بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

HISTOLOGY

﴿ وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ ﴾

Histology | Lecture 4

Epithelium pt2

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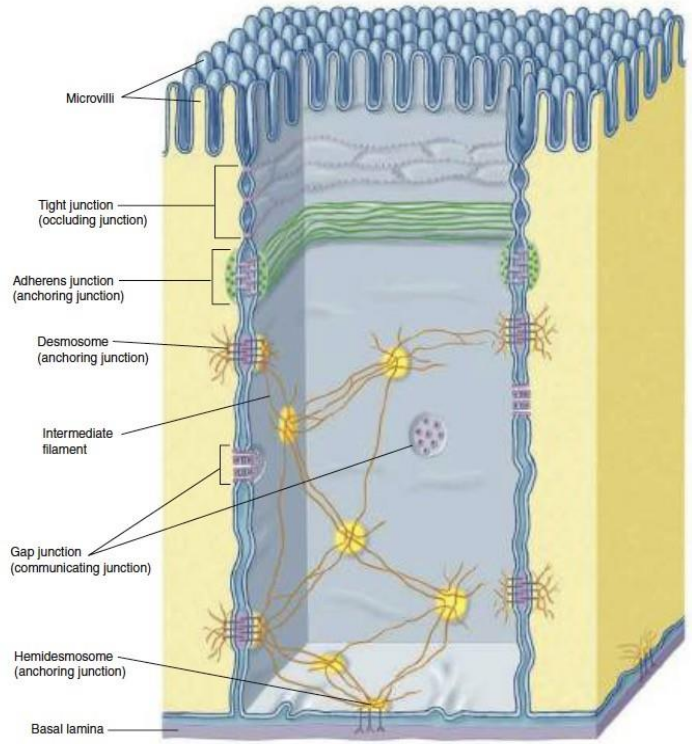
Junctional Complexes

Junctional Complexes

Recall that one of the features is that epithelial cells are well-adhered (glued) to each others which means they have strong bonding between the cells which fits the bell for being a protective tissue that prevents the passage of unwanted molecules and microorganisms and that's due to the presence of these junctions and each one has its own structure and location.

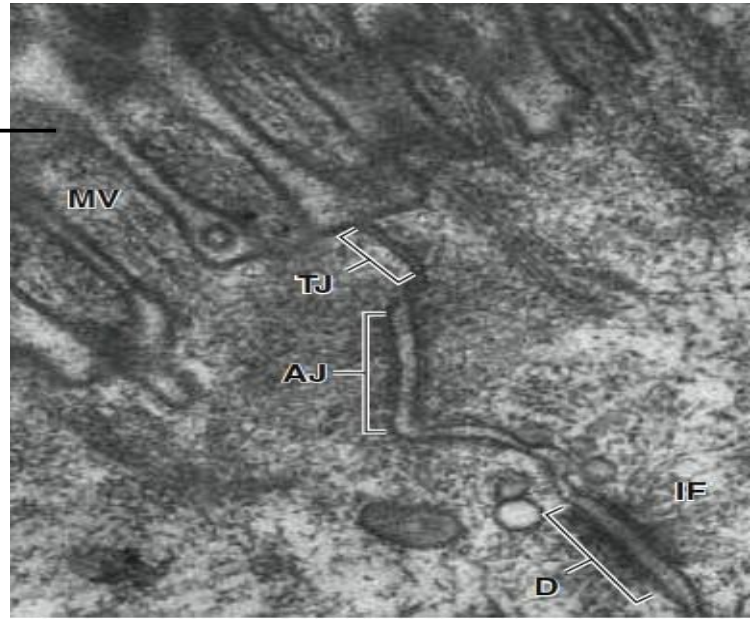
The junction complexes have an association with the cytoplasm through the cytoskeleton precisely with actin and intermediate filaments.

The epithelial cells are bound and adhere to the basil lamina due to the presence of Hemidesmosomes.



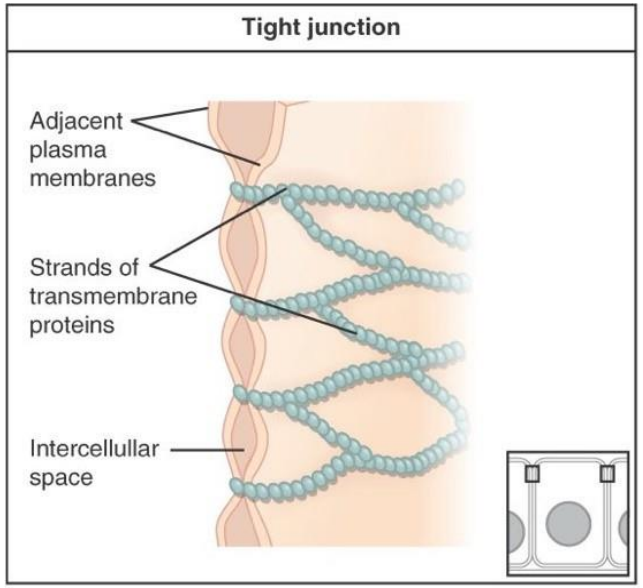
- Membrane-associated structures provide adhesion and communication between cells
- Epithelial cells adhere strongly to neighboring cells and basal laminae
- Tight or occluding junctions form a seal between adjacent cells.
- Adherent or anchoring junctions are sites of strong cell adhesion. **Pay attention to the Tight and Adherens junctions since these two members run more like a belt throughout the entire length and that's important to make sure that the cell is well separated from the external invornment.**
- Gap junctions are channels for communication between adjacent cells. **Gap junctions are more related to communication rather than adhering.**
- 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.

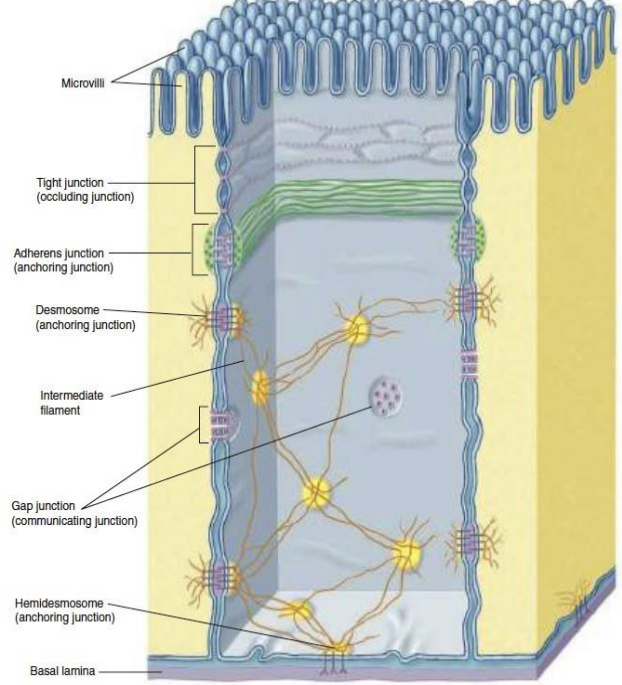
This is a TEM image (very detailed)



Tight Junction
Zonula occludens

)Belt)



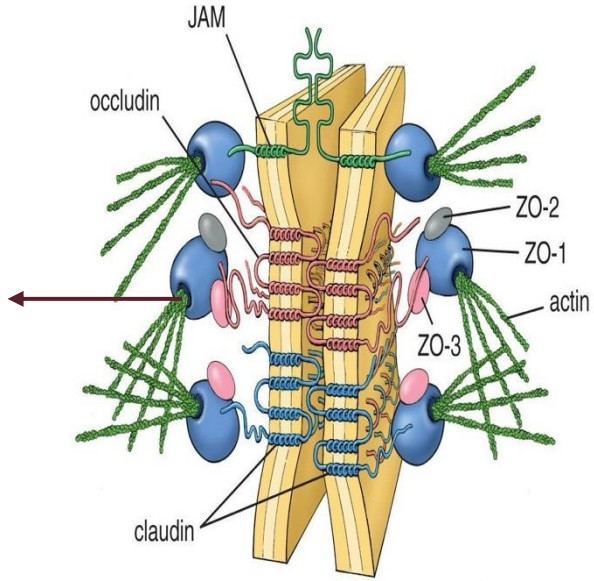


- Tight or occluding junctions form a seal between adjacent cells.
- They are the most apical

They play a major role in preventing the passage of molecules and microorganisms that attempt to gain access to the deeper structures, particularly the underlying connective tissue.

