

# RESPIRATORY SYSTEM

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ANATOMY



**Title:** Histology 1

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Whats written in purple is new....highlighted is all what the dr said throughout the lec, I didn't highlight the purple handwriting just so it could be easier to recognize

We must agree upon basic concepts we will go through them during histology lectures:

- ✦ The structures in the upper part of the respiratory tract have large diameter (trachea, bronchi [primary, secondary, tertiary]) then the diameter becomes smaller (the diameter of the bronchioles is 1mm).
- ✦ The lining epithelium starts as pseudo-stratified ciliated columnar epithelium then becomes simple columnar ciliated epithelium [in the bronchioles] then simple cuboidal ciliated and non-ciliated epithelium (clara cells) until we reach the respiratory portion of the respiratory tract where the lining epithelium is simple squamous epithelium (proper for gas exchange) – these changes are gradual.
- ✦ Goblet cells starts large in number (from the trachea) and become lesser as we go distally (to lungs) – so we don't find any of them in the respiratory bronchioles -for example-.
- ✦ Regarding the cartilages, they are C-shaped hyaline cartilages in the trachea, then they become plates of cartilage in the bronchi (these plates go circular around the bronchi), until we have no cartilages in the bronchioles.
- ✦ Whilst the smooth muscles start small in number and increase distally (to lungs) – so the bronchioles have large number of smooth muscles that are the cause of asthma when they become extensively contracted. smooth muscles decrease in respiratory portion where it gets replaced by elastic and reticular fibres

The dr mentioned the following note:

Long ago, any defect in the lungs (especially tumors) lobectomy would have been carried out, however, nowadays segmentectomy is rather carried out (bronchopulmonary segment is removed)

Note that we have 10 segments in each lung and 3 lobes in the right and 2 lobes on the left)

Regarding a clinical problem the dr mentioned; the effect of smoking :

Remember that lung epithelium is pseudostratified ciliated columnar (I think he didn't mean the whole respiratory tract as we mentioned earlier), these cilia are responsible with one direction movement of microbes, dust particles toward outside, what smoking does is that it prevent the formation of the protein responsible for the cilia movement which is called dynein; this will lead to chronic infection of the lung as microbes and other particles aren't being moved out. The dr mentioned that this problem regarding dynein can cause infertility in males. as dynein contributes to the formation of sperm flagella bending

In order to study the histology of the respiratory tract, we can divide it into two parts: conducting portion and respiratory portion. Let's first talk about the conducting portion.

## Conducting portion

We can consider it the upper part of the respiratory tract which includes nose, nasopharyngeal cavity, larynx, trachea, bronchi (primary, secondary, tertiary), large bronchioles, terminal bronchioles. It is involved **only in passage of air without gas exchange** and **its major function is to condition the inspired air**; so it becomes **cleansed (filtered), moistened, and warmed** before it enters the lungs.

**How the conducting portion can perform its major function?** \* Through the cilia that help in the filtration of air and can catch the foreign bodies and drive them outside the respiratory tract → air becomes cleansed / \* With the secretions of the seromucous glands → air becomes moistened / With the help of the plexus of venous blood present in the lamina propria (part of the mucosa) and submucosa → air becomes warmed

Now if we take a section through the trachea, what are the layers we can find?

1- **Mucosa:**

a- **Lining epithelium:** respiratory epithelium = pseudo-stratified ciliated columnar epithelium with goblet cells (this is true in trachea, but as we move distally it changes as we mentioned in the introduction). 5 types of cells (will be explained later in the sheet)

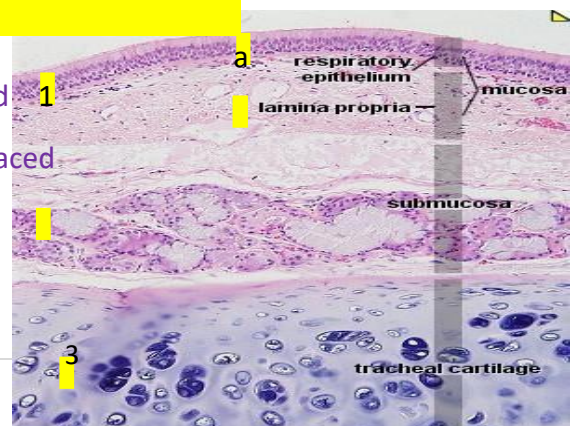
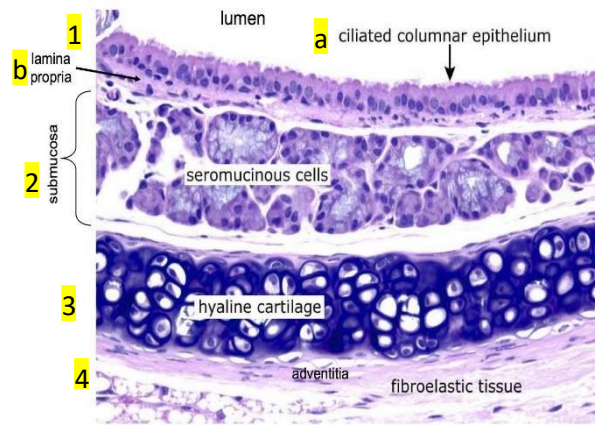
b- **Lamina propria:** loose CT contains blood vessels, lymphatics and seromucous glands whose ducts are directed toward the lumen.

c- **Muscularis mucosa:** two or three ribbons of smooth muscles. very thin (u can even barely see it in the microscopic image)

2- **Submucosa:** CT rich in (plexuses) blood vessels (warming), lymphatics and seromucous glands whose ducts are directed toward the lumen.

3- **Supportive layer:** contains hyaline cartilage as we said earlier regarding how hyaline cartilage change throughout the tract, as it decrease distally it gets replaced by smooth muscles and elastic fibers [in the GIT it is a muscular layer].

