visible (Stain brown with orcein)
- as seen with the electron microscope, elastic fibres consist of bundles of microfibrils embedded in an amorphous component called elastin.
- Elastin like collagen, contains glycine and proline but has little hydroxyproline and lacks hydroxylysin
- It has a high content of Valine and contains two amino acids desmosine and isodesmosine.

Figure 4–9 Note the presence of elastic fibers (*arrows*) in the matrix in this photomicrograph of elastic cartilage (×270).

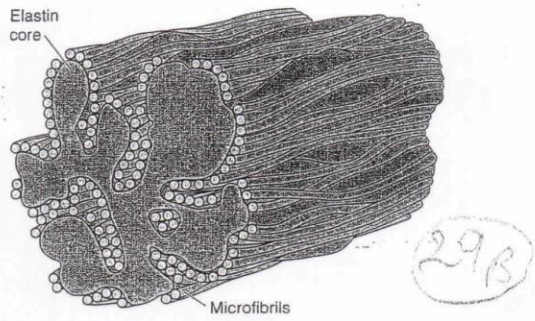


Figure 4–11 Schematic diagram of elastic fiber. Microfibrils surround the amorphous elastin.

29B

Elastic fibres

→ slender, long & branching in loose C-T

→ they may form bundles as in ligamentum flavum (vertebra column)

→ they may form sheets → in large blood vessels

→ manufactured by < fibroblasts of C-T.
Smooth muscle cells of blood vessels

→ Composed of ELASTIN → a protein rich in: glycine, alanine, lysine, valine, proline

No hydroxylysine

→ The CORE of elastic fibres is formed of elastin & is surrounded by a sheath of microfibrils formed of the glycoprotein fibrillin.

CLINICAL CORRELATIONS

The integrity of elastic fibers depends on the presence of microfibrils. Patients with **Marfan syndrome** have a defect in the gene on chromosome 15 that codes for fibrillin; therefore, their elastic fibers do not develop normally. People who are severely affected with this condition are predisposed to fatal rupture of the aorta.

Aurangi

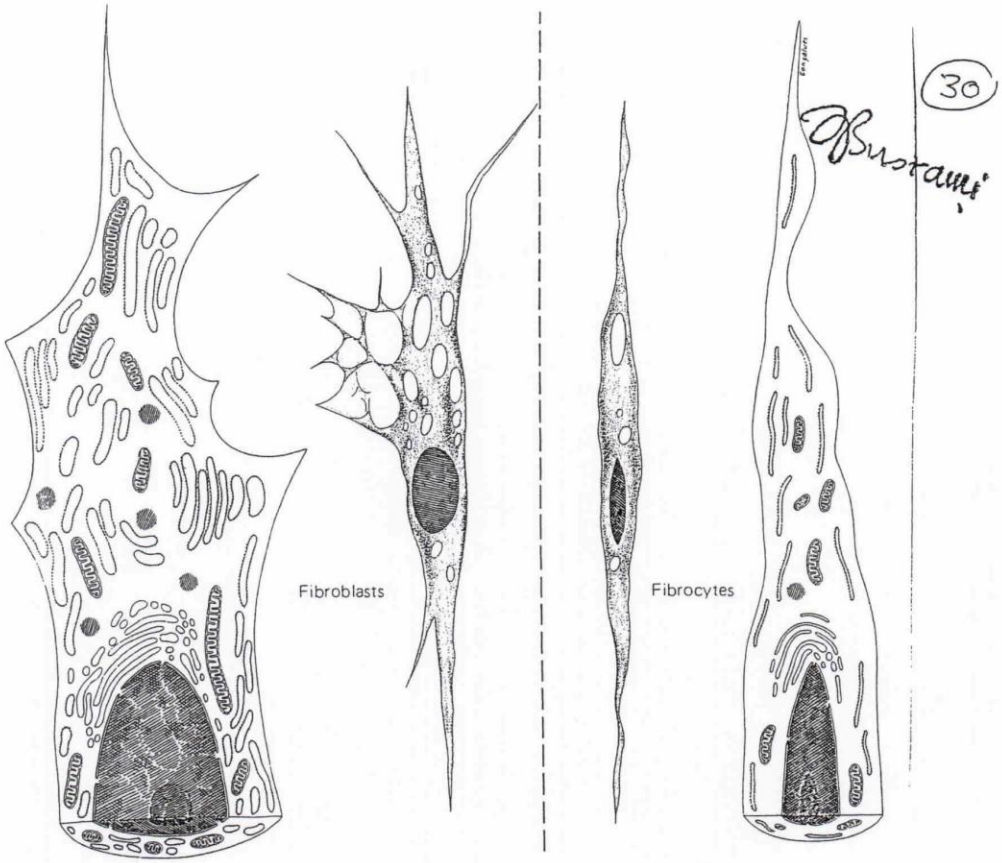


Figure 5–17. Active **(left)** and quiescent **(right)** fibroblasts. External morphologic characteristics and ultrastructure of each cell are shown. Fibroblasts that are actively engaged in synthesis are richer in mitochondria, lipid droplets, Golgi complex, and rough endoplasmic reticulum than are quiescent fibroblasts, often called fibrocytes.

Fibroblast → commonest C.T cell

↓

active in the formation of collagen, elastic & reticular fibres & the amorphous matrix

↓

cytoplasm is rich in Rough endoplasmic reticulum (RER)

⊕ well developed Golgi complex

→ basophilic cytoplasm

fibrocyte

↓

→ quiescent (less active)

→ smaller than fibroblast, spindle-shaped

seen in tendon & ligament

↓

small amount of RER → acidophilic cytoplasm

may revert to fibroblast during wound healing

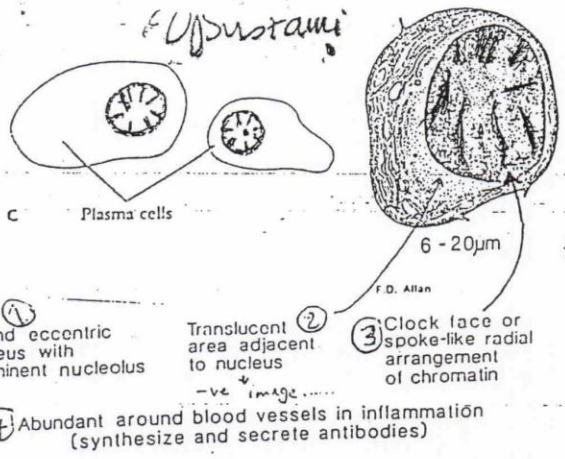
{Myofibroblast} !! → fibroblast

help wound closure so called wound contraction

⊕ actin & myosin filaments in its cytoplasm

PLASMA CELLS

31



* differentiate from B-lymphocyte
* Prime function → Synthesis & Secretion of antibodies (i.e immune globulins of the blood, which primarily act in the body's defenses against bacterial infections.

