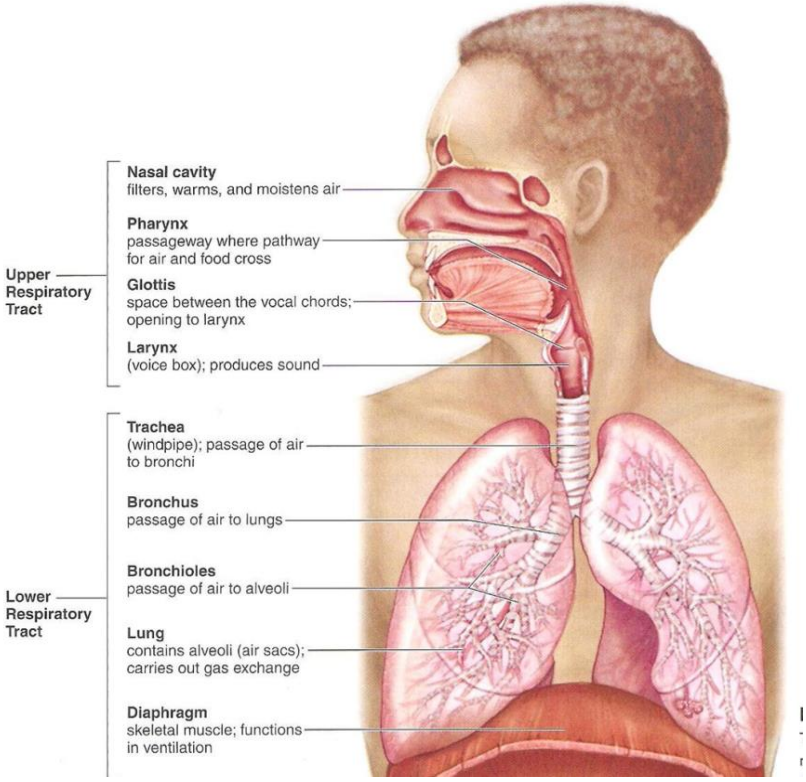
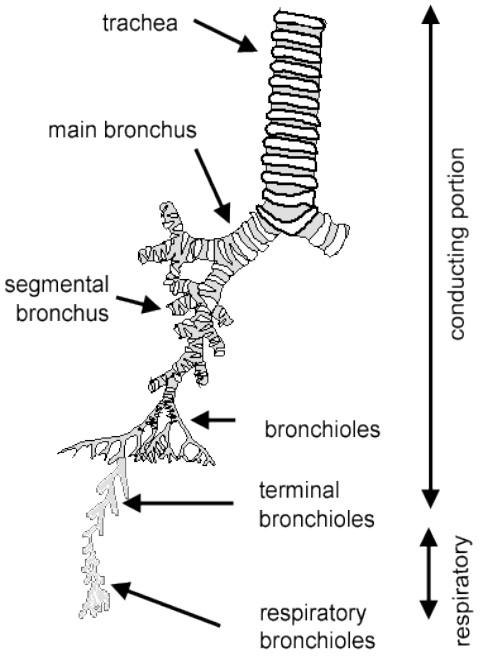
THE RESPIRATORY SYSTEM

The respiratory system includes the **lungs** and a branching system of tubes that link the sites of gas exchange with the external environment. The respiratory system is divided anatomically into structures of the upper and lower respiratory tracts. Functionally, these structures make up the system's **conducting portion**, which consists of the nasal cavities, nasopharynx , larynx , trachea , bronchi , bronchioles, and terminal bronchioles; and a **respiratory portion** (where gas exchange takes place) consisting of respiratory bronchioles, alveolar ducts, and alveoli.

The conducting portion serves to filter, warm and humidify air: **filtered** by particles being trapped in mucous secretions, and transported towards the throat, where the mucous is swallowed. **Warmed** by underlying blood vessels and **humidified** by serous and mucous secretions. Specialized portions of the conducting system also serve other functions, e.g., the nose in the sense of smell and the larynx in phonation.





The respiratory system consists of four main layers:

1. the respiratory mucosa (epithelium and supporting lamina propria)
2. Submuscosa
3. Cartilage and/or muscle layer
4. Adventitia / Serosa

The components of these layers in different regions of the respiratory system are related to the functions of each component of this system.