4- **Adventitia:** CT layer.



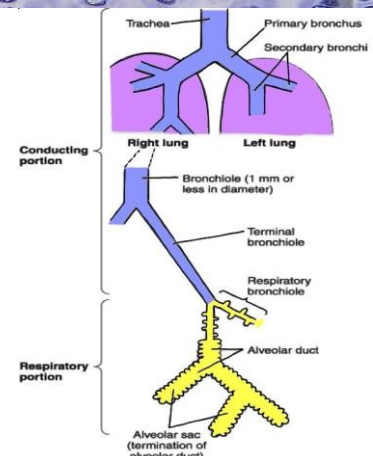
**Respiratory portion**

we can consider it the lower part of the respiratory tract which starts from the respiratory bronchioles (Region of transition) and includes the alveolar ducts, alveolar sacs and alveoli. In contrast to the conducting portion, the respiratory portion is the site where gas exchange takes place.

✓ Please notice that the alveoli are the main sites for the principle function of the lungs which is the exchange of O<sub>2</sub> and CO<sub>2</sub> between inspired air and blood.

If we studied the histology of the respiratory bronchioles carefully, we will find that the lining epithelium is simple squamous epithelium with no cartilages and a huge number of smooth muscles.

The same concepts can be applied on the alveoli, the lining epithelium is simple squamous epithelium with huge amount of elastic fibers in between [important for inflation of the lungs and for alveoli to become filled with air] and reticular fibers. Around the alveoli is a network of capillaries (you remember of course that the lining of capillaries is endothelium- special type of simple squamous epithelium)



This picture illustrates the conducting and respiratory portions of the respiratory tract. You can find two types of bronchioles: terminal bronchioles – belong to the conducting portion

Respiratory bronchioles – belong to the respiratory portion and they are considered the region of transition between the two portions

Of course, both types of alveoli differ in their diameter and the lining epithelium. refer to the beginning of the sheet and try to find the differences exactly-

# Gas exchange

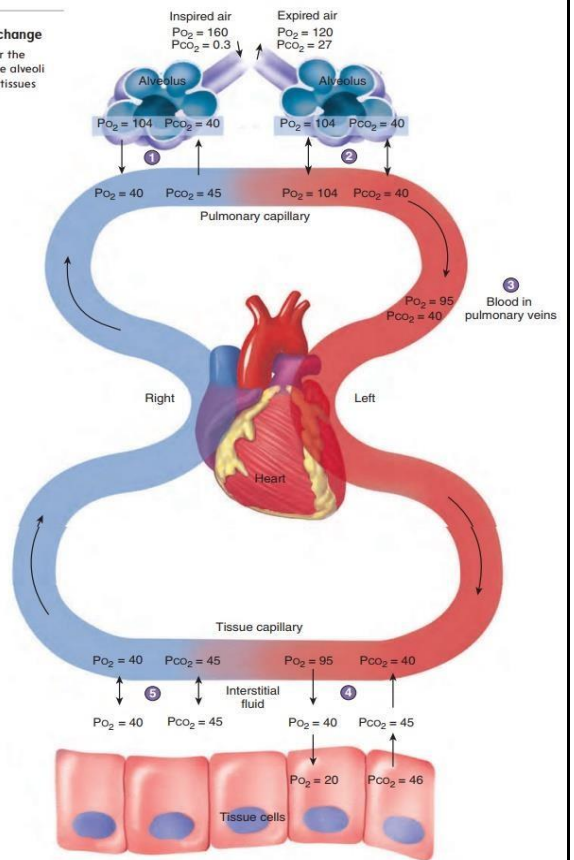
b

## PROCESS Figure **APR** Gas Exchange

Differences in partial pressure are responsible for the exchange of  $O_2$  and  $CO_2$  that occurs between the alveoli and the pulmonary capillaries and between the tissues and the tissue capillaries.

- 1 Oxygen diffuses into the arterial ends of pulmonary capillaries, and  $CO_2$  diffuses into the alveoli because of differences in partial pressures.
- 2 As a result of diffusion at the venous ends of pulmonary capillaries, the  $PO_2$  in the blood is equal to the  $PO_2$  in the alveoli, and the  $PCO_2$  in the blood is equal to the  $PCO_2$  in the alveoli.
- 3 The  $PO_2$  of blood in the pulmonary veins is less than in the pulmonary capillaries because of mixing with deoxygenated blood from veins draining the bronchi and bronchioles.

- 4 Oxygen diffuses out of the arterial ends of tissue capillaries, and  $CO_2$  diffuses out of the tissue because of differences in partial pressures.
- 5 As a result of diffusion at the venous ends of tissue capillaries, the  $PO_2$  in the blood is equal to the  $PO_2$  in the tissue, and the  $PCO_2$  in the blood is equal to the  $PCO_2$  in the tissue. Go back to step 1.



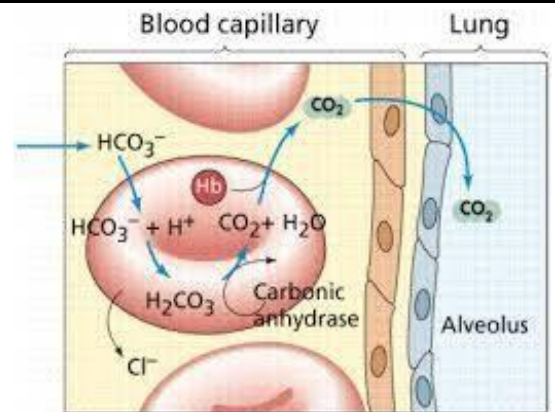
- O<sub>2</sub> is then taken by tissue cells for metabolic activity (tissue PO<sub>2</sub> = 40 mmHg)

