1. EPITHELIUM

Box 1-A | Main characteristics of epithelia

- Epithelia derive from the ectoderm, mesoderm, and endoderm.
- Epithelia line and cover all body surfaces except the articular cartilage, the enamel of the tooth, and the anterior surface of the iris.
- The basic functions of epithelia are **protection** (skin), **absorption** (small and large intestine), **transport of material** at the surface (mediated by cilia), **secretion** (glands), **excretion** (tubules of the kidneys), **gas exchange** (lung alveolus), and **gliding between surfaces** (mesothelium).
- Most epithelial cells renew continuously by mitosis.
- Epithelia lack a direct blood and lymphatic supply. Nutrients are delivered by diffusion.
- Epithelial cells have almost no free intercellular substances (in contrast to connective tissue).
- The cohesive nature of an epithelium is maintained by **cell adhesion molecules** and **junctional complexes**.
- Epithelia are anchored to a **basal lamina**. The basal lamina and connective tissue components cooperate to form the **basement membrane**.
- Epithelia have structural and functional **polarity**.

General classification of epithelia

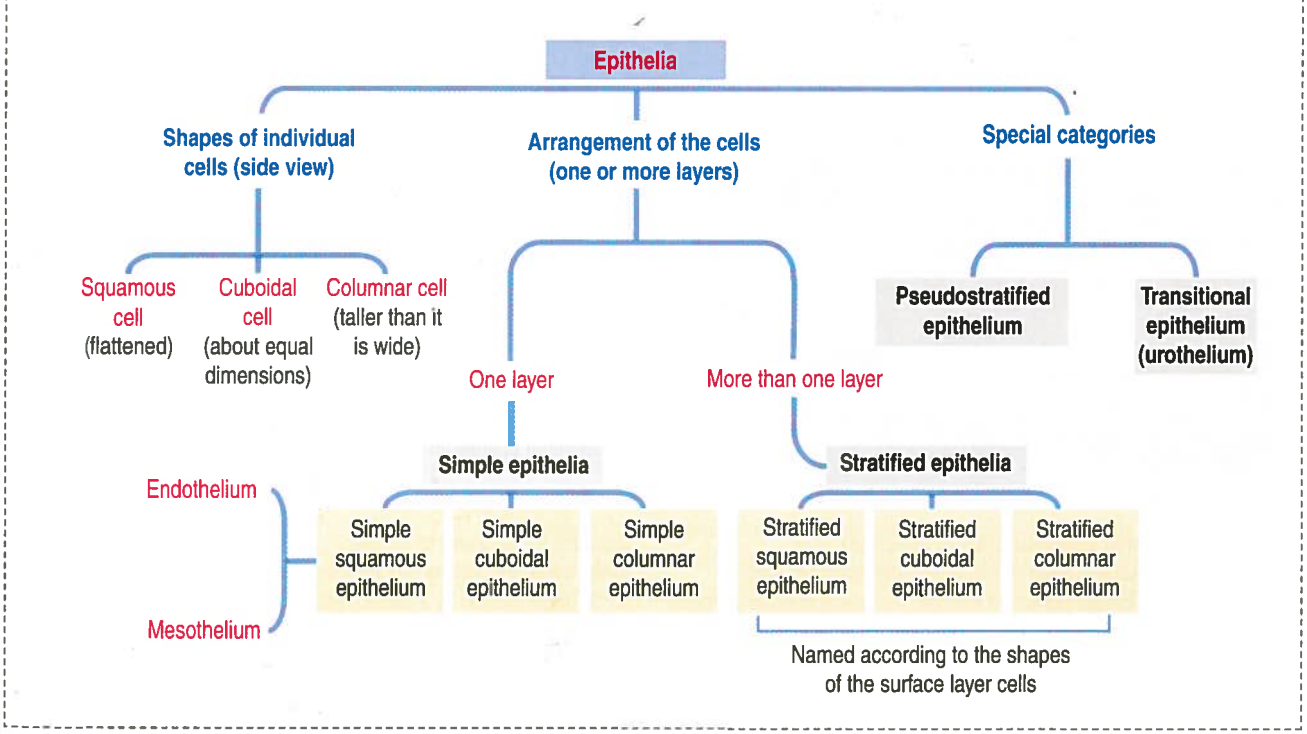
The epithelium is a tightly cohesive sheet of cells that covers or lines body surfaces (for example, skin, intestine, secretory ducts) and forms the functional units of secretory glands (for example, salivary glands, liver). The traditional classification and nomenclature of different types of epithelia are based on the shapes of individual cells and arrangement of the cells in one or more layers (Figure 1-1). The main characteristics of epithelia are listed in Box 1-A.

