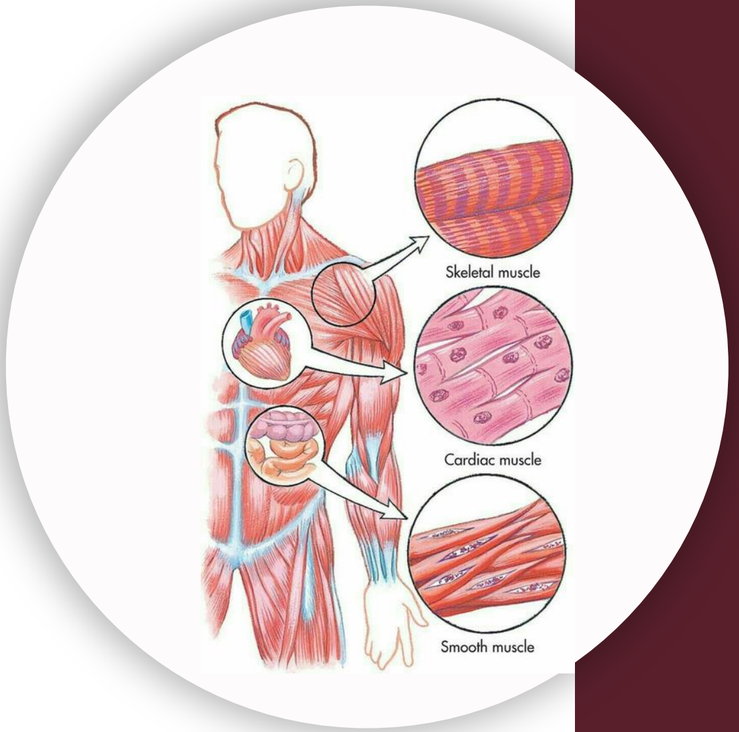
بسم الله الرحمن الرحيم

Histology - Lecture 4

Epithelium pt.2



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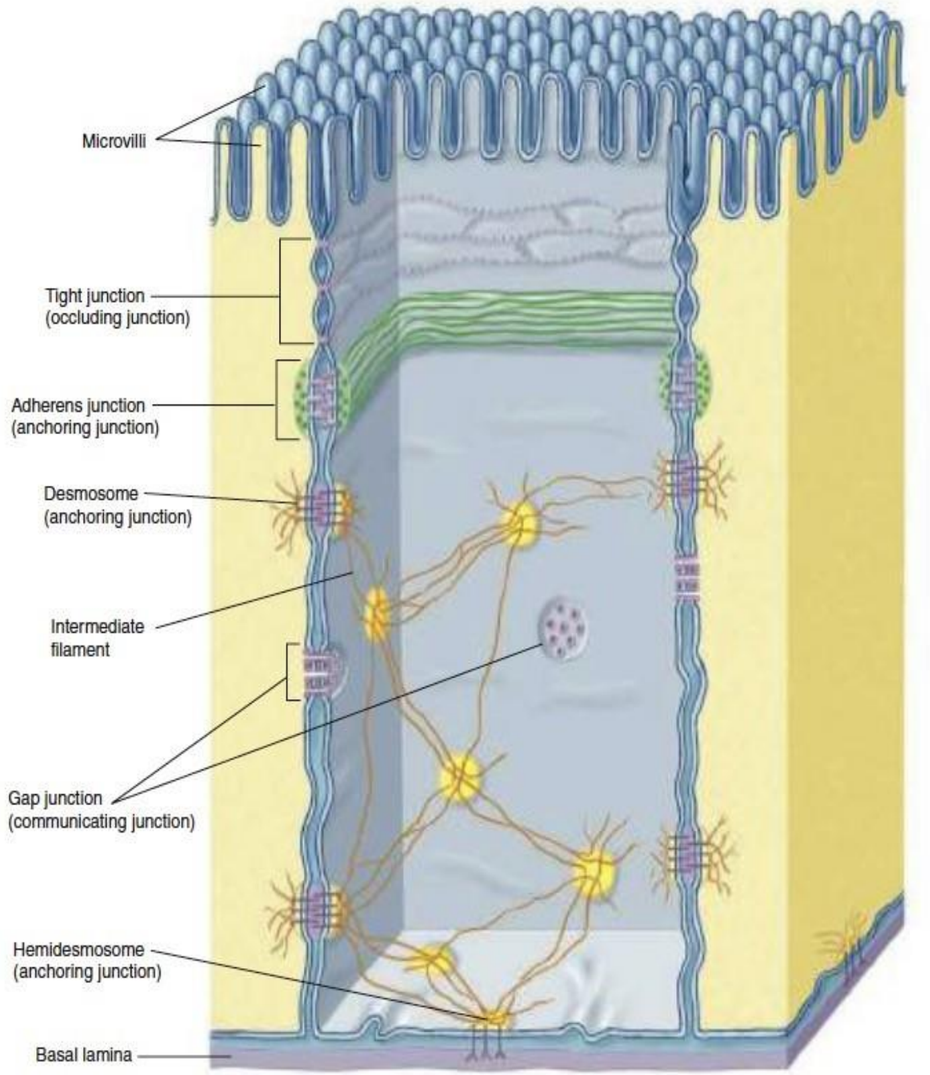
Junctional Complexes

We did talk about the features of epithelium, and one of these features is that the epithelial cells are well adhered to each other (glued together). They have strong bonds between the cells, which actually fits the role of being a protective tissue, preventing the passage of unwanted molecules and microorganisms.

There are different types of Junctional complexes with different structures and locations. These junctions communicate with the cytoplasm through the cytoskeleton, more specifically through actin and intermediate filaments.

Junctional Complexes

- Membrane-associated structures provide adhesion and communication between cells
- Epithelial cells adhere strongly to neighboring cells and basal laminae
- Tight or occluding junctions form a seal between adjacent cells.
- Adherent or anchoring junctions are sites of strong cell adhesion.
- Gap junctions are channels for communication between adjacent cells.
- Desmosome or macula adherens are disc-shaped structures at the surface of one cell that are matched with identical structures at an adjacent cell surface.

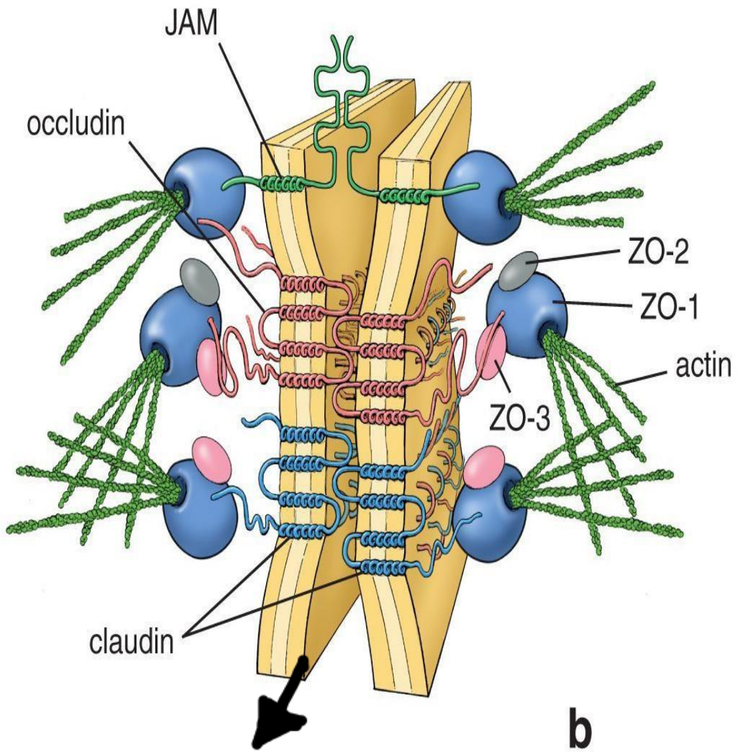


Tight Junction (Zonula occludens)

- Tight or occluding junctions form a seal between adjacent cells.

to make sure the cell is separated from the external environment

- They are the most apical.
- The intercellular seal of tight junctions ensures that molecules crossing an epithelium in either direction do so through transcellular route not the paracellular one
- The seal between the two cell membranes is due to tight interactions between the transmembrane proteins claudin and occludin.

