Histology –An Introduction

Histology:

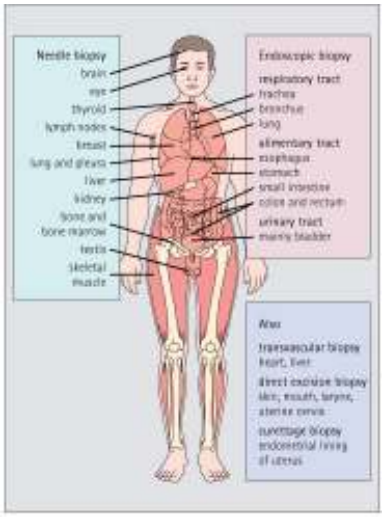
The study of the microscopic structure of biological material and the ways in which individual components are structurally and functionally related.

Critical to biological and medical science:

Bridge between biochemistry, molecular biology, physiology, disease processes and the effects of diseases.

Knowledge of normal histologic appearances is essential if abnormal diseased structures are to be recognized.

Histology at work:
Diagnostic Histology: Biopsies



Virchow's cellular theory: cell as the basic building block of most biological material.

Cell: an individual unit surrounded by a wall called cell membrane
Cell content: inside the cell membrane; the machinery of cell functions.

Tissues: collections of cells with similar morphological characteristics:

Original 4 types of tissues:

Epithelial tissues – surface coverage
Muscular tissues – contractile property
Nervous tissues – cells forming brain, spinal cord, and nerves
Connective tissues – to link or support other specialized tissues

Cells: basic functional units:

Functional classification of cells: cells of diverse morphologic appearance may be grouped together due to common functional attributes.

Cells are also adaptable.

Functional classification of cells:

Cell group	Epithelial cells	Support cells	Contractile cells	Nerve cells	Germ cells	Blood cells	Immune cells	Hormone-secreting cells
Example	gut and blood vessel lining, covering skin	fibrous support tissue, cartilage, bone	muscle	brain	spermatozoa	circulating red and white blood cells	lymphoid tissues and white cells (nodes and spleen)	thyroid and adrenal
Function	barrier, absorption, secretion	organize and maintain body structure	movement	direct cell communication	reproduction	oxygen transport, defence	defence	indirect cell communication
Special features	tightly bound together by cell junctions (see Chapter 3)	produce and interact with extracellular matrix material (see Chapter 4)	filamentous proteins cause contraction (see Chapter 5)	release chemical messengers on to surface of other cells (see Chapter 6)	half normal chromosome complement (see Chapters 16 and 17)	proteins bind oxygen, proteins destroy bacteria (see Chapter 7)	recognize and destroy foreign material (see Chapter 8)	secrete chemical messengers (see Chapter 14)

Tissue: an assembly of cells arranged in a specific organized fashion.

Simple tissue: cells forming the tissue are of the same structure.

e.g.: adipose tissue.

Compound tissue: containing a mixture of cells with different functions.

e.g.: nervous tissue – contains neurons, astrocytes, microglia, and ependymal cells.

Connective tissue: dominant extracellular matrix.

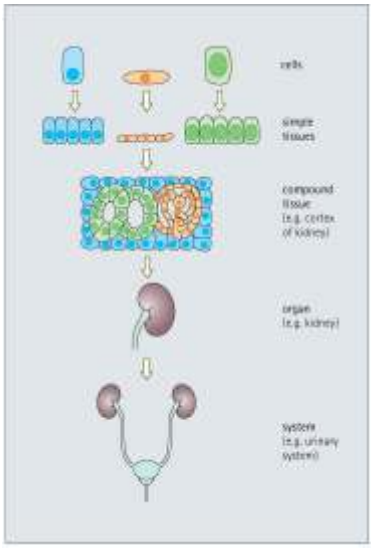
Tissue: forming organs and systems

System:

Cells of similar function but widely distributed in several anatomical sites; or

A group of organs having similar or related functional roles.

e.g.: the endocrine system in the GI tract and lung; GI system.



Cells, tissues, organs, and systems

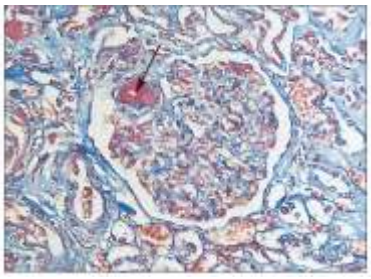
Histology and Pathology:

Histology: observe the conditions of cells and tissues under disease-free condition.

Pathology: observe the changes of cells and tissues by the disease processes.

e.g.: needle biopsy of a 20 y/o renal failure patient whose blood and radiology tests show negative findings.

The biopsy was stained with specialized dyes (MSB stain) to demonstrate the destruction of afferent arteriole of glomerulus by fibrinoid necrosis (arrow).

