

RESPIRATORY SYSTEM

جنا
ANATOMY



Title: Histology – sheet 2

Writer: Reham badayneh

Science: Raneem Mohammed

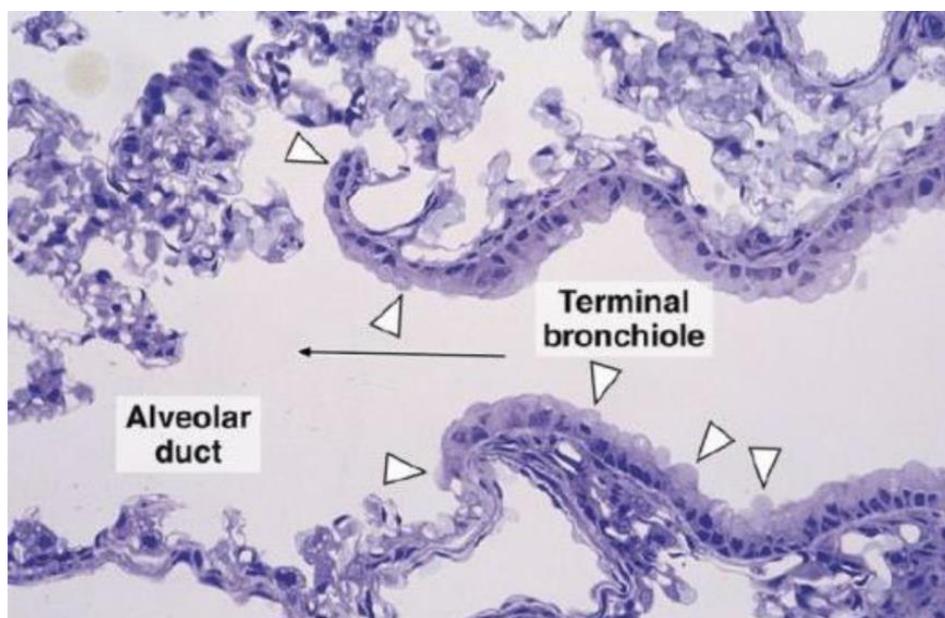
Final: Omar Ismail

Doctor: Mohammed Hisham Al-Muhtaseb

Bronchioles:

They are formed after about the 10th generation of branching.

- Intralobular airways with diameters of 1 mm or less (Large (1 mm) small (0.5mm)), Smaller bronchioles then divide into terminal bronchioles, these are the last component of the conducting zone of the respiratory tract.
- Have neither cartilage in the supporting layer nor mucosal glands (initially, there might be 1-2 glands in the mucosa of a large bronchiole. However, as we proceed, there won't be any). On the other hand, the smooth muscles increase as we go distally, so they are present in high numbers in the terminal bronchioles.
- No lymphatic nodules but lymphocytes are present. (lymphatic nodules are **absent** distally)
- There is gradual decrease of goblet cells and glands, scattered (few) goblet cells and glands within the epithelium of the initial segments, but they are absent distally.



- The lining epithelium of the initial (large) bronchioles is ciliated pseudostratified columnar epithelium , it will change gradually (decreases in height and complexity) into ciliated simple columnar and finally it will become simple cuboidal ciliated with Clara cells in the terminal bronchioles , and then simple squamous epithelium in respiratory bronchioles .

☺ Clara cells: -

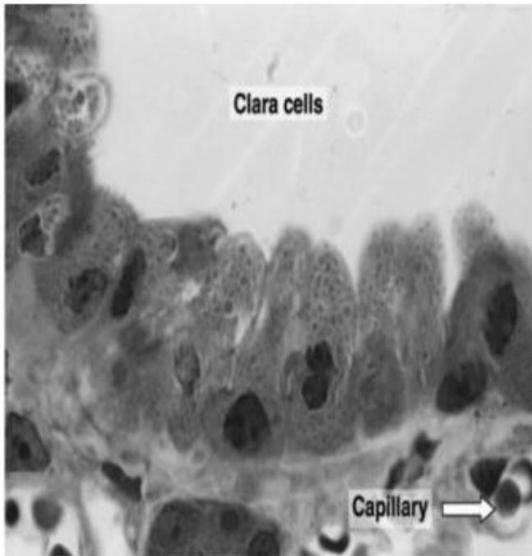
- Simple cuboidal non-ciliated cells.
- They're present in terminal bronchioles in high number.
- They have secretory granules at their apex

