HISTOLOGY OF EPITHELIUM & CONNECTIVE TISSUE

BY : DEPARTEMENT OF HISTOLOGY
Human body is composed of 4 basic types of tissue:

1. **Epithelial Tissues**
   Composed of closely aggregated polyhedral cells with very little extracellular substance.

2. **Connective Tissues**
   Characterized by the abundance of extracellular material produced by its cells.

3. **Muscle Tissues**
   Composed of elongated cells that have the specialized function of contraction.

4. **Nervous Tissues**
   Composed of cells with elongated processes extending from the cell body that have the specialized function of receiving, generating, transmitting nerve impulses.
EPITHELIUM

Derive from ectoderm, mesoderm, endoderm.

Epithelium:
• Covers and lines body surfaces (except articular cartilage, enamel of the tooth, anterior surface of iris)
• Forms the functional units of secretory glands → salivary glands, liver
Basic function:
1. Protection (skin)
2. Absorption (small and large intestine)
3. Transport of material (by cilia)
4. Secretion (gland)
5. Excretion (tubulus of the kidney)
6. Gas exchange (lung alveolus)
7. Gliding between surface (mesothelium)

Epithelia $\rightarrow$ anchored to a basal lamina.
Basal lamina + connective tissue component $\rightarrow$ basement membrant
Classified into 3 major categories:

1. **Simple epithelia**: 1 layer of cells
   a. simple squamous epithelium
   b. Simple cuboidal epithelium
   c. Simple columnar epithelium

   **Endothelium**: simple epithelium lining the blood and lymphatic vessel.
   **Mesothelium**: simple epithelium lining all body cavities.

2. **Stratified epithelia**: 2 or more cell layers
   a. Stratified squamous epithelium:
      1. Non keratinized
      2. Keratinized: (nuclei absent in the outer layer)
   b. Stratified cuboidal epithelium
   c. Stratified columnar epithelium

3. **Pseudostratified epithelium**: basal and columnar cells
   a. Pseudostratified columnar ciliated epithelium → trachea
   b. Pseudostratified columnar epithelium with stereocilia → epididymis
   c. Transitional epithelium → urinary passage (urothelium)
<table>
<thead>
<tr>
<th>Type</th>
<th>Cell Form</th>
<th>Examples of Distribution</th>
<th>Main Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>Squamous</td>
<td>Lining of vessels (endothelium). Serous lining of cavities; pericardium, pleura, peritoneum (mesothelium).</td>
<td>Facilitates the movement of the viscera (mesothelium), active transport by pinocytosis (mesothelium and endothelium), secretion of biologically active molecules (mesothelium).</td>
</tr>
<tr>
<td>Cuboidal</td>
<td></td>
<td>Covering the ovary, thyroid.</td>
<td>Covering, secretion.</td>
</tr>
<tr>
<td>Columnar</td>
<td></td>
<td>Lining of intestine, gallbladder.</td>
<td>Protection, lubrication, absorption, secretion.</td>
</tr>
<tr>
<td>Pseudostratified</td>
<td>Some columnar and some cuboidal</td>
<td>Lining of trachea, bronchi, nasal cavity.</td>
<td>Protection, secretion; cilia-mediated transport of particles trapped in mucus.</td>
</tr>
<tr>
<td>Stratified</td>
<td>Surface layer squamous keratinized (dry)</td>
<td>Epidermis.</td>
<td>Protection; prevents water loss.</td>
</tr>
<tr>
<td></td>
<td>Surface layer squamous nonkeratinized (moist)</td>
<td>Mouth, esophagus, larynx, vagina, anal canal.</td>
<td>Protection, secretion; prevents water loss.</td>
</tr>
<tr>
<td></td>
<td>Cuboidal</td>
<td>Sweat glands, developing ovarian follicles.</td>
<td>Protection, secretion.</td>
</tr>
<tr>
<td></td>
<td>Transitional: domelike to flattened, depending on the functional state of the organ</td>
<td>Bladder, ureters, renal calyces.</td>
<td>Protection, distensibility.</td>
</tr>
<tr>
<td></td>
<td>Columnar</td>
<td>Conjunctiva.</td>
<td>Protection.</td>
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</tbody>
</table>
SIMPLE EPITHELIUM