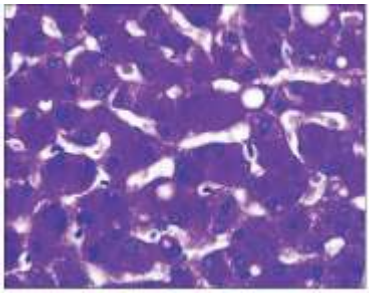


Tools of histology:

Tissue staining and Microscopes:

Tissue staining:

Emperical; e.g.: Trichrome method and van Gieson's method.
Histochemical; e.g.: periodic acid Schiff (PAS) stain.
Enzyme histochemical; e.g.: alkaline phosphatases
Immunohistochemical: detecting specific biomolecules with antibodies.



e.g.: PAS stain of glycogen in the liver paraffin section

Commonly Used Histological Stains:

Hematoxylin and Eosin (H&E): Nuclei: purple/black; cytoplasm: pink/red.

Van Gieson Method: Collagen: pinkish-red; muscle: yellow.

Trichrome Method: three color system to emphasize support fibers.

Silver Method: chemical reduction (black/dark deposit)

Periodic acid Schiff (PAS) Method: carbohydrates stained magenta.

Alcian blue Method: demonstrate acid mucin secretion.

May-Grünwald-Giemsa Method: blood and bone-marrow smear cells.

Myelin Methods: demonstrate normal myelin.

Tools of Histology (Cont.)

Microscopes:

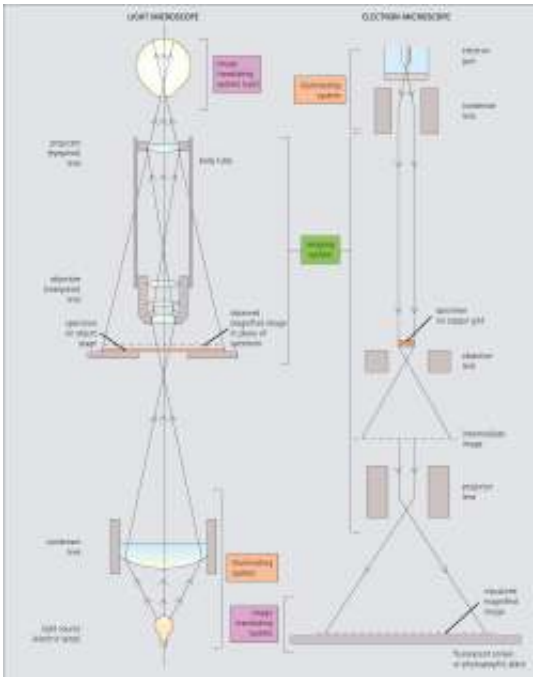
Light microscopes (LM): paraffin and thick plastic sections.

Electron microscopes: Transmission electron microscope (TEM): thin plastic sections.

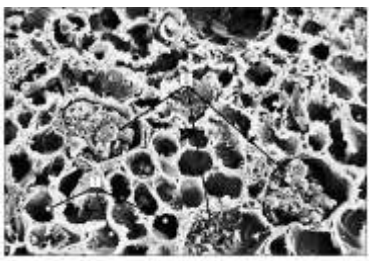
Scanning electron microscope (SEM): surface scanning using electron beams.

Resolution:

LM: no better than 0.6 µm
EM: subcellular structures.



SEM of the structure of kidney cortex at a sectional surface



Epithelial Cells

Epithelial cells:

A component of many organs specialized for absorption, secretion, and/or to act as a barrier.

They may cover or form a lining for body surfaces.

May form functional secretory glands.

Firmly joined together by adhesion specialization:

- To anchor the cytoskeleton of the neighboring epithelial cells together,
- To anchor the epithelial cells to the underlying/surrounding extracellular matrices.

Modified/specialized on the surface to fulfill their specific roles.

Classification of Epithelial cells: by their shape and their stacking pattern

By shape (morphology):

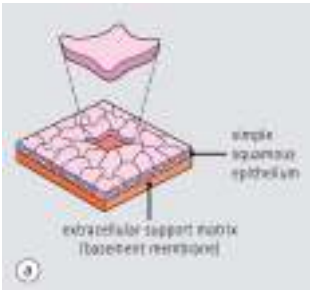
- Squamous (flat, plate-like)
- Cuboidal (height and width similar)
- Columnar (height = 2x – 5x greater than width)

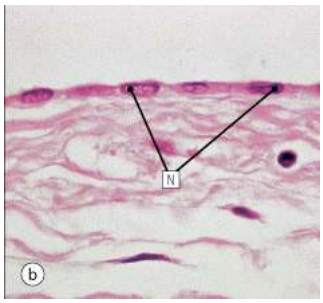
By stacking:

- Simple: forming a single layer, all the cells contact the underlying extracellular matrix.
- Stratified: multiple layer of cell stacking, where only the bottom layer is in contact with the extracellular matrix.
- Pseudostratified: cells appear arranged in layers, but all in contact with the extracellular matrix.
- Transitional: specialized epithelium only in the urinary tract, varies between cuboidal and squamous, depending on the degree of stretching.

