



RS

HISTOLOGY

MODIFIED NO.2







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Respiratory System 2

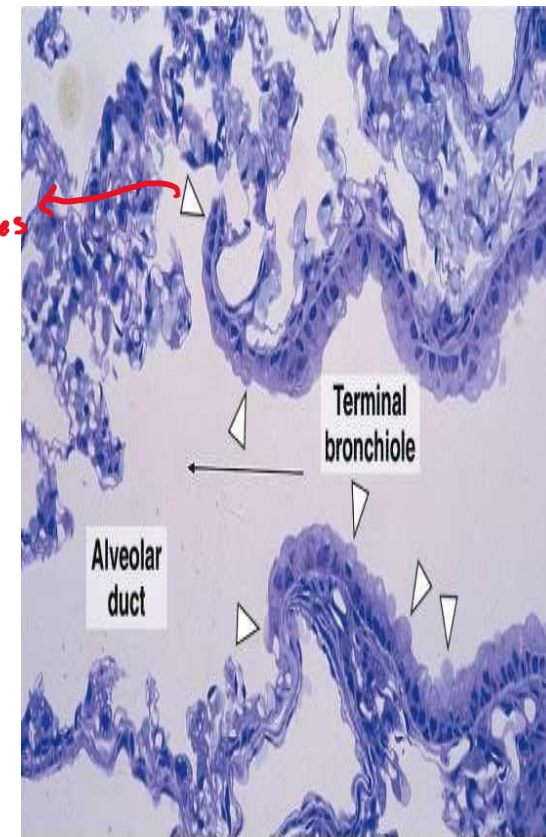
Color code

	Slides
	Doctor
	Additional info
	Important

Bronchioles

- intralobular airways with diameters of 5 mm or less
- Large (1 mm) small (0.5mm) it starts at 5mm then branches even more to a narrower bronchiole, so it ranges for 1mm to 0.5 mm.
- have neither cartilage nor glands in their mucosa
- **No lymphatic nodule**, there are lymphocytes in all of the respiratory tract.
- only **scattered** goblet cells within the epithelium of the initial segments The goblet cells are replaced by clara cells (simple cuboidal cells without cilia) as we move distally.
- In the larger bronchioles, the epithelium is ciliated pseudostratified columnar. As we move distally it decreases in height and complexity to become ciliated simple columnar or cuboidal epithelium in the smaller terminal bronchioles

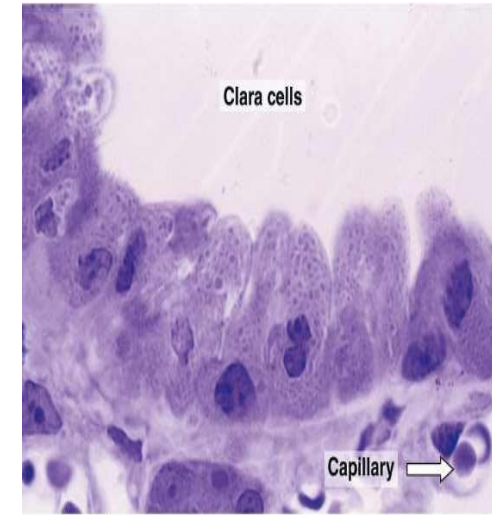
respiratory bronchioles



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Bronchioles

- The epithelium of terminal bronchioles also contains **Clara cells** which are devoid of cilia, have secretory granules in their apex known to secrete proteins that protect the bronchiolar lining against oxidative pollutants and inflammation.
 - They produce one of the components of the surfactants and also act as reserve cells
 - Bronchioles also exhibit specialized regions called neuroepithelial bodies
 - groups of cells (80-100) that contain secretory granules and receive cholinergic nerve endings it contains chemoreceptors which detects changes in CO₂ & O₂.
 - Their function is poorly understood, but they are probably chemoreceptors that react to changes in gas composition within the airway
 - They also seem involved in the reparative process of airway epithelial cell renewal after injury
- Important:** The clara cells are seen in the terminal bronchioles and at the beginning of the respiratory bronchioles.



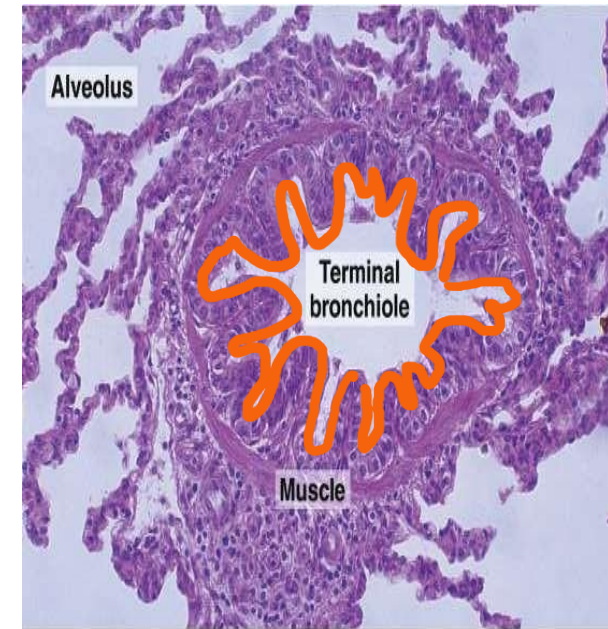
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Bronchioles

In the terminal bronchiole we can see prominent **folding of mucosa (in the pic)** due to the presence of smooth muscle in the lamina propria (it is responsible for asthma when the lumen becomes narrower in addition to it not having cartilage)

Remember: bronchi have cartilage that keep the lumen from narrowing

- lamina propria is composed largely of smooth muscle and elastic fibers (spiral and circular and folds)
- the lining epithelium of the terminal bronchi in the pic is simple columnar or cuboidal ciliated.
- musculature of both the bronchi and the bronchioles is under the control of the vagus nerve and the sympathetic nervous system
- Stimulation of the vagus nerve decreases the diameter of these structures (parasympathetic causes bronchoconstriction) ; sympathetic stimulation produces the opposite effect. so when patient with asthma come to the hospital we give him adrenaline).

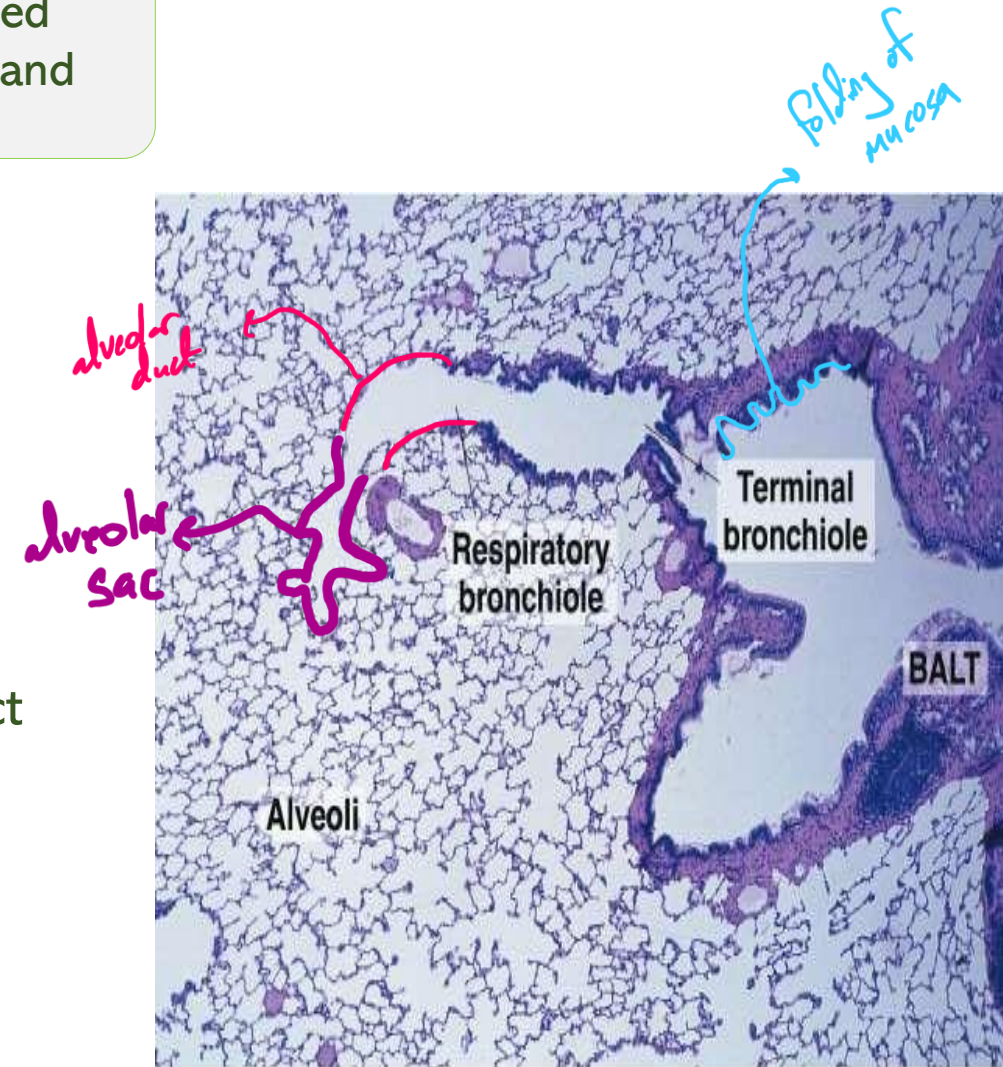


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Respiratory Bronchioles

The terminal bronchiole (conductive part) is a closed bronchiole (rounded closed lumen) In contrast to the respiratory which is open (not circular and open at an alveolar duct).

