

## ANATOMY / HISTOLOGY

☒ Sheet

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Number

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Subject

Histology of the respiratory tract

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Price:

**Note: it is important that you refer to the slides.**

➤ **Introduction**

- The respiratory system is divided into two parts, one that conducts the air through the respiratory tract and links the lungs to the external environment, the so-called conducting zone, and another that exchanges oxygen and carbon dioxide with the blood, the so-called respiratory zone.
- The main function of the lung is to exchange gases. This function occurs in the respiratory zone. However, the conducting zone is essential for warming, cleansing and moisturizing the inspired air.

➤ **Conducting Zone:**

- Nose, nasopharynx, larynx, trachea, bronchi, bronchioles and terminal bronchioles.
- The bronchi are divided into primary bronchi, which are extrapulmonary, and secondary and tertiary bronchi, which are intrapulmonary.
- Primary bronchi are the right and left main bronchi.
- Secondary bronchi are intrapulmonary, and each enters one lobe. So, there are three secondary bronchi on the right, and two on the left.
- Bronchioles can be conducting or respiratory. Large and terminal bronchioles are conducting, while the respiratory bronchioles are respiratory.

**A Step Forward**

The structure always fits the function.

Ex: Stratified epithelium fits protection, simple squamous epithelium fits diffusion, and ciliated epithelium fits sites where ciliary movement is needed ..etc.

Bear this in mind as we go through the lecture.

- Function of the Conducting Zone:

Cleansing, warming and moisturizing the inspired air.

➤ **Respiratory Zone:**

- Respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli.
- These are the main sites of gas exchange.
- The respiratory bronchioles are called the site of transition (will be explained later on).
- This area is rich in elastic and reticular fibers. These add to the elasticity of lung tissue to allow inflation and deflation.

## ➤ Layers of the Respiratory Wall:

Mucosa → Submucosa → Supportive layer → Adventitia

- The mucosa is composed of three layers:
  - 1- Epithelium: mostly pseudostratified ciliated columnar epithelium with goblet cells.
  - 2- Lamina propria: contains seromucous glands.
  - 3- Muscularis mucosa: contains smooth muscle cells.

- Submucosa: contains glands.
- Supportive layer: has cartilage and smooth muscle.

These two components vary in amount in different parts of the respiratory tract. As we go distally from the nose into the alveoli, the amount of cartilage decreases and the amount of muscle increases.

- Adventitia: a covering of connective tissue.

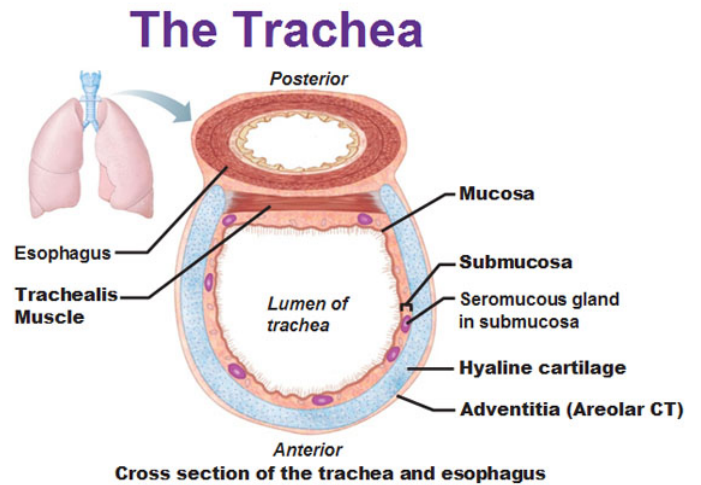
- Generally, the epithelial lining of the respiratory tract is pseudostratified ciliated columnar epithelium, but this doesn't fit the function all the way through the air passages. So, there must be a transition at some point (The conducting portion is responsible for passing the air, cleaning, warming and moisturizing it, so there fits the pseudostratified ciliated columnar epithelium. Whereas, the respiratory portion is responsible for gas exchange, where fits the thin simple squamous epithelium.)

This makes sense, right?

**This transition is gradual;**

Pseudostratified ciliated columnar → Simple ciliated columnar → Simple ciliated cuboidal → simple non-ciliated cuboidal (Clara cells) → Simple squamous epithelium.

- As we go distally, glands decrease in number. So, the lamina propria in the wall of upper parts contains more seromucous glands than the more distal parts.
- In the respiratory bronchioles, there are no glands.

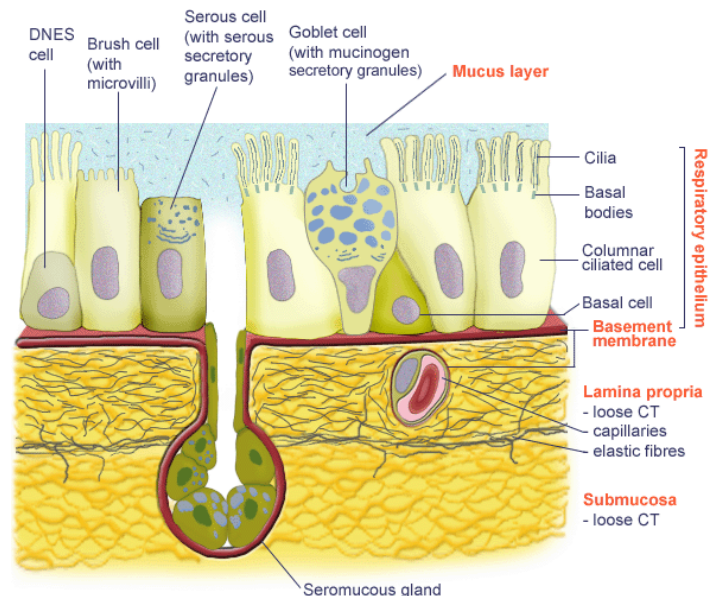


- As we go distally, cartilage in the supportive layer decreases. In the trachea, cartilage is in the form of C-shaped rings.
- These rings are not complete because the esophagus is posterior to the trachea. So, cartilage is replaced posteriorly with the trachealis muscle (this is smooth not skeletal muscle).
- The conducting zone filters the air. The cilia and mucous aid in this filtration.
- Mucous traps pathogens and foreign bodies, while the cilia move from inside to outside to propel anything trying to pass in, out of the respiratory tract.

