

Respiratory System 2

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Modified by: Rani Tachjian

Modified Key:

White Text: Information present in original presentation.

Underlined Text: Text read by the Doctor.

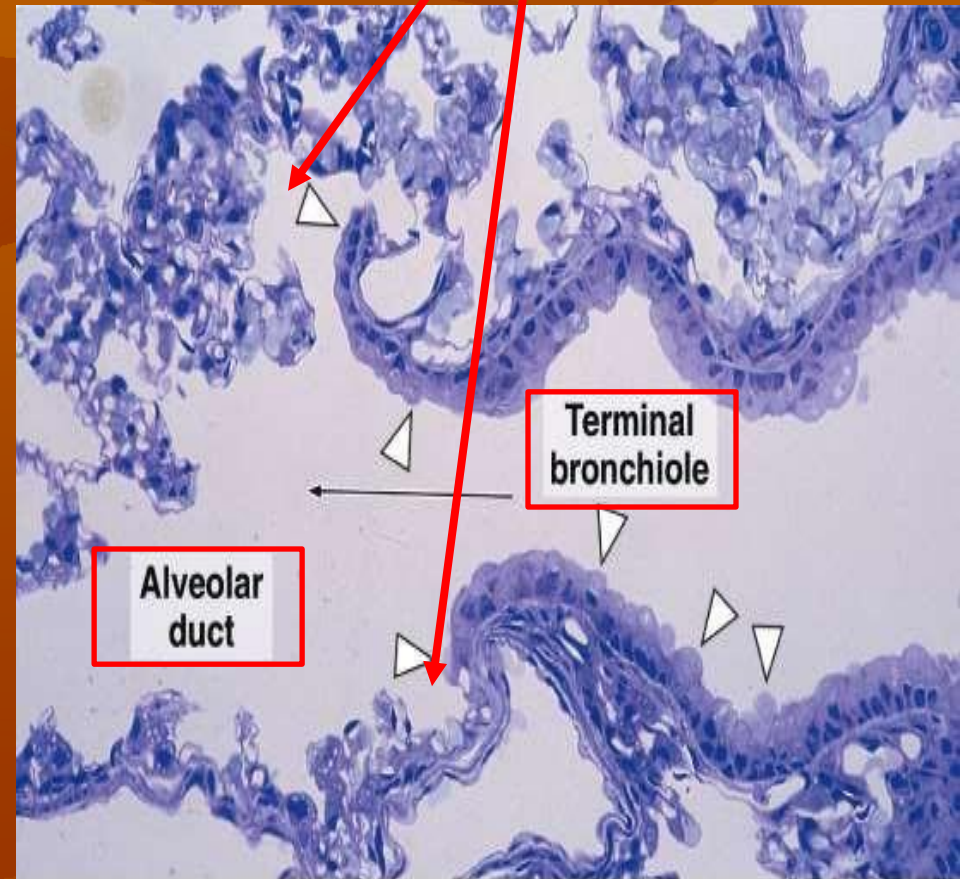
Light Yellow Text: Information stated by the Doctor, not present in original presentation file.

Blue Text: Additional information added for further comprehension.

Bronchioles

- intralobular airways with diameters of 5 mm or less
- Large (1 mm) small (0.5mm)
- have neither cartilage nor glands in their mucosa, characteristic feature
- No lymphocyte (more precisely, no lymphatic nodules. Lymphocytes are present all along the RT)
- only scattered goblet cells within the epithelium of the initial segments and replaced with clara cells (simple cuboidal cells, no cilia)
- In the larger bronchioles, the epithelium is **ciliated pseudostratified columnar**
- decreases in height and complexity to become **ciliated simple columnar or ciliated cuboidal** epithelium in the smaller terminal bronchioles. Even distally, we start seeing Clara cells (non-ciliated).
- Keep in mind, these changes are gradual and not sudden.

Respiratory Bronchioles

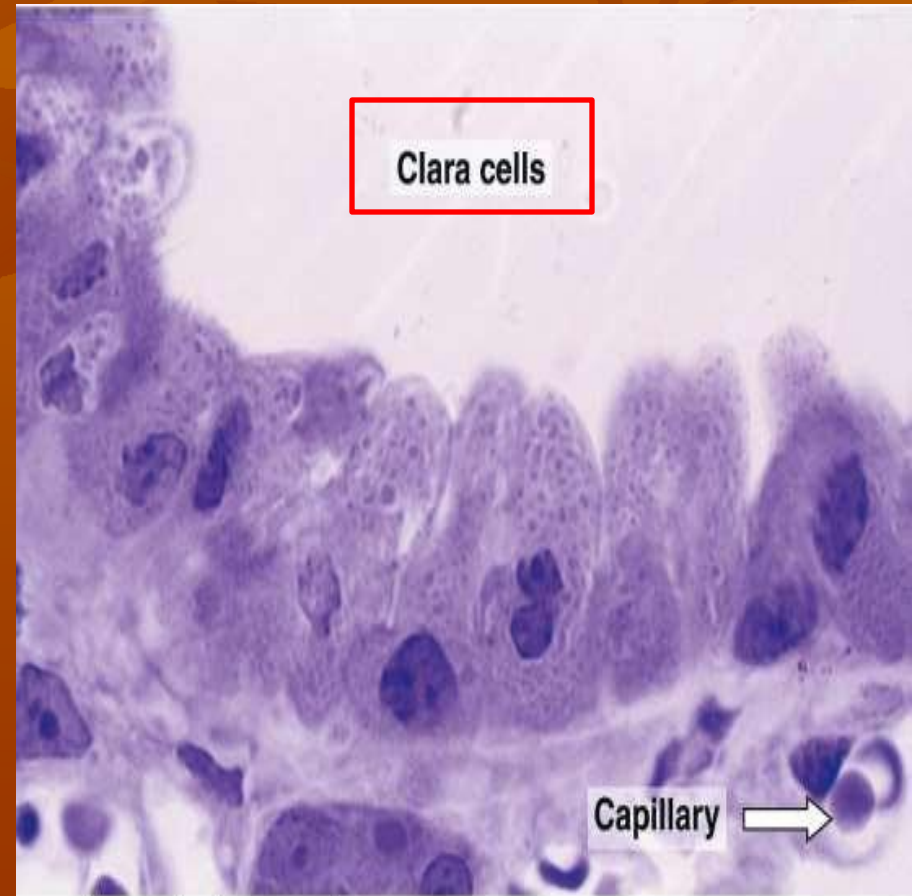


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Important question for the exam: characteristics of Clara cells. Study them well