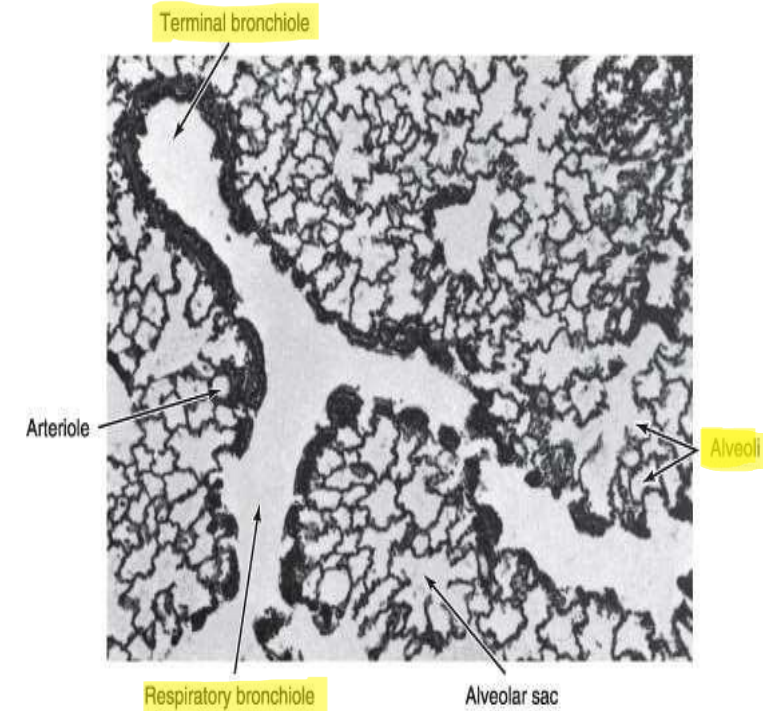
- Each terminal bronchiole subdivides into two or more respiratory bronchioles
- serve as regions of transition between the conducting and respiratory portions of the respiratory system
- **Epithelium:** there is a transition from simple cuboidal ciliated and non ciliated (clara cells) and as we move distally it becomes simple squamous epithelium that contain alveoli and alveolar duct
- mucosa is structurally identical to that of the terminal bronchioles . The folding of mucosa decreases because the smooth muscles decrease
- their walls are interrupted by numerous saclike alveoli where gas exchange occurs



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Respiratory Bronchioles

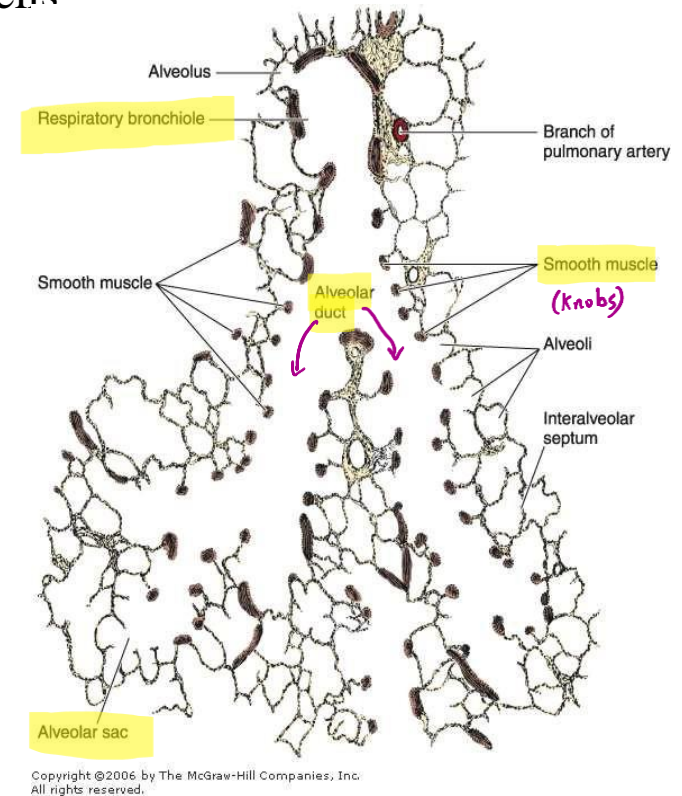
- lined with ciliated cuboidal epithelial cells and Clara cells (**non-ciliated cuboidal**), but at the alveolar openings the bronchiolar epithelium becomes continuous with the **simple squamous alveolar lining cells**
- Between alveoli, the bronchiolar epithelium consists of ciliated cuboidal epithelium
- Smooth muscle and elastic connective tissue lie beneath the epithelium The smooth muscles decrease and change their shapes from large folding to become **knobs** of smooth muscle **on the opening of alveoli.** (where gas exchange can occur)



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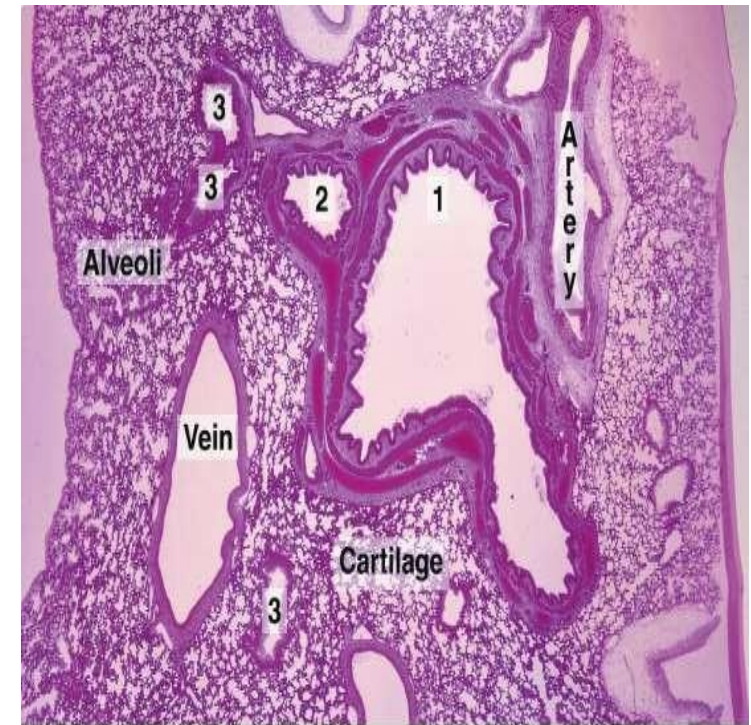
Alveolar Ducts

- Both the alveolar ducts and the alveoli are lined with extremely attenuated squamous alveolar cells
- When respiratory bronchioles open to 2 alveolar ducts its called **atria**.
- In the lamina propria surrounding the rim of the alveoli is a network of smooth muscle cells
- These sphincter like smooth muscle bundles appear as **knobs** between adjacent alveoli
- Smooth muscle disappears at the distal ends of alveolar ducts
- A rich matrix of elastic and reticular fibers provides the only support of the duct and its alveoli.
- Alveolar ducts open into **atria** that communicate with **alveolar sacs**
- The elastic fibers (**between alveoli**) enable the alveoli to expand with inspiration and to contract passively with expiration (inflation and deflation)
- The reticular fibers serve as a **support** that prevents overdistention (rupture) and damage to the delicate capillaries and thin alveolar septa.



Alveoli

- Alveoli are saclike evaginations (about 200 um in diameter)
- responsible for the spongy structure of the lungs (all of the lung is spongy because it's filled with air & there is elastic fibers between them)
- The structure of the alveolar walls is specialized for enhancing diffusion between the external and internal environments
- each wall lies between two neighboring alveoli and is therefore called an **interalveolar septum, or wall**
- Septum is what's between two alveoli & wall is the whole wall of alveolus.



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Interalveolar septum

- An interalveolar septum consists of two thin squamous epithelial layers between which lie capillaries, elastic and reticular fibers, and connective tissue matrix and cells

most of the **wall** (97%) is made of type 1 cells (simple squamous) and type 2 cells make only 3% of cells in the wall. But in the **septum** alone there is **more type 2 cells**, almost 16% is type 2 (septal cells) surfactant releasing septal cells that reside in the corners, and 8% is made from type 1 cells.