Note: The cilia move in one direction. They move from inside to outside to propel things out.

### ➤ Respiratory Epithelium

- Under the microscope, we see only pseudostratified ciliated columnar cells and goblet cells. However, there are 5 types of cells in the respiratory covering.
- These are:
  - 1- Ciliated columnar cells
  - 2- Goblet cells
  - 3- Brush cells
  - 4- Small granule cell (DNES cells)
  - 5- Basal cell
- The basement membrane of the respiratory system is unusually thick.



### ➤ Ciliated Columnar Cells

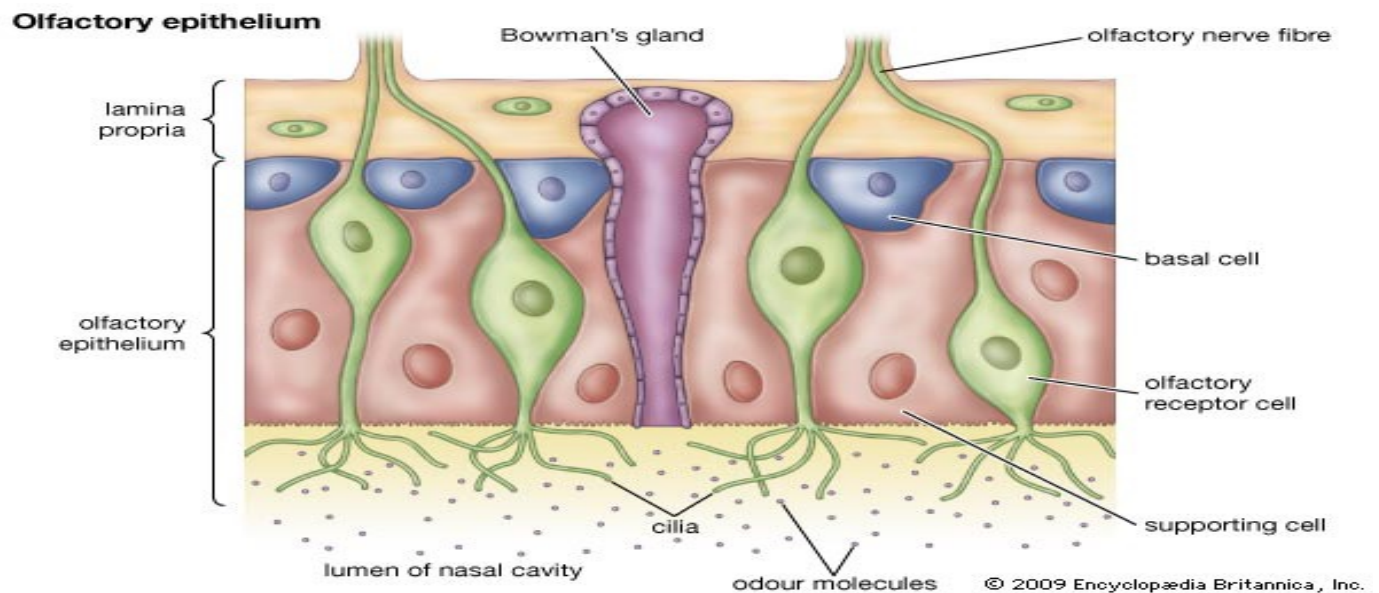
- The most abundant type.
- Each cell has 250-300 cilia on its surface.
- These cilia are inserted into the basal bodies in the apical part of the cell.
- The apical part of these cells is abundant in mitochondria, to provide the energy needed for ciliary movement.
- Cilia are composed of proteins. These are important for ciliary movement. Example of which is the dynein.
- Nicotine prevents the formation of dynein, which leads to improper movement of cilia.

- When the cilia don't move, the cleansing action of the cilia is lost. This predisposes the patient to recurrent chronic respiratory tract infections.
- The flagellum of the spermatozoon is a modified cilium, that's why anything affecting ciliary movement also affects the sperms.
- This loss of ciliary movement results in something called Immotile Cilia Syndrome.
- **Immotile Cilia Syndrome** متلازمة الأهداب الثابتة  
Aka Kartagner Syndrome
  - Smoking prevents the formation of dynein, resulting in immotile cilia syndrome.
  - This causes two things:
    - 1- Chronic respiratory tract infections
    - 2- Male infertility
- 2- Goblet cells:
  - present between ciliated columnar cells
  - secrete mucous that traps pathogens, and foreign bodies.
- 3- Brush cells:
  - have numerous microvilli on their apical surfaces.
  - These cells work as sensory receptors and they have afferent nerve endings at their basal surfaces.
- 4- Basal cells:
  - These are small round cells.
  - Mitotically active, generative stem cells that can differentiate into any of the other cell types.
- 5- Small granule cells:
  - These cells belong to the diffuse neuroendocrine system.
  - Also called Kulchitsky cells.
  - Regulate the local secretion of serous and mucous glands in the respiratory system.

