Ministry of Higher Education and Scientific Research

University of Baghdad

College of Science

Department of Biology

Theoretical Histology Lectures 2022-2023

المرحلة الثالثة/الدراستين الصباحية والمسائية

الفصل الدراسي الاول

تدريسو المادة

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LEC 1 : Epithelial tissues:

Tissues:

A level of organization in multicellular organisms; it consists of a group of structurally and functionally similar cells and their intercellular material.

Types of tissues:

A. **Epithelial** – lining, covering, and glandular.
B. **Connective** – support
C. **Muscle** – movement
D. **Nervous** – control

Epithelial tissues:

- An epithelium (**pl., epithelia**) is composed of one or more layers of closely aggregated polyhedral cells with very little extracellular substance(matrix) between these cells.
- These cells have strong adhesion due to adhesion molecules, membrane interdigitations, and intercellular junctions.
- These features allow the cells to form cellular sheets that cover the surface of the body and line its cavities or are arranged as three-dimensional secretory units.
- No blood vessels penetrate an epithelium.

Functions of epithelial tissues:

Epithelia have four functions, although no one epithelium performs all of them. These functions include the following:

- **Physical protection:** Epithelial tissues protect both external and internal surfaces from dehydration, abrasion, and destruction by physical, chemical, or biological agents.
- **Selective permeability:** All substances that enter or leave the body must pass through an epithelium, and thus epithelial cells act as "gatekeepers." An epithelium typically exhibits a range of permeability(semi-permeable); it may be relatively impermeable to some substances, while promoting and assisting the passage of other molecules.
- **Secretions:** Some epithelial cells are specialized to produce secretions. Individual gland cells may be scattered among other cell types in an epithelium, or a large group of gland cells may form either an exocrine gland or an endocrine gland that produces specific secretions.
- **Sensations**: Epithelial tissues contain nerve endings to detect changes in the external environment at their surface. These sensory nerve endings and those in the underlying connective tissue continuously supply information to the nervous system concerning touch, pressure, temperature, and pain. Additionally, several organs contain a specialized epithelium called a neuroepithelium, that houses specific cells responsible for the senses of sight, taste, smell, hearing, and equilibrium.

Basement membrane:

- A thin, fibrous, extracellular matrix that separates the epithelial tissue from underlying connective tissue.
- May be observed as a single layer internal to the epithelium using the **light microscope**.
- However, in reality it consists of two layers when viewed using an **electron microscope**:

A. **Basal lamina:** contains collagen fibers as well as specific proteins and carbohydrates macromolecules, some of which are secreted by the epithelial cells. This layer can be further subdivided into two layers: **The lamina lucida:** a clear layer closer to the epithelium, and the **lamina densa:** a dense layer closer to the connective tissue.

B. **Reticular lamina:** Cells in the underlying connective tissue secrete the reticular lamina and it contains protein fibers and carbohydrates.

Function of basement membrane:

1. Provides support to the overlying epithelium.
2. Anchoring down the epithelium to its loose connective tissue (the dermis) underneath.
3. Acts as a mechanical barrier, preventing malignant cells from invading the deeper tissues
4. Other roles for basement membrane have been found that include blood filtration and muscle homeostasis

Intercellular junctions:

- Specialized regions of contact between the plasma membranes of adjacent cells.
- They are present in most tissues but are prominent in epithelia.
- Intercellular adhesion is especially marked in epithelial tissues that are subjected to traction and pressure (e.g., the skin).
- The intercellular junctions include the following types:

a. Tight junctions (zonula occludens):

- Encircles epithelial cells near their exposed apical surface.
- completely attaches each cell to its neighbors.
- The plasma membrane of adjacent cells fuse, nothing passes.

b. Adherens junction (zonula adherens):

- Protein complexes that occur at cell-to-cell junctions in epithelial and endothelial tissues. They are deeper in position than tight junctions.
- A point of junction between cells at which **actin filaments (**microfilaments) from inside the cell pass across the adjacent cell membrane forming a belt-like adherence junction called an **adhesion belt**.

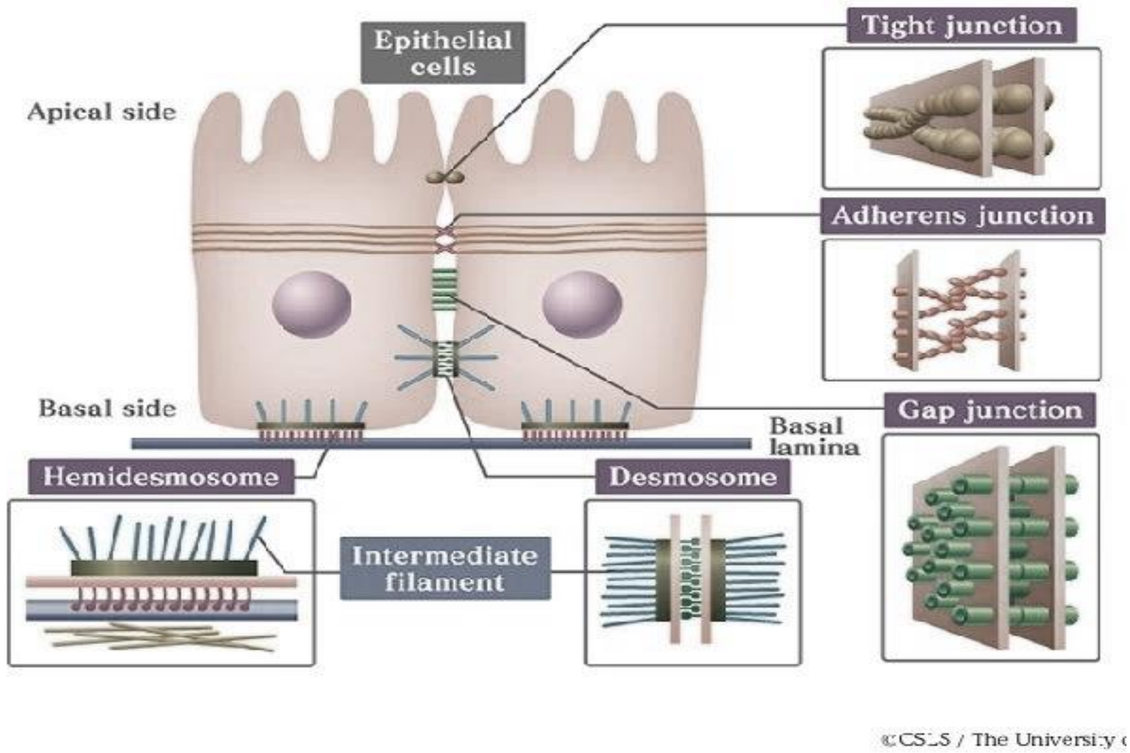
c. Gap junctions (macula communicans):

- An organized collections of protein channels in cell membranes that allows ions and small molecules to pass between adjacent cells.
- The protein channels consist of two **connexons proteins,** and each connexon consist of six subunits called **connexins.**
- Each connexon aligns and joins the connexon of the neighboring cell, forming a **continuous aqueous pathway** by which ions and small molecules can freely pass (passively) from one cell to the other.

d. Desmosomes (macula adhaerens):

- A complex disk-shaped structure at the surface of one cell that is matched with an identical structure at the surface of the adjacent cell.
- It is found in tissue that experience intense mechanical stress
- Button-like spots that are not totally encircle the cell.
- Desmosomes have **intermediate filaments** in the cells underneath that help anchor the junction.
- In the contact zone between certain epithelial cells and the basal lamina, **hemidesmosomes** can often be observed.
- These structures take the form of half a desmosome and bind the epithelial cell to the subjacent basal lamina.

Intercellular junctions



Classification of Epithelial Tissue

Epithelia are divided into two main groups according to **their structure and function**:

1. **Covering & lining epithelia** form the outer layer of the skin; lines open cavities of the digestive and respiratory systems; covers the walls of organs of the closed ventral body cavity.
2. **Glandular epithelia** form the glands within the body.

Covering & lining Epithelia:

- In which the cells are organized in layers that cover the external surface or line the cavities of the body.
- They can be classified according **to the number of cellular layers** into:
  - A. **Simple epithelium**
  - B. **Stratified epithelium**
  - C. **Pseudostratified**

A. Simple epithelium

- A simple epithelium is one cell layer thick, and all of the epithelial cells are in direct contact with the basement membrane.
- A simple epithelium is found in areas where stress is minimal and where filtration, absorption, or secretion is the primary function.
- **Examples of locations include** the lining of the air sacs of the lung, the intestines, and blood vessels.

B. Stratified epithelium

- Contains two or more layers of epithelial cells. Only the cells in the deepest (basal) layer are in direct contact with the basement membrane.
- A stratified epithelium resembles a brick wall, where the bricks in contact with the ground represent the basal layer and the bricks at the top of the wall represent the apical (superficial) layer.
- A stratified epithelium is found in areas likely to be subjected to abrasive activities or mechanical stresses, (**e.g.,** skin, internal lining of the pharynx and esophagus).
- Cells in the basal layer continuously regenerate as the cells in the apical layer are lost due to abrasion or stress.

C. Pseudostratified epithelium

- Looks layered (stratified) because the cells' nuclei are distributed at different levels between the apical and basal surfaces.
- Although all of these epithelial cells are attached to the basement membrane, some of them do not reach its apical surface.
- For studying purposes, pseudostratified epithelium has been classified as a type of simple epithelium, because all of the cells are attached to the basement membrane.

LEC 2: Simple epithelial tissues\ Classification by cell shape:

Simple epithelial tissues are generally classified **by the shape of their cells**. The four major classes of simple epithelium are:

1) **Simple squamous epithelium**
2) **Simple cuboidal epithelium**
3) **Simple columnar epithelium**
4) **Pseudostratified columnar epithelium**

1) Simple Squamous Epithelium:

- Simple squamous epithelium cells are flat in shape(scales) and arranged in a single layer, the cell is irregular in shape and has a disk-shaped flattened nucleus.
- This single layer is thin enough to form a membrane that compounds can move through via passive diffusion.
- Both the endothelial lining of blood vessels and the mesothelial lining of the body cavities (pericardial, pleural and peritoneal) as well as the external surfaces of visceral organs are simple squamous epithelium.
- The mesothelium gets its name from the germ layer mesoderm from which it derived.

2) Simple Cuboidal Epithelium

- Simple cuboidal epithelium consists of a single layer cell that are as tall as they are wide (appear to be square-shaped in cross section).
- Tissue cells have large, rounded, centrally located nuclei, and all the cells of this epithelium are directly attached to the basement membrane.
- The important functions of the simple cuboidal epithelium are secretion and absorption.
- This epithelial type is found in the small collecting ducts of the kidneys, pancreas, and salivary glands.

3) Simple columnar epithelium

- Simple columnar epithelium is a single layer of tall, closely packed cells, aligned in a row. Each cell has an oval nucleus that located close to the basal region of the cell.

- This type of epithelium is adapted for secretion and/or absorption, and can also be protective.
- It can be further divided into two categories: **ciliated and non-ciliated**.
- It lines the stomach and uterine cervix, also can be seen in areas with high secretory function (such as the wall of the stomach), or absorptive areas (as in small intestine).
- Non ciliated columnar epithelium often contains **cellular extensions (microvilli)** and scattering **unicellular glands (goblet cells)** as in the small intestine.

4) Pseudostratified Columnar Epithelium

- It may look stratified because the nuclei are scattered at different distances from the basal surface, but not all of the cells reach the apical surface in this epithelium.
- However, EM shows that **all of its cells are in direct contact with the basement membrane**, so this is a 'simple' epithelium. But it is called pseudostratified, because of its appearance.
- The columnar cells within this epithelium always reach the apical surface, and the shorter cells are stem cells that give rise to the columnar cells.

Pseudostratified columnar epithelium exists in two forms:

A. **pseudostratified ciliated columnar epithelium:** contains cilia in its apical surface. This type is found in the larger air passageways of the respiratory system.

B. **pseudostratified non-ciliated columnar epithelium:** lack cilia and goblet cells, occurs primarily in part of the male urethra and epididymis.

Stratified Epithelial Tissues\classification by cell shape:

It can be classified according to the shape of cells of its superficial layer into:

1. Stratified Squamous Epithelium:

- This tissue has multiple cell layers, and only the deepest layer of cells is in direct contact with the basement membrane.
- The cells in the basal layers have a cuboidal or polyhedral shape, whereas the apical cells display a flattened, squamous shape.
- Thus, stratified squamous epithelium is so named because of its multiple cell layers and the shape of the apical cells. This epithelium is adapted to protect underlying tissues from damage due to activities that cause abrasion and friction.
- This type of epithelium exists in two forms: **non keratinized and keratinized.**

A. Non keratinized stratified squamous epithelium:

- The cells in non-keratinized stratified squamous epithelium remain alive all the way to the tissue's apical surface, and they are kept moist with secretions such as saliva or mucus.
- These cells lack keratin; a tough protective protein that is abundant in the keratinized form of this epithelium.
- Because all of the cells are still alive, the flattened nuclei characteristic of squamous cells are visible throughout the tissue.
- Non keratinized stratified squamous epithelium lines the oral cavity (mouth), part of the pharynx (throat), the esophagus, the vagina, and the anus.

B. **Keratinized stratified squamous epithelium:**

- The superficial layers are composed of cells that are dead.
- These cells lack nuclei and all organelles when observed under the microscope, and instead are filled with the protein keratin.
- New cells produced in the basal region of the epithelium migrate toward the apical surface of the tissue.
- During their migration, the cells fill with keratin they produce, which makes them very strong, but as a consequence the cells lose their organelles and nuclei, and die.
- The epidermis (outer layer) of the skin consists of keratinized stratified squamous epithelium.