### CO<sub>2</sub> in the blood

7% dissolved in plasma

23% combine with hemoglobin to form carbaminohemoglobin

70% converted to protons by carbonic anhydrase and combines to hemoglobin (reversible reaction)(what the dr meant here by proton although he didn't mention it, remember that carbonic anhydrase catalyse the reversible reaction between CO<sub>2</sub> and H<sub>2</sub>O to form bicarbonate and a proton)



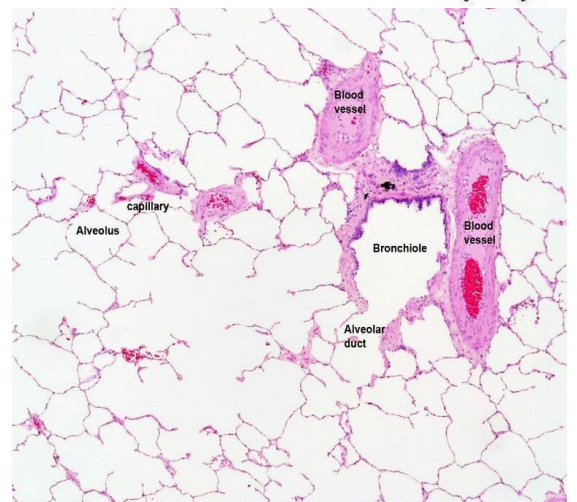
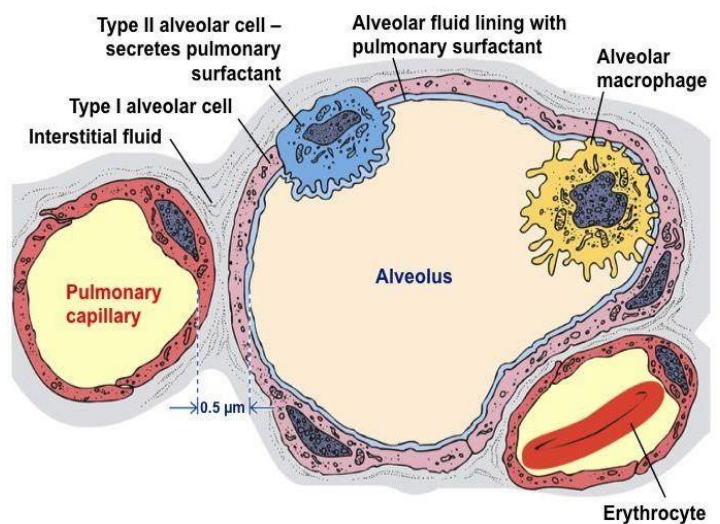
Along with **the simple squamous epithelium** which is composed of **extremely thin cells -flattened-** (covering 95% of alveolar surface) and are **called type 1 alveolar cells or type 1 pneumocytes** involved in **gas exchange**, another type of cells found in the alveoli are called **type 2 alveolar cells or type 2 pneumocytes** (covering the remaining 5% of alveolar surface) and are roughly **cuboidal** involved in **the secretion of surfactants**.

➔ surfactants are secreted at the end of the 8<sup>th</sup> month and the 9<sup>th</sup> month of the fetal life in large amounts because they are important at birth when there is inflation and therefore expansion of the lungs. If there is any decrease in surfactants in birth, a syndrome called **respiratory distress syndrome** will develop.

Dr said when the dr flip the newborn and hits him on the back we activate the respiratory center in medulla oblongata, so through phrenic diaphragm contracts and leads to inspiration.

So, if we notice any decrease in surfactants during fetal life, we can give artificial surfactants.

➔ we can call the simple squamous epithelial layer of the alveoli and the endothelial layer of the capillaries = **respiratory membrane** it includes **blood air barrier and the two simple squamous surfaces**, and both layers are flattened so they help in gas exchange.



the basal lamina of both epithelial layers is fused to form a very thin layer between the alveolar wall and the capillary wall. (blood air barrier)

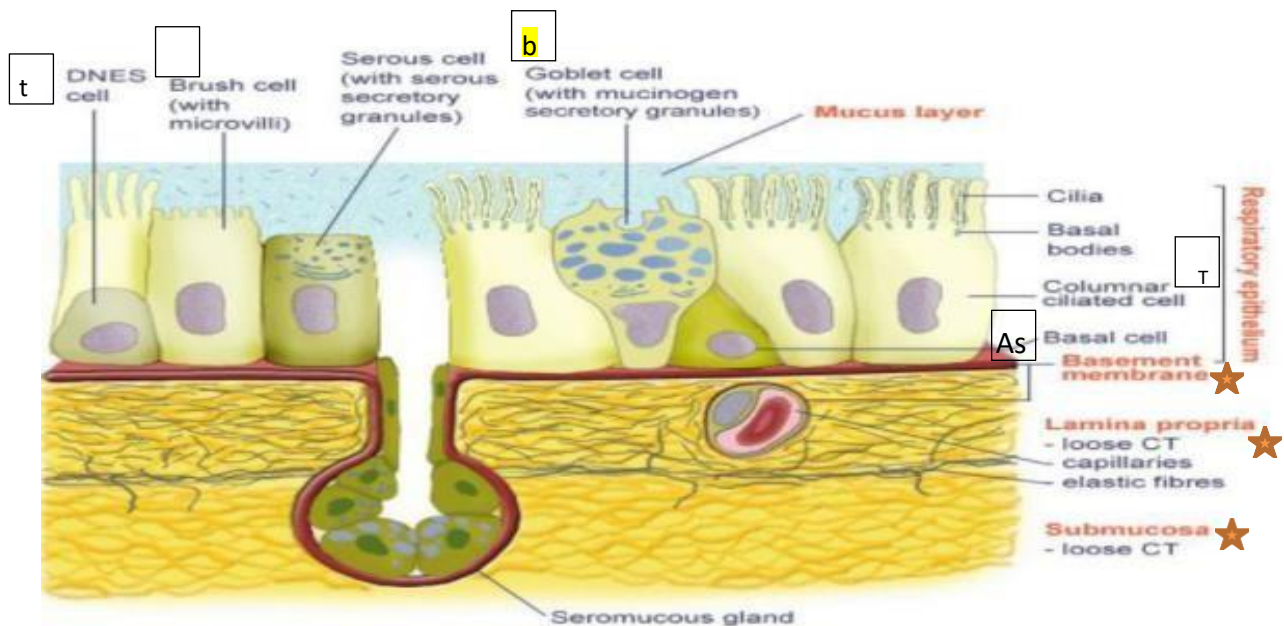
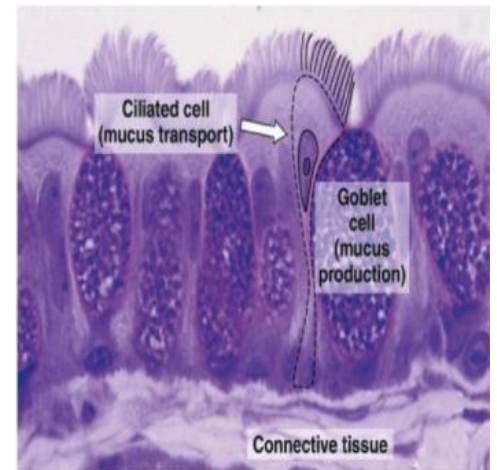
the surfactant layer covers the alveolar surface from inside [look to the pictures on the right]