Epithelia are classified into:

1. **Simple epithelia** (Figure 1-2), formed by only one layer of cells. They are subdivided into **simple squamous, simple cuboidal**, and **simple columnar**, according to the height and width of the cells. The specific name **endothelium** is used for the simple epithelium lining the blood and lymphatic vessels. **Mesothelium** is the simple epithelium lining all body cavities (peritoneum, pericardium, and pleura).

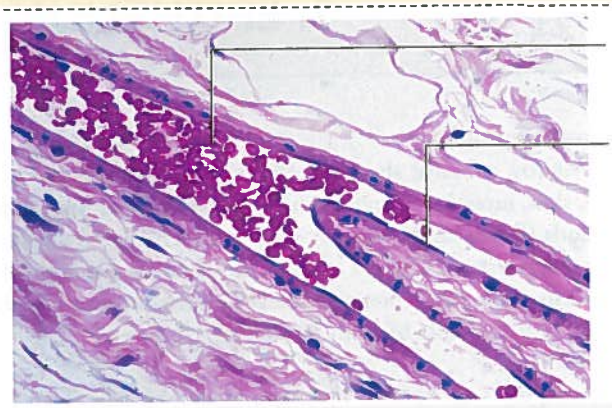
2. **Stratified epithelia** (Figure 1-3) are composed of two or more cell layers. Stratified epithelia are subclassified according to the shapes of the cells at the superficial or outer layer into **stratified squamous, stratified cuboidal**, and **stratified columnar**. Stratified squamous is the epithelium most frequently found and can be subdivided into **moderately keratinized** (also known as nonkeratinized) or **highly keratinized** types. The cells of the outer layer of a moderately keratinized squamous epithelium **can display nuclei** (for example, esophagus and vagina). **Nuclei are absent in the outer layer of the highly keratinized stratified squamous epithelium** (for example, the epidermis of the skin). The basal cells aligned along the basal lamina are mitotically active and replace the differentiating cells of the upper layers.

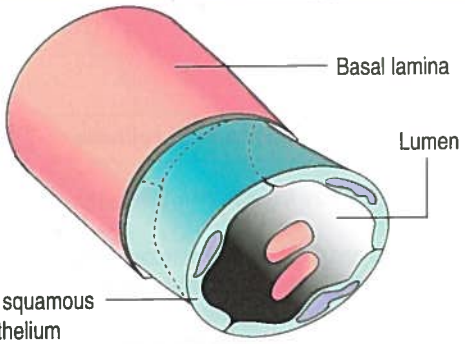
Figure 1-1. Concept mapping: Types of epithelia



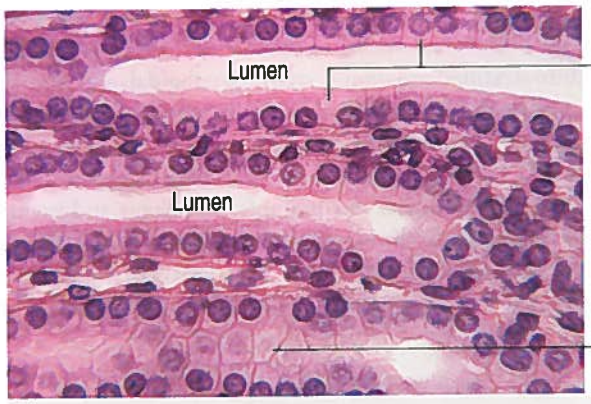
classification utilisé en cours de l'histologie (Prof. Soulié)

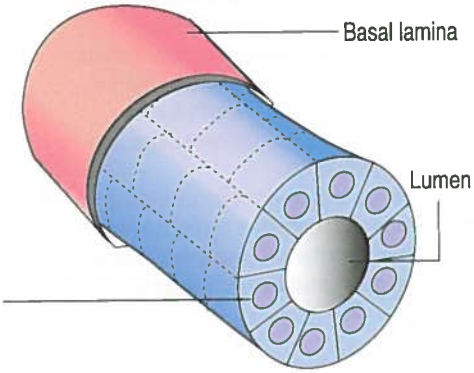
Figure 1-2. Simple epithelium



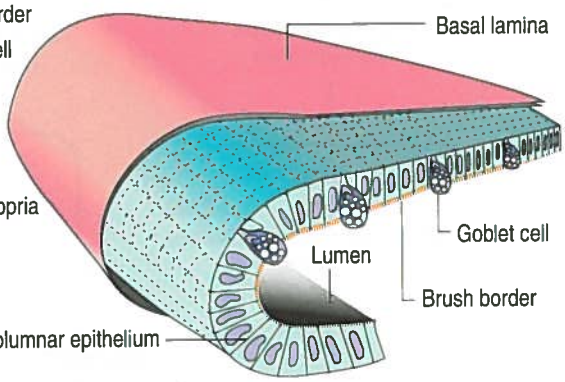


Simple squamous epithelium (endothelium)
The inner lining of all blood vessels consists of a single layer of squamous endothelial cells. The thinness of the simple squamous epithelial cells reflects their primary function in rapid exchange of substances between blood and tissue. A similar epithelium (called **mesothelium**) covers the peritoneum, pleura, and pericardium.



