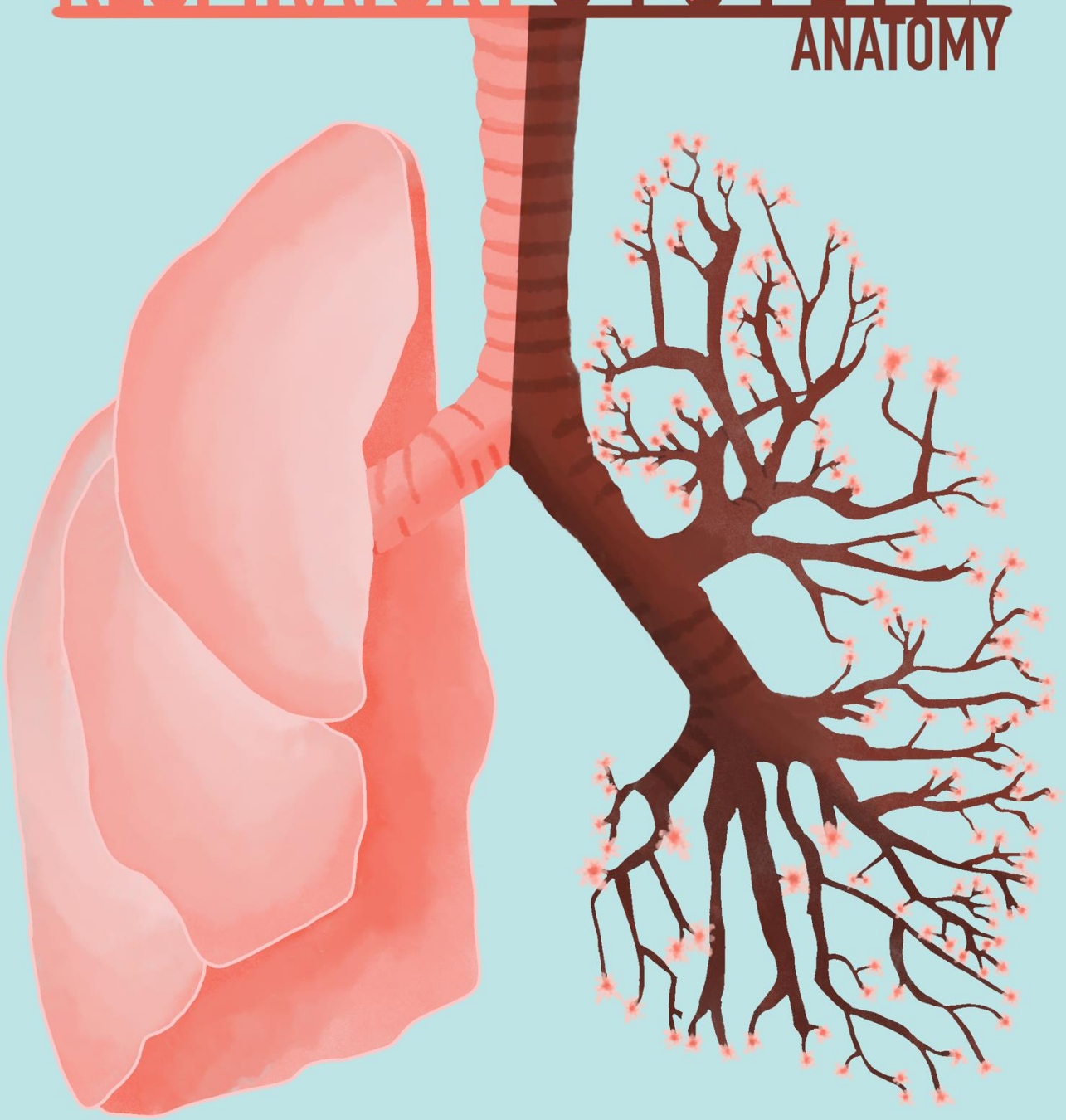
RESPIRATORY SYSTEM
ANATOMY



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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 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, 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.

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.