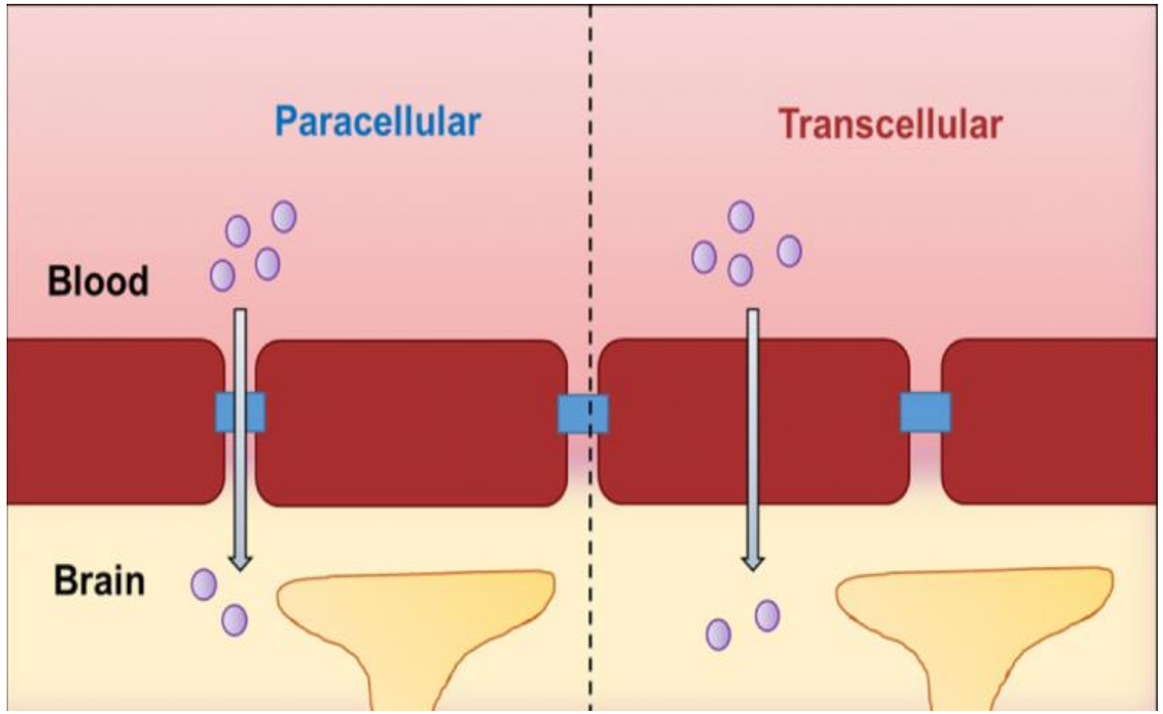


The close approximation between the two lateral sides of epithelial cells is due to the strong association between two proteins (occludin and claudin).

Tight junctions are associated with the cytoskeleton through actin filaments.

Tight junctions Participate heavily in the prevention of the passage of any molecule or microorganism that tries to access the deeper structures

A picture showing the difference between the transcellular and the paracellular route

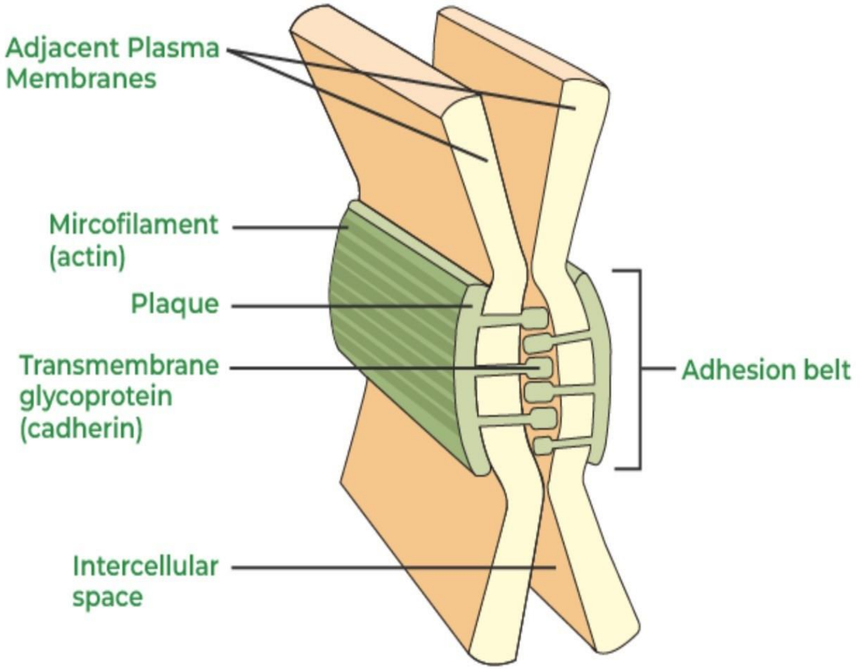


Adherent Junctions (Zonula adherens)

- Encircle the epithelial cell, usually below the tight junction.
- Firmly anchors cells to neighboring ones.

They heavily participate in anchoring and approximating the two lateral epithelial membranes.

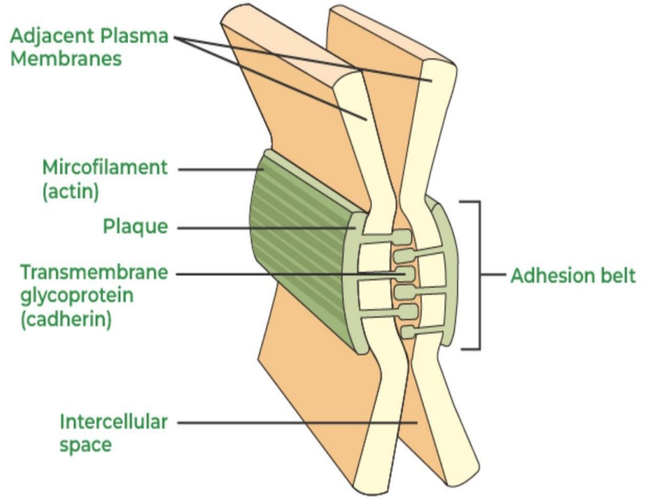
- Cell adhesion is mediated by **e-cadherin** (transmembrane glycoproteins) of each cell that bind each other in the presence of Ca2+



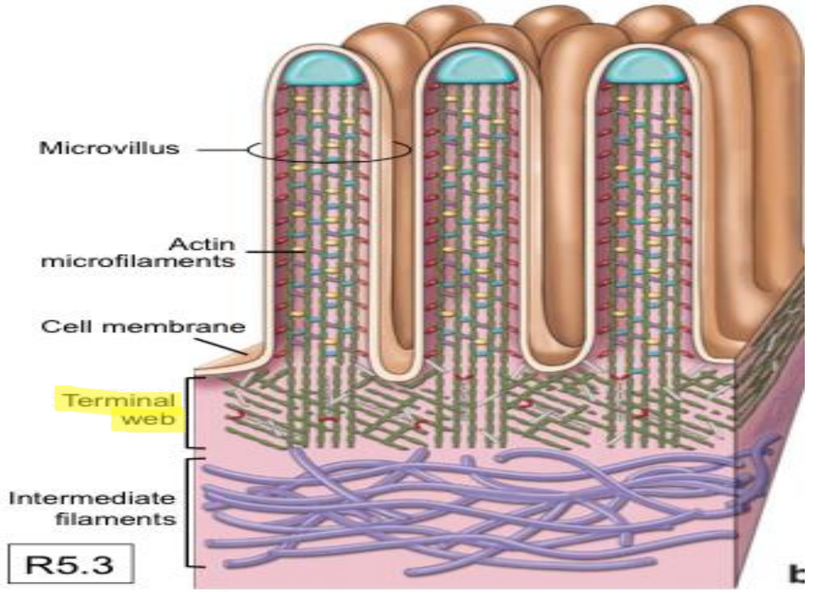
The transmembrane glycoproteins (cadherin) which are involved in the formation of adherent junctions, interact with each other outside the cells where they meet. Calcium ions enhance and maintain this interaction.