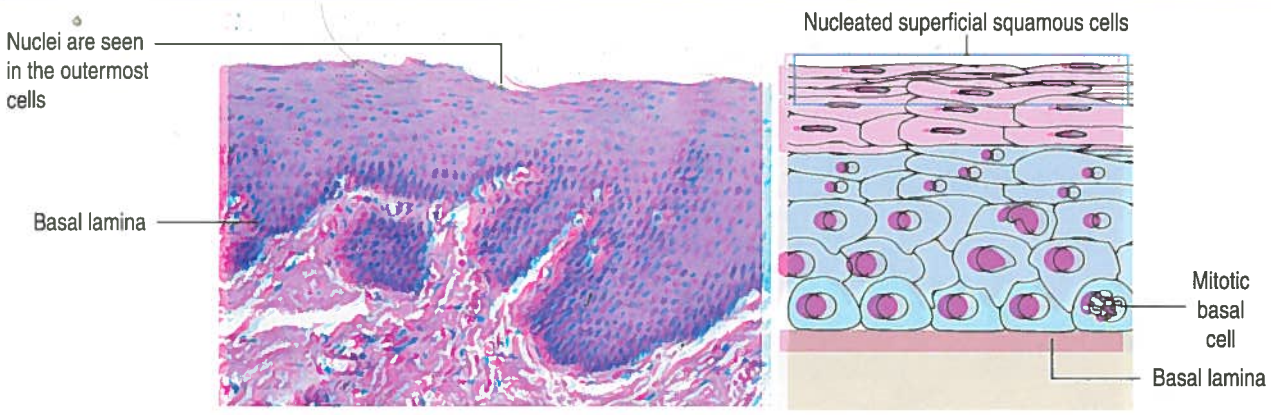


Simple cuboidal epithelium (collecting tubule, kidneys)
The inner lining of kidney tubules and thyroid follicles consists of a single layer of cuboidal cells. Cuboidal cells are highly polarized and participate in absorption, secretion (thyroid gland), and active ion transport (kidneys). Similar to the endothelium, a basal lamina attaches the cell to the subjacent connective tissue.

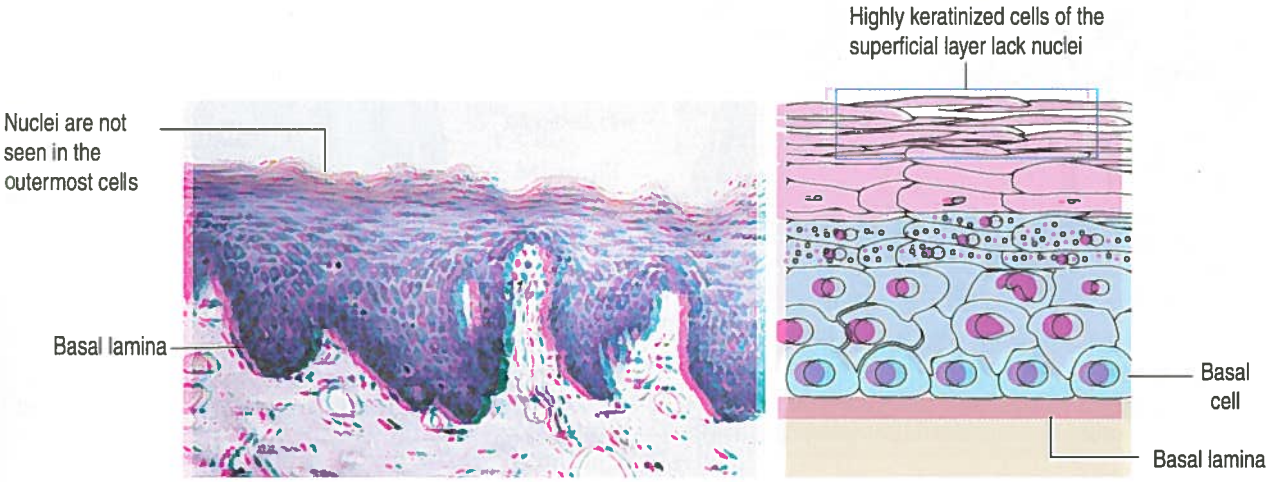


Simple columnar epithelium (small intestine)
The small intestine is lined by columnar epithelial cells with the nucleus in the medial portion of the cell. The apical domain contains finger-like projections called **microvilli** forming a **brush border**. Microvilli participate in the absorption of proteins, sugar, and lipids, which are released at the basolateral domain into the blood circulation for transport to the liver.
Goblet cells are present among the columnar epithelial cells. They can be distinguished by a dilated, goblet-like apical cytoplasm containing a light-stained mucus material. Mucus is released into the lumen and coats the epithelial cell surface. The **lamina propria** is indicated.