☺ Functions of Clara cells: -

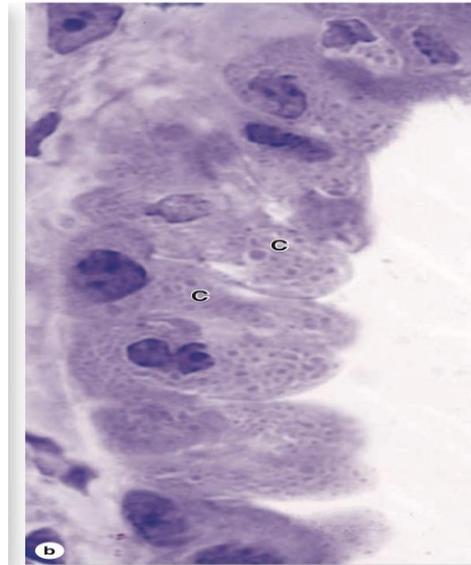
- Known to secrete proteins that protect the bronchiolar lining against oxidative pollutants and inflammation.
- They produce one of the components of the surfactants and act as reserve cells.

- They also seem involved in the reparative process of airway epithelial cell renewal after injury

☺ 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 within the airway.

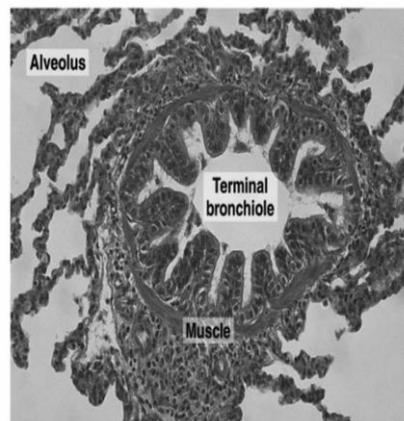
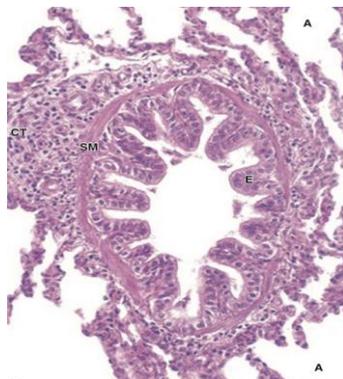


Copyright ©2006 by The McGraw-Hill Companies, Inc. All rights reserved.



In bronchioles, lamina propria is composed largely of smooth muscle and elastic fibers with no cartilage, that's why it looks folded. Smooth muscle cells are organized in a circular/spiral shape in the lamina propria.

- 1- These smooth muscles are under the control of the vagus nerve (parasympathetic) [which will make them contract → bronchoconstriction]
- 2- And the sympathetic nervous system [which will make them relax → bronchodilation].



This bronchoconstriction (contraction of smooth muscles of bronchioles by vagus nerve) will cause expiratory wheezing in asthmatic patients. (A wheeze is a whistling sound due to an obstruction or narrowing of the respiratory airways).

The purple box is extra

>> MEDICAL APPLICATION

Asthma is a common condition produced by chronic inflammation within the bronchial tree of the lungs. The disorder is characterized by sudden constrictions of the smooth muscle in bronchioles called **bronchospasms**, or bronchial spasms. Constriction is caused by mast cell degranulation triggered by the presence of specific antigens. The resulting difficulty in breathing can be very mild to severe. **Epinephrine** and other sympathomimetic drugs relax the muscle and increase the bronchiole diameter by stimulating the sympathetic nervous system, and they are administered during asthma attacks. When the thickness of the bronchial walls is compared with that of the bronchiolar walls, the bronchiolar muscle layer is seen to be proportionately greater.

Respiratory bronchioles:-

-Each terminal bronchiole subdivides into two or more respiratory bronchioles which serve as regions of transition between the conducting and respiratory portions of the respiratory system.

-They are always surrounded by blood vessels; either branches of pulmonary arteries or pulmonary veins tributaries.

-Its mucosa at first is structurally identical to that of the terminal bronchioles- ciliated simple cuboidal epithelial cells and clara cells (nonciliated), but at the alveolar openings (distally) the bronchiolar epithelium becomes continuous with the simple squamous alveolar lining cells.

Between alveoli, the bronchiolar epithelium consists of ciliated cuboidal epithelium

-They open upon alveolar ducts (unlike terminal bronchioles which are closed) , their walls are interrupted by numerous saclike alveoli where gas exchange occurs.

-In respiratory bronchioles there aren't any cartilage nor mucosal glands/goblet cells.