Adherent Junctions (Zonula adherens)

At their cytoplasmic ends, cadherins bind **catenins** that link to actin filaments with actin-binding proteins.



The actin filaments linked to the adherent junctions form part of the “terminal web” ,a cytoskeletal feature at the apical pole in many epithelial cells.



Desmosomes

- Disc-shaped structures that are matched with identical structures at an adjacent cell surface

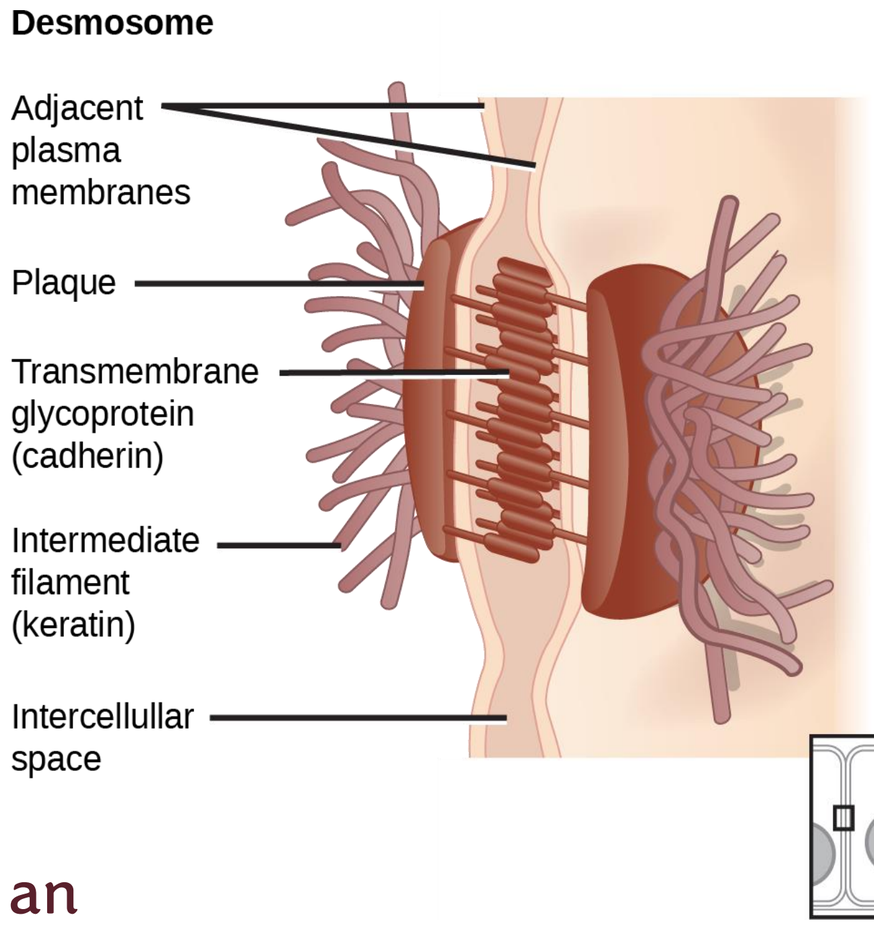
What distinguishes desmosomes is that they are disc-shaped, not forming a circular hole along the entire length of the epithelial membrane

- Desmosomes contain larger members of the cadherin family called desmogleins and desmocollins.

They are large, so they enhance the attachment and adhesion of the two lateral epithelial membranes.

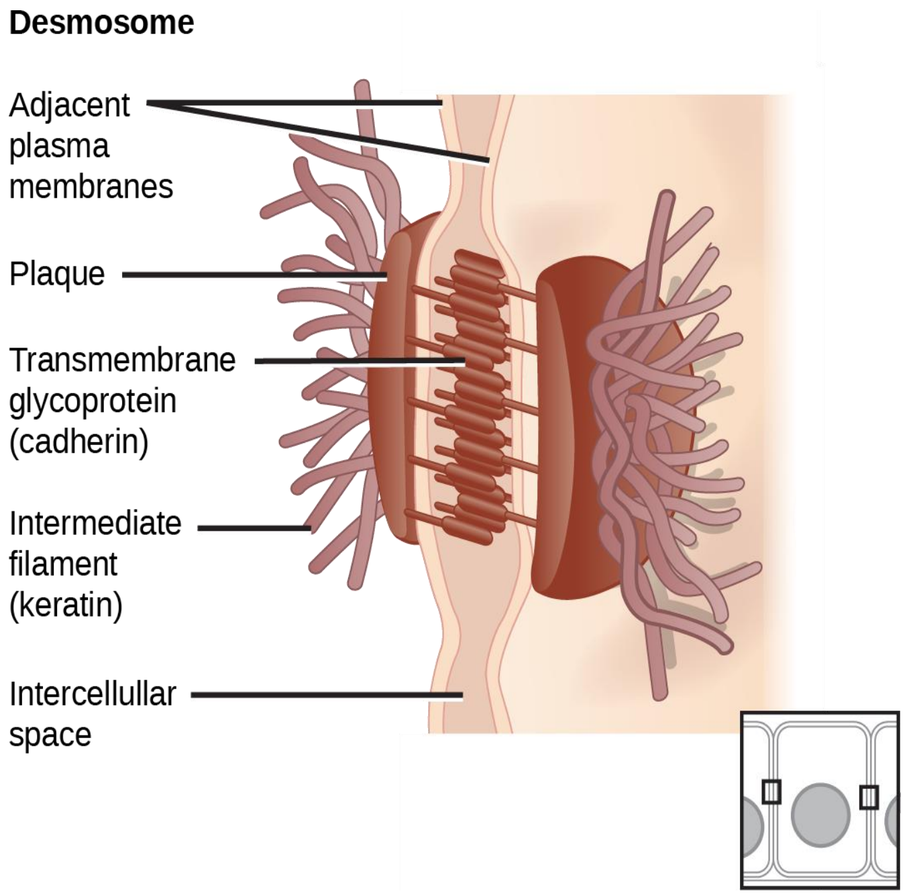
We can see desmosomes between epithelial cells under an electron microscope as a very dense patch.

These areas appear dense because of the protein complexes and structures involved in cell adhesion, which are visible due to their high electron density.



Desmosomes

- The cytoplasmic ends of these transmembrane proteins bind a catenin-like protein which bind intermediate filament proteins rather than actins.