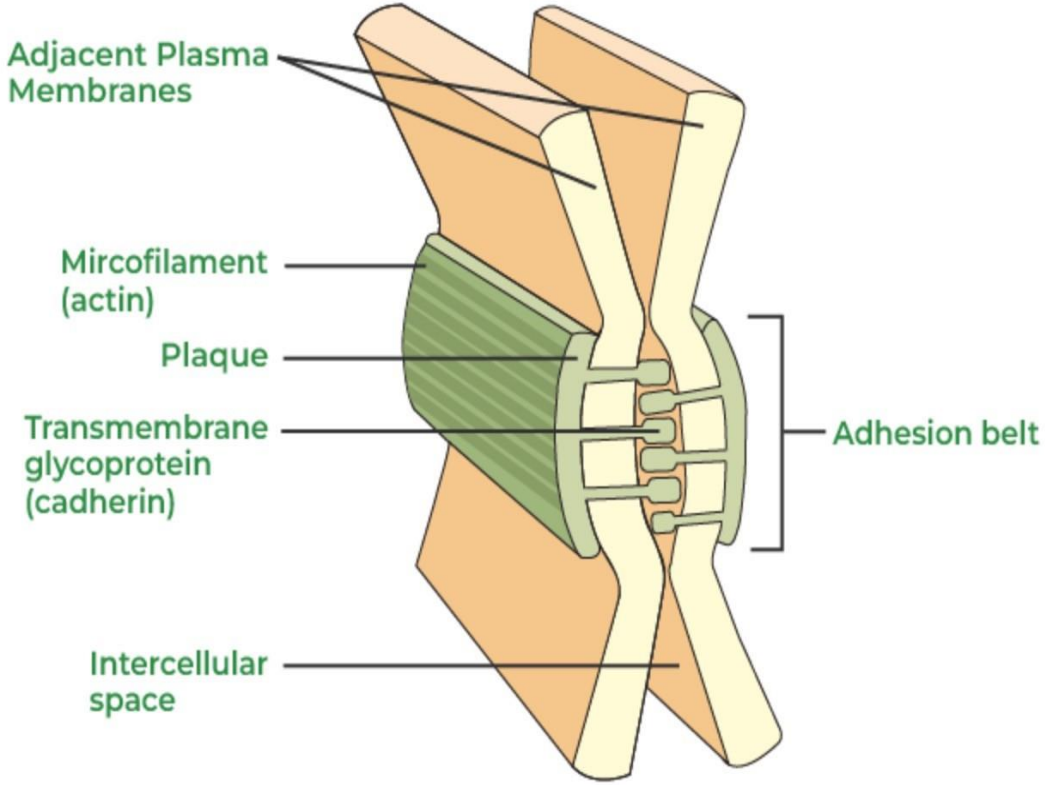
- The seal between the two cell membranes is due to tight interactions between the transmembrane proteins claudin and occludin.
- The intercellular seal of tight junctions ensures that molecules crossing an epithelium in either direction do so through transcellular route not the paracellular one .

This is a diagram that shows exactly the proteins that are presented in Tight junctions and the close approximation is due to the strong association between these proteins and these Tight junctions are associated with cytoskeleton (Actin filaments)



Adherent Junctions (Zonula Adherens)

- Encircle the epithelial cell, usually below the tight junction.
- Firmly anchoes cells to neighboring ones.
- Cell adhesion is mediated by **e-cadherin** (transmembrane glycoproteins) of each cell that bind each other in the presence of Ca^{2+}.



The transmembrane glycoproteins (Cadherin) interact with each others outside the cell then they meet providing that calcium ions enhance and maintain these interactions.

Cell adhesion in junctions is mediated by transmembrane glycoproteins such as cadherins.

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

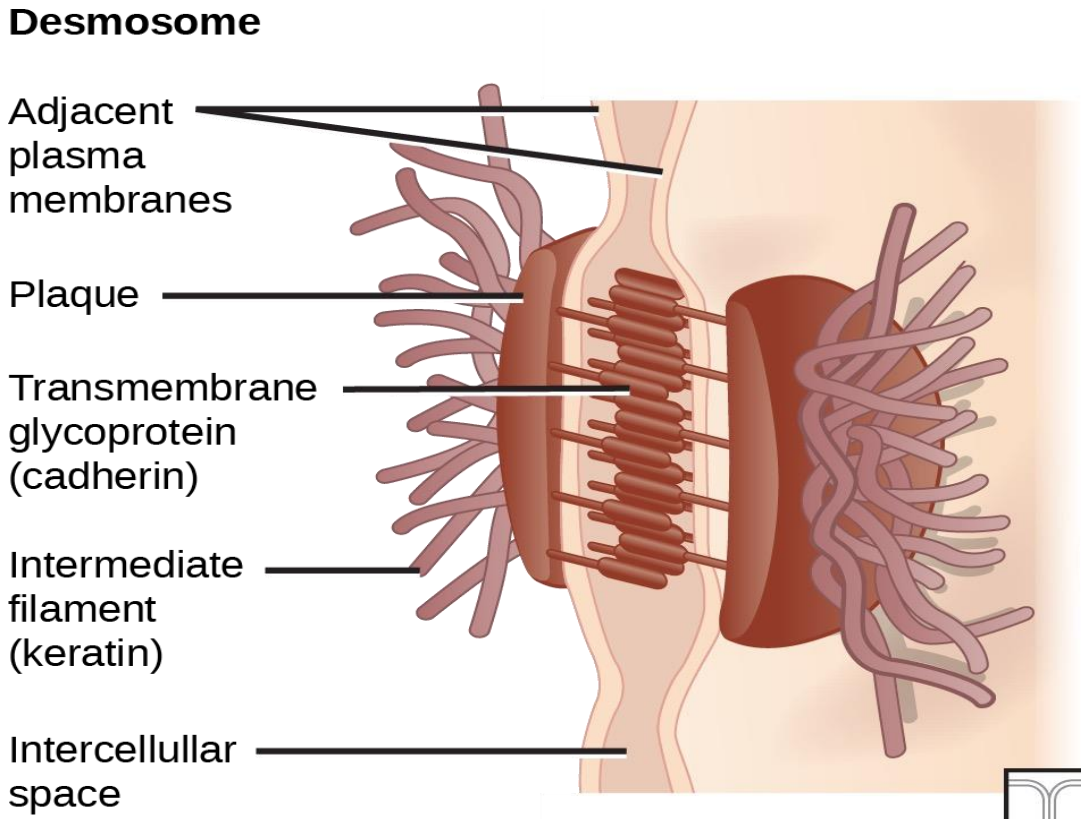
The Cadherin does not attach directly with Actin filaments)microfilaments(and that's why the catenin is existed Cadherin →Catenin →Actin filament

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

Desmosomes

One of the main difference between Desmosomes and pprevious two that it act presents as a disk shape it is not encircle a whole with the entire length of the epithelial membrane.