Bronchioles

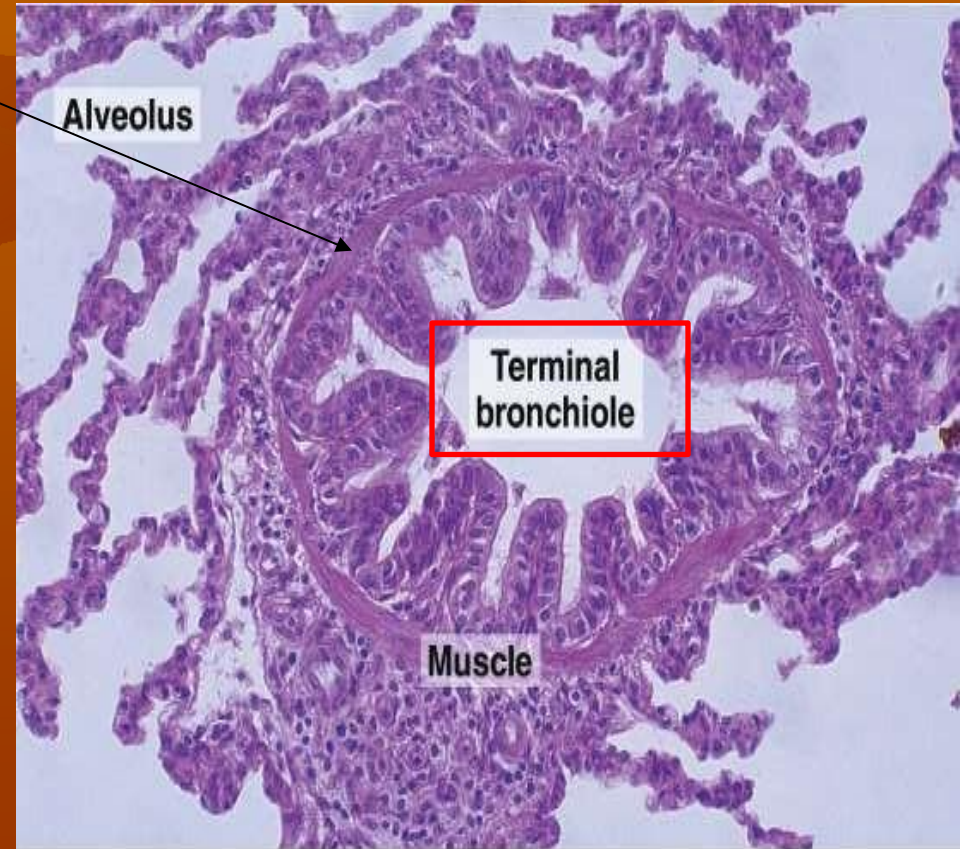
- The epithelium of terminal bronchioles and beginning of respiratory bronchioles also contains Clara cells
- which are devoid of cilia, have secretory granules in their apex
- known to secrete proteins that protect the bronchiolar lining against oxidative pollutants and inflammation of bacteria.
- They 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
- Their function is poorly understood, but they are probably chemoreceptors that react to changes in gas composition (O₂ & CO₂) within the airway
- They also seem involved in the reparative process of airway epithelial cell renewal after injury



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Terminal Bronchioles

- lamina propria is composed largely of spiral smooth muscle and elastic fibers, which produces prominent folding in the mucosa (simple ciliated columnar to cuboidal epithelium).
- 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; sympathetic stimulation produces the opposite effect.



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Doctor's Notes:

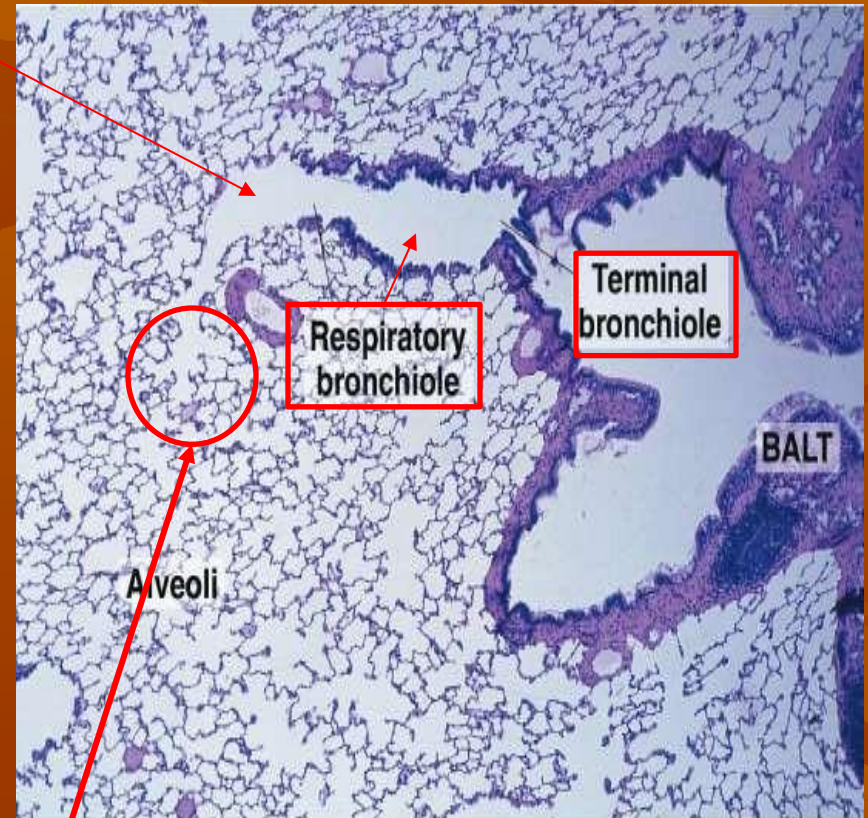
We said in the first lecture that smooth muscles increase as we move in the RT, especially in bronchioles, and cartilage is decreases, resulting in what we called asthma: smooth muscles contract and no cartilage is present to hold it open, resulting in obstruction of bronchioles.

Since sympathetic stimulation causes bronchodilatation, asthma patients can be given adrenaline to relieve their symptoms.

Respiratory Bronchioles

- Each terminal bronchiole subdivides into two or more respiratory bronchioles
- Terminal bronchioles serve as regions of transition between the conducting and respiratory portions of the respiratory system
- mucosa is structurally identical to that of the terminal bronchioles
- their walls are interrupted by numerous saclike alveoli where gas exchange occurs

Alveolar duct, similar to a corridor running through the alveolar sacs. The sacs are similar to flowers, petals connected together at the duct, with each leaflet representing an alveolus.



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Alveolar sac, similar to a flower petals.

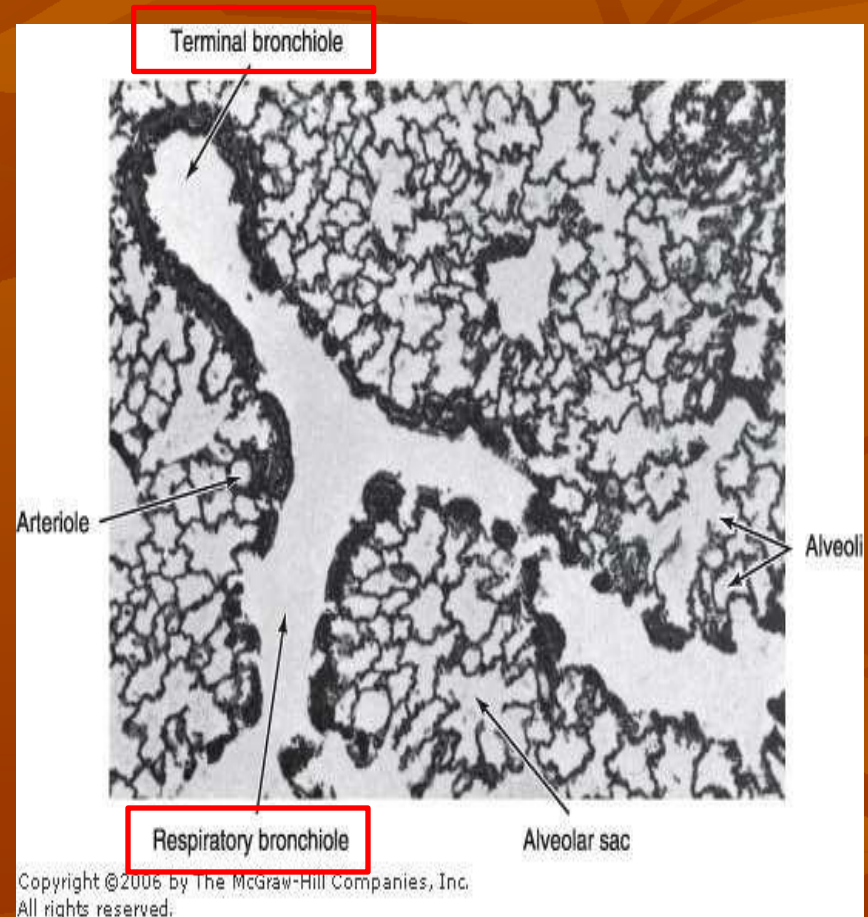
Doctor's Notes:

Under the microscope, pay attention to the continuity of the epithelium to differentiate between respiratory bronchioles and terminal bronchioles.