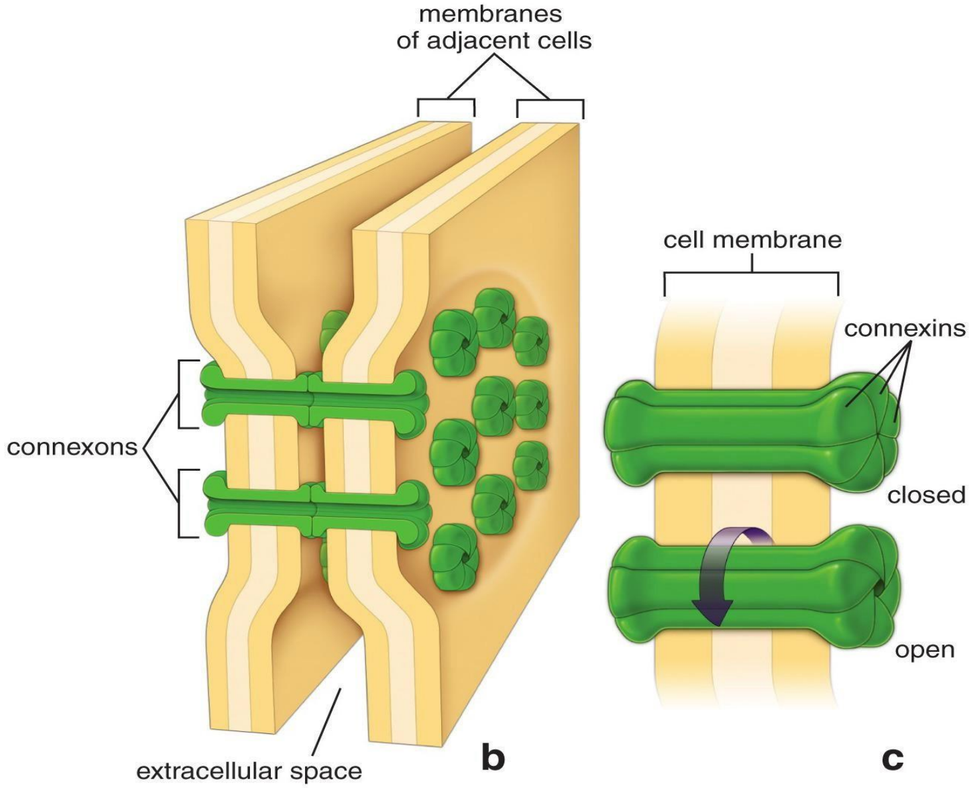
Gap Junctions

- Mediate intercellular communication.

Gap junctions have proteins that interact with each other at the two lateral epithelial membranes. They participate in adhesion, but communication seems to be their priority over adhesion.

- Present in many other cells.
- Connexins (transmembrane proteins) form hexameric complexes called connexons, each of which has a central hydrophilic pore about 1.5 nm in diameter.
- Permit intercellular exchange of molecules with small molecules < 1.5 nm in diameters.

Only hydrophilic and small molecules

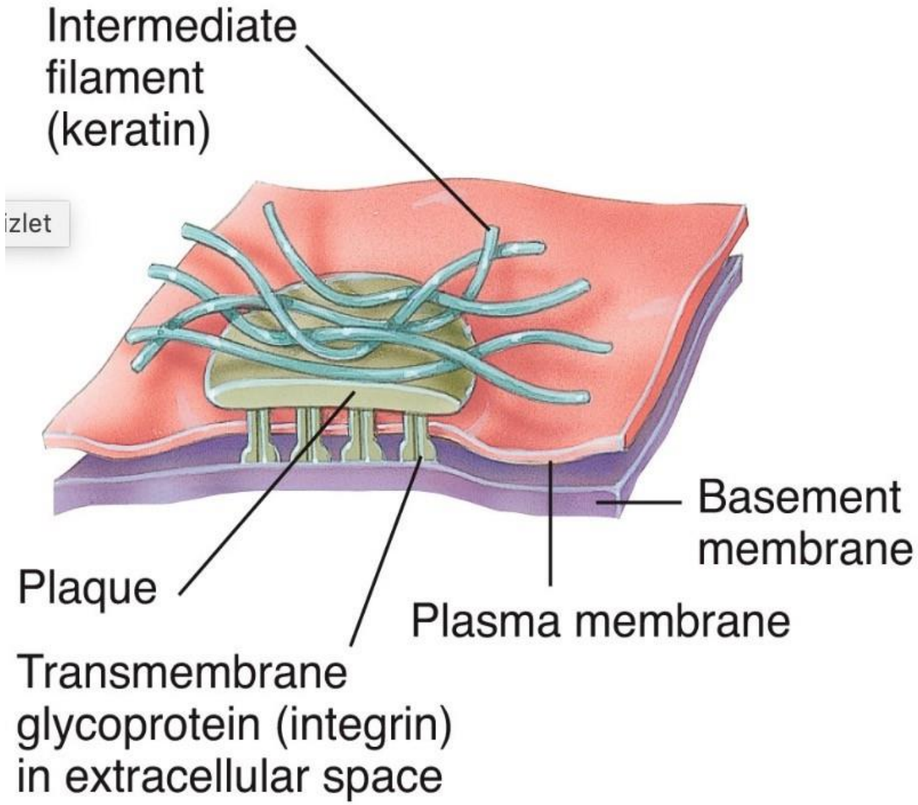


Hemidesmosomes

- Located on the basal epithelial surface.
- Attach cells to the basal lamina.
- Resemble a half-desmosome ultra structurally, but unlike desmosomes the transmembrane proteins that indirectly link to cytokeratin intermediate filaments are integrins rather than cadherins.

They don't use cadherins for the association with the proteins in the basement membrane, they use the glycoprotein (integrin) instead.

- The integrins of hemidesmosomes bind primarily to laminin molecules in the basal lamina.



This is a summary with an extra information about medical significance which is extremely important!

Junction	Tight Junction (Zonula Occludens)	Adherent Junction (Zonula Adherens)	Desmosome (Macula Adherens)	Hemidesmosome	Gap Junction (Nexus)
Major transmembrane link proteins	Occludins, claudins, ZO proteins	E-cadherin, catenin complexes	Cadherin family proteins (desmogleins, desmocollin)	Integrins	Connexin
Cytoskeletal components	Actin filaments	Actin filaments	Intermediate filaments (keratins)	Intermediate filaments	None
Major functions	Seals adjacent cells to one another, controlling passage of molecules between them; separates apical and basolateral membrane domains	Provides points linking the cytoskeletons of adjacent cells; strengthens and stabilizes nearby tight junctions	Provides points of strong intermediate filament coupling between adjacent cells, strengthening the tissue	Anchors cytoskeleton to the basal lamina	Allows direct transfer of small molecules and ions from one cell to another
Medical significance	Defects in occludins may compromise the fetal blood-brain barrier, leading to severe neurologic disorders	Loss of E-cadherin in epithelial cell tumors (carcinomas) promotes tumor invasion and the shift to malignancy	Autoimmunity against desmoglein I leads to dyshesive skin disorders characterized by reduced cohesion of epidermal cells	Mutations in the integrin-β4 gene are linked to some types of epidermolysis bullosa, a skin blistering disorder	Mutations in various connexin genes have been linked to certain types of deafness and peripheral neuropathy

A medical condition associated With those junction complexes is epidermolysis bullosa. This disease is rare and fortunately uncommon. Patients suffer from skin blistering because some of the epithelium doesn’t stay in place due to issues with the integrins. As a result, these patients develop blisters on their skin filled with fluid, and when one heals, another one appears