- **Disc-shaped** structures that are matched with identical structures at an adjacent cell surface
- Desmosomes contain larger members of the cadherin family called desmogleins and desmocollins.
- The cytoplasmic ends of these transmembrane proteins bind a catenin-like protein which bind intermediate filament proteins rather than actins.



The associations are quite strong and we see it under electron microscope EM as a very dense patch.

Although the discs are localized ,the proteins are large so they do enhance significantly to the attachment and the adhering the lateral two membranes

These interactions are mediated by cadherin like proteins .

Gap Junctions

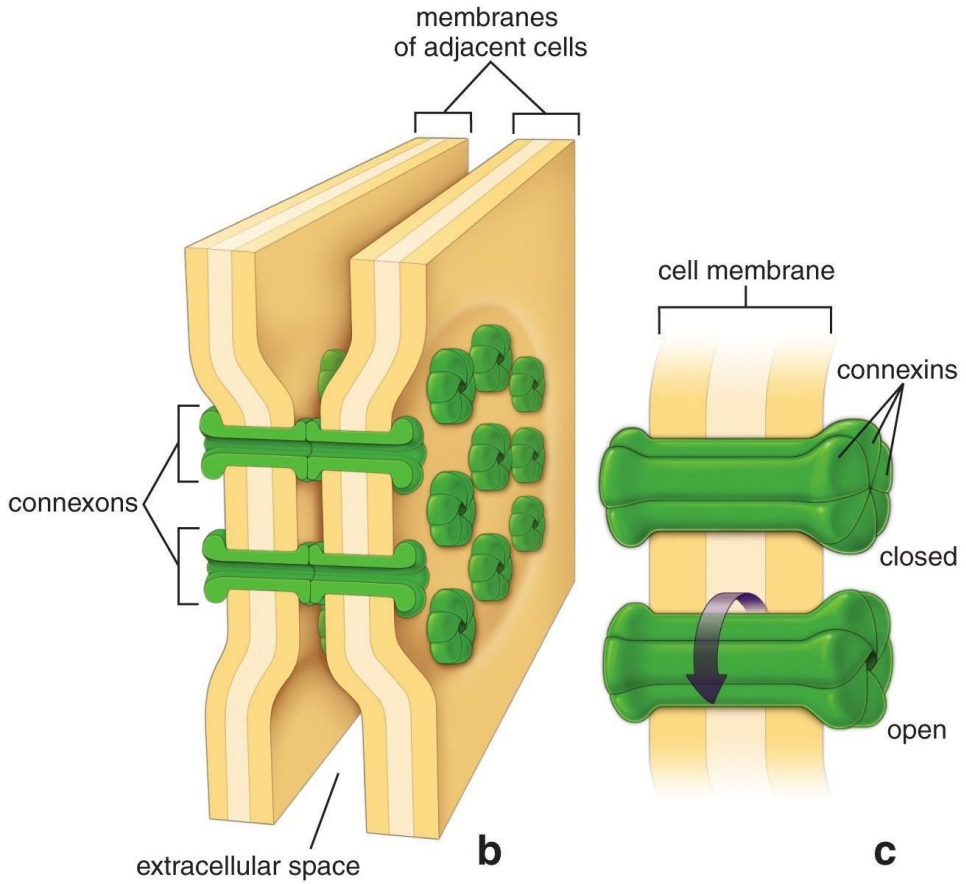
They do have proteins that participate in the adhesion, but the communication seems to be more of priority than the adhesion.

This type of junction is different from the previous ones because its main function is more into communication.

- Mediate intercellular communication.
- 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.

it has a hydrophilic channel thus it transfers extremely small (smaller than its diameter) hydrophilic molecules

- Permit intercellular exchange of molecules with small molecules < 1.5 nm in diameters.

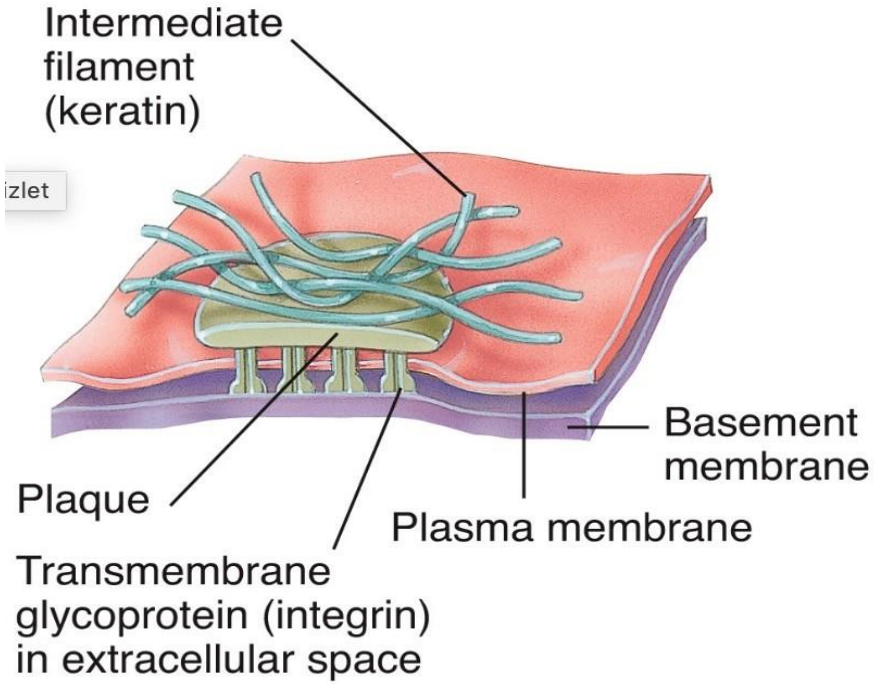


Half

Hemidesmosomes

There are some differences between Desmosomes and Hemidemosomes,it is smiliar to the Desmosomes in attaching to the intermediate filaments ,but they didn't use Cadherin for the associations with proteins in the basement membrane just like Desmosomes instead it has integrant.

- 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.
- 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