First of all, bronchioles are not surrounded by cartilage, so look for a lumen without any cartilage around it and, then, check if the epithelium is continuous: if it is, then it is terminal. If not, then it is a respiratory bronchiole and it opens into an alveolar duct.

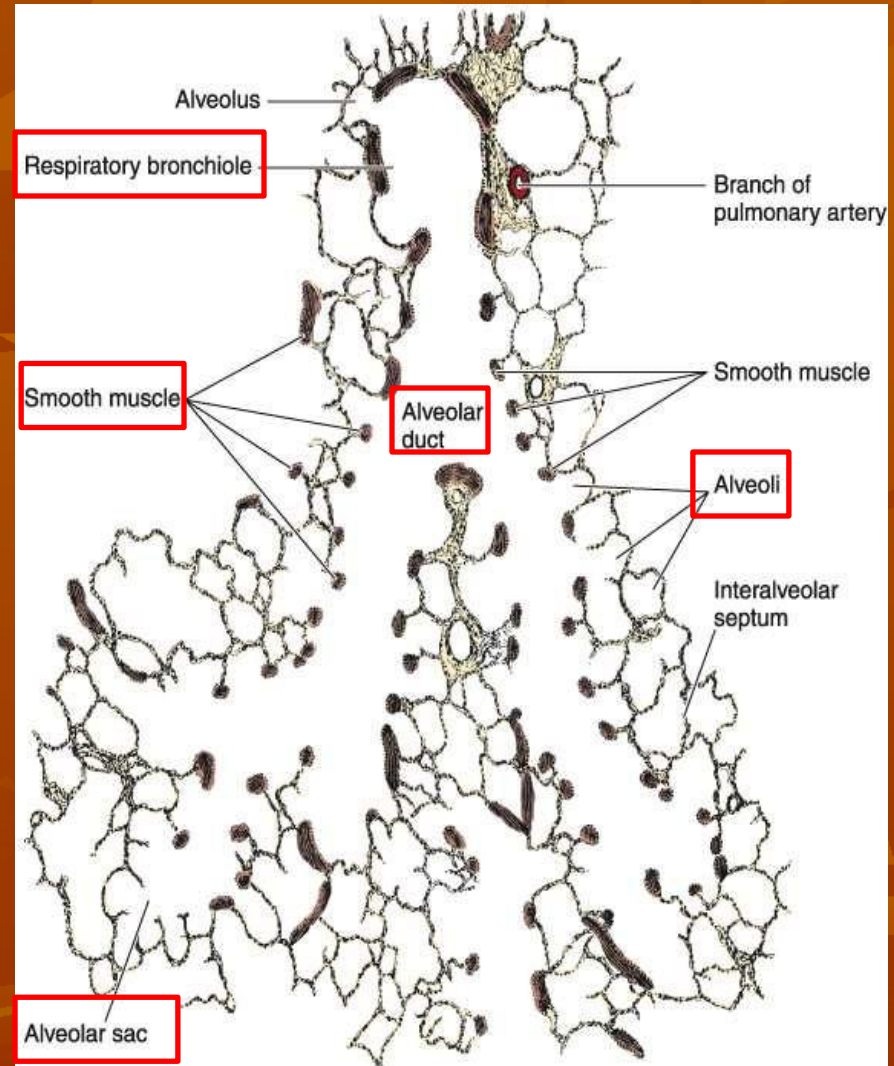
Respiratory Bronchioles

- lined with ciliated cuboidal epithelial cells and Clara cells (non ciliated cuboidal cells), but at the alveolar openings the bronchiolar epithelium becomes continuous with the squamous alveolar lining cells
- Between alveoli, the bronchiolar epithelium consists of ciliated cuboidal epithelium
- Smooth muscle and elastic connective tissue lie beneath the epithelium; however, smooth muscles and, therefore, folding of the mucosa decreases.



Alveolar Ducts

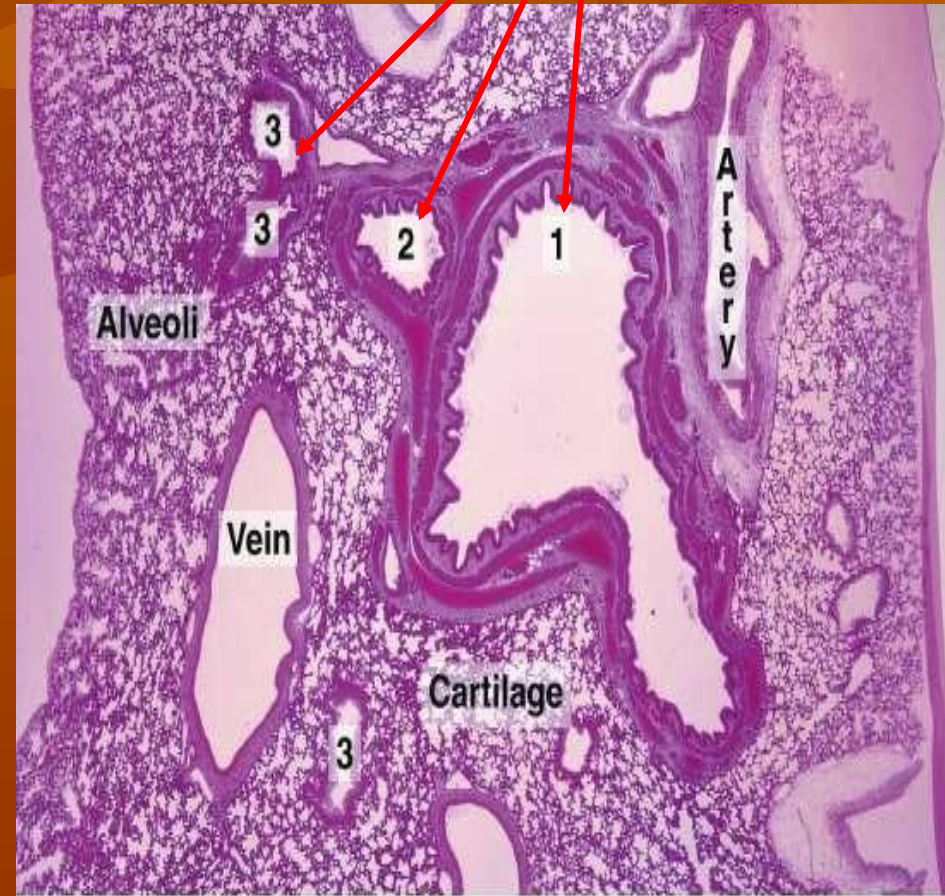
- Both the alveolar ducts and the alveoli are lined with extremely attenuated squamous alveolar cells
- In the lamina propria surrounding the rim of the alveoli is a network of smooth muscle cells
- These sphincterlike smooth muscle bundles appear as knobs/tags between adjacent alveoli
- Smooth muscle 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. Atria are basically the meeting of two alveolar ducts.
- The elastic fibers enable the alveoli to expand with inspiration and to contract passively with expiration
- The reticular fibers serve as a support that prevents overdistention and damage to the delicate capillaries and thin alveolar septa.