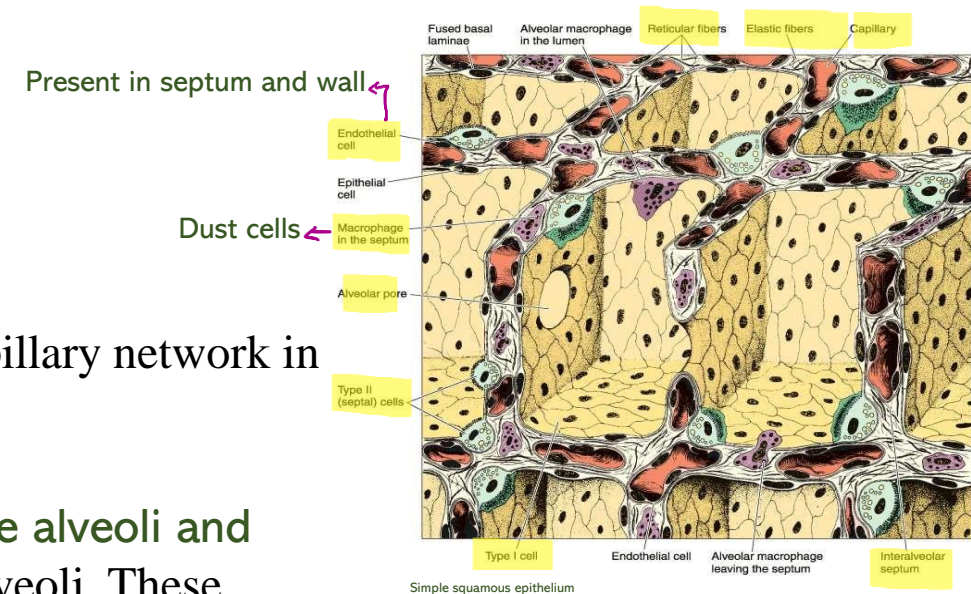
- The capillaries and connective tissue constitute the **interstitium**

- Connective tissue consist from :

- 1- cells: macrophages, mast cells, ... etc
- 2- **ECM** : Fibers (reticular,elastic,..)+ **ground substance**

- Within the interstitium of the interalveolar septum is found the richest capillary network in the body.

- The interalveolar septum contains **pores** Which distribute the oxygen the alveoli and maintain the balance. 10-15 um in diameter, that connect neighboring alveoli. These pores equalize air pressure in the alveoli and promote the collateral circulation of air when a bronchiole is obstructed.



Remember, the green text represents what the doctor said, while the black underlined text is what the doctor mentioned from the slides :)

Blood-air barrier (where gas exchange occurs) is between the capillary (endothelial cells) & type 1 alveolar cell.

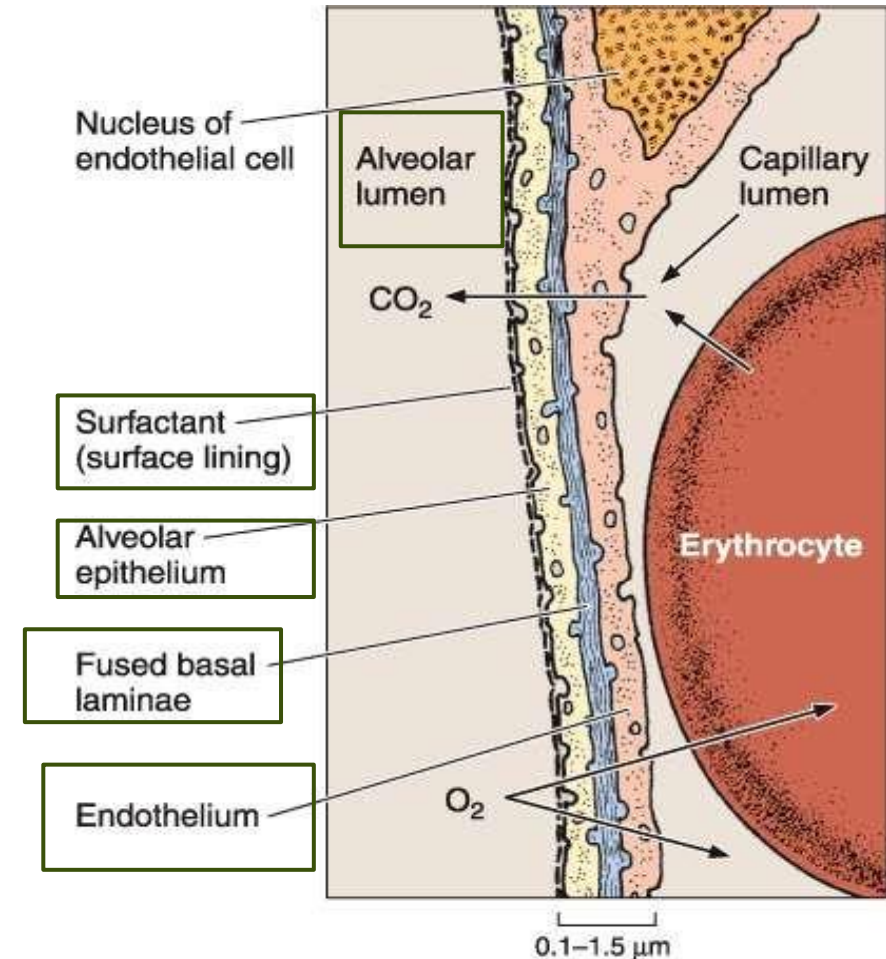
- The components of respiratory membrane or the BAB:
- 1. The surface lining and cytoplasm of the alveolar cells
 - Surfactant plays a crucial role in alveolar inflation, especially during labor.
- 2. The fused basal laminae of the closely apposed alveolar and endothelial cells
- 3. cytoplasm of the endothelial cells
- The total thickness of these layers varies from 0.1 to 1.5 μm (it is very thin).
- Oxygen goes to erythrocytes in capillaries.
- CO₂ goes to alveoli.

Gas exchange

Blood-air barrier

- Air in the alveoli is separated from capillary blood by three components referred to collectively as the **blood-air barrier**
- 1. The surface lining and cytoplasm of the alveolar cells
- 2. The fused basal laminae of the closely apposed alveolar and endothelial cells
- 3. cytoplasm of the endothelial cells
- The total thickness of these layers varies from 0.1 to 1.5 μm

Everything doctor mentioned from this slide was explained in the previous slide.



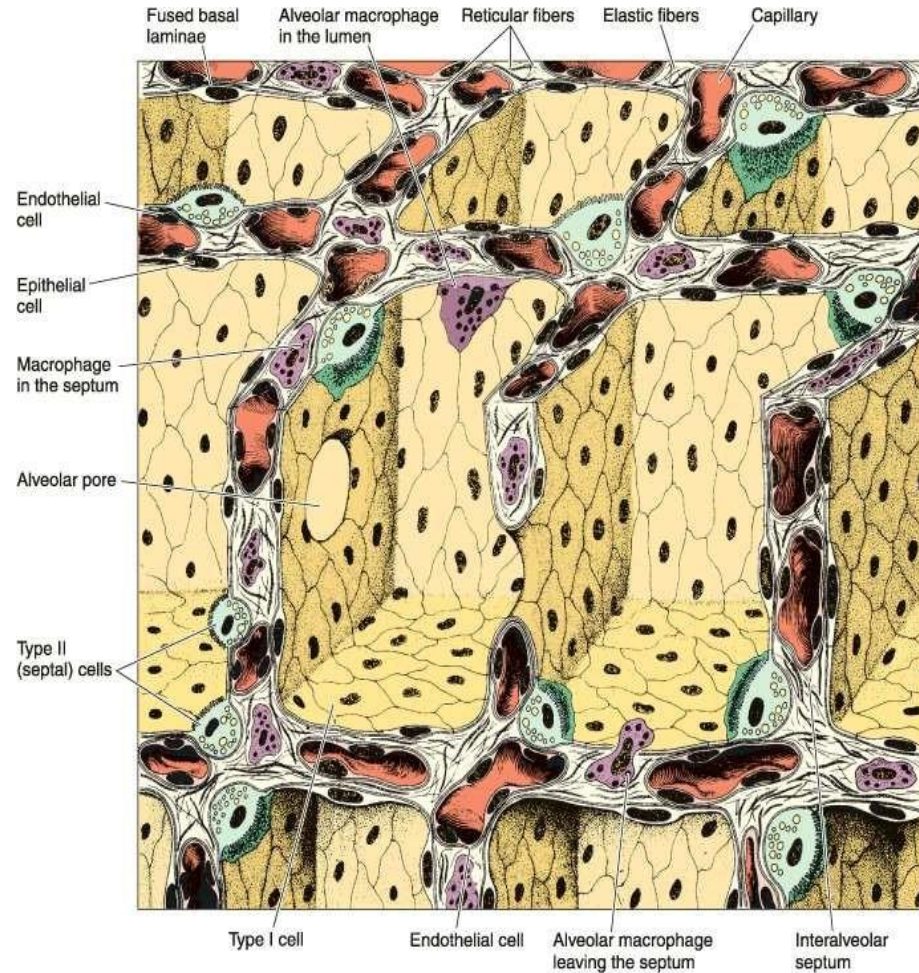
- Within the interalveolar septum, anastomosing pulmonary capillaries are supported by a meshwork of reticular and elastic fibers.
- The basement membrane, leukocytes, macrophages, and fibroblasts can also be found within the interstitium of the septum.
- When I say interstitium that means capillary + connective tissue.
- The fusion of two basal laminae produced by the endothelial cells and the epithelial (alveolar) cells of the interalveolar septum forms the basement membrane.

- Cells in the interstitium:
 1. Endothelial cells (capillaries) 30 %
 2. Fibroblasts and mast cells 36%
 3. Macrophages 10 %
- Cells in the septum:
 1. Type I cells 8 %
 2. Type II cells (called septal cells) 16%
 3. Leukocytes

Interalveolar septum

Everything doctor mentioned from this slide was explained in the previous slide.

