RESPIRATORY SYSTEM

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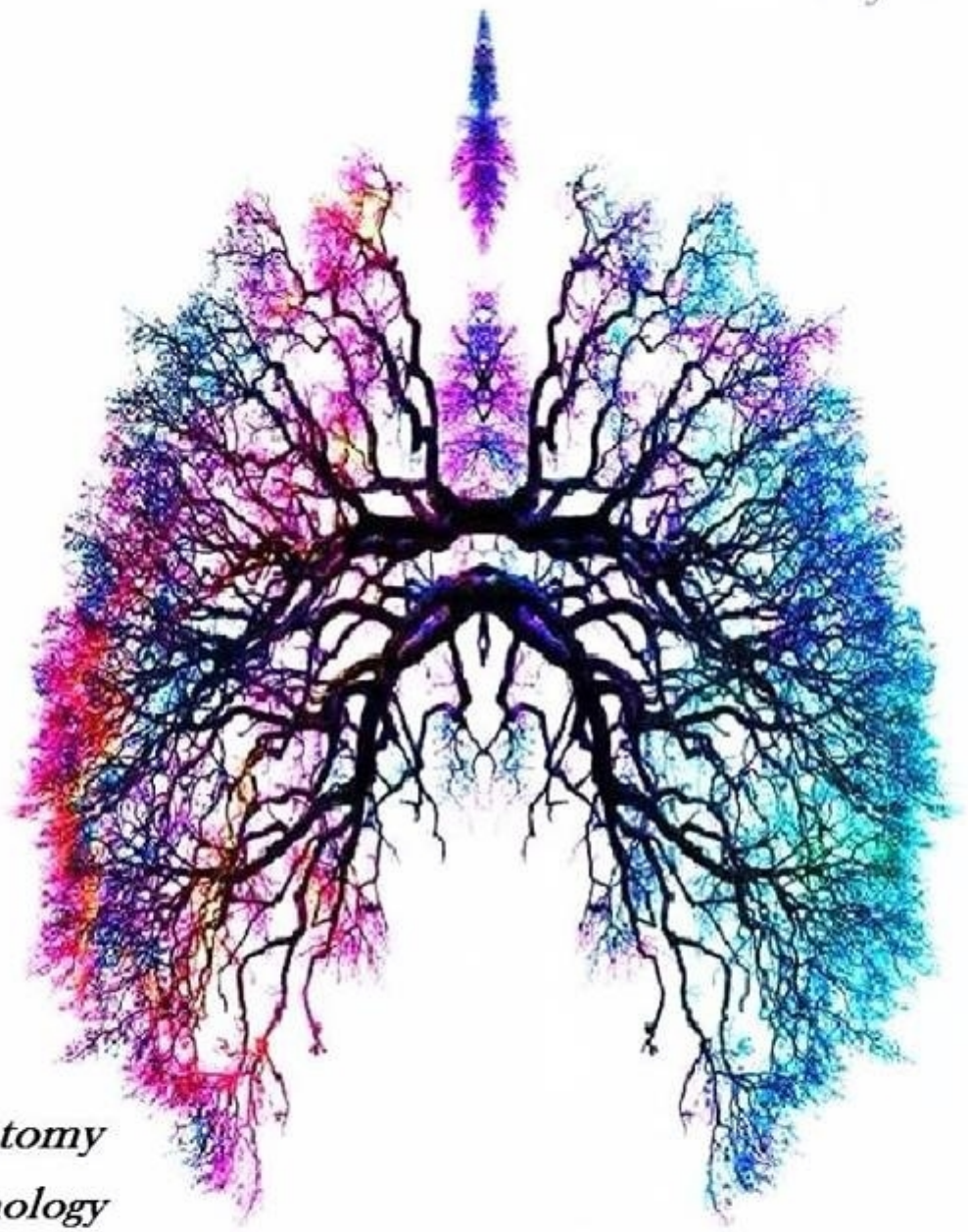

- Anatomy
- Pathology
- Physiology
- Pharmacology
- Microbiology
- PBL
- Histology