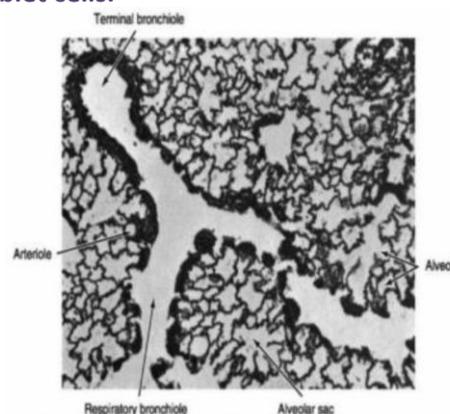
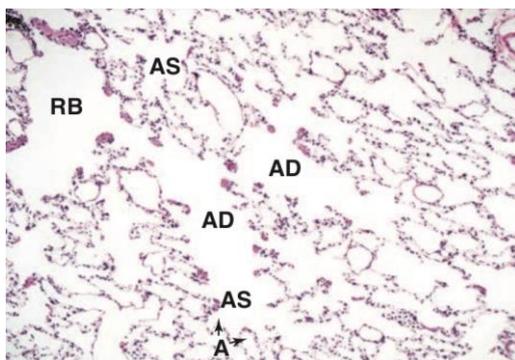
This figure is from the book:

RB : Respiratory bronchioles

AS : Alveolar Sac

AD : Alveolar Duct

A : Alveoli



Smooth muscle and elastic connective tissue lie beneath the epithelium. The entrances of alveoli contain very little amount of smooth muscle cells which form small knobs. As smooth muscles decrease, elastic and reticular fibers increase. Elastic fibers help in inflation of the lung, while reticular fibers maintain alveoli integrity and prevent rupturing of alveoli.

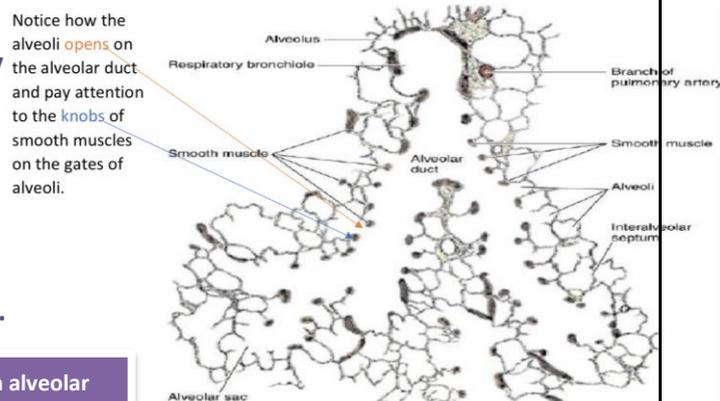
Alveolar ducts: - (10:00)

-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 and capillaries, the 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 (respiratory portion).

The elastic fibers enable the alveoli to expand with Inspiration (inflation) and to contract passively with expiration. Reticular fibers prevent overdistension of alveoli.



Alveoli:

-Alveoli are saclike invaginations (about 200 μm in diameter) that are responsible for the spongy structure of the lungs because of the elastic fibers.

-The structure of the alveolar walls is specialized for enhancing diffusion between neighboring alveoli (internal environments), and between the alveoli and capillaries (external environments). Each wall lies between two neighboring alveoli is called an interalveolar septum, or wall.

Interalveolar septum (wall):

An interalveolar septum consists of two thin squamous epithelial layers (type I pneumocytes) between which lie the capillaries, elastic and reticular fibers, and connective tissue matrix and cells.

At the corners, you have type II pneumocytes, which are cuboidal and secrete surfactant from their lamellar bodies. (VIP)

The interstitium of the interalveolar septum is composed of two things:

- 1-Connective tissue resting on basement membrane (cells of CT are: leukocytes, macrophages, fibroblasts)
- 2- A heavy network of capillaries (the richest capillary network in the body).

The interalveolar septum contains pores (10- 15 μm in diameter), that allow for passage of air between neighboring alveoli > equalize air pressure in the alveoli and promote the collateral circulation of air when a bronchiole is obstructed.

Cells in the interstitium:

- Leukocytes
- Endothelial cells (capillaries) 30 %
- Fibroblasts and mast cells 36%
- Macrophages 10 %
- Type I cells 8 %
- Type II cells 16%