- Within the interalveolar septum, anastomosing pulmonary capillaries are supported by a meshwork of reticular and elastic fibers
- These fibers are arranged to permit expansion and contraction of the interalveolar septum
- are the primary means of structural support of the alveoli
- The basement membrane, leukocytes, macrophages, and fibroblasts can also be found within the interstitium of the septum
- The fusion of two basal laminae produced by the endothelial cells and the epithelial (alveolar) cells of the interalveolar septum forms the basement membrane



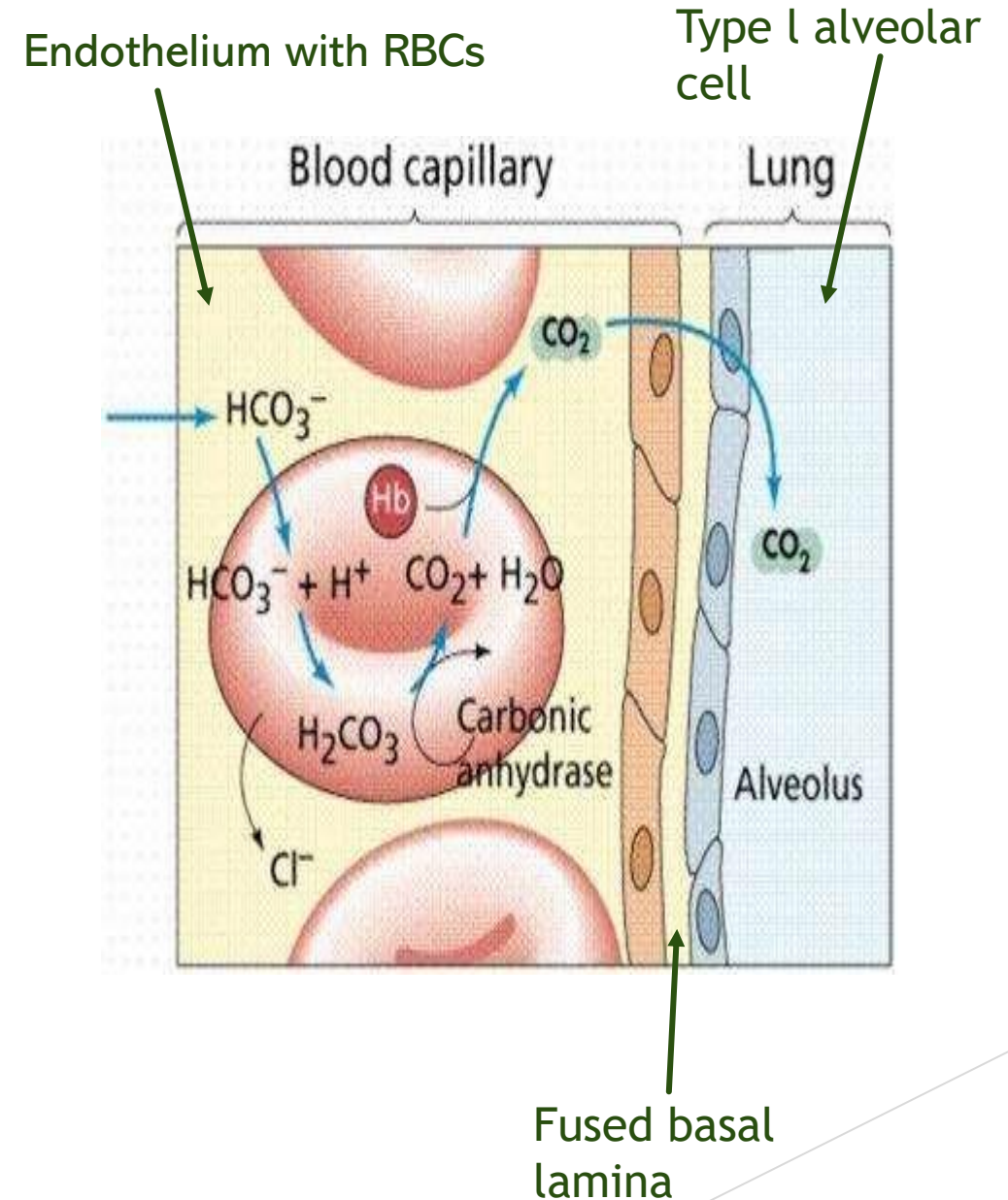
Interalveolar septum

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- leukocytes

Everything doctor mentioned from this slide was explained in the previous slide.

Gas Exchange

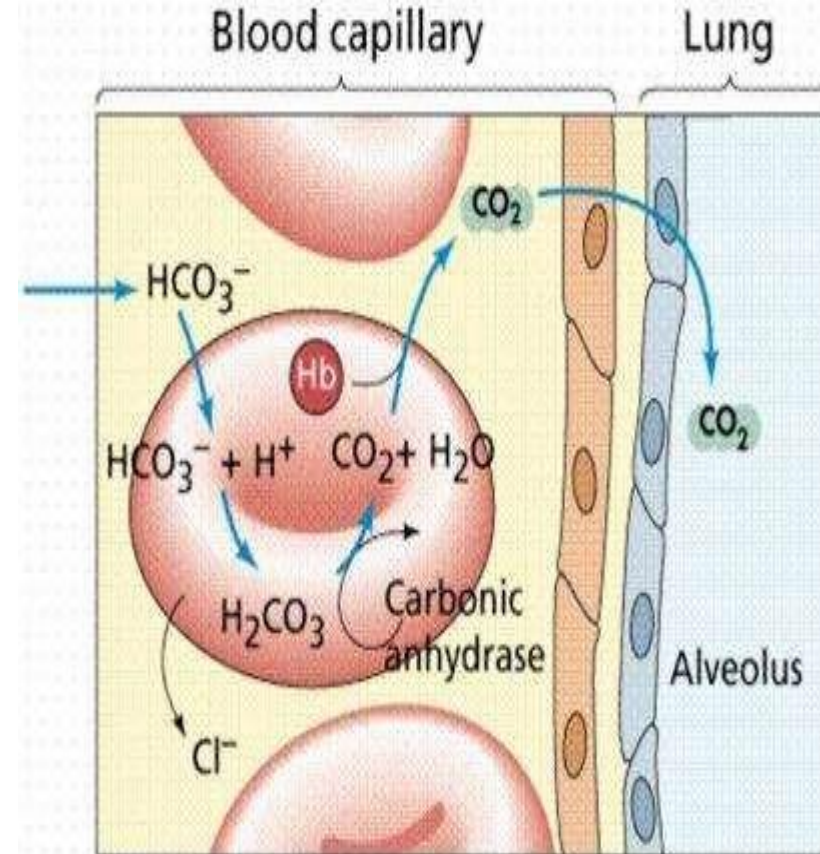
- O₂ comes from type I alveolar cell then it goes to endothelial cells and opposite to it is CO₂ (which through it there's a connection with carbonic anhydrase).
- The approximately 300 million alveoli in the lungs considerably increase their internal exchange surface, which has been calculated to be approximately 140 m². [Large surface area for gas exchange].



Gas exchange

Everything doctor mentioned from this slide was explained in the previous slide.

- O₂ from the alveolar air passes into the capillary blood through the blood-air barrier and CO₂ diffuses in the opposite direction
- Liberation of CO₂ from H₂CO₃ is catalyzed by the enzyme **carbonic anhydrase** present in erythrocytes
- The approximately 300 million alveoli in the lungs considerably increase their internal exchange surface, which has been calculated to be approximately 140 m²