Alveoli

Primary, secondary and tertiary bronchi

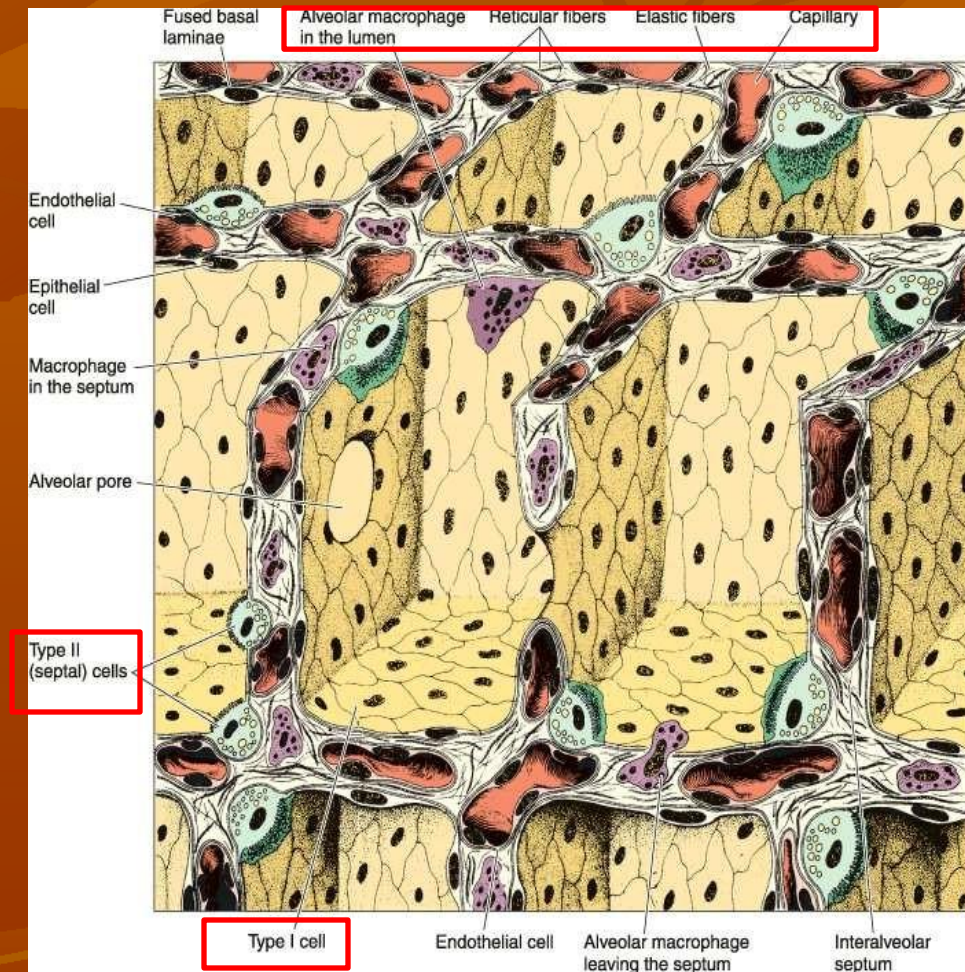
- Alveoli are saclike evaginations (about 200 um in diameter)
- responsible for the spongy structure of the lungs
- The structure of the alveolar walls is specialized for enhancing diffusion between the external and internal environments
- each wall lies between two neighboring alveoli and is therefore called an **interalveolar septum, or wall**
- **Alveolar wall = boundaries of the alveoli**
- **interalveolar septum = contact point of two or more alveolar walls**



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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
- The capillaries and connective tissue constitute the **interstitium**
- Within the interstitium of the interalveolar septum is found the richest capillary network in the body.
- The interalveolar septum contains **pores**
- 10-15 μm in diameter, that connect neighboring alveoli
- These pores equalize air pressure in the alveoli (by allowing oxygen diffusion between them) and promote the collateral circulation of air when a bronchiole is obstructed.



Doctor's Notes:

In the previous slide, the whitish tissue is the septa while the yellow-coloured cells are the walls of alveoli.

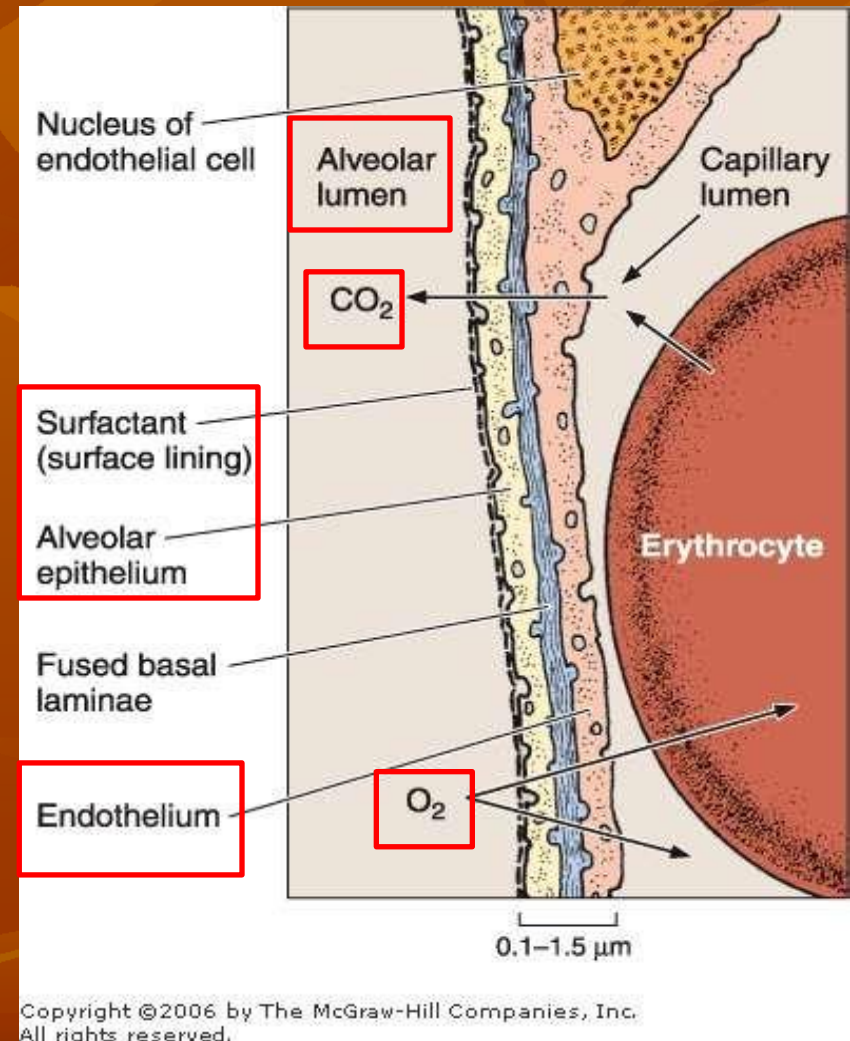
As we said in the 1st lecture, 97% of the cells in the alveolar wall (pay attention to walls and septa now because they differ in composition) are type 1 cells, while 3% are type 2 cells.