Most of the conducting portion is lined with ciliated pseudostratified columnar epithelium known as **respiratory epithelium**. This epithelium has at least five cell types, all of which touch the thick basement membrane:

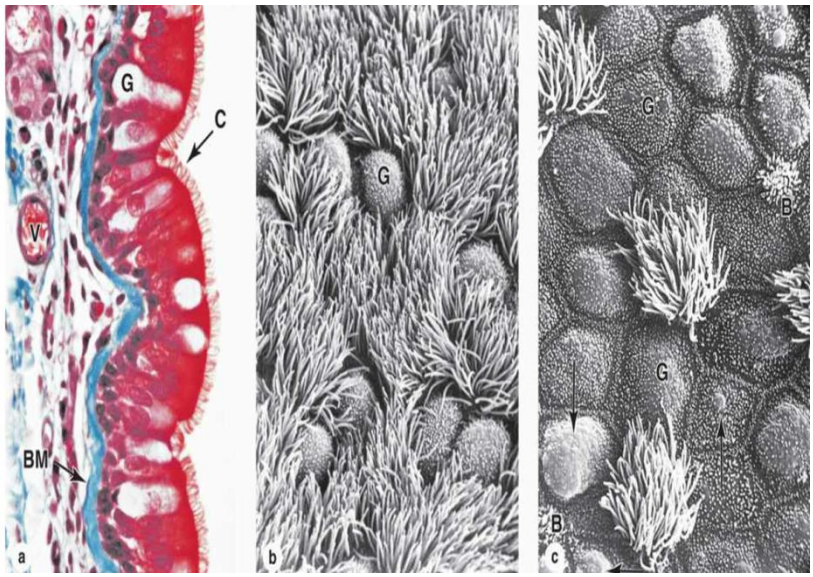
1- **Ciliated columnar cells** are the most abundant, columnar cells have cilia on its apical surface.

2- **Goblet cells** are also numerous and predominate in some areas with basal nuclei and apical domains filled with granules of mucin glycoproteins.

3- **Brush cells** columnar cells at apical surface bears sparse microvilli. Brush cells are chemosensory receptors.

4- **Small granule cells** are possess numerous dense core granules, are part of the diffuse neuroendocrine system.

5- **Basal cells** small rounded cells on the basement membrane and not extending to the luminal surface, are stem cells that give rise to the other cell types.

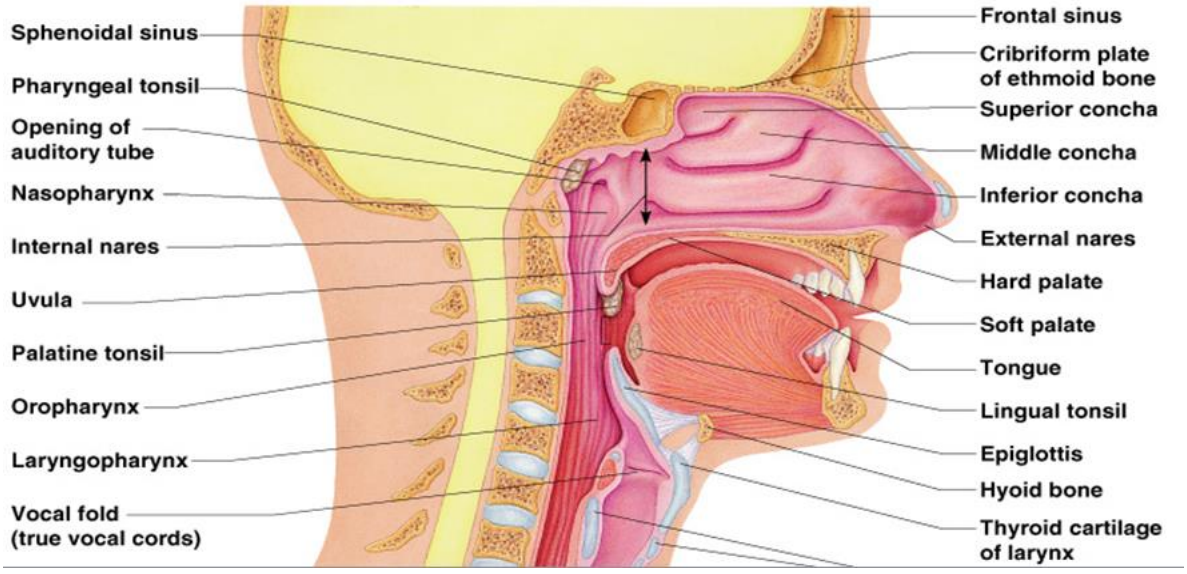


NASAL CAVITY

The left and right nasal cavity each has two components: the external **vestibule** and the internal **nasal cavity**. The **vestibule** is the most anterior and dilated portion of each nasal cavity, are lined with a keratinised stratified squamous epithelium and has sweat glands, sebaceous glands, and short coarse **vibrissae** (hairs) that filter out particulate material from the inspired air.

Within the vestibule, the epithelium loses its keratinized nature and undergoes a transition to typical pseudostratified columnar epithelium before entering the nasal cavities. The **nasal cavities** lie within the skull as two cavernous chambers separated by the osseous nasal septum. Extending from each lateral wall are three bony shelf like projections called **conchae**. **The middle and inferior conchae** are covered with **respiratory epithelium**; the roof of the nasal cavities and the **superior conchae** are covered with **specialized olfactory epithelium.**

The mucosa covering these and other parts of the nasal cavity walls has a lamina propria with important roles in conditioning inhaled air**.** The narrow passages between the conchae improve the conditioning of the inspired air by increasing the surface area of moist, warm respiratory epithelium and by slowing and increasing turbulence in the airflow.

