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Epithelia and Glands

I. EPITHELIA

A. Structure. Epithelia are specialized layers that line the internal and cover the external surfaces of the body. An epithelium consists of a sheet of cells lying close together with little intercellular space. These cells have distinct biochemical, functional, and structural domains that confer polarity, to epithelia.

1. The basement membrane separates the epithelium from underlying connective tissue and blood vessels.

2. Epithelia are avascular and receive nourishment by diffusion of molecules through the basal lamina.

B. Classification. Epithelia are classified into various types on the basis of the **number of cell layers** (one cell layer is **simple**; more than one is **stratified**) and **the shape of the superficial cells**. Pseudostratified epithelia appear to have multiple cell layers, but all cells are in contact with the basal lamina(basement membrane).

C. Function

1. Transcellular transport of molecules from one epithelial surface to another occurs by various processes, including the following:

a. Diffusion of oxygen and carbon dioxide across the epithelial cells of lung alveoli and capillaries

b. Carrier protein–mediated transport **of amino acids and glucose across intestinal epithelia**

c. Vesicle-mediated transport **of immunoglobulin A** (IgA) and other molecules

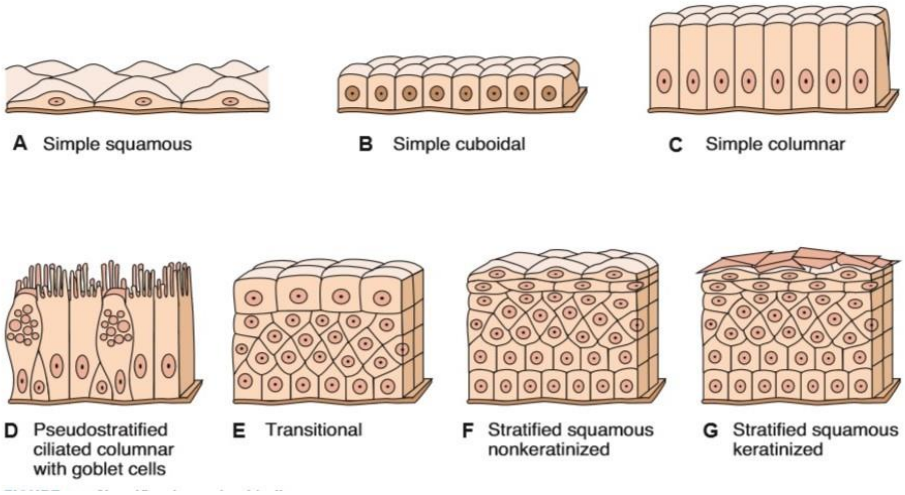
2. Absorption occurs via **endocytosis or pinocytosis** in various organs (e.g., the proximal convoluted tubule of the kidney).

3. Secretion of various molecules (e.g., hormones, mucus, proteins) occurs by **exocytosis**.

4. Selective permeability results from the presence of tight junctions between epithelial cells and permits fluids with different compositions and concentrations to exist on separate sides of an epithelial layer (e.g., intestinal epithelium).

5. Protection from abrasion and injury is provided by the epidermis, the epithelial layer of the skin.

Type	Shape of Superficial Cell Layer	Typical Locations
One cell layer		
Simple squamous	Flattened	Endothelium (lining of blood vessels), mesothelium (lining of peritoneum and pleura)
Simple cuboidal	Cuboidal	Lining of distal tubule in kidney and ducts in some glands, surface of ovary
Simple columnar	Columnar	Lining of intestine, stomach, and excretory ducts in some glands
Pseudostratified	All cells rest on basal lamina, but not all reach the lumen; thus, the epithelium appears falsely stratified	Lining of trachea, primary bronchi, nasal cavity, and excretory ducts in parotid gland
More than one cell layer		
Stratified squamous (nonkeratinized)	Flattened (nucleated)	Lining of esophagus, vagina, mouth, and true vocal cords
Stratified squamous (keratinized)	Flattened (without nuclei)	Epidermis of skin
Stratified cuboidal	Cuboidal	Lining of ducts in sweat glands
Stratified columnar	Columnar	Lining of large excretory ducts in some glands and cavernous urethra
Transitional	Dome-shaped (when relaxed), flattened (when stretched)	Lining of urinary passages from renal calyces to the urethra



II. LATERAL EPITHELIAL SURFACES

These surfaces contain specialized junctions that provide adhesion between cells and restrict movement of materials into and out of lumina.

A. The junctional complex is an intricate arrangement of membrane-associated structures that functions in cell-to-cell attachment of columnar epithelial cells. It corresponds to the terminal bar observed in epithelia by light microscopy and consists **of three distinct components** that are visible by **electron microscopy**.