Type 2 cells (also called septal cells) are mainly in the septa, especially in the corners. 16% of cells in the SEPTA are type 2 cells, while 8% are type 1.

We also have endothelial cells which are present in both the septa and the walls.

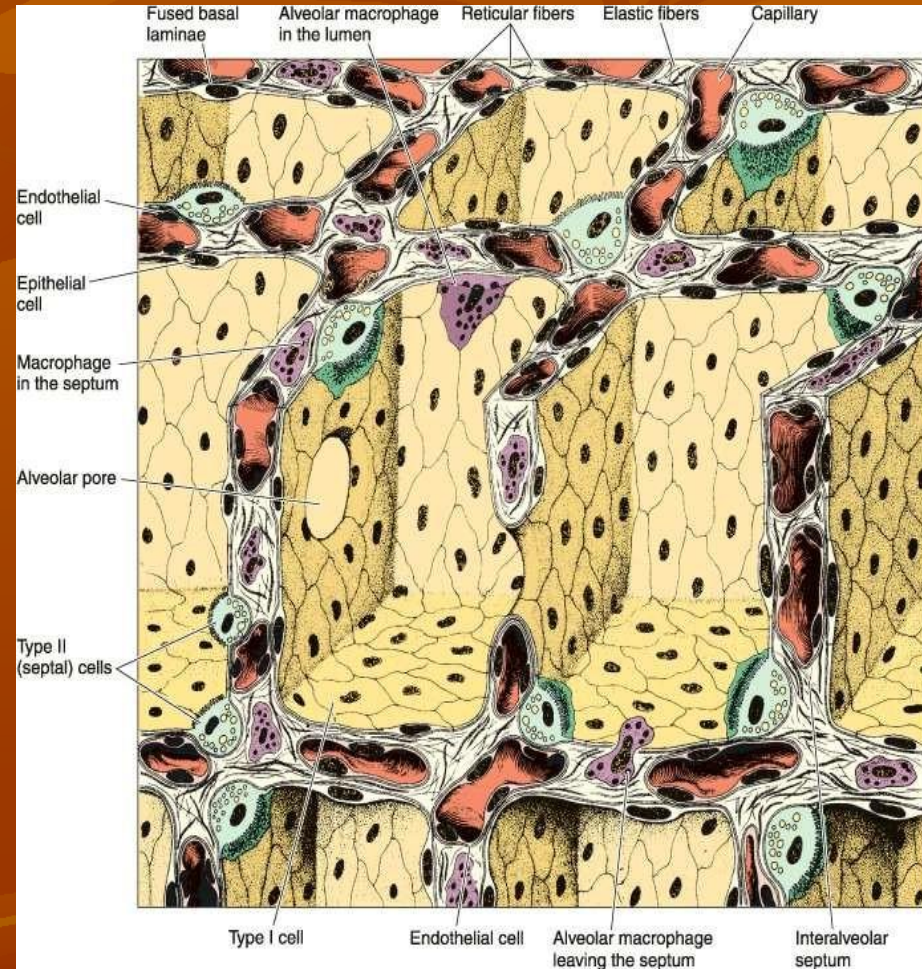
Blood-air barrier (i.e. respiratory membrane)

- 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 type 1 alveolar cells which is lined by a surfactant layer.
- 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 (very thin). Gas exchange occurs through part of the **SEPTUM**.



Interalveolar septum

- 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

- Cells in the interstitium

 - Endothelial cells (capillaries) 30 %

 - Fibroblasts and mast cells 36%

- Macrophages 10 % (i.e. dust cells, engulf foreign bodies)