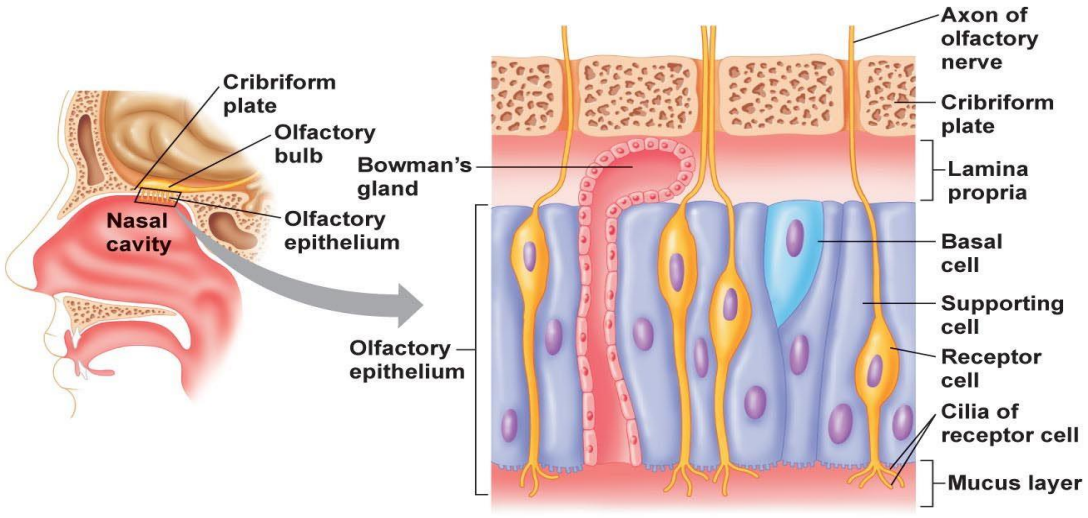


Olfactory epithelium

The olfactory chemoreceptors for the sense of smell are located in the olfactory epithelium, a specialized region of the mucous membrane covering the superior conchae at the roof of the nasal cavity. It is a pseudostratified columnar epithelium composed of three types of cells:

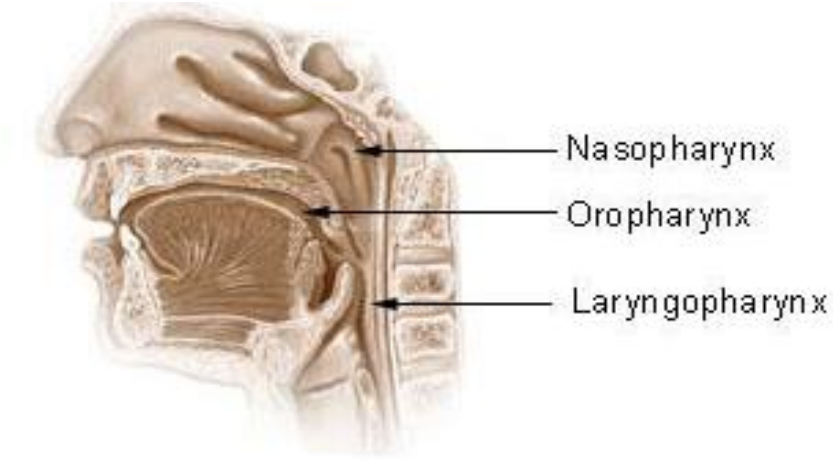
1- **Basal cells** are small, spherical or cone-shaped and form a layer at the basal lamina. They are the stem cells for the other two types.
2- **Supporting cells** are columnar, with broad, cylindrical apexes and narrower bases. On their free surface are microvilli submerged in a fluid layer.
3- **Olfactory neurons** are bipolar neurons present throughout this epithelium. They are distinguished from supporting cells by the position of their nuclei, which lie between those of the supporting cells and the basal cells. The dendrite end of each olfactory neuron is the apical (luminal) pole of the cell.

The lamina propria of the olfactory epithelium possesses large serous glands (glands of Bowman), which produce a flow of fluid surrounding the olfactory cilia and facilitating the access of new odoriferous substances.



NASOPHARYNX

The nasal cavities open posteriorly into the nasopharynx, which is the first part of the pharynx and continuous with the oropharynx, the posterior part of the oral cavity leading to the larynx which lined with stratified squamous epithelium. The nasopharynx is lined with respiratory epithelium, and its mucosa contains the medial pharyngeal tonsil.



LARYNX

The larynx is a rigid, short passage for air between the pharynx and the trachea. Its wall is reinforced by a set of hyaline cartilage and smaller elastic cartilages all connected by ligaments. In addition to maintaining an open airway, movements of these cartilages by skeletal muscles participate in sound production during phonation.

