

RESPIRATORY SYSTEM

Anatomy



Sheet



Slide

Number:

-Histo1

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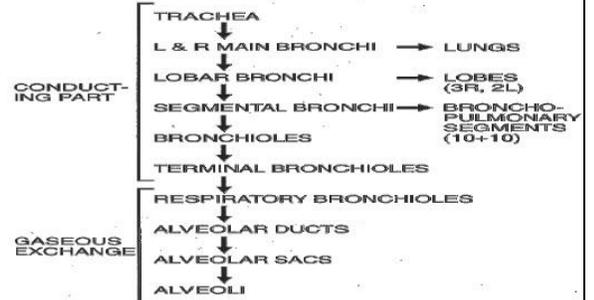
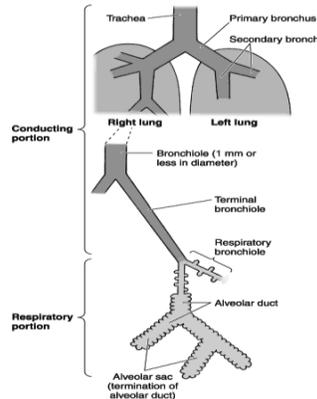
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Histology of the Respiratory Tract

This sheet includes all information and images within the slides.

The respiratory system starts by the nose, ends by the alveoli of the lungs, and is divided into a conducting part and a respiratory part.

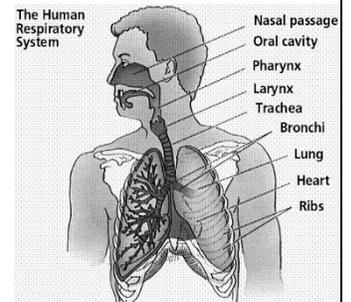


Conducting portion:

It consists of: *(their order is important)*

- **Nose; nasopharyngeal cavity; larynx; trachea; the primary, secondary and tertiary bronchi; large bronchioles; and the terminal bronchioles.**

The conducting portion provides passage of air, and *no* gaseous exchange occurs through it. Its major function is to condition the inspired air. Before it enters the lungs, inspired air is cleansed (protection role), moistened, and warmed through glandular secretions and the plexus of veins, which serves to warm the air mostly.

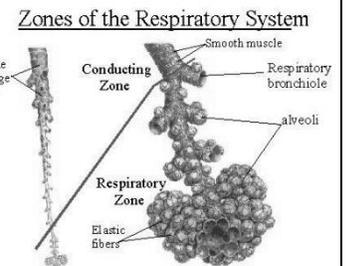


Respiratory portion:

It consists of: *(their order is important)*

- **Respiratory bronchioles (region of transition); alveolar ducts; alveolar sacs (at the end of the ducts); and alveoli (around the sacs and ducts).**

The respiratory portion is where gas exchange takes place.



Extremely important:

The respiratory tract is similar to the digestive tract in the fact that no sudden changes occur; *they are gradual*. An example is the transitional area between the esophagus and the stomach. The esophagus is lined by *stratified squamous non-keratinized epithelium* while the stomach is lined by *simple columnar epithelium*, and this change requires a transitional area, which is very commonly affected by cancer. Similarly, there is a transitional area separating the conducting and respiratory portions. Most of the tract is lined by *ciliated pseudostratified columnar epithelium with goblet cells*, which changes in the

terminal bronchioles to *simple columnar* and *simple cuboidal epithelium (ciliated cells)*, and *Clara cells*. Clara cells are simple cuboidal cells without cilia. Reaching the respiratory portion means that the lining epithelium turns into *simple squamous epithelium*, which is necessary for the process of gases exchange. Therefore, the capillaries are lined by simple squamous epithelium (endothelial cells) similar to the walls of the alveoli. (An area where diffusion occurs mandates the presence of simple squamous epithelium, just like the glomeruli of the kidneys where filtration of fluid takes place).