2. Stratified Cuboidal Epithelium

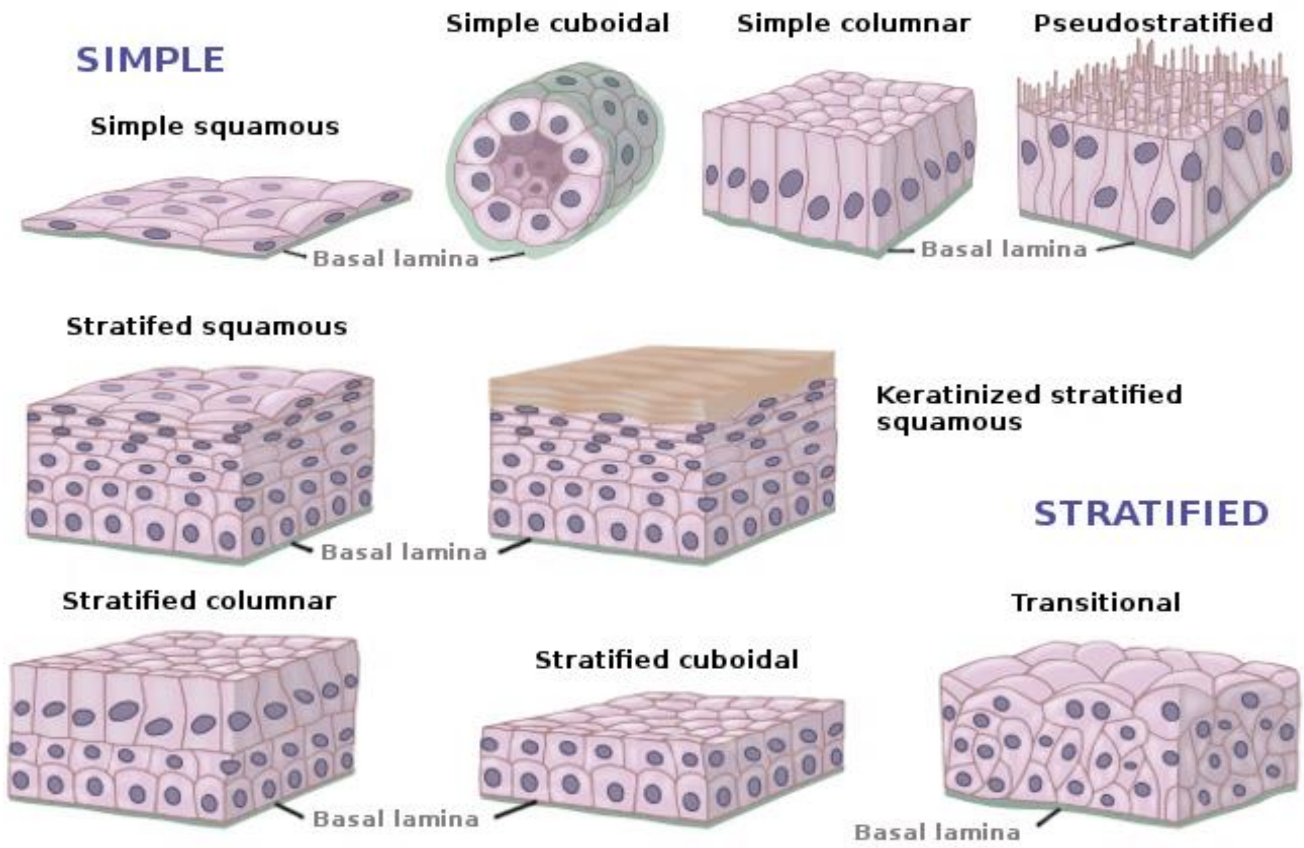
- This epithelium contains two or more layers of cells, and the superficial cells tend to be cuboidal in shape.
- This tissue forms the walls of the large ducts of most exocrine glands, such as the ducts of the sweat glands in the skin.
- Although the function of stratified cuboidal epithelium is mainly protective, it also serves to strengthen the walls of the gland ducts, and some sections of male urethra.

3. Stratified Columnar Epithelium:

- This epithelium is relatively rare in the body.
- It consists of two or more layers of cells, but only the cells at the apical surface are columnar in shape.
- This type of epithelium protects and secretes. It is found in the large ducts of salivary glands and in the membranous segment of the male urethra.

4. Transitional Epithelium:

- This epithelium is limited to the urinary tract (urinary bladder, ureters, and part of the urethra).
- It varies in appearance, depending upon whether it is in a relaxed state or a stretched state.
- In a relaxed state, the basal cells appear cuboidal or polyhedral, and the apical cells are large and rounded.
- When transitional epithelium stretches, it thins and the apical cells flatten and become almost squamous in shape.
- At the distended state, it may difficult to distinguish transitional epithelium from non-keratinized stratified squamous epithelium.
- One distinguishing feature of transitional epithelium is the presence of some binucleated (containing two nuclei) cells.

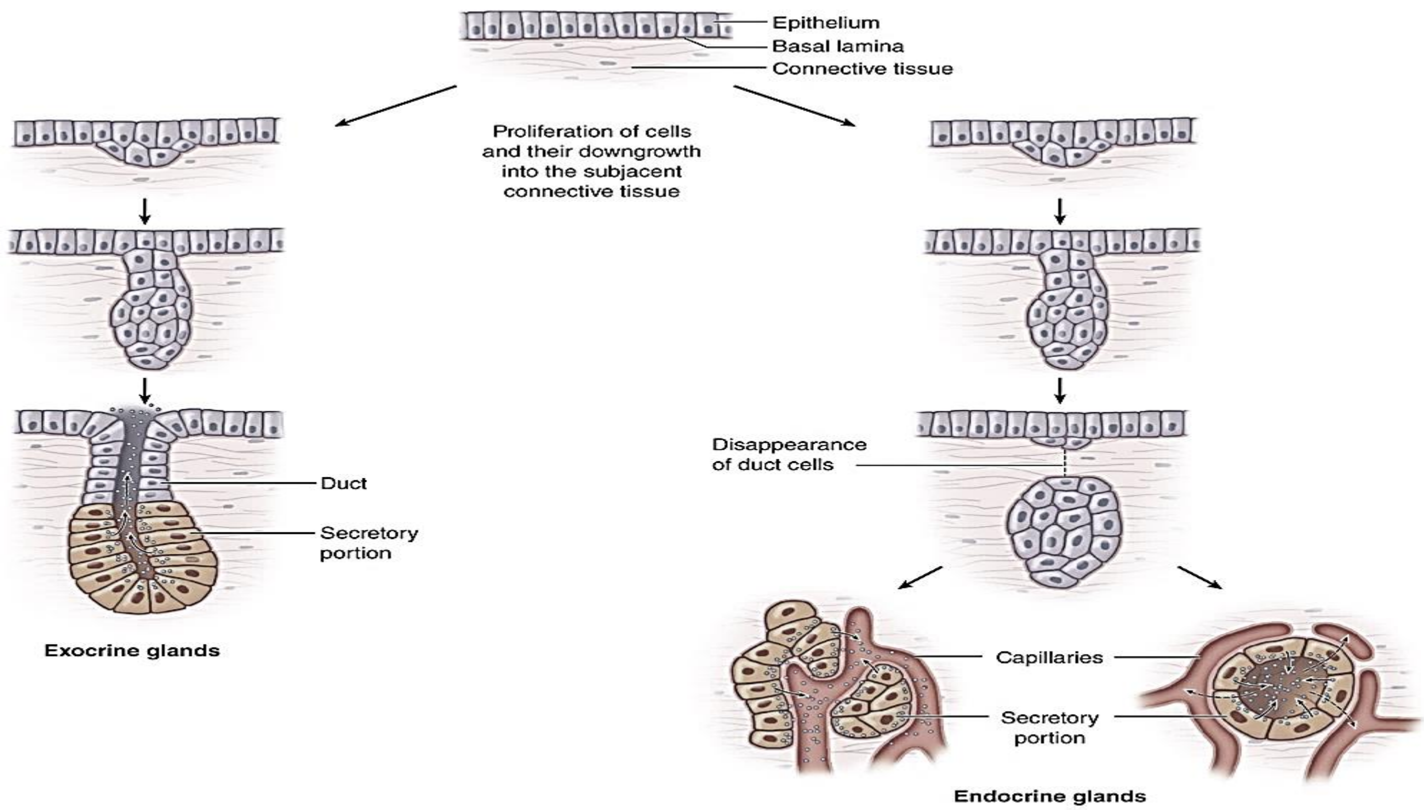


LEC 3: Glandular Epithelial Tissue:

- Formed by cells specialized to produce secretion.
- As epithelial tissue develops in the embryo, small invaginations from this epithelium into the underlying connective tissue give rise to specialized structures called **glands**
- **Glands** are either **individual cell (unicellular)** or **multicellular organs** composed predominately of epithelial tissue.
- **Glands** perform a secretory function by producing substances either for use elsewhere in the body or for elimination from the body.
- Glandular secretions include **mucin, hormones, enzymes, and waste products.**
- Glands are classified as **endocrine &exocrine** depending upon whether they have a duct connecting the secretory cells to the surfaces of an epithelium.
- **Endocrine glands** lack ducts and secrete their products directly into the interstitial fluid and bloodstream.
- The secretions of the endocrine glands, called **hormones,** act as chemical messengers to influence cell activities elsewhere in the body.

Exocrine glands:

- Typically originate from an invagination of the epithelium that burrows into the deeper connective tissues.
- These glands usually maintain their contact with the epithelial surface by means of **a duct**.
- **A duct** is an epithelium-lined tube through which secretions of the gland are discharged onto the epithelium surface.



- An exocrine gland may be **unicellular or multicellular**.
- **A Unicellular exocrine gland** is an individual exocrine cell located among non-secretory epithelial cells.
- Unicellular exocrine glands typically **do not contain a duct,** and they are located close to the surface of the epithelium in which they reside.
- The most common type of unicellular exocrine gland is the **goblet cell in respiratory tract and in intestine.**

Multicellular exocrine glands may be classified **according to 3 criteria**:

1. **Form and structure (Morphology):** considered as an anatomic classification
2. **Type of secretion**
3. **Method of secretion**

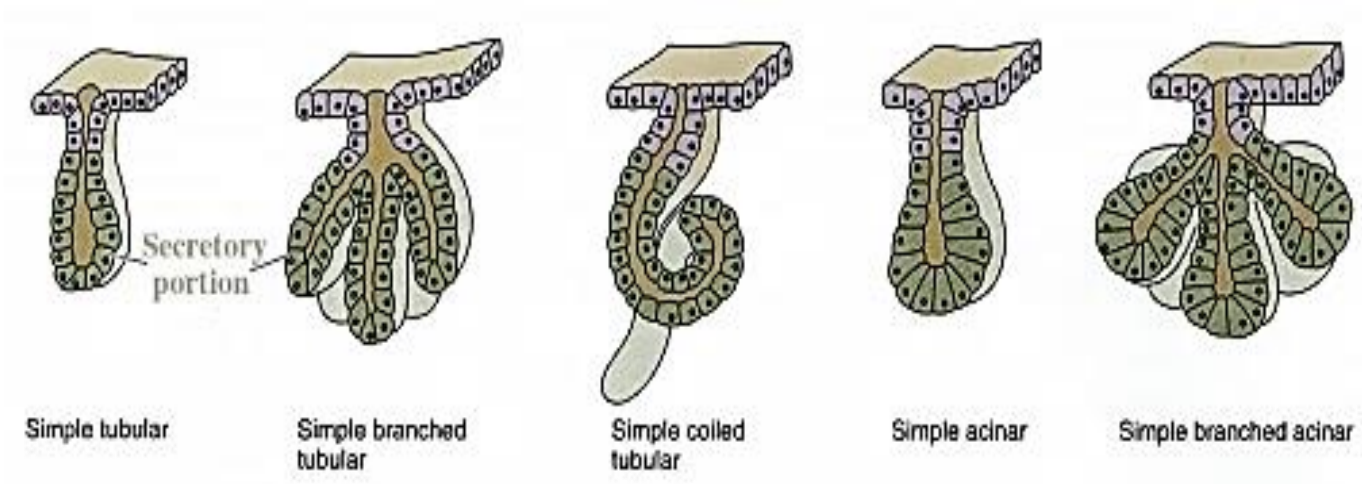
(2 and 3) } considered as physiologic classifications

Form and Structure:

Based on the structure and complexity of their ducts, exocrine glands are considered either **simple or compound.**

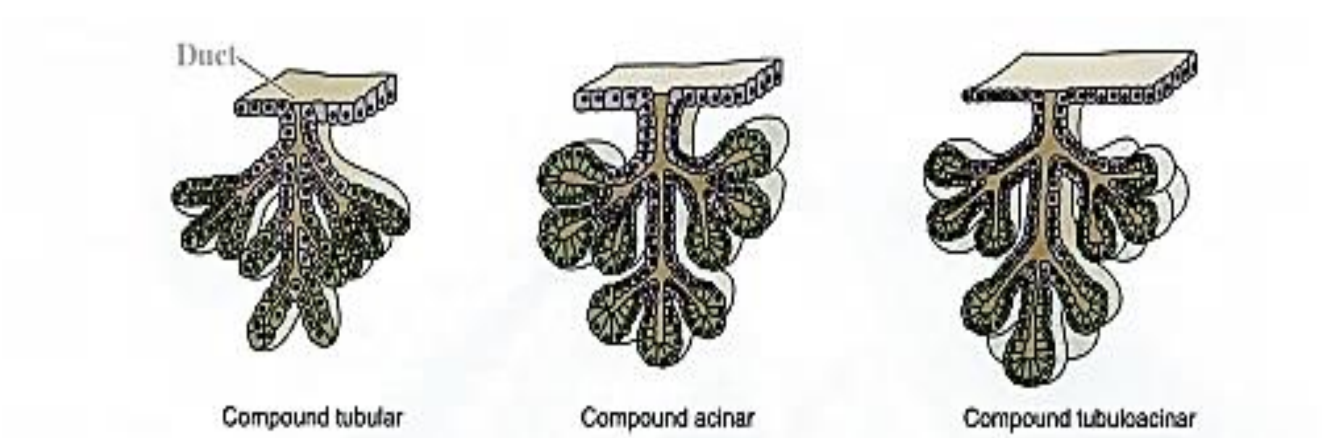
- **Simple Glands** have a single, unbranched duct.
- **Compounds Glands** have ducts that branch repeatedly.
- **Simple exocrine glands** are classified **according to the shape or organization of their secretory portions**:

1. If the secretory portion and the duct are of uniform diameter, the gland is called **Tubular.** It can be further subdivided into
   (A) simple tubular
   (B) simple coiled tubular
   (C) simple branched tubular
2. If the secretory cells form an expanded sac the gland is called **Acinar (alveolar).** It can be further subdivided into:
   (A)simple acinar or alveolar
   (B) simple branched acinar



Compound exocrine glands:

- Consist of a varying number of simple glands whose small excretory ducts join to form progressively larger and larger ducts which carry the secretion onto an epithelial surface.
- They are also classified **according to the shape or organization of their secretory portions**:
  (A) **compound tubular.**
  (B) **compound acinar(alveolar).**
  (C) **compound tubuloacinar:** it is so called because the gland has both secretory tubules and secretory acini.



Types of Secretion:

Exocrine Glands are classified by the nature of their secretions as **serous glands, mucous glands,** or **mixed glands (seromucous)**.

A. **Serous Glands:** produce and secrete a non-viscous, watery fluid, such as sweat, milk, tears, or digestive juices. This fluid carries wastes(sweat) to the surface of the skin, nutrients(milk), to a nursing infant, or digestive enzymes from the pancreas to the lumen of the small intestine.
B. **Mucous Glands:** secrete mucins, which forms mucus when mixed with water. Found in such places as the roof of the oral cavity and the surface of the tongue.
C. **Mixed Glands(seromucous):** such as the salivary glands inferior to the oral cavity, contains both serous and mucous cells, and produce a mixture of the two types of secretions.