After talking about the two portions of the respiratory tract, we can now talk about the histology of the structures in the respiratory tract in more details

## Respiratory epithelium

as we said earlier, in the conducting portion specifically the trachea a type of respiratory epithelium is present which is a lining with **ciliated pseudo-stratified columnar epithelium with goblet cells (common type).**

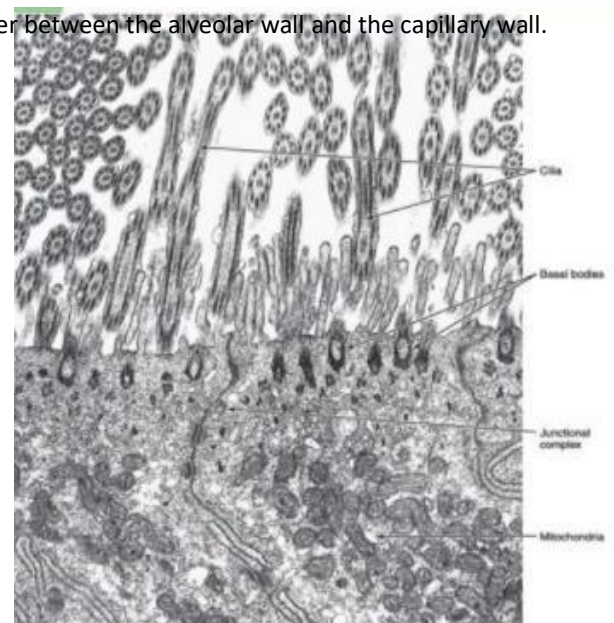
Under EM We can find 5 types of cells in the respiratory tract, all of them are resting on a **thick** basement membrane but not all of them reach the surface.



Notice the thick and prominent basement membrane / the lamina propria (loose CT) containing capillaries and elastic fibres / the submucosa (loose CT) / the seromucous gland found in the lamina propria and submucosa with its duct opening into the lumen. We can see the pseudo-stratified columnar epithelium and goblet cells only using the LM.

the basal lamina of both epithelial layers is fused to form a very thin layer between the alveolar wall and the capillary wall. (blood air barrier)

the surfactant layer covers the alveolar surface from inside [look to the pictures on the right]



A common disease in the respiratory tract is **Immotile cilia syndrome (Kartagner syndrome)**.

- ❖ Dynein is a protein that normally participates in the ciliary movement.
- ❖ Nicotine (found in cigarettes) prevents formation of dynein, which leads to improper movement of cilia.
- ❖ This syndrome is caused by immobility of cilia and flagella. Induced, in some cases, by deficiency of dynein.
- ❖ Therefore, it causes **chronic respiratory tract infections in both sexes** (because the damage of cilia permits entering of foreign bodies and bacteria to the respiratory tract leading to bronchitis and pneumonia) and **infertility in men** (because sperms also need flagella for motility)

## 2-Mucous goblet cells

Contains apical mucous droplets, composed of **glycoproteins and contains polysaccharides**, important for trapping of foreign bodies.

filtration

## 3-Brush cells

Have **numerous microvilli** on their apical surface and **sensory receptors** (afferent nerve endings) on their basal surface.

Important for secretion

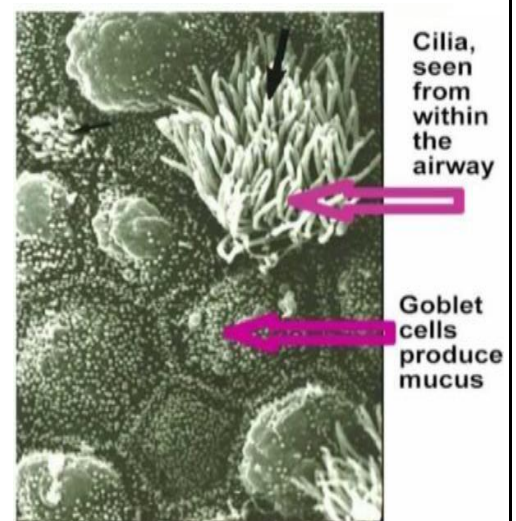
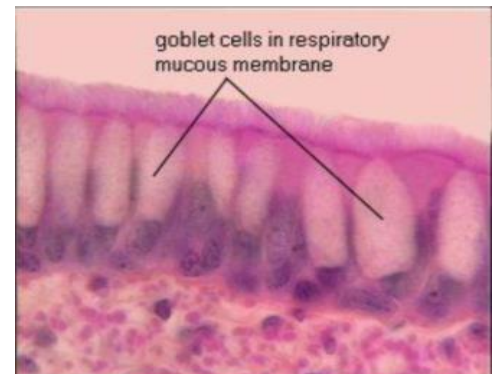
## 4-Basal (short) cells

Small rounded cells **rest on the basement membrane** but don't reach the surface.