Simple squamous epithelium:

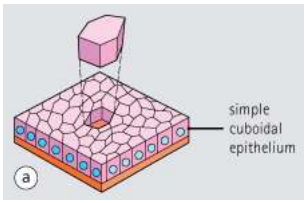
Consisted of a single layer of cells that are flat and plate like.
Many having such characteristics have specialized name, such as endothelium.

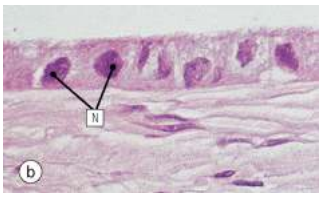




Simple cuboidal epithelium:

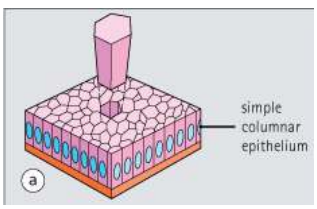
A single layer of cells whose height, width, and depth are almost the same.

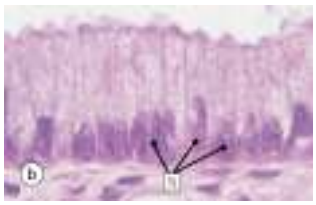




Simple columnar epithelium:

A single layer of cells whose height is two to five times greater than its width.

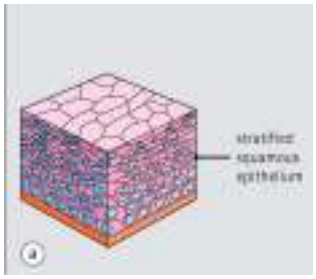


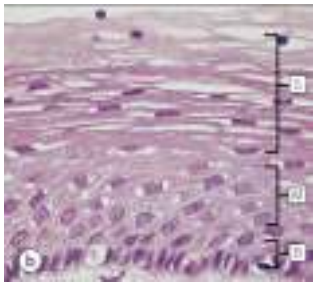


Stratified squamous epithelium:

Multiple layers of stacked cells.

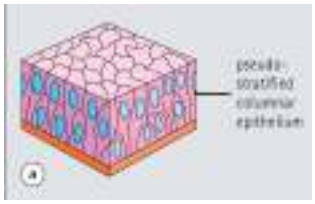
Upper layer: squamous (flattened) shape.
Middle and basal (bottom) layer: pyramidal or polygonal shape.

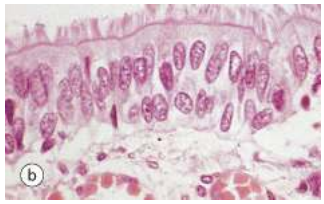




Pseudostratified columnar epithelium:

Multiple layers of nuclei, suggesting multiple layer of cells
But all the cells are in contact with the underlying extracellular matrix (basal membrane).





Epithelial Cell Junctions:

Junction: specialized structures in the epithelia that link (adhere) individual cells together to form a functional unit.

Two main systems involved in the cell adhesion:

Cell membrane proteins function as specialized cell adhesion molecules.
Specialized areas of cell membrane incorporated into cell junctions.

Three types of cell junctions:

Occluding junctions: Link cells to form impermeable barrier.
Anchoring junctions: Link cells to provide mechanical strength.
Communicating junctions: Allow movement of molecules between cells.

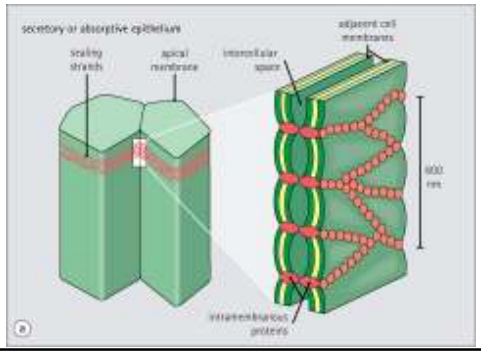
Occluding junctions: Bind cells together and maintain the integrity of epithelial cells as a barrier.

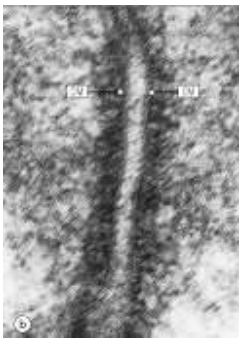
Function: Prevention of diffusion of molecules between adjacent cells.
Prevention of lateral migration of specialized cell membrane proteins.
Delineating and maintaining specialized cell membrane domains.

Also known as tight junction ultrastructurally.

Well developed in the intestinal epithelia:

Prevent digested macromolecules from passing between the cells.
Confine specialized area of cell membrane involved in absorption or secretion to the luminal side of the cell.