However, that's not the case in alveolar epithelium,

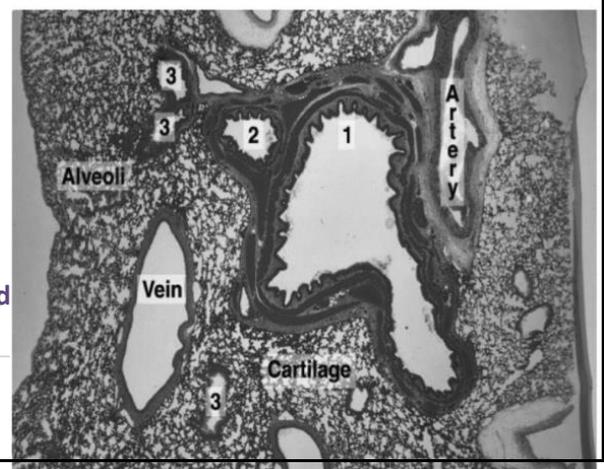
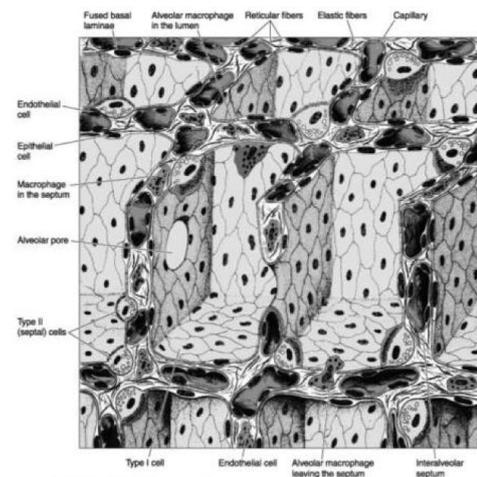
Where type I pneumocytes make about 97% of the alveolar lining and type II pneumocytes make only about 3%.

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. They are the primary means of structural support of the alveoli.

Here we can see the alveoli with a vein and artery.

Differences between alveolar veins and artery:

- 😊 Arteries:- Have thin walls-Low pressure -Carry deoxygenated blood
- 😊 Veins: -Have thick walls-High pressure- Carry oxygenated blood



The basement membrane is generally thick in the interalveolar septum except in the respiratory membrane, where two thin basal laminae of the endothelial cells and the epithelial (alveolar) cells of the interalveolar septum fuse to form the basement membrane.

Blood-air barrier (respiratory membrane):- (20:00)

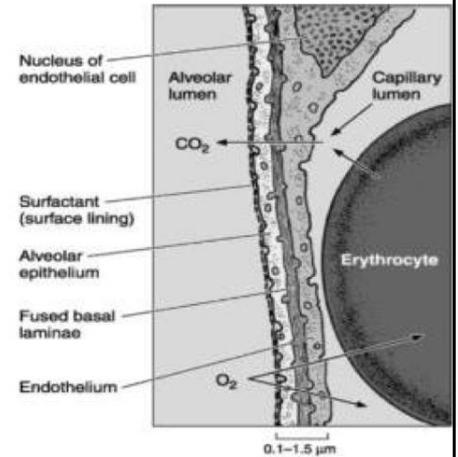
Air in the alveoli is separated from capillary blood by three components referred to collectively as the blood-air barrier or respiratory membrane (because gas exchange happens across it).

The components of the blood-air barrier are:-

- 1.The surface lining and cytoplasm of the alveolar cells (simple squamous epithelium).
2. Cytoplasm of Endothelial cells (also simple squamous).
- 3-The fused basal laminae of the previous two components lie in-between.
4. Although it's not a tissue component, the surfactant layer that lines the alveoli (called the surfactant lining surface) is considered as a part of this membrane.

The total thickness of these layers varies from 0.1 to 1.5 μm .

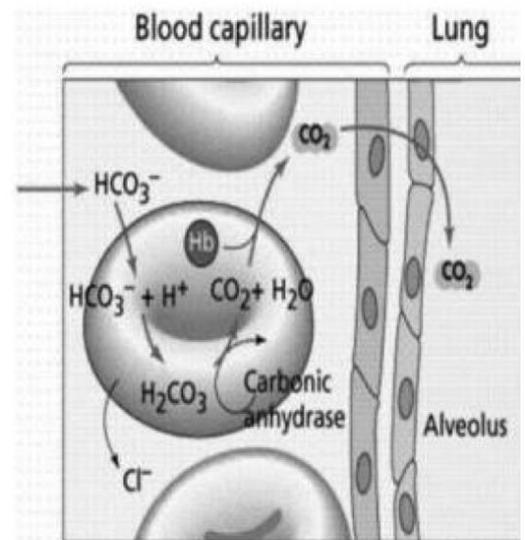
There are no other structures, and that's to ensure minimal thickness of the membrane.