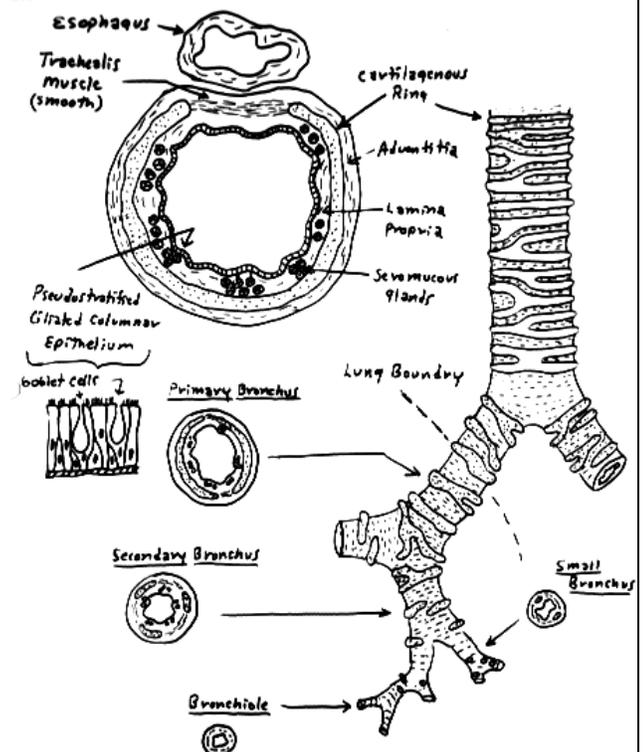
Pseudostratified ciliated columnar → simple columnar → simple cuboidal → Clara cells without cilia → simple squamous epithelium

Notice that the bronchioles have a *conducting part* (primary or large bronchioles, and terminal or small bronchioles) and a *respiratory part* (respiratory bronchioles). The terminal bronchioles of the conducting part are followed by the respiratory bronchioles, and the difference between them is histological. The terminal bronchioles are lined by simple columnar, simple cuboidal, or Clara cells, while the respiratory bronchioles are lined by simple squamous epithelium.

Also note that the conducting bronchioles have a diameter of approx. 1 mm and no cartilage, since cartilage is completely replaced by smooth muscles – the most important characteristic of both types of bronchioles is that they contain no cartilage.

Observe the following section in the trachea and the esophagus posterior to it. There are 4 layers in the histology the respiratory tube:

- 1- **Mucosa :**
 - a. **Lining epithelium (pseudostratified ciliated columnar)** resting on a basement membrane and goblet cells
 - b. **Lamina propria** (loose connective tissue containing seromucous glands)
 - c. **Muscularis mucosa** (2 or 3 ribbons of smooth muscle)
- 2- **Submucosa:** a connective tissue layer that contains lymphatics and blood vessels and houses mucous and seromucous glands.
- 3- **Supportive layer:** *smooth muscle and cartilage*
- 4- **Adventitia:** connective tissue coverings that are always present. They cover the alveoli, although in small quantities.



The third layer in the trachea, *the supportive layer*, is in the form of C-Shaped Hyaline Cartilage, which is open posteriorly; meaning that there is no cartilage in the back to interfere with the esophagus's

peristaltic movements. If the cartilage was in the form of a full ring, it would stop the flow of food in its tracks. Instead, there is a smooth muscle posteriorly, called the trachealis muscle, that can help in the peristaltic movement. In the bronchi (right and left main bronchus), the C-shaped cartilage is replaced by **plates** of cartilage that are circular. The more distal you go, the less the cartilage becomes, to the point that you will only find 1 or 2 pieces of cartilage when you reach the tertiary (segmental) bronchi. It is completely absent in the bronchioles. Smooth muscles replace the gradually dwindling cartilage. In the beginning, smooth muscles are small in number, nearly absent, and the more distal you go, the more they become. In the trachea, smooth muscles are present in the form of the trachealis muscle. In the bronchioles, smooth muscles have crossing/spiral, prominent and abundant fibers. However, they decrease between the alveoli. So, it can be deduced that since asthma causes the contraction of smooth muscle, it will mainly affect the bronchioles, and there will be no cartilage to prevent it from doing so.

The number of goblet cells decreases as you go distally. By the beginning of the bronchioles, there are few goblet cells, while the respiratory bronchioles contain no goblet cells.

The glands are present in the beginning and decrease in number distally. There are few glands in the beginning of the bronchioles, but no glands in the terminal bronchioles.

There are few scattered lymphocytes in the beginning which increase distally to provide immunity. In the bronchioles, the lymphocytes are present in the form of lymphatic nodules.

Elastic fibers are initially absent but are numerous between the alveoli.

Having discussed the histological layers of the respiratory tract, notice how they differ between the conducting and respiratory portions:

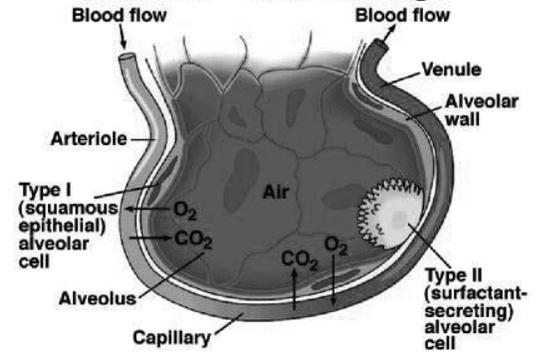
- **Conducting portion:**

- Mucosa of the conducting portion is lined with a specialized **respiratory epithelium**
- Numerous mucous and serous glands as well as a rich superficial vascular network in the lamina propria mainly; they can also be present in the submucosa.