A Simple squamous epithelium

B Simple cuboidal epithelium

C Simple ciliated columnar epithelium

- Epithelium
- Basement membrane
- Lamina propria
- Capillaries
- Terminal bars
- Cilia
- Baseline membrane
- Lamina propria
Simple squamous epithelium
Figure 4—13. Section of a vein containing red blood cells. All blood vessels are lined with a simple squamous epithelium called endothelium (arrowheads). Pararosaniline–toluidine blue (PT) stain. Medium magnification.
Simple cuboidal epithelium

Figure 4—15. Simple cuboidal epithelium from kidney collecting tubules. Cells of these tubules are responsive to the antidiuretic hormone and control the resorption of water from the glomerular filtrate, thus affecting urine density and helping retain the water content of the body. PT stain. Low magnification.

Figure 21—18. High magnification of a section of a thyroid. Calcitonin-producing parafollicular cells can be distinguished from the follicular epithelial cells because they are larger and their nuclei stain lighter. H&E stain. High magnification.
Simple columnar epithelium

Figure 4—16. Simple columnar epithelium formed by long cells with elliptical nuclei. The epithelium rests on the loose connective tissue of the lamina propria. A basal lamina (not visible) is interposed between the epithelial cells and the connective tissue. The round nuclei within the epithelial layer belong to lymphocytes that are migrating through the epithelium (arrows). H&E stain. Medium magnification. (Courtesy of PA Abrahamsohn.)
STRATIFIED EPITHELIUM

A  Stratified squamous epithelium

- Epithelium
- Basement membrane
- Lamina propria

B  Transitional epithelium

- Surface epithelium (facet cells)
- Basal epithelium
- Basement membrane
- Lamina propria

C  Ciliated pseudostratified epithelium

- Mucus
- Cilia
- Terminal bars
- Epithelial cell
- Goblet cells
- Basal cell
- Basement membrane
- Lamina propria
Stratified squamous keratinized epithelium

Connective tissue
Stratified squamous non keratinized epithelium
Stratified cuboidal epithelium
Epithelial membranes are classified according to the number of cell layers between the basal lamina and the free surface and by the morphology of the epithelial cells (Table 5–1). If the membrane is composed of a single layer of cells, it is called **simple epithelium**; if it is composed of more than one cell layer, it is called **stratified epithelium** (Fig. 5–1). The morphology of the cells may be squamous (flat), cuboidal, or columnar when viewed in sections taken perpendicular to the basement membrane. Stratified epithelia are classified by the morphology of the cells in their superficial layer only. In addition to these two major classes of epithelia, which are further identified by cellular morphology, there are two other distinct types: pseudostratified and transitional.

Ciliated pseudostratified columnar epithelium

trachea
Transitional epithelium
EPITHELIAL CELL POLARITY

1. On apical polarity :
   a. Cilia → trachea
      • For protection
      • Motile cell projection originating from basal bodies
   b. Microvilli → intestine
      • For absorption
      • Finger like projections of the apical epithelial cell surface
   c. Stereocilia → epididymis
      • Long and branching finger like projections of the apical epithelial cell surface

2. Basolateral domain :
   a. Cell adhesion molecules
   b. Junctional complexes
stereosilia

Spermatozoa
a. Cell adhesion molecules:
   1. Ca2+ dependent: chaderin and selectin
   2. Ca2+ independent: cell adhesion of the immunoglobulin superfamily (CAMs) and integrins

b. Junctional complexes:
   1. Tight Junction
   2. Anchoring Junction
   3. Gap junction
1. Tight junction

Function:
- Determine epithelial cell polarity and preventing the free diffusion of lipids and proteins between them
- Prevent of free passage of substance across an epithelial cell layer (paracellular pathway barrier)