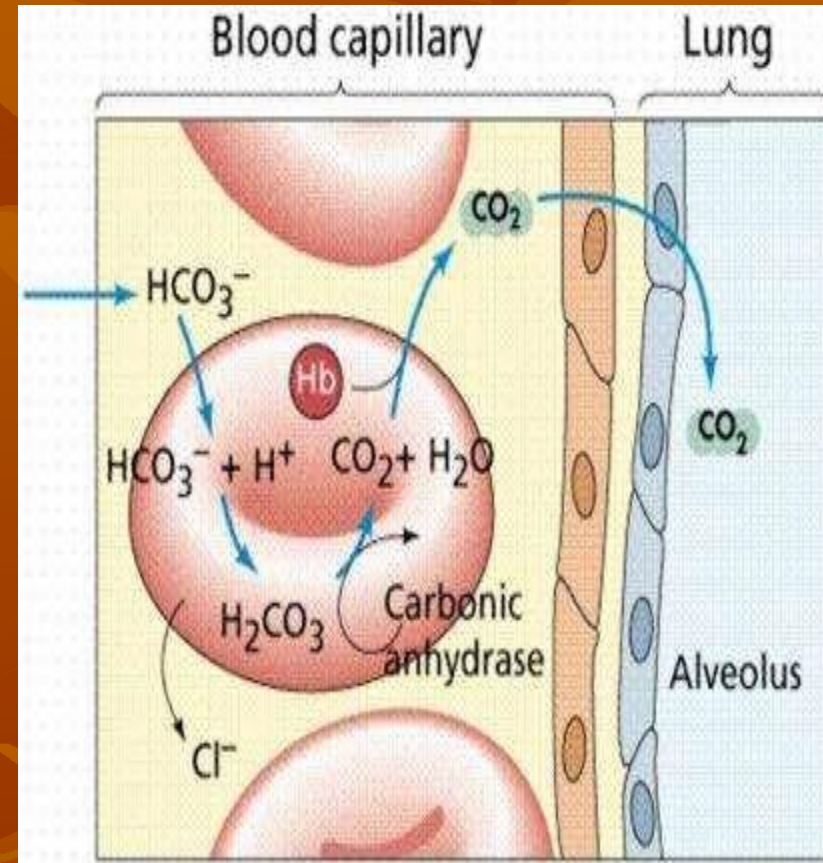
- Type I cells 8 %

- Type II cells (septal cells) 16%

- leukocytes

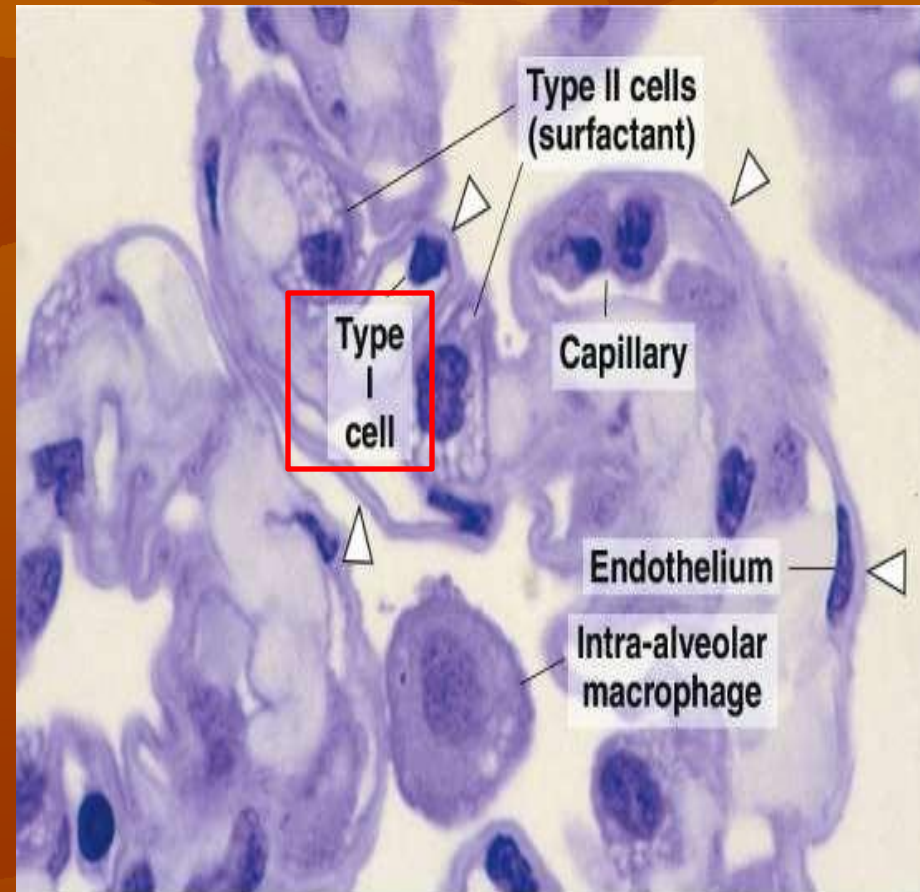
Gas exchange

- 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

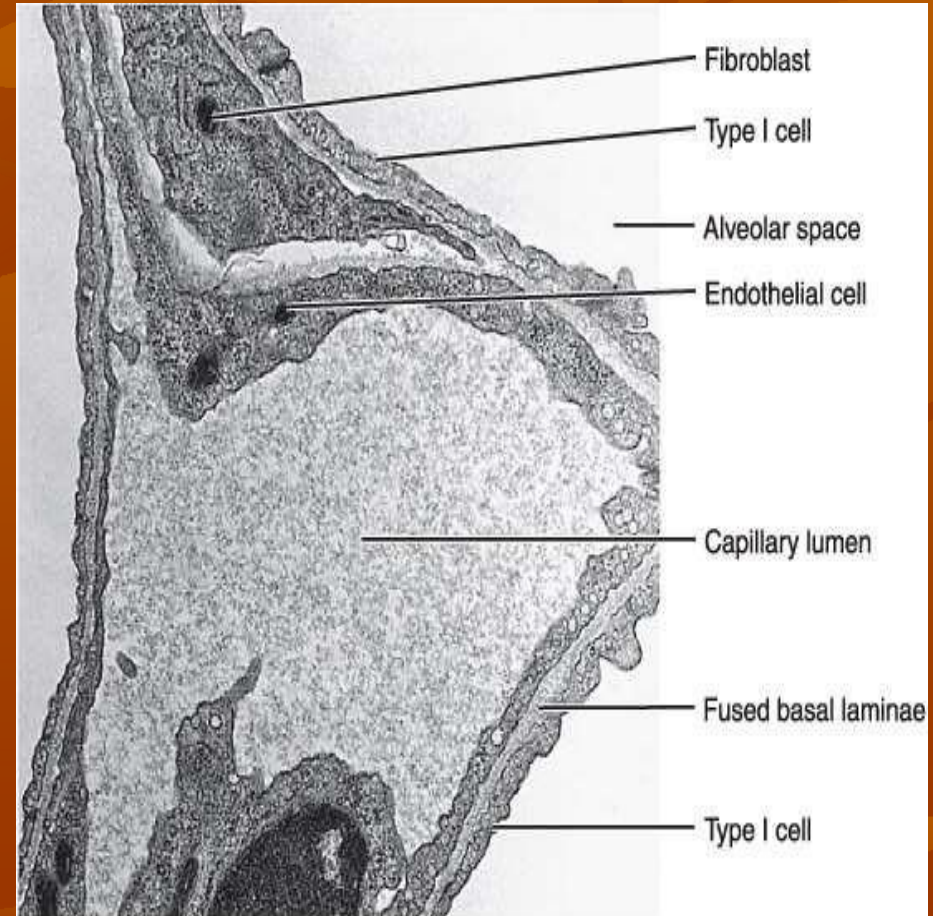
- extremely thin and can be easily confused with type I alveolar epithelial cells, differentiated under the microscope by presence of RBCs.
- endothelial lining of the capillaries is continuous and not fenestrated
- Clustering of the nuclei and other organelles allows the remaining areas of the cell to become extremely thin increasing the efficiency of gas exchange
- The most prominent feature of the cytoplasm in the flattened portions of the cell is numerous pinocytotic vesicles.



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Type I cells

- Simple 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%).
- 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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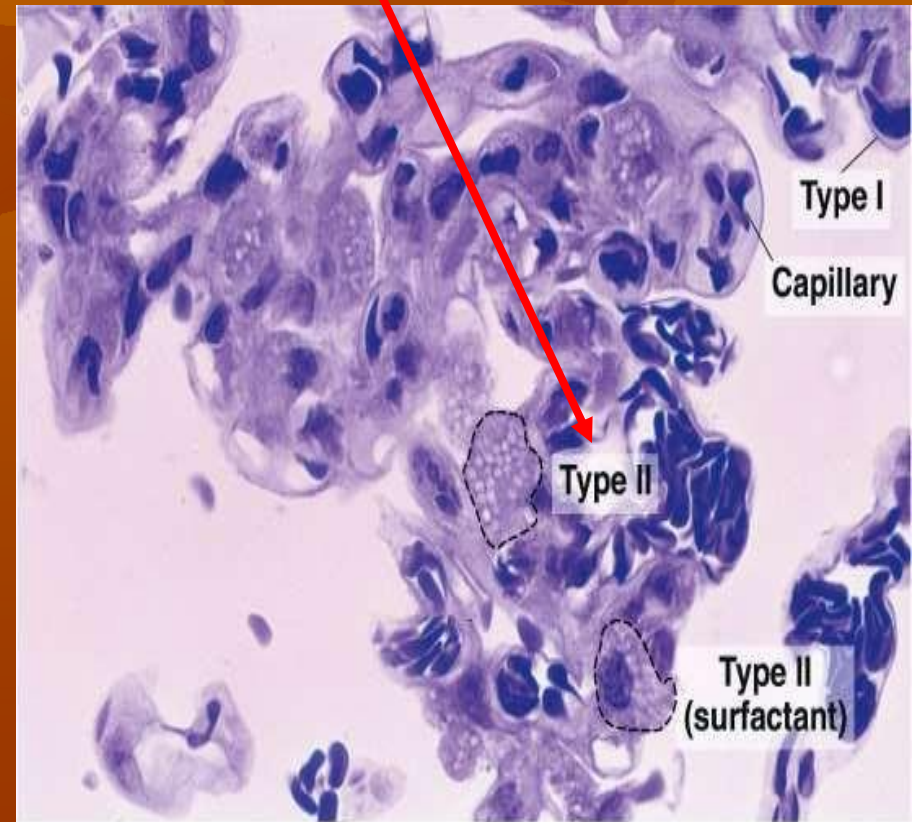
Type I cells

- 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 (between type 1 and type 2 cells) that prevent the leakage of tissue fluid into the alveolar air space
- The main role of these cells is to provide a barrier of minimal thickness that is readily permeable to gases.