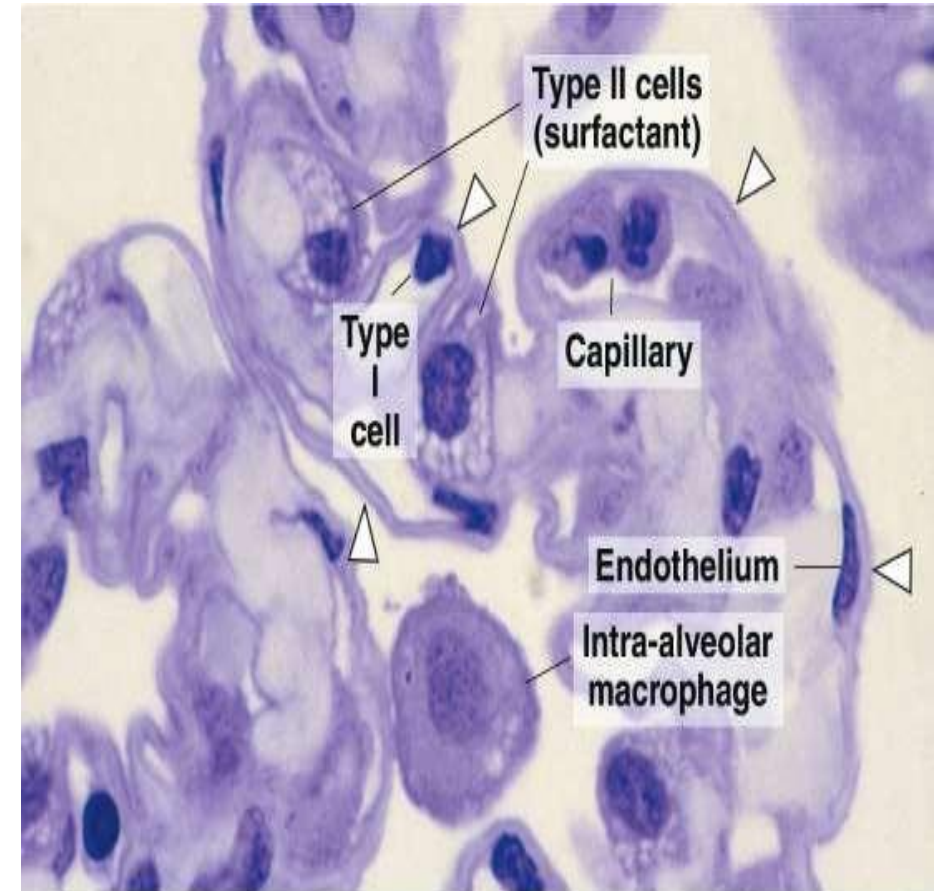
Capillary endothelial cells

- Extremely thin and can be easily confused with type I alveolar epithelial cells. Why are they confused? Because both are of simple squamous epithelium, so how to differentiate them under the microscope? Endothelial cells are surrounded with RBCs.
- Endothelial lining of the capillaries is continuous and not fenestrated.
- Clustering of the nuclei and other organelles allows the remaining areas of the cell to become extremely thin increasing the efficiency of gas exchange (clustering means we can find mitochondria, Golgi complex close to the nuclei and the rest of cytoplasm is empty, to leave a space for oxygen).
- The most prominent feature of the cytoplasm in the flattened portions of the cell is numerous pinocytotic vesicles.

Capillary endothelial cells

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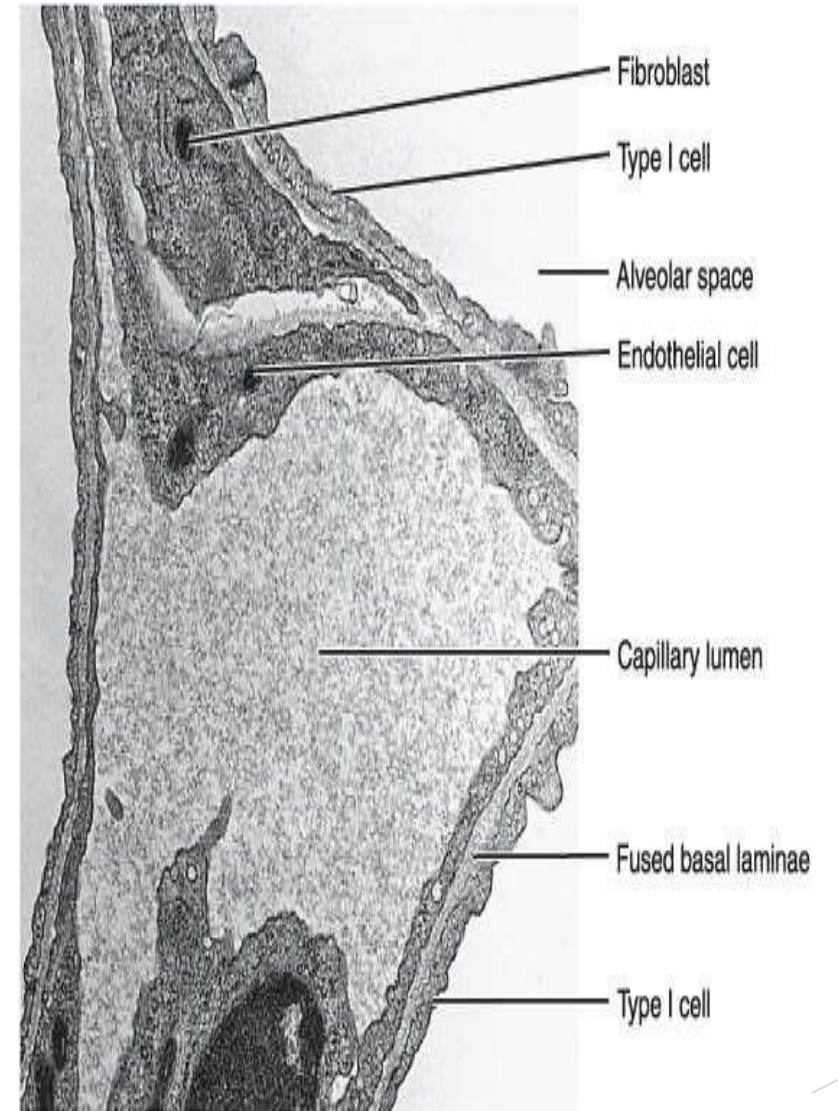
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Type I cells

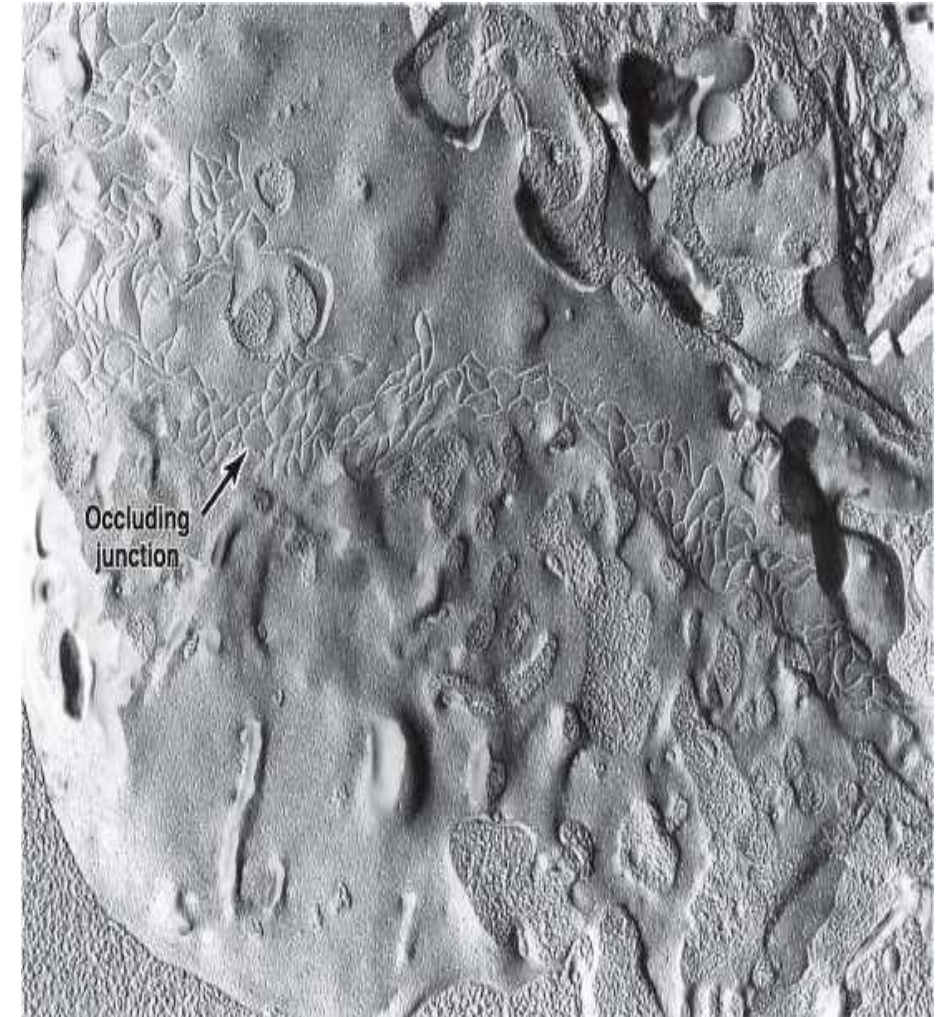
- squamous alveolar cells
- extremely attenuated cells that line the alveolar surfaces
- Type I cells make up 97% of the alveolar surfaces (type II cells make up the remaining 3%).
- While in septum : type I → 8% , Type II → 16%.
- are so thin (sometimes only 25 nm) that the electron microscope was needed to prove that all alveoli are covered with an epithelial lining
- Organelles such as the Golgi complex, endoplasmic reticulum, and mitochondria are grouped around the nucleus, reducing the thickness of the blood-air barrier and leaving large areas of cytoplasm virtually free of organelles