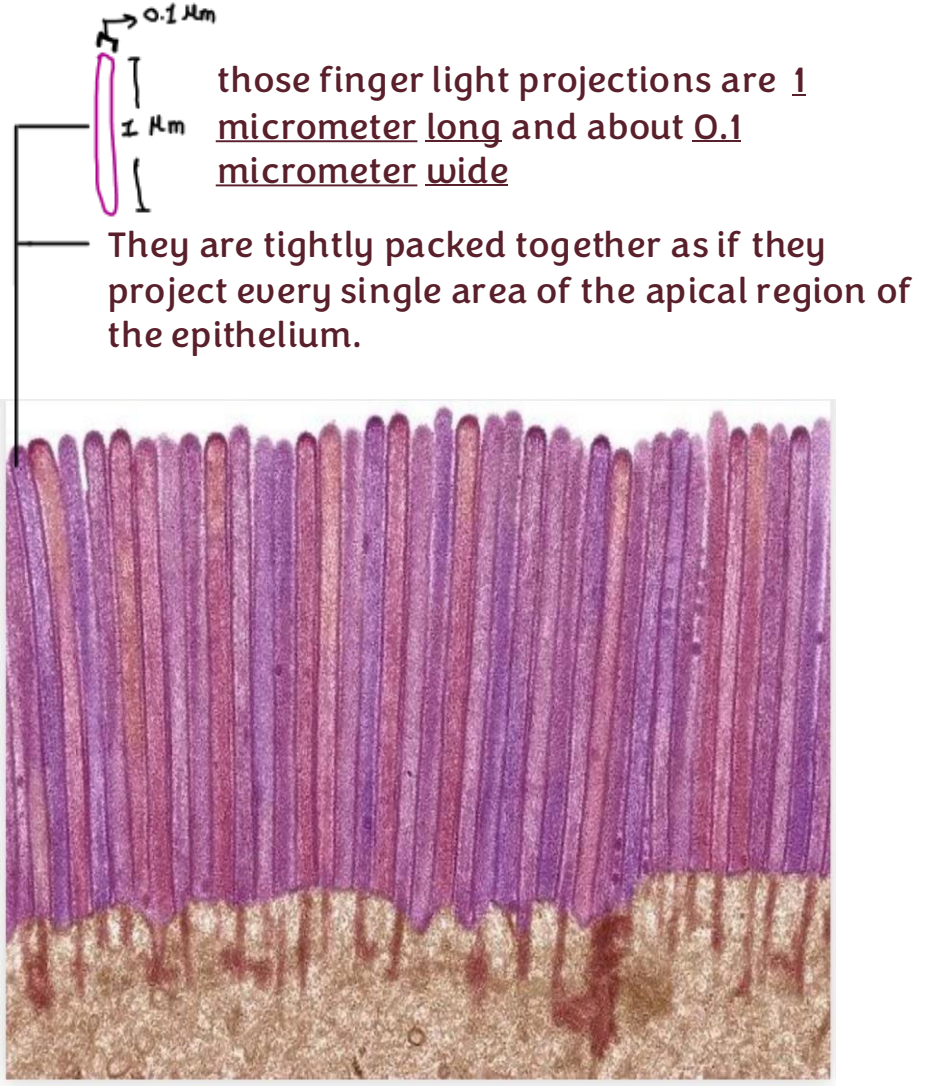
This condition is quite nasty and luckily I is quite rare ,patients suffer from skin blistering because simply the epithelium will not stay on its place because there is something wrong with the integrin and their skin will be filled in fluids

Specialized apical structures

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

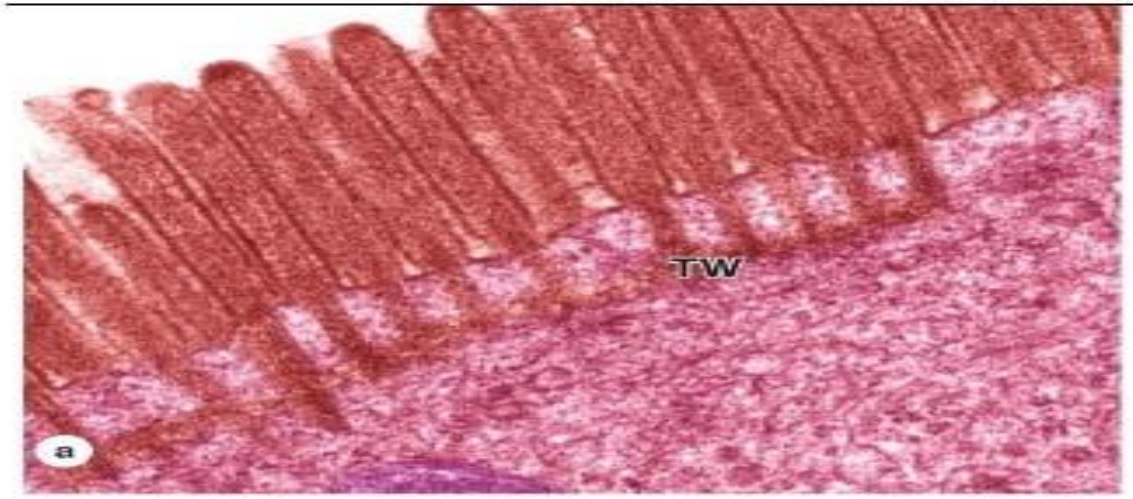
  - Microvilli
  - Cilia
  - Stereocilia

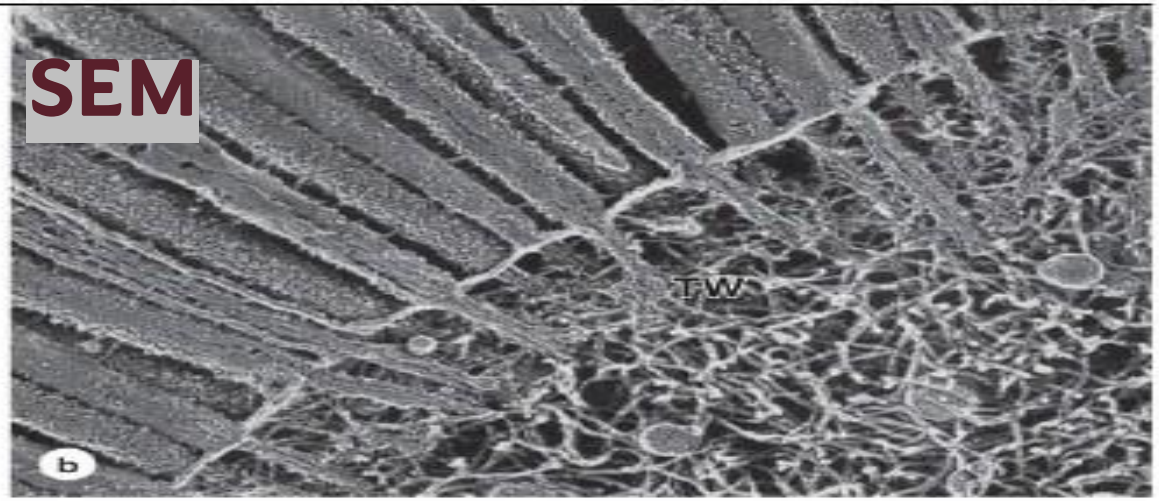
Microvilli

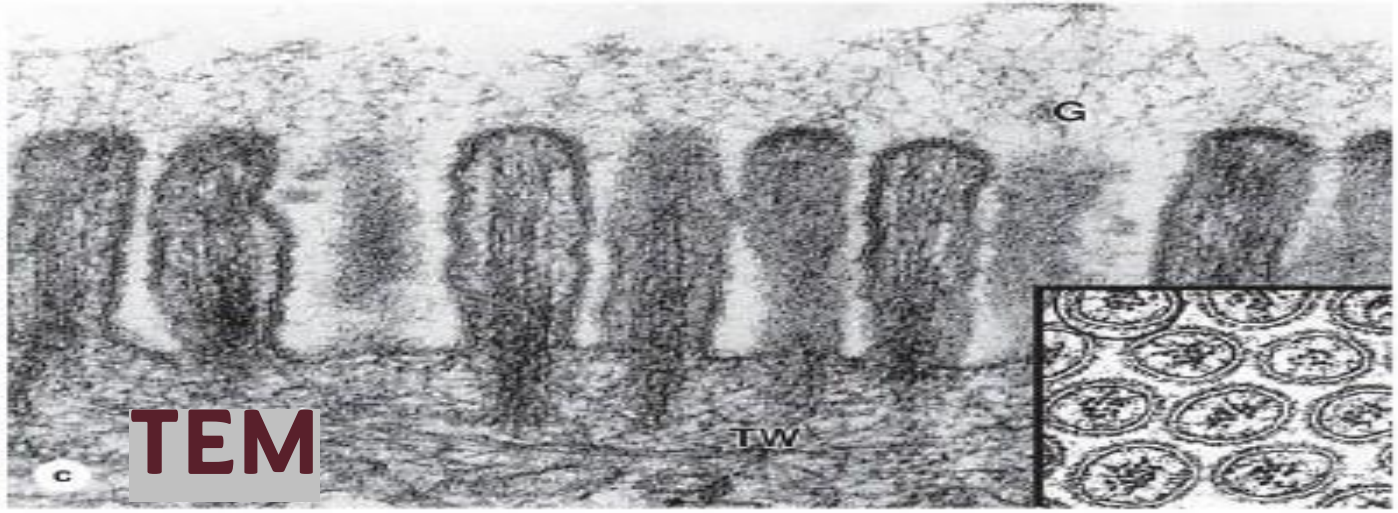


- Finger-like extensions of plasma membrane of apical epithelial cell.
- Contains bundled actin filaments capped and bound to the surrounding plasma membrane by actin binding proteins
- Present mainly in **absorptive cells (columnar (usually)/cuboidal(sometimes)**.
- Main function is the absorption of nutrients from intestines and glomerular filtrate: Striated border in the intestine. Brush border in the kidney).
- **Increase the surface area for absorption.**