1. The tight junction (zonula occludens) is a zone that surrounds the entire apical perimeter of adjacent cells and is formed by fusion of the outer leaflets of the cells' plasma membranes.

a. In freeze-fracture preparations of this zone, the tight junction is visible as a branching anastomosing network of intramembrane **strands** on the plasma membrane inner leaflet next to the cytoplasm and **grooves** on the corresponding external, the inner aspect of the outer. The strands consist of transmembrane proteins of each cell **attached directly to one another**, thus sealing off the intercellular space.

b. The tight junction prevents movement of substances into the intercellular space from the lumen. This ability (its tightness) is directly related to the number and complexity of the intramembrane strands.

c. The tight junction is analogous to the fascia occludens, a ribbon like area of fusion between transmembrane proteins on adjacent endothelial cells lining capillaries.

2. The intermediate junction (**belt desmosome; zonula adherens**) is the zone that surrounds the entire perimeter of epithelial cells just basal to the tight junction

a. It is characterized by a 10- to 20-nm separation between the adjacent plasma membranes, where the extracellular portions of cadherin molecules occupy the intercellular space.

b. A mat of **actin filaments** is located on each of its cytoplasmic surfaces. The actin filaments are linked, alpha actinin and vinculin to the transmembrane glycoprotein **E-cadherin.** This protein is markedly dependent on calcium ions for promoting adhesion at this structurally supportive junction.

c. It is analogous to the **fascia adherens**, a ribbon like adhesion zone in the **intercalated disks** of cardiac muscle**.**

3. A desmosome (**macula adherens**) is a small, discrete, disk-shaped adhesive site. It is also commonly found at sites other than the junctional complex, where it joins epithelial cells.

a. It is characterized by a dense plaque of intracellular attachment **proteins**, called **desmoplakins**, on the cytoplasmic surface of each opposing cell.

b. Keratin intermediate filaments in bundles (tonofilaments) loop into and out of the dense plaque from the cytoplasm.

c. Between the adjacent cells are transmembrane linker glycoproteins, called **desmogleins** and **desmocollins**, that are cadherin molecules.

B. The gap junction(communicating junction; nexus) is not part of the junctional complex and is common in certain tissues other than epithelia (e.g., central nervous system, cardiac muscle, and smooth muscle).

1. Gap junctions couple adjacent cells metabolically and electrically.

2. The gap junction is a plaquelike entity composed of an **ordered array of subunits** called **connexons**, which extend beyond the cell surface into the gap to keep the opposing plasma membranes approximately 2 nm apart.

a. Connexons consist of six cylindrical subunits (composed of proteins called **connexins**), which are arranged radially around a central channel with a diameter of 1.5 nm.

b. Precise alignmentof connexons on adjacent cells produces a junction where cell-to-cell channels permit passage of ions and small molecules with a molecular weight of less than 1,200 d (daltons).

c. Connexins may alter their conformation to shut off communication between cells.

C. Lateral interdigitations are irregular fingerlike projections that interlock adjacent epithelial cells.

III. BASAL EPITHELIAL SURFACES.

A. The basal lamina is an extracellular supportive structure 20 to 100 nm thick that is visible only by electron microscopy. It is produced by the epithelium resting upon it and is composed mainly of **type IV collagen**, **laminin**, **entactin**, and **proteoglycans** (rich in heparan sulfate).

1. It consists of two zones: **the lamina lucida** (or lamina rara), which lies next to the plasma membrane, and **the lamina densa**, a denser meshwork of type IV collagen, glycoproteins, and glycosaminoglycans, which lies adjacent to the reticular lamina of the deeper connective tissue.

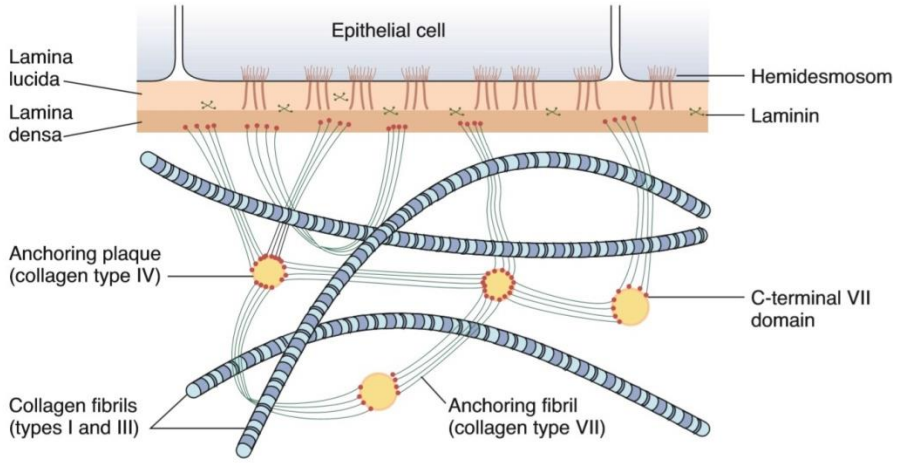
2. The basal lamina plus the underlying **reticular lamina** constitute the **basement membrane**, which is observable by light microscopy.