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Type I cells

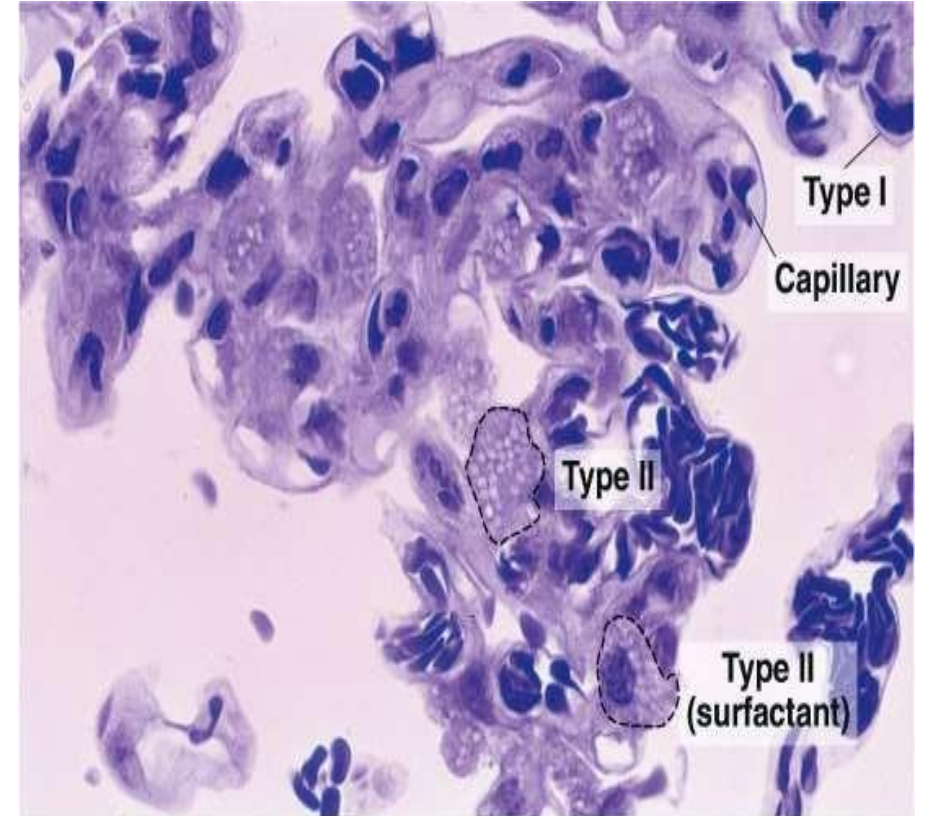
- The cytoplasm in the thin portion contains abundant pinocytotic vesicles, which may play a role in the turnover of surfactant and the removal of small particulate contaminants from the outer surface
- In addition to desmosomes, all type I epithelial cells have occluding junctions that prevent the leakage of tissue fluid into the alveolar air space.
- - Desmosomes are presented between type I and type II cells, and from the desmosomes there's occluding junction between type I and type II cells.
- The main role of these cells is to provide a barrier of minimal thickness that is readily permeable to gases.



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Type II cells

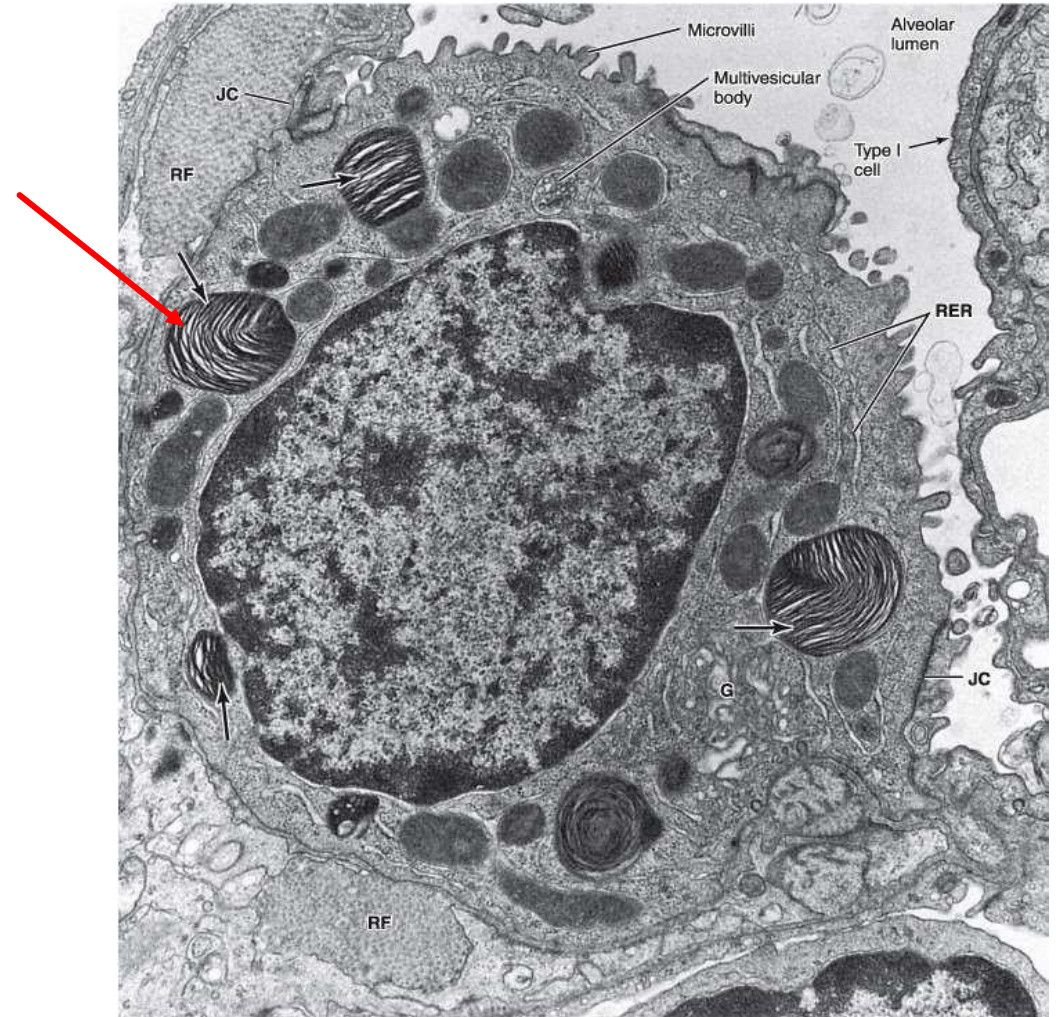
- They are Cuboidal cells. They secrete surfactant which is very important to decrease surface tension of the alveoli and that helps in inflation especially for delivery.
 - interspersed among the type I alveolar cells with which they have occluding and desmosomal junctions
 - rounded cells that are usually found in groups of two or three along the alveolar surface at points at which the alveolar walls unite and form angles
 - rest on the basement membrane, are part of the epithelium, with the same origin as the type I cells
 - divide by mitosis to replace their own population and also the type I population.



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Type II cells (great alveolar cells) (septal cells)

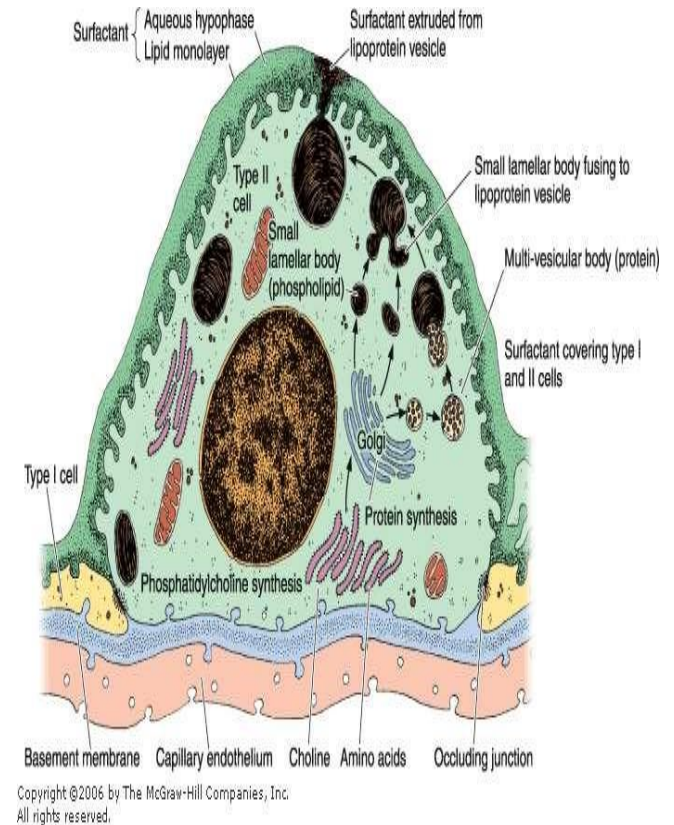
- By Electron Microscope: they exhibit a characteristic vesicular or foamy cytoplasm. These vesicles are caused by the presence of lamellar bodies
- Lamellar bodies, which average 12µm in diameter, contain concentric or parallel lamellae limited by a unit membrane
- these bodies, which contain phospholipids, glycosaminoglycans, and proteins, are continuously synthesized and released at the apical surface of the cells
- The lamellar bodies give rise to the pulmonary surfactant, a material that spreads over the alveolar surfaces, providing an extracellular alveolar coating, that lowers alveolar surface



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Pulmonary surfactant

- The surfactant layer consists of proteinaceous hypophase covered with a phospholipid film that is primarily composed of **dipalmitoyl phosphatidylcholine** and **phosphatidylglycerol**.
- Surfactant also contains several types of proteins (A,B,C,D)
- Pulmonary surfactant serves several major functions in the lung, but it primarily aids in reducing the surface tension of the alveolar cells
- The reduction of surface tension means that less inspiratory force is needed to inflate the alveoli, and thus the work of breathing is reduced
- without surfactant, alveoli would tend to collapse during expiration
- have a bactericidal effect and lysosomal effect.
- In fetal development, surfactant appears in the last weeks of gestation and coincides with the appearance of lamellar bodies in the type II cells. (Resp. distress. Syndrome.)