- **Respiratory portion:**

- Contains simple squamous epithelium
- Rich in elastic fibers, which constitute most of its connective tissue. Their presence is especially important in the walls of the alveoli for the process of inflation and deflation, during inspiration and expiration, respectively.
- The alveoli are surrounded by a network of capillaries lined by endothelial cells (simple squamous epithelium).
- Between the capillaries and the alveoli lies a membrane, called the respiratory membrane, through which occurs the process of gases exchange, whereby oxygen diffuses to the capillaries to be transported to the cells, while CO₂ diffuses to the alveoli and outside the body through expiration.

Alveolus — Gas Exchange

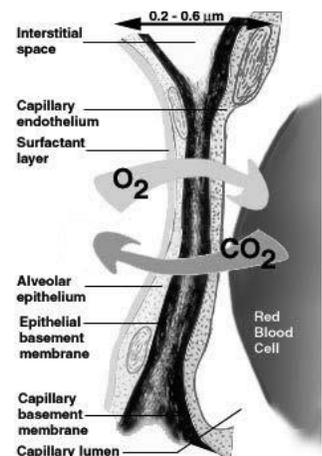


In the adjacent image of the alveolus, notice the Type 1 Alveolar Cell, also called Pneumocyte Type 1, which is a squamous epithelial cell. It constitutes 98% of the alveolar wall. The Type 2 Alveolar Cells are cuboidal, with lamellar bodies (responsible for the secretion of surfactant) and smaller in number 2%. They are present between the corners of the alveoli and secrete a surfactant.

The surfactant is formed during the 7th month of pregnancy and increases in amount during the 8th. By the 9th month, it should be in amounts sufficient to decrease the surface tension when the baby is born and respiration starts, so that the alveoli are filled with air. Since the baby receives oxygen from the blood of its mother during pregnancy, it should be gently slapped on the legs or the back as soon as it is born in order to stimulate the respiratory center, which through the phrenic nerve causes the lung to inflate and fill with air. The baby's first cry signals the beginning of respiration (this coincides with expiration). Thus, the surfactant must be in sufficient amounts for the inflation of the lungs, otherwise resulting in Respiratory Distress Syndrome. This requires immediate intervention since the baby isn't able to fill their lungs with air and the alveoli are abnormal. The baby will need the incubator in addition to the deficient surfactant that is required for the completion of the alveoli's growth.

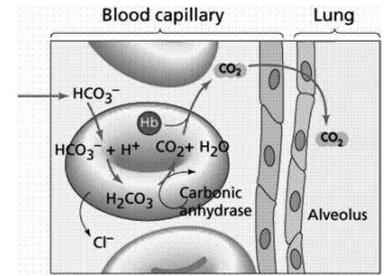
Gas exchange

- Alveoli are the main sites for the principal function of the lungs; that is the exchange of O₂ and CO₂ between inspired air and blood.
- Since alveolar ducts also contain simple squamous epithelium, gases exchange can occur in the ducts but is mainly in the alveoli and the capillaries surrounding them.
- The exchange of gases (O₂ & CO₂) between the alveoli & the blood occurs by passive diffusion. When blood first arrives at the pulmonary capillary at its arteriolar end, the partial pressures of carbon dioxide and oxygen are:
PCO₂ = 45 mm Hg (high)
PO₂ = 40 mm Hg (low)
- In the alveoli:
PO₂ = 105 mmHg
PCO₂ = 45 mmHg
- O₂ is taken up by RBCs and CO₂ is released due to difference in pressure
- After the net diffusion of oxygen, PO₂ in the venous end equals **95mmHG**, which heads to the left atrium through the pulmonary veins and then to the aorta through the ventricle.
- Oxygen is then taken up by tissue cells for metabolic activity (tissue PO₂ = 40 mmHg)
- Notice the simple squamous epithelia in both the capillaries and alveoli in the picture.