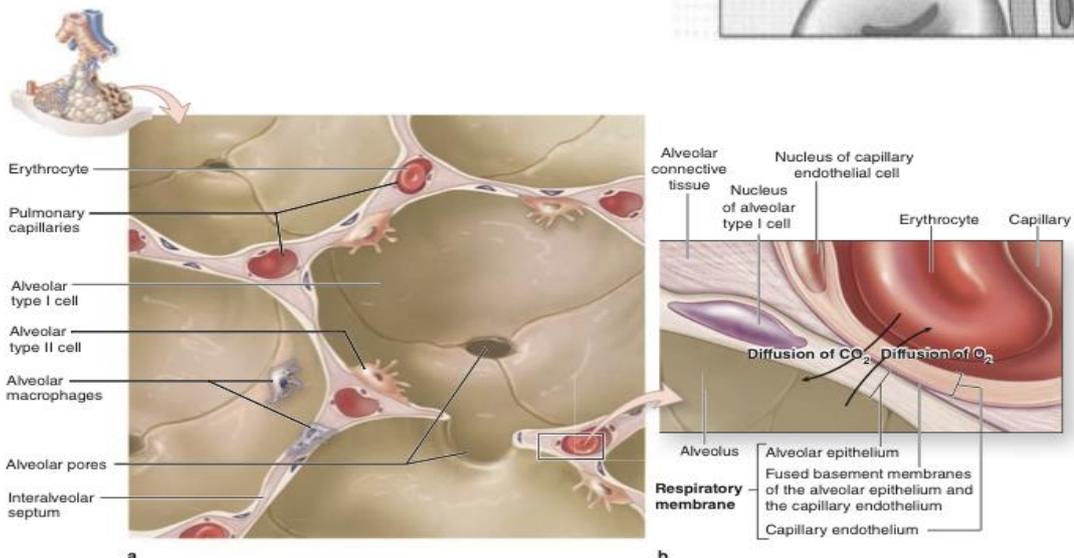
Gas exchange across the respiratory membrane

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.



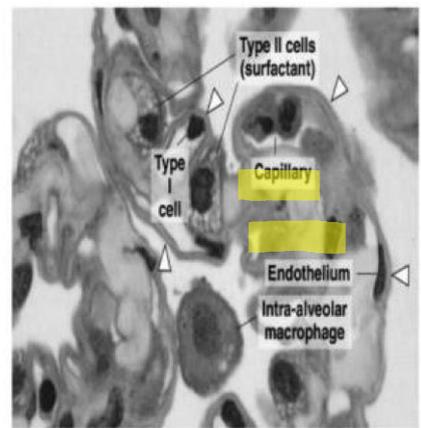
The below figure is from the book (not in the slides) :-



Capillary endothelial cells:

Extremely thin and can be easily confused with type I alveolar epithelial cells under the microscope because both are simple squamous epithelium, we can differentiate between them by the presence of red blood cells in the capillaries.

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.



Copyright © 2006 by The McGraw-Hill Companies, Inc. All rights reserved.

Alveolar epithelial cells: -

As we've mentioned, there are two types of alveolar epithelial cells: -

1. Type I Pneumocytes:

-Squamous cells, extremely attenuated, that line the alveolar surfaces.

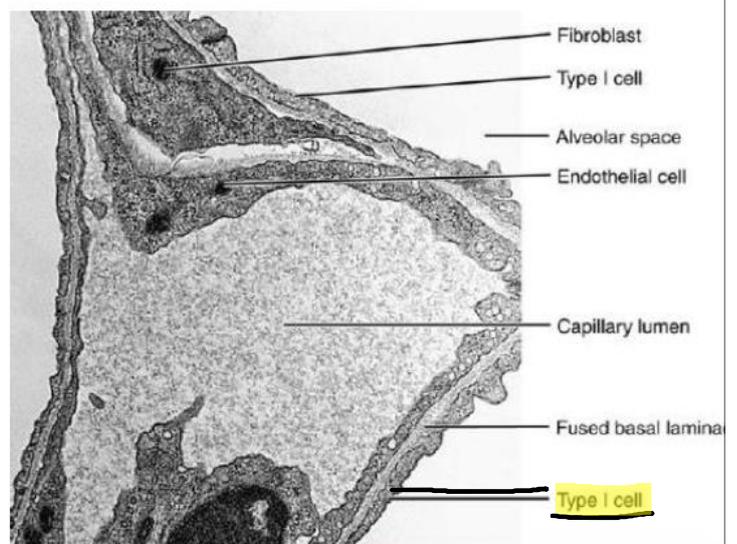
- Make up to 97% of the alveolar surfaces.

- 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.

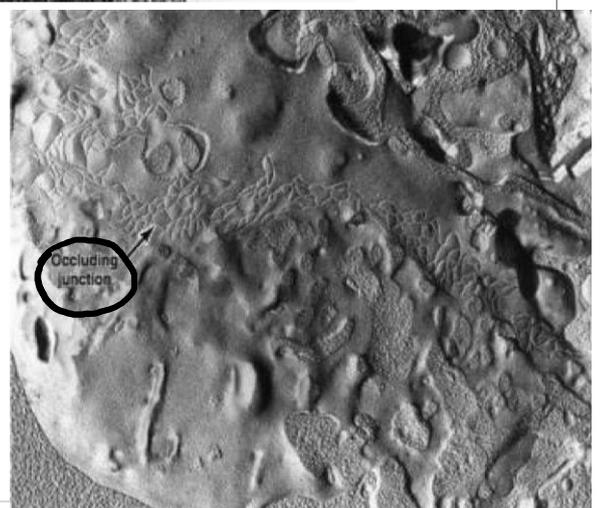
-The cytoplasm in the thin portion contains abundant pinocytotic vesicles, which may play a role in the turnover of surfactant and the removal of small particulate contaminants from the outer surface.