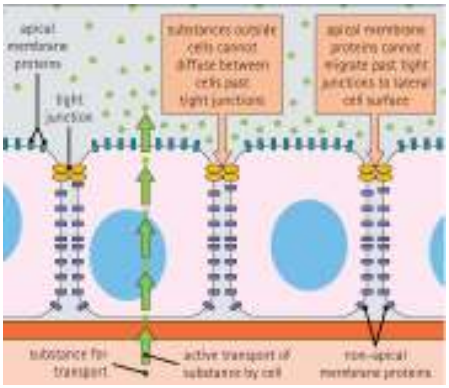




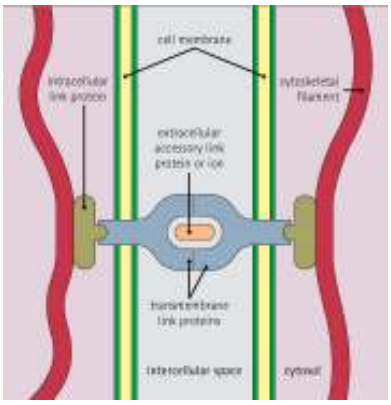
Occluding Junction: Also found in cells actively transport substances.

Prevent the back-diffusion of the transported substance.

Occludin and claudin are involved in the formation of occluding junctions.



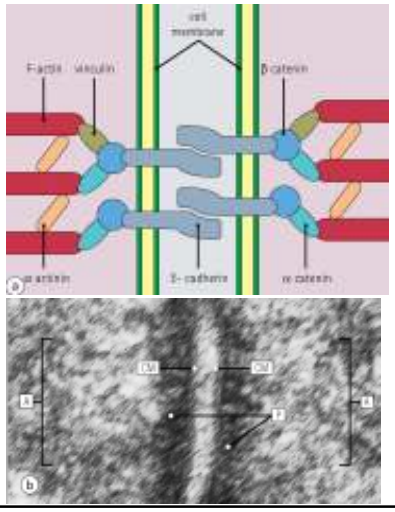
Anchoring Junction:
Provide mechanical stability to groups of epithelial cells.
Extracellular interaction may be mediated by additional extracellular proteins or ions (such as cadherins).



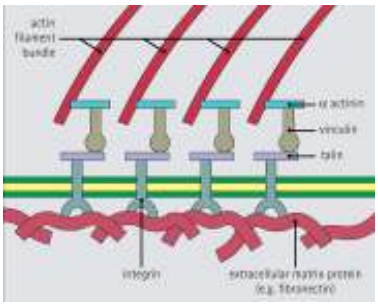
Actin network interact with two types of junctions:

Adherent junctions link the actin filament network between adjacent cells.
Focal contacts link the actin filament network of a cells to the extracellular matrix.

Adherent Junction:



Focal Contact:



Adherent Junctions:

Most common toward the apex of adjacent columnar and cuboidal epithelial cells.

Forms adhesion belt by linking the submembranous actin bundles.

Prominent in the cells lining the small intestine, forming an eosinophilic band (terminal bar).

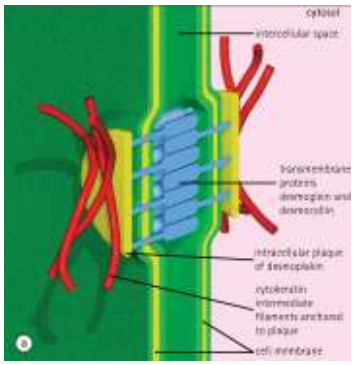
Transmit motile forces generated by the acting filaments across the whole sheets of cells.

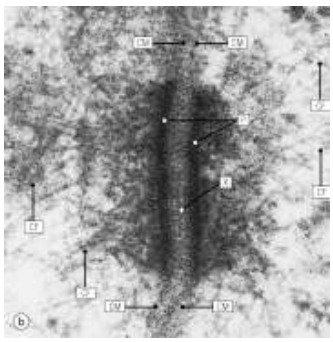
Essential in mediating folding of epithelial sheet to form early organs in the embryo.

Intermediate filament network interact with two different types of junctions:

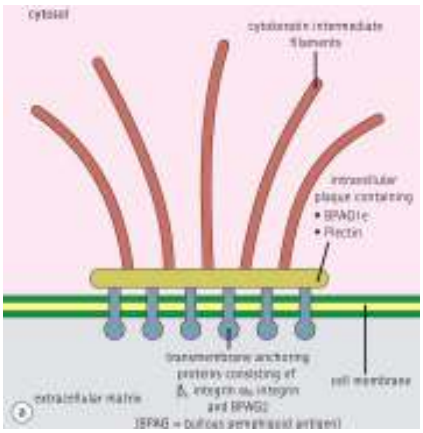
Desmosomes that connect the intermediate filament networks of adjacent cells.
Hemidesmosomes connect the intermediate filament network of cells to extracellular matrix.