2. Anchoring junction → below the tight junction
   
   a. **Zonula adherens or belt desmosome**

   a beltlike junction associated with actin microfilament → mediated by interaction of cadherin with catenins.
b. **Macula adherens or spot desmosome**: a spot like junction
   - Associated with keratin intermediate filament (tonofilament)
   - Provide strength and rigidity to an epithelial cell layer

c. **Hemidesmosome** → **asymmetrical structure**
   - Link the basal domain of an epithelial cell to the basal lamina
   - Increase the overall stability of epithelial tissues by linking intermediate filament of cytoskeleton with component of the basal lamina

3. **Gap Junction**
   - Form by integral membrane protein called connexins
   - 6 connexin monomer → a connexon
   - End to end ligament of connexons in adjacent cells provides a direct channel of communication between cytoplasm of two adjacent cells
<table>
<thead>
<tr>
<th>name</th>
<th>function</th>
</tr>
</thead>
<tbody>
<tr>
<td>tight junction</td>
<td>seals neighboring cells together in an epithelial sheet to prevent leakage of molecules between them</td>
</tr>
<tr>
<td>adherens junction</td>
<td>joins an actin bundle in one cell to a similar bundle in a neighboring cell</td>
</tr>
<tr>
<td>desmosome</td>
<td>joins the intermediate filaments in one cell to those in a neighbor</td>
</tr>
<tr>
<td>gap junction</td>
<td>allows the passage of small water-soluble ions and molecules</td>
</tr>
<tr>
<td>hemidesmosome</td>
<td>anchors intermediate filaments in a cell to the basal lamina</td>
</tr>
</tbody>
</table>
**Zonulae occludentes**
Extend along entire circumference of the cell. Prevent material from taking paracellular route in passing from the lumen into the connective tissues.

**Zonulae adherentes**
Basal to zonulae occludentes. E-cadherins bind to each other in the intercellular space and to actin filaments, intracellularly.

**Maculae adherentes**
E-cadherins are associated with the plaque. Intermediate filaments form hairpin loops.

**Gap junctions**
Communicating junctions for small molecules and ions to pass between cells. Couple adjacent cells metabolically and electrically.

**Hemidesmosomes**
Attach epithelial cells to underlying basal lamina.
LAMININ, FIBRONECTIN AND THE BASEMENT MEMBRANE

Laminin + Fibronectin:
- Distinct protein of ECM
- Associated with collagens, proteoglycans and other protein → organize a basement membrane

Basement membrane consists of 2 components:
1. Basal lamina: result from lamina molecules with type IV collagen, entactin and proteoglycans
2. Reticular lamina: formed by collagen fibers

Basal and reticular lamina → can be distinguished by electron microscopy

Basement membrane → can be recognized by the Periodic Acid-Schiff (PAS) stain → light microscopy
Figure 1.7 PAS-positive basement membrane.
GLANDULAR EPITHELIA

• Tissue formed by cells specialized to produce secretion
• Molecules → secrete → secretory granules
• Synthesize, store, secrete: protein (pancreas), lipid (adrenal, sebaceous gland), carbohydrate + protein (salivary gland)
  Secrete all substance: mammary glands

Type of Glandular Epithelia:
• Unicellular glands: consists of isolated glandular cells → goblet cells
• Multicellular glands: composed of cluster of cells

Glands → covering epithelia → proliferation and invasion → further differentiation.
Proliferation of cells and their downgrowth into the subjacent connective tissue.

Exocrine gland formation

Cords of cells forming endocrine gland

Follicular endocrine gland formation

Epithelium
Basal lamina
Connective tissue

Duct

Disappearance of duct cells

Capillaries

Secretory portion

Secretory portion
Principal types of exocrine glands. The part of the gland formed by secretory cells is shown in black; the remainder shows the ducts. The compound glands have branching ducts.
ENDOCRINE

- Lack an excretory duct
- Their product released into the blood circulation
- Surrounded by fenestrated capillaries
- Synthesize and release after stimulation by chemical or electrical signals

