General Histology Lec:5/

The Respiratory System

The respiratory system is divided into 2 principal regions (**Figure 1**):

1. **The Conducting Portion:** Consisting of the nasal cavity, nasopharynx, larynx, trachea, bronchi, bronchioles, and terminal bronchioles.

2. **The Respiratory Portion:** Consisting of respiratory bronchioles, alveolar ducts, and alveoli.

Alveoli: Are specialized saclike structures that make up the greater part of the lungs. They are the main sites for the principal function of the lungs-the exchange of O_2 and CO_2 between inspired air and blood.

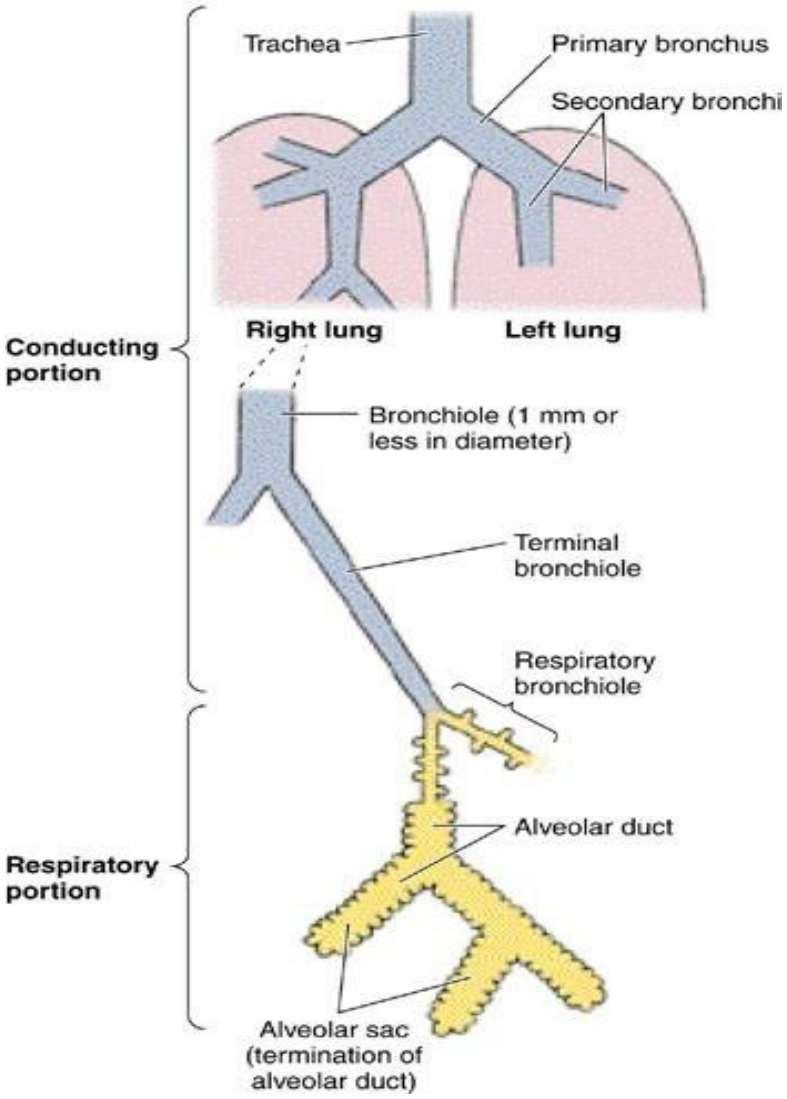


Figure 1. The main divisions of the respiratory tract.

1- The Conducting Portion of the Respiratory System

Most of the conducting portion is lined with ciliated pseudostratified columnar epithelium that contains a rich population of goblet cells and is known as **respiratory epithelium** (**Figure 2**).

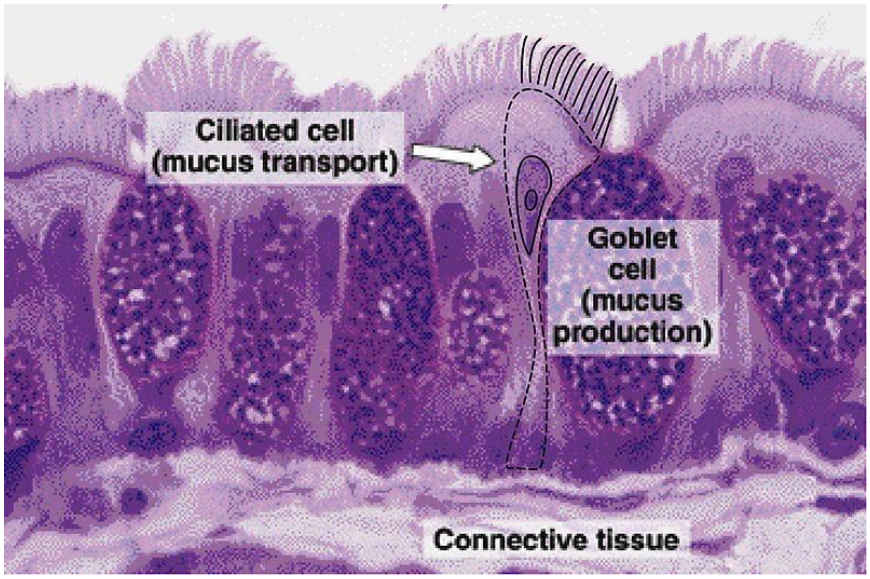


Figure 2. Photomicrograph illustrating the main components of the respiratory epithelium.