Figure 1-3 Stratified epithelium



Stratified squamous epithelium with moderate keratin (esophagus)
This epithelium consists of undifferentiated **basal cells** specialized for **mitotic division**. Stratified cells covering the basal layer are differentiating cells. Cells of the outer layer are highly differentiated: they increase their **keratin content** to protect the tissue from the mechanical action of ingested food. The **outermost cells retain their nuclei**. This epithelium is also known as **nonkeratinizing**.

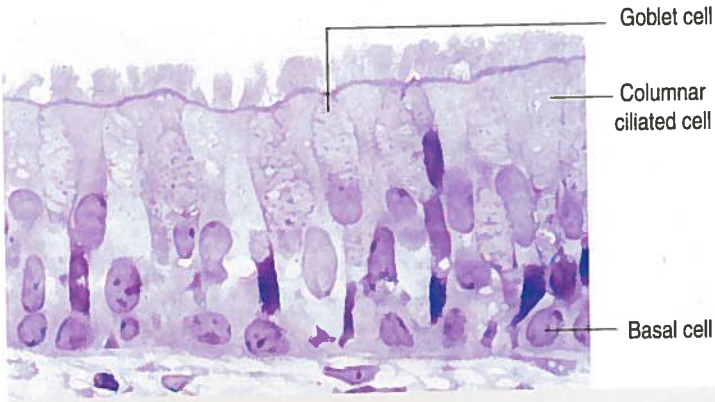


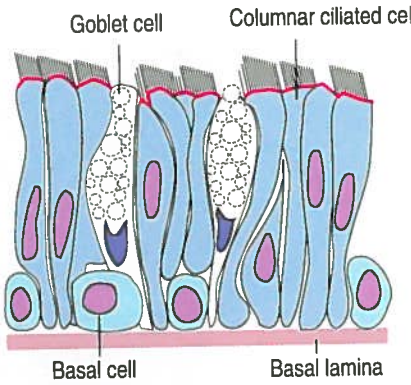
Stratified squamous epithelium with abundant keratin (epidermis)
This highly keratinized epithelium consists of undifferentiated **basal cells** specialized for **mitotic division**. Stratified cells covering the basal layer are differentiating cells. Cells of the outer layer contain abundant **keratin** to prevent water loss and penetration of chemical and physical insults. The **outermost cells lack nuclei**. This epithelium is also known as **keratinizing**.

3. Two special categories are the **pseudostratified epithelium** and the **transitional epithelium** (Figure 1-4). The pseudostratified epithelium consists of basal and columnar cells resting on the basal lamina. Only the columnar cells reach the luminal surface, however. Because the nuclei of the basal and columnar cells are seen at different levels, one has the impression of a stratified epithelial organization. Within this category are the **pseudostratified columnar ciliated epithelium** of the trachea and the **pseudostratified columnar epithelium with stereocilia** of the epididymis. The **transitional epithelium** of the urinary passages is also referred to as **urothelium**. The urothelium also consists of basal and columnar dome-shaped cells. An important feature of this epithelium is that its height varies with distention and contraction of the organ (see Chapter 14, Urinary System).

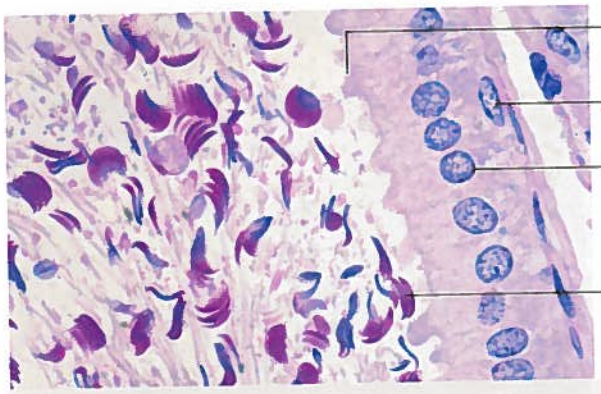
An important aspect of epithelia is its **polarity**. Most epithelial cells line surfaces and cavities and have three domains (Figure 1-5):