Methods of Secretion:

Glands also can be classified by their mechanism of discharging secretory product as **merocrine glands, holocrine glands, or apocrine glands**

A. Merocrine Glands:

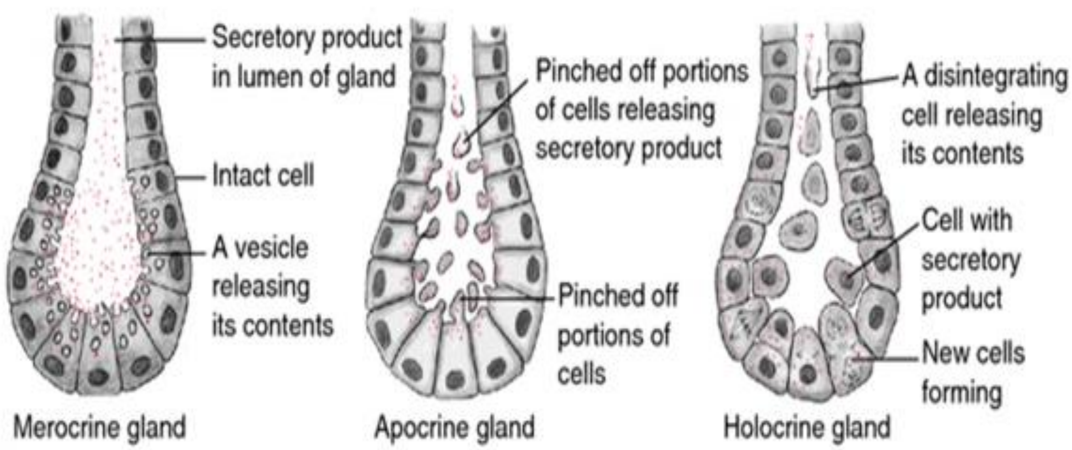
- They package their secretions in structures called **secretory vesicles**.
- The secretory vesicles travel to the apical surface of the glandular cells, and leave the cell by **exocytosis** with no loss of other cellular material.
- Lacrimal(tear) glands, salivary glands, some sweat glands, the exocrine glands of the pancreas, and the gastric glands of the stomach are examples of merocrine glands.

B. Holocrine Glands:

- Formed from cells that accumulate a product and then the entire cell disintegrates. Thus, a holocrine secretion is a mixture of cell fragments and the product the cell synthesized prior to its destruction.
- The ruptured dead cells are continuously replaced by other epithelial cells undergoing mitosis.
- The oil-producing glands (sebaceous glands) in the skin are an example of holocrine glands.

C. Apocrine Glands:

- Composed of cells that accumulates their secretory products within the apical portion of their cytoplasm.
- The secretion follows as this apical portion decapitates .So, their mode of secretion is a decapitation.
- The apical portion of the cytoplasm begins to pinch off into the lumen of the gland for the secretory product to be transported to the skin surface.
- Mammary glands and ceruminous glands (special types of sweat glands) are apocrine glands.



LEC 4: Connective Tissues

- The most diverse, abundant, widely distributed tissues.
- It is designed **to support, protect,** and **bind organs.**
- It is the **"glue"** that binds body structures together.
- Structurally, connective tissue **is formed by three classes of components:**
  - **a. Cells**
  - **b. Fibers**
  - **c. Ground Substance.**
- The major constituent of connective tissue is the **extracellular matrix.**
- Extracellular matrix consists of different combinations of **protein fibers** (collagen, reticular, and elastic) and **ground substance.**

a) Cells:

- Each type of connective tissue contains specific types of cells. **For example;** connective tissue proper contains fibroblast, fat contains adipocytes, cartilage contains chondrocytes, and bone contains osteocytes.
- Most connective tissue cells are not in direct contact with each other, but are scattered throughout the tissue.
- This differs markedly from epithelial tissue; whose cells crowd closely together with little to no extracellular matrix surrounding them.

b) Protein Fibers:

- Most connective tissue contains protein fibers throughout.
- These fibers strengthen and support connective tissue.
- The 3 types of proteins fibers found connective tissue are:
  - I. **Collagen Fibers**, which are strong and stretch resistant
  - II. **Elastic Fibers**, which are flexible and resilient
  - III. **Reticular Fibers**, which form an interwoven framework

c) Ground Substance:

- Both the cells and the protein fibers reside within a material called **ground substance.**
- This nonliving material is **produced by the connective tissue cells.**
- It primarily consists of **protein and carbohydrates molecules** and variable amounts of **water**.
- The Ground substance may be **viscous** (as in blood), **semisolid** (as in cartilage), or **solid** (as in bone)
- Together the ground substance and the protein fibers form an **extracellular matrix.**

Functions of Connective Tissue:

1. **Physical Protection**: The bones of the cranium, sternum, and thoracic cage protect delicate organ, such as the brain, heart, and lungs; fat packed around the kidneys and at the posterior side of the eyes within the skull protect these organs.
2. **Support and Structural Framework**: Bones provide the framework for the adult body and support the soft tissues; cartilage supports such body structures as the trachea, bronchi, ears, and nose; connective tissue sheets form capsules to support body organs such as the spleen and kidneys
3. **Binding of Structures:** Ligaments bind bone to bone; tendons bind muscle to bone; dense irregular connective tissue binds skin to underlying muscle to bone.
4. **Storage function**: Fat is the major energy reserve in the body; bone is a large reservoir for calcium and phosphorus.

5. **Transport**: Blood carries nutrients, gases, hormones, wastes, and blood cells between different regions of the body.
6. **Immune Protection:** Many connective tissue types contain white bloods cells (leukocytes) which protect the body against disease and mount an immune response when the body is exposed to something foreign.

Development of connective tissues

- The primary germ layer mesoderm forms all connective tissues.
- There are 2 types embryonic connective tissue: **mesenchyme**, and **mucous** connective tissue

A. Mesenchyme Embryonic Tissue:

- The first type of connective tissue to emerge.
- It has star-shaped (stellate) or spindle-shaped mesenchyme cells dispersed within a gel-like ground substance that contains fine, immature protein fibers.
- There is proportionately **more ground substance** than mesenchyme cells in this type of embryonic connective tissue.
- Mesenchyme is the source of all other connective tissues.
- Adult connective tissues often house numerous mesenchymal (stem) cells that support the repair of the tissue following damage or injury.

B. Mucous connective tissue:

- The immature protein fibers in mucous connective tissue are more numerous than those within mesenchyme.
- Mucous connective tissue is located within the umbilical cord only. It is absent in adults.

Classification of Connective Tissue

The connective tissues types presented at birth are classified into 3 broad categories: **connective tissue proper, supporting connective tissue, and fluid connective tissue.**

Connective Tissue Proper: Includes those types of connective tissue that exhibit a variable mixture of both connective tissue cell types and extracellular protein fibers suspended within a viscous ground substance.

Cells of connective tissue proper:

The two classes of cells that form the connective tissue proper: **Residential and Wandering Cells**

Residential Cells of Connective Tissue Proper:

1. Fibroblasts:

- Large, relatively flat cells with tapered ends.
- They are the most abundant resident cells in connective tissue proper.
- They produce the fibers and ground substance components of the extracellular matrix.

2. Adipocytes:

- Also called fat cells.
- They often appear in small clusters within some types of connective tissue proper.
- If a larger cluster of these cells dominates an area, the connective tissue is called adipose connective tissue.

3. Fixed Macrophages:

- Relatively large, irregular shaped cells with numerous surface folds and projections.
- They are derived from one type of leukocyte (called a monocyte) and dispersed throughout the extracellular matrix, where they **phagocytize damaged cells or pathogens.**

- When fixed macrophages encounter foreign materials, the cells release chemicals that stimulate the immune system and lure numerous wandering cells involved in body defense to the foreign materials.

4. Mesenchymal Cells:

- A type of embryonic stem cell contained within connective tissue.
- As a result of local injury or connective tissue damage, mesenchyme stem cells divide.
- One of the cells produced is the replacement mesenchymal cell and the other becomes a committed cell that moves into the damaged or injured area and differentiates into the type of connective tissue cell that is needed.

Wandering cells of the connective tissue proper

1. Mast Cells:

- These small mobile cells contain a granule- filled cytoplasm.
- They are usually found close to blood vessels
- They secrete heparin to inhibit blood clotting and histamine to dilate blood vessels and increase blood flow.

2. Plasma Cells:

- When B-Lymphocytes (a type of white blood cell) are activated by exposure to foreign materials, the cells mature into plasma cells.
- These cells are small "factories" that synthesize disease fighting proteins called "antibodies"
- Antibodies attach to foreign material and prevent it from causing further damage
- Usually, Plasma Cells are found in the intestinal walls, spleen, and lymph nodes.

3. Free Macrophages:

- These mobile phagocytic cells are formed from monocytes (a type of white blood cell) that migrate out of the blood stream.
- They wander through connective tissue and engulf destroy any bacteria foreign particles or damaged cells and debris they encounter.

4. Other Leukocytes:

- Other leukocytes migrate through the blood vessel walls in the connective tissue where they spend most of their time.
- The majority of these leukocytes are **neutrophils**, a type of white blood cell that seeks out and phagocytizes bacteria. The rest are **lymphocytes** which attack and destroy foreign materials.

Protein Fibers Found in Connective Tissue Proper:

- There are 3 types of protein fibers found in connective tissue Proper: **collagen, elastic, and reticular fibers**
- **Fibroblasts synthesize** the components of collagen, Elastic, and Reticular Fibers and then secrete these protein subunits into the interstitial fluid.

I. Collagen Fibers:

- Long, unbranched extracellular fibers composed of the protein collagen.
- They are strong, flexible, and resistant to stretching.
- Collagen forms about 25% of the body protein, making it the most abundant protein in the body.
- In fresh tissue collagen fibers appear white and thus they are often called white fibers to give contrast
- In tissue sections stained with hematoxylin and eosin collagen fibers appear pink
- In tissue sections collagen forms coarse, sometimes wavy bundles

- The parallel structure and arrangement of collagen bundles in tendons and ligaments allow them to withstand enormous forces in one direction.

II. Elastic Fibers:

- They are made of the protein elastin and are thinner than collagen fibers.
- Stretch easily, branch then rejoin.
- Coiled structure allows them to stretch and recoil; allows lungs, arteries, and skin to return to normal shape after stretching.

III. Reticular Fibers:

- Thinner than collagen fibers.
- They contain the same protein subunits that collagen has, but their subunits are combined in a different way and they are coated with a glycoprotein (a protein with some carbohydrate attached to it).
- These fibers form a branching interwoven framework that is tough but flexible.
- Reticular Fibers are especially abundant in the **stroma**; a structural connective tissue frame work in organs such as the lymph nodes, spleen, and liver.
- The mesh-like arrangement of the reticular fibers permits them to physically support organs and resist external forces that may damage the organs cells and blood vessels.

Ground Substance of Connective Tissue proper:

- The cellular and fibrous components of the connective tissue proper are suspended within the ground substance, a colorless, featureless, viscous solution.
- Ground substance usually has a gelatinous, almost rubbery consistency due to the mixture of its component molecules, which vary both in their size and in their proportions of proteins and carbohydrates.
- The different molecules in the ground substance are called **glycosaminoglycans, proteoglycans, and structural glycoproteins.**

LEC 5: Proper Connective Tissue:

Connective tissue proper is divided into 2 broad categories: **Loose connective tissue** and **Dense connective tissue.**

A. Loose Connective Tissue:

- Contains relatively **fewer** cells and protein fibers than dense connective tissue.
- The protein fibers in loose connective tissue are **loosely arranged** rather than tightly packed together.
- Usually, this tissue occupies the spaces between and around organs.
- It supports the overlying epithelia as well as many structures that are normally under pressure and low friction. Thus, provides cushioning around organs.
- It supports and surrounds blood vessels and nerves.
- Stores lipids and provides a medium for the diffusion of materials.
- It is also found in the dermis and the hypodermis.
- Loose connective tissue contains all the main components of connective tissue proper. There is no predominant element in this tissue. The most numerous cells are **fibroblasts and macrophages**, but all the other types of connective tissue cells are also present.
- A moderate amount of collagen, elastic, and reticular fibers appears in this tissue.

There are **3 main types** of loose connective tissue:

- **Areolar connective tissue**
- **Adipose connective tissue**
- **Reticular connective tissue.**

Areolar Connective tissue:

- Highly variable in appearance and the least specialized connective tissue in the body.
- It has a loosely array of collagen and elastic fibers and an abundant distribution of blood vessels.
- Contains all of the cell types of connective tissue proper, although, the predominant cell is the **fibroblast**.
- In areolar connective tissue, a **viscous ground substance** occupies the spaces between fibers and accounts for most of the volume of areolar connective tissue.
- Areolar Connective Tissue is found nearly everywhere in the body. It surrounds nerves, blood vessels, and individual muscle cells. It is also a major component of the subcutaneous layer deep to the skin.

Adipose Connective tissue

- Commonly known as "fat".
- It is a loose connective tissue composed primarily of cells called **Adipocytes.**
- Adipose Connective Tissue serves as packing around structures and provides padding, cushions shocks, and acts as an insulator to slow heat loss through the skin.
- Adipose connective is commonly found throughout the body in such diverse locations as a fat capsule surrounding the kidney, the pericardial and abdomino-pelvic cavities and the subcutaneous layer.

Reticular Connective Tissue:

- Contains a mesh-work of reticular fibers, fibroblasts, and leukocytes.
- This connective tissue forms the stroma of many lymphatic organs such as the spleen, thymus, lymph nodes, and bone marrow.

B. Dense Connective Tissue

- Composed primarily of protein fibers, and has proportionally **less ground substance** than loose connective tissue.
- Dense connective tissue is sometimes called **collagenous tissue** because collagen fibers are the dominant fiber type.
- There are **3 categories** of dense connective tissue: **dense regular** connective tissue, **dense irregular** connective tissue, and the **elastic connective tissue.**

a. Dense Regular Connective Tissue

- A category of dense connective tissue in which collagen fibers are **packed tightly** and **aligned parallel** to an applied force.
- This tissue type is found in tendons and ligaments, where stress is applied in a single direction.
- Dense Regular Connective Tissue has few blood vessels and thus it takes long time to heal following injury since a rich blood supply is necessary for goes healing.

b. Dense irregular connective tissue:

- Composed of individual bundles of collagen fibers **extended in all directions** in a scattered meshwork.
- These bundles of collagen fibers appear **in clumps** throughout the tissue, rather than arranged in parallel as seen in dense regular connective tissue.
- Dense irregular connective tissue provides support and resistance to stress **in multiple directions**.
- An example of dense irregular connective tissue is the deep portion of the dermis, which lends strength to the skin and permits it to withstand applied forces from any direction.