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Lecture # 4 (2-histology)
Done By: Hamzeh Salameh & Tareq Bushnaq

Sheet ■
Slide □
Other □

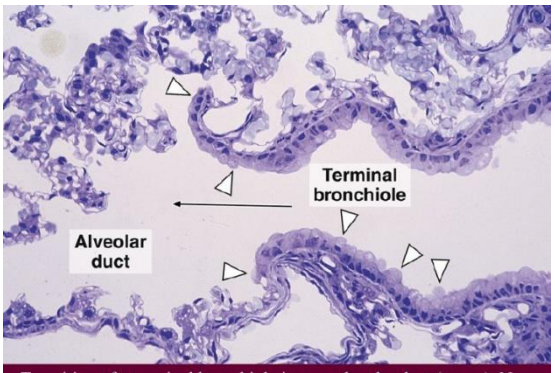
Histology of the Bronchioles and Alveoli

Lecture #2

We previously discussed the histology up to the bronchi.
Today, we'll continue.

- **Bronchioles**

Seen in the image is a Terminal Bronchiole. Bronchioles are divided into**Terminal/Conducting bronchioles** and**Respiratory bronchioles**. Bronchioles are intra-pulmonary, which means they are surrounded by lung tissue.



Transition of a terminal bronchiole into an alveolar duct (arrow). Note the Clara cells (arrowheads). Medium magnification.

No sudden changes in the epithelium are seen as we go from bronchioles to bronchi; instead, the changes occur*gradually*. So, at the very beginning of a bronchiole, the lining epithelium is**pseudostratified ciliated columnar epithelium** just like the bronchus. As we go farther away towards the terminal bronchioles, it becomes **simple columnar ciliated epithelium**or **simple cuboidal ciliated epithelium.** This is what we mean by **"gradual changes in epithelium".**
More distally (in respiratory bronchiole) you will find **Clara Cells.

- **Characteristics of a bronchiole:**

  - ✓ **No** Hyaline cartilage.
  - ✓ **No** glands. (remember as you go distally glands decrease)
  - ✓ Epithelium: at the beginning it may be pseudostratified ciliated columnar epithelium, and then it becomes simple columnar ciliated and simple cuboidal ciliated epithelia. (generally we consider it as simple columnar ciliated epithelium)
  - ✓ As you go distally the diameter decreases. In the bronchiole the diameter is 1mm for large bronchioles and 0.5mm for Small bronchioles and then <0.5mm as we go distally.
  - ✓ **No** Lymphatic Nodules. (the slide mentions there are no lymphocytes and this is incorrect, there are actually scattered lymphocytes in bronchioles)
  - ✓ Goblet cells decrease distally. Generally,the beginning of Terminal bronchioles has few or scattered Goblet cells. As we go distally - last part of terminal bronchiole and Respiratory bronchioles-there will be **NO** Goblet cells.

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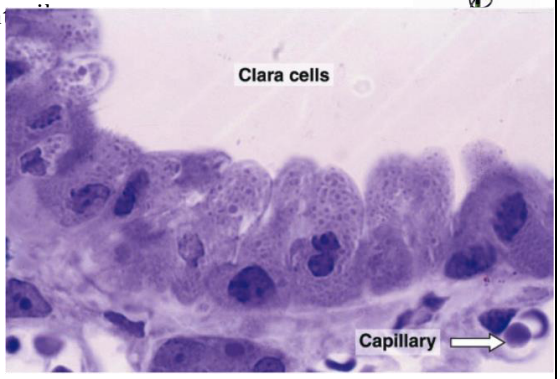
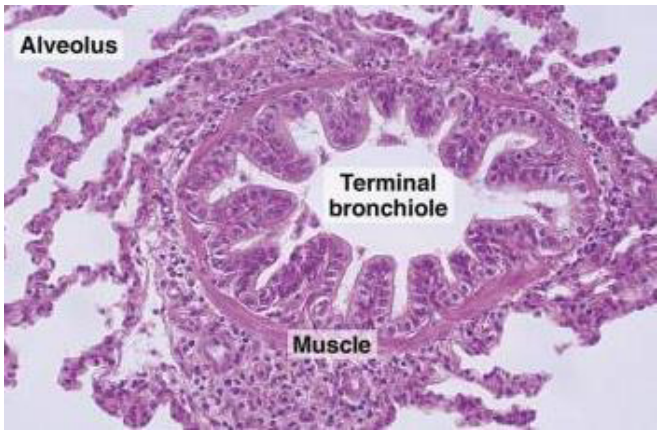
You can find **Clara cells**(simple cuboidal cells without cilia) in bronchioles.