Types of endocrine glands:
- The agglomerated cells → form anastomosis cords interspersed between dilated blood capillaries (adrenal gland, parathyroid, anterior lobe of pituitary)
- The cell line a vesicle or follicle filled with noncellular material (thyroid gland)
EXOCRINE

Connected to the surface of the epithelium by an excretory duct

• A secretory portion:
  – Contains the cells responsible for the secretory process
  – One cell type (unicellular) → goblet cell
  – Many cells (multicellular)
  – Shape: tubular (large intestine), coiled (sweat glands of the skin), alveolar (sebaceous gland)
  – Classified:
    • Simple gland: have only one unbranched duct
    • Compound gland: have ducts that branch repeatedly

• Excretory duct:
  – Transport the secretion to the exterior of the gland
LIVER

- One cell type may function both ways: endocrine + exocrine
- Cells that secrete bile into the duct system and also secrete some of their products into the bloodstream

PANCREAS

- Endocrine secretion: the islet cells secrete insulin and glucagon into the bloodstream
- Exocrine secretion: the acinar cells secrete digestive enzymes into the intestinal lumen
Types of secretion:

- Mucous glands: glycoprotein + water
- Serous glands: protein + water
- Mixed glands: mucous + serous cells

Mechanism of secretion:

- Merocrine: the secretory granul leave the cell by exocytosis with no loss of other cellular material → skin
- Apocrine: the secretory products is discharge together with parts of the apical cytoplasm → axilla
- Holocrine: the secretory product constitute the entire cell and its product → sebaceous gland
CONNECTIVE TISSUE

Provides the supportive ang connecting framework (or stroma) for all the other tissues of the body.

Connective tissue is formed by:
1. Cells
2. Extracellular matrix (ECM): fiber and ground substance
<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Representative Product or Activity</th>
<th>Representative Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroblast, chondroblast, osteoblast</td>
<td>Production of fibers and ground substance</td>
<td>Structural</td>
</tr>
<tr>
<td>Plasma cell</td>
<td>Production of antibodies</td>
<td>Immunological (defense)</td>
</tr>
<tr>
<td>Lymphocyte (several types)</td>
<td>Production of immunocompetent cells</td>
<td>Immunological (defense)</td>
</tr>
<tr>
<td>Eosinophilic leukocyte</td>
<td>Participation in allergic and vasoactive reactions, modulation of mast cell activities and the inflammatory process</td>
<td>Immunological (defense)</td>
</tr>
<tr>
<td>Neutrophilic leukocyte</td>
<td>Phagocytosis of foreign substances, bacteria</td>
<td>Defense</td>
</tr>
<tr>
<td>Macrophage</td>
<td>Secretion of cytokines and other molecules, phagocytosis of foreign substances and bacteria, antigen processing and presentation to other cells</td>
<td>Defense</td>
</tr>
<tr>
<td>Mast cell and basophilic leukocyte</td>
<td>Liberation of pharmacologically active molecules (e.g., histamine)</td>
<td>Defense (participate in allergic reactions)</td>
</tr>
<tr>
<td>Adipose (fat) cell</td>
<td>Storage of neutral fats</td>
<td>Energy reservoir, heat production</td>
</tr>
</tbody>
</table>
CELLS

1. **FIBROBLAST**
   - Synthesize collagen, elastin to form collagen, reticular, and elastic fiber; and glycosaminoglikans, proteoglycans and multiadhesive glycoproteins of the ECM
   - The most common cells in connective tissue
   - Responsible for the synthesize of ECM
   - 2 stages of activity:
     - active (fibroblast): abundant and irregularly cytoplasm, nucleus is ovoid and large, pale staining
     - quiscent (fibrocyte): smaller than fibroblast, spindle-shaped
Quiescent fibroblasts are elongated cells with thin cytoplasmic extensions and condensed chromatin. Parosaniline–toluidine blue stain. Medium magnification.
2. MACROPHAGE

– When trypan blue or India ink is injected into an animal, macrophage engulf and accumulate the dye in their cytoplasm in the form of granules or vacuoles visible in the light microscope.

– Have phagocytic properties and derive from monocytes, cells formed in the bone marrow.