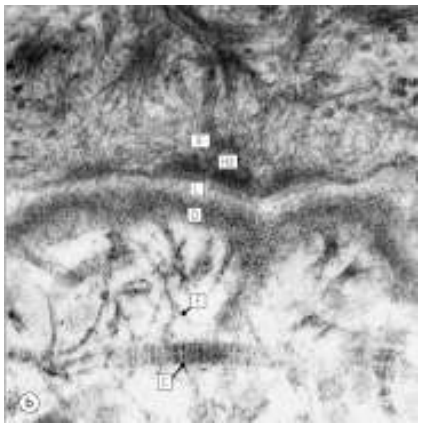
Desmosome:





Hemidesmosome:





Desmosomes:

Very good characteristics of epithelial cells.

Provide mechanical stability in epithelial cells subject to tensile and shearing stresses.

Well developed in stratified squamous epithelium covering the skin.

A biomarker in differentiating the origin of the invasion in the malignant tumors of uncertain nature.

Junctional Complex:

The close association of several types of junction between adjacent epithelial cells.

A manifestation of the requirement for several types of attachment between epithelial cells to maintain structural and functional integrity.

Disease related to hemidesmosome:

Bullous pemphigoid:

Antibodies generated by the body (auto antibodies) that attack proteins called bullous pemphigoid antigens 1 and 2 (BPAG1 and BPAG 2) in hemidesmosomes, causing inflammation and separation of epithelium from the basal lamina, leading to blistering.

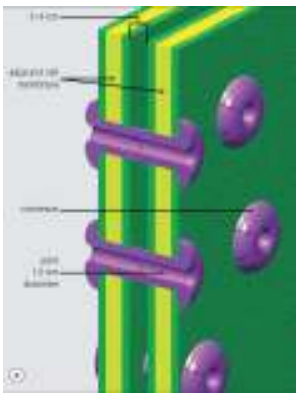
Disease related to desmosome:

Pemphigus (Pemphigus Vulgaris):

Auto antibodies attack the proteins forming desmosome junctions in the skin, also causing skin and mucous membrane blistering.

Communication Junction (Gap Junction):

Allow selective diffusion of molecules between adhacent cells and faciliate cell-cell direct communication.
Found mostly in embryogenesis.
In cardiac and smooth muscle: signal passage between cells.
In some cerebellar synapses: direct synapses.

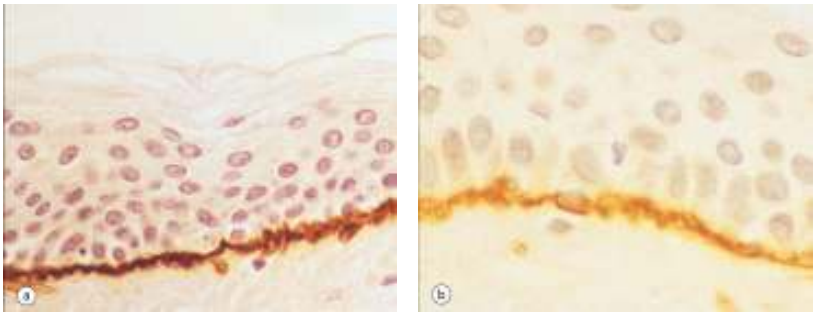


Basement Membrane:

Anchors epithelial cells to the underlying tissues.

Contains Type IV collagen synthesized by the epithelial cells.

Appears as a linear structure at the base of epithelia, can be stained with PAS stain.



Epithelial Cell Surface Specialization:

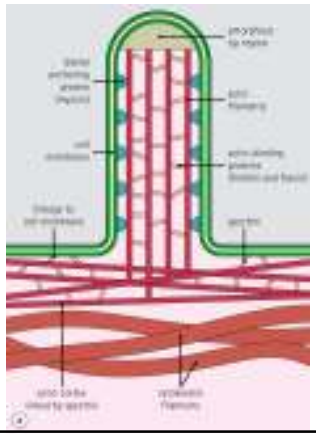
Developed to fulfill specialized functions:

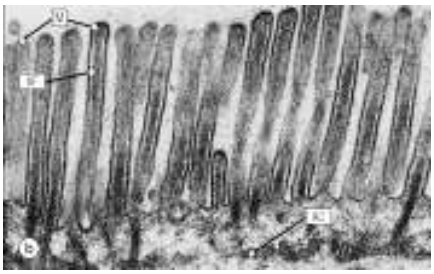
•Increase of surface area by microvilli, basolateral folds, and membrane plaques.

•To move substance over the surface by motile cell projections called cilia.