Believed to be **generative stem cells** which differentiate into the other cell types (**reserve cells**).

## 5-Small granule cells

Cells of the **DNES** (diffuse neuroendocrine system) **regulate locally the excretions or secretions of mucous and serous glands** in the respiratory tract. Also called **Kulchitsky Cells**.



## Nasal Cavity

Subdivided into **the vestibule**, **the respiratory area** and **the olfactory region**.

**The vestibule:** Most anterior and dilated portion of the nasal cavity. The beginning of the lateral wall of the nasal cavity above the anterior nares.

- ✓ Lined by **modified skin** (keratinized stratified squamous epithelium) that contains **sebaceous and sweat glands and thick short hairs called vibrissae**. filtration
- ✓ Tarps and filters out large particles from the inspired air.
- ✓ Epithelium loses its keratinized nature **and undergoes transition** into typical respiratory epithelium **before** entering the nasal fossae.

**The respiratory area:** it is the lateral wall of the nasal cavity with the septum middle and inferior concha

- ✓ Covered with **pseudo-stratified columnar epithelium with goblet cells**
- ✓ The sub epithelial connective tissue is rich with blood vessels **plexus of veins** for warming and **seromucous glands**

**Olfactory region:** present in the roof and upper parts of the nasal cavity above superior concha

- ✓ Covered by **olfactory mucosa**, which contains:
- ✓ **Olfactory epithelium:** it is a **pseudo-stratified columnar epithelium** composed of three types of cells: (the dr said if a question here asking about how many types of cells is present here the answer is 5 as there r the pseudostratified columnar cells and goblet cells plus these three.

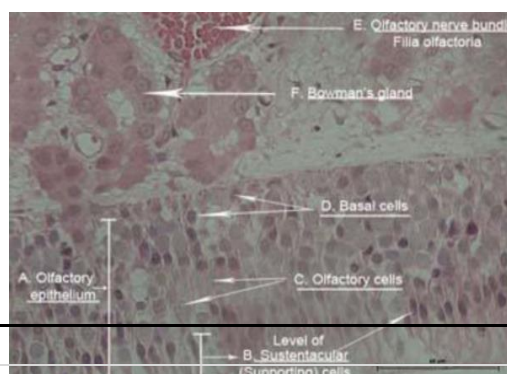
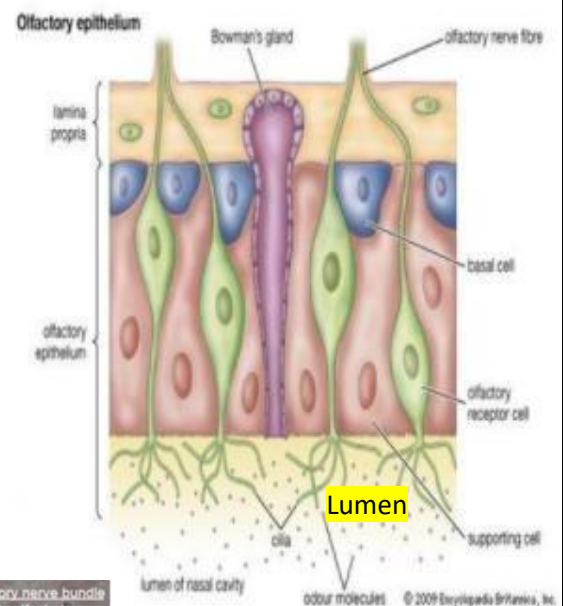
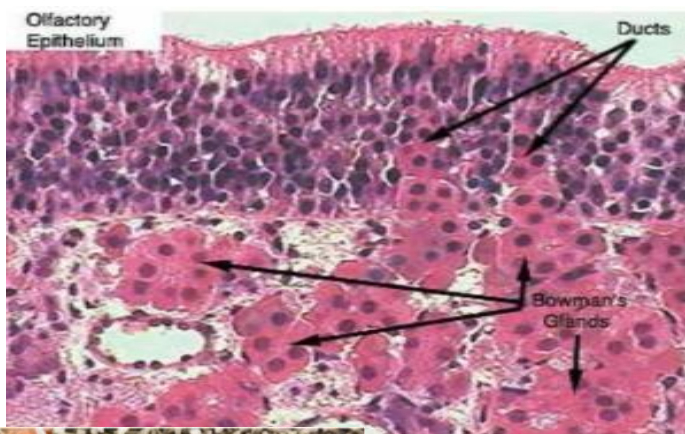
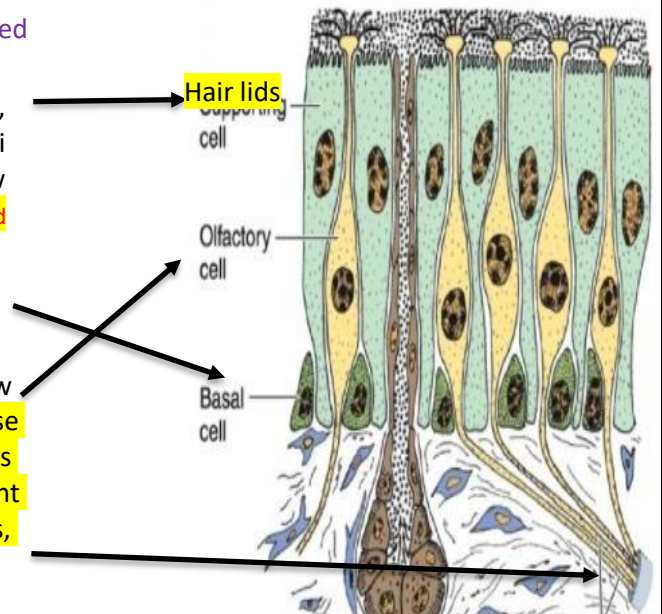
1- **Supporting (sustentacular) columnar cells:** broad, cylindrical apices and narrower bases. Microvilli submerged in a fluid layer. Contain a light yellow pigment. - are connective tissue cells that are supportive and nutritive to the bipolar cells