Specialized apical structures

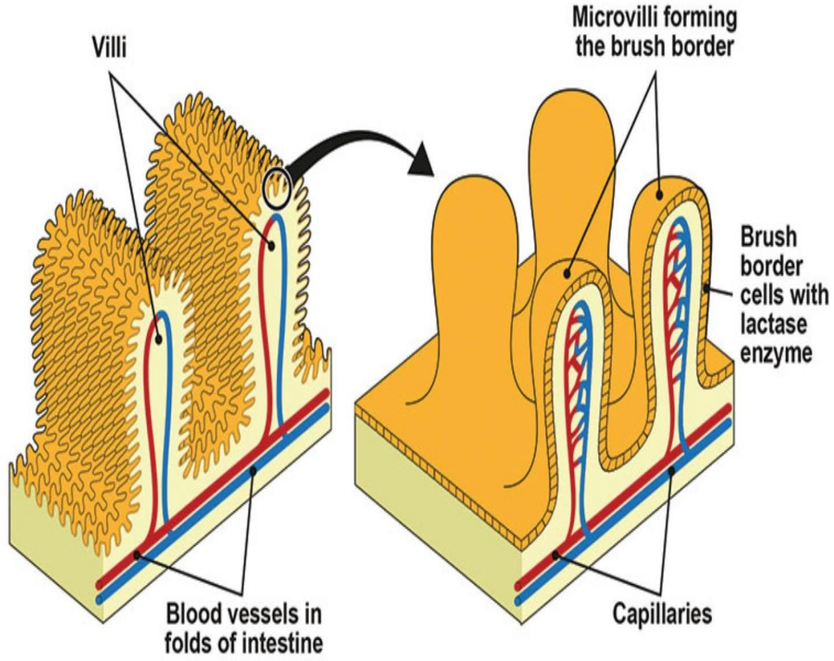
According to the functional need, the apical surface of epithelial cells shows certain surface modifications. These are:

- Microvilli
- Cilia
- Stereocilia

Microvilli

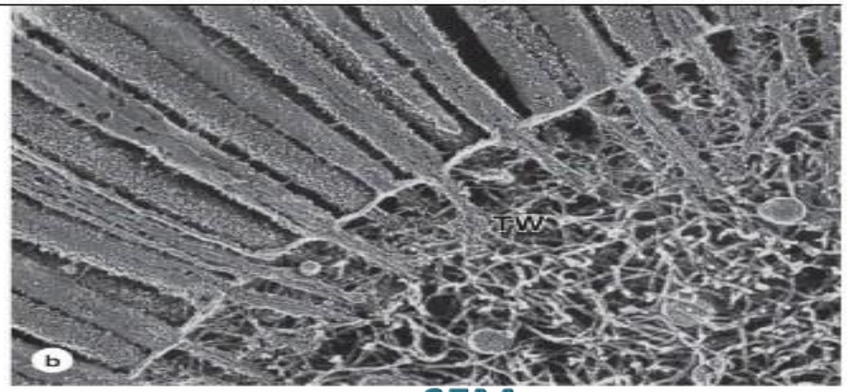
- Finger-like extensions of plasma membrane of apical epithelial cell.
- Present mainly in **absorptive cells (columnar/cuboidal)**.
- Main function is the absorption of nutrients from intestines and glomerular filtrate (in kidney):
- Striated border in the intestine.
  Bruch border in the kidney).
- **Increase the surface area for absorption.**

When microvilli are present in **the small intestine** in large numbers, they form what is called the **striated border.** Whereas, in **the kidney**, they are referred to as the **brush border**.
• **Different names are used, but they share the same fundamental function and structure, adapted to their specific roles in absorption.**

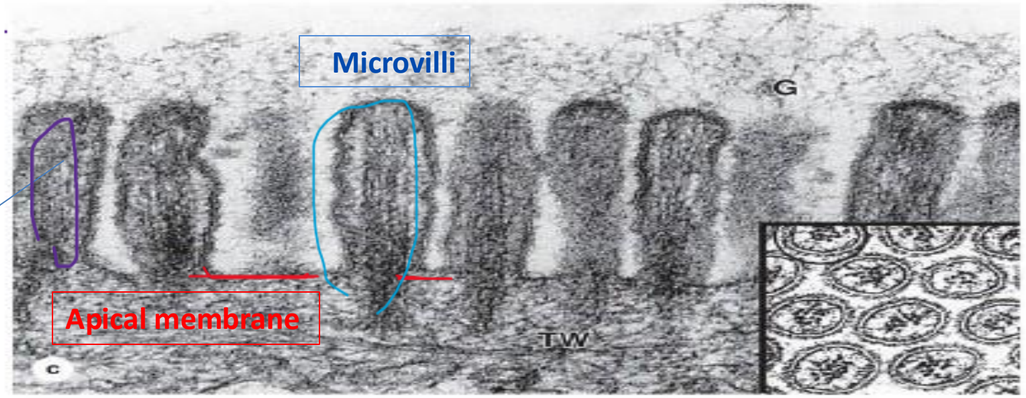


Finger like projections are simply one micrometer long and about 0.1 micrometer wide.

The main function of microvilli is simply to increase the surface area. If we rely only on the plasma membrane area of these cells, it would not be sufficient for absorption processes. Therefore, these finger-like projections amplify the surface area, which enhances the efficiency of these cells in nutrient absorption.
For example, in the small intestine or certain parts of the kidney, microvilli play a crucial role in reabsorbing essential nutrients that have been filtered.

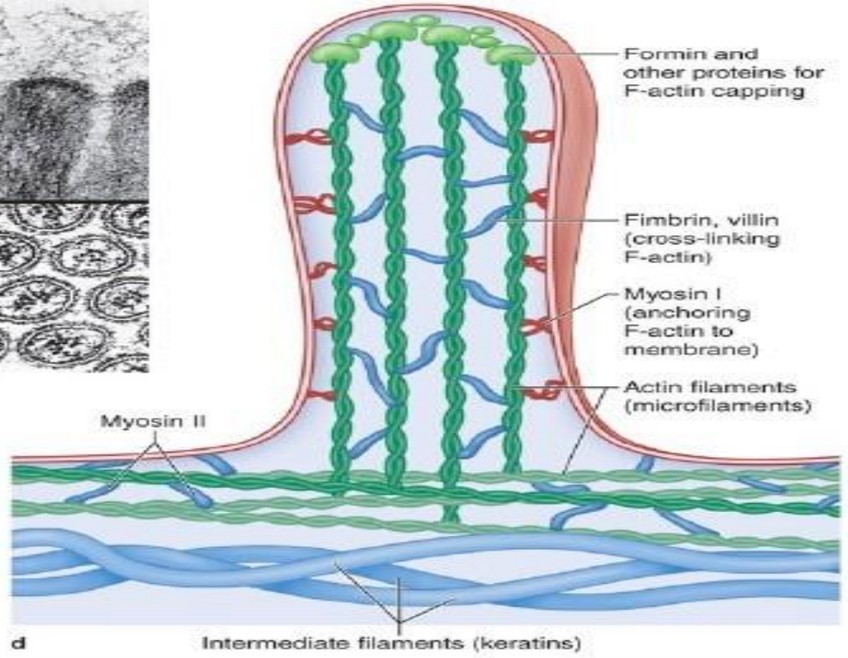


SEM



TEM

This is the core of the microvilli and the various binding or linking proteins



Microvilli

As you see, the microvilli are **tightly packed**, appearing as if they project from every single area in the apical region of the epithelium.

The core of microvilli is composed of actin filaments along with capping proteins and other binding proteins that help connect actin filaments to other molecules.