Microvilli:

Finger-like projections of the apical cells surface.
Most developed in absorptive cells like kidney tubule cells and epithelia of small intestine.
Morphology: maintained by bundle of actin filaments that anchored to the actin cortex.
Surface of microvilli: specific cell surface glycoprotein and enzymes related to absorption process.





Basolateral Folds: increase the cell surface area:

- Prominent in cells involved in fluid or ion transport.
- Commonly associated with high concentration of mitochondria.
- Gives the "striped" appearance to the basal cytoplasm of those cells.
- Often see in renal tubular cells and ducts of secretory glands.

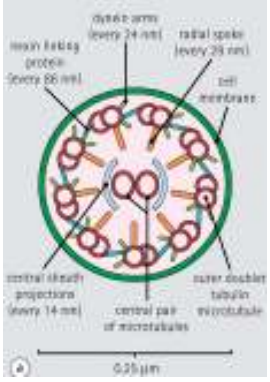
Membrane plaques:

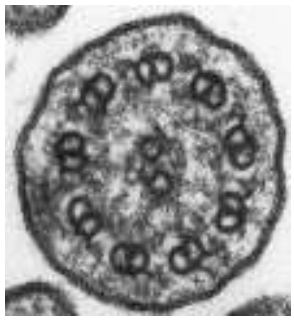
Rigid areas of the apical cells membrane found only in epithelium lining the urinary tract.

Fold down into cells when the surface tension is low, and unfold (extend) upon subjecting mechanical stretch.

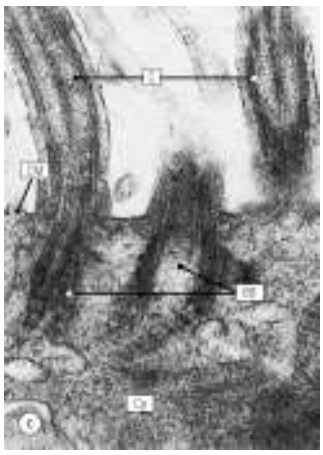
Cilia:

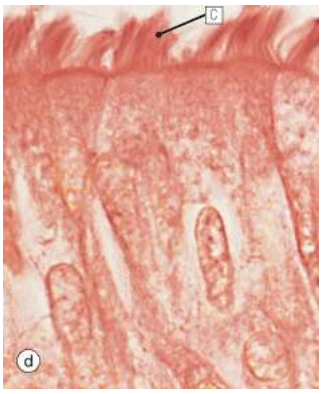
Hair-like projections, ~ 0.2 μm in diameter, arise from the surface of certain specialized cells.
Involved in moving fluid over the surface of the cell or to give cells motility.
Highly specialized extension of cytoskeleton (microtubules).
Microtubules bound with other proteins to produce energy-dependent movement, causing side-to-side beating.
Evident in respiratory tract epithelium (moving mucus), epithelium of fallopian tube (moving ova to the uterus)





Cilia in longitudinal section:

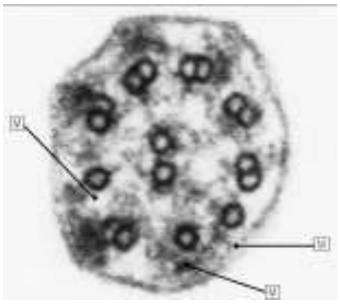




BB: basal body

Cross section of cilia from Immotile Cilia Syndrome:

Duplex structure is missing in some of the microtubule bundle.
Dynein arms are missing.



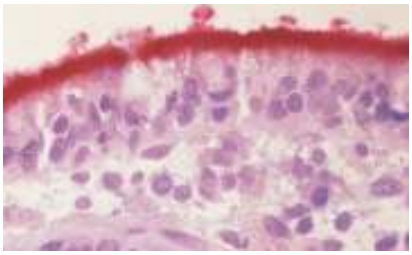
Abnormality resulted:

- During embryogenesis: cilia unable to move cell layer correctly; major organs unable to position correctly.
- Develop impaired air sinuses in the skull.
- Failure of mucus removal from the lungs/airways – causing repeated respiratory system infection.
- Infertility due to impaired ovum transport along the fallopian tube.

Cell surface proteins act as:

Enzymes
Adhesion molecules
Cell recognition molecule

Glycocalyx:
An amorphous fuzzy coating on the cell membrane surface containing sugar residues, proteins, or glycoprotein stainable by PAS method.



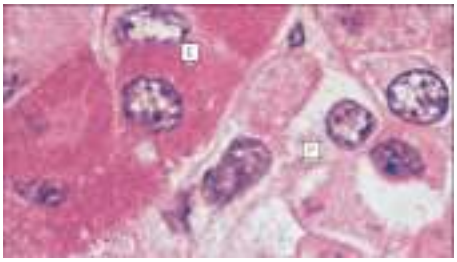
Alkaline phosphatase (stained in red) on the apical surface of the small intestine epithelia.

Secretory Adaptation of epithelia:

Organelles modification/development to adapt a cell for secretion of macromolecules.