- Dense irregular connective tissue also forms a supporting layer around cartilage (called the **perichondrium**) and around bone (called the **periosteum**), except at joints.
- In addition, it forms a thick, fibrous capsule that supports and houses internal organs, such as the liver, kidneys, and spleen.

c. Elastic Connective Tissue

- A type of dense connective tissue, has **branching elastic fibers** and **more fibroblast** than loose connective tissue in addition to **packed collagen fibers**.
- The elastic fibers provide resilience and the ability to deform and then return to normal shape.
- Examples: the vocal cords, the ligament of the penis, and some ligaments of the spinal column. Also, it found as wavy sheets in the walls of the large and medium arteries.

Supporting Connective Tissue

- Cartilage and bone are types of supporting connective tissue, because they form a strong, durable framework that protects and supports the soft body tissues.
- The **extracellular matrix** in supporting connective tissue contains many **protein fibers and a ground substance that ranges from semisolid to solid.**
- In general, cartilage has a **semisolid** extracellular matrix; while-bone has a **solid** extracellular matrix.

A. Cartilage

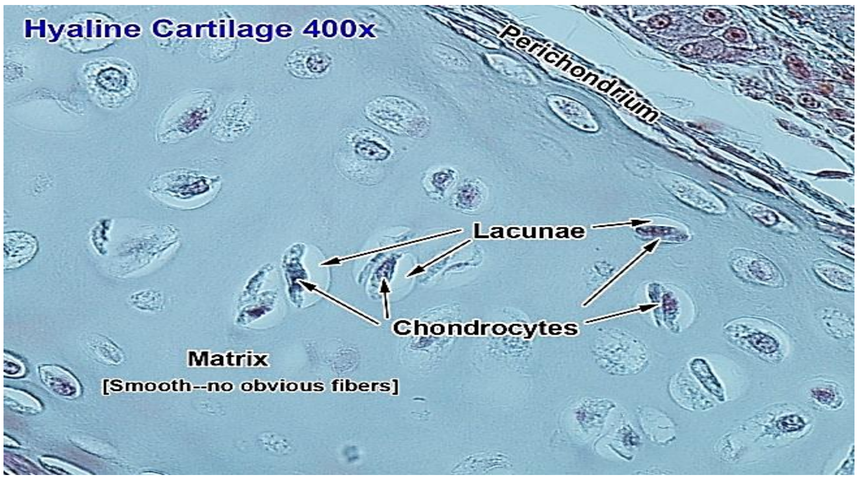
- A specialized form of connective tissue in which the firm consistency of the extracellular matrix allows the tissue to **bear mechanical stresses without permanent distortion**.
- Another function of cartilage is to **support the soft tissues**.
- Cartilage consists of cells called **chondrocytes** and an extensive firm **gel-like extracellular matrix** composed of fibers and ground substance.
- Chondrocytes synthesize and secrete the extracellular matrix, and the cells themselves are located in matrix cavities called **lacunae.**
- Cartilage is stronger and more resilient than any previous discussed connective tissue type, and it provides more flexibility than bone.
- Collagen fibers within the matrix give cartilage its tensile strength.
- Cartilage is found in areas of the body that need support and must withstand deformation, such as the tip of the nose or the external part of ear (auricle).
- Chondrocytes produce a chemical that prevents blood vessel formation and growth within the extracellular matrix. Thus, mature cartilage is **avascular**, meaning without blood vessels.
- Therefore, the chondrocytes must exchange nutrients and waste without blood vessels outside the cartilage **by diffusion.**
- Cartilage usually has a covering sheath called **Perichondrium**; composed of **2 distinct layers**:
  - **The outer fibrous region (fibrous perichondrium)** of dense irregular connective tissue provides protection and mechanical support, and secures the perichondrium to the cartilage and to the other structures.
  - **The inner cellular layer (chondrogenic perichondrium)** contains stem cells (chondroblasts) necessary for the growth and maintenance of the cartilage.

Types of Cartilage:

There are 3 major types of cartilage: **Hyaline** Cartilage, **Fibro**cartilage, and **Elastic** Cartilage.

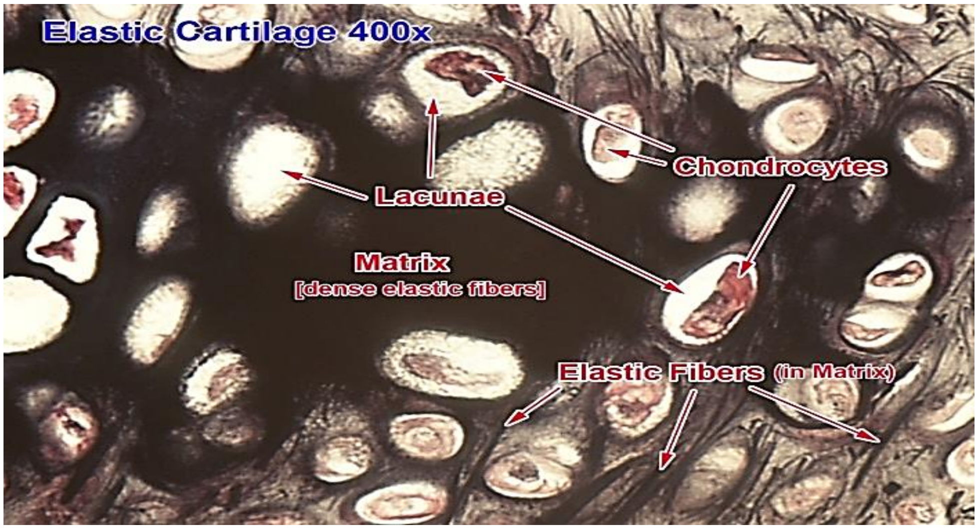
I. Hyaline Cartilage:

- The most common type of cartilage and also the weakest. It is named for its **clear glassy** appearance under microscope.
- The chondrocytes within their lacunae are **irregularly scattered** throughout the extracellular matrix.
- The collagen within the matrix is **not readily observed** by light microscopy because it is primarily in the form of submicroscopic fibrils.
- It provides support through flexibility and resilience.
- Hyaline cartilage is surrounded by a perichondrium
- Hyaline cartilage has many functions in addition to its primary one of supporting soft tissue; it forms most of the fetal skeleton and is the model for most future bone growth.
- Hyaline cartilage is found in many other areas of the body including the nose, the trachea, most of the larynx, coastal cartilage (cartilage attached to ribs) and the articular ends of long bones.



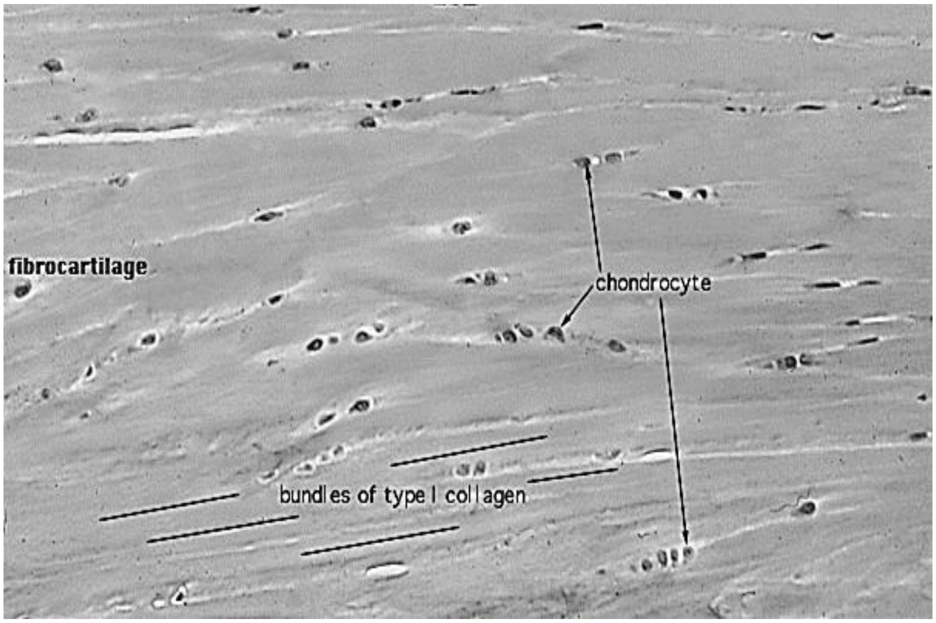
II. Elastic cartilage:

- It is so named because it has numerous **elastic fibers** in its matrix.
- The higher concentration of elastic fibers in this cartilage causes it to appear yellow in fresh sections.
- The chondrocytes of elastic cartilage are almost indistinguishable from those of hyaline cartilage. They are typically **closely packed** and surrounded by only a small amount of extracellular matrix.
- The elastic fibers are both denser and more highly branched in the central region of the extracellular matrix, where they form a web-like mesh around the chondrocytes within the lacunae.
- These fibers ensure that elastic cartilage is extremely resilient and flexible.
- Elastic cartilage is surrounded by perichondrium.
- Elastic cartilage is found in epiglottis and in the external ear



III. Fibrocartilage

- Fibrocartilage is a tissue intermediate between dense connective tissue and hyaline cartilage.
- the strongest type of cartilage; it has numerous coarse, readily visible fibers in its extracellular matrix.
- The fibers are arranged as **irregular bundles** between large chondrocytes.
- There is only a sparse amount of ground substance, and often the chondrocytes are **arranged in parallel long rows** separated by **coarse collagen type I fibers**
- The densely interwoven collagen fibers contribute to the extreme durability of this type of cartilage.
- There is no identifiable perichondrium in fibrocartilage
- Fibrocartilage is found in the intervertebral discs where it acts as a shock absorber and resists compression.



Growth Patterns of Cartilage

Cartilage grows in two ways: **Interstitial Growth and Appositional Growth.**

A. Interstitial Growth:

a) Chondrocytes housed in lacunae undergo mitotic cell division.
b) The two new cells occupy a single lacuna

c) Cells synthesize and secrete new cartilage matrix; they are pushed apart and now reside in their own lacunae
d) The new individual cells within their own lacunae are called chondrocytes. new matrix has been produced internally, and thus interstitial growth has occurred.

B. Appositional Growth:

A growth that occurs later in life after full maturity due to injury or healing. This growth occurs only at the periphery of the tissue:

a) Undifferentiated stem cells at the internal edge of the perichondrium begin to divide forming new stem cells and **committed cells** (a type of stem cell that can produce a subset of like cells; ex. Hematopoietic cells - blood stem cells).
b) The committed cells differentiate into chondroblasts
c) These chondroblasts, located at the periphery of the old cartilage, begin to produce and secrete new cartilage matrix, they are pushed apart and become chondrocytes, each occupying its own lacuna. The cartilage continues to grow at the periphery as chondrocytes continue to produce more matrix.
d) The new matrix has been produced peripherally, and thus appositional growth has occurred. During early embryonic development, both interstitial and appositional cartilage growth occur simultaneously.
e) The interstitial growth declines rapidly as the cartilage matures because the cartilage becomes semi-rigid, and it is no longer able to expand.
f) Further growth can occur only at the periphery of the tissue, so later growth is primarily appositional.
g) Once the cartilage is fully mature, new cartilage growth typically stops.
h) Thereafter, cartilage growth usually occurs only after injury to the cartilage, yet this growth is limited due to the lack of blood vessels in the tissue.

LEC 6: B. Bone:

- Bone is a specialized connective tissue composed of intercellular calcified material, the **bone matrix,** and three cell types: **osteocytes**, **osteoblasts** and **osteoclasts.**
- Because metabolites are unable to diffuse through the calcified matrix of bone, the exchanges between osteocytes with one another and with blood capillaries depend on communication through minute passageways in the matrix called **canaliculi** which are defined as thin, cylindrical spaces that perforate the matrix.

Functions of bone:

1. Support
2. Protection
3. Assistance in movement
4. Mineral homeostasis
5. Blood cell production
6. Triglyceride storage

Periosteum & Endosteum:

External and internal surfaces of bone are covered by layers of bone-forming cells and connective tissue called **periosteum;** consists of an outer layer of collagen fibers and fibroblasts. And an inner cellular layer, composed of fibroblast-like cells called **osteoprogenitor cells**.), and **endosteum** which lines all internal cavities within the bone.

Composition of Bone Matrix:

- **Organic composition:** About 1/3 of bone mass is composed of organic components, including cells, collagen fibers, and ground substance. The collagen fibers give a bone tensile strength by resisting stretching and twisting, and contribute to its overall flexibility.
- **Inorganic composition:** About 2/3 of bone mass is hydroxyapatite (calcium phosphate + calcium hydroxide) deposited into the framework formed by collagen fibers in a process called calcification. It is responsible for bone hardness and ability to resist compression.

Cell Types of Bone:

1. **Osteoprogenitor cells:**
   - Stem cells derived from mesenchyme.
   - When they divide, they produce another stem cell and a "committed cell" that matures to become an osteoblast.
   - These stem cells are located in both the periosteum and the endosteum.
2. **Osteoblasts:**
   - Formed from osteoprogenitor stem cells.
   - Often, osteoblasts are positioned side by side on bone surfaces.
   - Active osteoblasts exhibit a somewhat cuboidal shape and have abundant rough endoplasmic reticulum and Golgi apparatus, reflecting the activity of these cells.
   - Osteoblasts perform the important function of synthesizing and secreting the initial semisolid organic form of bone matrix called osteoid
   - Osteoid later calcifies as a result of salt crystal deposition.
   - As a consequence of this mineral deposition on osteoid, osteoblasts become entrapped within the matrix they produce and secrete, and thereafter they differentiate into osteocytes.
3. **Osteocytes**
   - Mature bone cells derived from osteoblasts that have become entrapped in the matrix they secreted.
   - They reside in small spaces within the matrix called lacunae
   - Osteocytes maintain the bone matrix and detect mechanical stress on a bone.
   - If stress is detected, osteoblasts are signaled, and it may result in the deposition of new bone matrix at the surface.
4. **Osteoclasts**
   - Large, multinuclear, phagocytic cells.
   - They appear to be derived from fused bone marrow cells similar to those that produce monocytes .
   - These cells exhibit a ruffled border where they contact the bone, which increases their surface area exposure to the bone.
   - An osteoclast is often located within or adjacent to a depression or pit on the bone surface called **a resorption lacuna (Howship's lacuna).**

<u>Osteoclasts are involved in an important process called **bone resorption** that takes place as follows</u>:

1. Osteoclasts secrete hydrochloric acid, which dissolves the mineral parts (calcium and phosphate) of the bone matrix, while lysosomes within the osteoclasts secrete enzymes that dissolve the organic part of the matrix.

2. The release of the stored calcium and phosphate from the bone matrix is called osteolysis.

3. The liberated calcium and phosphate ions enter the tissue fluid and then the blood.
4. Osteoclasts remove matrix and osteoblasts add to it, maintaining a delicate balance.
5. If osteoclasts resorb the bone to remove calcium salts at a faster rate than osteoblasts produce matrix to stimulate deposition, bones lose mass and become weaker; in contrast, when osteoblast activity outpaces osteoclast activity, bones have a greater mass.