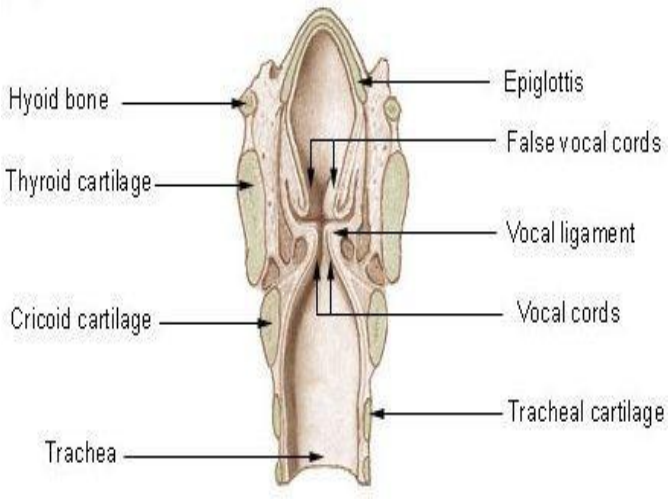
The epiglottis, a flattened structure projecting from the upper rim of the larynx, serves to prevent swallowed food or fluid from entering that passage , extends into the pharynx and has lingual and laryngeal surfaces. The entire lingual surface and the apical portion of the laryngeal surface are covered with stratified squamous epithelium. At variable points on the laryngeal surface of the epiglottis the epithelium undergoes a transition to ciliated pseudo stratified columnar epithelium. Mixed mucous and serous glands are found in the lamina propria beneath the epithelium.

Below the epiglottis and laryngeal vestibule, the mucosa projects into the lumen bilaterally with two pairs of folds separated by a narrow space or ventricle. **The upper pair**, the immovable vestibular folds (false vocal cord) is partly covered with **typical respiratory epithelium**. The **lower pair** of folds, the vocal folds (or cords), have features important for phonation or sound production:

- They are covered with stratified squamous epithelium that protects the mucosa from abrasion and desiccation from rapid air movement.

- A dense regular bundle of elastic connective tissue, the vocal ligament supports the free edge of each vocal fold.

- Deep to the mucosa of each vocal fold are large bundles of striated fibers that comprise the **vocal muscle**.

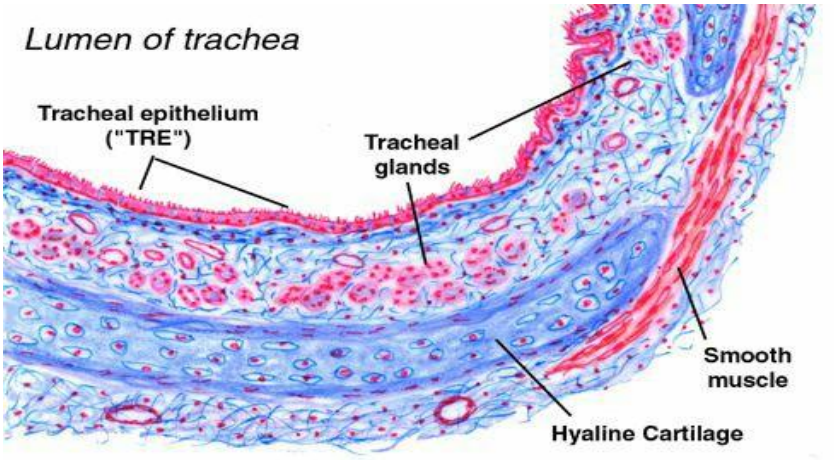


TRACHEA

The trachea is a long flexible, tubular airway is lined with typical respiratory mucosa in which the lamina propria contains numerous seromucous glands producing watery mucus.