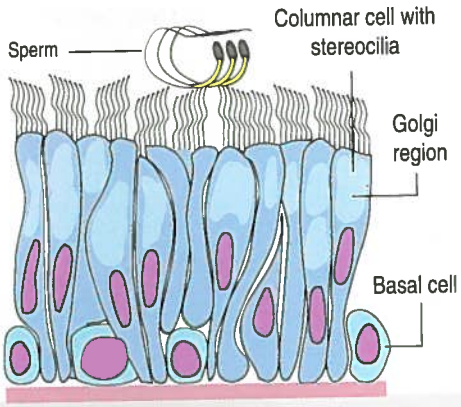
Figure 1-4. Pseudostratified and transitional epithelia



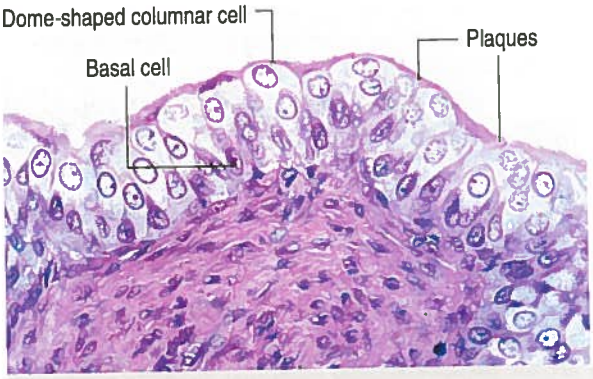


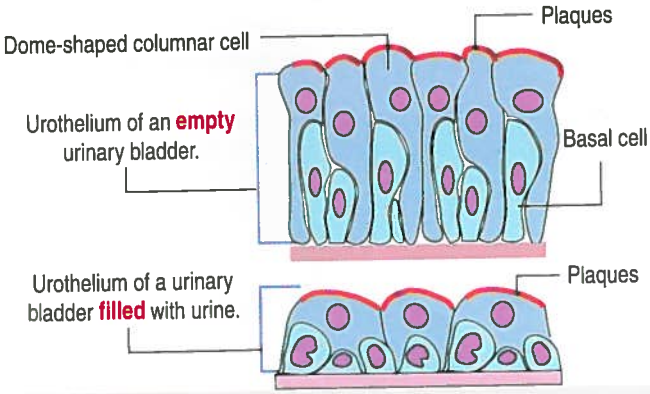
Pseudostratified columnar ciliated epithelium (trachea)
This epithelium consists of three major cell types: (1) **Columnar cells** with **cilia** on their apical domain. (2) **Basal cells** anchored to the basal lamina. (3) **Goblet cells**, mucus-secreting epithelial cells. Columnar ciliated and goblet cells attach to the basal lamina and reach the lumen. Basal cells do not reach the lumen.





Pseudostratified columnar epithelium with stereocilia (epididymis)
The epididymal epithelium contains two major cell types. (1) **Columnar cells** with stereocilia and highly developed Golgi apparatus (called principal cells). (2) **Basal cells** attached to the basal lamina. Basal and principal cells are associated with the basal lamina. Only principal cells reach the lumen. Sperm can be visualized in the lumen.





Transitional epithelium (urinary bladder)
The transitional epithelium, lining the urinary passages (also called **urothelium**), consists of two cell types. (1) **dome-shaped columnar cells** extending from the basal lamina to the lumen. (2) **Basal cells** attached to the basal lamina. In some species, the urothelium appears as a pseudostratified epithelium; in other species it has the appearance of a stratified squamous epithelium. A characteristic of the urothelium is that superficial cells respond to tensional forces—caused by urine—by changing their geometry and surface dome-shape configuration. **Plaques** of aggregated proteins are found on the apical plasma membrane of the columnar cells.

1. The **apical domain** is exposed to the lumen or external environment.
2. The **lateral domain** faces neighboring epithelial cells linked to each other by cell adhesion molecules and junctional complexes.
3. The **basal domain** is associated with a **basal lamina** that separates the epithelium from underlying connective tissue. The basal lamina is reinforced by components of the connective tissue. The basal lamina–connective tissue complex is designated the **basement membrane**.

Epithelial cells are attached to each other by junctional complexes and adhesion molecules. Epithelial cells are specialized to fulfill important roles, such as absorption and secretion or to act as a water or gas barrier. Several cell barriers and their functional significance are studied.

EPITHELIAL CELL POLARITY

Epithelial cells have two major domains (Figure 1-5):

1. An **apical domain**
2. A **basolateral domain**

Each domain is defined by specific structural and functional characteristics. For example, the apical domain has structures important for the **protection** of the epithelial surface (such as **cilia** in the respiratory tract) or for the **absorption** of substances (such as **microvilli** in the intestinal epithelium).

Junctional complexes and **cell adhesion molecules** are present at the basolateral domain to anchor epithelial cells to each other and to the basement membrane.