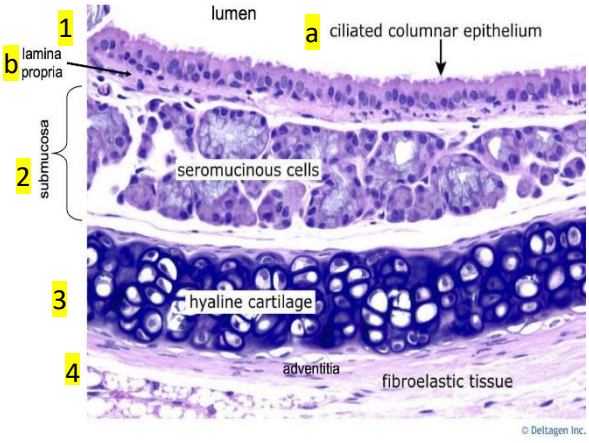
Conducting portion

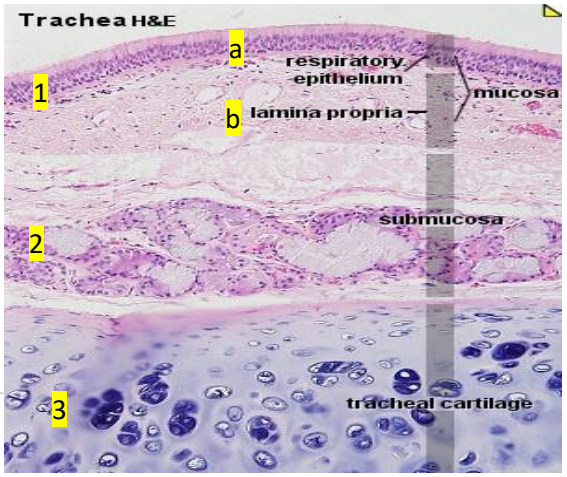
We can consider it the upper part of the respiratory tract which includes *nose, nasopharyngeal cavity, larynx, trachea, bronchi (primary, secondary, tertiary), large bronchioles, terminal bronchioles*. It is involved ***only in passage of air without gas exchange*** and **its major function is to condition the inspired air,** so it becomes **cleansed**, **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).
   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.
2- **Submucosa:** CT rich in blood vessels, lymphatics and seromucous glands whose ducts are directed toward the lumen.
3- **Supportive layer:** contains hyaline cartilage, smooth muscles and elastic fibers [in the GIT it is a muscular layer].
4- **Adventitia:** CT layer.





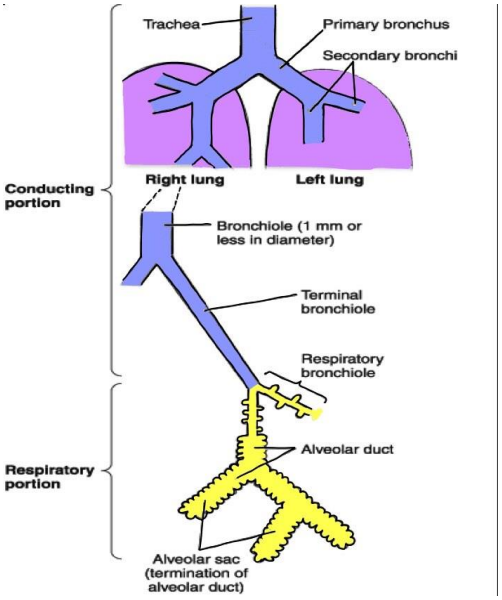
Respiratory portion

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 O2 and CO2 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* [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

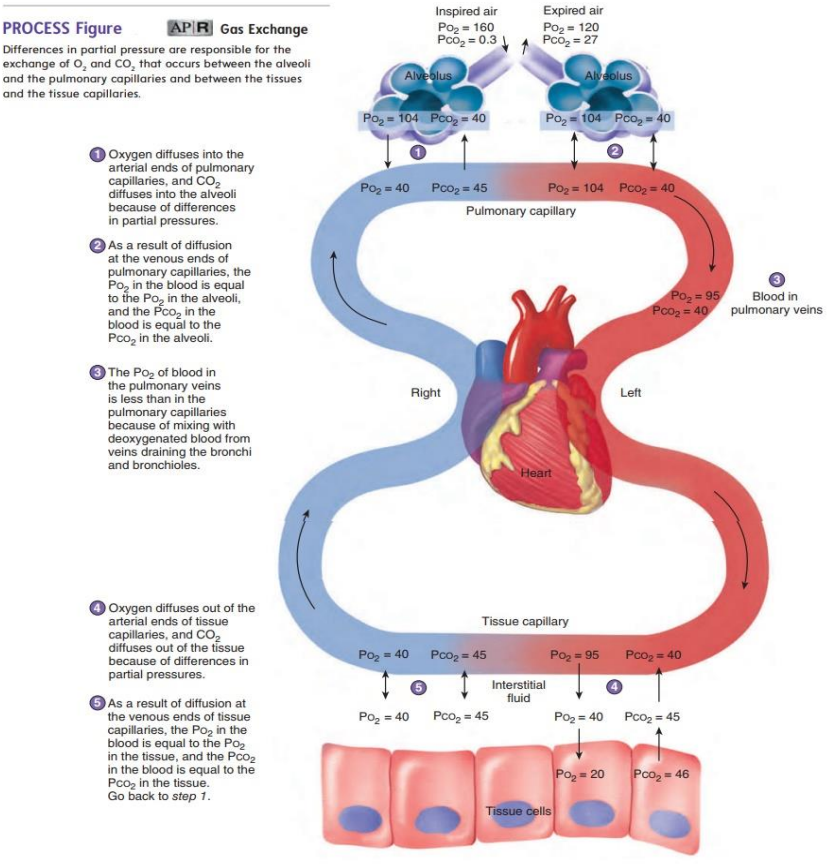
Respiratory bronchioles – belong to the respiratory portion and they are considered *the region of transition* between the two portions