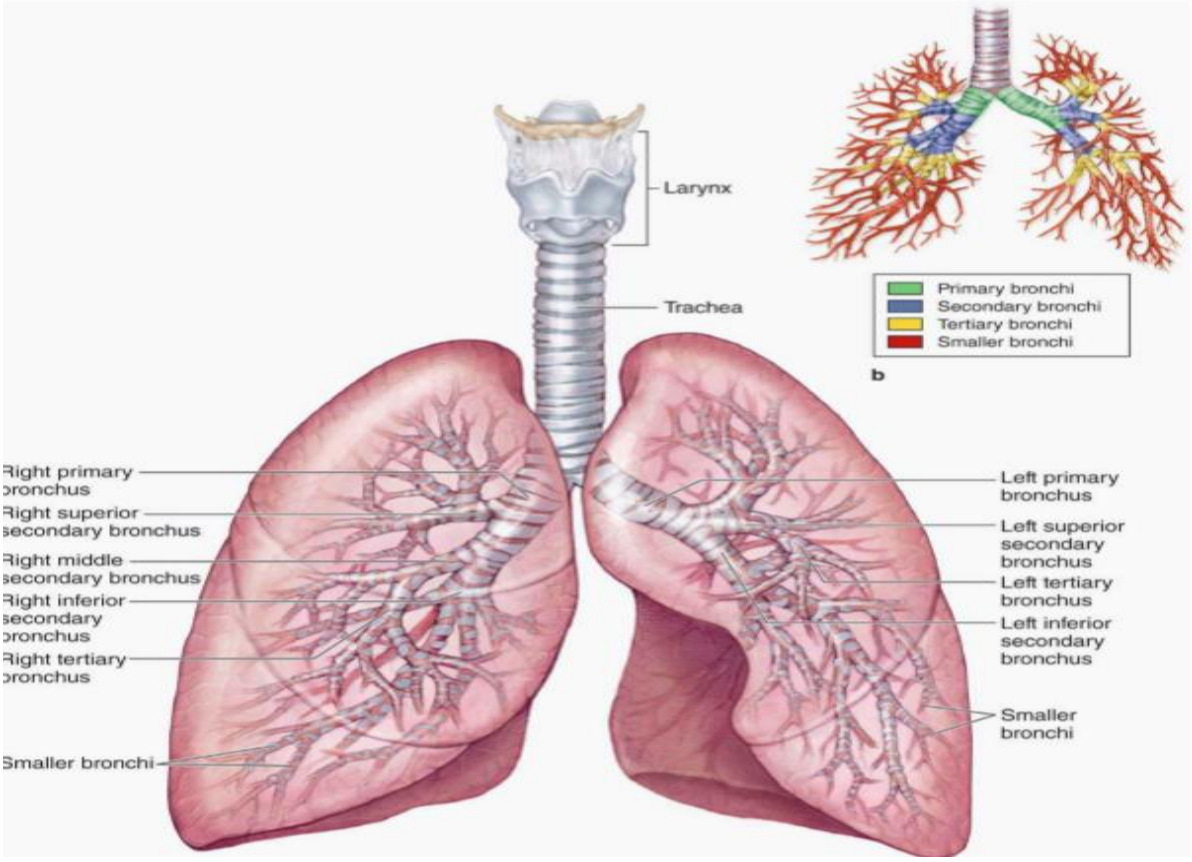
A series with about a dozen C-shaped rings of hyaline cartilage in the submucosa reinforces the wall and keeps the tracheal lumen open . The open ends of the cartilage rings are on the posterior surface, against the esophagus, and are bridged by a bundle of smooth muscle called the **trachealis muscle** and a sheet of fibroelastic tissue attached to the perichondrium.

Together these hold the lumen of the trachea open, but allow flexibility during inspiration and expiration. The trachealis muscle relaxes during swallowing to facilitate the passage of food by allowing the esophagus to bulge into the lumen of the trachea. The entire organ is surrounded by adventitia.



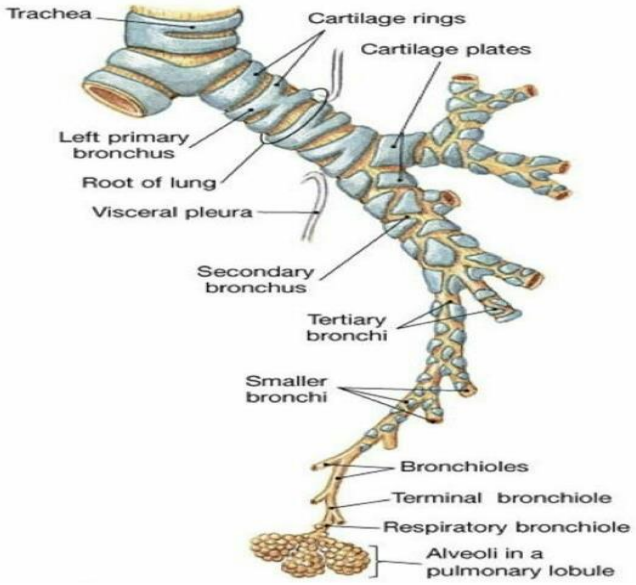
BRONCHIAL TREE & LUNG

The trachea divides into two primary bronchi that enter each lung at the hilum, along with arteries, veins, and lymphatic vessels. After entering the lungs, the **primary bronchi** divided to **three secondary** (lobar) bronchi in the right lung and two in the left lung , each of which supplies a pulmonary lobe. These lobar bronchi again divide, forming **tertiary bronchi**. The tertiary bronchi give rise to smaller and smaller bronchi, whose terminal branches are called **bronchioles.** Each bronchiole enters a pulmonary lobule, where it branches to form five to seven **terminal bronchioles**. The histologic organization of both the epithelium and the underlying lamina propria gradually becomes more simplified.