Apical differentiations

The **apical domain** of some epithelial cells can display three types of differentiation:

1. **Cilia**
2. **Microvilli**
3. **Stereocilia**

Cilia (singular, **cilium**; Figure 1-6) are **motile** cell projections originating from **basal bodies** anchored by **rootlets** to the apical portion of the cytoplasm. A basal body contains nine **triplet** microtubules in a **helicoid array** without a central microtubular component. By contrast, a cilium consists of an assembly called an **axoneme, formed by a central pair of microtubules surrounded by nine concentrically arranged microtubular pairs. This assembly is known as the 9 + 2 microtubular doublet arrangement.** The axoneme is also a component of the sperm tail, or **flagellum.**

Figure 1-5. Domains of a polarized epithelial cell

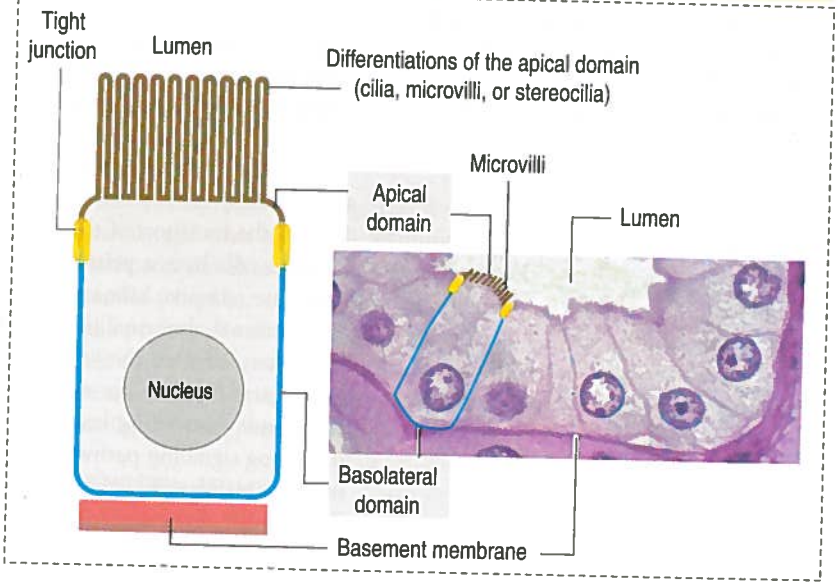
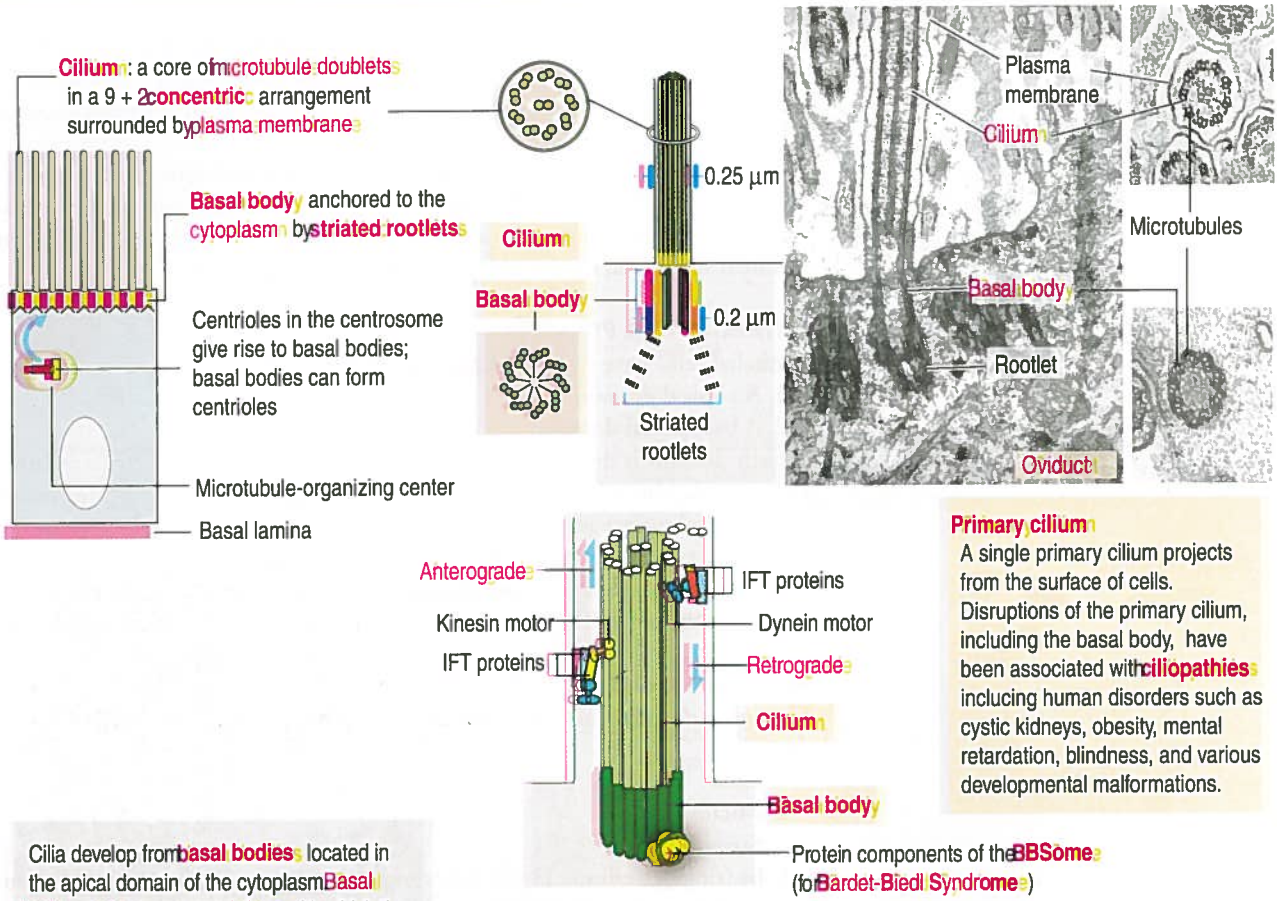