Question: What is its importance?

1) It secretes a type of protein which helps in the formation of the Surfactant.
2) It secretes a type of protein that helps in the protection of the lining epithelium of the bronchioles. (defense mechanism: against inflammation)
3) It has neuro-epithelial bodies which are groups of cells (80-100) that contain secretory granules and receive cholinergic nerve endings.

✓ "Clara cells are very prominent in **Respiratory bronchioles**."



This is a section of a terminal bronchiole.

Notice the *abundance of smooth muscle* cells in a helical or spiral form that surrounds the whole lumen; this abundance along with the *absence of cartilage*➔responsible for the **folding of mucosa in bronchioles**.

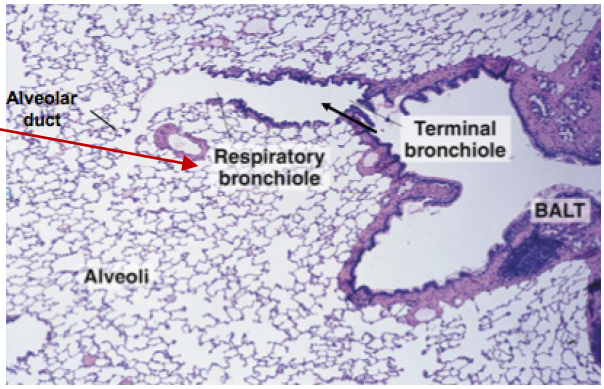
Bronchioles are intrapulmonary; you can notice the presence of lung tissue around them.

- The most common disease affecting the bronchiole is **Asthma**. During Winter or Spring season, pollen in the atmosphere causes an allergic reactionin the respiratory system. You find the patients struggling to take their breath, and there is **wheezing** upon expiration. The reason behind this is the contraction of the smooth muscle layer, and without cartilage, the lumen narrows very much.

➔You have to treat Asthma with Adrenaline; a sympathetic bronchodilator.

- Stimulation through the Vagus nerve – Parasympathetic stimulation – decreases the diameter/lumen of bronchioles, while sympathetic stimulation does the opposite.

**Respiratory Bronchiole:

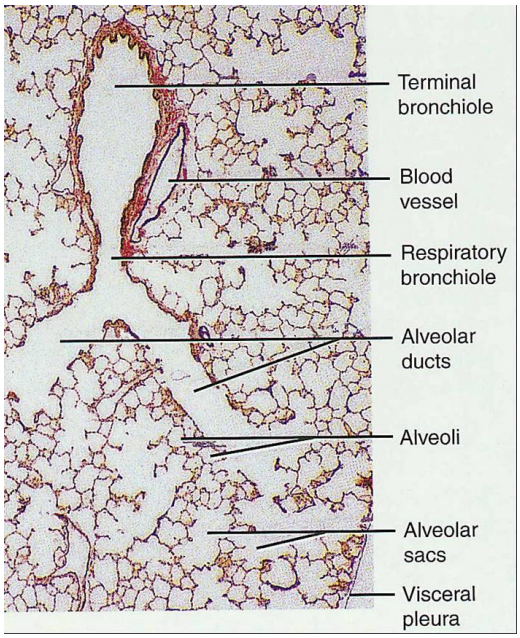


- ✓ Opens into alveolar ducts.
- ✓ Lining epithelium: simple columnar ciliated – simple cuboidal ciliated with prominent Clara cells.

Remember when we said that Clara Cells are most commonly found in respiratory bronchioles.

- ✓ Decreased smooth muscle cells.