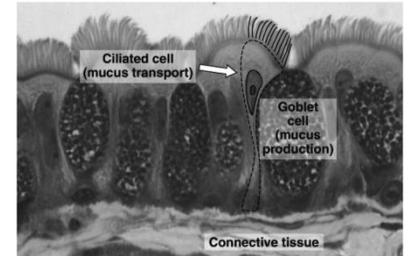
Carbon-dioxide in the blood

- 7% dissolved in plasma
- 23% combine with hemoglobin to form **carbaminohemoglobin**
- 70% converted to protons by **carbonic anhydrase** and combine to hemoglobin (reversible reaction)

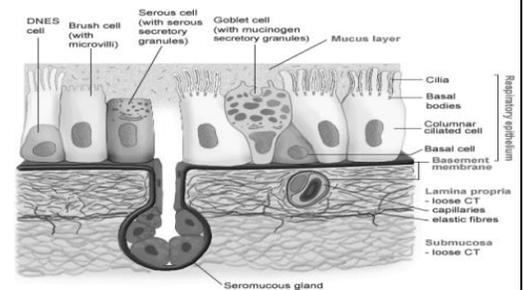


Respiratory Epithelium

- Lined with ciliated **pseudostratified columnar epithelium**
- Contains 5 types of cells all of which rest on a **thick** basement membrane, but not all of them reach the surface (some are short)

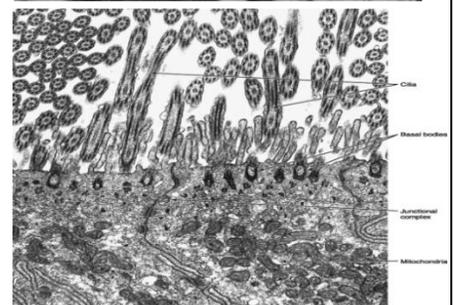
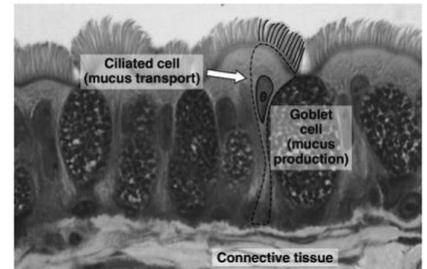


- Of these 5 types, the most common is the pseudostratified columnar cells which can be seen under the light microscope.
- Notice the seromucous gland in the lamina propria in the picture on the right.



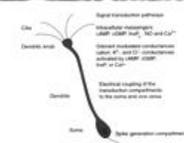
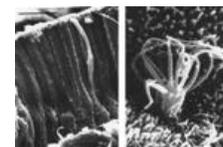
Ciliated columnar cells

- Most abundant type
- Each cell has about 300 cilia on its apical surface
- **Basal bodies:** concentrated on the apex where cilia is inserted in the apical part of the cell
- **Apical mitochondria (below the bodies)** supply adenosine triphosphate (ATP) as energy for ciliary beating.



Ciliary movements

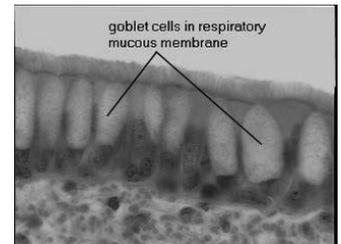
- Dynein is a protein that normally participates in the ciliary movement
- The ciliary movement is in one direction, and that is to the outside. This movement is of utmost importance in expelling bacteria, viruses, foreign bodies, sputum etc. through coughing.



- Nicotin prevents formation of dynein, which leads to improper movement of cilia.
- Immotile cilia syndrome (Kartagener syndrome) is caused by immobility of cilia and flagella and induced, in some cases, by deficiency of dynein. It results in infertility in men (since sperm need to be motile in order to reach the fallopian tube) and chronic respiratory tract infections in both sexes.

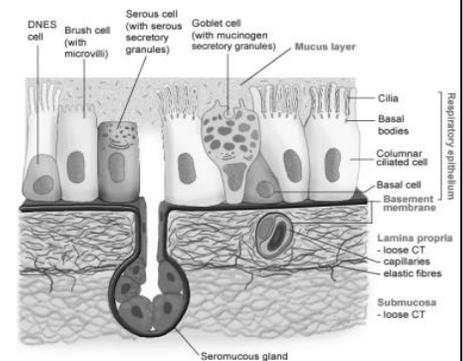
Mucous goblet cells

They secrete mucin and contain apical mucous droplets composed of **glycoproteins** and containing **polysaccharides**. Mucus is necessary for the lubrication and the entrapment of bacteria and viruses.



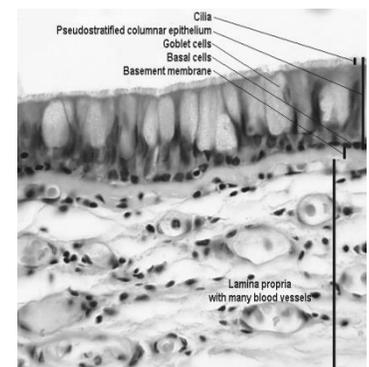
Brush cells

- Numerous microvilli on their apical surface
- Sensory receptors (afferent nerve endings on their basal surfaces)