Protein-secreting epithelial cells:

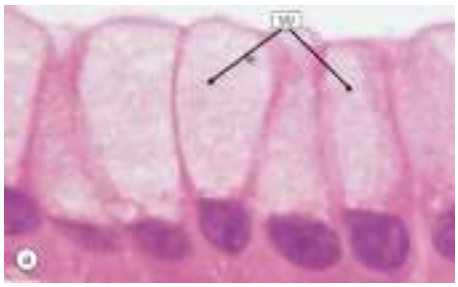
- A well-developed rER system that appears purple in color in the cytoplasm by H&E staining.
- Distinct polarity with basal rER, a supranuclear Golgi (ill-defined lucent cytoplasmic area)
- Apical zone containing granules filled with secretory proteins.

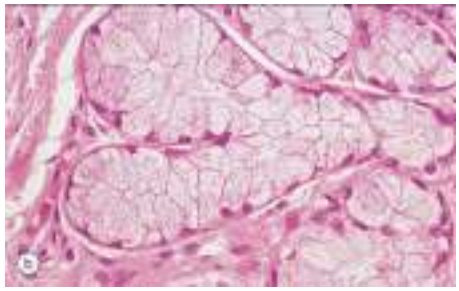


Mucin-secreting epithelial cells: contains greatly expanded Golgi system:

Mucins: mixture of glycoproteins and proteoglycans.

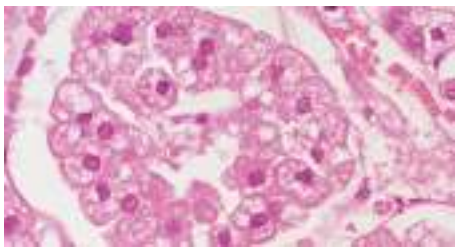
Features:
- Well-developed basal rER (stained faint blue) to the basal cytoplasm.
- Well-developed supranuclear Golgi for protein glycosylation (seen in TEM).
- Large secretory vesicles of mucins at cell apex impart an unstained vacuolated appearance to the apical cell cytoplasm.
- May be part of the surface epithelium which is called goblet cell.
- May aggregate into specialized glands.





Steroid secreting epithelial cells: extensive smooth endoplasmic riticulum (sER):

Location: adrenal gland, ovary, testis
Features:
- Well-developed sER that makes the cytoplasm a granular pink appearance.
- Free lipids in vacuoles → fine, vacuolated appearance to the cells.
- Mitochondria with tubular cristae.



Ion-pumping epithelial cells: high density of mitochondria and large surface area

In: kidney tubules, secretory glands (ions and waters), acid-producing cells (stomach).

Features:
•Cell membrane folded to increase surface area that harboring ion pumping proteins.
•Large number of mitochondria closely apposed to the membrane folds.
•Tight junctions between cells to prevent backward leakage.

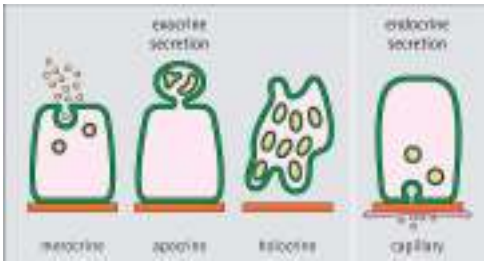
Direction of secretion and ion movement:

Salivary gland duct cells.

Four types of secretion by epithelial cells:

Exocrine secretion:
Merocrine, apocrine, and holocrine: deliver through the apex of cell into a lumen.

Endocrine secretion: secretion from the side or the base of cells into bloodstream.

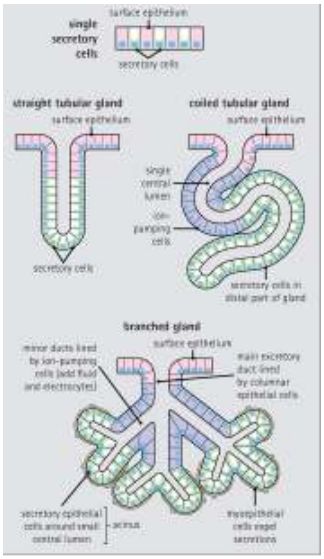


Epithelial cells grouped into secretory glands:

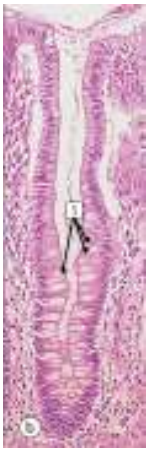
Gland: organized collection of secretory epithelial cells.

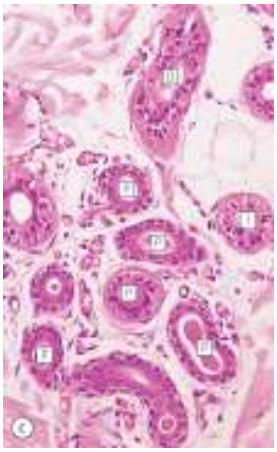
Invagination of surface epithelial cells to form the straight or coiled ducts, or more complex, branched glands.