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

Gas exchange

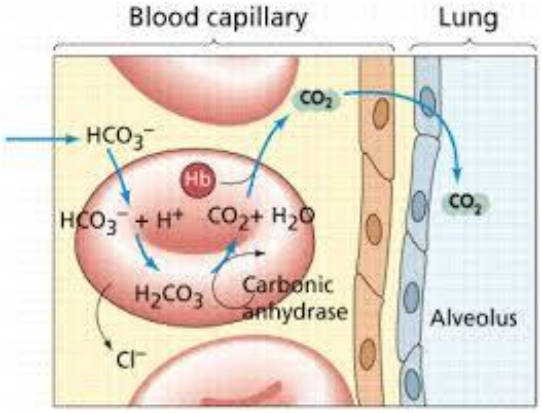
As we said earlier, the exchange of gases (O2 & CO2) occurs between the alveoli and the blood capillaries and this happens by passive diffusion.

- ➢ When blood first arrives at the pulmonary capillary at its arteriole end, the partial pressure of CO2 and O2 are:
  PCO2 = 45 mmHg, PO2 = 40 mmHg (PCO2 > PO2)
- ➢ In the alveoli
  PCO2 = 45 mmHg, PO2 = 105 mmHg (PO2 > PCO2)
- ➢ Due to the difference in pressure, O2 is taken up by RBCs and CO2 is released (to the alveoli)
- ➢ After the net diffusion of oxygen, PO2 in the venous end equals **95 mmHg**



- O2 is then taken by tissue cells for metabolic activity (tissue PO2 = 40 mmHg)

CO2 in the blood

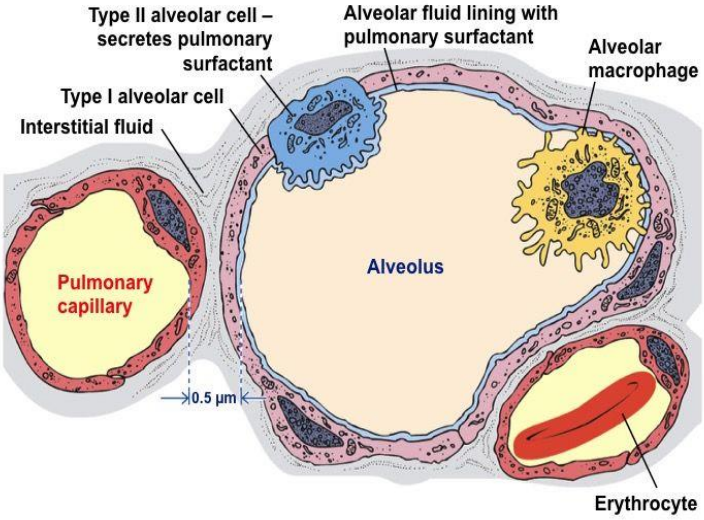


7% dissolved in plasma

23% combine with hemoglobin to form carbaminohemoglobin

70% converted to protons by carbonic anhydrase and combines to hemoglobin (reversible reaction)

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.**

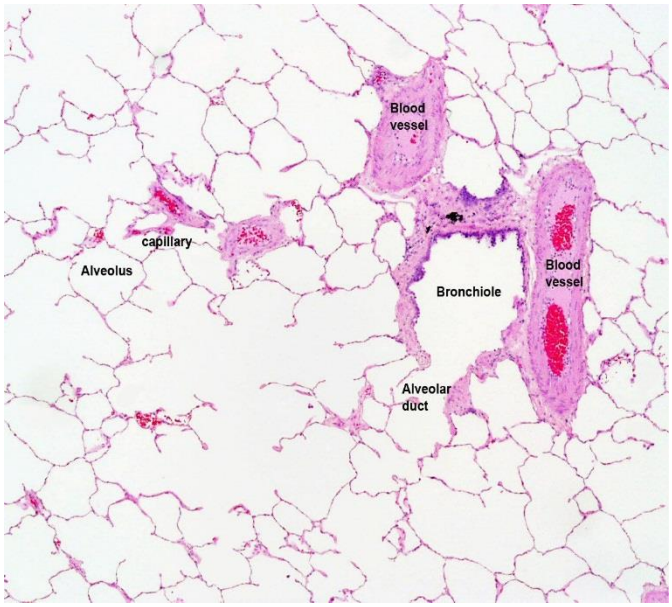


➔ surfactants are secreted at the end of the 8th month and the 9th month of the fetal life in large amounts because they are important at birth when there is inflation and therefore expansion of the lungs. If there is any decrease in surfactants in birth, a syndrome called respiratory distress syndrome will develop. 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**, and both layers are flattened so they help in gas exchange.