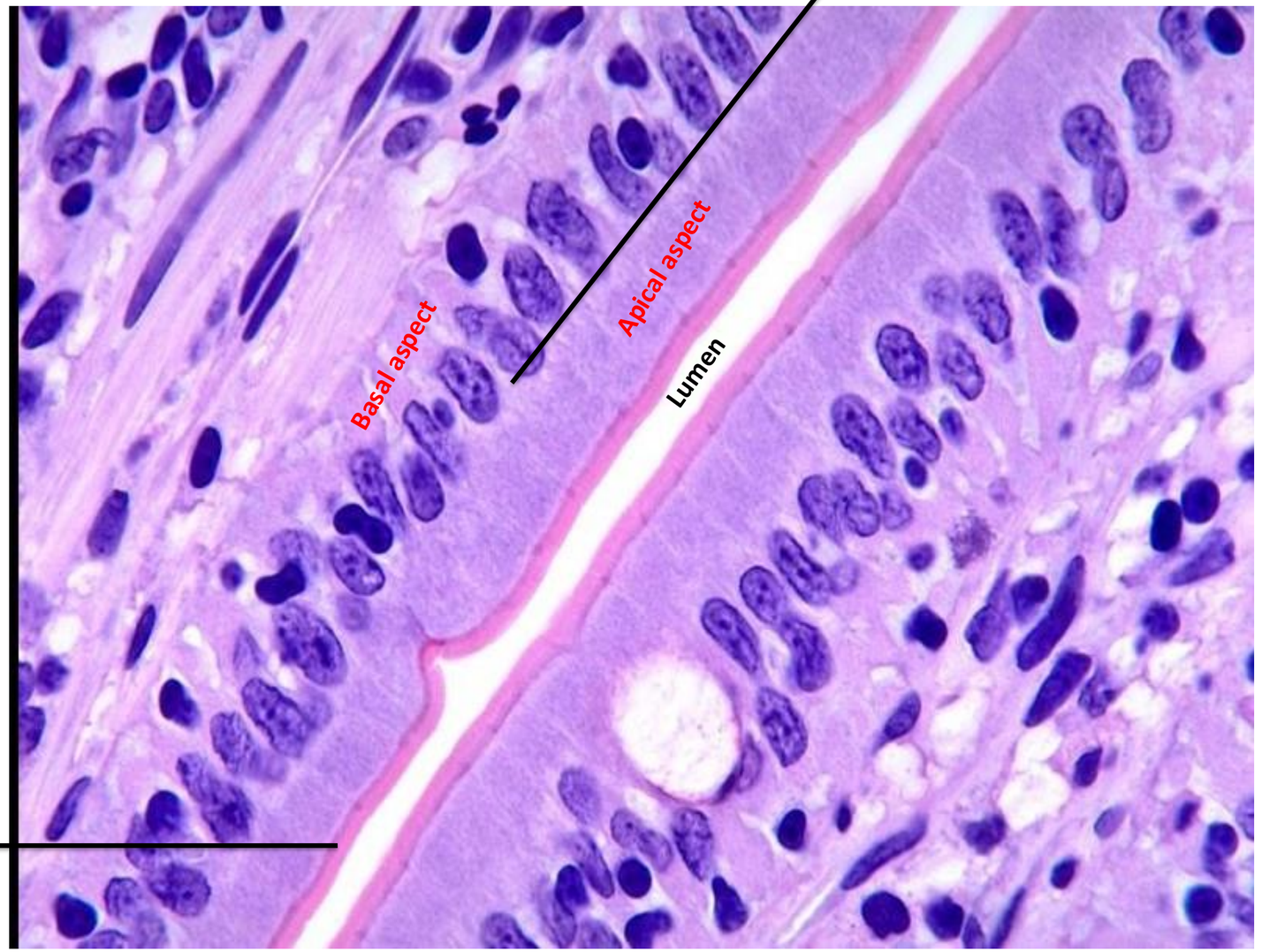
- ***Functions of Microvilli:***
- ***Increase surface area***
- ***Absorption.***

Why does it hold its shape? Why is it steady? Because of the presence of internal support.

Microvilli

This is a hematoxylin and eosin stain , and the image was acquired by a bright field light microscope.

This is simple epithelium because we have one row of cells



Microvilli are usually on the apical surface, and here they are actually represented by this dark pink color.

Cilia

- **Motile cytoplasmic hair like projections capable of moving fluid and particles along epithelial surfaces.**
- **Line cells in the respiratory organs, uterine tubes, and efferent ducts in testes.**
- **They move rhythmically and rapidly in one direction. (motor protein).**
- **Abundant on cuboidal or columnar cells**
- **Each cilium has a core structure (internal organization) consisting of nine peripheral microtubule doublets arrayed around two central microtubules---9 + 2 assembly---is called an axoneme**

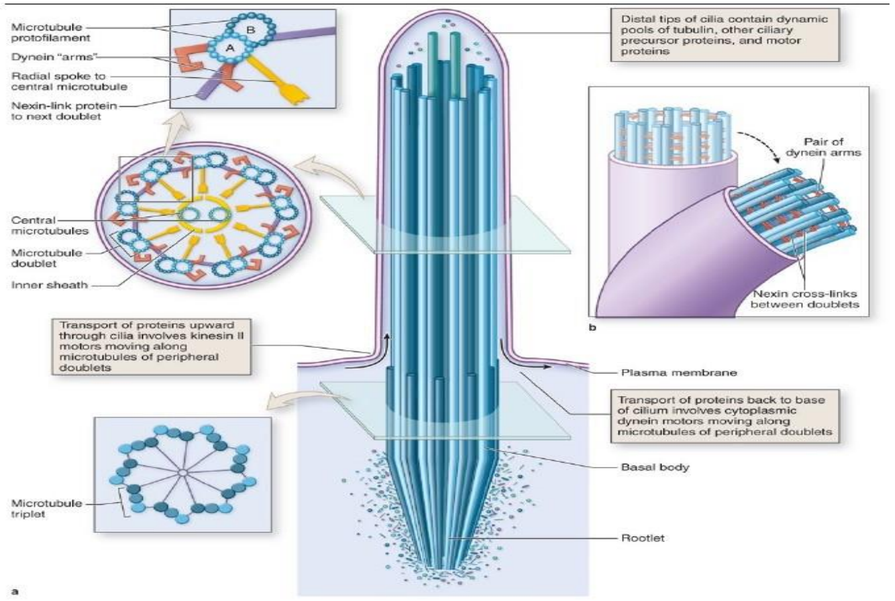
Cilia are significantly longer than Microvilli. Their core structure is different from that of Microvilli, and their function also differs. The primary function of Microvilli is to increase the surface area for absorption, whereas Cilia are primarily involved in motility. Microvilli are immotile and remain stationary for absorption, whereas Cilia are equipped with motor proteins that facilitate their movement.

We usually find cilia in the respiratory tract, as well as in the female and male reproductive tracts. In the respiratory system, cilia are located on the apical surface of epithelial cells, playing a crucial role in clearing mucus. This mucus serves an important function, but when it becomes old and loaded with unnecessary molecules, it must be expelled. The movement of the cilia helps the body remove the old mucus, allowing new mucus produced by the cells to replace it.

In the female reproductive system, cilia in the uterine (fallopian) tubes facilitate the movement of the ovum, helping to push it toward the uterus after ovulation.

CILIA

- **A microtubule** of the doublet is composed of **13tubulin dimers** arranged in a side-by-side configuration.
- **B microtubule** is composed of **10 tubulin dimers** and shares the remaining dimers with those of the A microtubule.
- The **dynein arms** extend from the **A microtubule** and make temporary cross-bridges with the **B microtubule** of the adjacent doublet.
- The basal body is anchored by the striated rootlet within the cell cytoplasm.
- A cross section of the basal body shows the arrangement of nine microtubule triplets.



When looking at the central microtubules, you can see what is called the inner sheath, which surrounds the single microtubules. The doublets are connected to this sheath through what is called the radial spoke.

When we look at the cross-section of a cilium, we can see both its external and central aspects. The external aspect is primarily composed of microtubules, which are arranged in pairs, forming nine doublets. In the center, there are two single microtubules.

