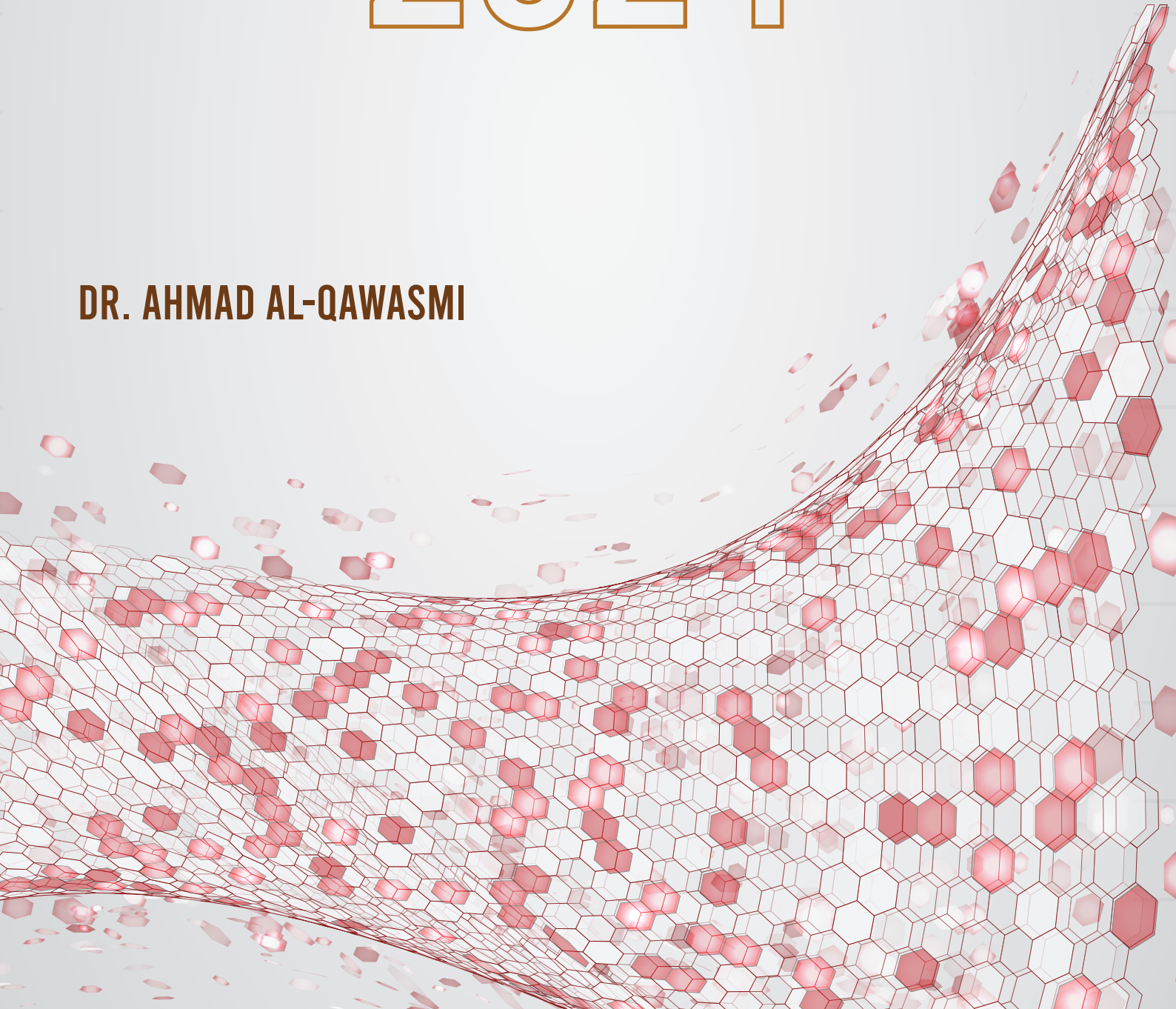


HISTOLOGY

2024

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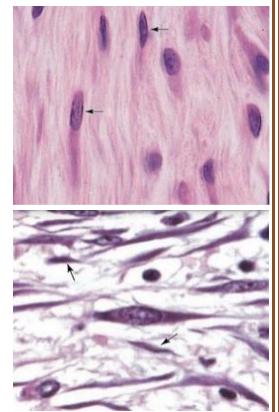
❖ Connective Tissue

- Connective tissue consists of cells, fibers and ground substance
 - **Ground substance:** It is a complex of anionic hydrophilic proteoglycans, glycosaminoglycans (GAGs) and multi adhesive glycoproteins (laminin, fibronectin, and others)
- Connective tissue originates from the *mesoderm* which differentiate into *mesenchymal cells*
- Functions of the connective tissue:
 - Structural *framework*
 - *Supports*, surrounds, and connects other tissues
 - *Transportation of fluids* and dissolved substances (by blood)
 - *Protection* of delicate organs such as capsules surrounding organs
 - *Storage of energy* in the form of lipids (Adipose tissue)
 - *Defend* the body against microorganisms