## ➤ Nasal Cavity

The nasal cavity is divided into three parts:

- Vestibule: the anterior, dilated part.
  - Respiratory area: Contains the conchae and meatuses.
  - Olfactory region: roof and upper parts of the nasal cavity.
- Vestibule:
  - The most anterior and dilated part of the nasal cavity.
  - Lined by modified skin, that initially contains sebaceous and sweat glands, but it then loses its keratinization nature and undergoes a transition into typical respiratory epithelium as it goes into the nasal cavity.
  - It contains thick hairs (vibrissae).
- Respiratory Area:
  - Covered by pseudostratified ciliated columnar epithelium with goblet cells.
  - The sub-epithelial connective tissue is rich in blood supply, and this is important for warming the air.



- Olfactory Area:
  - Present in the roof and at the upper part of the nasal cavity.
  - Covered by olfactory mucosa.

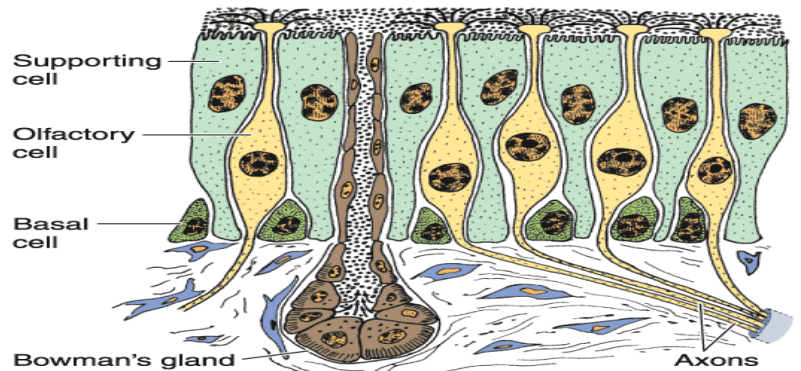
- Olfactory mucosa contains olfactory epithelium, lamina propria (corium) and Bowman's glands.

- Olfactory epithelium:  
Pseudostratified  
epithelium with 3 types of  
cells:

1- Olfactory cells (olfactory  
neurons).

- These are bipolar cells  
present throughout the  
epithelium.

- Their nuclei are below the level of the nuclei of supporting cells.
- Bipolar cells: its apical part is its dendrite and has about a dozen basal bodies.
- From these basal bodies, long non-motile cilia emerge. These cilia respond to odoriferous substances by generating action potentials that would be transmitted through the axons into the olfactory nerve. Then, they go to the brain to be interpreted.
- These axons unite in the lamina propria (see the figure), they pass through the foramina in the cribriform plate where they form the olfactory nerve which eventually synapses with other neurons in the olfactory bulb.



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## 2- Supporting cells:

- columnar cells, with broad apices and narrower bases.
- May be protective or nutritive.

## 3- Basal cells:

stem cells for other cells.

- Bowman's glands are present in the lamina propria (secrets watery mucous.)

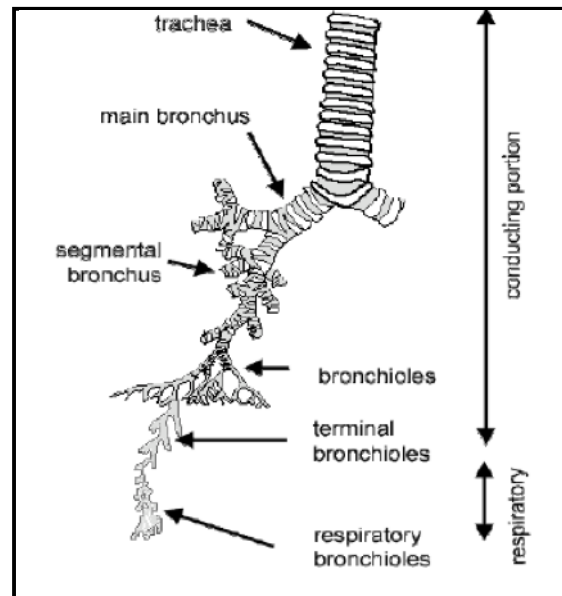


### ➤ Paranasal Sinuses

- Small cavities in the bones of the skull.
- Characterized by thin mucosa (thinner respiratory epithelium with fewer goblet cells).
- Few goblet cells.
- Contains small glands.
- The lamina propria contains only a few small glands and is continuous with the underlying periosteum.

### ❖ **Bronchial tree histology:**

- Remember that bronchial tree consists of:  
trachea → left and right main bronchus → secondary (lobar) bronchus → segmental bronchus → conducting bronchioles - including terminal bronchioles- → respiratory bronchioles that open into alveolar ducts.
- Only the first two are **extrapulmonary**. The rest structures (*starting from the secondary bronchus (or the lobar bronchi)*) are **intrapulmonary** structures –inside the lungs-.