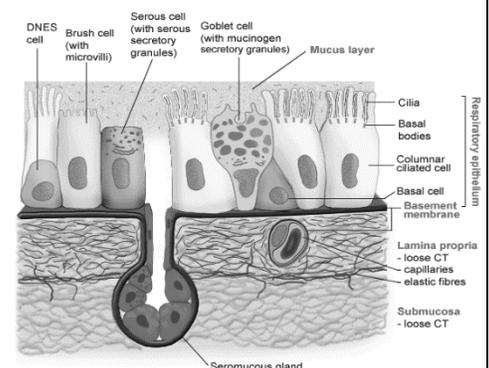
Basal (short) cells

- Small rounded cells located at the base
- Believed to be generative stem cells (responsible for mitosis)
- Differentiate into the other cell types (are considered **reserve cells**)



Small granule cell

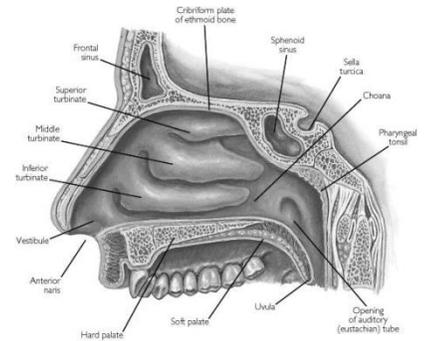
- Cells of the **DNES** (diffuse neuroendocrine system)
- Locally regulate the excretions or secretions of mucous and serous glands in the respiratory tract
- Also called **Kulchitsky Cells** (the name of the discoverer).



Nasal Cavity:

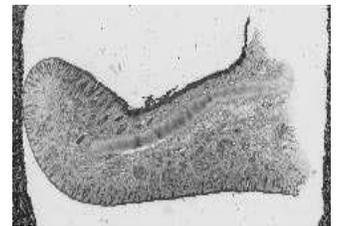
Subdivided histologically into:

- The vestibule
- The respiratory area (the area related to the conchae and meatuses and is a thick mucosa; meaning that it can result in obstruction in cases such as rhinitis. It contains a plexus of veins in the thick submucosa that warms and moisturizes the air)
- Olfactory region (contains respiratory epithelium plus olfactory bipolar cells) the bipolar cell is important in the smell sensation.



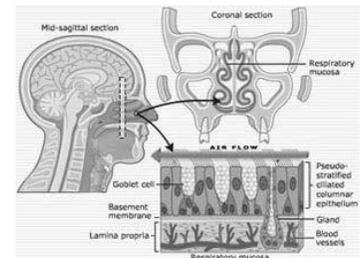
The vestibule

- Most anterior and dilated portion of the nasal cavity
- Lined by skin
- Contains sebaceous and sweat gland
- Thick short hairs, or **vibrissae**
- Traps and filters out large particles from the inspired air
- Epithelium loses its keratinized nature and undergoes a **transition** into typical respiratory epithelium **before** entering the nasal fossae



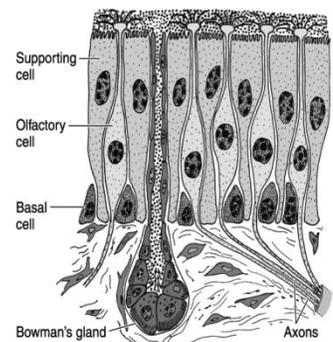
The respiratory area

- Covered with pseudostratified columnar and goblet cells
- The sub. Epithelial connective tissue is rich with blood vessels and seromucous glands.
- It covers the lateral wall of the nasal cavity.



Olfactory region

- Present in the roof and upper parts of the nasal cavity
- Covered by **olfactory mucosa** which contains:
Olfactory epithelium
Corium (lamina propria)
Bowman's gland in lamina propria whose secretions reach the surface to aid in dissolving the odor



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Olfactory epithelium

- It is a pseudostratified columnar epithelium composed of three types of cells:

1- Supporting (sustentacular) columnar cells

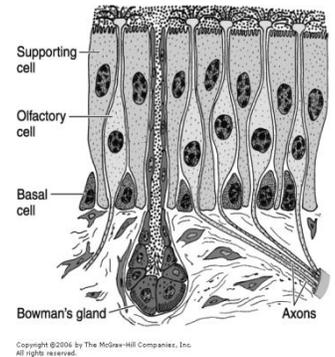
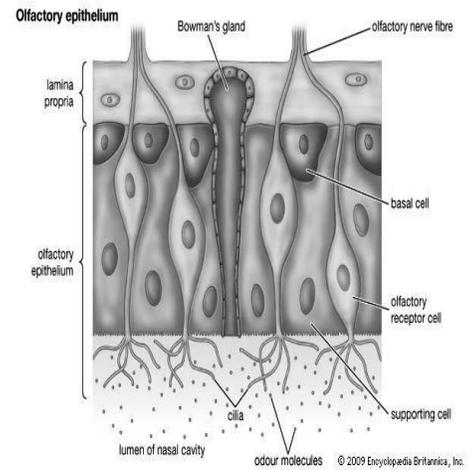
- broad, cylindrical apices and narrower bases
- microvilli submerged in a fluid layer
- contain a light yellow pigment
- are connective tissue cells that are supporting and nutritive to the bipolar cells