Type II cells

- interspersed among the type I alveolar cells with which they have occluding and desmosomal junctions. Cuboidal cells, larger than type 1 cells
- 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)

- they exhibit a characteristic vesicular or foamy cytoplasm. These vesicles are caused by the presence of **lamellar bodies**

- Lamellar bodies, which average 12um 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

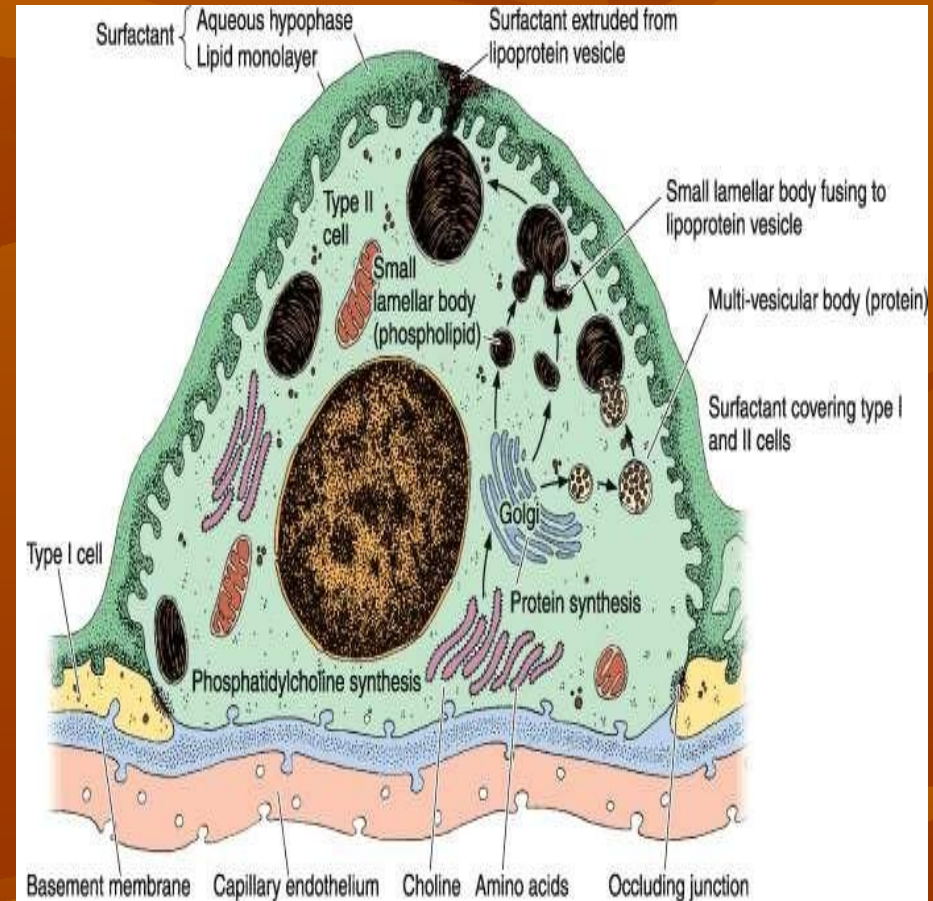
- The lamellar bodies give rise to the **pulmonary surfactant**, a material that spreads over the alveolar surfaces, providing an extracellular alveolar coating, that lowers alveolar surface tension.



Pulmonary surfactant

Biochemistry, Doctor didn't really focus on it

- 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
- 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.)



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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. That's why, when an infant is born, suctioning of the RT is done to shift these fluids which also contain the surfactant.
- The bronchoalveolar fluid contains several lytic and antibacterial enzymes (eg, lysozyme, collagenase, -glucuronidase) that are probably derived from the alveolar macrophages.

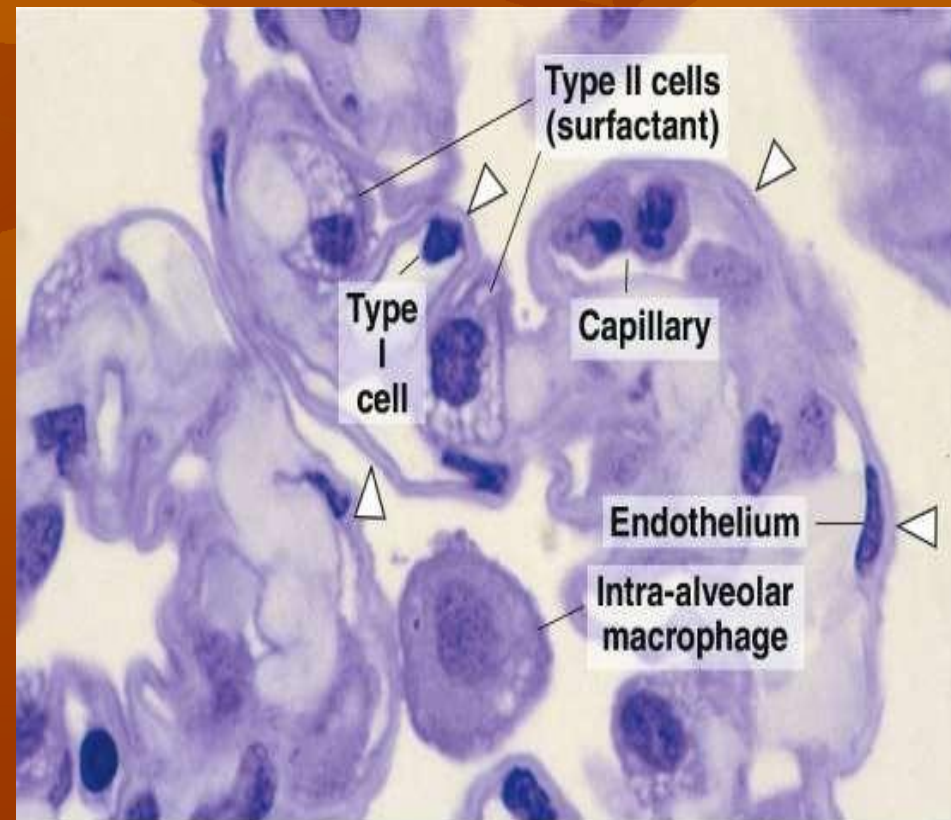
Alveolar-Lining Regeneration

- 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

IMPORTANT NOTE:
number of dust cells is
LARGER than number of
type 1 cells.

- also called **dust cells**, originate from monocytes of the blood.
- are found in the interior of the interalveolar septum and are often seen on the surface of the alveolus or on the pleura, appear as black dots under the microscope.
- 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 bronchioles, bronchi & pharynx, where they are swallowed (Doctor said expectorated, stick to it).
- 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