– Macrophage in the liver: Kupffer cells, in bone: Osteoclast, in the central nervous system: microglial cells.

– Constitute the mononuclear phagocyte system.
Section of lymph node showing blood cells (*) and macrophages. Note the cytoplasm of one of the macrophages (arrow). High magnification. (Courtesy of TMT Zorn.)
Figure 5—6. Section of pancreas from a rat injected with the vital dye trypan blue. Note that 3 macrophages (arrows) have engulfed and accumulated the dye in the form of granules. H&E stain. Low magnification.
<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Location</th>
<th>Main Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocyte</td>
<td>Blood</td>
<td>Precursor of macrophages</td>
</tr>
<tr>
<td>Macrophage</td>
<td>Connective tissue, lymphoid organs, lungs, bone marrow</td>
<td>Production of cytokines, chemotactic factors, and several other molecules that participate in inflammation (defense), antigen processing and presentation</td>
</tr>
<tr>
<td>Kupffer cell</td>
<td>Liver</td>
<td>Same as macrophages</td>
</tr>
<tr>
<td>Microglia cell</td>
<td>Nerve tissue of the central nervous system</td>
<td>Same as macrophages</td>
</tr>
<tr>
<td>Langerhans cell</td>
<td>Skin</td>
<td>Antigen processing and presentation</td>
</tr>
<tr>
<td>Dendritic cell</td>
<td>Lymph nodes</td>
<td>Antigen processing and presentation</td>
</tr>
<tr>
<td>Osteoclast</td>
<td>Bone (fusion of several macrophages)</td>
<td>Digestion of bone</td>
</tr>
<tr>
<td>Multinuclear giant cell</td>
<td>Connective tissue (fusion of several macrophages)</td>
<td>Segregation and digestion of foreign bodies</td>
</tr>
</tbody>
</table>
3. MAST CELLS
   - oval to round connective tissue, basophilic secretory granules, spherical nucleus is centrally
   - principal function: storage of chemical mediators of the inflammatory response
   - pre formed mediator such as histamine and proteoglycans
   - 2 populations of mast cells:
     ▪ connective tissue mast cell → skin
     ▪ mucosal mast cell → intestinal mucosa

4. PLASMA CELLS
   - large, ovoid, basophilic cytoplasm due to their richness in RER, nucleus spherical and eccentrically placed.
Figure 4.5 Elastin fibres Spread preparation, elastin/H [amp ] E ×320; Cap capillary E elastin fibre F fibroblast L collagen fibres in longitudinal section M microfibrils in transverse section Ma mast cells ML microfibrils in longitudinal section T collagen fibres in transverse section
Section of rat tongue. Several mast cells in the connective tissue surround muscle cells and blood vessels. PT stain. Medium mag.
Plasma cells

Villar epithelium
5. ADIPOSE CELL

- colour: white to dark yellow, polyhedral, eccentric and flattened nuclei

Figure 6—1. Photomicrograph of unilocular adipose tissue of a young mammal. Arrows show nuclei of adipocytes (fat cells) compressed against the cell membrane. Note that, although most cells are unilocular, there are several cells (asterisks) with small lipid droplets in their cytoplasm, an indication that their differentiation is not yet complete. Pararosaniline—toluidine blue (PT) stain. Medium magnification.

Figure 6—5. Photomicrograph of multilocular adipose tissue (lower portion) with its characteristic cells containing central spherical nuclei and multiple lipid droplets. For comparison, the upper part of the photomicrograph shows unilocular tissue. PT stain. Medium magnification.
6. LEUCOCYTE
– migrate through the walls of capillaries and post capillary venules from the blood to connective tissue by a process called diapedesis
– this process increases greatly during inflammation