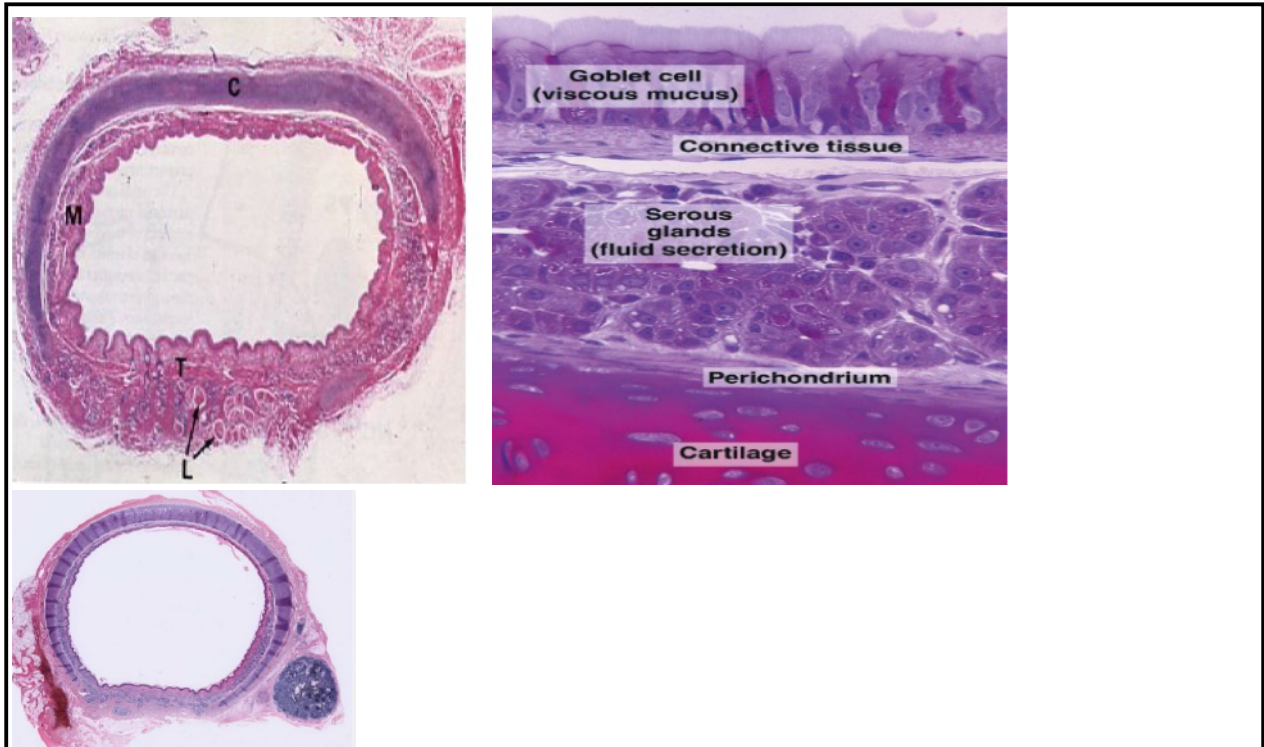


### ▶ the trachea:

- ▶ Layers that are found are: mucosa → sub mucosa → hyaline cartilage- C shaped- → Trachealis muscle, which is a smooth muscle found posteriorly.
- ▶ Sero-mucous glands are found in lamina propria and sometimes in sub-mucosa.

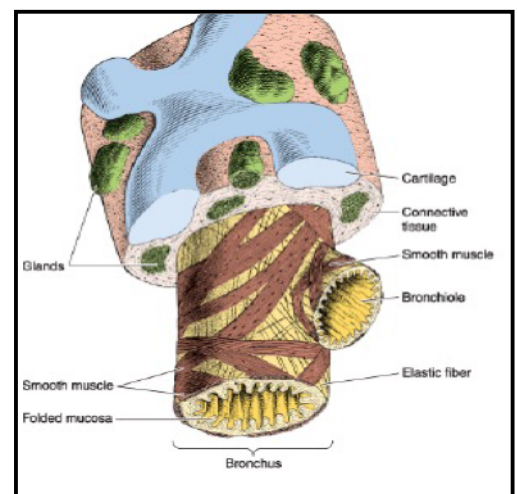


- ▶ Trachea ends at the level of T4 (angle of Louis/ sterna angle) then divides into right and left main bronchi.



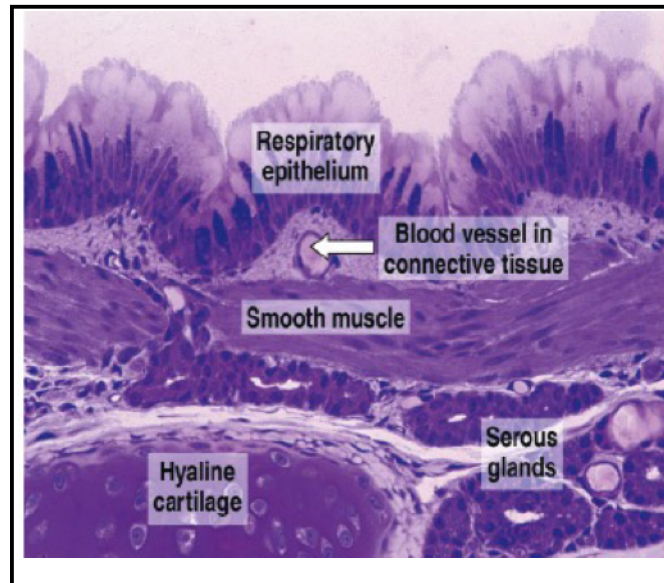
### ▶ **Bronchus:**

- ▶ Irregular plates of hyaline cartilage are seen.
- ▶ *Glands number decreases as we go distally-*
- ▶ Spiral smooth muscles also start to appear at the level of bronchi.
- ▶ Remember that the tertiary bronchus has very little amount of cartilage.