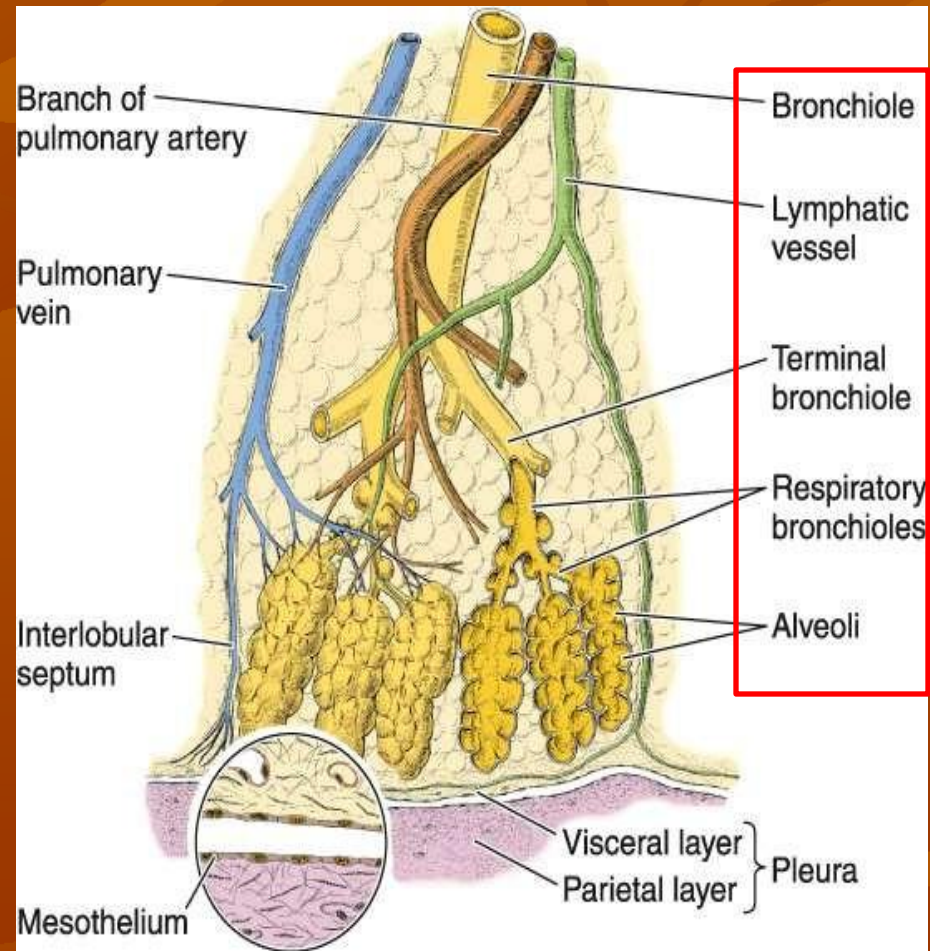


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Pulmonary Blood Vessels

Doctor revised some notes here about the blood supply and lymphatics, you can find them in the Trachea Modified slides.

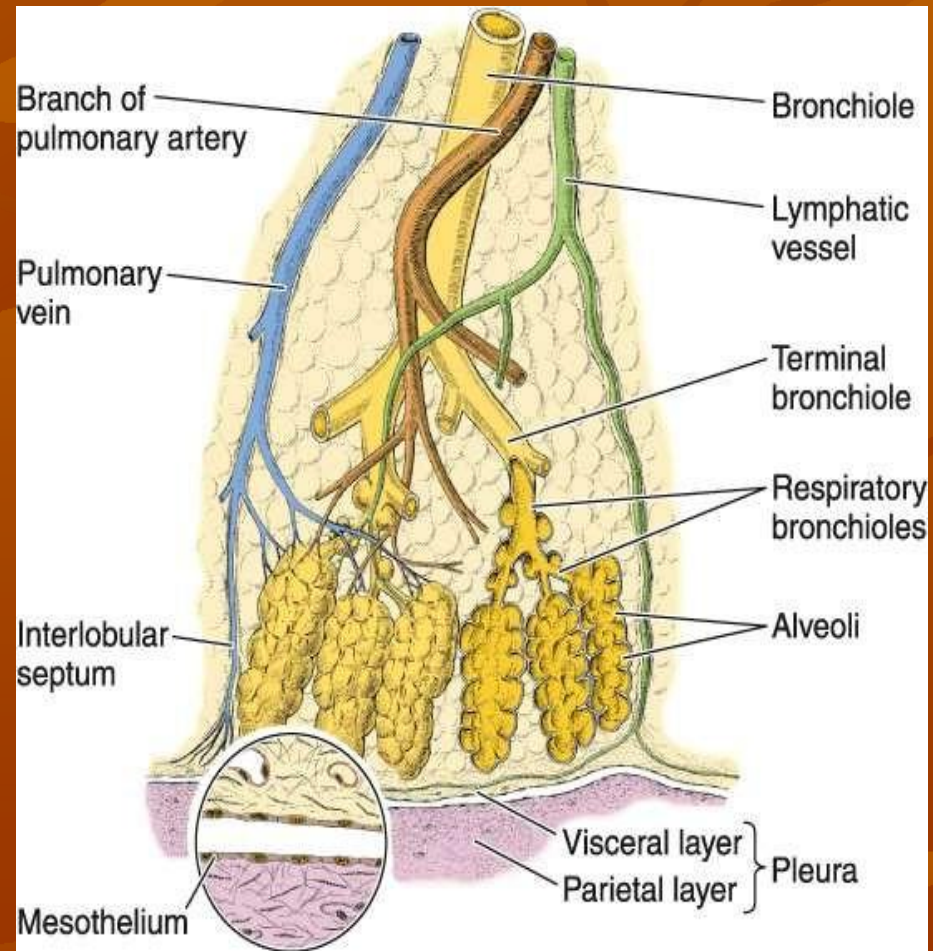
- Circulation in the lungs includes both nutrient (systemic) and functional (pulmonary) vessels
- Pulmonary arteries are thin walled as a result of the low pressures (25 mm Hg systolic, 5 mm Hg diastolic)
- Within the lung the pulmonary artery branches, accompanying the bronchial tree
- Its branches 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

- Venules 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

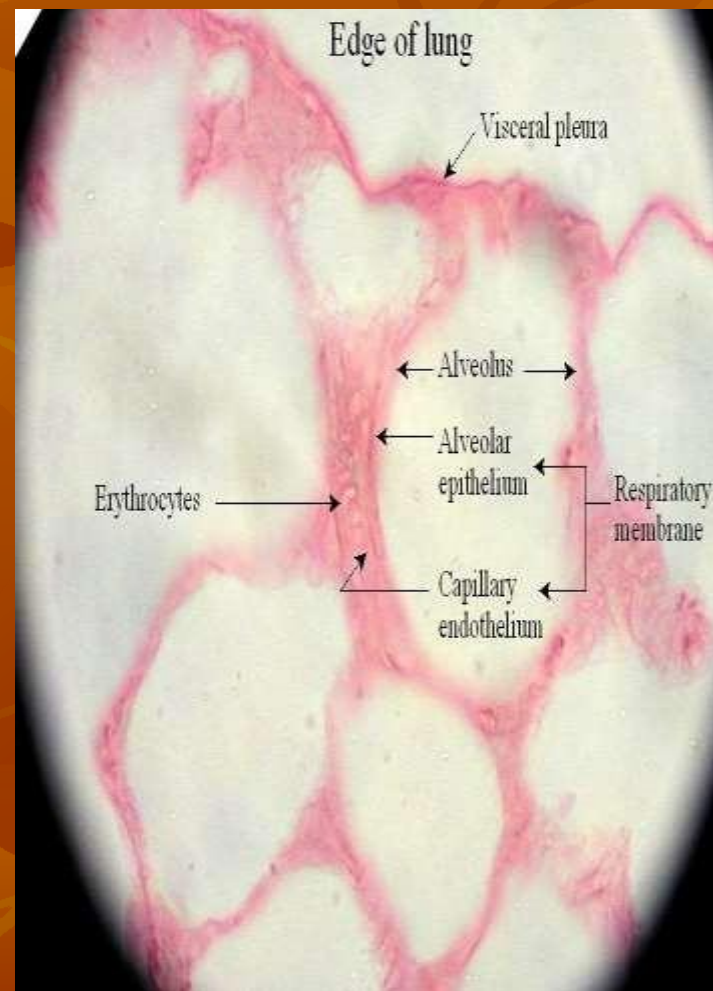
- follow the bronchi and the pulmonary vessels; they are also found in the interlobular septum,
- they all drain into lymph nodes in the region of the hilum (**deep network**)
- **superficial network** includes the lymphatic vessels in the visceral pleura
- The lymphatic vessels of the superficial network 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 and visceral pleura (only somatic to parietal pleura)
- general visceral afferent fibers, carrying poorly localized pain, touch and temperature 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) resting on a fine connective tissue layer that contains collagen, elastic and reticular 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





Thank you