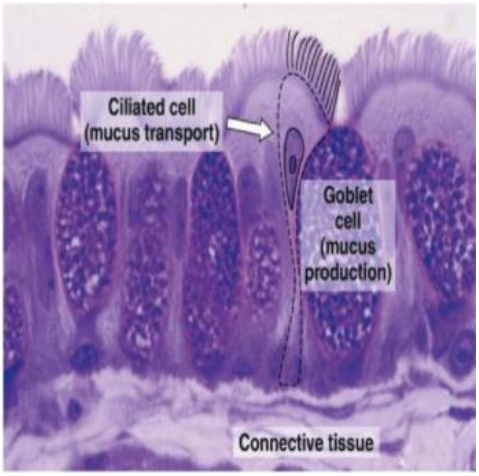
➔ the basal lamina of both epithelial layers is fused to form a very thin layer between the alveolar wall and the capillary wall.

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



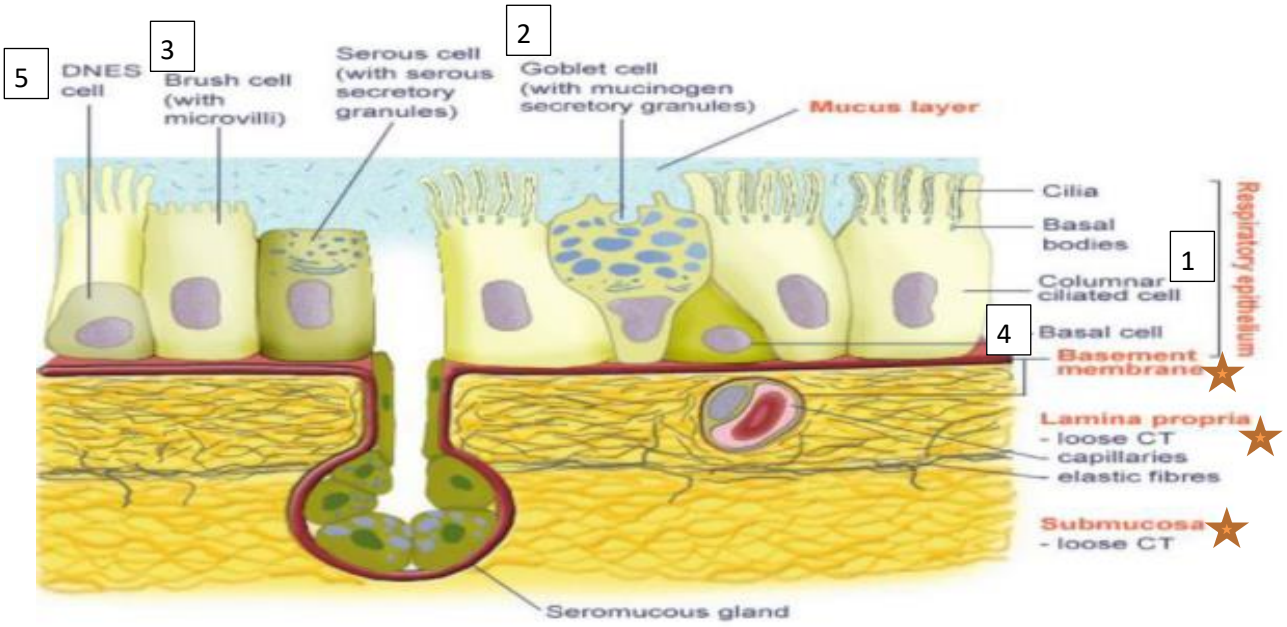
After talking about the two portions of the respiratory tract, we can now talk about the histology of the structures in the respiratory tract in more details

Respiratory epithelium



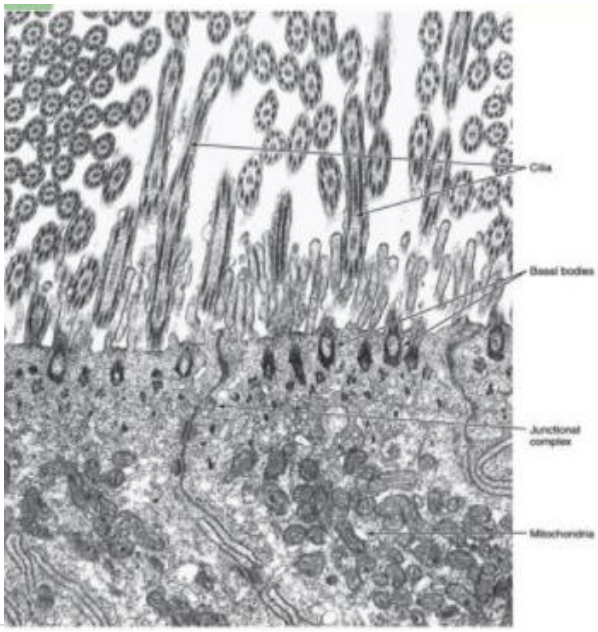
as we said earlier, in the conducting portion specifically the trachea a type of respiratory epithelium is present which is a lining with ciliated pseudo-stratified columnar epithelium with goblet cells (common type).