FIBERS

2 system of fibers:
1. Collagen system: collagen, reticular fibers
2. Elastic system: oxytalan, elaunin, elastic fibers
1. COLLAGEN FIBERS
   – a famili of proteins
   – the most abundant protein in the human body
   – classified in the following groups:
     1. form long fibril: type I, II, III, V, XI
        collagen type I → collagen fibers
     2. fibril associated collagens: type IX, XII, XIV
     3. form networks: type IV
     4. form anchoring fibrils: type VII
   – fresh collagen are colorless strands, in great numbers (eg. tendons) are white
   – in the light microscope: collagen fibers are acidophilic, they stain pink with eosin, blue with Mallory’s trichrome stain, green with Masson’s trichrome stain, red with sinus red
2. **RETICULAR FIBERS**

- consist mainly of collagen type III
- thin, not visible in HE preparations
- stain black by impregnation with silver salts, are called argyrophilic
- abundant in smooth muscle, endoneurium, hematopoietic organs

![Figure 5—48. Reticular connective tissue showing only the attached cells and the fibers (free cells are not represented). Reticular fibers are enveloped by the cytoplasm of reticular cells; the fibers, however, are extracellular, being separated from the cytoplasm by the cell membrane. Within the sinuslike spaces, cells and tissue fluids of the organ are freely mobile.](image-url)
Figure 4.3 Reticulin fibres Silver impregnation method/neutral red ×800
3. **ELASTIC FIBER SYSTEM**

The structure develop through 3 stages:

1. oxytalan → not elastic
2. elaunin
3. elastic fibers:
   a. the most numerous component
   b. rich in protein elastin, stretch easily
   c. contain desmosin and isodesmosine

**GROUND SUBSTANCE**

- Colorless and transparent
- Formed of:
  - glycosaminoglycans
  - proteoglycans
  - multiadhesive glycoproteins
Connective Tissue

Connective tissue proper
- Loose
- Dense
- Regular
- Irregular

Connective tissue with special properties
- Adipose tissue (Chapter 6)
- Elastic tissue
- Hematopoietic (lymphatic and myeloid) (Chapter 13)
- Mucous tissue

Supporting connective tissues
- Cartilage (Chapter 7)
- Bone (Chapter 8)
LOOSE CONNECTIVE TISSUE

- Found in the papillary layer of dermis, hypodermis, in the serosal linings of peritoneal and pleural cavities
- Comprise all the main components
- **Cells > fibers**
- The most numerous cells: fibroblast, macrophage
- Collagen, elastic, reticular fibers → moderate
- Flexible, well vascularized, not very resistant to stress
Figure 5—41. Section of rat skin in the process of repair of a lesion. The subepithelial connective tissue (dermis) is loose connective tissue formed soon after the lesion occurs. In this area, the cells, most of which are fibroblasts, are abundant. The deepest part of the dermis consists of dense irregular connective tissue, which contains many randomly oriented thick collagen fibers, scarce ground substance, and few cells. H&E stain. Medium magnification.
DENSE IRREGULAR CONNECTIVE TISSUE

- Less flexible and more resistant to stress than connective tissue
- Collagen fibers are arranged in bundles without a definite orientation, such areas as the dermis
- Fibers > cells

DENSE REGULAR CONNECTIVE TISSUE

- Collagen bundle are arranged according to a definite pattern
- Great resistance to traction forces, ex.tendons
- Fibers > cells
Figure 5—41. Section of rat skin in the process of repair of a lesion. The subepithelial connective tissue (dermis) is loose connective tissue formed soon after the lesion occurs. In this area, the cells, most of which are fibroblasts, are abundant. The deepest part of the dermis consists of dense irregular connective tissue, which contains many randomly oriented thick collagen fibers, scarce ground substance, and few cells. H&E stain. Medium magnification.
Figure 5—46. Longitudinal section of dense regular connective tissue from a tendon. A: Thick bundles of parallel collagen fibers fill the intercellular spaces between fibroblasts. Low magnification. B: Higher magnification view of a tendon of a young animal. Note active fibroblasts with prominent Golgi regions and dark cytoplasm rich in RNA. PT stain.
DENSE REGULAR CONNECTIVE TISSUE

Muscle-Tendon Junction van Gieson

- Collagen fibres
- Fibrocyte nuclei
- Skeletal muscle fibres
THANK YOU....