(it increase the efficiency of the absorption, as if it only have this flat plasma membrane area, it would not be enough -not efficient- when we need it. This function appears highly in the small intestine or certain parts of the kidney, microvilli play a crucial role in reabsorbing essential nutrients that have been filtered.)

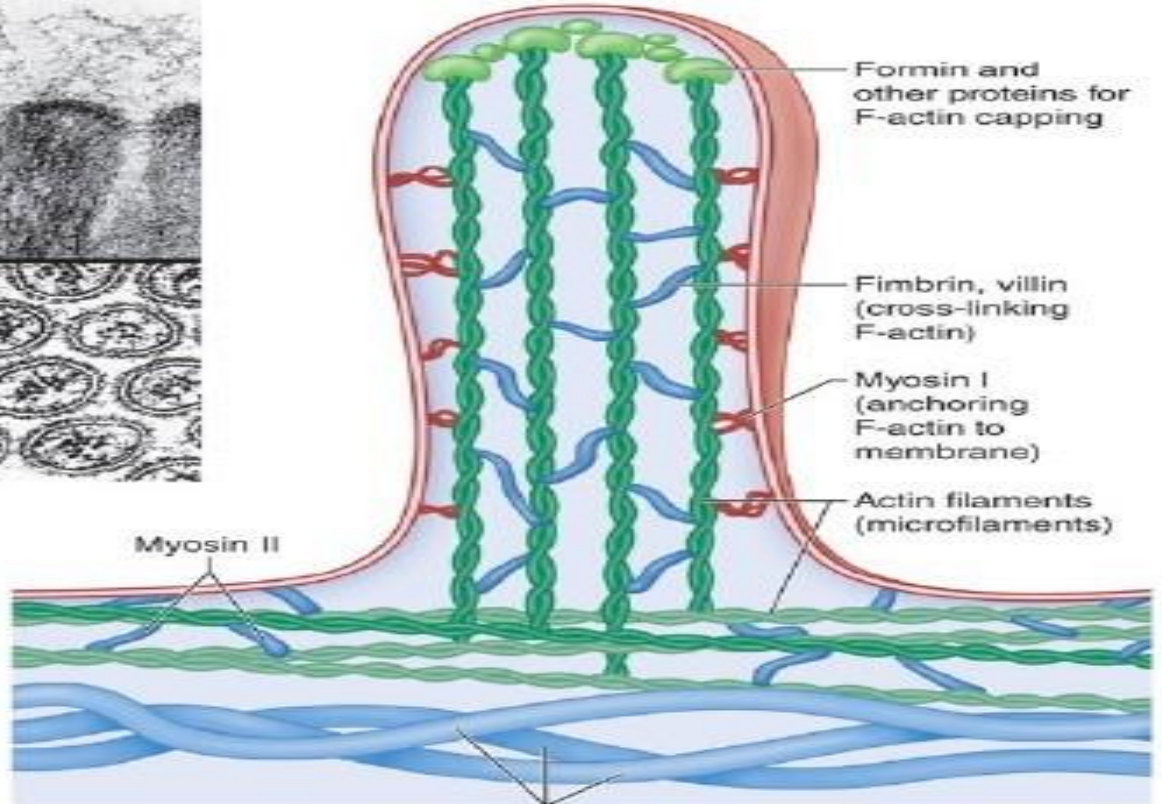




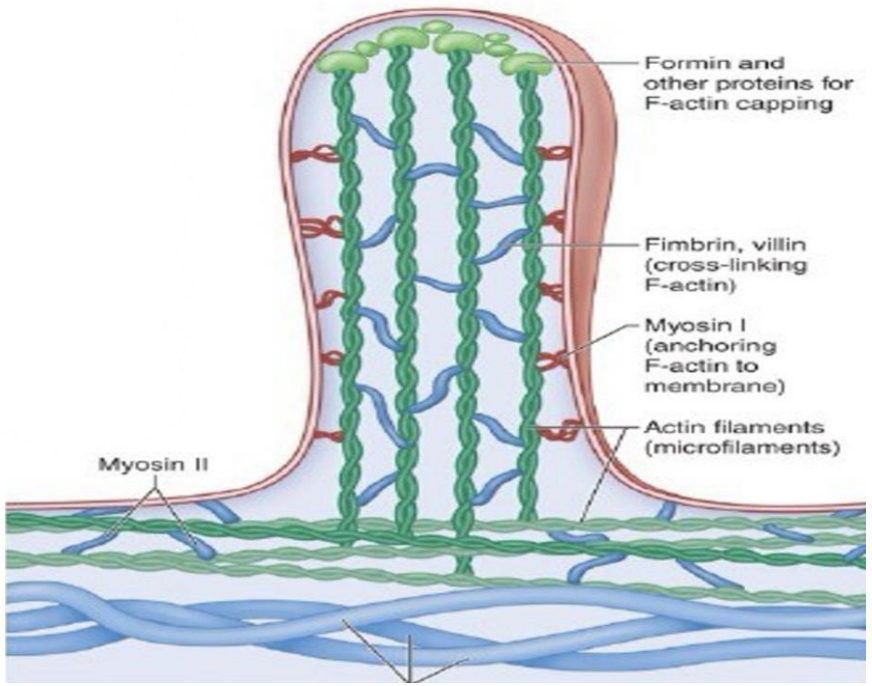


Microvilli

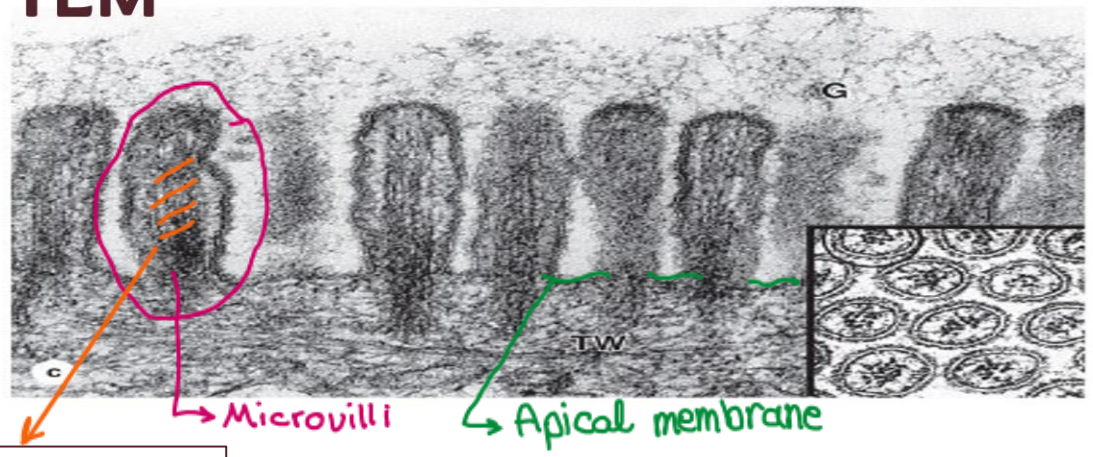
- Increase surface area
- Absorption.