B. Hemidesmosomes are specialized junctions that resemble half of a desmosome. They mediate **adhesion** of epithelial cells to the underlying extracellular matrix.

1. These junctions are present on the basal surface of **basal cells** in certain epithelia (e.g., tracheal epithelium and stratified squamous epithelium) and on myoepithelial cells, where they lie adjacent to the basal lamina.

2. They consist of a **dense cytoplasmic plaque**, which is linked via transmembrane receptor proteins (**integrins**) to laminins in the basal lamina. Anchoring filaments (type VII collagen) from the basal lamina extend deeper into the underlying connective tissue and insert into plaques of type IV collagen.

3. Keratin filaments (tonofilaments) in the cell terminate in the hemidesmosome plaque, allowing these junctions to **link** the cytoskeleton with the extracellular matrix.



C. Basal plasma membrane infoldings are common **in ion-transporting epithelia** (e.g., distal convoluted tubule of the kidney, striated ducts in salivary glands).

1. They form deep invaginations that compartmentalize mitochondria.

2. Function. They increase the surface area and bring ion pumps (Na–K adenosine triphosphatase ATPase) in the plasma membrane close to their energy supply (ATP produced in mitochondria).

IV. APICAL EPITHELIAL SURFACES

These surfaces may possess specialized structures such as **microvilli**, **stereocilia**, and **cilia**.

A. **Microvilli** are fingerlike projections of epithelia approximately 1µm long that extend into a lumen and increase the cell's surface area.

1. A glycocalyx (sugar coat) is present on their apical.

2. A bundle of approximately 30 actin filaments runs longitudinally through the core of each microvillus and extends into the terminal web, a zone of intersecting filaments in the apical cytoplasm.

3. Microvilli constitute the brush border of kidney proximal tubule cells and the striated border of intestinal absorptive cells.

B. **Stereocilia** are very long microvilli (not cilia) in the epididymis and vas deferens of the male reproductive tract.

C. Cilia are actively motile processes 5 to 10 µm long extending from certain epithelia (e.g., tracheobronchial and oviduct epithelium) that propel substances along their surfaces. They contain a core of longitudinally arranged microtubules (the axoneme), which arises from a basal body during ciliogenesis.

1. The axoneme consists of nine doublet microtubules uniformly spaced around two central microtubules, as well as the following components:

a. Ciliary dynein arms, which extend unidirectionally from one member of each doublet microtubule and interact with adjacent doublets, so that they slide past one another. These arms consist of ciliary dynein, with a head that is an ATPase that splits ATP to liberate the energy necessary for active movement of a cilium.

b. Radial spokes that extend from each of the nine outer doublets toward the central sheath.

c. Central sheath, which surrounds the two central microtubules; it and the radial spokes regulate the ciliary beat.

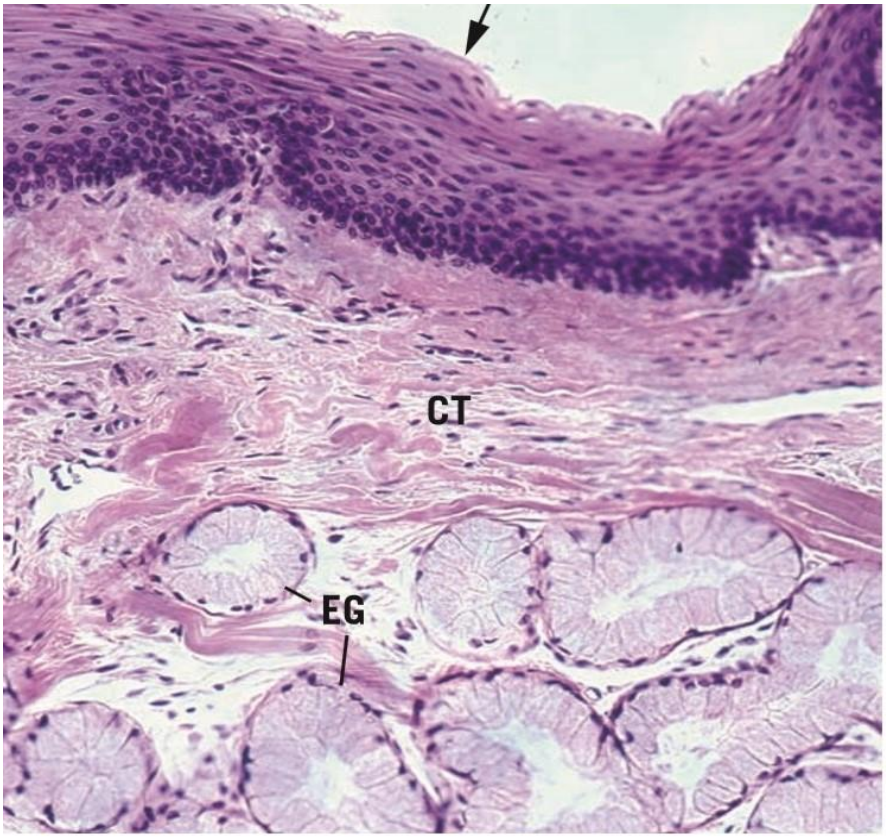
d. Nexin, an elastic protein that connects adjacent doublet microtubules and helps maintain the shape of the cilium.