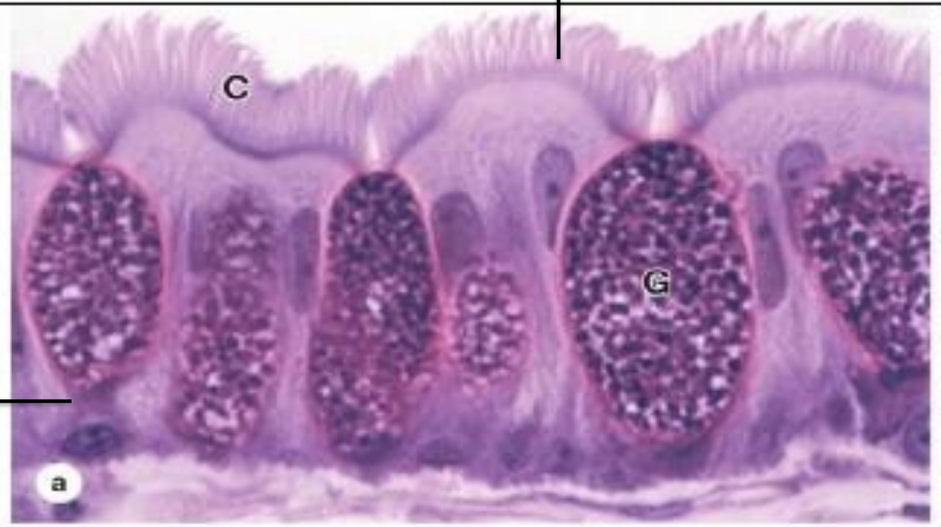
Each doublet consists of microtubule (A)and microtubule (B), which are bonded together. Extending from microtubule A are the dynein arms, which play a crucial role in initiating movement. These dynein arms are the sites where ATP is utilized, providing the energy required for ciliary motion.

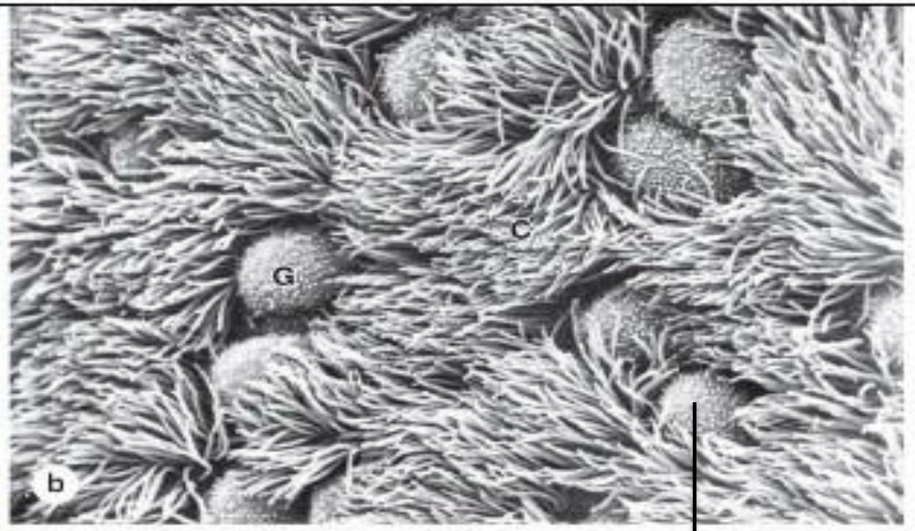
The dynein arms extending from microtubule(A) attach to microtubule(B)of the adjacent doublet. Their attachment changes dynamically depending on the motion required. However, cilia typically move in one direction only.

- In the respiratory tract, cilia beat upward, facilitating the clearance of old mucus.
- In the female reproductive tract, cilia beat toward the uterus, helping to transport the ovum to its final destination, the uterus.

Cilia

Stained by haematoxylin and eosin



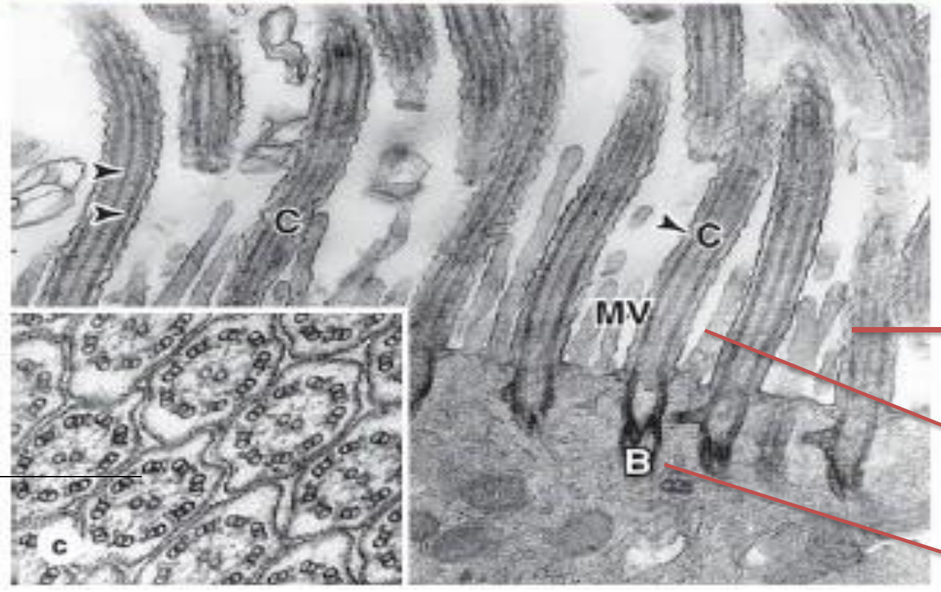


This is a goblet cell, which is responsible for producing mucus that will be secreted and will cover the apical surface of the epithelium.

This is done by SEM(gives 3D image),so the image is quite obvious

Those round structures represent the apical part of goblet cells, which produce mucus.