This is how the structure of microvilli looks like



TEM



The core of it and the various binding or linking proteins

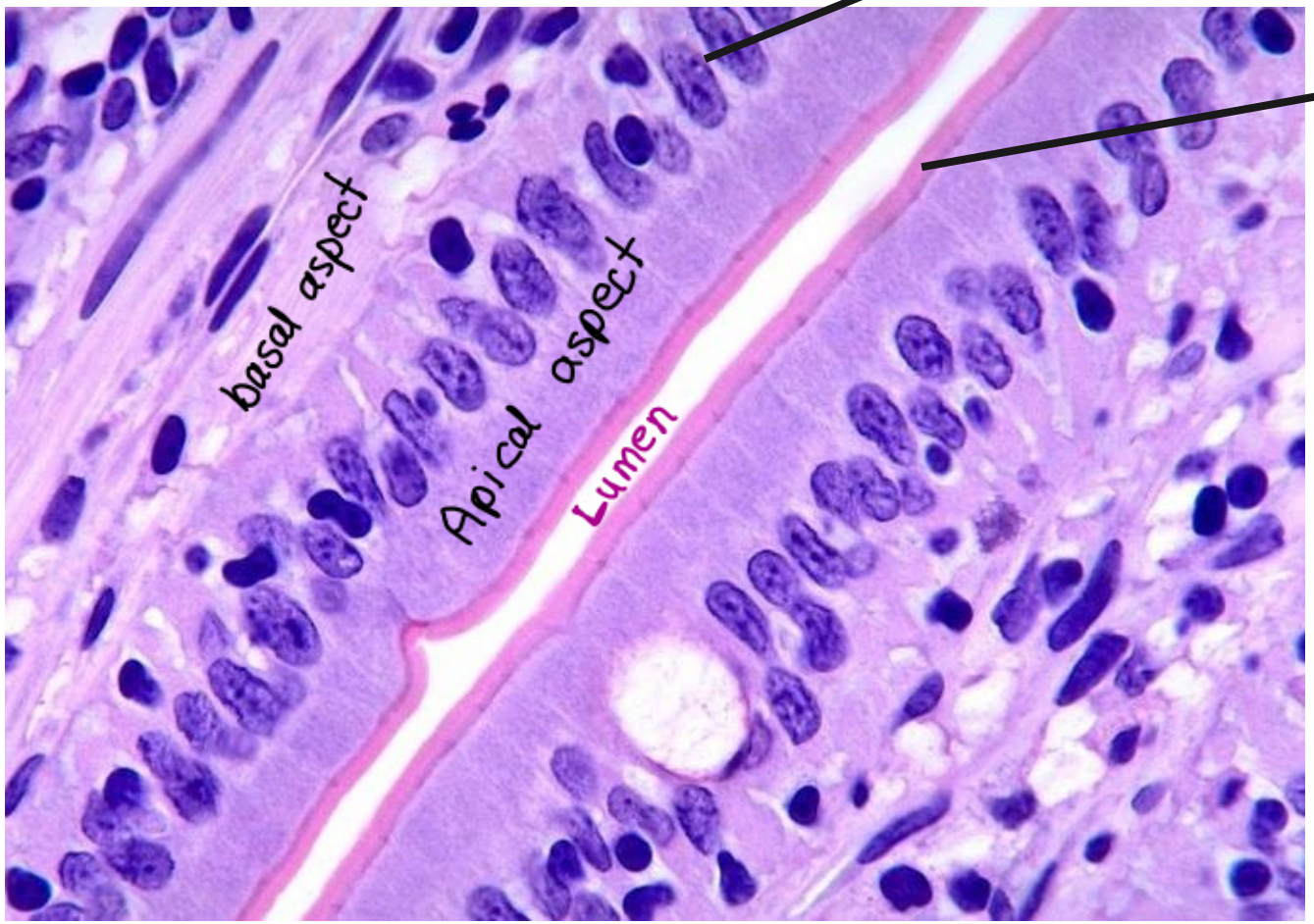
Because of the presence of internal support the shape is hold and the microvilli is stead.

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.

Microvilli

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.



This image was taken by *a-bright field light microscope*

H&E stain is used

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**

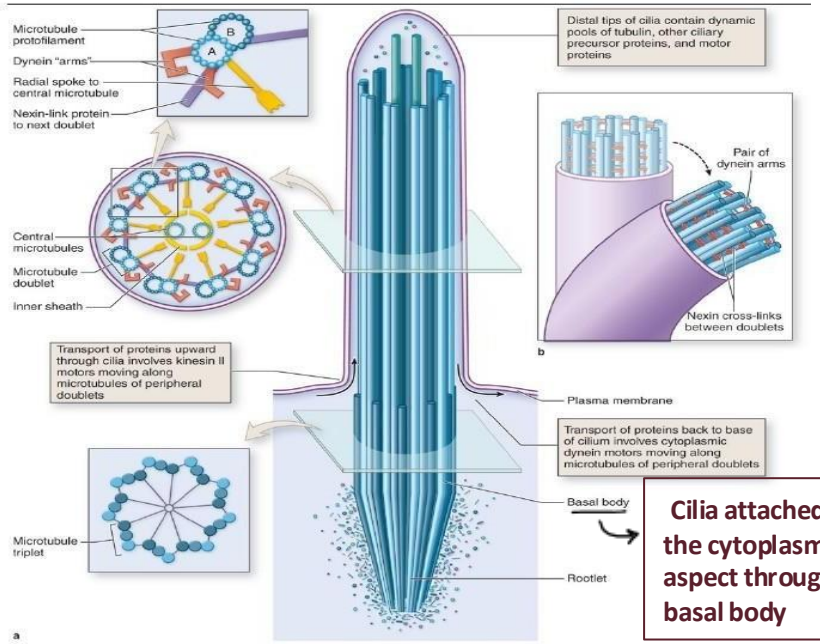
Cilia are significantly longer than Microvilli. Their core structure is different from that of Microvilli, and their function also differs. The primary function of Microvilli is to increase the surface area for absorption, whereas Cilia are primarily involved in motility. Microvilli are immotile and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

- **Amicrotubule** 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 Amicrotubule.
- The **dynein arms** extend from the **Amicrotubule** 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.
- Across section of the basal body shows the arrangement of nine microtubule triplets.



Cilia attached on the cytoplasmic aspect through the basal body

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.