There are 2 forms of bone connective tissue: **compact bone** and **spongy bone.**

A. Compact Bone:

- Appears solid but is in fact perforated by a number of vascular canals.
- It usually forms the hard outer shell of the bone.
- A cylindrical osteon or Haversian system, is the basic functional and structural unit of mature compact bone.
- Osteons run parallel to the diaphysis of the long bone.

Compact Bone Microscopic Anatomy: An osteon composed of the following components:

- **The central canal** (Haversian canal) is a cylindrical channel that lies in the center of the osteon. Traveling within the central canal are the blood vessels and nerves that supply the bone.
- **Concentric lamellae** are rings of bone connective tissue that surround the central canal and form the bulk of the osteon. The numbers of concentric lamellae vary among osteons. Each lamella contains collagen fibers oriented in one direction; fiber direction gives bone part of its strength and resilience.
- **Osteocytes** are housed in lacunae and are found between adjacent concentric lamellae.
- **Canaliculi** are tiny, interconnecting channels within the bone connective tissue that extend from each lacuna, travel through the lamellae, and connect to other lacunae and the central canal. Canaliculi house osteocyte cytoplasmic projections that permit intercellular contact and communication. Thus, nutrients, minerals, gases, and wastes can travel through these passageways between the central canal and the osteocytes.
- **Perforating canals** (Volkmann canals) resemble central canals in that they also contain blood vessels and nerves. However, perforating canals run perpendicular to the central canals and help connect multiple central canals, thus creating a vascular and innervation connection among the multiple osteons.
- **Circumferential lamellae** are rings of bone immediately internal to the periosteum of the bone (external circumferential lamellae) or internal to the endosteum (internal circumferential lamellae). These two distinct regions appear during the original formation of the bone.
- **Interstitial lamellae** are the leftover parts of osteons that have been partially resorbed. They often look like a "bite" has been taken out of them. The interstitial lamellae are incomplete and typically have no central canal.

B. Spongy Bone

- Also called cancellous or trabecular bone).
- appears more porous, like a sponge, forms an open lattice of narrow plates of bone, called **trabeculae.**
- spongy bone is located internally, primarily within the epiphyses.

Spongy Bone Microscopic Anatomy:

- Spongy bone contains **no osteons**.
- Instead, the **trabeculae** of spongy bone are composed of **parallel lamellae**.

- Between adjacent lamellae are osteocytes resting in lacunae, with numerous canaliculi radiating from the lacunae.
- Nutrients reach the osteocytes by diffusion through canaliculi that open onto the surfaces of the trabeculae.
- The trabeculae often form a meshwork of crisscrossing bars and plates of bone pieces.
- This structure provides great resistance to stresses.

Ossification:

- Refers to the formation and development of bone connective tissue.
- Ossification begins in the embryo and continues as the skeleton grows during childhood and adolescence.
- **Endochondral** and **intramembranous** are the two methods of ossification in the fetus and young children.

A. **Endochondral Ossification:** the most common bone formation process, which involves the replacement of hyaline cartilage with bone.
B. **Intramembranous Ossification:** the process of bone formation in the flat bones of the skull, where bone forms directly within mesenchyme arranged in sheet-like layers that resemble membranes.

LEC 7: Fluid Connective Tissue

- Blood is a fluid connective tissue, approximately 8% of an adult's body weight made up of blood (about 5.5 L in a man).
- It has a pH of (7.35-7.45), making it slightly basic (less than 7 is considered acidic).
- Blood is 5 times thicker than water, indicating that it is more resistant to flow than water.
- Blood in the arteries is a brighter red than blood in the veins because of the higher levels of oxygen found in the arteries.
- Hematology is the study of blood.

Composition of blood

Blood is classified as a connective tissue, and consists of two main components:

A. Plasma

- The liquid extracellular matrix.
- It is composed of water, dissolved & suspended molecules that flow in a regular unidirectional movement within the closed circulatory system.

B. Formed elements

- Which are made up of the **blood cells** and **platelets**.
- The formed elements are so named because they are enclosed in a plasma membrane and have a definite structure and shape.
- <u>All formed elements are cells</u> except for the <u>platelets</u>, which are <u>tiny fragments</u> of bone marrow cells.

Functions of blood

Blood has three main functions: **transport, protection and regulation.**

1. **Transport**

   Blood transports the following substances:
   - Gases, namely oxygen (O_2) and carbon dioxide (CO_2), between the lungs and rest of the body
   - Nutrients from the digestive tract and storage sites to the rest of the body
   - Waste products to be detoxified or removed by the liver and kidneys
   - Hormones from the glands in which they are produced to their target cells

2. **Protection:**
   - Blood contains leukocytes, plasma proteins, and various molecules that help protect the body against potentially harmful substances. They are part of the immune system.
   - Blood has several roles in inflammation:
     a. Leukocytes, or white blood cells, destroy invading microorganisms and cancer cells
     b. Antibodies and other proteins destroy pathogenic substances.
     c. Platelet factors initiate blood clotting and help minimize blood loss.
3. **Regulation**

   Blood participated in the regulation of:

   a) Body temperature: Blood absorbs heat from body cells then releases it at the body surface.

   b) Body pH- Blood: because it absorbs acids and base from body cells, helps maintain the pH of cells.

   c) Fluid balance: There is a constant exchange of fluid between the blood plasma in the capillaries and the interstitial fluid surrounding the cells of the body's tissues.

Blood Plasma:

- The fluid portion of blood; i.e. blood minus formed elements
- A straw-colored sticky fluid that is composed primarily of water (about 92% or its volume)
- It also contains plasma proteins, electrolytes, hormones, nutrients, and byproducts of metabolism.
- Plasma proteins comprised about 7% of its volume.

Plasma Proteins:

1. **Albumins**
   - The smallest and most abundant of the plasma proteins, making up approximately 58% of total proteins.
   - Synthesized in liver.
   - Regulate water movement between blood and interstitial fluid. Thus, it plays an important role in the maintenance of osmotic pressure and fluid distribution between blood and tissues.
   - Act as transport proteins that carry ions, hormones, and some lipids in the blood.

2. Globulins

- The second largest group of plasma proteins synthesized in liver, forming about 37% of all plasma proteins.
- The smaller **alpha-globulins (**α) and the larger **beta-globulins** (β) primarily bind and transport certain water-insoluble molecules and hormones, some metals, and ions.
- **Gamma-globulins** (¥)are also called **immunoglobulins**, or antibodies, which play a part in the body's defenses.

3. Fibrinogen

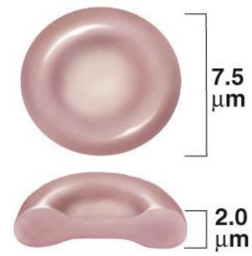
- Makes up about 4% of all plasma proteins.
- Responsible for blood clot formations.
- When the clotting proteins are removed from plasma, the remaining fluid is termed **serum**.
- Following trauma to the walls of blood vessels, fibrinogen is converted into long, insoluble strands of **fibrin**, which helps form a blood clot.

4. Regulatory proteins

- Form a minor class of plasma proteins (less than 1% of total plasma proteins)
- Includes **enzymes** to accelerate chemical reactions in the blood and some **hormones** being transported throughout the body to target cells.

Erythrocytes (Red Blood Cells)

- Transport oxygen and carbon dioxide to and from the tissues and lungs.
- Life span in blood: About 120 days.
- Its unique, biconcave disc structure allows respiratory gases to be loaded and unloaded efficiently.
- Erythrocytes which are anucleate, are packed with the O_2-carrying protein hemoglobin.
- Under normal conditions, these corpuscles never leave the circulatory system.
- The biconcave shape provides erythrocytes with a large surface-to-volume ratio, thus facilitating gas exchange
- When suspended in an isotonic medium, human erythrocyte are 7.5 m in diameter, 2.6 m thick at the rim, and 0.8 m thick in the center.
- The normal concentration of erythrocytes in blood is approximately 3.9–5.5 million per microliter in women, and 4.1–6 million per microliter in men.



- The erythrocyte is quite flexible, a property that permits it to adapt to the irregular shapes and small diameters of capillaries.
- Erythrocytes lose their mitochondria, ribosomes, and many cytoplasmic enzymes during their maturation.
- The source of energy for erythrocytes is glucose, which is anaerobically degraded to lactate.
- The plasma membrane of a mature RBC has glycoproteins and glycolipids that determine a person's blood type.
- Erythrocytes line up in a single column called **Rouleau**, as they pass through small blood vessels.

Hemoglobin:

- Every erythrocyte is filled with about 280 million molecules of the red-pigmented protein called hemoglobin that Makes up 33% of RBC cytoplasm.
- It transports oxygen and carbon dioxide and is responsible for the characteristic color of blood.
- Each hemoglobin molecule consists of four polypeptide chains called **globins.**
- Two of these globins are called **alpha** chains and **beta** chains.
- These globin chains each contain a non-protein (**heme**) that is in the shape of a ring with an iron ion in the center.

Heme

- Oxygen binds to the iron ion (Fe++) in heme for transport in the blood.
- Because each hemoglobin has 4 chains with 4 hemes, each hemoglobin is capable of carrying 4 molecules of oxygen.

Main Functions of Hemoglobin:

1. Helps maintain homeostatic balance by facilitating cellular respiration.
2. Delivers oxygen from lungs to the body's tissues.
3. Pulls carbon dioxide away from tissues.
   Keeps blood in balanced pH.

Life Cycle of an Erythrocyte:

Step 1: Macrophages phagocytize worn-out red blood cells

Step 2: Hemoglobin is split into heme and globin

Step 3: Globin is broken down into amino acids

Step 4: Iron is removed from heme and transported to the liver via a protein named **transferrin**

Step 5: Iron is stored on **ferritin** in the liver

Step 6: Iron is released from storage, reattaches to transferrin and is transferred to bone.
Step 7: Iron is reused to make new hemoglobin
Step 8: New RBCs are made and released into circulation
Step 9: Heme is converted to **biliverdin** then to **bilirubin**
Step 10: Bilirubin is transported to the liver
Step 11: Bilirubin is released into bile and then into the small intestines where it is then converted to **urobilinogen**
Step 12: Urobilinogen is converted into **urobilin** and **stercobilin** and excreted.

Leukocytes (white blood cells):

- They are the least abundant formed elements, totaling only 5,000 to 10,000 WBCs/microliter.
- Very motile and flexible, most leukocytes function in the body tissues.
- leukocytes are larger than erythrocytes, the nucleus is very noticeable.
- Help initiate an immune response and defend against pathogens.
- Migrate to the tissues, where they perform multiple functions.
- Unlike mature erythrocytes, leukocytes are true cells that have organelles and a nucleus and they retain their organelles throughout life.
- Among these organelles are the usual instruments of protein synthesis; the nucleus, rough ER, ribosomes, and Golgi complex, for WBCs must synthesize proteins in order to carry out their functions.

Medical cases:

- **Leukopenia** is a serious disorder resulted from reduced number of leukocytes, usually due to viral/bacterial infection, certain types of leukemia, or toxins that damage the bone marrow.
- **Leukocytosis:** Results from an elevated leukocyte count, indicating infection, inflammation, or extreme physiological stress.
- **According to the type of granules in their cytoplasm and the shape of their nuclei**, leukocytes are divided into **two groups:**
  - **A. Granulocytes** (polymorphonuclear leukocytes)
  - **B. Agranulocytes** (mononuclear leukocytes).

  Both granulocytes and agranulocytes are spherical while suspended in blood plasma, but some become amoeboid after leaving the blood vessels and invading the tissues.

LEC 8: Granulocytes:

- Granulocytes have various types of specific granules that stain conspicuously and distinguish each cell type from the others. They include: **neutrophils, eosinophils** and **basophils.**

Neutrophils

- The most abundant WBCs constituting 60%-70% of the circulating WBCs.
- Nucleus usually with 3-5 lobes.
- Contain fine reddish to violet specific granules in cytoplasm which contain lysozyme and other antimicrobial agents.
- Neutrophils also called **polymorphonuclear leukocytes** because of their varied nuclear shapes.
- Their numbers rise, a condition called **neutrophilia,** in response to bacterial infections.

Functions:

1. Neutrophils are antibacterial cells, they phagocytize (digest) bacteria via **lysozymes**. (**Lysozyme**: an enzyme that destroys bacterial cell walls, found in sweat, tears, and saliva).
2. Neutrophils secrete antimicrobial chemicals.

Eosinophils

- Harder to find in a blood film. Percentage of WBCs 2-4%.
- The eosinophil has bilobed nucleus; i.e., the nucleus usually has two large lobes connected by a thin strand, and the cytoplasm has an abundance of coarse rosy to orange-colored (pink/red) specific granules.

Functions:

1. Eosinophils secrete chemicals that weaken or destroy relatively large parasites such as hookworms and tapeworms, which are too big for any one WBC to phagocytize.
2. They also phagocytize antigen-antibody complexes, and allergens.

Basophils:

- Percentage of WBCs <0.5%.
- Nucleus large and irregularly shaped, typically S or U shaped obscured from view.
- Coarse, abundant, dark violet specific granules in cytoplasm.

Functions:

1. Basophils secrete histamine (vasodilator) which speeds flow of blood to an injured area.
2. Secretes heparin (anticoagulant) which promotes the mobility of other white blood cells to the area.
3. They also release chemical signals that attract eosinophils and neutrophils to a site of infection.

- **Histamine:** a vasodilator that widens the blood vessels, speeds the flow of blood to an injured tissue, and makes the blood vessels more permeable so that blood components such as neutrophils and clotting proteins can get into the connective tissues more quickly.
- **Heparin:** an anticoagulant that inhibits blood clotting and thus promotes the mobility of other WBCs in the area.

A. Agranulocytes:

- Lack specific granules.
- Nonspecific granules are inconspicuous to the light microscope, and these cells therefore have relatively clear-looking cytoplasm.
- Two types of Agranulocytes: **Lymphocytes** and **Monocytes**

Lymphocytes:

- Percentage of WBCs 25-33%.
- They represent the smallest WBCs
- There are small, medium and large lymphocytes.
- Nucleus is round, ovoid, or slightly dimpled on one side, of uniform dark violet color.
- In small lymphocytes, nucleus fills nearly all of the cell and leaves only a scanty rim of clear, light blue cytoplasm.
- In larger lymphocytes, cytoplasm is more abundant; larger lymphocytes may be hard to differentiate from monocytes.

Functions of lymphocytes:

a) Destroy cancer cells, cells infected with viruses, and foreign cells.
b) Present antigens to activate other cells of immune system.
c) Coordinate actions of other immune cells, secrete antibodies, serve in immune memory.