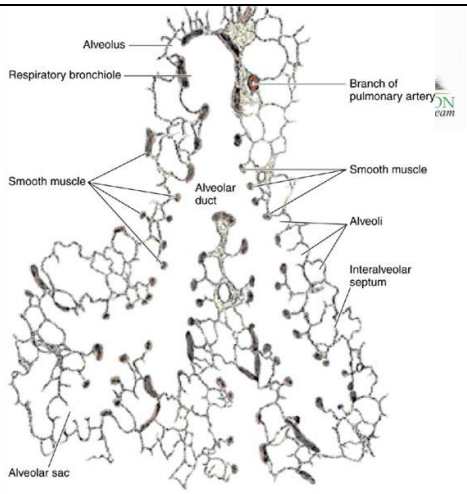
Elastic, reticular, and collagen fibers are between alveoli (in lung tissue) to help in inflation and deflation.



- This is a slide of lung tissue filled with alveoli with inter-alveolar septum in between.
- Smooth muscle cells are arranged as tags or knobs. The sphincter –like bundles appear as knobs between adjacent alveoli.
- Alveolar ducts open into**Atria**that communicate with alveolar sacs.
- The end of an alveolar duct is called an **alveolar sac**.

Alveoli are small sac – like invaginations, about 200 micrometers in diameter. They are responsible for the spongy appearance of the lungs.You can think of alveoli as being small tennis balls stacked next to each other.

ALL alveoli are surrounded by a network of capillaries, but gas exchange does NOT occur across all parts of the capillary network. Gas Exchange occurs ONLY at the respiratory membrane (or blood – air barrier).
So, in other words, not all parts of the alveoli are meant for gas exchange.
*why is the respiratory membrane the site for gas exchange?
ANS: because it is *thin* and contain capillaries.



This slide shows alveoli as pockets. You can notice Type 1 alveolar cells forming the wall. **Type I cells** constitute **97%** of cells in the WALL of the alveolus.

Type II cells constitute **3%** of the WALL of the alveolus, but it's very abundantin the interalveolar septum mostly around the corners.

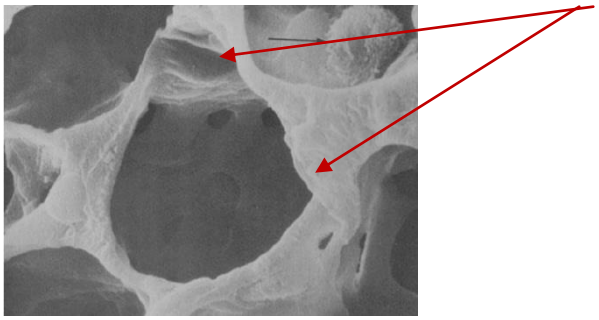
Type I cells are the most abundant type of cells in the alveolar walls, but at the corners of the septum it's **Type II cells** that are more abundant.

**Interalveolar septum:

A septum found between two adjacent alveoli, and characterized by the presence of supporting meshwork of reticulum or elastic fibers to give a kind of elasticity that help in the inflation; it's also responsible for supporting the alveoli.

Constituents of the interalveolar septa:

1-Alveolar pores:



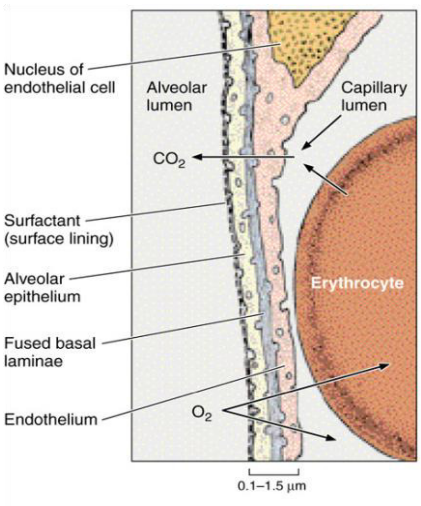
Alveolar pores are present between adjacent alveoli, with a diameter of 10 to 15 micrometers. Alveolar pores are responsible for the *collateral air circulation* between adjacent alveoli. This serves to equalize air pressure between adjacent alveoli.