We can find 5 types of cells in the respiratory tract, all of them are resting on a 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 fibers / 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.

1-Ciliated columnar cells



Most abundant type. Starts from the basement membrane and ends into the surface. Each cell has about 300 cilia on its apical surface. As we said, cilia are important in filtration of air and with their outward movement they can expel the foreign bodies outside the respiratory tract.

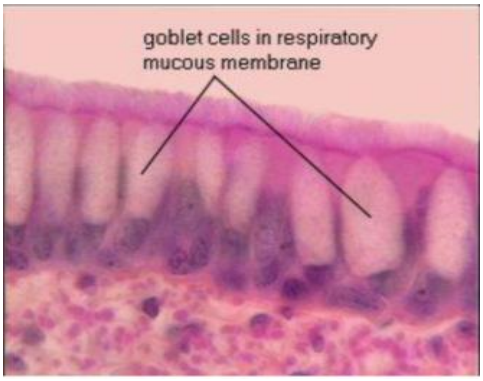
Where cilia are inserted *in the apical part of the cell*, we can find **basal bodies**.

And *below the basal bodies*, we can find many **apical mitochondria** that supply ATP (energy) for ciliary beating.

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.

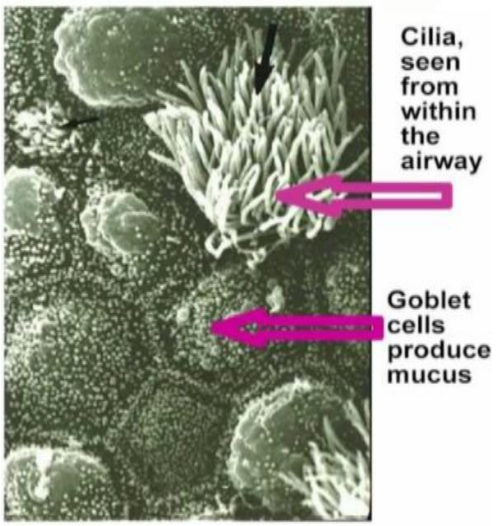
3-Brush cells

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

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.

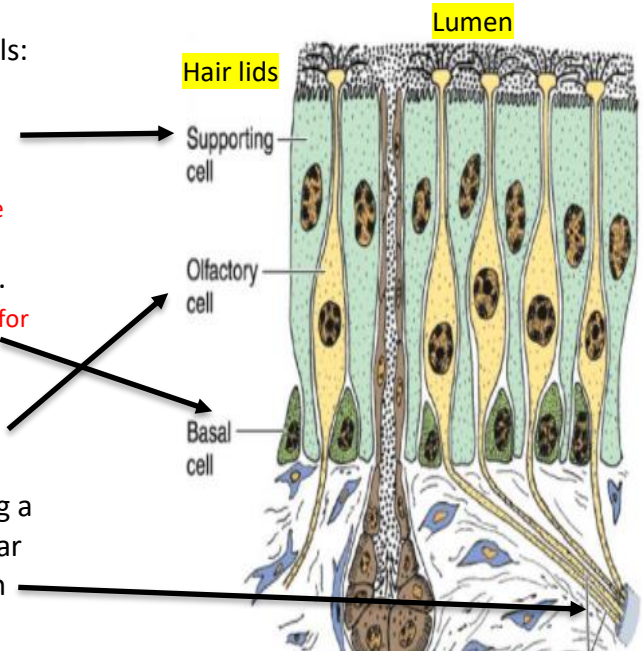
- ✓ Lined by modified skin (keratinized stratified squamous epithelium) that contains sebaceous and sweat glands and thick short hairs called **vibrissae**.
- ✓ Tarps and filters out large particles from the inspired air.
- ✓ Epithelium loses its keratinized nature and undergoes **transition** into typical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

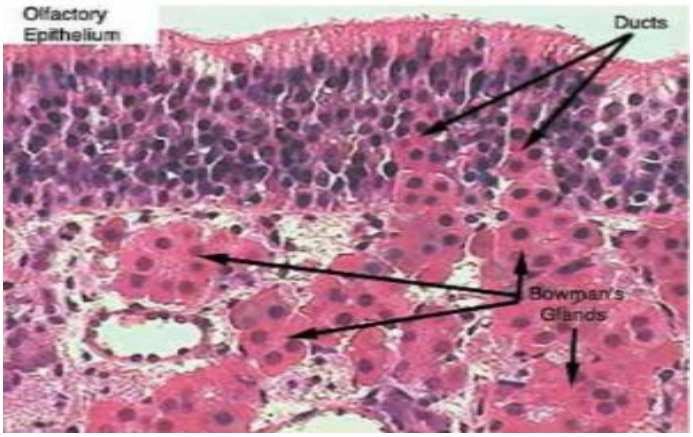
The respiratory area: it is the lateral wall of the nasal cavity with the septum