2- Basal cells: single layer at the base of the epithelium

- spherical or cone shaped
- important in mitosis and replacement of other cells

3- Olfactory cells: bipolar neurons

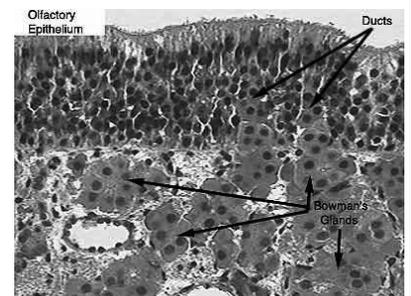
- their nuclei lie below the nuclei of the supporting cells
- cilia (nonmotile) rise from their apices (dendrites)
- respond to odoriferous substances by generating a receptor potential
- afferent axons of these bipolar neurons unite in small bundles, and synapse with the olfactory lobe.



The bipolar cells (also named the olfactory cells, or bipolar nerve cells), are called as such because at one pole they have “tiny hairs” responsible for the reception of odor, and on the other pole, an axon of the olfactory nerve. After the odor is dissolved, it generates an impulse that travels through the axon to the smell center, which in turn provides the interpretation of the impulse to recognize the smell. Each type of smell has its own special impulse. The axons (olfactory filaments) pass through the cribriform plate.

Lamina propria

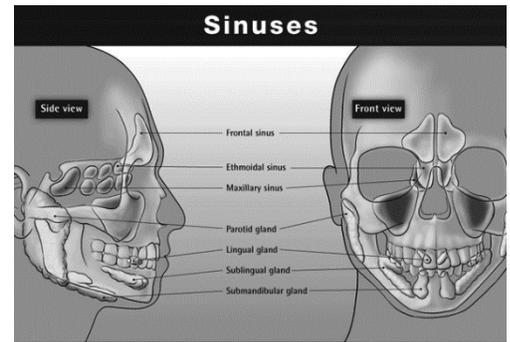
- **Corium** (lamina propria) is rich in blood vessels.
- Contains **Bowman's gland** that secretes watery mucous, facilitating the access of new odoriferous substances.



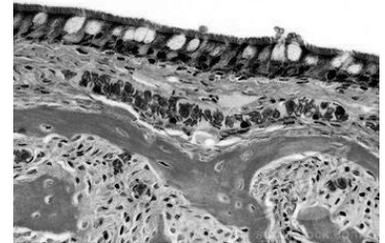
Olfaction is not required

Nasal sinuses:

- 1- Frontal sinus
- 2- Maxillary sinus
- 3- Ethmoidal sinus
- 4- Sphenoidal sinus, which lies behind the ethmoidal.

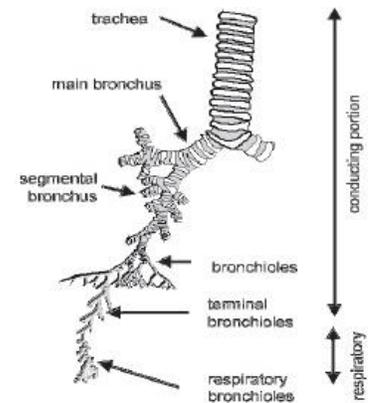


- Nasal sinuses are lined with a thinner respiratory epithelium (thin mucosa)
- Contain few goblet cells
- The lamina propria contains only a few small glands
- Continuous with the underlying periosteum
- Inflammation of these sinuses is called sinusitis
- They have ducts that open in the lateral wall of the nose

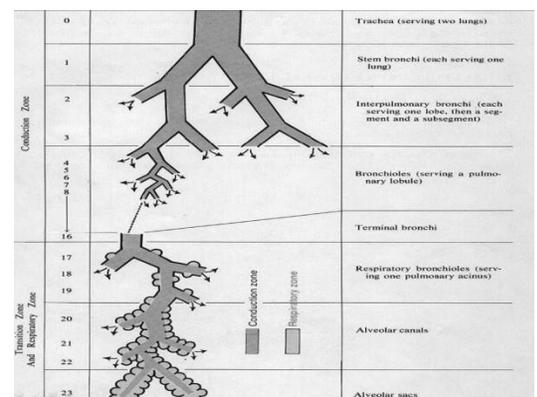


Structural changes in the bronchial tree

- The trachea extends from the level of C6 to the thoracic vertebra T4 opposite to the sternal angle anteriorly (angle of Louis) between the manubrium and the body of the sternum (bifurcation point)
- Only the trachea and the primary 1ry (main) bronchus are extra-pulmonary
- We have **three** lobar (secondary 2ndry) bronchi in the right and **two** in the left lung
- Tertiary 3ry bronchi have 10 segments in the right and 10 segments in the left lung.
- So if you look at a slide under the microscope and see lung tissue, then the bronchus you're looking at is either 2ndry or 3ry. Otherwise, it's 1ry.