-They have renewal capacity – they can undergo mitoses – but they only replace similar type I cells.



- They have many junctions between them – like desmosomes – to maintain their integrity. In addition to desmosomes, all type I epithelial cells have occluding junctions 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.



2. Type II pneumocytes: -

-Interspersed among the type I alveolar cells with which they have occluding and desmosomal junctions.

- Make the remaining 3% of the alveolar surface.

-They are found mainly on the corners of the interalveolar septum.

-Rounded (cuboidal) 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.

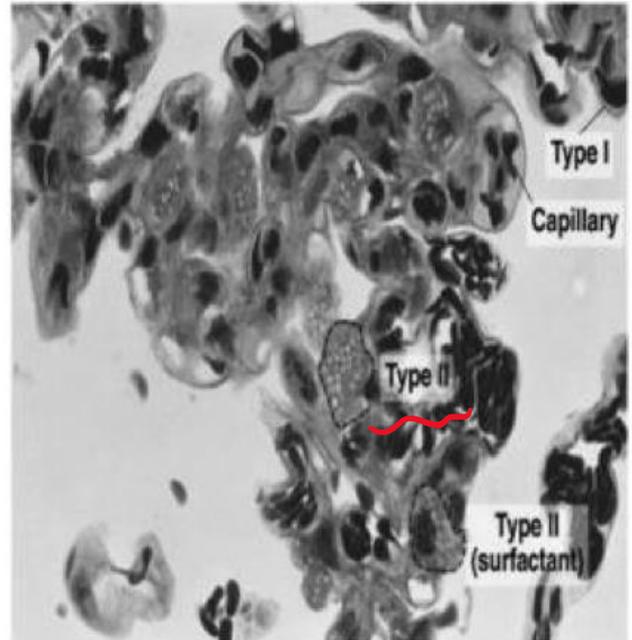
- Divide by mitosis to replace themselves and the type I alveolar cells.

- They are also called: great alveolar cells or septal cells.

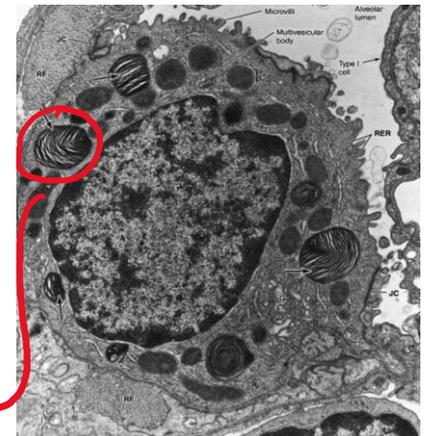
-They contain a large central nucleus. They exhibit a characteristic vesicular or foamy cytoplasm.

-They contain lamellar bodies which average 12 um in diameter, contain concentric or parallel lamellae limited by a unit membrane and are responsible for the production of surfactant.

- These bodies, which contain phospholipids, glycosaminoglycans, and proteins, are continuously synthesized and released at the apical surface of the cells.



Copyright ©2006 by The McGraw-Hill Companies, Inc.



Lamellar bodies

Pulmonary surfactant: - (30:00)

- 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
- Has a bactericidal effect

In fetal development, surfactant appears in the last weeks of gestation –during 8th month- and coincides with the appearance of lamellar bodies in the type II cells. But it won't reach its normal level until the end of the 8th month of gestation.

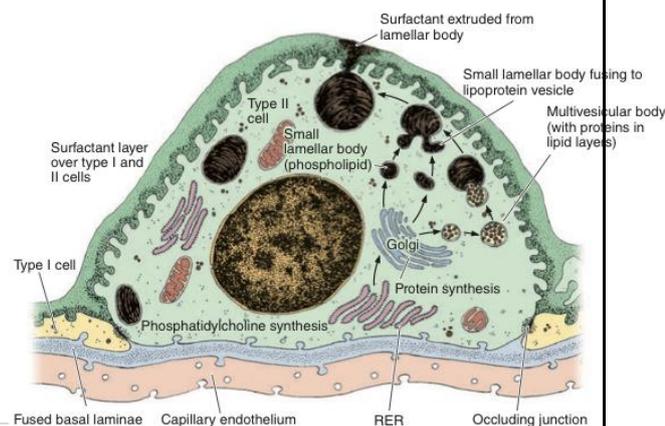
We can measure the level of surfactant in the fetal lungs; if it's

low, we give the mother hydrocortisone injections to

enhance surfactant production in the fetus. If the baby

was born with low level of surfactant, the lungs won't be able to inflate and the alveoli will collapse; this condition is called