► **The histological difference between trachea and bronchi:**

- The main difference is the **presence of hyaline cartilage**. In the trachea, it is **C shaped** while in the bronchus, cartilage is found as **plates**.
- Plates decrease as we go distally, and in the tertiary bronchus there are only one or two plates.

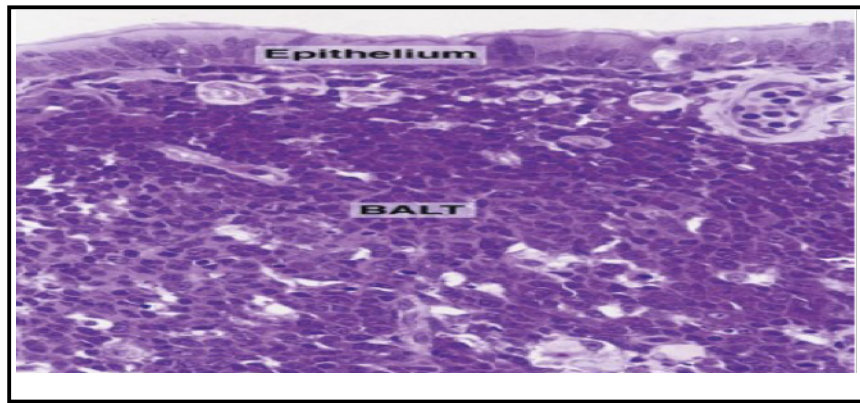


► **Lymphatic nodules in the respiratory tract:**

- They are called "**BALT**".
- Lymphocytes are found along the whole respiratory tract as scattered cells but they accumulate forming nodules in certain areas.
- Nodules are mainly found in the **bronchus**. They become scattered once again when reaching the bronchioles.

*\*Scattered cells → nodules in the bronchus only → scattered cells from the bronchioles till the end of the tract.\**

- Like the smooth muscles and elastic fibers, BALT also becomes more abundant as bronchi become smaller.