CILIA



Cilia

Microvilli

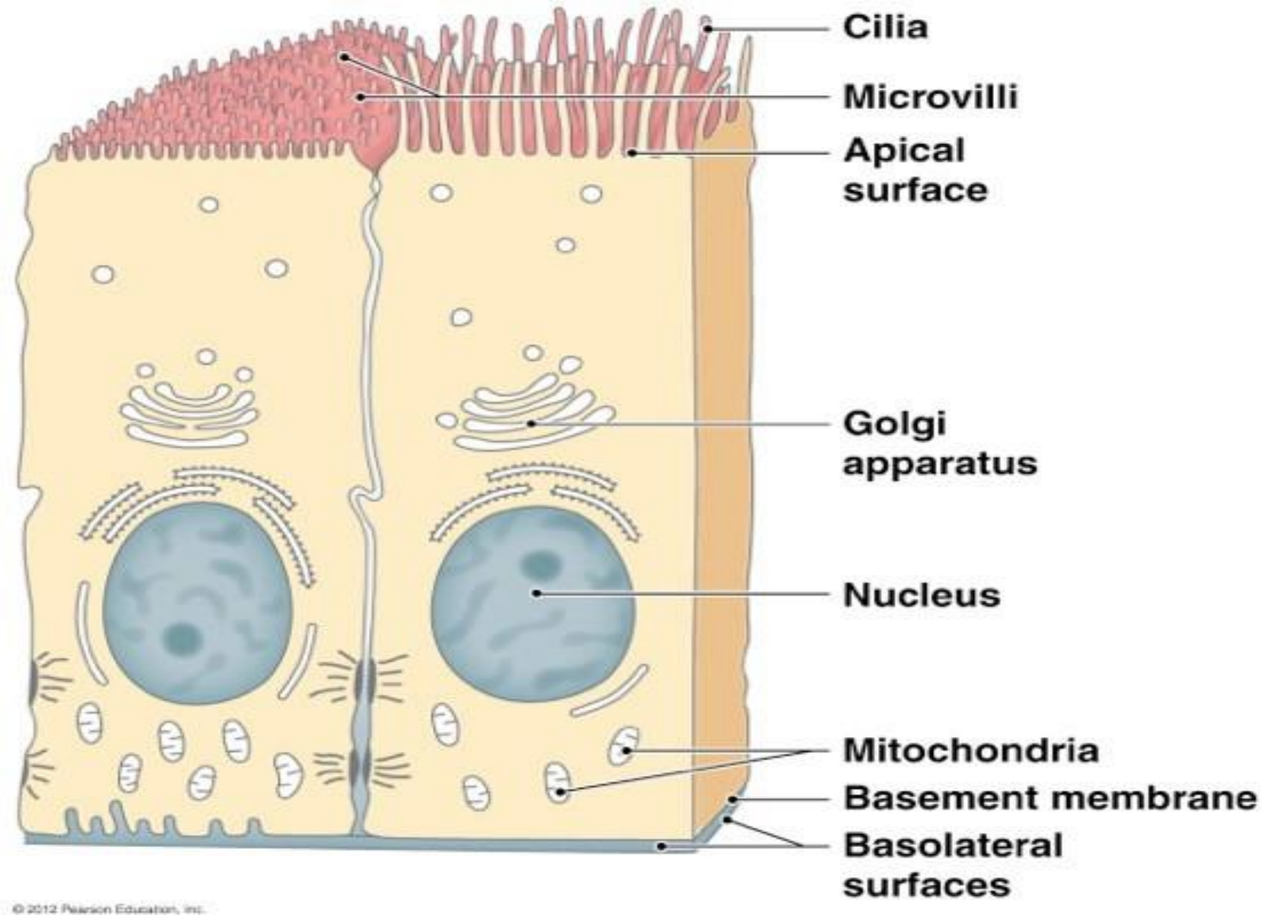
Basal body

This cross-section of the cilia shows the 9 doublets and 2 central single microtubules.

This is done by TEM (gives 2D image)

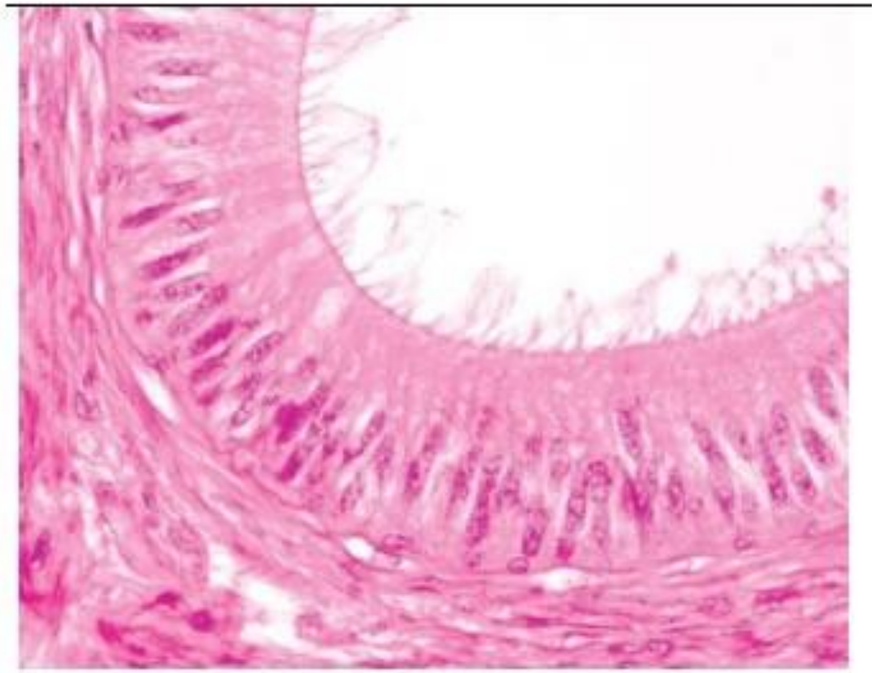
Cilia And Microvilli

This diagram shows the difference between cilia and microvilli in terms of their size.



Stereocilia are the least common type as they are not usually observed. They behave more like microvilli than typical cilia.

Stereocilia

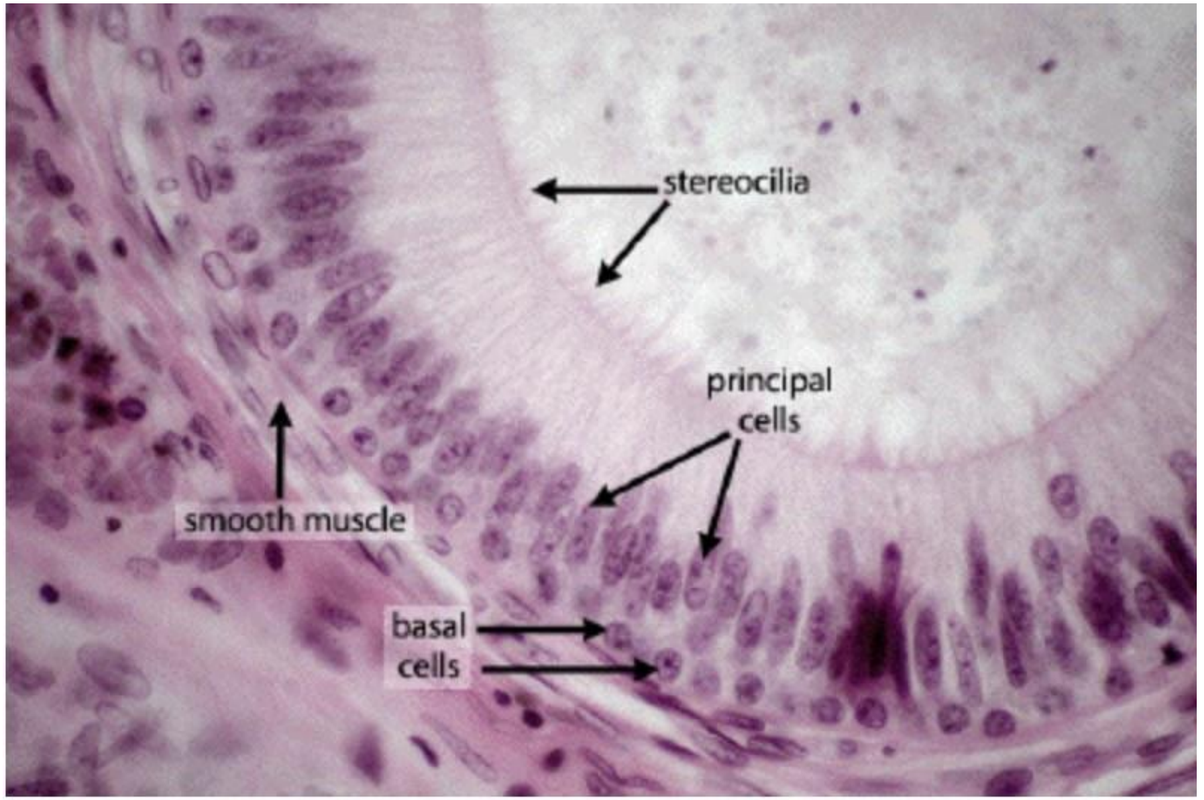


- They are similar to **microvilli** **BUT**longer.
- Branched.
- Found in epididymis and ductus deferens (males)
- They have an absorptive function.
- In the internal ear they have a sensory function—detection of motion.

-In the epididymis and ductus deferens, stereocilia function primarily to increase absorption. This is why they resemble microvilli; however, they are slightly longer and branched, whereas microvilli are not branched.

-In the inner ear, stereocilia are present on what are called hair cells, where they play a crucial role in translating mechanical stimuli into electrical signals. This process is essential for both hearing and balance (equilibrium). The ability to perceive sound and maintain balance relies on the presence of these specialized structures in the inner ear.

Stereocilia



This is in male genital tract

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			

رسالة من الفريق العلمي:

قال رسول الله ﷺ:

"ثلاثة لا ترد دعوتهم: الإمام العادل، والصائم حتى يفطر، ودعوة المظلوم"

(رواه الترمذي وابن ماجه).