2-Respiratory membrane/blood-air barrier:

*site of**gas exchange**.

*Very thin; with a diameter ranging from 0.1 to 1.5 micrometers.

*Characterized by the presence of a fused basal lamina, Endothelial cells of the capillary, alveolar epithelium (of type I cells), and surfactant lining (present on the inner side of the alveolar wall).



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*NO interstitium: we need the membrane to be as thin as possible for gas exchange

NOTE: the Fused basal lamina takes 2 layers and fuse them tightly together: One layer from the capillary endothelium and the other from the alveolar epithelium.

NOTE: Each alveolus can have one or more respiratory membranes.

3- Pulmonary capillary network:
Please note that since the pulmonary artery carries de-oxygenated blood, it will be thin-walled; on the other hand, the pulmonary veins will have thicker walls because of the oxygenated blood it carries.

4-Interstitium:

A layer of connective tissue present between the alveoli; this *connectivetissue* along with the *capillaries* forms the **Interstitium**.

*Interstitium = connective tissue + capillaries. (IMPORTANT)

Now, what are the types of cells found in the interstitium?

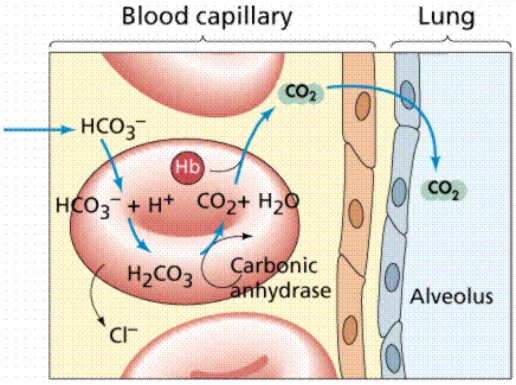
- Endothelial cells (capillaries) 30 %
- Fibroblasts and mast cells 36%
- Macrophages 10 % (like dust cells, for example)
- Type I cells 8 %
- Type II cells 16%
- Leukocytes

So these are the cells found in the interstitium (which contains connective tissue & capillaries).

But once we talk about the **Alveolar Walls**, then you must know that the most prominent cells are **Type I Alveolar Cells** which constitute around 97% of the cells (while only 3% for **Type II Alveolar Cells**).

"Remember, this is only in the alveolar walls."

These alveolar walls are lined by surfactant film.



Now, this shows the gas exchange that occurs between the alveoli & blood capillaries, here you can see what is called **(The Respiratory Membrane)-** between the alveolar wall & capillary.

*(From image) You notice that CO2 is firstly converted into HCO3- (bicarbonate ion), and by entering the RBC it will combine with a hydrogen ion(proton, H+) to become H2CO3. By the action ofthe enzyme **Carbonic Anhydrase,** H2CO3will be split into water & CO2; CO2 then diffuses into the alveoli and out of the body within the next exhalation.

It is found that there are around 300 million of alveoli in the two lungs. Their surface area is around 140 meter square.

Now, let's start talking about the different types of cells & their characteristics:

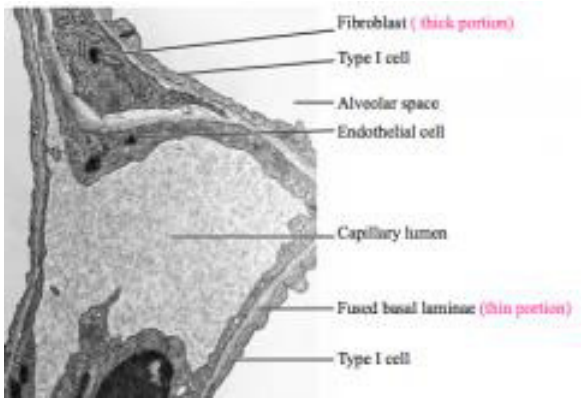
1) Capillary Endothelial Cells:

Found at the wall of capillaries

- ✓ Simple squamous epithelial cells found at the wall of capillaries.
- ✓ Nucleus and organelles➔ found on one side to allow for effective gas exchange.
- ✓ Cytoplasm ➔thin. Except at oneplace where it contains the organelles.
  - **So, Clustering of the nuclei and other organelles allows the remaining areas of the cell to become extremely thin, thus, increasing the efficiency of gas exchange.**
- ✓ Under the microscope, you can easily differentiate the capillary endothelial cells due to the presence of SURROUNDING RBCs.

used to differentiate it from Type I cell

- ✓ An important characteristic is that the endothelial lining of the capillaries is continuous and *not fenestrated* (very important).