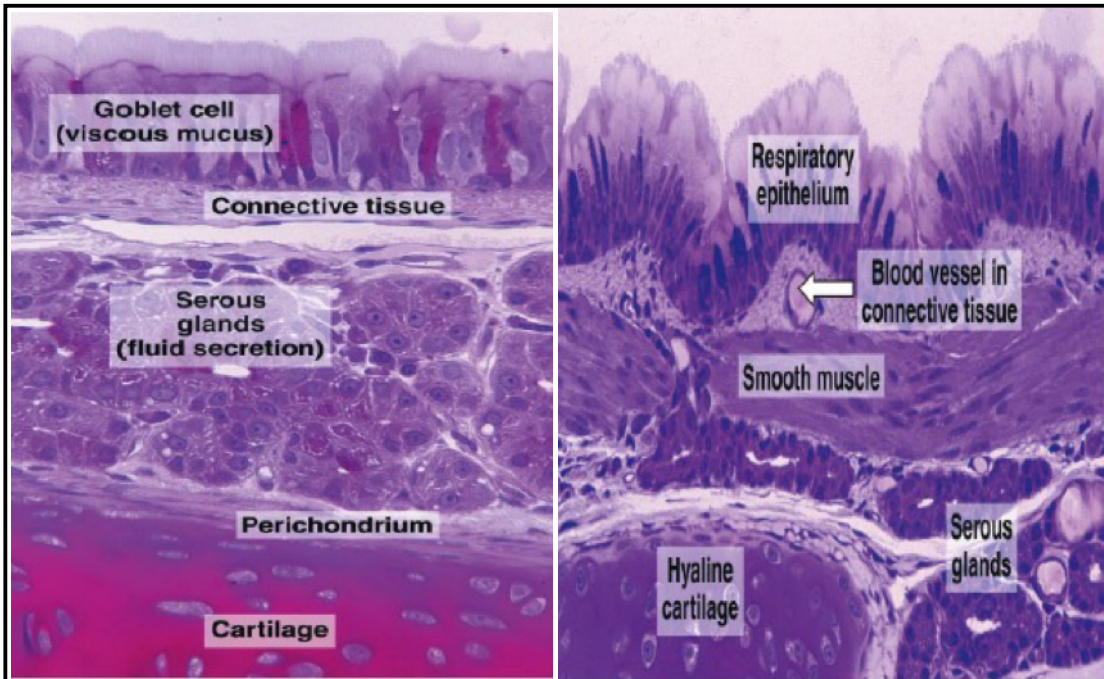


### ➤ Bronchioles:

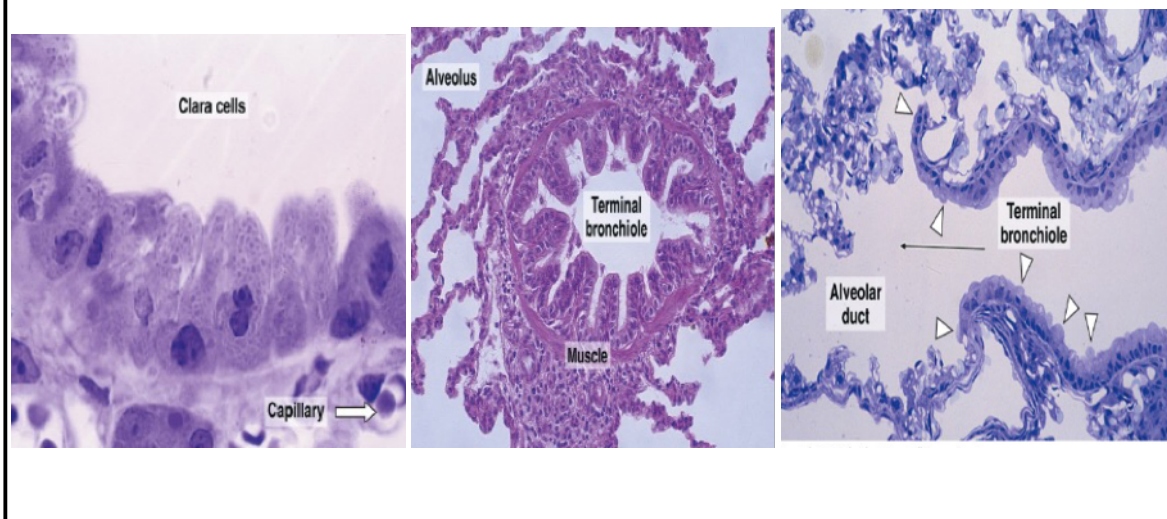
- ▶ There are large conducting bronchioles → terminal bronchioles → respiratory bronchioles -narrower than the terminal- .
- ▶ In general, the diameter in small bronchioles is around .5 mm while in the large ones the diameter is around 1mm. ( *simply, the diameter decreases as we go distally*)
- ▶ No cartilage found in them.
- ▶ No glands.
- ▶ No lymphatic nodules -Only scattered lymphocytes- .
- ▶ Spiral smooth muscles are found.
- ▶ Goblet cells are few at the proximal parts and then they disappear in more distal areas.
- ▶ Each large bronchiole has a diameter of 1 mm and terminates by dividing into around 5-7 terminal bronchioles.
- ▶ **NOTE:** In extra pulmonary areas, elastic fibers are few in amount however; elastic fibers increase as we go distally.
- ▶ **In terminal bronchioles** there is folding of the lining epithelium due to the presence spiral smooth muscle between lamina propria and submucosa, and absence of cartilage.
- ▶ **In respiratory bronchioles,**
  - Clara cells start to appear -*they are only seen in respiratory bronchioles*-. Clara cells are cuboidal cells with no cilia containing secretory granules that are related to formation of **surfactant**.
  - Neuroepithelial bodies, which are groups of cells that receive cholinergic nerve endings and are thought to be chemoreceptors that react to changes in gas composition within the airway, are also seen.
  - Elastic fibers are mainly found between the alveoli as it is responsible for the inflation of the lung and deflation.
  - No goblet cells.

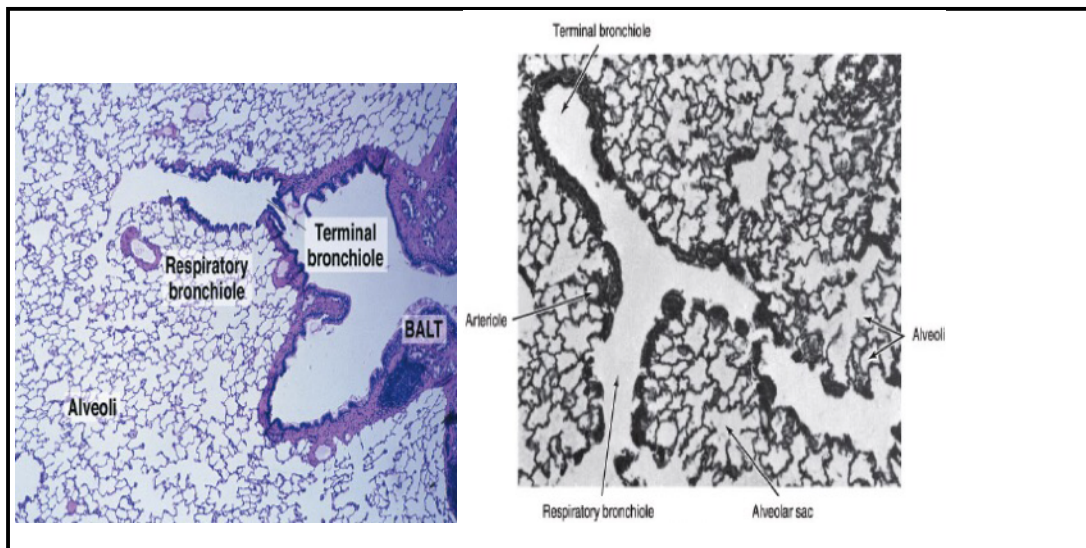
- The respiratory bronchioles terminate by opening into alveolar ducts, thus it is always opened unlike the terminal bronchioles.
- ▶ Keep in mind that the changes in the lining epithelium in the respiratory tract are **gradual** and never sudden. Thus the lining epithelium in the bronchioles changes in the following order:
  - **At the most proximal parts of bronchioles the epithelium is pseudo-stratified columnar epithelium** → **simple columnar ciliated** → **simple cuboidal ciliated** - *terminal bronchioles* - → **Clara cells** - *respiratory bronchioles* - → **simple squamous cells in the alveoli.**
- ▶ **NOTE:** the Alveolar ducts open into alveolar sac.
- ▶ Smooth muscles are found in terminal bronchioles → then they start to decrease in the respiratory bronchioles → becoming knobs of smooth muscles -i.e. small pieces of smooth muscles- at the beginning of the alveoli. But elastic and reticular fibers are abundant in these regions.
- ▶ **To sum up:**
  - *Cartilage, glands and goblet cells **decrease** as we go distally.*
  - *On the other hand, elastic and reticular fibers **increase** as we go distally.*
- ▶ **NOTE:** Pulmonary artery and vein are very close to the terminal bronchiole.