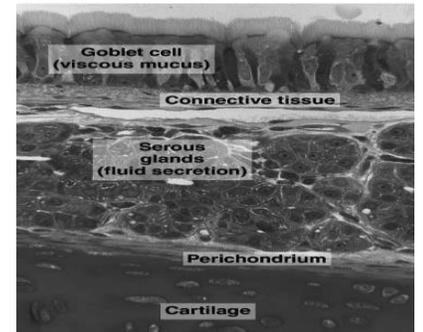
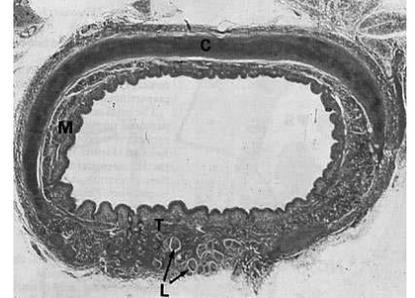
- The segmental (tertiary) bronchus is almost 5mm or less in diameter
- Each bronchiole enters a pulmonary lobule
- Each large bronchiole (1mm) gives 5-7 terminal ones
- Terminal bronchioles (0.5mm) contain **Clara cells** (no cilia) and **neuroepithelial bodies** (chemoreceptor)
- Note that the diameters decrease distally



- “Terminal bronchi” in the image refer to the tertiary bronchi. The image doesn’t show the terminal (conducting) bronchioles that precede the respiratory ones.

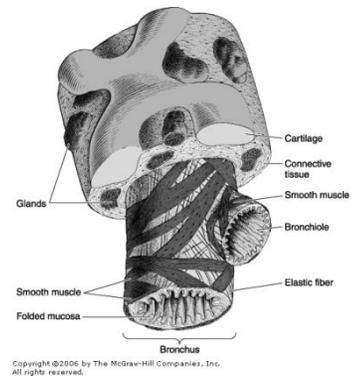
Trachea

- Lined with a typical respiratory mucosa, and contains **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**
- Some longitudinal muscles may be found behind the trachealis
- The trachealis is innervated by the sympathetic and the parasympathetic nervous system.
- Numerous seromucous glands that produce a more fluid mucus (in the submucosa and lamina propria)
- Contains 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



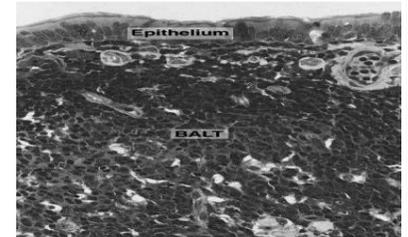
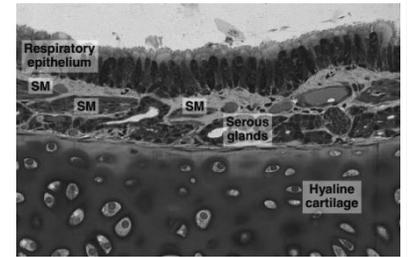
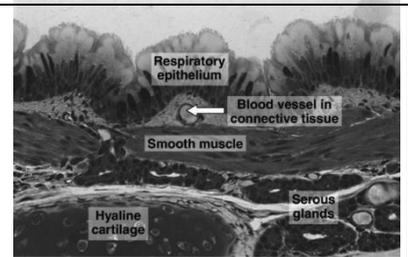
Bronchi

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



Differences between the trachea and bronchi: (Characteristics of the bronchi):

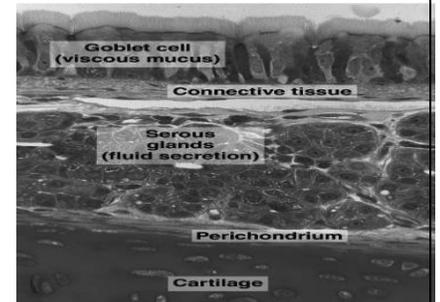
1. Narrower lumen (small bronchus is 5mm or less)
2. Irregular bronchial cartilage plates
3. Smooth muscle layer consisting of **spirally arranged bundles** between the lamina p. and submucosa
Contraction of this muscle layer and decreased cartilage plates are responsible for the folded appearance of 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)