* Shape → oval or rounded (marked resemblance to lymphocytes)
* Size → from 6 - 20 μm
* cytoplasm → homogenous basophilic, suggestive of abundant rough endoplasmic reticulum
  → closely adjacent to the nucleus is a clear translucent area → the negative image of Golgi
  Unstained with H & E
  occasionally the cytoplasm contains acidophilic inclusion bodies

* THE PLASMA cell's MOST DISTINCTIVE FEATURE IS ITS UNUSUAL NUCLEUS which is round ECCENTRIC in position and has a Prominent nucleolus
Its chromatin is arranged in darkly staining CLUMPS along the inner surface of the nuclear membrane. Such a unique radial arrangement suggests the SPOKES of a WHEEL or a CLOCK FACE PATTERN.

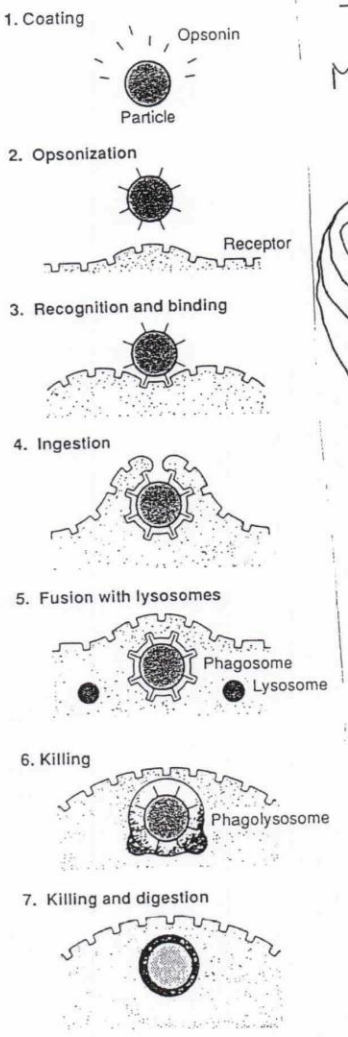
* plasma cells → occasionally found in the subcutaneous loose connective tissue EXCEPT IN INFECTION when they are VERY NUMEROUS especially around blood vessels

PLASMA CELLS ARE THE HALLMARK of SUBACUTE & CHRONIC INFLAMMATION

→ Macrophages

↓

Mononuclear Phagocyte System (MPS)



→ derived from → Precursors of monocytes in the bone marrow

→ almost as abundant as fibroblast

↓

→ difficult to distinguish from fibroblasts unless the macrophages show evidence of Phagocytosis

↓

→ they are actively phagocytic ingesting a variety of materials from inert matter (carbon Particles) to bacteria, tissue debris & whole dead cells

→ influence activation of immune response

↓

Macrophages can be identified readily in the tissues of animals that have been injected with colloidal materials such as trypan blue or india ink

→ the phagocytosed particles in the cytoplasm distinguish macrophages from fibroblasts

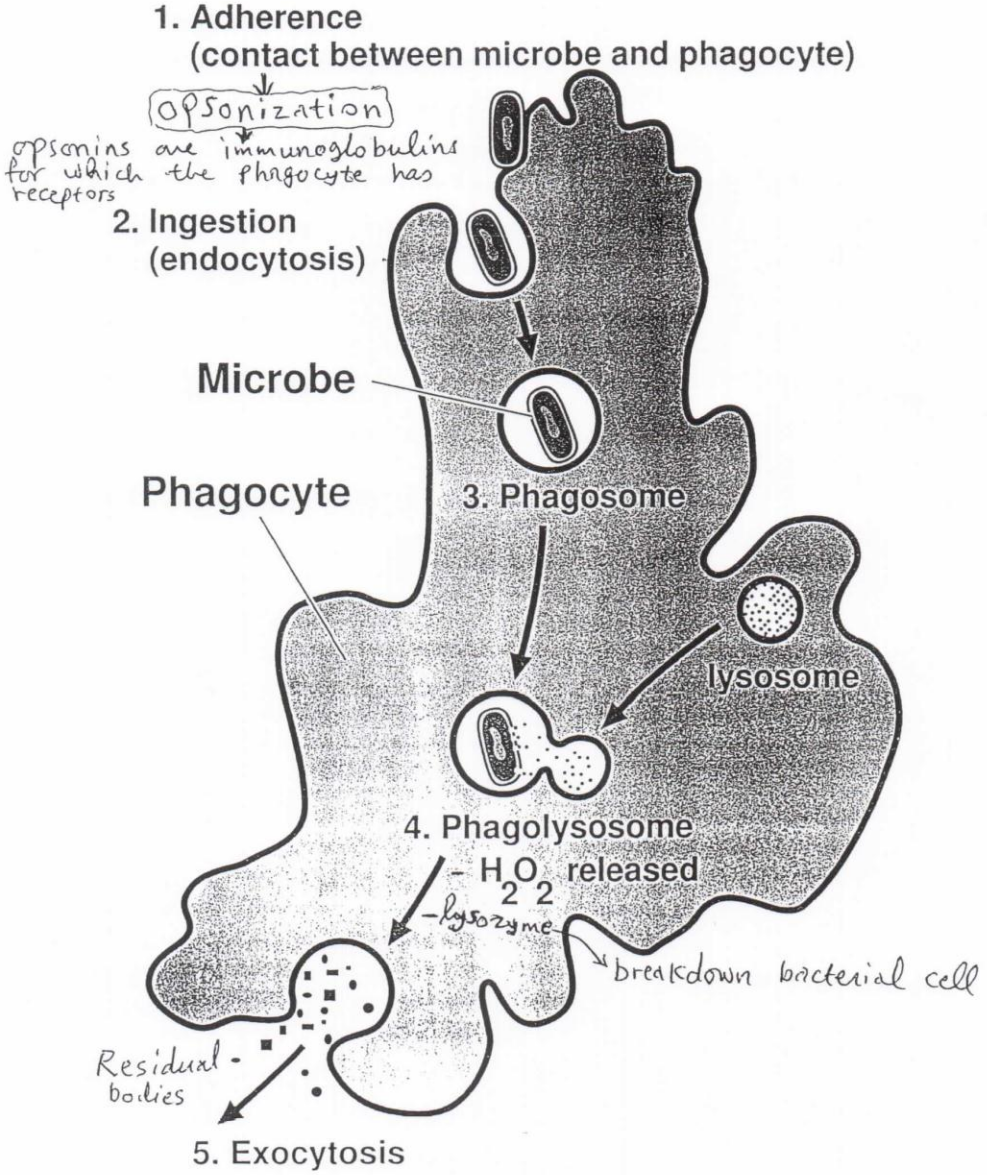
The macrophages of loose connective tissue are part of a generalized system of mononuclear phagocytes which includes phagocytes of liver → Kupffer cells of lung → alveolar macrophages of bone → osteoclasts of nervous system → microglial cells, of spleen & lymph node