extra-pulmonary bronchus VS intra-pulmonary





### ➤ The alveoli:

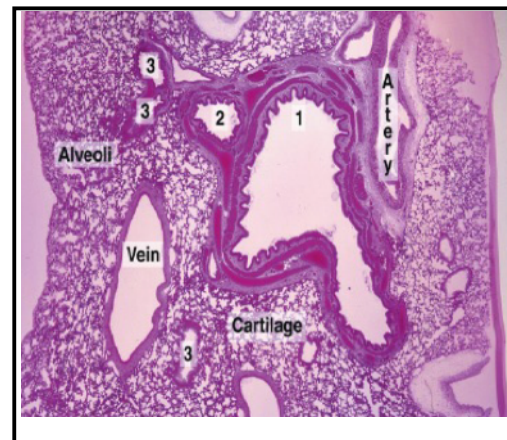
- The alveoli are sac-like evaginations.
- Their size is around 200  $\mu\text{m}$ .
- Massive networks of capillaries are found around the alveoli.

❖ Cells of the alveoli:

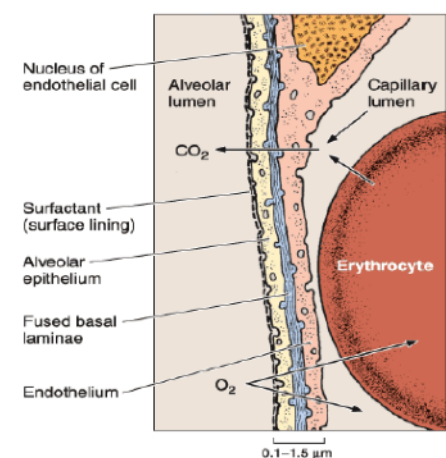
### • Type 1 alveolar cells:

- ➔ Simple squamous epithelial cells that line the whole alveolar wall.
- ➔ Between adjacent cells "Alveolar pores" are found sometimes, which is a pore with a diameter of 10-15  $\mu\text{m}$  that allows the air passage between the adjacent alveoli.
- ➔ They constitute 97% of the alveolar surface (remaining 3% are type 2 cells.)
- ➔ It has a size of 25 nm.
- ➔ Its organelles are found at one side.
- ➔ High rate of mitosis.
- ➔ Connected to type 2 cells by desmosomes or occluding junctions.

➔ Respiratory membrane "blood-air barrier-":  
important



Blood air barrier



❖ It is formed by three layers:

- ▶ The **endothelial cells** at the capillary side.
- ▶ The epithelial cells-**type 1 cells**- at the alveolar side lined by a surfactant.
- ▶ Between the two cells there is fused **basal lamina**.

***\*thus it is made of simple squamous cell at both sides and basal lamina in between only\****

❖ It is the place at which the gas exchange occurs.

❖ It has thickness of 0.1-1.5  $\mu\text{m}$ .

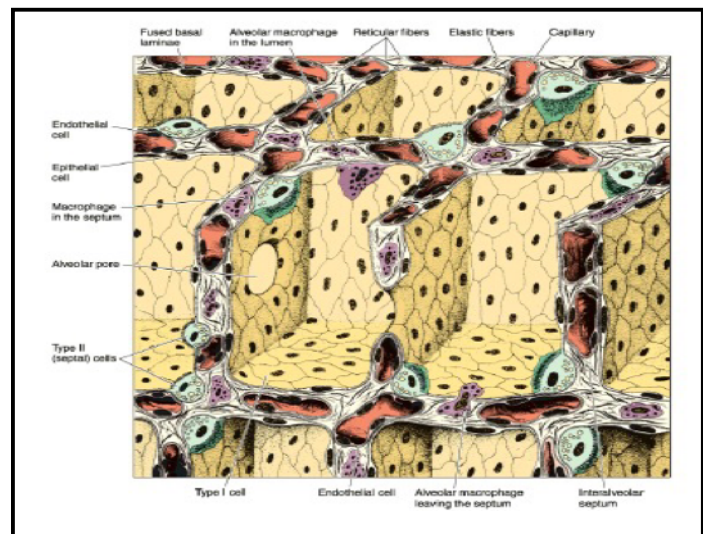
• **Type 2 alveolar cells:**

- Cuboidal cells with large nucleus.
- Secret surfactant that lines type 1 cells to **decrease the surface tension** so inflation of the alveoli can occurs.
- Common at the corners between the alveoli.
- Have the ability for mitosis and the replacement of other cells including type 1 cells.
- Contain lamellar bodies which give rise to the pulmonary surfactant.

❖ **Inter-alveolar septum:**

→ Between adjacent alveoli, there is **inter-alveolar septum** in which capillaries are found forming respiratory membrane with the alveolar cells.

→ **Interstitium:** Is the part of the inter-alveolar sputum that is made of connective tissue and capillaries. cells that are found in it include: Fibroblast, macrophages and plasma cells, leukocytes, mats cells, type1 and 2 alveolar cells and endothelial cells of the capillaries. It is different from the respiratory membrane.