Pulmonary surfactant

- The surfactant layer is not static but is constantly being turned over
- The lipoproteins are gradually removed from the surface by the pinocytotic vesicles of the squamous epithelial cells, by macrophages, and by type II alveolar cells.
- Alveolar lining fluids are also removed via the conducting passages as a result of ciliary activity
- As the secretions pass up through the airways, they combine with bronchial mucus, forming a **bronchoalveolar fluid** (This is why the respiratory tract of newborns is suctioned).
- The bronchoalveolar fluid contains several lytic enzymes (eg, lysozyme, collagenase, -glucuronidase) that are probably derived from the alveolar macrophages.

Alveolar-Lining Regeneration

- Inhalation of **NO₂** destroys most of the cells lining the alveoli (type I and type II cells).
- The action of this compound or other toxic substances with the same effect is followed by an increase in the mitotic activity of the remaining type II cells
- The normal turnover rate of type II cells is estimated to be 1% per day and results in a continuous renewal of both its own population and that of type I cells.

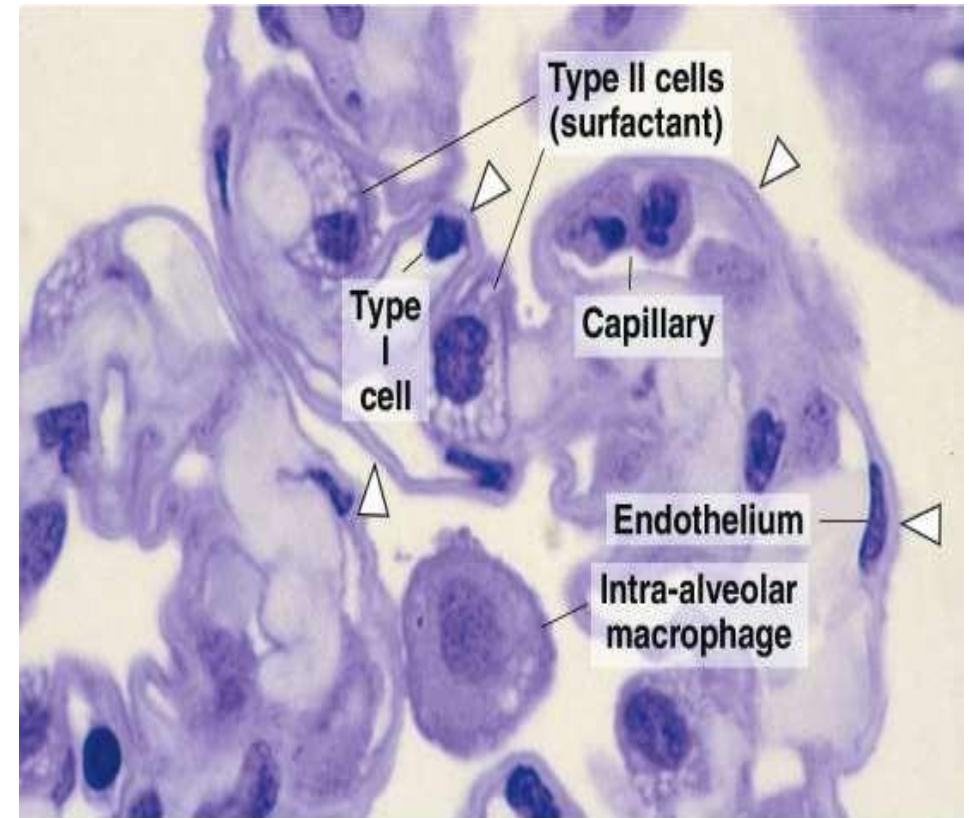
Lung Macrophages

- Also called dust cells.
- They are found in the interior of the interalveolar septum and are often seen on the surface of the alveolus.
- The phagocytosed debris within these cells was passed from the alveolar lumen into the interstitium.
- Could be seen on the surface of pleura or appear as black dots in the lungs.
- They originate from monocytes (WBCs) in the blood stream.
- They can pass through bronchioles into the bronchi, then enter the pharynx where they are expectorated with saliva.
- They are more numerous in number, even in comparison to type 1 alveolar cells.

Lung Macrophages

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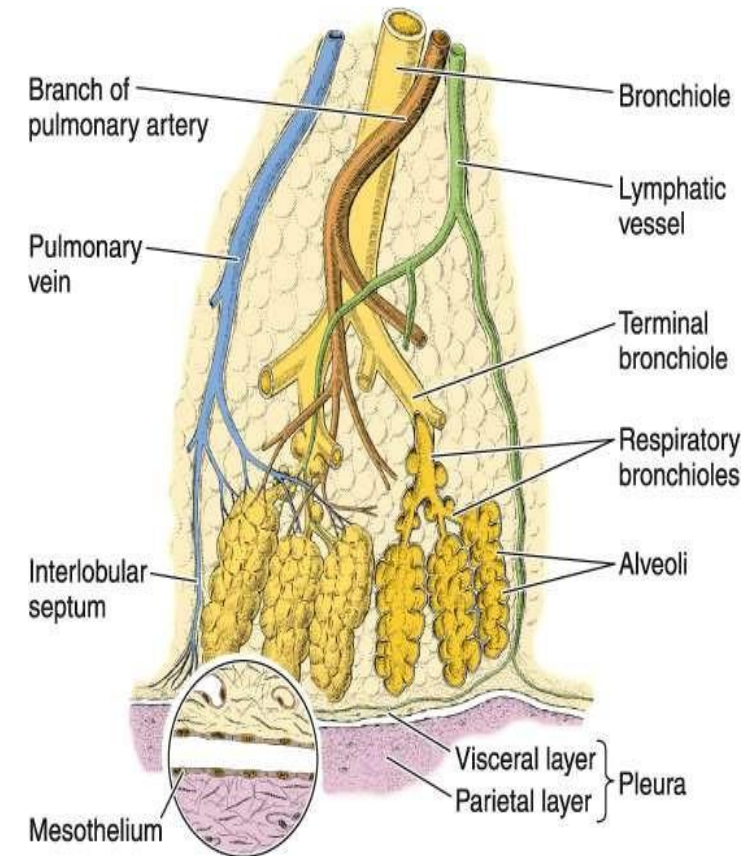
- also called **dust cells**
- are found in the interior of the interalveolar septum and are often seen on the surface of the alveolus
- The phagocytosed debris within these cells was passed from the alveolar lumen into the interstitium by the pinocytotic activity of type I alveolar cells
- The alveolar macrophages that scavenge the outer surface of the epithelium within the surfactant layer are carried to the pharynx, where they are swallowed.
- Numerous dust-laden macrophages in the connective tissue around major blood vessels or in the pleura probably are cells that have never passed through the epithelial lining



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Pulmonary Blood Vessels

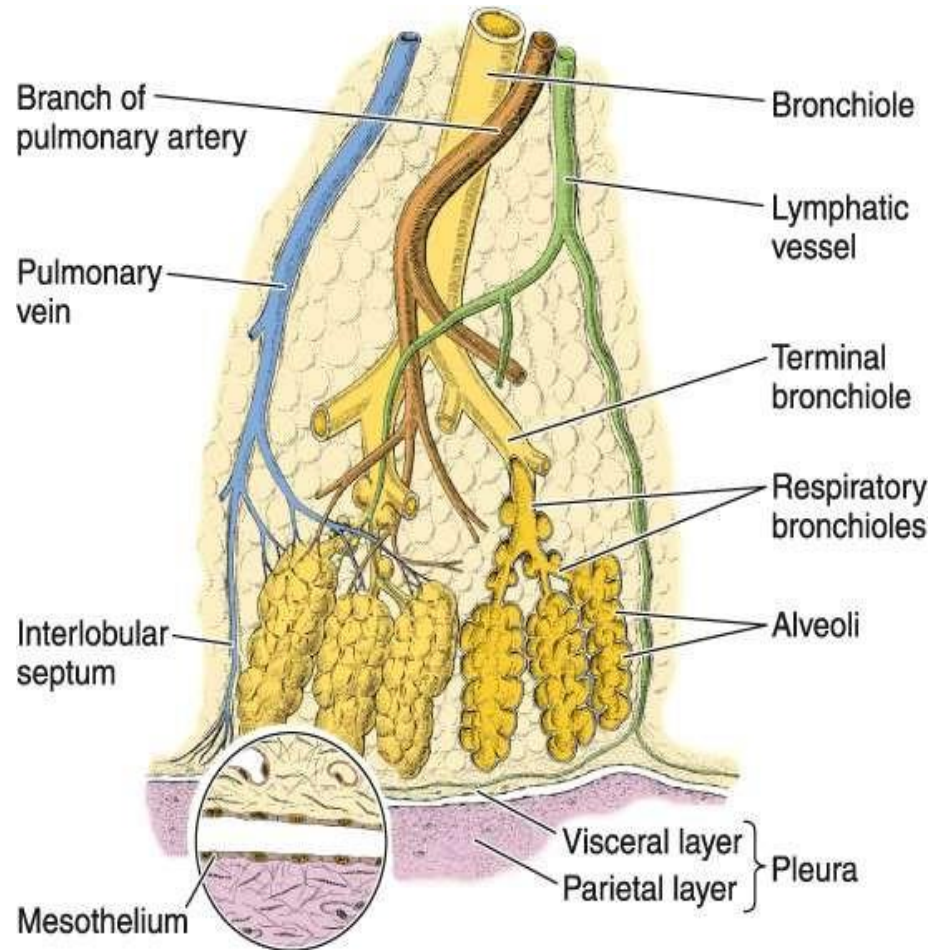
- Pulmonary artery carries deoxygenated blood to the lungs.
- Bronchial arteries provide the main blood supply to the lung tissue.
- Pulmonary veins carry oxygenated blood from the lungs to the heart, and finally 4 pulmonary veins will go to the left atrium then to the left ventricle then to the aorta.
- Pulmonary veins are Bi-laterally located as shown in the following figure.
- Nutrient vessels are the bronchial arteries which are coming from Descending thoracic aorta.