- Cells of the connective tissue:

1) Fibroblasts

- They are **active** cells with a *large euchromatic nucleus (pale stained)*, large amount of cytoplasm, abundant organelles and highly developed RER and Golgi
 - ✓ The **most common** cells of the general connective tissue
 - ✓ **Produce** the **fibers** (including collagen and elastin) and **ground substance**
 - ✓ Produce **growth factors** which stimulate cell differentiation and growth
- **Fibrocytes** are **inactive (quiescent)** cells with smaller spindle shape, fewer processes, *darker smaller nucleus*, and tiny amount of cytoplasm
 - ✓ **Maintain** the fibers (including collagen and elastin) and ground substance



2) Adipocytes

3) Immune cells

- They include: Mast cells, Plasma cells, macrophages, White blood cells (WBC)
- **WBCs (leukocytes)** include neutrophils, eosinophil, basophil, lymphocytes and monocytes
- **Macrophages** have a *kidney-shaped nucleus* and undergo phagocytosis, clearing of the dead cells and tissue debris, inflammation and representation of the antigen by Major histocompatibility complex (**MHC**) molecules
 - ✓ Macrophages originate from the *monocytes*
 - ✓ Monocytes leave the blood into the tissues forming **Kupffer cells** (liver), **microglial cells** (CNS), **langerhans cells** (epidermis), **osteoclast** (bone, regulate calcium levels), **dendritic cells** (spleen, lymph nodes) and **dust cells** (lungs)

Permanent (resident) cells:

- Fibroblast
- Macrophage
- Adipocytes

Transient cells:

- Mast cells
- Leukocytes (WBC)
- Plasma cells

- **Mast cells** are oval or *irregularly shaped* cells of connective tissue between 7 and 20 micrometers in diameter, they are filled with *basophilic secretory granules*
- The major product of mast cells is *histamine (vasodilator)* and *heparin (anticoagulant)* which is important in **allergies** and inflammation
- **Metachromasia:** The ability to **change the color** of the cell
 - ✓ Mast cells undergo metachromasia due to the high content of acidic radicals in their GAGs and so can change their color in the basic dyes (such as toluidine blue) from **blue to red** or purple

- **Plasma cells:** They are *lymphocyte*-derived, **antibody-producing** cells, and they are relatively large ovoid cells with basophilic cytoplasm rich in RER and a large Golgi apparatus near the nucleus that may **appear pale** in routine histologic preparations (negative Golgi staining)
 - ✓ The nucleus of the plasma cell is generally spherical eccentrically placed, which regions of euchromatin and regions of heterochromatic (*car-wheel shape*, clock-like shape)
 - ✓ Their average lifespan is only **10-20 day**

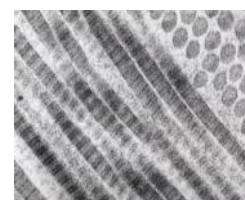
- Fibers of the connective tissue:

1) Collagen

- The **most common** type of proteins and stained with H&E where it appears *pinkish (eosinophilic)*
- Undulating longitudinally striated (Gapping lighter) bundles form **non-extensible** meshwork
- Gives the **strength** of the connective tissue
- Synthesized by fibroblasts
- It is subdivided into subfamilies:

a) Fibrillar collagens

- Include collagen **I, II, III**, and form bundles (fibrils, fibers)
- Form the *tendons, capsules* and *dermis*
- It is the **most common** (widely spread subfamily), and especially collagen type I is the most common
- They are synthesized in the **RER** as Procollagen → Collagen fibril → Collagen Fiber → Collagen bundle



b) Network or sheet-forming collagens

- Type **IV** collagen have subunits produced by **epithelial cells** (major structure of basal laminae)

c) Linking/anchoring collagens

- Short and small proteins (type **VII**) link or connect different proteins together

Disorder	Defect
Ehlers-Danlos type IV	Faulty transcription or translation of collagen type III
Ehlers-Danlos type VI	Faulty lysine hydroxylation
Ehlers-Danlos type VII	Decrease in procollagen peptidase activity
Scurvy	Lack of vitamin C, a required cofactor for prolyl hydroxylase
Osteogenesis imperfecta	Change of 1 nucleotide in genes for collagen type I

2) Elastic fibers

- **Poorly stained with H & E**, stained brown-black *orcein, resorcin fuchsin* and *Verhoeff van Gieson's*
- In the *dermis*, you need collagen to resist tension and elastic fibers for recoiling
- You can find it in *lungs* and the wall of large **blood vessels**, especially arteries (aorta)
- Synthesized by fibroblasts

3) Reticular fibers

- Delicate extensible network, **unstained** by H & E
- Stained by **PAS (+ve)**, stained black in *AgNO₃ (Argyrophilic)*
- Found in such as **bone marrow, liver** (hematoxylin), **lymph nodes** and **spleen**, which are structures associated with blood cells formation and maturation
- **Surround adipocytes, smooth muscle** and **nerve fibers**, and **small blood vessels**
- Serve as the supportive **stroma** for the parenchymal secretory cells, liver, and endocrine glands
- Mainly composed of **collagen type III** with some modifications
- Synthesized by **reticular cells**