- **NOTES:**

- Inflation of the lung (الانتفاخ الرئة) is important as it makes the respiratory membrane more thin thus increasing the **efficiency of gas exchange process**.
- Alveoli looks like tennis balls, so if you place a 1000 ball next to each other, you can see spaces and corners. The same principle applies here, in which the balls are the alveoli themselves and the spaces are the inter-alveolar septum. Corners are filled with connective tissue, elastic fibers and other cells .
- If the fetus is born with few amount of surfactant, then he will suffer from **respiratory distress syndrome**, in such case the baby requires to be placed in incubator and rapid treatment. Nowadays pregnant women are tested to see the amount of the surfactant that their fetus has, and if it is low, they are given cortisone as it helps in the surfactant formation.
- Both types of alveolar cells have the ability for regeneration and they are also affected by the NO<sub>2</sub> (damages the cells, thus induces regeneration.)

- ❖ **Endothelial cells:**

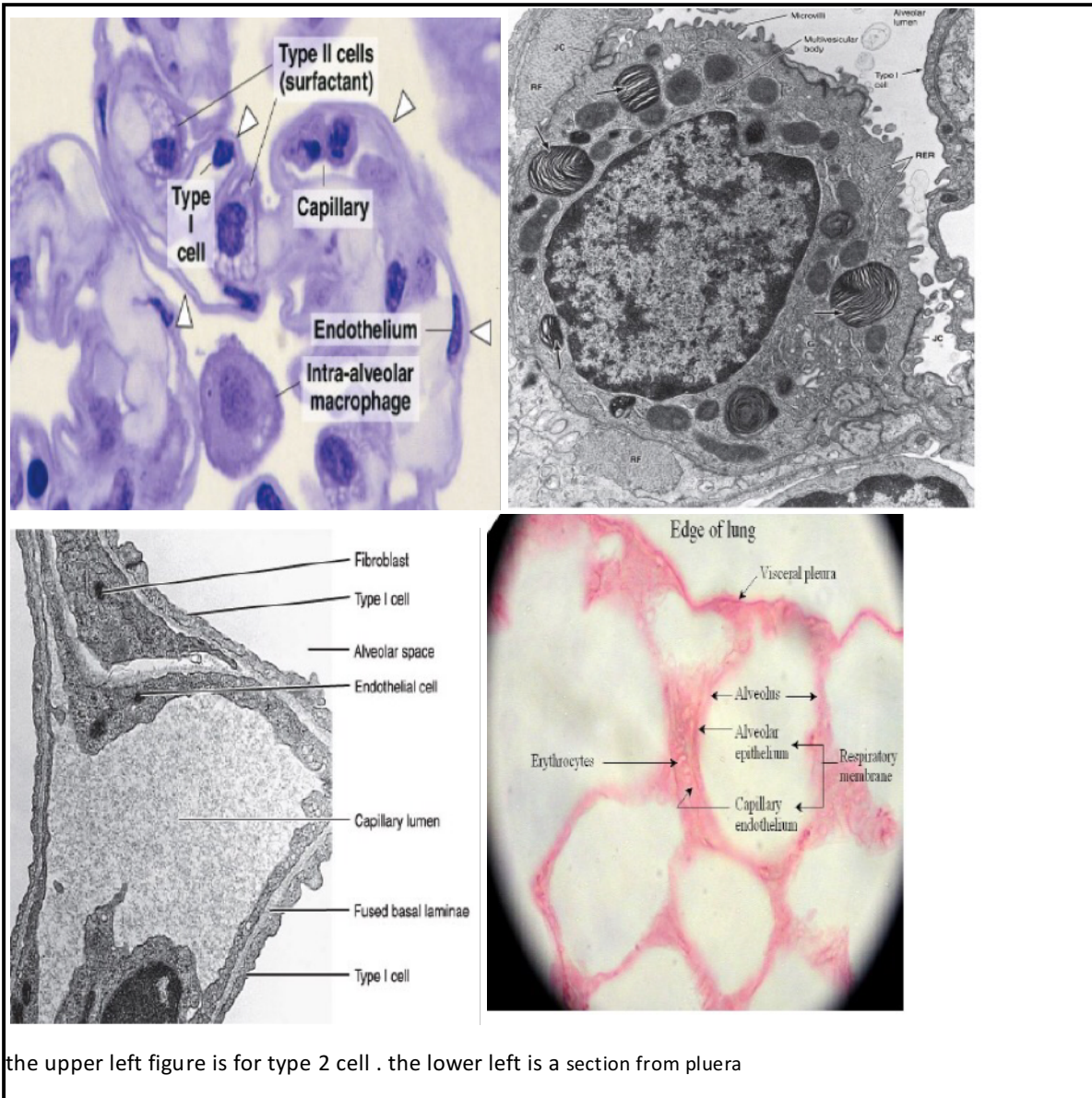
- ▶ They are simple squamous epithelial cells
- ▶ Have clustering of nuclei and many organelles (allows other areas in the cytoplasm to become thin-> important for gas exchange.)
- ▶ They are continuous and not fenestrated type.

- ❖ **Macrophages :**

- ▶ Macrophages of the alveoli are called **dust cells** (الخلايا الغبارية).
- ▶ Originate from monocytes that circulate in the microvasculature.
- ▶ Most numerous cells in the respiratory system -*even more than type 1 cells*-.
- ▶ They are responsible for the **engulfment** of bacteria, foreign bodies and nicotine particles.
- ▶ Found in the lung tissue, pleura, between blood vessels and in the connective tissue between the alveoli.
- ▶ Once macrophages are filled with engulfed material, it can pass upwards and by the ciliary movement it reaches the pharynx to be expectorated (swallowed.)

➤ **Pleura:**

- ▶ The lining epithelium of both layer of the pleura; parietal and visceral, is **mesothelium** (i.e. simple squamous epithelium).



**NOTE:** Blood vessels will be discussed in anatomy lectures.

Sorry for any mistakes~