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Pulmonary Blood Vessels

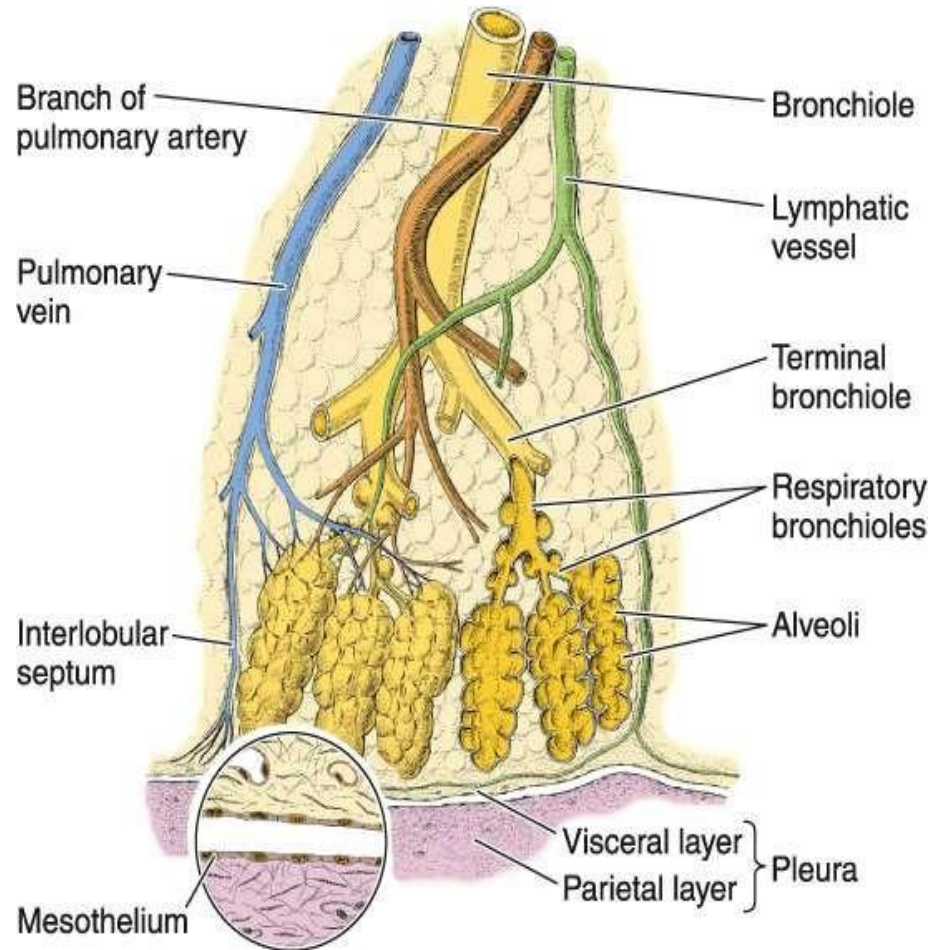
- Circulation in the lungs includes both nutrient (systemic) and functional (pulmonary) vessels
- Pulmonary arteries are thin walled as a result of the low pressures (25 mm Hg systolic, 5 mm Hg diastolic)
- Within the lung the pulmonary artery branches, accompanying the bronchial tree
- Its branches are surrounded by adventitia of the bronchi and bronchioles
- At the level of the alveolar duct, the branches of this artery form a capillary network in the interalveolar septum
- The lung has the best-developed capillary network in the body, with capillaries between all alveoli, including those in the respiratory bronchioles



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Pulmonary Blood Vessels

- Venues that originate in the capillary network are found singly in the parenchyma
- supported by a thin covering of connective tissue and enter the interlobular septum
- After veins leave a lobule, they follow the bronchial tree toward the hilum.
- Nutrient vessels follow the bronchial tree and distribute blood to most of the lung up to the respiratory bronchioles, at which point they anastomose with small branches of the pulmonary artery.



Pulmonary Lymphatic Vessels

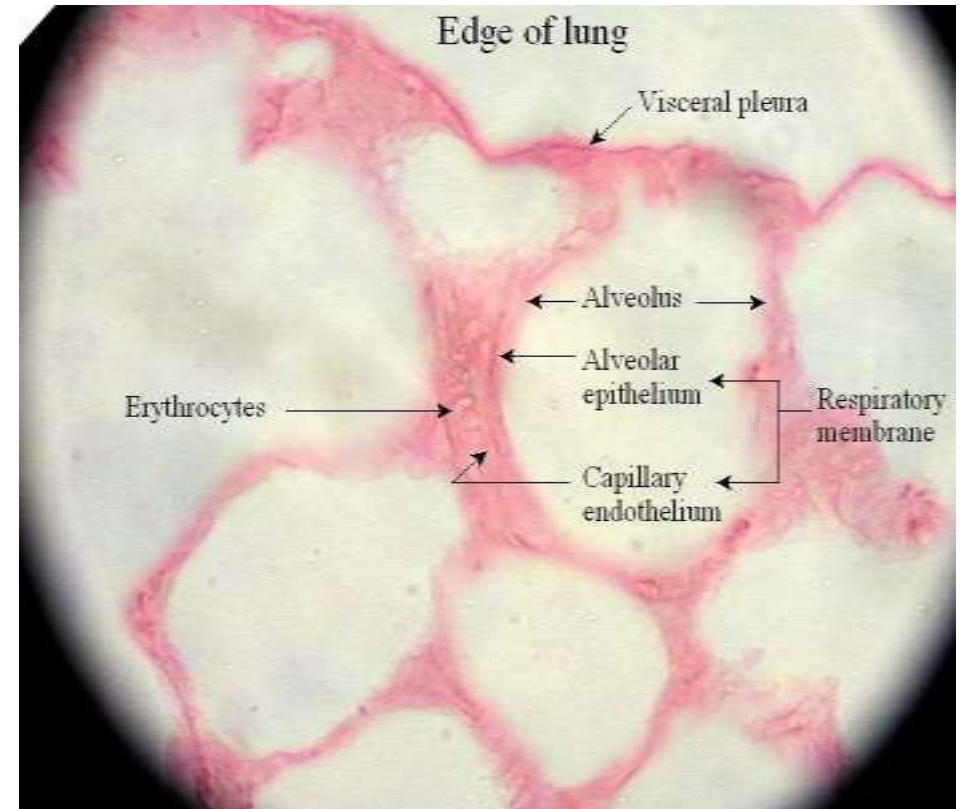
- follow the bronchi and the pulmonary vessels; they are also found in the interlobular septum,
 - they all drain into lymph nodes in the region of the hilum (deep network),
 - Lymph nodes in the hilum/ mediastinum are called mediastinal lymph nodes.
 - superficial network includes the lymphatic vessels in the visceral pleura.
 - Lymphatic vessels drain into the thoracic duct on the left side, and the right lymphatic duct on the right side, which will drain into the respective brachiocephalic veins.
 - The lymphatic vessels of the superficial network drain toward the hilum. They either follow the entire length of the pleura or penetrate the lung tissue via the interlobular septum.
- Lymphatic vessels are not found in the terminal portions of the bronchial tree or beyond the alveolar ducts

Nerves

- Both parasympathetic and sympathetic efferent fibers innervate the lungs.
Sympathetic innervation causes bronchodilation.
Parasympathetic innervation causes bronchoconstriction.
- general visceral afferent fibers, carrying poorly localized pain sensations, are also present
- Most of the nerves are found in the connective tissues surrounding the larger airways.

Pleura

- It consists of two layers, parietal and visceral, that are continuous in the region of the hilum
- ▶ Both membranes are composed of mesothelial cells (simple squamous epithelial cells), resting on a fine connective tissue layer that contains collagen and elastic fibers
- The elastic fibers of the visceral pleura are continuous with those of the pulmonary parenchyma.
- pleural cavity contains only a film of liquid that acts as a lubricant, facilitating the smooth sliding of one surface over the other during respiratory movements.
- This fluid is derived from the blood plasma by exudation



E learning quiz

The respiratory membrane composed of all of the following except:

- A) Type 1 Alveolar cells
- B) Endothelial cells
- C) Fused Basal lamina
- D) Surfactant layer
- E) Dust Cell

Answer: E

the lining epithelium of the following Respiratory organs is **not** respiratory:

- A) Nasal Cavity
- B) Intrapulmonary Bronchi
- C) True Vocal Cord
- D) False Vocal Cord
- E) Trachea

Answer: C

Additional sources

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1 → V2	35		We add not to Q2
V2 → V3			



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