Figure 1-6. Apical differentiations of epithelial cells: cilia and primary cilium



Primary cilium
A single primary cilium projects from the surface of cells. Disruptions of the primary cilium, including the basal body, have been associated with **ciliopathies** inclucing human disorders such as cystic kidneys, obesity, mental retardation, blindness, and various developmental malformations.

Cilia develop from **basal bodies** located in the apical domain of the cytoplasm. Basal bodies derive from **centrioles** with which they share a similar substructure: **nine peripheral microtubule triplets** in a **helicoidal** arrangement.

Rootlets anchor the basal body to the cytoplasm. Central microtubules are not present in basal bodies and centrioles. **Centrioles**, but not basal bodies, are surrounded by a dense material called the **microtubule-organizing center**.

The cilium consists of a concentric array of nine microtubule doublets surrounding a central pair of microtubules (9 + 2 organization).

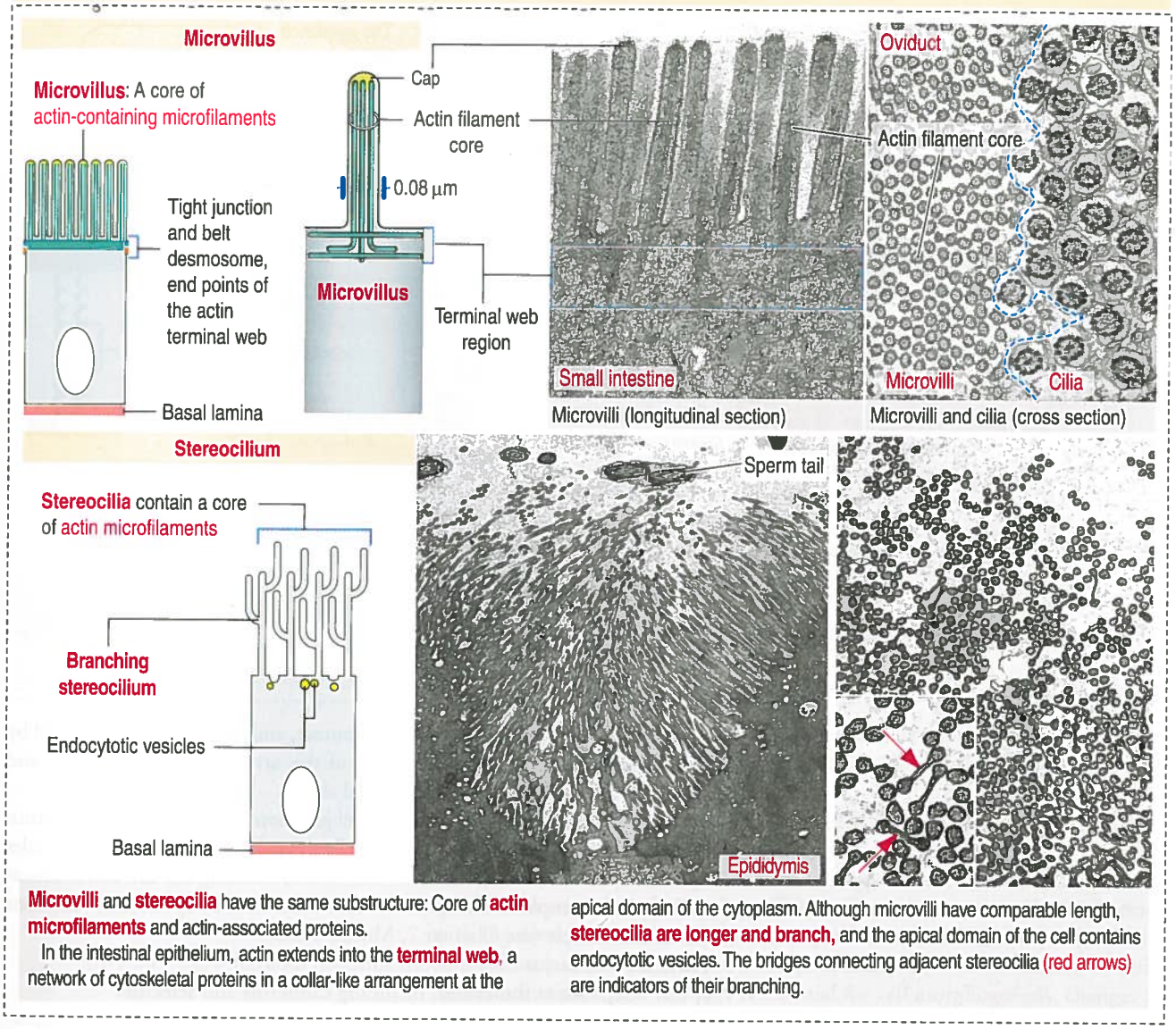
Assembly of the cilium
The cilium is formed and maintained by the transport of tubulins along the axoneme mediated by proteins of the **intraflagellar transport** (**IFT**) system. IFT trafficking from the base of the cilium to the tip (**anterograde transport**; to the microtubule plus end) is mediated by **kinesin motor proteins** mobilizing IFT protein complexes. **Dynein motor** participates in **retrograde transport** (to the microtubule minus end; base of the cilium). IFT proteins form a platform for transporting cargo between the base and tip of the cilium.