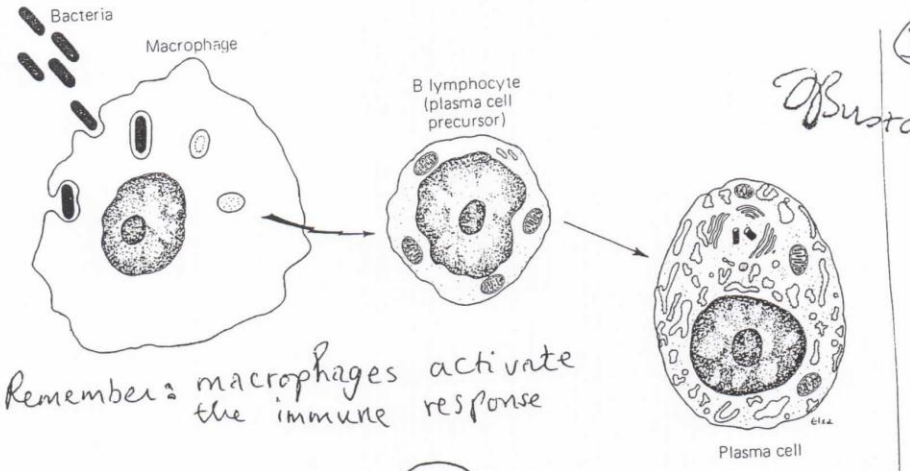
Regardless of where found → macrophages have a common origin from Precursors in the bone marrow

The monocyte of the blood represent a transit form of macrophages (wandering macrophages) → once they migrate to connective tissue they form (fixed macrophages)

PHAGOCYTOSIS

Neutrophils and macrophages phagocytize bacteria, virus-infected cells, cancer cells, and foreign materials





Remember: macrophages activate the immune response

Figure 5–21. Possible relationships between macrophages and plasma cells. It has been shown that some kind of information passes from macrophages to plasma cell precursors.

→ What is an activated macrophage? When the macrophages are stimulated e.g by infection → They change their metabolism & shape ① they show increase in their capacity for phagocytosis & intracellular digestion → increased lysosomal activity

→ What is the life span of a macrophage?

Normally about 2 months (Remember the life span of plasma cells 2-3 weeks)

→ Phagocytosis can be performed by cells other than macrophages, what are these cells??

① Neutrophils → most active phagocytic type of White blood cells
they are the first phagocytes to arrive at the site of infection or tissue damage

puss is an accumulation of dead neutrophils & bacteria

② Eosinophils → like neutrophils are attracted to the site of inflammation by leukocyte chemotactic factors
they combat parasites by releasing cytotoxins

They are also attracted to the site of allergic inflammation where they moderate the allergic reaction & phagocytose antibody-antigen complex

→ Sequence of events in phagocytosis

① Adherence (Contact between microbe & Phagocyte) followed by opsonization ② Ingestion (endocytosis) using Pseudopodia formed of plasma membrane ③ fusion of phagosome & lysosome to form Phagolysosome ④ Killing of microbe ⑤ exocytosis of Residual Body

MAST CELLS

Bustami

Main function → storage of chemical mediators of the inflammatory response

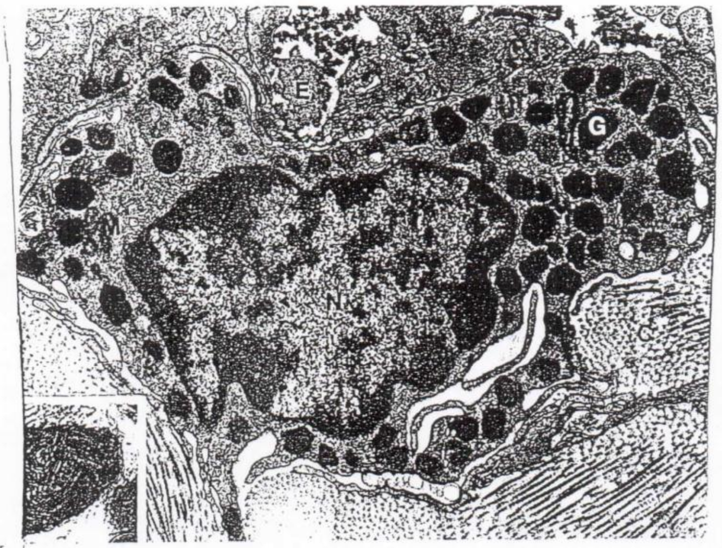


Figure 5–23. Thin section of connective tissue. Four mast cells appear with their conspicuous granules, stained by toluidine blue. × 800.

→ oval to round C-T cells 20-30 μm in diameter

→ centrally located nucleus

→ cytoplasm → contains closely packed large coarse granules that often obscure the small pale nucleus

يحتوي السيتوبلازم على حُبيبات كبيرة مزدحمة غالباً ما تُغطّي وتُخفي نواة الخلية

→ secretory granules are metachromatic i.e colour of granules (purple-red) is not the true colour of the applied dye (blue)

→ Secretory granules contain

a. Heparin (anticoagulant يمنع تجلط الدم) → This is connective tissue mast cell, another type of mast cell → mucosal mast cell → its granules contain chondroitin sulphate

b. Histamine → it causes dilation توسع of arterioles & تضيق constriction of venules → increase hydrostatic pressure within capillaries → increase filtration out of capillaries → edema → ورم النسيج زيادة السائل بين الخلايا

(Cause contraction of smooth muscles mainly of bronchioles)

c. ECF-A → eosinophilic chemotactic factor of anaphylaxis
This factor attracts blood eosinophils to the site of inflammation → eosinophils can modulate inflammation by inactivating histamine & leukotrienes produced by other cells

d. Neutrophil chemotactic factor → attracts neutrophil to the site of inflammation

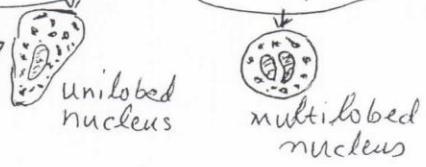
e. Leukotriens derived from membrane lipid (36) (arachidonic acid) → Vasodilator (يوسع الأوعية الدموية) increases permeability of capillaries, causes contraction of bronchial smooth muscles

f. Prostaglandin D_2 → derived from membrane lipid causes Vasoconstriction (يضيق الأوعية الدموية) & contraction of bronchial smooth muscles

G. Bradykinin → has similar effects to histamine. In addition it is responsible for pain sensation

The Relation between mast cell & Basophil

Mast cell is often referred to as connective tissue basophil !!