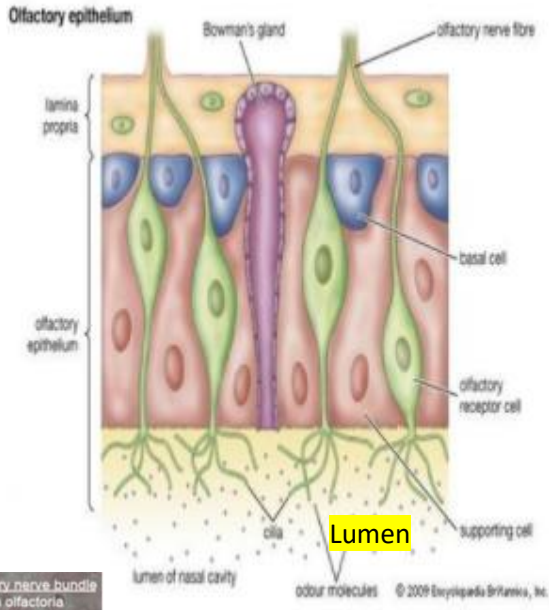
- ✓ Covered with pseudo-stratified columnar epithelium with goblet cells
- ✓ The sub epithelial connective tissue is rich with blood vessels and seromucous glands

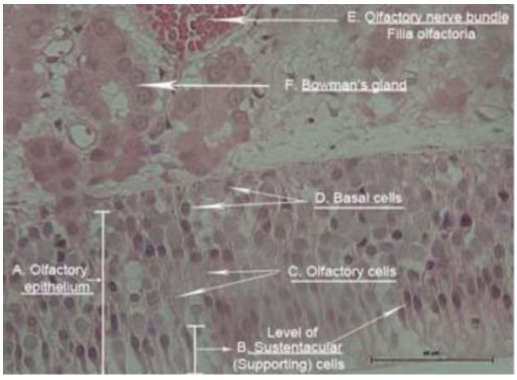
Olfactory region: present in the roof and upper parts of the nasal cavity

- ✓ Covered by **olfactory mucosa**, which contains:
- ✓ **Olfactory epithelium:** it is a pseudo-stratified columnar epithelium composed of three types of cells:
  1- **Supporting (sustinacular) columnar cells**: broad, cylindrical apexes 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 apexes (dendrites). Respond to odoriferous substances by generating a receptor 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.

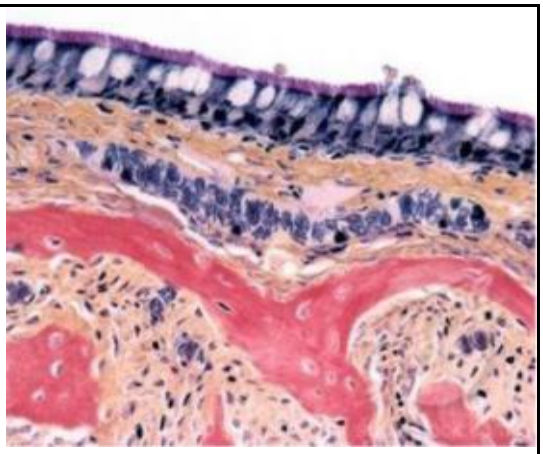






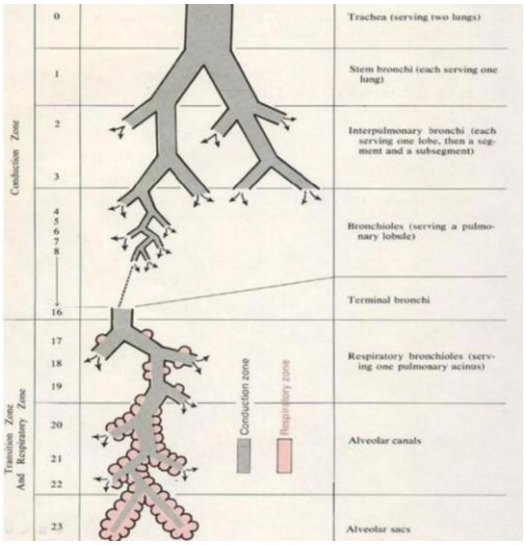


Nasal sinuses: Frontal sinus, Maxillary sinus, Ethmoidal sinus, Sphenoidal sinus. [air sinuses important for resonance of the voice]