Infant respiratory distress syndrome



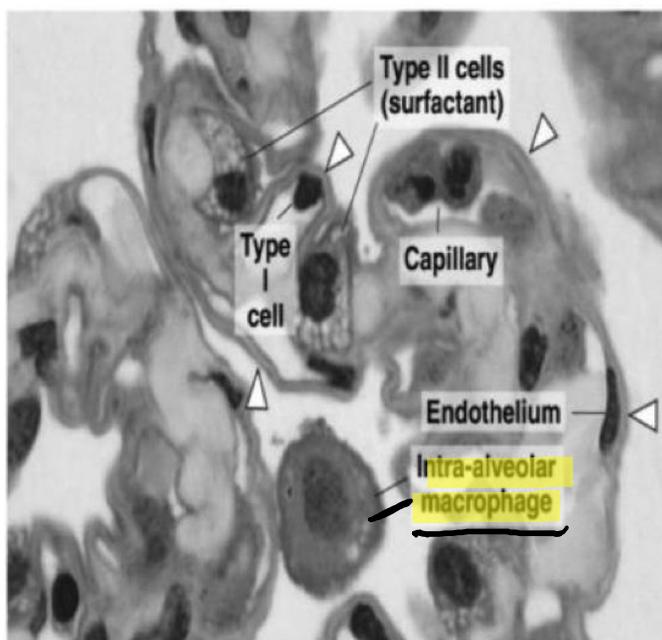
- The surfactant layer is not static but is constantly being turned over and gradually removed by pinocytosis in both types of alveolar cells and by macrophages. It consists of proteinaceous hypophase covered with a phospholipid film that is primarily composed of dipalmitoyl phosphatidylcholine and phosphatidylglycerol.
- The lipoproteins are gradually removed from the surface by the pinocytotic vesicles of the squamous epithelial cells, macrophages, and 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. The bronchoalveolar fluid contains several lytic enzymes (e.g., lysozyme, collagenase, glucuronidase) that are probably derived from the alveolar macrophages. Bronchoalveolar fluid is then expelled as sputum.
- In infants who can't clear their own airway, we perform aspiration of sputum by an endotracheal tube.

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 results in a continuous renewal of both type 1 and 2 cells.
- The normal turnover rate of type II cells is estimated to be 1% per day.

Lung Macrophages: -

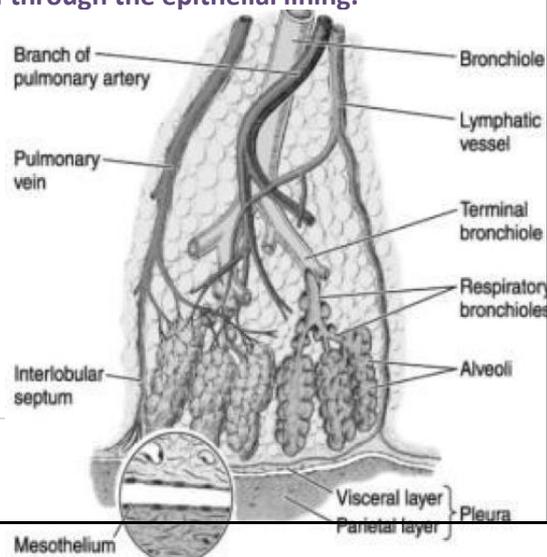
- Also called dust cells, these are the most abundant cells in the lungs (more than type I/II or endothelial cells or any other cells).
- Are found in the interior of the interalveolar septum and are often seen on the surface of the alveolus and are also found in the pleura.
- The phagocytosed debris 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 converge at the hilum of the lungs and then they are carried with sputum to the pharynx, where they are swallowed or expelled.
- 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.



Pulmonary Blood Vessels:

Circulation in the lungs includes both nutrient (systemic) and functional (pulmonary) vessels

The image here shows you a bronchopulmonary segment, notice bronchioles, pulmonary arteries, veins, and lymphatics. Gas diffusion occurs through capillaries NOT pulmonary arteries nor veins.



- ***Pulmonary arteries:*** -

- Are thin walled as a result of the low pressures: 25/5 mmHg.

- 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.

- Capillaries are lined by mesothelium or endothelium

- ***Pulmonary veins:***

- Thick wall, high pressure= 120/80 mmHg equals systemic arterial blood pressure

- 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 > 2 pulmonary veins for each lung > total of 4 pulmonary veins > go to the left atrium.

☺ ***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).