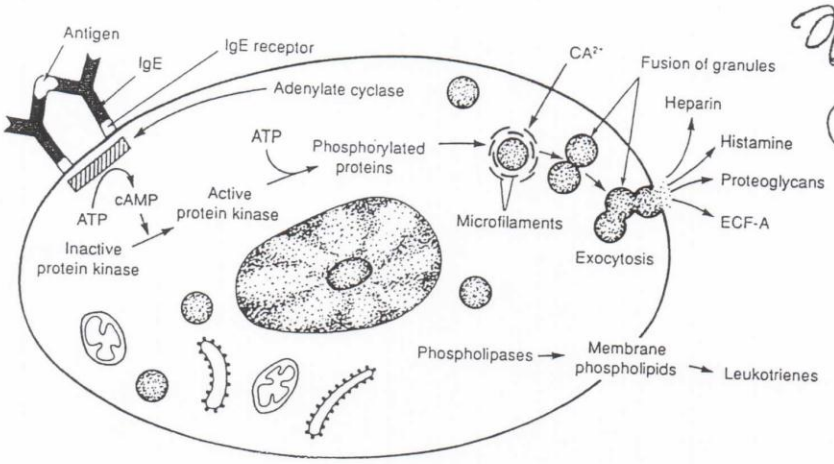
① Both cells (mast cell / basophil) → have metachromatic membrane-bound granules that contain (histamine / heparin / ECF-A) as well as Leukotriens (from cell membrane phospholipids)
↳ previously called (slow reactive substances of anaphylaxis)

These substances are called MEDIATORS !!
→ they are released in immediate hypersensitivity reactions e.g anaphylactic shock

② Both cells (mast cell / basophil) can attach IgE antibodies causing them to release their mediators e.g histamine .....etc

③ The two cells (mast- / basophil) originate from separate bone marrow stem cell

④ Mast cell is a fixed (Resident) C.T cell, present close to small blood vessels in the dermis of skin and mucosa of digestive & respiratory systems
basophil is a visitant C.T cell coming from the blood.



Mediator release from mast cells & basophil (mast cell secretion)

↓

Release of the chemical mediators stored in mast cells promotes the allergic reactions known as <u>immediate hypersensitivity reactions</u> because ?? they occur within a few minutes after exposure to an antigen of an individual previously sensitized to the same or a very similar antigen

e.g anaphylactic reaction → bee venom, certain drugs ... etc.

↓

first exposure to an antigen → formation of IgE antibodies which bind to special receptors on the plasmalemma of mast cells

↓

subsequent exposure to the SAME antigen → the antigen BINDs to the IgE on the mast cell causing CROSS-linking of the bound IgE antibodies and accumulation of receptors ⇒ Activation of adenylate cyclase the enzyme responsible for the conversion of ATP to cAMP → Activation of Protein Kinases → enzymes that catalyze the transfer of phosphate from a molecule of ATP to a protein → This changes the shape of the protein and therefore its function → The protein may be an enzyme or ion-channel

↓

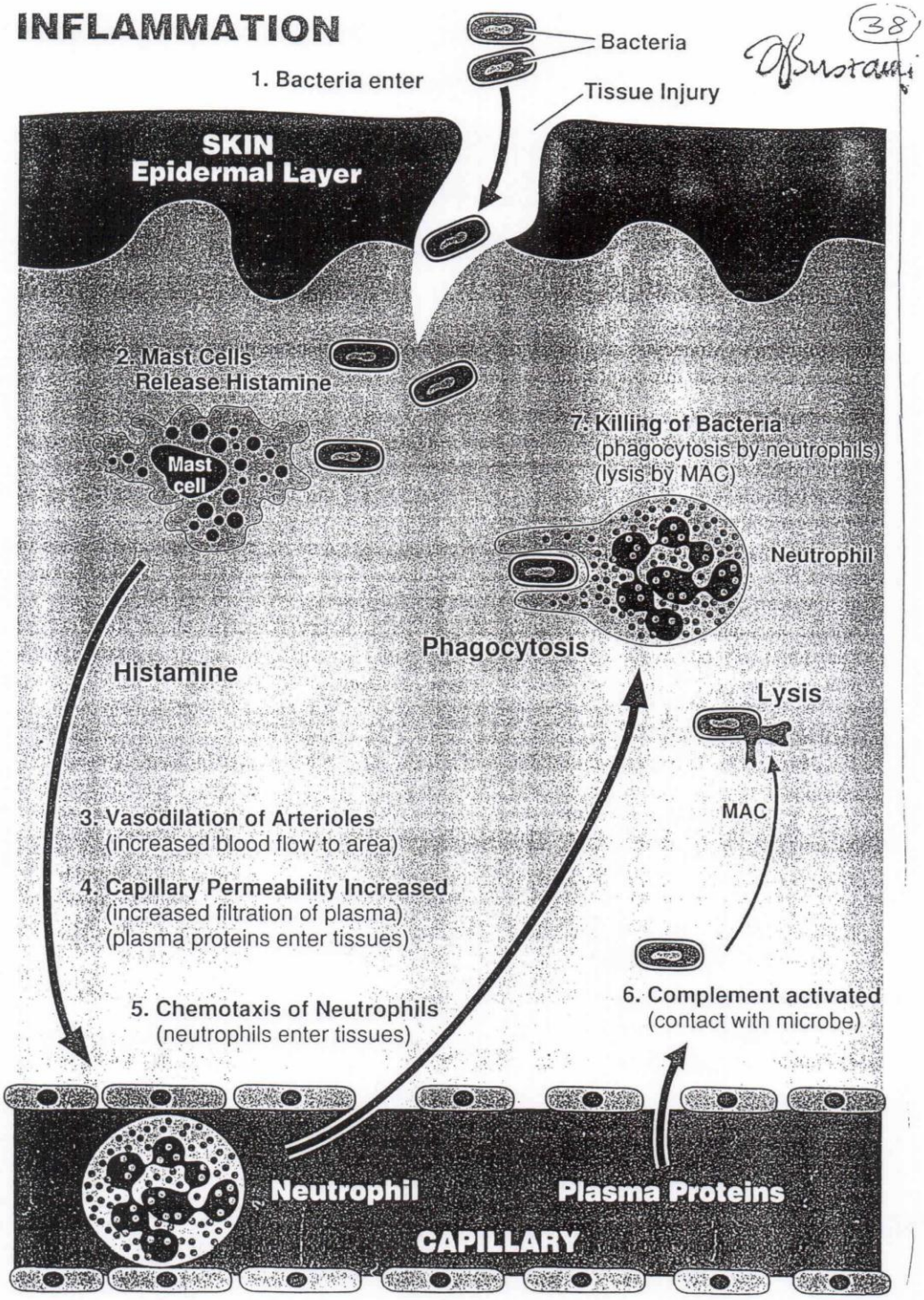
↑ in cytosolic Ca^{2+} ← release from intracellular storage (ER)

↓ ← influx from extracellular source

(Degranulation)

↓

the secretory granules fuse with one another as well as with cell membrane → Release of granule content .....