Regions of glands are divided into specialized zones for the secretion of different products.

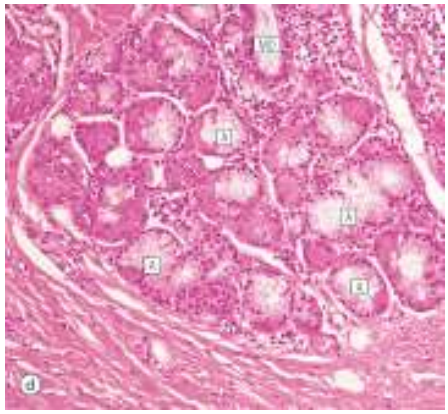


Single secretory cells

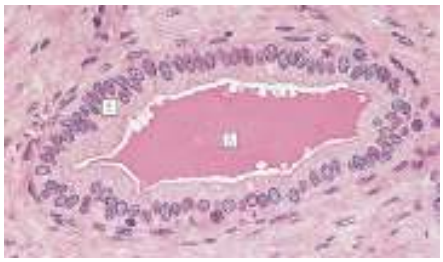




Straight and coiled tubular glands



Branched gland arranged into acini and excretory ducts

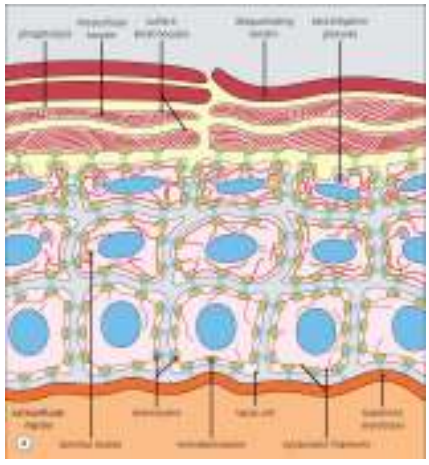


Glandular duct: columnar epithelial cells

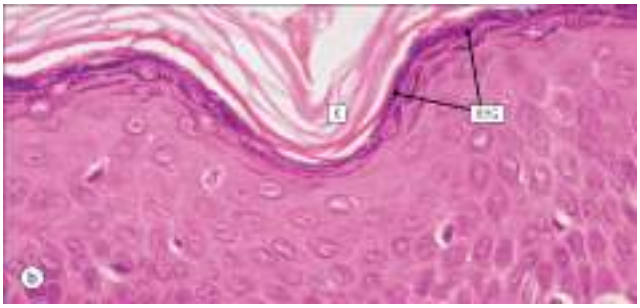
Barrier function of epithelium:

Specializations for barrier function:

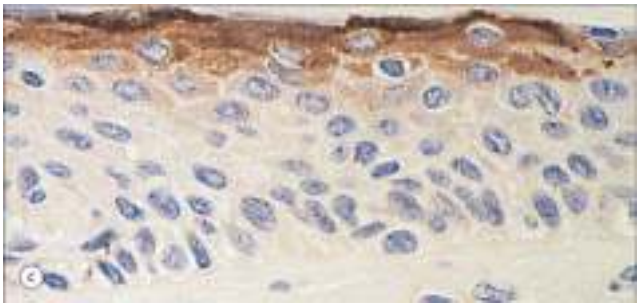
- Occluding junctions: prevent backward diffusion.
- Apical membrane of urinary tract contains high proportion of sphingolipids: forming membrane plaques and resist fluid and electrolyte movement according to osmotic effect.
- Tight mechanical linkage between cells and cell-extracellular matrix by desmosome and hemidesmosome.
- Stratified squamous epithelial cells: keratinization→ turn cells into non-living, proteinaceous material (kreatin) that is impervious and tough.



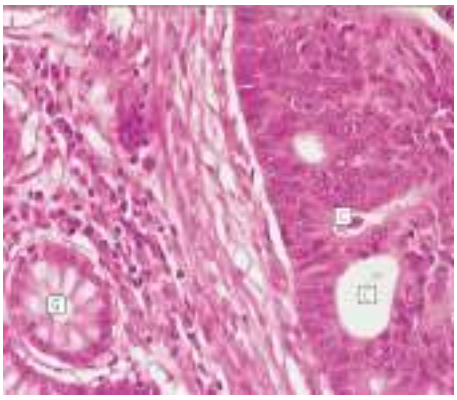
Keratinization of epithelium



KGH:keratohyaline granules.



Brown substance: involucrin that present in only the upper keratinizing part of the epithelium.



Adenocarcinoma of colonic epithelium: H&E stain:
G: normal glandular epithelium; C: carcinoma.