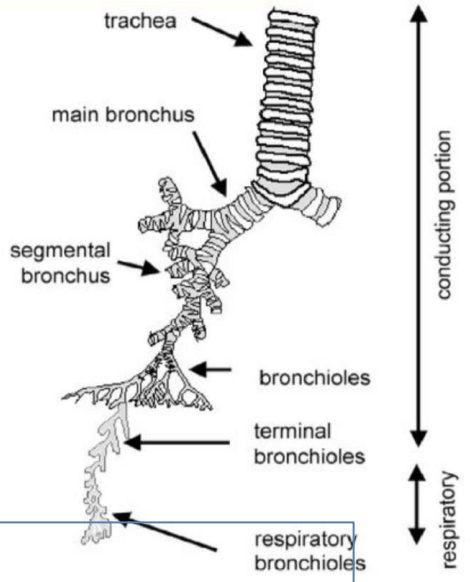


- lined with a **thinner** respiratory epithelium
- contains few goblet cells
- the lamina propria contains only a few small glands
- continuous with the underlying periosteum
- have ducts that open into the lateral wall of the nasal cavity

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)

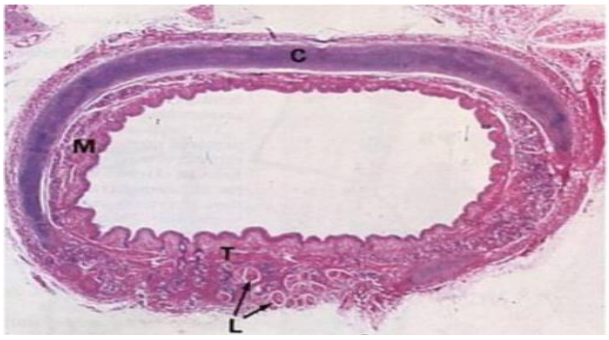
  Notice that the diameter decreases distally

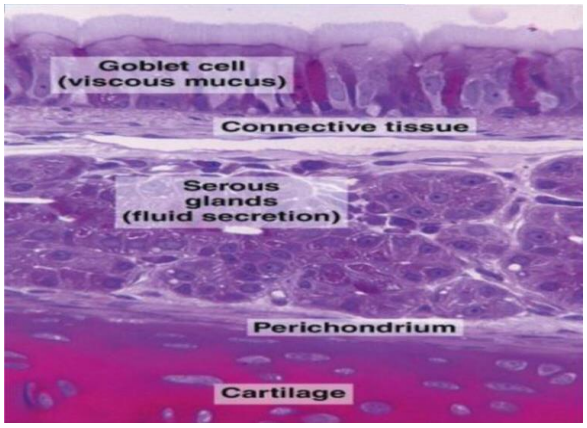
Clara cells: devoid of cilia, secrete proteins that protect the bronchiolar lining against oxidative pollutants and inflammation.

Neuroepithelial bodies: contain secretory granules and receive cholinergic nerve endings + **chemoreceptors** that react to changes in gas composition within the airway

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 overdistention 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**

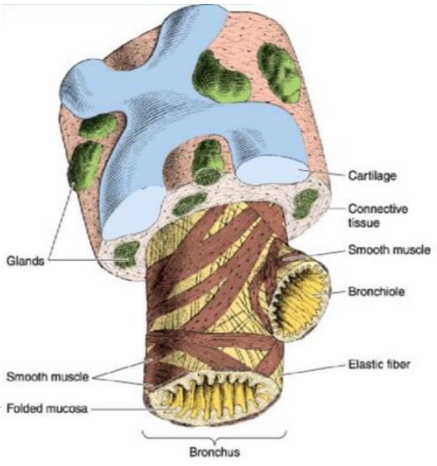




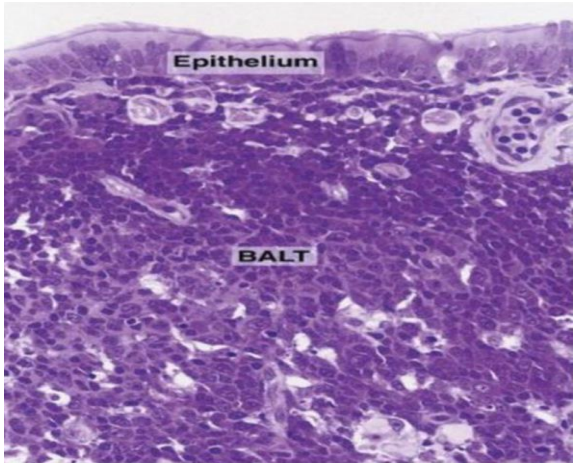
Bronchi

- Divided into:
  1- **Extrapulmonary (primary bronchus):** Resembles trachea in structure
  2- **Intrapulmonary (2ndry and tertiary):** They have complete muscular layer. Cartilaginous plates instead of rings.

Notice that as we go distally, smooth muscles, elastic fibers and lymphocytes increase in number while goblet cells and the glands decrease in number.