During the initial or acute phase of inflammation the neutrophils predominate → when the inflammation persists & enters the chronic phase → cells change → lymphocytes & macrophages come from blood & plasma cells originate from B lymphocytes

Cross-linking of the membrane-bound IgE also activates phospholipase A2 which acts on membrane phospholipids to form arachidonic acid converted into secondary mediators (leukotriens, Prostaglandins) (39)

NONSPECIFIC RESISTANCE / Inflammation

Definition Inflammation is a local, nonspecific response to tissue damage. The tissue damage may be due to microbes, chemical irritants, physical trauma, or exposure to extreme temperatures. Regardless of the cause, the response is basically the same. The key role is played by phagocytes, which engulf the microbes or damaged cells and destroy them.

SEQUENCE OF EVENTS (for a bacterial infection)

(1) Bacteria Enter the Tissues Bacteria penetrate the skin or mucous membrane, multiply, and cause tissue damage. (Tissue damage without bacterial invasion causes the same response.)

(2) Mast Cells Release Histamine Mast cells in the connective tissue are stimulated by the presence of bacteria and damaged tissue cells to release histamine. Mast cells also release prostaglandins and leukotrienes. Damaged tissue cells also release histamine and prostaglandins. The released chemical mediators diffuse to nearby blood capillaries and arterioles.

(3) Vasodilation of Arterioles Histamine causes local arterioles to dilate, increasing the flow of blood to the infected area.

(4) Capillary Permeability Is Increased Histamine causes local capillaries to become permeable to plasma proteins by inducing endothelial cells to contract, opening the spaces between them. Plasma proteins that mediate inflammation are able to pass through the capillary wall into the infected area. Histamine triggers the conversion of an inactive plasma protein (kininogen) into peptides called kinins. Kinins enhance vasodilation and capillary permeability and function as chemotaxins (chemicals that attract phagocytes). Prostaglandins (released by damaged tissue cells) intensify the effects of histamine and kinins. Clotting factors are activated, forming a mesh of fibrin that helps to isolate the infected area and prevent the spread of bacteria. Increased permeability of capillaries increases the filtration of plasma, resulting in a buildup of fluid in the tissue spaces (edema).

(5) Chemotaxis of Neutrophils Chemotaxis is the attraction of phagocytes to microbes or damaged tissue by a chemical stimulus. Neutrophils migrate to the infected area attracted by chemotactic chemicals. They squeeze through capillary walls into the tissue spaces, a process called diapedesis.

(6) Activation of Complement Complement proteins are activated by contact with bacterial surfaces. Activated complement proteins cause vasodilation, increased capillary permeability, and chemotaxis of neutrophils. One complement protein (C3b) coats bacteria (opsonization), enhancing phagocytosis.

(7) Killing of Bacteria Neutrophils (a type of white blood cell) phagocytize bacteria, digesting and killing them. Five of the activated complement proteins, called the membrane attack complex (MAC), become embedded in the bacterial plasma membrane; channels are formed in the membrane, causing the bacterial cell to burst (lysis) and die.

(8) Tissue Repair Fibroblasts divide rapidly and secrete collagen, forming scar tissue. Usually local tissue cells divide, forming new organ-specific cells.

SYMPTOMS

(1) Redness The redness is a result of increased blood flow to the infected area.
(2) Pain Pain may be caused by the stimulation of pain receptors by kinins, injury of nerve fibers, and irritation by toxic chemicals released by microbes.
(3) Heat The heat is due to the large amount of warm blood flowing to the area and the increased metabolic activities occurring in the area.
(4) Swelling An increase in the permeability of the capillaries permits more fluid to move from the blood into the tissue spaces.

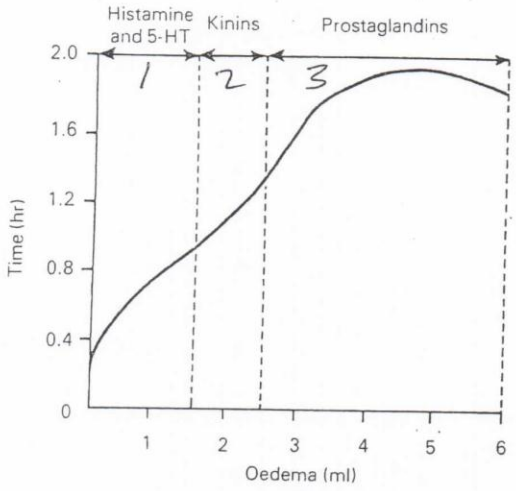


Fig. 10.8 Sequential release of mediators of increased vascular permeability.

40

Bustamante

1→ Remember that (histamine) is released from mast cell stimulated by bacteria & damaged tissue cells → diffuse to nearby capillaries & arterioles

⇩

Vasodilation of arteriales ⊕ ↑ capillary permeability

<To plasma proteins>

↙

2→ inactive plasma protein (Kininogen) —Histamine→ Kinin → ↑ vasodilation & capillary permeability; Chemotaxin

3→ Prostaglandins (released by damaged tissue cells)

⇩

intensify the effects of histamine & Kinins

In summary, increased vascular permeability can be due both to direct ethothelial damage affecting capillaries and venules, and to the action of chemical mediators causing endothelial contraction only in venules.

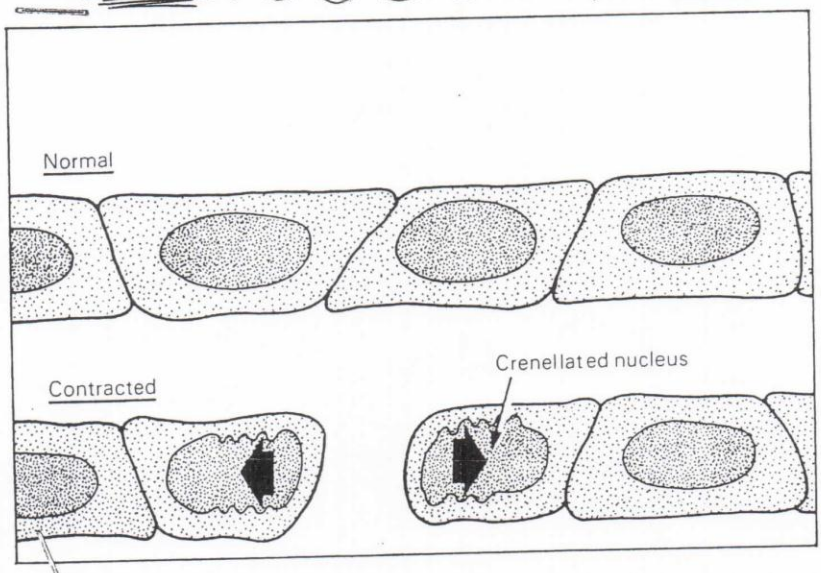


Fig. 10.5 Contraction of vascular endothelium to allow escape of plasma protein.