Disruption of the kinesin motor or IFT proteins blocks cilia formation. Basal body proteins influence ciliary trafficking. Among these are components of the **BBSome**, which are named after their association with **Bardet-Biedl syndrome** (**BBS**). BBSome proteins may help loading protein cargo to the ciliary axoneme. Proteins of the **hedgehog signaling pathway** participate in intraciliary and intraflagellar transport (not shown).

The trachea and the oviduct are lined by **ciliated** epithelial cells. In these epithelia, ciliary activity is important for the local defense of the respiratory system and for the transport of the fertilized egg to the uterine cavity.

Some cells have a **primary cilium**. The importance of primary cilia emerges from rare recessive human disorders known as **ciliopathies** caused by structural or functional abnormalities of cilia. The structure and mechanism of assembly of primary cilia are shown in Figure 1-6. The significant aspects of the primary cilium are: (1) they are **non-motile**; (2) they participate in the early stages of embryonic patterning leading to organogenesis; (3) many components of the hedgehog signaling pathway, essential at least in early development, are present in primary cilia; and (4) the position of the primary cilium, called **kinocilium**, of the hair cell of the organ of Corti in the inner ear determines the correct polarity of the actin-containing stereocilia (see Chapter 9, Sensory Organs: Vision and

Figure 1-7. Apical differentiations of epithelial cells: microvilli and stereocilia



Microvilli and **stereocilia** have the same substructure: Core of **actin microfilaments** and actin-associated proteins.

In the intestinal epithelium, actin extends into the **terminal web**, a network of cytoskeletal proteins in a collar-like arrangement at the apical domain of the cytoplasm. Although microvilli have comparable length, **stereocilia are longer and branch,** and the apical domain of the cell contains endocytotic vesicles. The bridges connecting adjacent stereocilia (red arrows) are indicators of their branching.

Hearing).

Microvilli (singular, **microvillus**; Figure 1-7) are finger-like cell projections of the apical epithelial cell surface containing a core of cross-linked microfilaments (a polymer of G-actin monomers). At the cytoplasmic end of the microvillus, bundles of **actin** and other proteins extend into the **terminal web**, a filamentous network of cytoskeletal proteins running parallel to the apical domain of the epithelial cell.

The intestinal epithelium and portions of the nephron in the kidney are lined by epithelial cells with microvilli forming a **brush border**. In general, a brush border indicates the **absorptive** function of the cell.

Stereocilia (singular, **stereocilium**; see Figure 1-7) are long and **branching** finger-like projections of the apical epithelial cell surface. Similar to microvilli, stereocilia contain a core of cross-linked actin with other proteins. **Stereocilia do not have axonemes.** Stereocilia are typical of the epithelial lining of the epididymis and contribute to the process of sperm maturation occurring in this organ.

CELL ADHESION MOLECULES

A sheet of epithelial cells results from the tight attachment of similar cells to each other and to the **basal lamina**, a component of the extracellular matrix. **Cell adhe-**