2- **Basal cells:** single layer at the base of epithelium. Spherical or cone shaped. - are stem cells important for replacement of other cells

3- **Olfactory cells:** bipolar neurons. Their nuclei lie below the nuclei of the supporting cells. Cilia (nonmotile) rise from their apices (dendrites). Respond to odoriferous substances by generating areceptor potential. Afferent axons of these bipolar neurons unite in small bundles, and synapse with the olfactory lobe.

- ✓ **Corium (lamina propria):** rich in blood vessels, contains **Bowman's gland** that secrete watery mucous facilitating the access of new odoriferous substances

Lumen



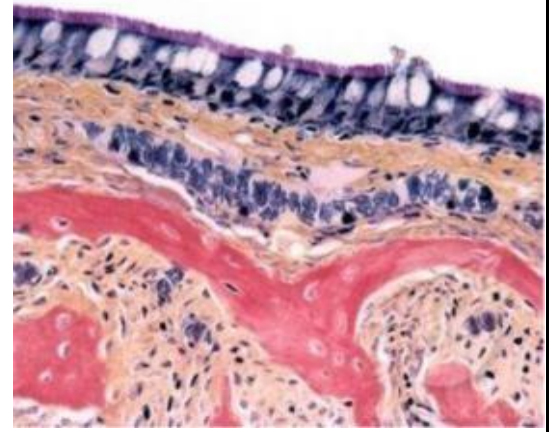


**Nasal sinuses:** Frontal sinus, Maxillary sinus, Ethmoidal sinus, Sphenoidal sinus. [air sinuses important for resonance of the voice]

- lined with a **thinner respiratory epithelium**
- contains **few goblet cells**
- the lamina propria contains only a **few small glands**
- continuous with the underlying periosteum**

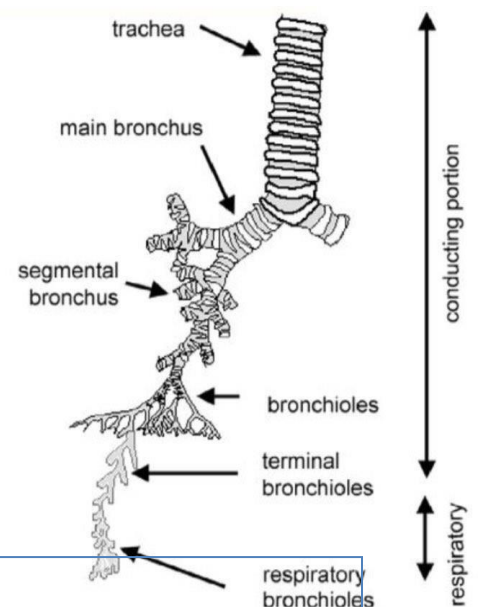
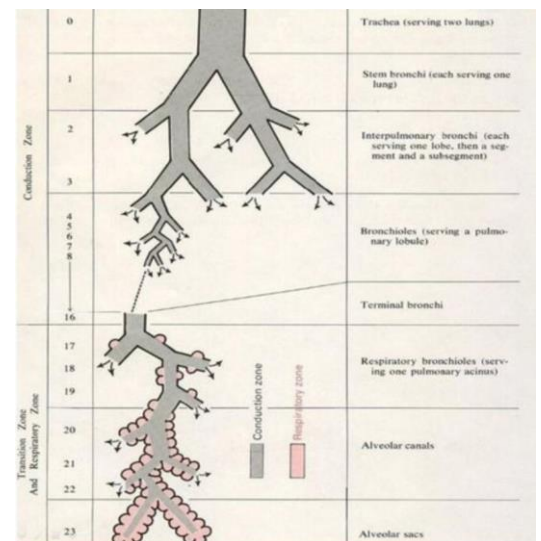
Since it is a cavity in the bone