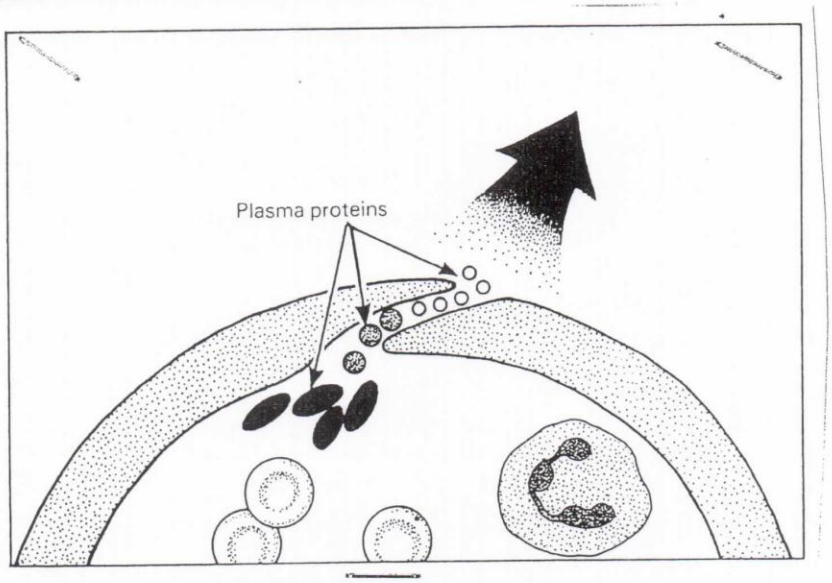


Fig. 10.4 Increased permeability of venule to plasma proteins. The proteins escape in inverse proportion to the molecular size (molecular sieving).

Complement ----> plasma protein (activated) by contact with bacterial surfaces

Vasodilation ⊕ ↑ capillary permeability
⊕ chemotaxis of neutrophils
⊕ C_3b → coats bacteria (opsonization) enhancing phagocytosis

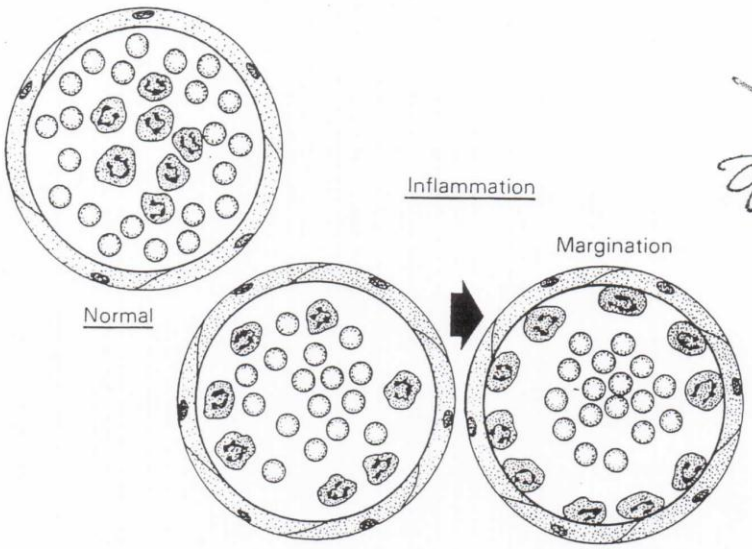


Fig. 10.3 Margination of leucocytes in acute inflammation

the leucocytes, leave the centre of the stream which they normally occupy to move to the periphery. They then form a layer against the inner surface of the cells which line the lumen of the blood vessels, the vascular endothelium, a process known as margination and which is a prelude to the migration of leucocytes through the vessel wall into the adjacent tissues (Fig. 10.3).

At the same time a crucial change occurs in the wall of the venules and capillaries. These vessels are normally freely permeable to water and small solutes but only slightly permeable to plasma proteins, i.e. albumin, the globulins and fibrinogen. In fact, it is the oncotic pressure of these retained molecules which counters the hydrostatic pressure of the blood. This oncotic pressure keeps water inside the vessels whereas the tangential thrust of the blood pressure pushes it out through the vessel wall like a positive pressure filter. In inflammation, hydrostatic pressure inside the vessel may rise, the balance be upset and more water may leave the blood and enter the tissues. More important, the wall of the venule and capillary now loses its impermeability to protein. As a result, albumin, globulins and fibrinogen pour out through the wall into the tissues, which thus come to contain fluid with a composition similar to that of blood plasma (Fig. 10.4). The swelling of the tissues is known as oedema and the fluid itself is the fluid exudate. The change in the properties of the vessel wall is called increased vascular permeability.

DIAPEDESIS

Bustami

43

Leukocytes (White blood cells) are frequently found in connective tissue

↓

There is a continuous movement of leukocytes from blood to connective tissue across the walls of capillary & venule ⟹ Diapedesis → increases greatly during inflammation

↓

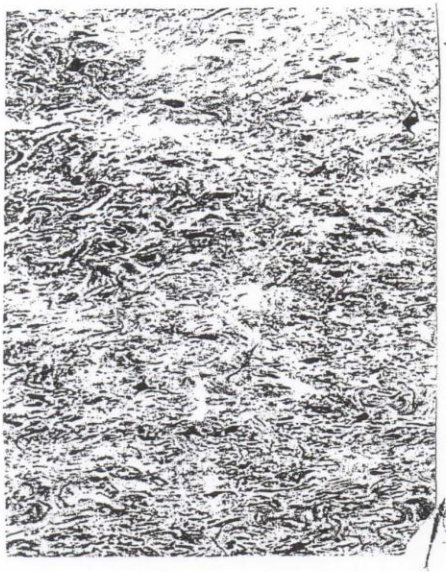
These cells (leukocytes) DO NOT move back into the blood after reaching connective tissue → the only exception is the lymphocyte.