- The deep network then drains to: paratracheal lymph nodes → tracheobronchial lymph nodes → Broncho-mediastinal lymph nodes → thoracic duct > veins.

- Superficial network includes the lymphatic vessels in the visceral pleura and it drain at the end in the thoracic duct > 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 fibers innervate the lungs and the visceral pleura (autonomic innervation) and they are sensitive to stretch only (afferents). Those fibers act mainly on bronchioles (efferent). Most of the nerves are found in the connective tissues surrounding the larger airways. The parietal pleura is innervated by somatic nerves that are very sensitive to pain, touch and temperature therefore pleuritis is painful.

Effect of parasympathetic (VIP) = bronchoconstriction

Effect of sympathetic (VIP) = bronchodilation

Slide: general visceral afferent fibers, carrying poorly localized pain sensations, are also present.

Pleura: -

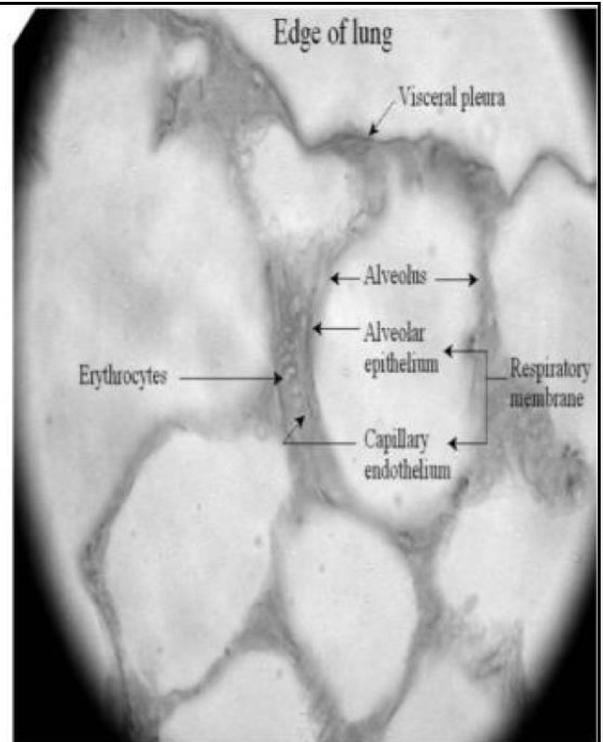
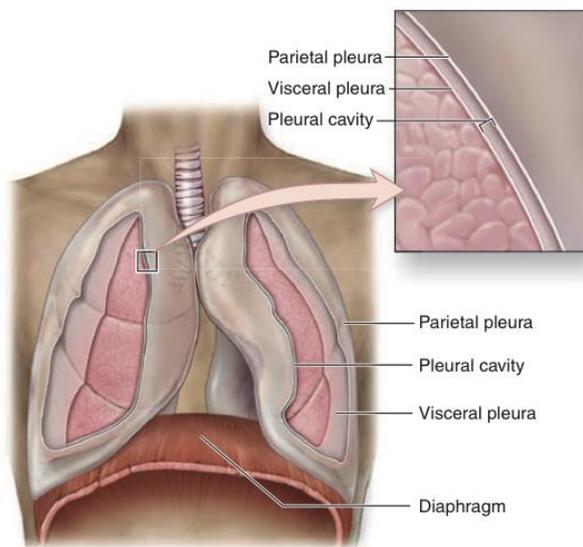
- It consists of two layers, parietal and visceral, that are continuous in the region of the hilum

- Both membranes are composed of mesothelial cells (simple squamous) resting on a fine connective tissue layer that contains collagen, reticular 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 (fluid leaked from capillaries)



Test yourself: -

1. Which of the following components increase(s) as a proportion of the respiratory tract wall from trachea to alveoli?
 - a. Cilia
 - b. Elastic fibers
 - c. Smooth muscle
 - d. Cartilage
 - e. Goblet cells

2. Which structural feature distinguishes between terminal and respiratory bronchioles?
 - a. Alveoli
 - b. Cilia
 - c. Exocrine bronchiolar cells
 - d. Mucous glands in lamina propria
 - e. Smooth muscle

3. Which of the following features distinguishes a bronchus within a lung from the primary bronchi?
 - a. Glands in the submucosa
 - b. Pseudostratified ciliated columnar epithelium
 - c. Smooth muscle in the wall
 - d. Irregular plates of cartilage
 - e. Goblet cells in the epithelium

4. Which of the following is true of pulmonary surfactant?
 - a. Secreted by type I pneumocytes
 - b. Forms layer rich in phospholipid overlying a thin aqueous phase
 - c. Prevents alveolar collapse by increasing surface tension
 - d. Does not affect bacterial survival
 - e. Is secreted by goblet cells