Types of lymphocytes:

1. **T-Lymphocytes (T-cells) (T=thymus)**
   - Makes up approximately 80% of circulating lymphocytes.
   - Produced in red bone marrow, mature thymus; responsible for attacking & destroying foreign cells (direct cellular immunity)
2. **B-Lymphocytes (B-cells) (B=bone)**
   - Make up approximately 10-15% of circulating lymphocytes.
   - Differentiated into Plasma Cells.
   - Produce antibodies which target specific antigens (antibody-mediated immunity).
3. **Natural Killer Cells**
   - Makes up 5-10% of circulating lymphocytes.
   - NK cells are responsible for immunological surveillance & destroy foreign cells, virus-infected cells, and cancer cells.

Monocytes:

- Percentage of WBCs 3-8%.
- Nucleus is ovoid, kidney-shaped, or horseshoe-shaped.
- Abundant light violet cytoplasm with sparse, fine, nonspecific granules.
- Sometimes very large with stellate or polygonal shapes.

Functions:

1. Differentiate into macrophages.
2. Phagocytize pathogens, dead neutrophils, and debris of dead cells.
3. Present antigens to activate other cells of immune system.

Platelets:

- Blood platelets are irregular, membrane enclosed fragments, also called (**thrombocytes**)
- They are non-nucleated, disk-like shaped.
- Platelets originate from the fragmentation of giant **megakaryocytes** that reside in the bone marrow.
- Platelets promote blood clotting and help repair gaps in the walls of blood vessels, preventing loss of blood.
- Normal platelet counts range from 200,000 to 400,000 per microliter of blood.
- Platelets have a life span of about 10 days.
- In stained blood smears, platelets often appear in clumps. Each platelet has a peripheral light blue-stained transparent zone, the **hyalomere,** and a central zone containing purple granules, called the **granulomere.**

Medical case: Thrombocytopenia; reveals a small number of platelets.

Functions of platelets

1. They secrete **vasoconstrictors**; chemicals that cause spasmodic constriction of broken vessels and thus help reduce blood loss.
2. They stick together to form temporary platelet plugs to seal small breaks in injured blood vessels.
3. They secrete procoagulants, or clotting factors, which promote blood clotting.
4. They internalize and destroy bacteria.
5. They secrete chemicals that attract neutrophils and monocytes to sites of inflammation.

LEC 9: Muscle Tissue

- The muscular system is responsible for the movement of the human body.
- Muscle tissue is composed of **differentiated cells** containing **contractile proteins**.
- Most muscle cells are of **mesodermal origin**, and they are differentiated mainly by a gradual process of lengthening, with simultaneous synthesis of myofibrillar proteins.
- For some muscle types, the cells are **non-proliferative** due to this high degree of specialization and differentiation.
- Muscle contraction is accomplished by the reciprocating sliding of intracellular filaments composed of **actin** and **myosin**.
- Muscle tissue comprises the "flesh" of the body and much of the walls of hollow organs.

  Due to its high degree of specialization, unique terms are used for certain structures in muscle cells:
- Individual muscle cell is called **muscle fiber.**
- The cytoplasm of muscle fiber is called **sarcoplasm.**
- The muscle fiber plasma membrane (plasmalemma)is called the **sarcolemma.**
- The smooth endoplasmic reticulum is called the **sarcoplasmic reticulum.**

Classification of Muscles:

1- Functional classification is based on the **type of neural control**:

- Voluntary
- Involuntary

2- Structural classification is based on the **presence or absence of cross striations:**

- Striated
- Non striated (smooth)

3- Combined functional and structural classification:

Upon it, three types of muscle tissue in mammals can be distinguished on the basis of morphological and functional characteristics, and each type of muscle tissue has a structure adapted to its' physiological role:

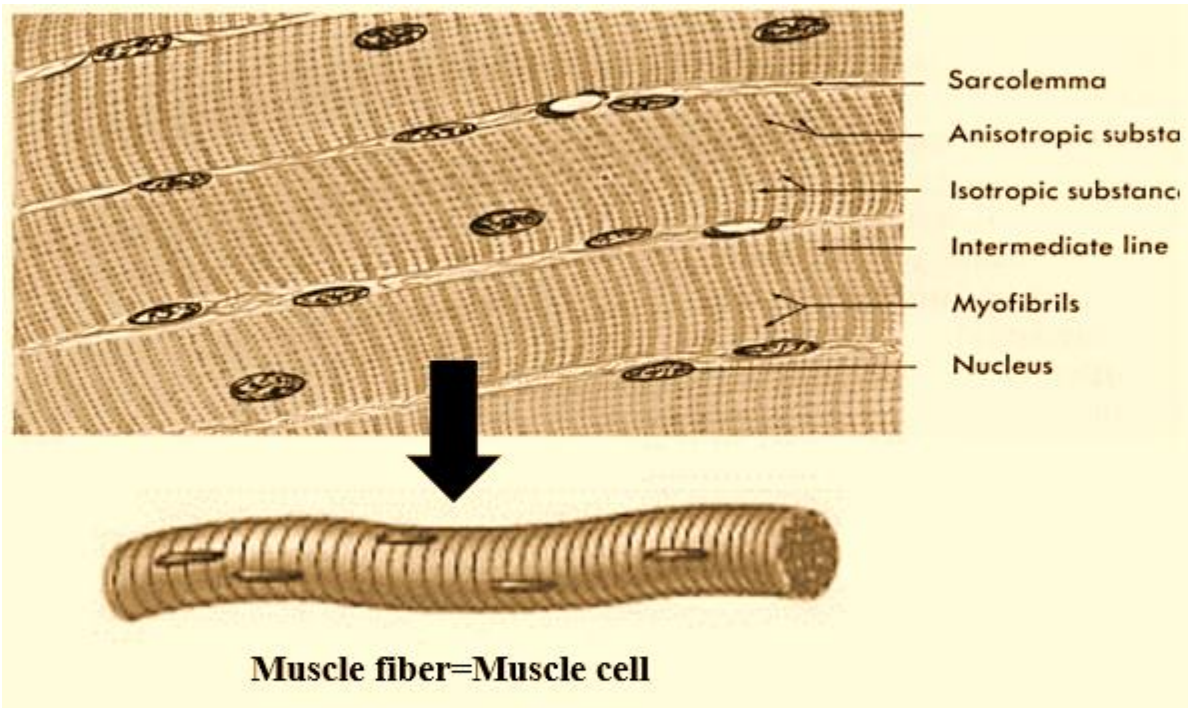
1. **Skeletal muscle:**
   - ➢ Striated and voluntary
   - ➢ Found mostly attached to the skeleton
2. **Cardiac muscle**
   - ➢ Striated and involuntary
   - ➢ Composes the majority of the heart wall (myocardium)
3. **Smooth (visceral) muscle**
   - ➢ Non striated and involuntary
   - ➢ Found mostly in the walls of hollow organs and vessels

Skeletal muscle tissue:

Structure & characteristics of skeletal muscle:

- Composed of bundles of long, cylindrical, multinucleated cells (muscle fibers) that show cross-striations.
- The oval nuclei are usually found at the periphery of the cell under the cell membrane (sarcolemma).
- Skeletal muscle fiber considered largest fiber type, (1–30mm) in length and (10–100) microns in diameter.
- Fibers can increase in size but not in number.

- Contains glycogen, which provides energy for muscle contraction.
- Abundant of myoglobin, an oxygen binding protein.
- The characteristic nuclear location is helpful in distinguishing skeletal muscle from cardiac and smooth muscle, both of which have centrally located nuclei.
- The contraction of skeletal muscle is quick, forceful, and usually under voluntary control.
- The contraction is caused by **the interaction of thin actin filaments and thick myosin filaments,** whose molecular configuration allows them to slide upon one another. The forces necessary for sliding are generated by weak interactions in the bridges that bind actin to myosin.
- This movement of actin filaments in relation to myosin filaments is called **Sliding Filament Theory**
- binding protein.



Organization of <u>Skeletal Muscle</u>:

The masses of fibers that make up the muscle **are not grouped in random fashion**, but are arranged in regular bundles surrounded by **connective tissue investments(sheathes). Three types of sheathes are found:**

- **A. Epimysium:** an external sheath of dense connective tissue surrounding the entire muscle.
- **B.** From the epimysium, thin septa of connective tissue extend inward, surrounding the bundles of fibers within a muscle. The connective tissue around each bundle of muscle fibers is called the **Perimysium**.
- **C.** Each muscle fiber is itself surrounded by a delicate layer of connective tissue, the **Endomysium**, composed mainly of a basal lamina and reticular fibers.

Blood Supply of skeletal muscle:

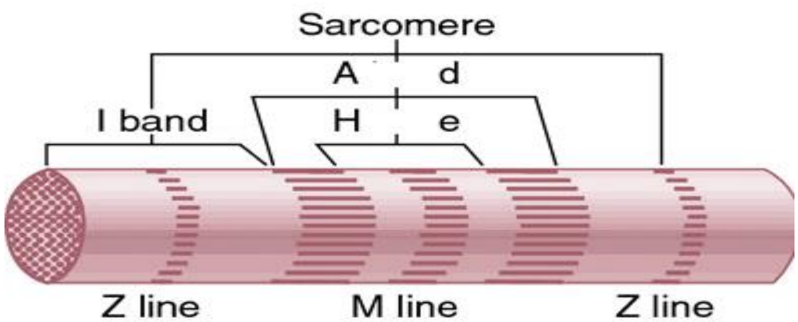
- Blood vessels penetrate the muscle within the connective tissue septa and form a rich capillary network that runs between and parallel to the muscle fibers.
- The capillaries are of the **continuous type**, and lymphatic vessels are found in the connective tissue.

Organization of <u>Skeletal Muscle Fibers</u>:

- As observed with the light microscope, the longitudinally sectioned muscle fibers show cross-striations of alternating light and dark bands:
- The darker bands are called **A bands** (**anisotropic,** i.e., are birefringent in polarized light), composed mainly of **thick filaments** in addition to **portions of overlapping thin filaments**. (i.e. Contain actin and myosin).
- The lighter bands are called **I bands** (**isotropic,** i.e., do not alter polarized light), contains actin only.
- In the electron microscope, **each I band** is bisected by a dark transverse line, the **Z line,** which composed of alpha-actinin protein, and located in the center of the I band.
- Close observation of the A band shows the presence of a lighter zone in its center, the **H band,** which represents the area where actin is not present, consisting only of the rod-like portions of the myosin molecule
- Bisecting the H band is the **M line;** a region at which lateral connections are made between adjacent thick filaments (myosin filaments).

Sarcomere:

- The smallest repetitive subunit of the contractile apparatus of striated muscle fibers.
- Seen in both skeletal and cardiac muscle fibers.
- About 2.5 mm long in resting muscle.
- Extends from z-line to z-line.



Hierarchy of skeletal muscle organization:

1. **Myofilaments*:*** Visible only with the electron microscope; composed primarily of actin, which forms 5-nm wide thin filaments, and myosin, which forms 15-nm wide thick filaments.
2. **Myofibrils:** Visible with the light microscope, 1–2 microns wide, oriented parallel to the long axis of the cell; composed of bundles of overlapping myofilaments that are arranged in register, producing an alternating light-dark, striated banding pattern.
3. **Muscle fiber**: Specialized term for a muscle cell, 10–100 microns wide; sarcoplasm is filled with hundreds of myofibrils, which are oriented parallel to each other and to the long axis of the muscle fiber.
4. **Muscle fascicle**: Collection of muscle fibers surrounded by perimysium; collections of muscle fascicles are surrounded by the epimysium and form a muscle.

Alterations in sarcomeres during contraction according to (Sliding Filament Model):

1. Sarcomeres shorten.
2. Z-line interval narrows.
3. Width of H and I bands decrease as actin is pulled past the myosin.
4. A band width remains unchanged.

Sarcotubular system:

Myofibrils are surrounded by structures made up of membranes in the form of vesicles and tubules which form two systems:

1. **Transverse T tubules:**
   - Deep invaginations of the sarcolemma
   - Function: play important role in the physiology of muscle contraction (how?):
   - Muscle **action potential** (which is the movement of electrical charges) that travelling along t tubules, triggers the release of calcium ions from sarcoplasmic reticulum.
2. **Sarcoplasmic reticulum:**
   - Runs longitudinally and surrounds each myofibril.
   - Form chambers called **terminal cisternae** on either side of the T- tubules.
   - A single T-tubule and the 2 terminal cisternae form a **triad**.
   - SR stores Ca^{++} when muscle not contracting.
   - When stimulated, calcium released into sarcoplasm
   - SR membrane has Ca^{++} pumps that function to pump Ca^{++} out of the sarcoplasm back into the SR after contraction.

- **Triad:** is a structure formed by **a single T tubule with 2 terminal cisternae** of the sarcoplasmic reticulum on either side.
- **The main function of the triad** is to transmit the electrical impulse from the sarcolemma to the sarcoplasmic reticulum, effecting calcium flow into the cytoplasm and the initiation of muscle contraction.

LEC 10: Contractile proteins:

Striated muscle filaments contain several proteins; the four main proteins **are actin, tropomyosin, troponin, and myosin.**

- **Thin filaments** are composed of the first three proteins.
- **Thick filaments** consist primarily of myosin.
- Myosin and actin together represent 55% of the total protein of striated muscle.

1. **Actin**:
   - The primary structural protein presents as long filamentous (F-actin) polymers consisting of two strands of globular (G-actin) monomers, twisted around each other in a double helical formation
   - G-actin molecules are structurally asymmetric. When G-actin molecules polymerize to form F-actin, they bind back to front, producing a filament with distinguishable polarity.
   - Each G-actin monomer contains a binding site for myosin
2. **Tropomyosin:**
   - A long, thin molecule about 40 nm in length, contains two polypeptide chains.
   - These molecules are bound head to tail, forming filaments that run over the actin subunits alongside the outer edges of the groove between the two twisted actin strands.
   - It is the major regulatory protein of contractile systems.
3. **Troponin:**
   - A complex of three subunits: **TnT,** which strongly attaches to tropomyosin; **TnC,** which binds calcium ions; and **TnI,** which inhibits the actin-myosin interaction.
   - A troponin complex is attached at one specific site on each tropomyosin molecule.

4. **Myosin:**

- Each molecule consists of **linear tail + globular head**
- A much larger complex than actin, can be dissociated into two identical heavy chains and two pairs of light chains (four light chains).
- Myosin heavy chains are thin, rod-like molecules made up of two heavy chains twisted together.
- Small globular projections at one end of each heavy chain form the heads, which have **ATP-binding sites,** as well as **ATP-hydrolyzing sites** that have the enzymatic capacity to hydrolyze ATP (ATPase activity), and **actin binding sites** which have the ability to bind to actin.
- The head form cross bridges, projects from the tail and bind the thin filaments during contraction.
- The four light chains are associated with the head.
- Several hundred myosin molecules are arranged within each thick filament with their rod-like portions overlapping (tail to tail aggregation), and their globular heads directed toward either end.
- Analysis of thin sections of striated muscle shows the presence of cross-bridges between thin and thick filaments.
- These bridges, which are known to be formed by the head of the myosin molecule plus a short part of its rod-like portion, are involved in the conversion of chemical energy into mechanical energy

Types of skeletal muscle fibers:

- There are 3 types of skeletal muscle fibers, **fast contracting, intermediate contracting,** and **slow contracting** fibers.
- Each skeletal muscle contains a percentage of each of these types.