- have ducts that open into the lateral wall of the nasal cavity**



## The bronchial tree

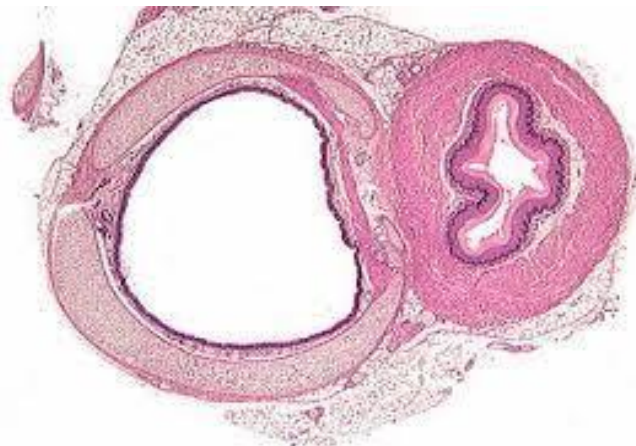
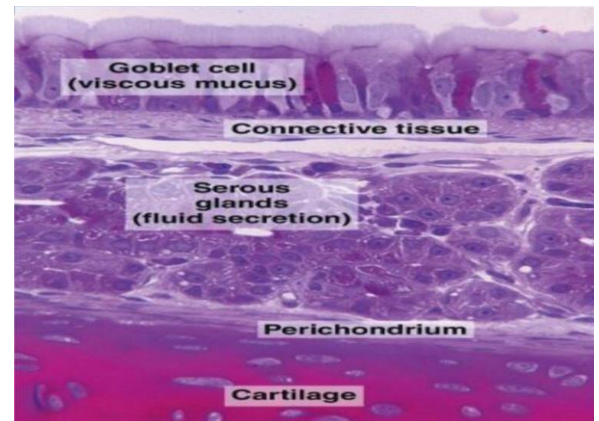
- The trachea extends from the level of C6 to T4 (bifurcation point – angle of Louis / sternal angle)
  - Only the trachea and the **primary 1ry (main) bronchus** are extrapulmonary
  - Secondary (lobar) and tertiary (segmental) bronchi** are intrapulmonary
  - So, if you don't see any lung tissue, you're in the trachea or the primary bronchi. And if you see a lung tissue, you're in the secondary or tertiary bronchi
  - Trachea is divided into 2 main bronchi (right + left), each main bronchus divides into lobar bronchi depending on the number of lobes each lung has. And then they divide into segmental bronchi.
  - We have **three** lobar bronchi in the right and **two** in the left lung (RL have three lobes and LL have 2 lobes)
  - And we have **10** tertiary bronchi in the right and **10** tertiary bronchi in the left lung
  - The **segmental (tertiary) bronchus** is almost 5mm or less in diameter.
  - Each bronchiole enters a pulmonary lobule
  - Each large bronchiole (1mm) gives 5-7 terminal ones
  - Terminal bronchioles (0.5mm) contain **Clara cells** (no cilia) and **neuroepithelial bodies** (chemoreceptor)
- Notice that the diameter decreases distally



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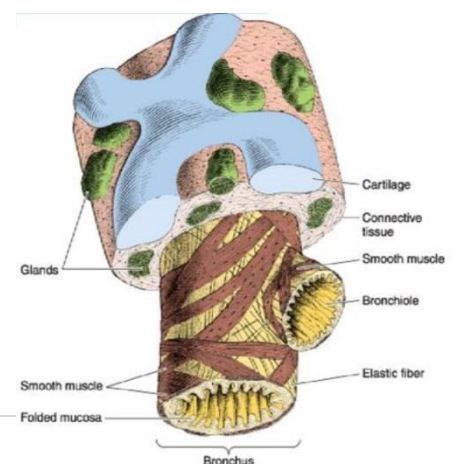
## Trachea

- ❖ Lined with a typical respiratory mucosa
- ❖ C-shaped rings of hyaline cartilage that keep the tracheal lumen open (in the lamina propria).
- ❖ Fibroelastic ligament and bundle of smooth muscle (**Trachealis**) bind to the perichondrium and close the rings **posteriorly** (remember that the esophagus is present posterior to the trachea, so the presence of trachealis allows the peristaltic movements of the esophagus)
- ❖ Some longitudinal muscles may be found behind the trachealis
- ❖ Numerous seromucous glands that produce a more fluid mucus
- ❖ Contain the same 5 types of cells in the mucosa
- ❖ The ligament prevents overdilatation of the lumen
- ❖ The muscle allows regulation of the lumen
- ❖ Contraction of the Trachealis muscle and the resultant narrowing of the tracheal lumen are involved in the **cough reflex**



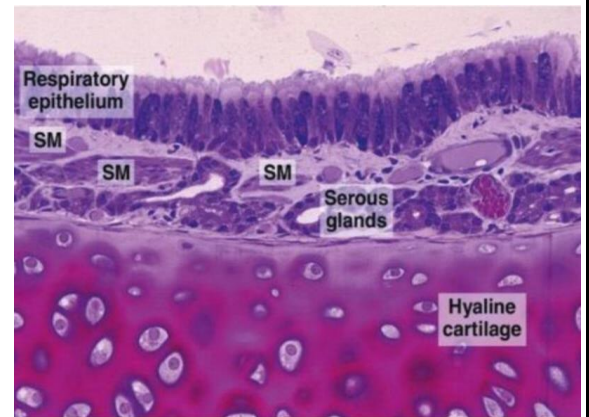
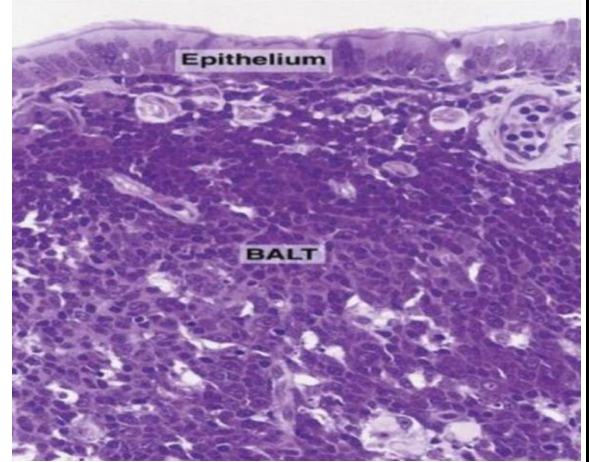
## Bronchi

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## Differences between the trachea and bronchi (*characteristics of the bronchi*)