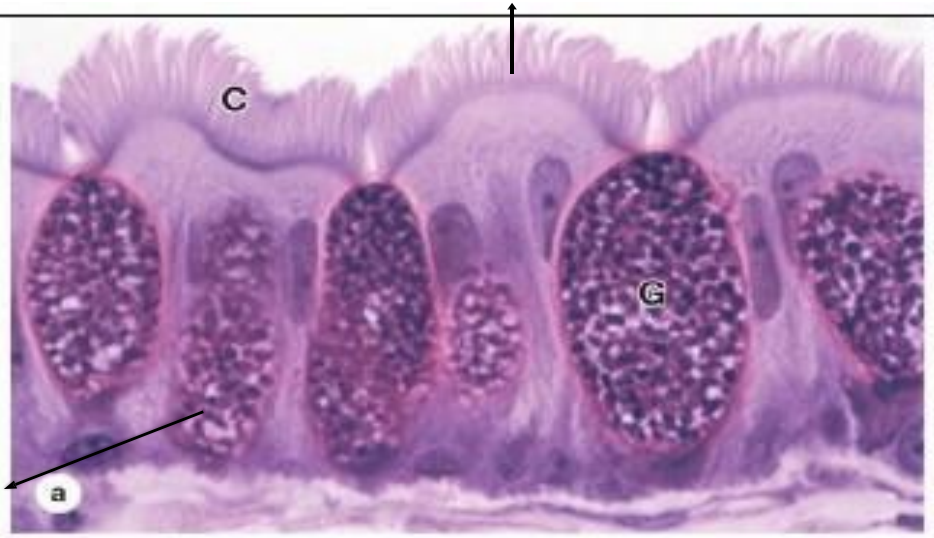
Each doublet consists of microtubule (A)and microtubule (B), which are bonded together. Extending from microtubule A are the dynein arms, which play a crucial role in initiating movement. These dynein arms are the sites where ATP is utilized, providing the energy required for ciliary motion.

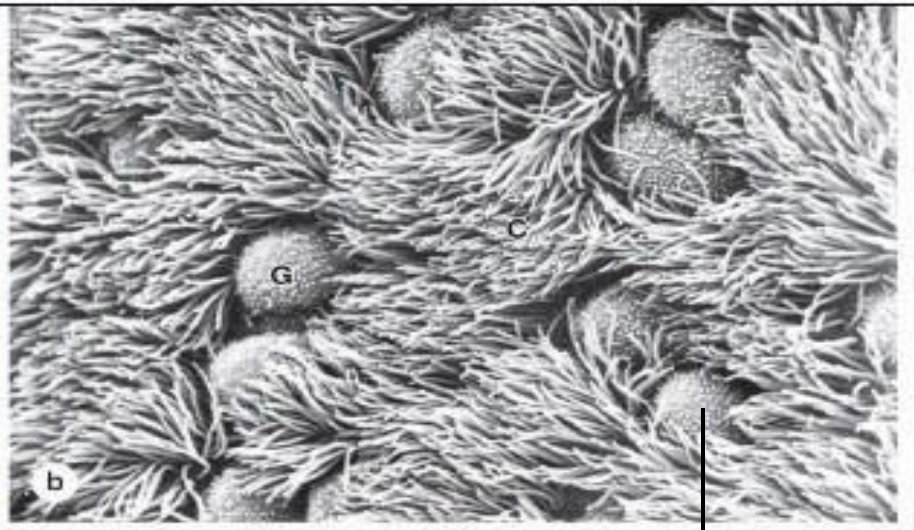
The dynein arms extending from microtubule(A) attach to microtubule(B)of the adjacent doublet. Their attachment changes dynamically depending on the motion required. However, cilia typically move in one direction only.

- 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 H&E

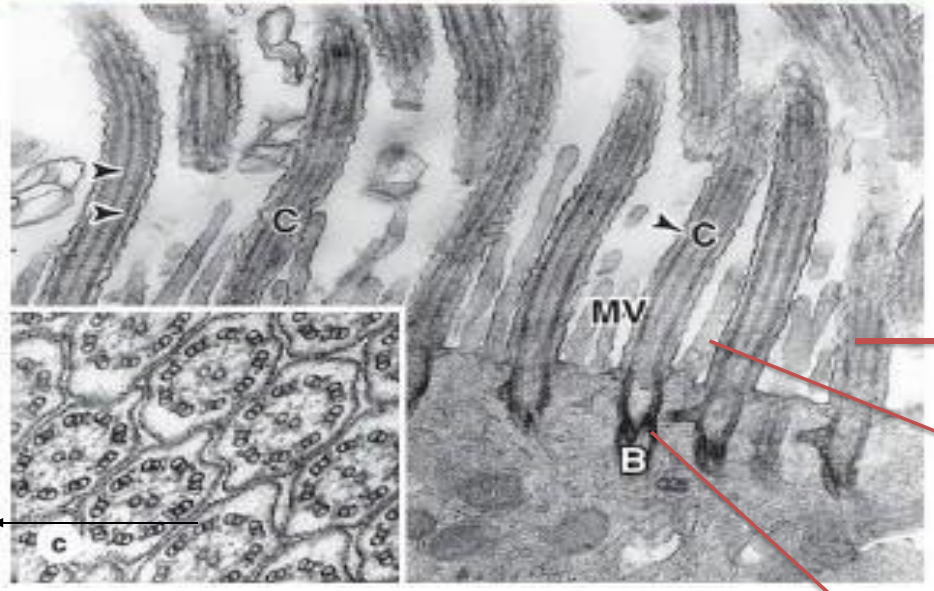




This is a goblet cell, which is responsible for producing mucus that will be secreted and will cover the apical surface of the epithelium.

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

Microvilli

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

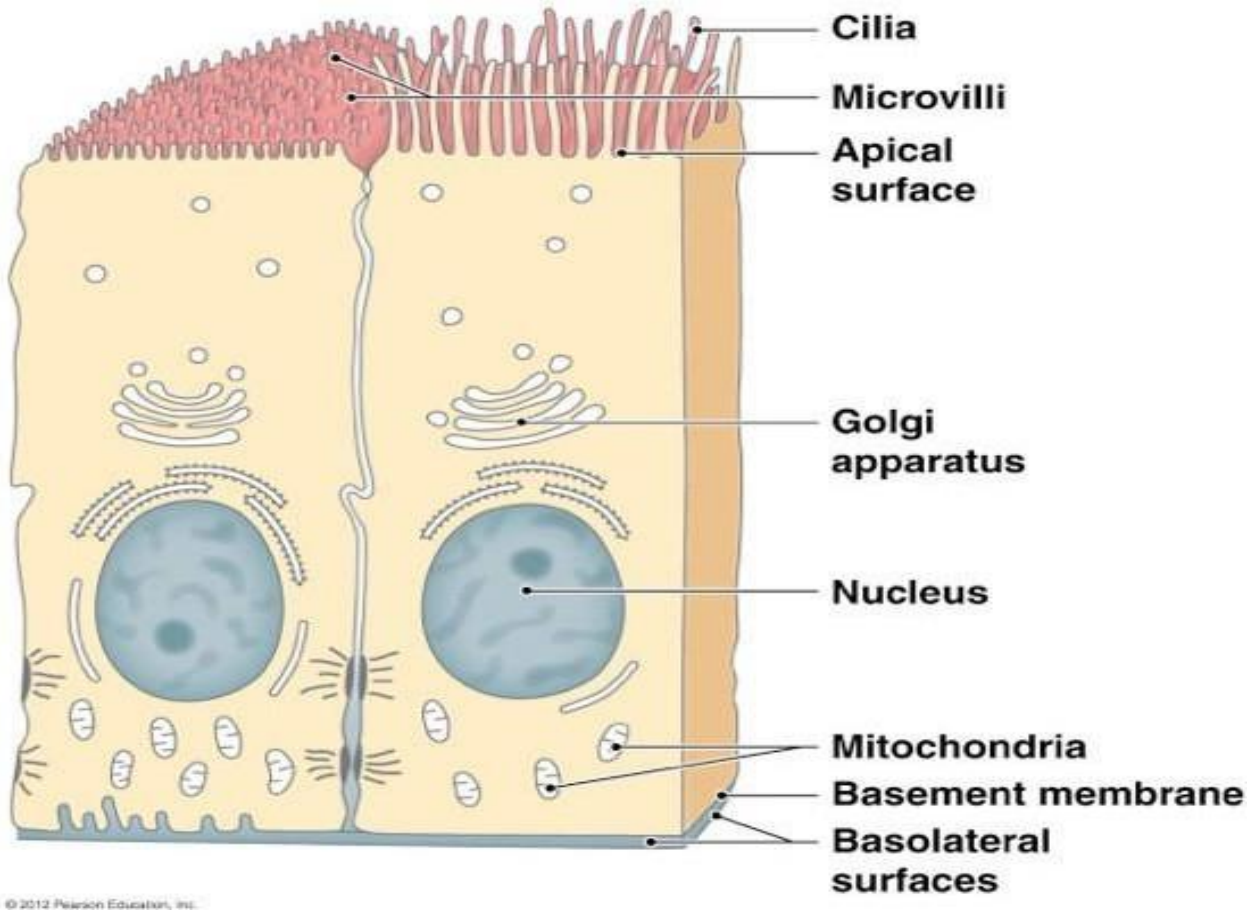
** notice the difference in length and width
Cilia is longer