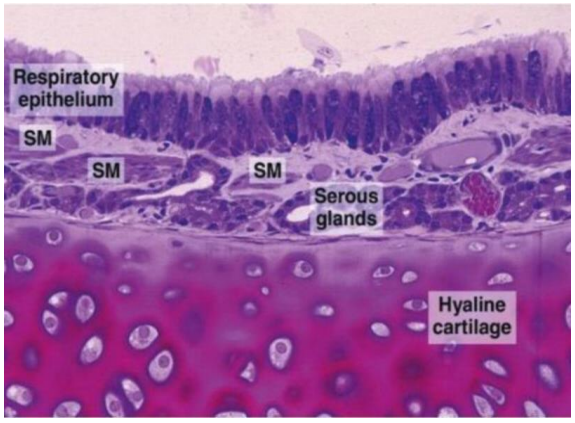
Differences between the trachea and bronchi *(characteristics of the bronchi)*



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.

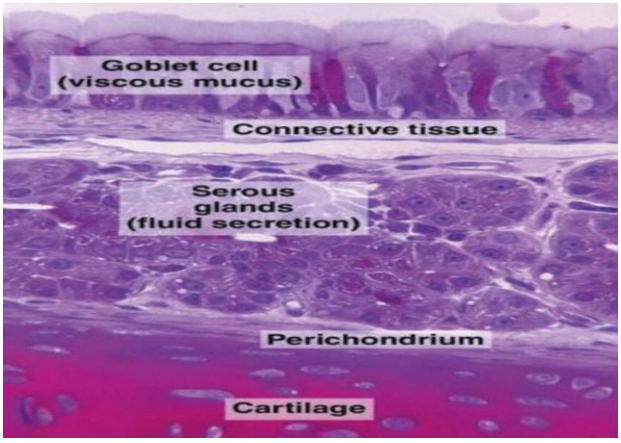


4. lamina propria is rich in elastic fibers and contains an abundance of mucous and serous glands

5. respiratory epithelium with fewer goblet cells

6. Numerous lymphocytes and lymphatic nodules (BALT) are present (infiltrated by the adventitia)

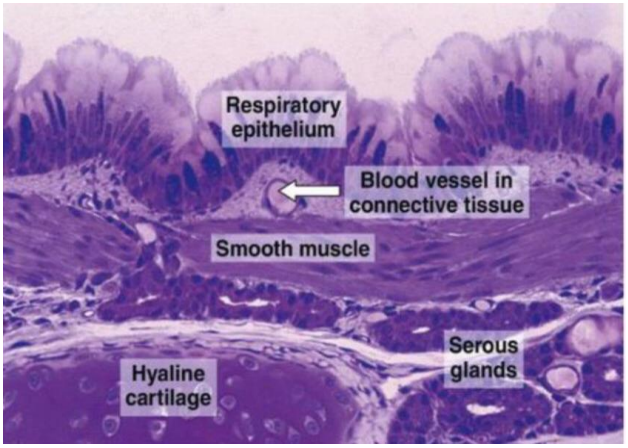
Structural changes in the conducting portion of the respiratory tract:



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

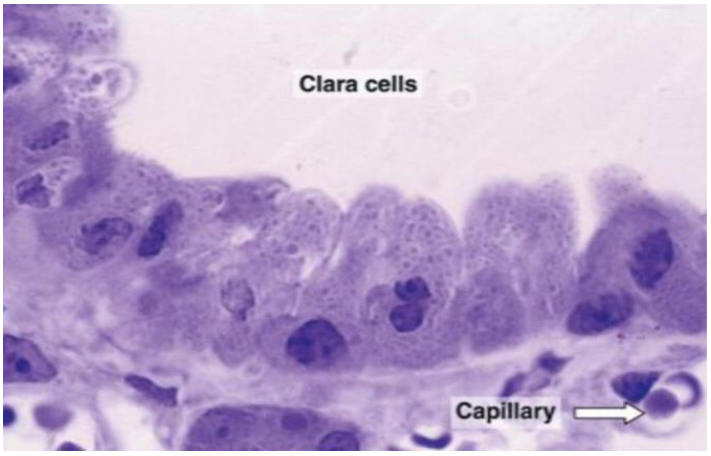
Intrapulmonary bronchi



- ✓ **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

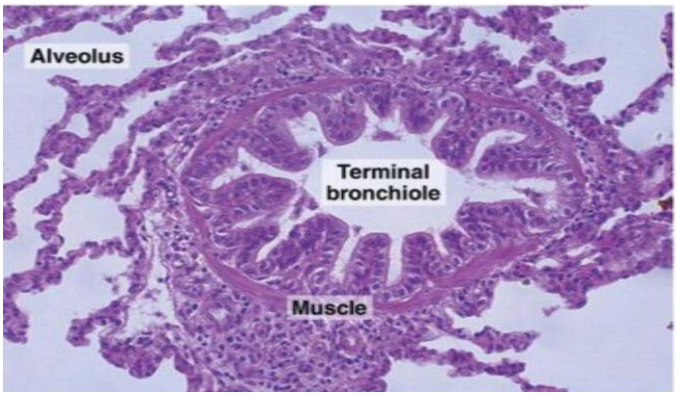
Bronchioles (1 mm or less)

- ✓ **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



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.