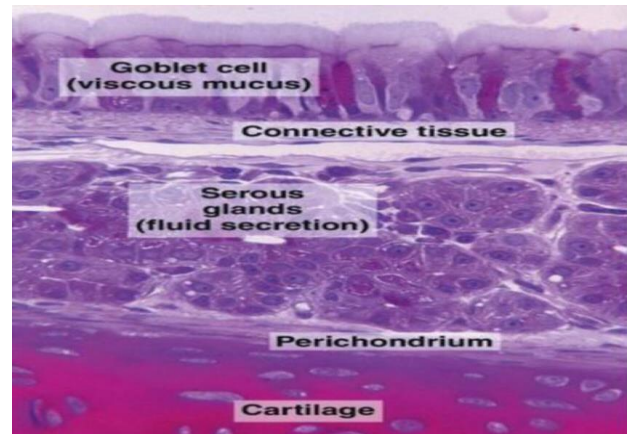
1. narrower lumen (small bronchus 5mm or less)
2. irregular bronchial cartilage plates
3. smooth muscle layer consisting of spirally arranged bundles between the lamina propria and submucosa. Contraction of this muscle layer is responsible for the folded appearance of the bronchial mucosa.
4. lamina propria is rich in elastic fibers and contains an abundance of mucous and serous glands
5. respiratory epithelium with fewer goblet cells
6. Numerous lymphocytes and lymphatic nodules (BALT) are present (infiltrated by the adventitia)



## Structural changes in the conducting portion of the respiratory tract:

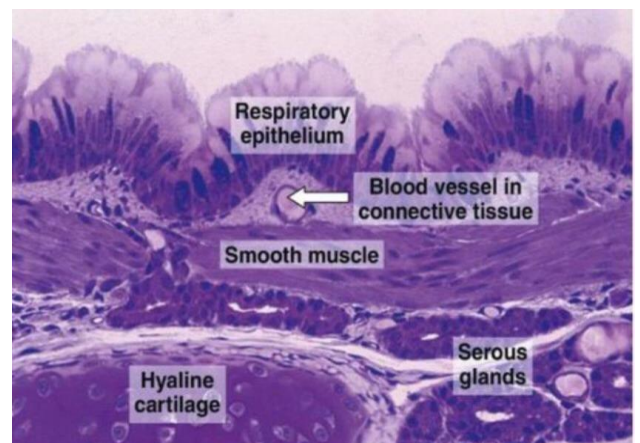
### Extra-pulmonary bronchi

- ✓ Pseudostratified ciliated columnar epithelium with goblet cells.
- ✓ Prominent basement membrane
- ✓ Relatively thin lamina propria (elastic layer at base)
- ✓ Submucosa with seromucous glands
- ✓ "C" shaped hyaline cartilage rings w/ smooth muscle between ends of cartilage



### Intrapulmonary bronchi

- ✓ Pseudostratified ciliated columnar changing to ciliated simple columnar in smaller branches. Goblet cells at all levels.
- ✓ Below lamina propria are interlacing spirals of smooth muscle
- ✓ Seromucous glands decrease as bronchi get smaller.
- ✓ Plates of cartilage gradually disappear

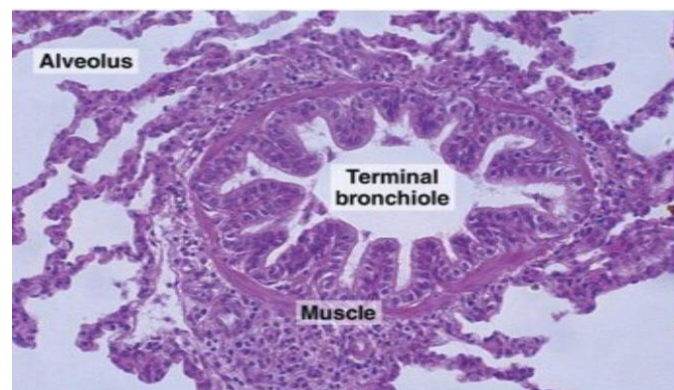
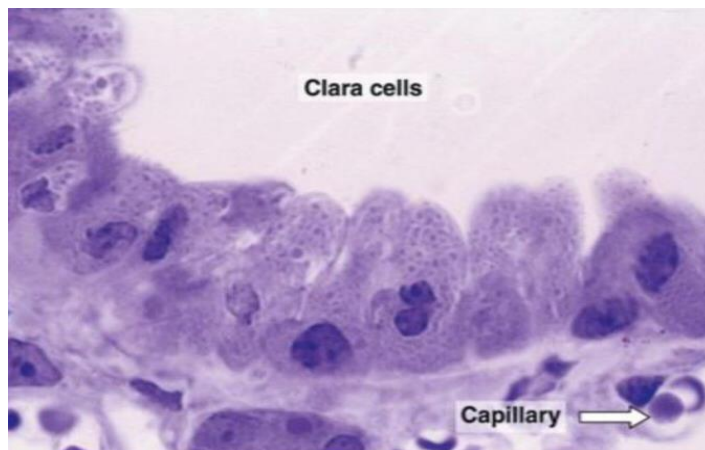


### Bronchioles (1 mm or less)

- ✓ Ciliated simple columnar to ciliated simple cuboidal
- ✓ Goblet cells decrease and Clara cells (simple cuboidal non-ciliated) appear
- ✓ Spirals of smooth muscle relatively heavier than elsewhere (gradually decrease in amount)
- ✓ No seromucous glands
- ✓ No cartilage
- ✓ balt

### Terminal bronchioles

- ✓ Cuboidal epithelium with some cilia.
- ✓ Clara cells and no goblet cells.
- ✓ Thin supporting wall of C.T. and an incomplete layer of smooth muscle.
- ✓ Outpocketings of alveoli, numbers increase at lower levels.
- ✓ Folding of bronchioles is due to contraction (the presence of smooth muscles and absence of cartilage)



Note: Elastic fibers – Longitudinal elastic fibers are present in all the segments of the bronchial system (in the L. propria) - The smaller the bronchiole the higher proportions of elastic fibers. It increases around the lung and alveoli due to its role in inflation.