BRONCHI

The mucosa of the larger bronchi is structurally similar to the tracheal mucosa except for the organization of cartilage and smooth muscle. In the primary bronchi most cartilage rings completely encircle the lumen, but as the bronchial diameter decreases, cartilage rings are gradually replaced with isolated plates of hyaline cartilage. Small mucous and serous glands are abundant, with ducts opening into the bronchial lumen. The lamina propria contains crisscrossing bundles of spirally arranged smooth muscle and elastic fibers which become more prominent in the smaller bronchial branches. Contraction of this muscle layer is responsible for the control of diameter and length of the bronchi - it contracts during expiration to help expel the air.



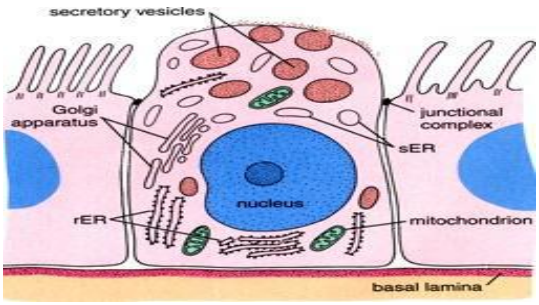
BRONCHIOLES

The tertiary bronchi branch into the bronchioles. These are histologically distinct from the tertiary bronchi in that their walls, they lack both mucosal glands and cartilage, although dense connective tissue is associated with the smooth muscle. In the larger bronchioles, the epithelium is still ciliated pseudostratified columnar, but this decreases in height and complexity to become ciliated simple columnar or simple cuboidal epithelium in the smallest **terminal bronchioles**, which are the last parts of the air conducting system. Most numerous in the cuboidal epithelium of terminal bronchioles are **Clara cells**, or exocrine bronchiolar cells, which have nonciliated, dome-shaped apical ends with secretory granules. Clara cells have various functions, including the following:

-Secretion of surfactant lipoproteins and mucins in the fluid layer on the epithelial surface.

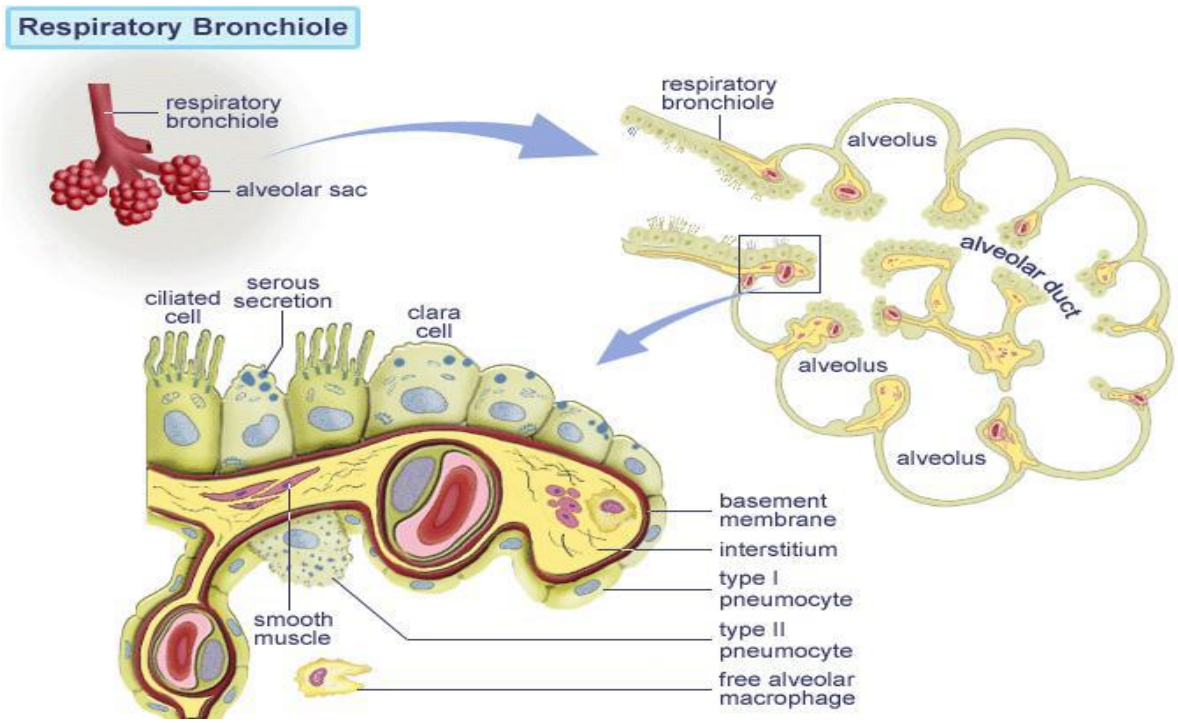
- Detoxification of inhaled xenobiotic compounds by enzymes of the SER.

-Secretion of antimicrobial peptides and cytokines for local immune defense.