2) Type I Alveolar Cells:

Found at the wall of alveoli

This shows the appearance of Type I alveolar cells under the electron microscope.

- ✓ These cells also resemble simple squamous epithelial cells.
- ✓ They constitute about 97% of the wall of alveoli (while the remaining 3% is made up by Type II alveolar cells).
- ✓ Diameter ➔ around 25 nm.
- ✓ Nucleus & organelles (like Golgi Apparatus & Endoplasmic Reticulum) are found on one side to reduce the overall thickness for effective gas exchange. There are large areas of cytoplasm virtually free of organelles.
- ✓ 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+Occluding junctions are seen in both Type I & II alveolar cells).**
- ✓ Can divide by mitosis to replace their own cells/population only (not like Type II cells which can replace both, their own population & Type I population).

Finally, DON'T forget that the best way for differentiating between **Capillary Endothelial Cells** and **Type I Alveolar Cells**, depends on the surrounding RBCs. (Since both are made of Simple Squamous Epithelial Cells, so they might be easily confused).

Capillary Endothelial Cells ➔ surrounded by RBCs. (Found in Capillaries walls)

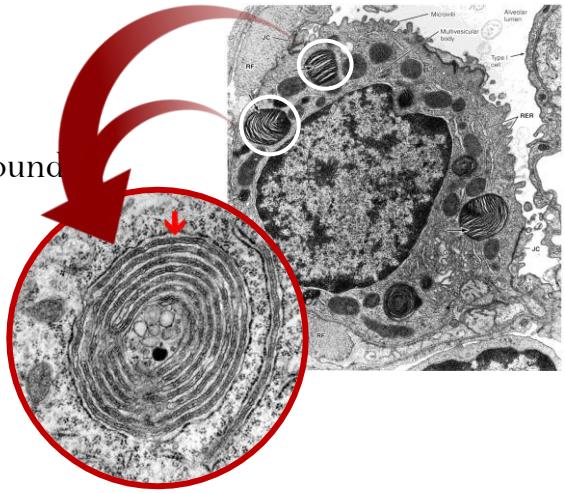
Type I Alveolar Cells➔not surrounded by RBCs. (Found in Alveolar walls)

3) Type II Alveolar Cells:

Also called (Surfactant Secreting Cells) or (Great Alveolar Cells)

- ✓ Appear as large Cuboidal Cells with large nucleus.
- ✓ They exhibit a characteristic vesicular or foamy cytoplasm. These vesicles are caused by the presence of **lamellar bodies.**
- ✓ Found mainly in the corners between the alveoli.
- ✓ Make up around 16% of cells in the interstitium (More than type I).
- ✓ Divide by mitosis to replace their own population and also the type I population.

These bodies give rise to the Pulmonary Surfactant.



This is a picture for electron microscope, it shows the **Lamellar Bodies**that are found around thenucleus in the cytoplasm of type II cells.

The surfactants are secreted in the last 2 months of pregnancy (in the 8th& 9th months) ➔ during that period, doctors can make some tests to find out if the amount of surfactant is low or not.