2. The basal body is a cylindrical structure at the base of each cilium that consists of nine triplet microtubules arranged radially in the shape of a pinwheel . It resembles a centriole but has a less complex central organization. The inner two triplets of the basal body give rise to the doublet microtubules of the cilium axoneme.

V. GLANDS

They originate from an epithelium that penetrates the connective tissue and forms **secretory units**.

A. **Structure**. A gland consists of a functional portion (**parenchyma**) of secretory and ductal epithelial cells, which is separated by a basal lamina from supporting connective tissue elements (**stroma**).



B. Classification.

Glands are classified into three types on the basis of the site of secretion. **Exocrine glands secrete** into a duct or onto a surface. **Endocrine glands secrete** into the bloodstream. **Paracrine glands secrete** into the local extracellular space.

1. Exocrine glands

a. Unicellular glands are composed of a single cell (e.g., goblet cells in tracheal epithelium).

b. Multicellular glands: Classification

Classification is based on two criteria:

i- Multicellular glands are classified according to duct branching as simple glands (duct does not branch) or compound glands (duct branches)

ii- They are further classified according to the shape of the secretory unit as **acinar** or **alveolar** (saclike or flasklike) or **tubular** (straight, coiled, or branched).

A connective tissue capsule may surround the gland, or septa of connective tissue may divide the gland into lobes and smaller lobules.

Glands may have ducts between lobes (**interlobar**), within lobes (**intralobar**), between lobules (**interlobular**), or within lobules (**intralobular**), such as striated and intercalated ducts.

Multicellular glands secrete various substances.

(a) Mucus is a viscous material that usually protects or lubricates cell surfaces.

(b) Serous secretions are watery and often rich in enzymes.

(c) Mixed secretions contain both mucous and serous components.

Mechanisms of secretion vary.

(a) In **merocrine** glands (e.g., parotid gland), the secretory cells release their contents by **exocytosis.**

(b) In **apocrine** glands (e.g., lactating mammary gland), part of the apical cytoplasm of the secretory cell is released along with the contents.

(c) In **holocrine** glands (e.g., sebaceous gland), the entire secretory cell along with its contents is released.

2. Endocrine glands

may be **unicellular** (e.g., individual endocrine cells in gastrointestinal and respiratory epithelia) **or multicellular** (e.g., adrenal gland), and they lack a duct system. In multicellular glands, secretory material is released into **fenestrated capillaries**, which are abundant just outside the basal lamina of the glandular epithelium.

CLINICAL CONSIDERATIONS

A- Epithelia sometimes undergo **metaplasiain** response to persistent injury.

Metaplasia is the conversion of one type of differentiated epithelium into another. Most commonly a glandular epithelium is transformed into a squamous epithelium. However, in cases of chronic acid reflux from the stomach into the lower esophagus, the stratified squamous nonkeratinized epithelium is replaced by a glandular mucus-secreting epithelium (**Barrett epithelium**) similar to that found lining the cardia of

the stomach. This helps protect the esophagus against the injurious effects of the acid and pepsin, but is also a well-known precursor of esophageal adenocarcinoma.

B. Epithelial cell tumors occur when cells fail to respond to normal growth regulatory mechanisms.

1. These tumors are **benign** when they remain local.
2. They are malignant when they invade neighboring tissues. Then, they may (or may not) metastasize to other parts of the body.
    a. Carcinomas are malignant tumors that arise from surface epithelia.
    b. Adenocarcinomas are malignant tumors that arise from glands.