❖ Ground substance

- A semi-fluid gel (highly hydrated) and transparent material represents a medium for passage of materials

- Composed of:
 - *Adhesive glycoproteins*: have major component (proteins), and minor component (sugar)
 - *Proteoglycans*: responsible for the **gel state** of the ECM because of its ability to hold water, major component (sugar of GAGs) and minor component (proteins)

- *Glycosaminoglycans (GAGs)*: repeated disaccharide connected together contain sugar that contains amine

Glycosaminoglycan	Distribution
Hyaluronic acid	Umbilical cord, synovial fluid, vitreous humor, cartilage
Chondroitin 4-sulfate	Cartilage, bone, cornea, skin, notochord, aorta
Chondroitin 6-sulfate	Cartilage, umbilical cord, skin, aorta (media)
Dermatan sulfate	Skin, tendon, aorta (adventitia)
Heparan sulfate	Aorta, lung, liver, basal laminae
Keratan sulfate	Cartilage, nucleus pulposus, annulus fibrosus

- Hyaluronic acid (hyaluronan)*
 - The **longest GAG**

❖ Classification of connective tissue

- Embryonic connective tissue includes:

1. *Mesenchyme CT*

- Sparse, **undifferentiated** cells, uniformly distributed in matrix with sparse collagen fibers
- Found in the **mesodermal** layer of early embryo, where mesenchymal cells are **stem cells** of the CT

2. *Mucuos (Mucoïd tissue)*

- They are random fibroblasts and collagen fibers in viscous matrix
- A **gel-like** connective tissue with **few cells** found most abundantly around blood vessels
- It is formed in **embryo umbilical cord** which is attached to the mother placenta
 - ✓ The filling of the umbilical cord is also called **Whrton's jelly**
- It provides **support and cushion** for the structures (such as blood vessels)

- Adult connective tissue is divided into:

- **General (Proper) CT**, which includes **Loose (areolar) CT** and **Dense CT**
- **Specialized CT**

- Loose (areolar) connective tissue*

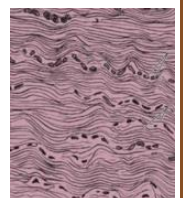
- It consists of all 3 types fibers, several types of cells and it is **randomly** distributed
- Semi-fluid ground substance (relatively **more ground substance and cells** and **less fibers** than dense)
- Found in **substance layer, mucous membranes, around blood vessels** and **nerves** and **organes**
- Its function is to provide **strength, support, cushioning** and **elasticity**
- Form **lamina propria** underlying the connective tissue

- Dense connective tissue*

- **Less ground substance and cells** but **thicker and more fibers** that tightly backed together, includes:

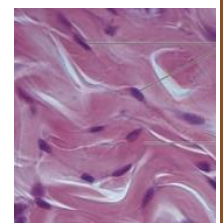
Regular dense CT

- ✓ It consists **bundles** of collagen fibers and fibroblasts, and it runs in **one direction**
- ✓ Found mainly in the **tendons** and **ligaments**
- ✓ It provides strong **connections with musculoskeletal** system, strong resistance force



A. Irregular dense CT

- ✓ Contain a little more ground substance than regular
- ✓ The fibers run in **all directions**
- ✓ Much collagen in randomly arranged fibers
- ✓ Found in **dermis** of skin, organ **capsules** and **submucosa** of digestive tract
- ✓ **Protects** and **supports** organs, **resists tearing**



- **Specialized connective tissue**
 - It includes cartilage, bone, blood, adipose and reticular tissues
- Reticular CT consists of fine irregular reticular fibers and reticular cells
 - Present in the Liver, Spleen, Lymph Nodes and the stroma
- **Adipose CT** consist of a **loose connective** tissue with **adipocytes (fat cells)**
 - Adipocytes are **ring shaped** cells
 - 15-20 % of body wight of a man body (slightly more in women)
 - Mostly contain neutral fats, mainly **triglycerides**
 - Fat is cleared during tissue preparation and fixation, so it appears negative under the microscope

- There are 2 types of adipose tissue:

1. White (yellow) adipose tissue

- Found in the **bellies** and **hips**
- Contain one large droplet of fat
- When completely developed, a white adipocyte is very large (50-150 micrometer) called **unilocular**
- Fat level is regulated by the metabolism of glycogen

By aging, White adipose is distributed differently between men (bellies) and women (hips)

2. Brown adipose (heater)

- Low amount, and its maximum amount is 2-5% of body weight in newborns
- Keeps body warm and **resist temperature changes** (**thermogenesis, heat production**)
- Found mainly in the **back, neck** and **shoulders**
- In **adults**, it is found in **scattered areas** (around kidneys, adrenal glands, aorta and mediastinum)
- Its color is due to the **abundant mitochondria** and blood vessels
- Contain many small lipid inclusions called **multilocular**
- Their cells are smaller and their nuclei are more centrally located