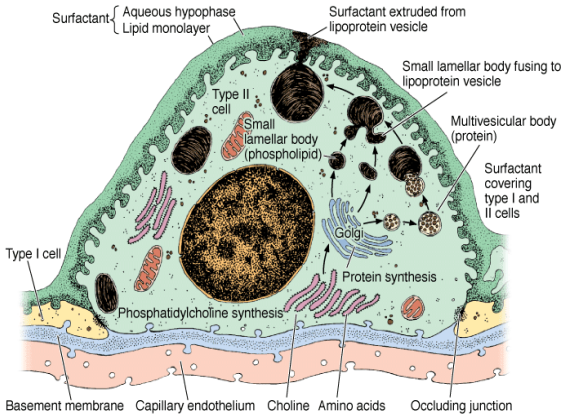
The function of these surfactants is to decrease the surface tension of the alveoli ➔ which help in the expansion of the alveoli ➔ This expansion is needed immediately after delivery for breathing to take place.

So, once the baby is delivered, the doctor should hold him from his legs and hit him either on his legs or back. This process is very important since it works as stimulation to the nervous system. So the impulses will travel to the respiratory center in the medulla oblongata and once this area receives the impulses, it will send other impulses through the Phrenicnerve to the diaphragm. The diaphragm will contract and descend downward, allowing the lungs to expand and fill with air.At this time, the baby will start crying (serves as an evidence for respiration).

- ✓ ***What helps this inflation process to occur is the presence of surfactants.***

Now, if the baby has no enough surfactants and does not cry, this means that he has Respiratory Distress Syndrome (RDS). Here, the doctor must interfere by giving him oxygen and stimulating the surfactants (one way is by giving the baby injections of cortisone). Cortisone aids in the production of surfactant.

So here you can see the Pulmonary Surfactant.



> As we said before, **Clara Cells** can also secrete a type of protein, which play a role in the formation of the surfactants.

Surfactant is mainly made of Amino Acids (Proteins), it contains several proteins (A,B,C&D).

Surfactant layer is found on the inner side of the alveolar wall, and it makes up part of the respiratory membrane.

There are other secretions apart from surfactant. The secretions pass up through the airways and combine with bronchial mucus to form bronchoalveolar fluid.

Once the baby is delivered, the doctor will pass a tube through the baby's mouth & start suctioning the Bronchoalveolar Fluid out.

Both **Surfactants** &**Secretions of fluids** -before birth- are very important for the development of respiratory tract (especially for Lungs).

- However, after delivery, this fluid must be removed ➔allowing normal respiration to take place.

The BronchoalveolarFluid contains several lytic enzymes, like, lysozyme(antibacterial), collagenase, glucuronidasethat are probably derived from the alveolar macrophages ➔ all of these will be removed after birth.

> "Inhalation of NO2 destroys most of the cells lining the alveoli (type I and type II cells), so it is considered to be a toxic substance".

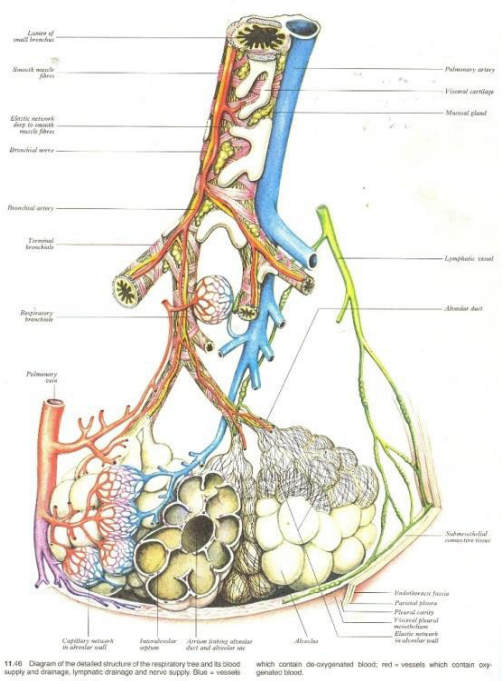
- Type II alveolar cells are "non-static" (they go through normal turnovers: a continuous cycle of secretion & absorption). However, their amounts stay fixed or slightly increased. The normal turnover of type II alveolar cells is 1%.

Now, let's talk about the **Macrophages Cells**:

- ✓ They are known as scavenger cells: cells that can ingest bacteria, foreign particles, and other cells.
- ✓ Origin ➔ from Monocytes.
- ✓ Those found in the lungs are called Dust Cells.
- ✓ They are found in all parts of respiratory tract, but are more prominent in the Lungs, Pleura, connective tissue surrounding the alveoli, and between bronchi.