Types of Connective tissue > C-T

- (A) Embryonic C.T. < Mesenchymal C-T, Mucous C-T
- (B) C.T. Proper
  - ① Loose (areolar) C.T
  - ② Dense C-T
    - regular
      - collagenous (tendon)
      - elastic
    - irregular → (Dermis)
  - ③ Reticular
  - ④ adipose
- (C) special C.T. → cartilage, bone, blood

Mesenchymal C-T

- Present only in the embryo
- formed of mesenchymal cells which resemble fibroblasts → cytoplasm send processes in different directions ⊕ gel-like matrix ⊕ few reticular fibres
- can differentiate into a variety of adult C-T cells
- In the adult (Pericytes) correspond to mesenchymal cells, present along capillaries, can differentiate into other C.T cells



Mucous (mucoid) tissue

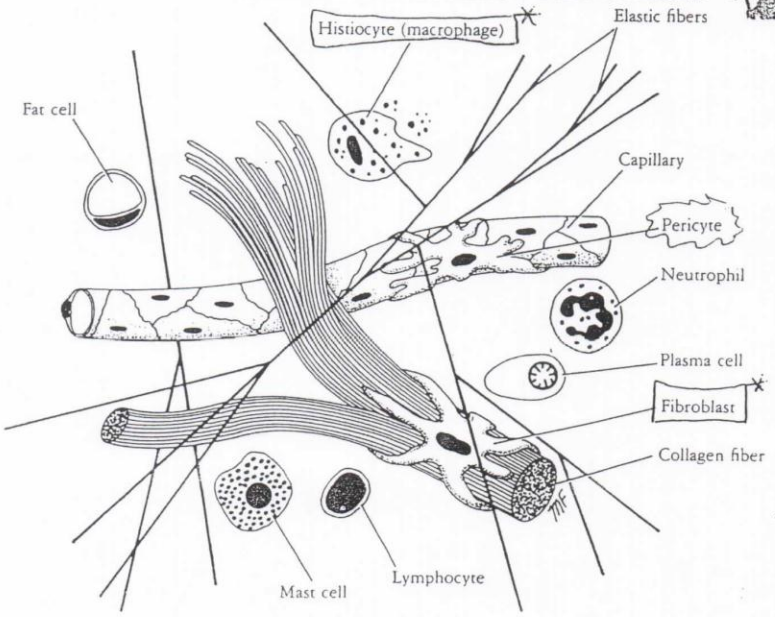
- Jelly-like matrix primarily composed of hyaluronic acid
- ⊕ few collagen fibres (type I, type III)
- ⊕ cells have differentiated into fibroblasts (stellate-shaped)

This tissue is also known as Wharton's jelly → present in Umbilical cord

Loose (areolar) C.T

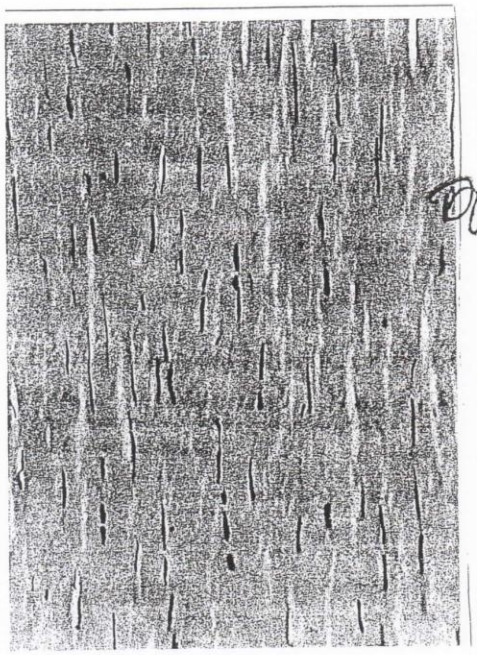
has abundance of cells & ground substance but relatively sparse fibre development

- * The most numerous cells are fibroblasts & macrophages but all other types of C.T cell are present also
- * Collagen, elastic & reticular fibres are present



Loose C.T

- → supports most epithelial tissues
- → forms septa that separates organs into lobes
- → forms a layer that ensheaths blood vessels
- → forms subcutaneous tissue (superficial fascia)
- → forms the lamina propria (deep to epithelium that forms mucosa of alimentary canal)



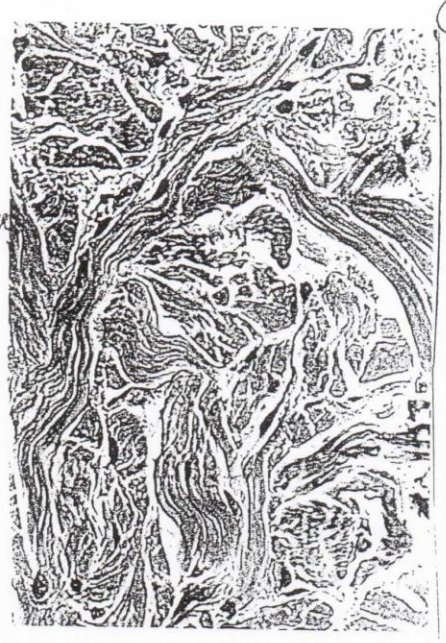
Dense "Regular" C-T

↓ e.g

TENDON

↓

Parallel closely Packed bundles of collagen → Their fibrocytes contain elongated nuclei parallel to the fibres → their cytoplasm is rarely revealed in H & E stains because it stains the same colour as the fibres → Notice the direction of collagen bundles in the line of Pull of a tendon



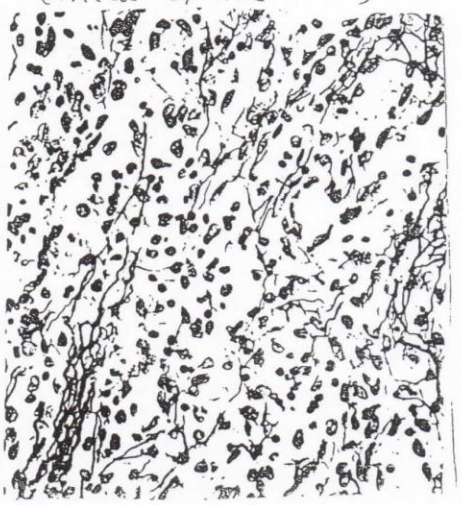
Dense "Irregular" C-T

↓ e.g

DERMIS

↓

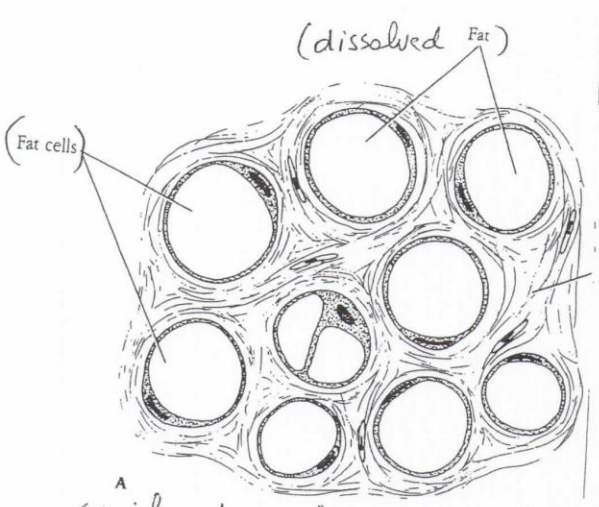
collagen fibres are arranged in bundles without a definite orientation. The collagen fibres provide resistance to stress from all directions → fine network of elastic fibres are present between collagen bundles (need special stain)