A. Fast contracting (white) type:

- most skeletal muscles fibers are of this type
- large in diameter
- Abundance of glycogen
- Extensive sarcoplasmic reticulum, this allows rapid release and uptake of Ca^{++}.
- few mitochondria
- depend largely on anaerobic metabolism
- fatigue rapidly
- appear pale to the naked eye because of low number of capillaries per unit

B. Slow contracting (red) type:

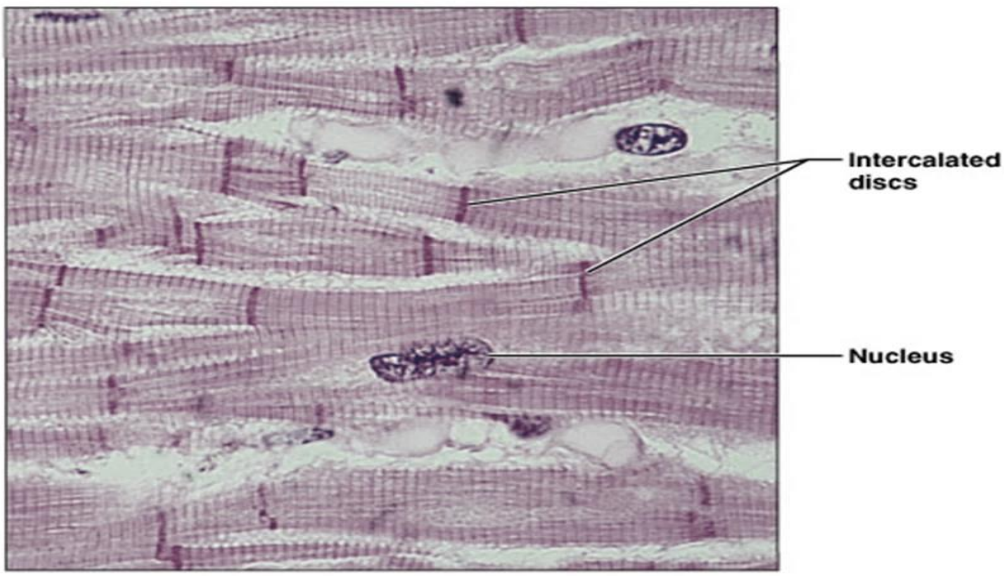
- are smaller than fast type.
- take about three times longer to contract after receiving stimulus.
- many mitochondria, little glycogen
- Rich capillary supply
- contain a large amount of myoglobin, which carry oxygen to muscle fibers, suggesting aerobic energy pathways

C. Intermediate type:

- have properties of both fast and slow fibers
- similar in appearance to fast fibers
- similar in endurance to slow fibers

Cardiac Muscle Tissue:
Structure & characteristics of cardiac Muscle:

- Cardiac muscle occurs only in the myocardium of the heart and in the roots of large vessels where they join the heart.
- Intermediate in size between skeletal and smooth muscle.
- Fibers are cylindrical, branch, and form interwoven bundles.
- Usually, one nucleus per fiber located in the center (mononucleated)
- Organelles are clustered at the poles of the nucleus.
- Myofilament organization into myofibrils is identical to skeletal muscle; cross-striations and bands which identical to skeletal muscle are present, but not as prominent.



Intercalated discs

- Microscopic identifying features of cardiac muscle.
- Dark-staining transverse lines that cross the chains of cardiac cells at irregular intervals.
- Junctional complexes that are unique to cardiac muscle fibers, consist of specialized cell junctions and interdigitations of the sarcolemma at the ends of the fibers.
- There are <u>three main junctional specializations</u> within the intercalated disk:

1. **Fascia adherens**: Acts as a hemi-Z-line; serve to attach cardiac muscle fibers and anchor actin filaments of the terminal sarcomeres at the ends of the cell.
2. **Desmosomes**: Bind ends of fibers together preventing them from pulling apart under constant contractile activity.
3. **Gap junctions**: provide ionic continuity between adjacent cells.

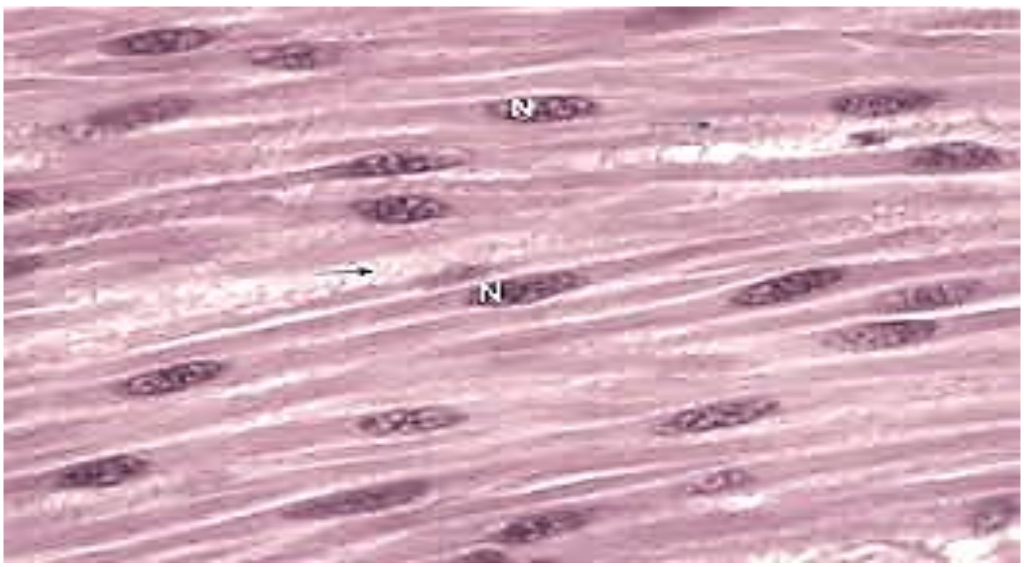
Purkinje fibers:

- One of the specialized cardiac muscle fibers, they are often binucleated cells.
- They are part of the impulse-conducting network of the heart, that rapidly transmit impulses from the atrio-ventricular node to the ventricles.
- They are larger than cardiac muscle cells, but have fewer myofibrils, lots of glycogen and mitochondria.
- These cells are connected together by desmosomes and gap junctions, but not by intercalated discs.

Smooth Muscle Tissue:
Structure & characteristics of smooth muscle:
- Spindle-shaped cells with central nuclei
- No striations
- Occurs mostly as sheets, which form the walls of most hollow organs **with the exception of the heart**.
- Prominent in the walls of blood vessels, many respiratory passageways, and some genital ducts.
- Smooth muscle usually has spontaneous activity in the absence of nervous stimuli.
- Therefore, its nerve supply has the function of modifying activity rather than initiating it as in skeletal muscle.

Q Where can you see the smooth muscles?

Answer: Smooth Muscle found in six areas of the body: blood vessel walls, respiratory tract, digestive tubes, urinary organs, reproductive organs, and the eye.



Structure of smooth muscle fibers
- Smallest fiber type, length varies from 20 microns in blood vessels to 500 microns in the uterus.
- Unbranched spindle-shaped (fusiform) fibers are elongated with tapering ends, each of which is enclosed by a basal lamina and a network of reticular fibers.
- Possess a single, centrally placed, oval nucleus, which can appear spiraled shaped when the fiber is contracted.
- Organelles are clustered at the poles of the nucleus.
- Nonstriated; no myofibrils are present.
- Abundant gap junctions.

Organization of the contractile proteins
- Actin and myosin myofilaments are present, but **they are not organized into myofibrils**.
- Myofilaments overlap as in striated muscle and crisscross throughout the sarcoplasm, forming a reticulum.

Dense bodies
- Two types of **dense bodies** appear in smooth muscle cells; One is **membrane** associated; the other is **cytoplasmic**.
- Both contain alpha-actinin, and are thus similar to the Z lines of striated muscles.

- Serve as insertion points for myofilaments to transmit the force of filament sliding. i.e. myofilaments insert into dense bodies transmit contractile force to adjacent smooth muscle cells and their surrounding network of reticular fibers.

Regeneration of Muscle Tissue

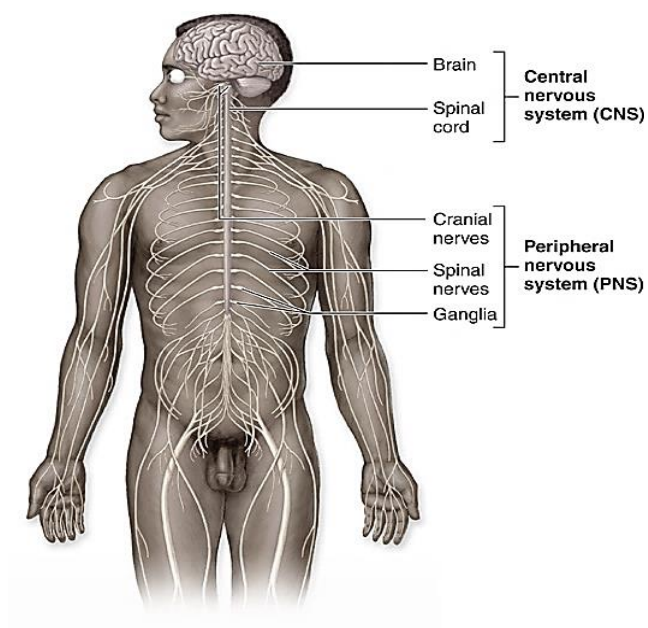
- The three types of adult muscle have different potentials for regeneration after injury.
- **In skeletal muscle**, although the nuclei are incapable of undergoing mitosis, the tissue can undergo limited regeneration.
- **Cardiac muscle** has almost no regenerative capacity beyond early childhood. Defects or damage in heart muscle are generally replaced by the proliferation of connective tissue, forming myocardial scars.
- **Smooth muscle** is capable of an active regenerative response.

LEC 11: Nervous Tissue

- Nerve tissues develop from **embryonic ectoderm**.
- The human nervous system, the most complex system in the human body, is formed by a network of more than 100 million nerve cells (**neurons**), assisted by many more **glial cells**.
- Each neuron has, on average, at least 1000 interconnections with other neurons, forming a very complex system for communication.
- The nervous system consists of the **brain**, **spinal cord**, **sensory organs**, and all of the **nerves** that connect these organs with the rest of the body.
- Together, these organs are responsible for the control of the body and communication among its parts.

Anatomical subdivisions of nervous tissue:

1. ***Central nervous system (CNS) includes:***
   - *Brain*
   - *Spinal cord*
2. ***Peripheral nervous system (PNS) includes:***
   - *Nerves*
   - *Ganglia (singular: ganglion)*



- The brain and spinal cord form the **central nervous system (CNS);** the control center where information is evaluated and decisions are made.
- The sensory nerves and sense organs of the **peripheral nervous system (PNS)** monitor conditions inside and outside of the body and send this information to the CNS.
- **The Efferent nerves** in the PNS carry signals from the control center to the muscles, glands, and organs to regulate their functions.

Cells of Nervous Tissue:

1- Neurons:

- They are the functional units of the nervous system.
- **Functions:**
  - **a)** Receive, process, store, and transmit information (stimuli) to and from other neurons, muscle cells, or glands.
  - **b)** Triggering of certain cell activities; and the release of **neurotransmitters** and other informational molecules.
  - **c)** Form complex and highly integrated circuits.

2- Supportive cells:

- Have short processes, support and protect neurons, and participate in neural activity, neural nutrition, and the defense processes of the central nervous system. It comprised of:
  - **A. Astrocytes, Oligodendrocytes, Microglia, and Ependymal cells** in the <u>**CNS**</u>**.**
  - **B. Schwann cells** in the <u>**PNS**</u>.

Structure of a Typical Neuron:

Most neurons consist of three parts: **cell body, dendrites and Axon.**

I.Cell body (or perikaryon): the trophic center for the whole nerve cell and is also receptive to stimuli. It contains:

A. **Nucleus:**
- Large, spherical, usually centrally located in the cell body.
- Highly euchromatic with a large, prominent nucleolus.

B. Cytoplasm which contains**:**
- Well-developed cytoskeleton.
- Intermediate filaments (*neurofilaments) which* are abundant in cell body as well as cell processes.
- Abundant rough endoplasmic reticulum and ***Nissl's bodies****; the* large granular bodies consisting of rough endoplasmic reticulum and ribosomes, that <u>occurs in nerve cell bodies and dendrites</u>, and are the site of protein synthesis.
- Well-developed Golgi apparatus.
- Numerous mitochondria.

II. Dendrites (dendron):
- Usually multiple and highly branched at acute angles.
- Collectively, form the majority of the receptive field of a neuron; conduct impulses toward the cell body.

- Organelles present in dendrites include**:**
  a) Neurofilaments
  b) Rough endoplasmic reticulum and nissl's bodies.
  c) Smooth endoplasmic reticulum
  d) Mitochondria
  e) Dendrites devoid of Golgi bodies

III. Axon:

- A cylindrical process that varies in length and diameter according to the type of neuron.
- The plasma membrane of the axon is called the **axolemma**, and its contents are known as **axoplasm**.
- Usually only one axon per neuron
- Generally, of smaller caliber and longer than dendrites
- Branches at right angles, fewer branches than dendrites
- **Organelles contained in the axon:**
  a. Neurofilaments
  b. Smooth endoplasmic reticulum
  c. Mitochondria
  d. Axon lacks rough endoplasmic reticulum and Nissl's bodies

Type of Neurons by Function:

1. **Sensory neurons:** Transmit nerve impulse from sensory receptors to the CNS
2. **Motor neurons:** Transmit nerve impulse from CNS to muscles or glands
3. **Interneurons (association neurons)**:
   - A neuron that lies entirely within the CNS.
   - Multipolar type.
   - Connect between sensory and motor neurons.

Types of Neurons by Shape:

Based on the size and shape of their processes, most neurons can be placed in one of the following categories: **multipolar neurons, bipolar neurons,** and **Pseudounipolar neurons.**

1. ***Multipolar neuron:***
   - *Most numerous and structurally diverse type*
   - Have short dendrites emanating from the cell body and one long axon
   - Found throughout the CNS and in autonomic ganglia in the PNS.