RESPIRATORY BRONCHIOLES

Respiratory bronchioles is a regions of transition between the conducting and respiratory portions of the respiratory system , which lead to alveolar ducts , alveolar sacs and alveoli. The mucosa lining consists of Clara cells and ciliated cuboidal cells, with simple squamous cells at the alveolar openings and extending into the alveolus. Proceeding distally along the respiratory bronchioles, alveoli are more numerous and closer together. Smooth muscle and elastic connective tissue make up the lamina propria.



Alveolar Ducts

Distal ends of respiratory bronchioles branch into tubes called alveolar ducts that are completely lined by the openings of alveoli. Both the alveolar ducts and the alveoli themselves are lined with **squamous cells**. In the thin lamina propria, a **strand of smooth muscle cells** surrounds each alveolar opening and a matrix of elastic and collagen fibers supports both the duct and its alveoli. Larger clusters of alveoli called **alveolar sacs** form the ends of alveolar ducts distally and occur occasionally along their length. The lamina propria is thin, consisting essentially **of a network of elastic and reticular fibers** that encircles the alveolar openings and closely surrounds each alveolus. Network of capillaries also surrounds each alveolus.

ALVEOLI

Alveoli are responsible for the spongy structure of the lungs. The structure of alveolar walls is specialized to enhance diffusion between the external and internal environments. Between neighboring alveoli lie thin inter alveolar septa consisting of elastic and reticular fibers, of connective tissue. The arrangement of elastic fibers enables alveoli to expand with inspiration and contract passively with expiration; reticular fibers prevent both collapse and excessive distention of alveoli.

The epithelium of the alveoli, contains two main types of cells:

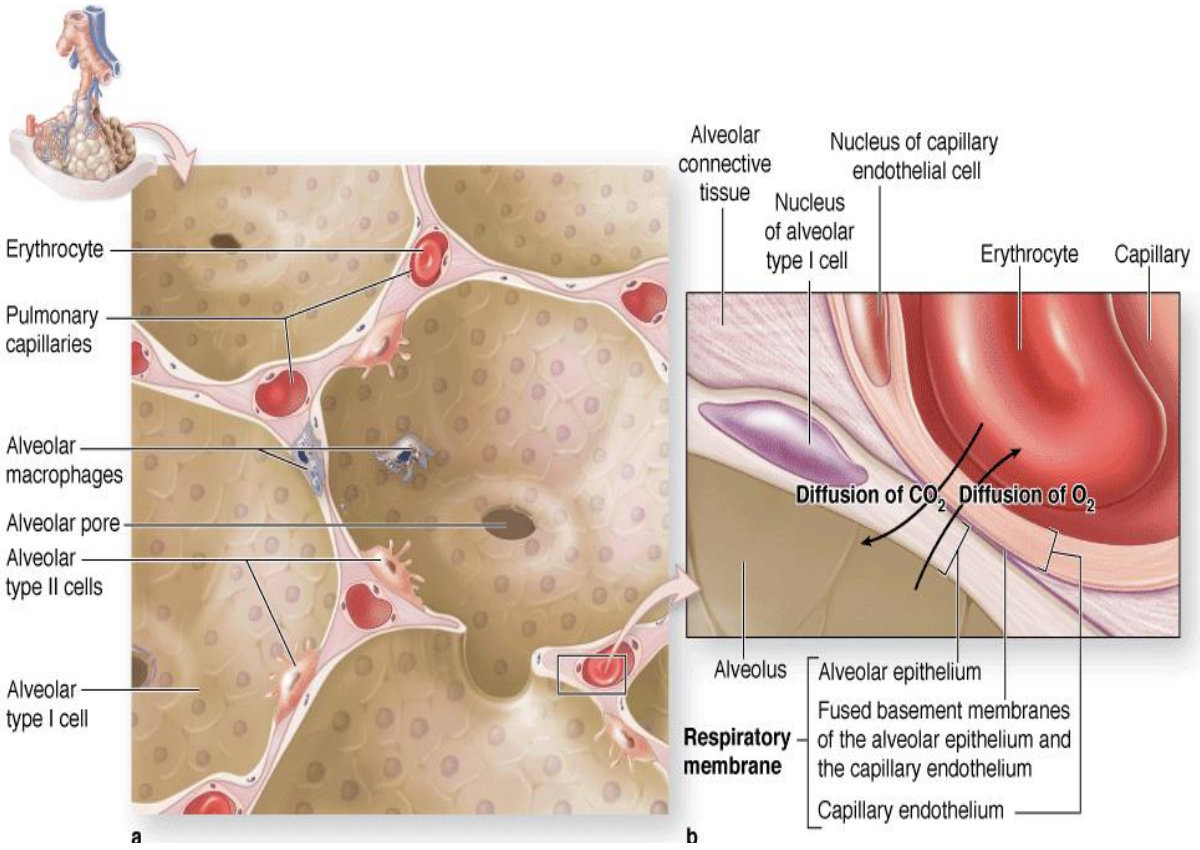
1. type I pneumocytes: called type I pneumocytes or squamous alveolar cells, large flattened cells (95% of the total alveolar). which present a very thin diffusion barrier for gases. They are connected to each other by tight junctions.