Dust cells are usually accumulated in the Hilum, but sometimes ascend upwards towards the pharynx by the action of cilia. Once they reach the pharynx, they will be expelled outside through sputum.

The dust cells are considered the most numerous cells in the Lungs, or even
In the whole respiratory tract…
(More than Type I Alveolar Cells).
But remember that, Type I Alveolar Cells are the most prominent cells **in the wall of Alveoli.**



11.46 Diagram of the detailed structure of the respiratory tree and its blood supply and drainage, lymphatic drainage and nerve supply. Blue = vessels which contain de-oxygenated blood; red = vessels which contain oxygenated blood.

**Bronchopulmonary segments:

- ✓ Here we have a bronchopulmonary segment. It is a common site for Surgeries, especially in emergency cases where extraction of a part of a lung is needed.
- ✓ Each lung has 10 bronchopulmonary segments. We might find small lobules inside these segments.
- ✓ These bronchopulmponary segments are filled with alveoli. They are pyramidal in shape with an **Apex**➔ directed towards the Hilum,

And a **Base** ➔directed towards the surface of thelung.

Very Important:Each bronchopulmponary segment has its own vein, artery, lymphatic vessel, bronchioles, and alveoli.➔That is why

LOBECTOMY (or resection of abronchopulmonarysegment) is possible without any problem.

A Land Mark used by Surgeons for recognizing abronchopulmponary segment ➔**The pulmonary vein-it is found on the edges of a segment-**, so the surgeon will use this land mark to verify the area he'll cut in. (He should cut from outside the vein).

- ✓ As we know the vein will carry oxygenated blood, so its wall is thicker than that of the artery.
- ✓ While the pulmonary artery is found in the middle of the bronchopulmponary segment and it carries non-oxygenated blood, so its wall is thinner (the opposite).

Pulmonary blood vesselstarts as a venule, and then it will form 4 pulmonary veins, while the artery is converted into arteriole.

So, don't be confused, this is a special case for the pulmonary vessels. However, other parts of the body have their oxygenated blood in their arteries and non-oxygenated blood in their veins.

**Pleura:

- It consists of two layers, **parietal** and **visceral**, that become continuous as we reach theHilum.
- The parietal layer lines the thoracic cage from inside.
  - ⇨ Made of simple squamous epithelium.
- While the visceral layer is adherent to the lung, it is also known asMESOTHELIUM.
  - ⇨ Also Made of simple squamous epithelium.

"Even the alveolar epithelium is made of simple squamous epithelium for facilitating GAS EXCHANGE".

**Pulmonary lymphatic vessel:

- ✓ There are both - **Deep lymphatic plexus**➔ between the alveoli inside

the lungs.

- **Superficial lymphatic plexus➔**on the surface.

✓ But at the end, both Deep & Superficial branches reach the Hilum, which contains Lymphatic nodules. In smokers, these lymphatic nodules usually appear dark-contain black spots.

✓ After that they travel to the bronchopulmponary lymph nodes, then to the paratracheal lymph nodes.

✓ From there they will go up until they reach the thoracic duct(on the left side) and the right lymphatic duct on the right side.

✓ At the end, they will drain to the venous blood (at the beginning of the Brachiocephalic Vein). The brachiocephalic vein will continue its path until it reaches the superior vena cava and then the right atrium.

**Nerves:

Both parasympathetic (By vagus nerve) and sympathetic (By superior cervical sympathetic ganglia) efferent fibers innervate the lungs➔**Autonomic Nervous System.**

Parasympathetic and Sympathetic efferent fibers work in opposite manners, since the parasympathetic causes vasoconstriction (spasm) to the whole Respiratory Tract while the sympathetic causes vasodilation.

-General visceral afferent fibers, carrying poorly localized pain sensation, are also present.

-Most of the nerves are found in the connective tissues surrounding the larger airways.

By HamzehSalameh...

&Tariq Bushnaq··Good Luck...