Types of multipolar neurons in CNS according to the variations in size, position and shape:

	Type	Position
1.	Motor neuron	ventral horn of spinal cord
2.	Pyramidal cells	in cerebral cortex
3.	Purkinje cells	in cerebral cortex
4.	Stellate cells	in cerebellum
5.	Basket cells	in cerebellum

2. ***Pseudounipolar neuron:***

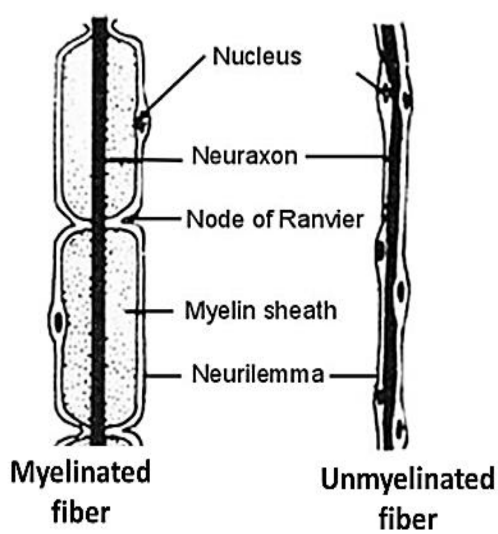
- Neurons with a short extension that quickly divides into two branches, one of which functions as a dendrite, the other as an axon
- Found in selected areas of the CNS and in sensory ganglia of cranial nerves and spinal nerves (dorsal root ganglia)

3. ***Bipolar neuron:***

- Have two main extensions of similar lengths.
- Found associated with organs of special sense (retina of the eye, olfactory epithelium)
- Developmental stage for all neurons

Nerve Fibers :

- Nerve fibers consist of **axons** enveloped by a special sheath derived from cells of ectodermal origin.
- Groups of nerve fibers constitute the tracts of the **brain, spinal cord, and peripheral nerves.**
- Nerve fibers exhibit differences in their enveloping sheaths, related to whether the fibers are part of the central or the peripheral nervous system.
- Single or multiple folds of a sheath cell cover most axons in adult nerve tissue.
- In peripheral nerve fibers, the sheath cell is the **Schwann cell,** while in central nerve fibers it is the **oligodendrocyte.**
- Axons of small diameter are usually **unmyelinated nerve fibers**.
- Progressively thicker axons are generally sheathed by increasingly numerous concentric wrappings of the enveloping cell, forming the **myelin sheaths.** These fibers are known as **myelinated nerve fibers**.



Nerve fibres

Myelin:

- An insulating layer around a nerve, formed by oligodendrocytes in CNS and Schwann cells in PNS.
- It is composed of a lipoprotein with phospholipids, glycolipids and cholesterol.
- Myelin allows nerve conduction to be 150 x faster than unmyelinated nerves.
- **Myelination** is the process of myelin formation.

Myelinated Fibers:

- In myelinated fibers of the peripheral nervous system, the plasmalemma of the covering Schwann cell winds and wraps around the axon.
- The layers of membranes of the sheath cell unite and form myelin.
- The myelin sheath shows gaps along its path called the **nodes of Ranvier**; these represent the spaces between adjacent Schwann cells along the length of the axon.
- The distance between two nodes is called an **internode** and consists of one Schwann cell. The length of the internode varies between 1 and 2 mm.

Unmyelinated Fibers :

- In both the central and peripheral nervous systems, not all axons are sheathed in myelin.
- In the peripheral system, all unmyelinated axons are enveloped within simple clefts of the Schwann cells
- Unmyelinated nerve fibers do not have nodes of Ranvier, because neighboring Schwann cells are united to form a continuous sheath.
- The central nervous system is rich in unmyelinated axons; unlike those in the peripheral system.

LEC 12: Ganglia:

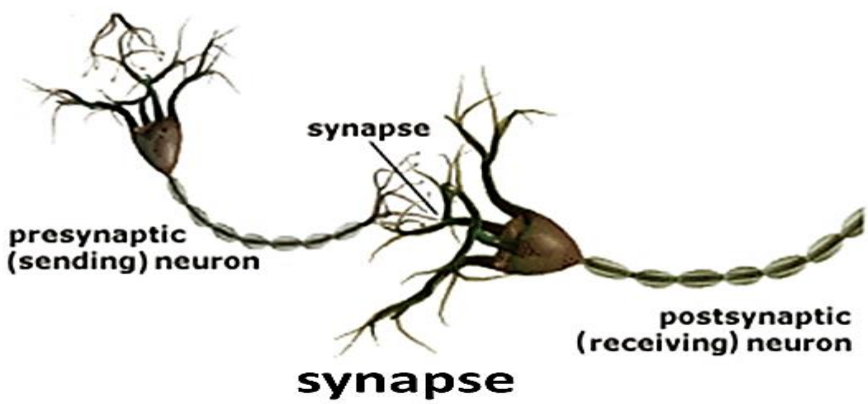
- Ganglia are ovoid structures containing neuronal cell bodies and glial cells supported by connective tissue.
- Because they serve as relay stations to transmit nerve impulses, one nerve enters and another exits from each ganglion.

Types of Ganglia:

1. **Sensory Ganglia:**
   - Sensory ganglia receive afferent impulses that go to the central nervous system.
   - Two types of sensory ganglia exist:
     A. **Cranial ganglia:** associated with cranial nerves.
     B. **Spinal ganglia**: associated with the dorsal root of the spinal nerves.
       - A connective tissue framework and capsule support the ganglion cells.
       - The type of neurons of sensory ganglia are **Pseudounipolar,** and relay information from the ganglion's nerve endings to the gray matter of the spinal cord via synapses with local neurons.
2. **Autonomic Ganglia:**
   - Autonomic ganglia appear as bulbous dilatations in autonomic nerves.
   - Some are located near or within certain organs, especially in the walls of the digestive tract, where they constitute the **intramural ganglia.**
   - These ganglia are devoid of connective tissue capsules, and their cells are supported by the stroma of the organ in which they are found.
   - Autonomic ganglia usually have multipolar neurons.

Synapse:

- A **synapse** is a structure that permits a neuron to pass an electrical or chemical signal to another neuron.
- The synapse is responsible for the unidirectional transmission of nerve impulses.
- Synapses are sites of functional contact between neurons or between neurons and other effector cells (eg, muscle and gland cells).
- The function of the synapse is to convert an electrical signal (impulse) from the **presynaptic cell** into a chemical signal that acts on the **postsynaptic cell**.
- Most synapses transmit information by releasing **neurotransmitters** during the signaling process.
- **Neurotransmitters** are chemicals that, when combined with a receptor protein, either open or close ion channels or initiate second-messenger cascades.
- **Neuromodulators** are chemical messengers that do not act directly on synapses but modify neuron sensitivity to synaptic stimulation or inhibition.
- Some neuromodulators are neuropeptides or steroids produced in the nerve tissue; others are circulating steroids.
- **Composition of synapse** the synapse itself is formed by an axon terminal (**presynaptic terminal**) that delivers the signal to a region on the surface of another cell at which a new signal is generated (**postsynaptic terminal**), and a thin intercellular space called the **synaptic cleft;** a fluid filled space or gap between presynaptic and postsynaptic terminals.



Types of synapses

- If an axon forms a synapse with a cell body, the synapse is called **axosomatic**
- If it forms a synapse with a dendrite, it is called **axodendritic**
- If it forms a synapse with an axon, it is called **axoaxonic**
- A **neuromuscular junction** is a **chemical synapse** formed by the contact between a motor neuron and a muscle fiber.
- It is at the neuromuscular junction that a motor neuron is able to transmit a signal to the muscle fiber, causing muscle contraction.

Nerve Endings:

- There are several structural types of receptors in the skin (cutaneous receptors).
- These fall into the category of **encapsulated** and **non-encapsulated** receptors.
- The **non-encapsulated** endings include free nerve endings, which are mostly respond to noxious (pain) and thermal stimuli, ex: **Merkle's cells**.
- The **encapsulated endings** include **Meisner's corpuscles, Pacinian corpuscles** and **Ruffini endings.**

Meissner's corpuscle:

- A type of mechano-receptor.
- A type of nerve ending located near the surface of the skin and responsible for sensitivity to light touch.
- Most concentrated in thick hairless skin, especially at the finger pads.
- Meissner's corpuscle is <u>encapsulated unmyelinated nerve endings</u>, which consist of flattened supportive cells arranged as <u>horizontal lamellae</u> surrounded by a connective tissue capsule.
- A single nerve fiber meanders between the lamellae and throughout the corpuscle.

Pacinian's corpuscle:

- Another type of mechano-receptor.
- A specialized bulb-like nerve ending located in the subcutaneous tissue of the skin and scattered within the body, particularly around muscles and joints.
- Occurs abundantly in the skin of palms, soles, joints and genitals, and respond only to mechanical deformation.
- Larger and fewer in number than Miessner's.
- Pacinian's corpuscles are built in a way that gives them a fast response and quick recovery.
- They contain a central nerve fiber surrounded by onion like layers of connective tissue that behave like a shock absorber.
- In addition to cutaneous receptors, there are muscle receptors that are involved in detecting muscle stretch (**muscle spindle**) and muscle tension (**Golgi tendon organs**).
- Muscle spindles are located in the muscle belly and consist of **intrafusal muscle fibers** that are arranged in parallel with the majority of fibers comprising the muscle (**extrafusal fibers**).

Supportive cells of the nervous system

I. **Supporting cells of the <u>CNS</u>** (neuroglial cells); outnumber neurons 10:1

1. ***Astrocytes:***

- Star-shaped cells with multiple radiating processes.
- Astrocytes bind neurons to capillaries and to the pia mater (a thin connective tissue that covers the central nervous system).
- Astrocytes are by far the most numerous glial cells and exhibit an exceptional morphological and functional diversity.

Types:

- ***Fibrous astrocytes:*** astrocytes with few long processes *located in white matter*
- ***Protoplasmic astrocytes:*** astrocytes with many short-branched processes located *in gray matter*

Functions of Astrocytes:

- Physical support
- Transport nutrients
- Maintain ionic homeostasis
- Absorb local excess of neurotransmitters

2. ***Oligodendrocytes:***
   - Present in white and gray matter.
   - produce the myelin sheath that provides the electrical insulation of neurons in the central nervous system
   - These cells have processes that wrap around axons, producing a myelin sheath

3. ***Ependymal cells:***
   - Ependymal cells are low columnar epithelial cells lining the ventricles of the brain and central canal of the spinal cord.
   - In some locations, ependymal cells are ciliated, which facilitates the movement of cerebrospinal fluid.

4. ***Microglia:***
   - Not a true neuroglial cell; derived from mesoderm whereas neuroglial cells, as well as neurons, are derived from ectoderm.
   - small elongated cells with short irregular processes
   - Microglia are phagocytic cells that represent the mononuclear phagocytic system in nerve tissue

   Functions:
   1. They are involved with inflammation and repair in the adult central nervous system
   2. they produce and release neutral proteases and oxidative radicals.
   3. Microglia secrete a number of immunoregulatory cytokines and dispose of unwanted cellular debris caused by central nervous system lesions.

II. Supporting cells of the PNS:

Schwann cells:

- Schwann cells have the same function as oligodendrocytes but are located around axons in the peripheral nervous system.
- One Schwann cell forms myelin around a segment of one axon, in contrast to the ability of oligodendrocytes to branch and serve more than one neuron and its processes.

Types:

1. ***Satellite Schwann cells*** surround cell bodies in ganglia.
2. ***Ensheathing Schwann cells*** surround unmyelinated axons and produce myelin around axons.

Connective Tissue Investments of Nervous Tissue:

A. Peripheral nervous system:

- Nerves have an external fibrous coat of dense connective tissue called **epineurium,** which also fills the space between the bundles of nerve fibers.
- Each bundle is surrounded by the **perineurium,** a sheath formed by layers of flattened epithelium-like cells.
- The cells of each layer of the perineurial sleeve are joined at their edges by tight junctions, an arrangement that makes the perineurium a barrier to the passage of most macromolecules and has the important function of protecting the nerve fibers from aggression.
- Within the perineurial sheath run the Schwann cell-sheathed axons and their enveloping connective tissue, the **endoneurium** which consists of a thin layer of reticular fibers, produced by Schwann cells.

B. Central nervous system

Meninges:

- The skull and the vertebral column protect the central nervous system.
- It is also encased in membranes of connective tissue called the **meninges**
- Starting with the outermost layer, the meninges are the **dura mater, arachnoid,** and **pia mater.**
- The arachnoid and the pia mater are linked together and are often considered a single membrane called the **pia-arachnoid**
- **The primary function of the meninges** is to protect the central nervous system.

a) ***Pia mater***

- The pia mater is a loose connective tissue containing many blood vessels.
- Although it is located quite close to the nerve tissue, it is not in contact with nerve cells or fibers.
- The pia mater follows all the irregularities of the surface of the central nervous system and penetrates it to some extent along with the blood vessels. Squamous cells of mesenchymal origin cover pia mater.

b) ***Arachnoid membrane***

- Separated from pia mater by connective tissue trabeculae
- Together with pia mater, constitute the *leptomeninges*
- *Inflammation* of these membranes produces meningitis

c) ***Dura mater***

- The dura mater is the external layer and is composed of dense connective tissue continuous with the periosteum of the skull.
- The dura mater that envelops the spinal cord is separated from the periosteum of the vertebrae by the epidural space, which contains thin-walled veins, loose connective tissue, and adipose tissue.
- The dura mater is always separated from the arachnoid by the thin subdural space.
- The internal surface of all dura mater, as well as its external surface in the spinal cord, is covered by simple squamous epithelium of mesenchymal origin.

Brain and Spinal cord:

- The brain is the control center of the body.
- It consists of three main components: the **forebrain**, the **mid brain(brainstem)**, and the **hindbrain**.
- **The spinal cord** is a cylindrical shaped bundle of nerve fibers that is connected to the brain.
- It is located inside the vertebral canal.
- Spinal cord nerves transmit information from body organs and external stimuli to the brain and send information from the brain to other areas of the body.
- The nerves of the spinal cord are grouped into bundles of nerve fibers that travel in two pathways:
- **Ascending nerve** tracts carry sensory information from the body to the brain.
- **Descending nerve** tracts send information pertaining to motor function from the brain to the rest of the body.
- When sectioned, the spinal cord show regions that are white (**white matter**) and that are gray (**gray matter**).
- The differential distribution of myelin in the central nervous system is responsible for these differences.
- The main component of white matter is **myelinated axons,** and **the myelin-producing oligodendrocytes**.
- White matter does not contain neuronal cell bodies.

- Gray matter contains neuronal cell bodies, dendrites, and the initial unmyelinated portions of axons and glial cells.
- In cross sections of the **spinal cord,** white matter is peripheral and gray matter is central, assuming the shape of an **H.**
- In the horizontal bar of this **H** is an opening, the **central canal,** which is a remnant of the lumen of the embryonic neural tube. It is lined with ependymal cells.
- The gray matter (the legs of the **H)** forms the **anterior horns,** which contain motor neurons whose axons make up the ventral roots of the spinal nerves.
- Gray matter also forms the posterior horns (the arms of the **H**), which receive sensory fibers from neurons in the spinal ganglia (dorsal roots).
- Spinal cord neurons are large and multipolar, especially in the anterior horns, where large motor neurons are found.