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Extra-pulmonary bronchi

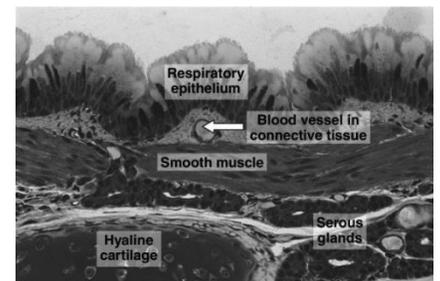
- **Pseudostratified ciliated columnar epithelium with goblet cells.**
- Prominent basement membrane.
- Relatively thin lamina propria (elastic layer at base)
- Submucosa with **seromucous glands**
- "C" shaped hyaline **cartilage rings** w/ smooth muscle between ends of cartilage *according to the slides*. *The doctor insisted during and after the lecture that it turns into plates as we go distally.



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Intrapulmonary bronchi

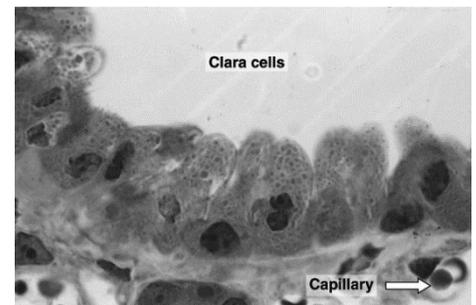
- **Pseudostratified ciliated columnar** changing to **ciliated simple columnar** in smaller branches. **Goblet cells** at all levels. (but in less numbers)
- Below lamina propria are interlacing **spirals of smooth muscle**
- Seromucous glands decrease as bronchi get smaller.
- **Plates of cartilage**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



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Bronchioles (1 mm or less) (very small)

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

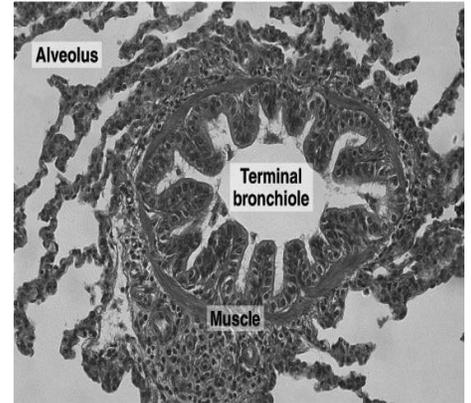


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Respiratory bronchioles

- **Cuboidal epithelium with some cilia**, Clara cells, and **no goblet cells** at the beginning, then turns into **simple squamous epithelium**.
- Thin supporting wall of C.T. and an incomplete layer of smooth muscle.
- **Outpocketings of alveoli**, numbers increase at lower levels.

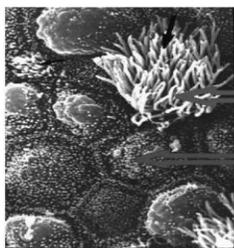
Notice the folding of mucosa in the terminal bronchioles due to the absence of cartilage and the presence of the spiral smooth muscles that pull on the epithelium causing its folding.



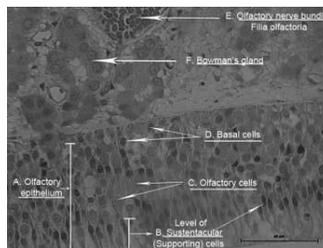
Bronchioles

- **Clara cells**
 - Devoid of cilia, cuboidal
 - Secrete proteins that protect the bronchiolar lining against oxidative pollutants and inflammation. They were found to be involved in the formation of the surfactant.
 - They are present near the end of the conducting bronchioles and the beginning of the respiratory bronchioles (between the ending of simple cuboidal and the beginning of the simple squamous epithelium)
- **Neuroepithelial bodies**
Contain secretory granules and receive cholinergic nerve endings
- **Chemoreceptors** that react to changes in gas composition within the airway
- Longitudinal elastic fibers are present in all the segments of the bronchial system (in the L. propria)
- The smaller the bronchiole, the higher the proportions of elastic fibers present. They are most in the walls of the alveoli.

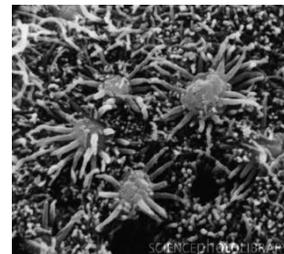
Additional images in the slides:



Cilia and Goblet Cells



Olfactory epithelium



Olfactory cells

"A flower does not think of competing to the flower next to it. It just blooms."