This is done by TEM (gives 2D image)

Basal body

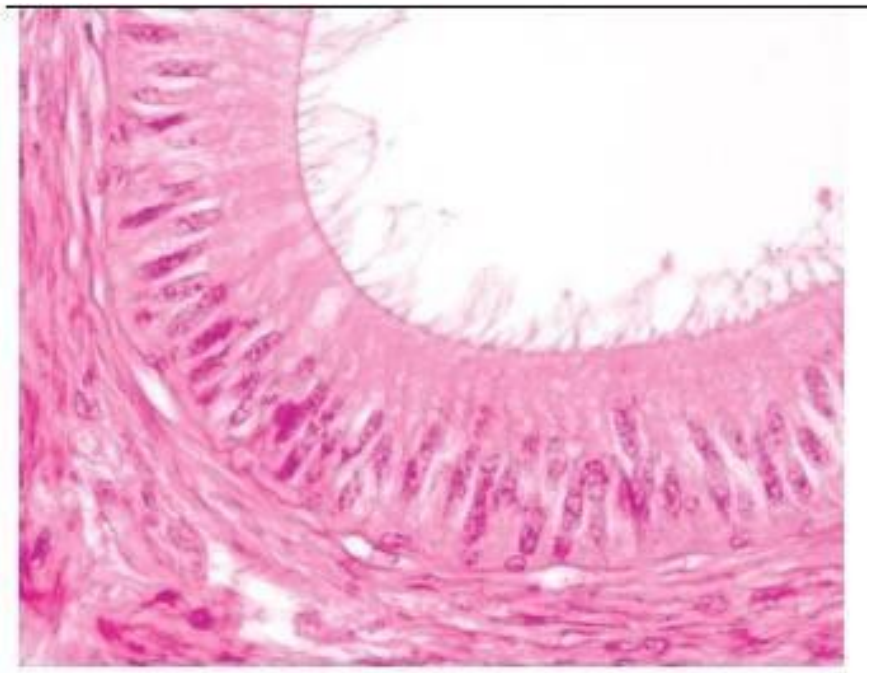
Cilia And Microvilli

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



Stereocilia

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

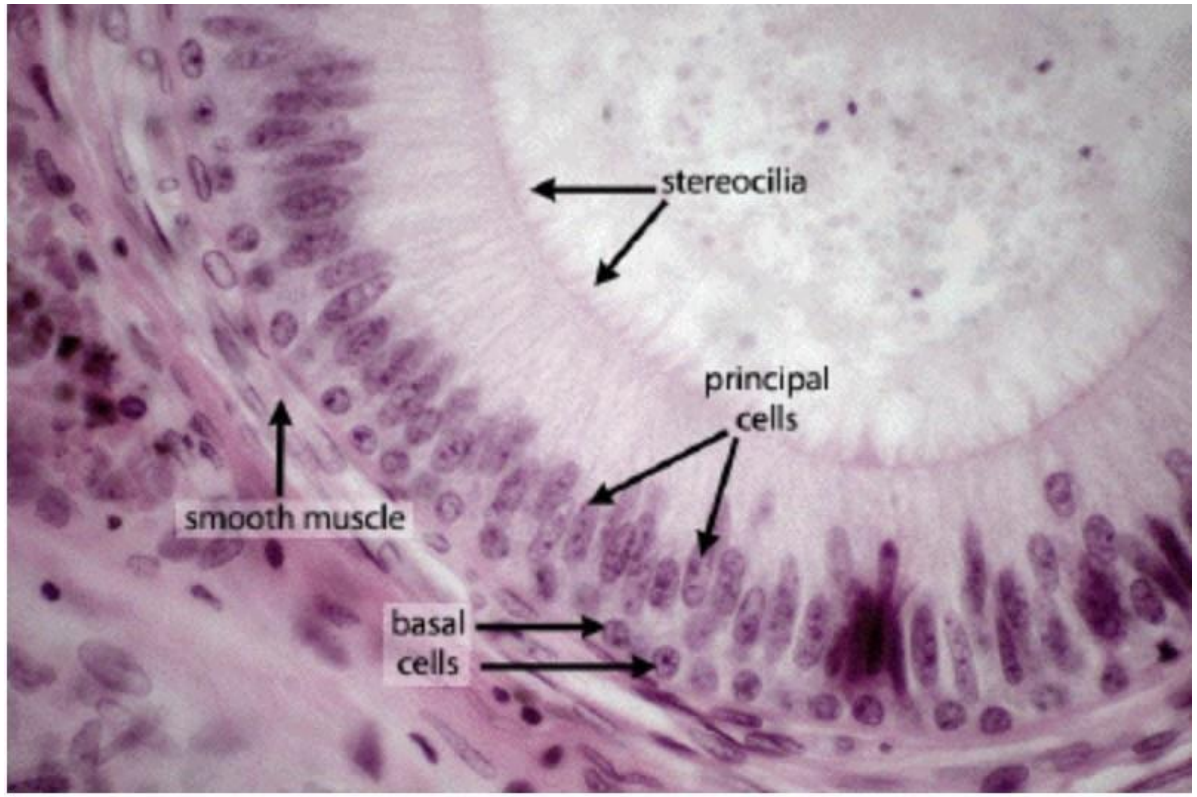


- They are similar to **microvilli BUT** longer.
- Branched.
- Contains array of microfilaments and acting-binding proteins.
- Found in epididymis and ductus deferens (males)
- They have an absorptive function.
- In the internal ear they have a sensory function—detection of motion.

-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 stimulation 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			

Additional Resources:

رسالة من الفريق العلمي:

ولَقَدۡ ءَاتَيۡنَا دَاوُۥدَ وَسُلَيۡمَٰنَ عِلۡمٗاۖ وَقَالَا ٱلۡحَمۡدُ لِلَّهِ ٱلَّذِي فَضَّلَنَا عَلَىٰ كَثِيرٖ مِّنۡ عِبَادِهِ ٱلۡمُؤۡمِنِينَ (15) وَوَرِثَ سُلَيۡمَٰنُ دَاوُۥدَۖ وَقَالَ يَٰٓأَيُّهَا ٱلنَّاسُ عُلِّمۡنَا مَنطِقَ ٱلطَّيۡرِ وَأُوتِينَا مِن كُلِّ شَيۡءٍۖ إِنَّ هَٰذَا لَهُوَ ٱلۡفَضۡلُ ٱلۡمُبِينُ (16)

سورة النمل

Reference Used:
(numbered in order as cited in the text)

1. ***Dr. Ghada Abu Al-Ghanem's lecture***