2. **type II pneumocytes**: type II pneumocytes are interspersed among the type I alveolar cells (making up 5% of the total alveolar area) These cells secrete 'surfactant' which decreases the surface tension between the thin alveolar walls, and stops alveoli collapsing when you breathe out.

Macrophages are important for ingesting bacteria and particles, and arise from monocytes, which have escaped from the blood capillaries.

Air in the alveoli is separated from capillary blood by three components referred to collectively as the **respiratory membrane or blood-air barrier**:

- Surface lining and cytoplasm of the alveolar cells (type I pneumocytes and type II pneumocytes).
- The fused basal laminae of these cells and capillary endothelial cells.
- Cytoplasm of the endothelial cells.

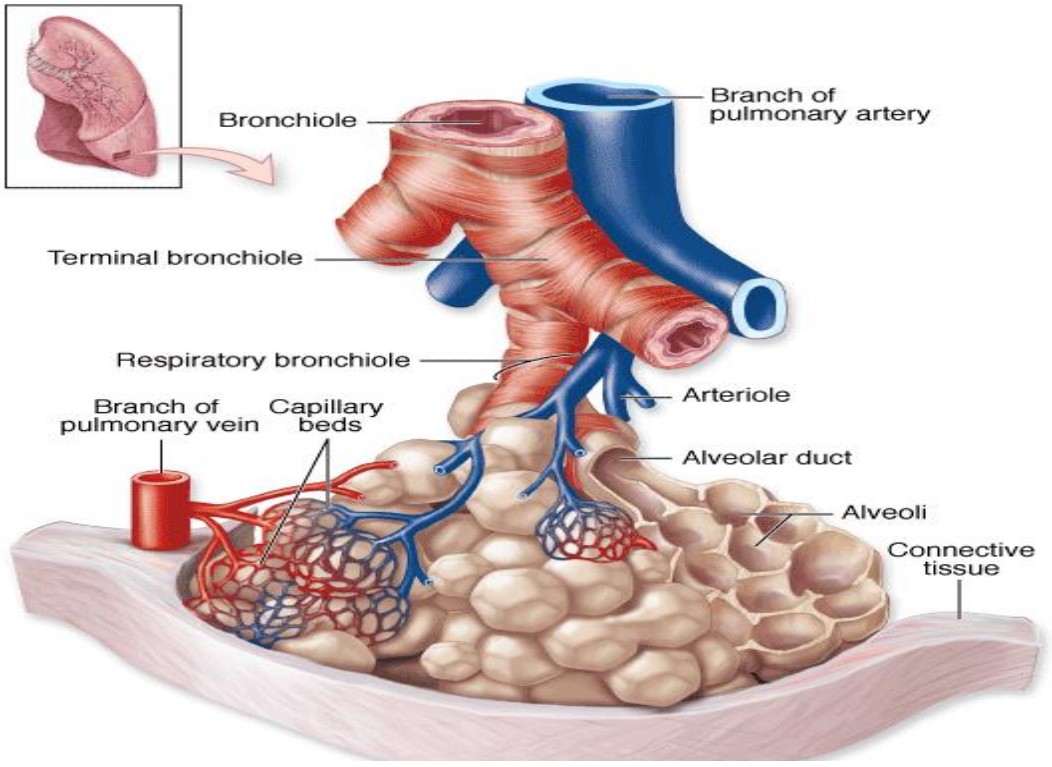


LUNG VASCULATURE & NERVES

Blood circulation in the lungs includes both the pulmonary circulation. Within the lung, the pulmonary artery branches and accompanies the bronchial tree. At the level of the alveolar duct, the branches of this artery form the dense capillary networks in the interalveolar septa that contact the alveoli.

Venules arising from the capillary networks are found singly in the lung parenchyma, somewhat removed from the airways supported by a thin covering of connective tissue. After small pulmonary veins leave a lobule, they follow the bronchial tree toward the hilum. The lymphatic vessels originate in the connective tissue of bronchioles. They follow the bronchioles, bronchi, and pulmonary vessels and all drain into lymph nodes in the region of the hilum.

Both parasympathetic and sympathetic autonomic fibers innervate the lungs and control reflexes regulating smooth muscle contractions which determine the diameters of the airways.



PLEURAL MEMBRANES

The lung's outer surface and the internal wall of the thoracic cavity are covered by a serous membrane called the pleura. The membrane attached to lung tissue is called the visceral pleura and the membrane lining the thoracic walls is the parietal pleura. The two layers are continuous at the hilum and are both composed of simple squamous mesothelial cells on a thin connective tissue layer containing collagen and elastic fibers. The elastic fibers of the visceral pleura are continuous with those of the pulmonary parenchyma.