Reticular tissue → forms the stroma (framework) of bone marrow, lymph nodes & spleen

→ Reticular cells are simply fibroblasts specialized for secreting reticular fibres which are collagen type III fibres

→ Reticular fibres are argyrophilic (stained with silver)



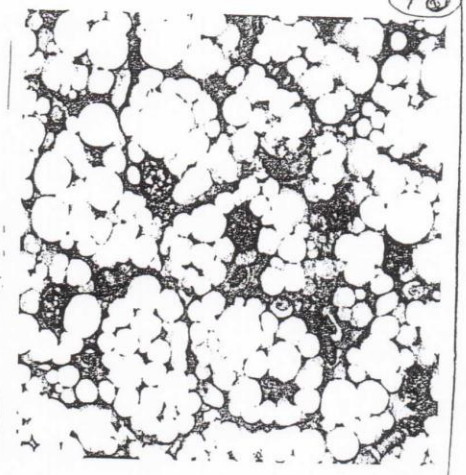


Figure 6–5. Photomicrograph of multilocular adipose tissue with its characteristic cells containing central spherical nuclei and multiple lipid droplets. × 1000.

<Unilocular adipose tissue>

Adipose tissue is a special type of connective tissue in which adipose cells (adipocytes) predominate

Unilocular adipose tissue	Multilocular adipose tissue
1. fat cell contains a single lipid droplet. The cell (50-150 μm) in diameter has a signet-ring appearance → it appears as a thin ring of cytoplasm surrounding the vacuole left by the dissolved lipid droplet with eccentric flattened nucleus	1. fat cells contain multiple lipid droplets with a central rounded nucleus
2. Colour → **white or yellow** (yellow when the food is rich in caritenoids e.g carrots)	2. **Brown** in colour due to (a) large number of blood capillaries (b) numerous mitochondria that contain cytochrome
3. Site → throughout the body e.g Subcutaneous tissue (superficial fascia), neck, shoulders buttocks, breast in females, anterior abdominal wall	3. mainly in the newly born → In the neck or interscapular region

4. **Both are richly innervated by Sympathetic nerves**

In Unilocular adipose tissue nerve endings are found only in the wall of blood vessels ⟹ nerve endings are present in blood vessels as well as adipocytes

Basement membrane

↓

① Narrow Acellular region present between epithelium and connective tissue

② due to the presence of GAGS (glycosaminoglycans) it is well stained by the PAS reaction & silver salts

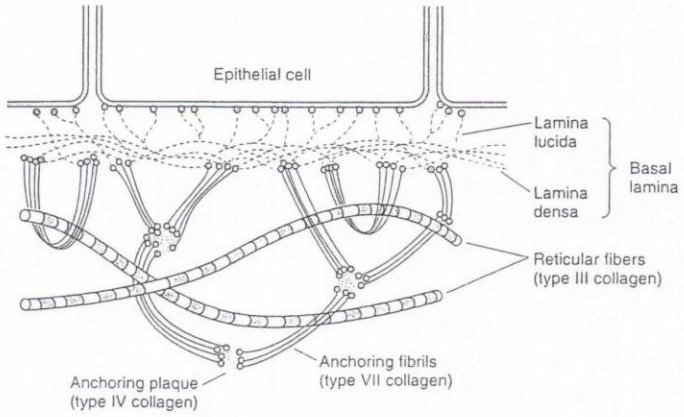
⊗ What is the External lamina → a structure similar to the basement membrane that surrounds Smooth & Skeletal muscle cells, adipocytes & Schwann cells

↓

Basement membrane is visible by light microscopy

↓

by electron microscopy (EM) it is better defined into 2 constituents



- Basal lamina → lamina lucida / lamina densa
- lamina reticularis

Basal lamina → produced by epithelial cells

lamina reticularis → produced by connective tissue cells

- By (EM) → Basal lamina → lamina lucida / lamina densa

- lamina lucida → consists mainly of the extracellular glycoproteins laminin & entactin as well as integrins that project from the epithelial cell membrane into the basal lamina

- lamina densa → formed of a meshwork of type IV collagen (coated on both the lamina lucida & lamina reticularis sides by a proteoglycan Perlecan

What connects the basal lamina to the reticular lamina? several substances including fibronectin anchoring fibrils (type VII) & microfibrils (fibrillin) ⟹ all produced by connective tissue (C-T) cells (fibroblasts)

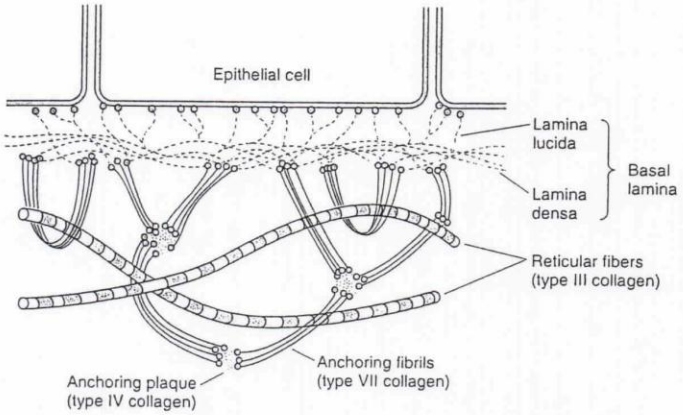
Basal lamina function → Both as molecular filter & Support for the overlying epithelium

Basement membrane

① Narrow Acellular region present between epithelium and connective tissue

② due to the presence of GAGs (glycosaminoglycans) it is well stained by the PAS reaction & Silver salts

⊛ What is the External lamina → a structure similar to the basement membrane that surrounds Smooth & Skeletal muscel cells, adipocytes & Schwann cells



Basement membrane is visible by light microscopy

↓

by electron microscopy (EM) it is better defined into 2 constituents

- Basal lamina → produced by epithelial cells
- lamina reticularis → produced by connective tissue cells

- By (EM) → Basal lamina
  - lamina lucida
  - lamina densa

- lamina lucida → consists mainly of the extracellular glycoproteins ⇄ laminin ⇄ entactin as well as integrins that project from the epithelial cell membrane into the basal lamina
- lamina densa → formed of a meshwork of type IV collagen (coated on both the lamina lucida & lamina reticularis sides by a proteoglycan perlecan

What connects the basal lamina to the reticular lamina?

several substances including fibronectin anchoring fibrils (type VII) & microfibrils (fibrillin) ⟹ all Produced by Connective tissue (C-T) cells (fibroblasts)

Basal lamina function → Both as molecular filter & support for the overlying epithelium