Typical respiratory epithelium consists of 5 cell types (as seen in the electron microscope):

A. **Ciliated Columnar Cells:** Constitute the most abundant type. Each cell has about 300 cilia on its apical surface (see Figure 2) and (**Figure 3**); beneath the cilia, in addition to basal bodies, are numerous small mitochondria which supply ATP for ciliary beating.
B. **Mucous Goblet Cells:** The next most abundant cells in the respiratory epithelium (see Figure 2). The apical portion of these cells contains the mucous droplets composed of glycoproteins.
C. **Brush Cells:** The remaining columnar cells (**Figure 4**) because of the numerous microvilli on their apical surface. Brush cells have afferent nerve endings on their basal surfaces and are considered to be chemosensory receptors.
D. **Basal (Short) Cells:** Are small rounded cells that lie on the basal lamina but do not extend to the luminal surface of the epithelium.These cells are believed to be generative stem cells that undergo mitosis and subsequently differentiate into the other cell types.

E. Small Granule Cells: (or **Kulchitsky Cells**) are difficult to distinguish in routine preparations, but possess numerous dense core granules 100 to 300 nm in diameter. **Like enteroendocrine cells of the gut, they are part of the diffuse neuroendocrine system (DNES).**

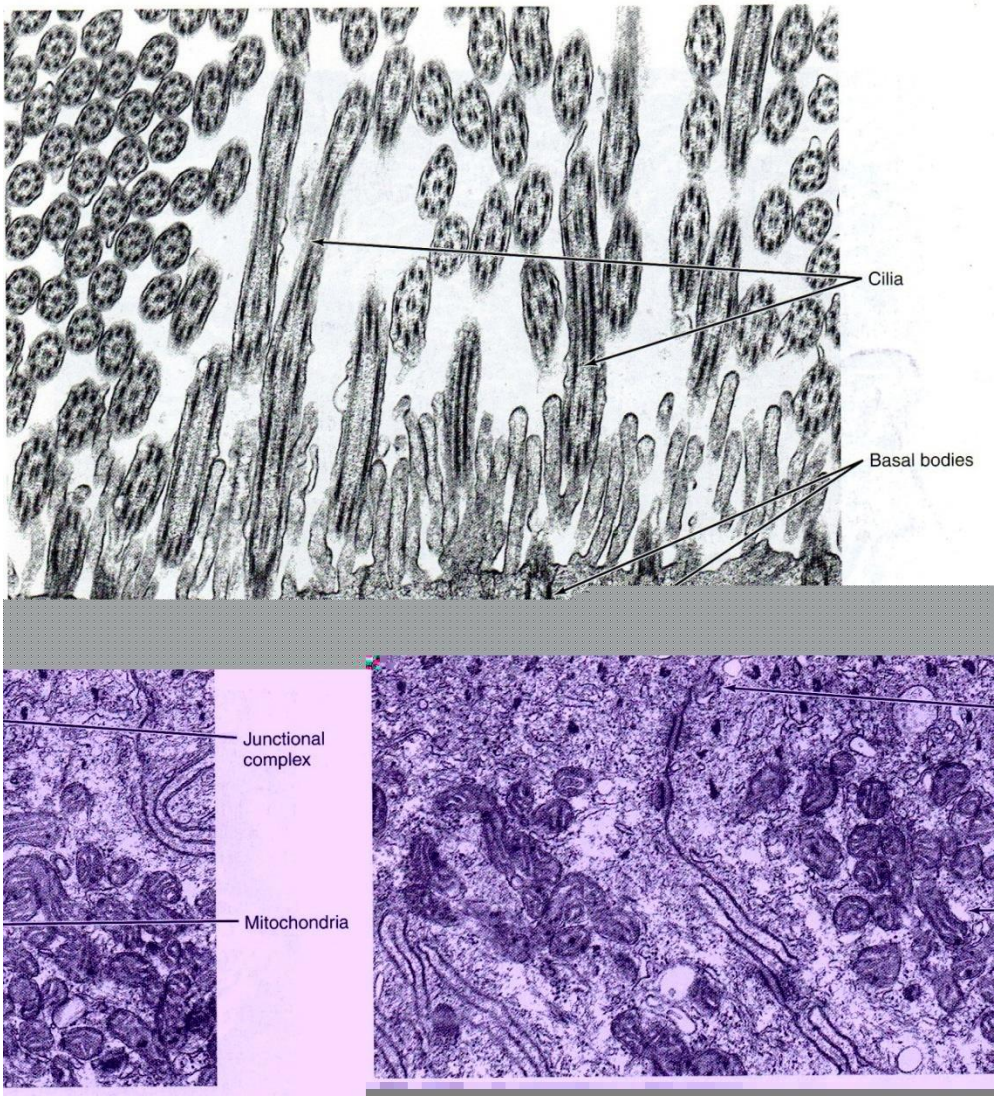


Figure 3. Electron micrograph of ciliated columnar cells of the respiratory epithelium, showing the ciliary microtubules in transverse and oblique section. In the cell apex are the U-shaped basal bodies that serve as the source of, and anchoring sites for, the ciliary axonemes. The local accumulation of mitochondria is related to energy production for ciliary movement. Note the junctional complex.

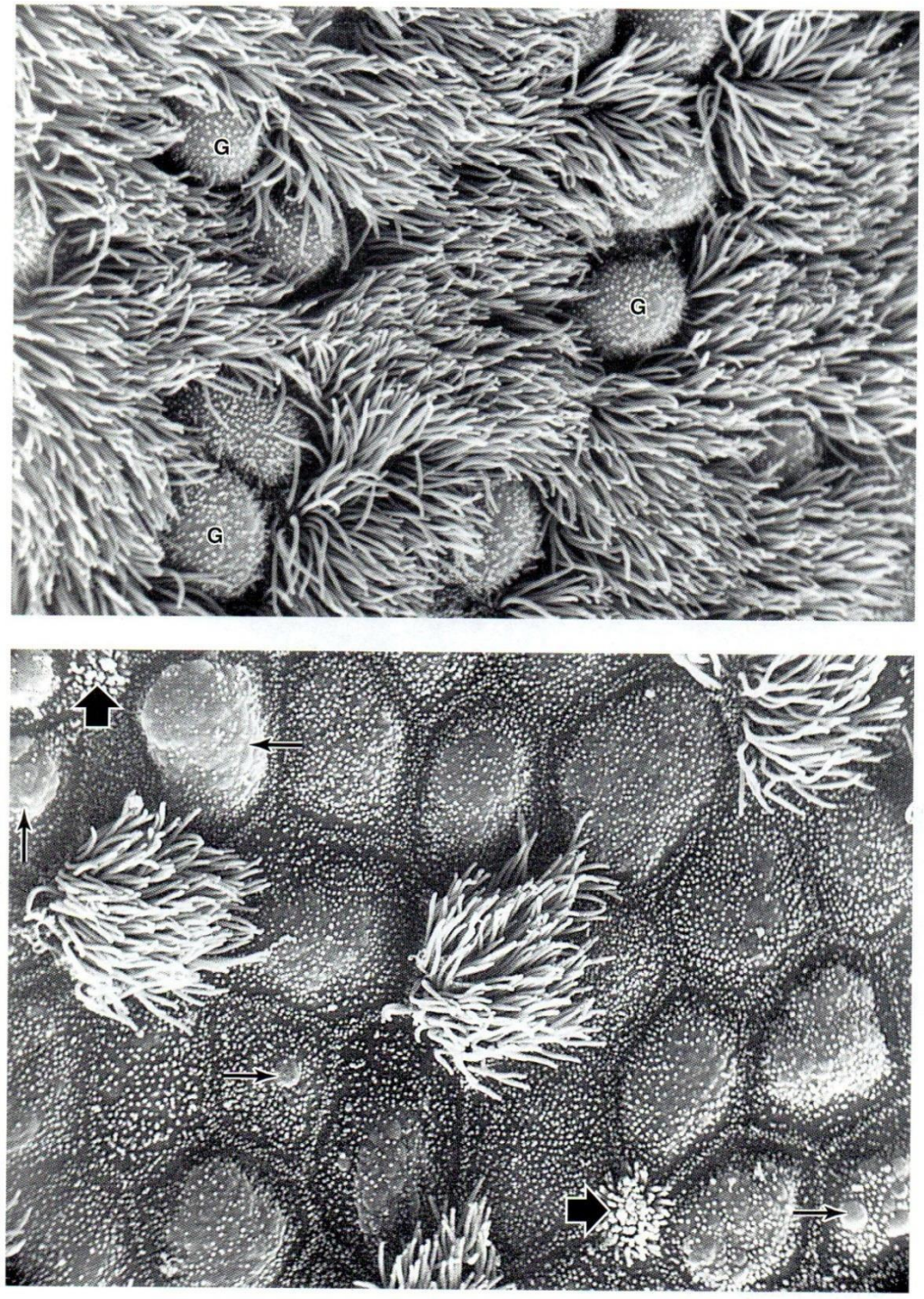


Figure 4. Scanning electron micrographs of the surface of respiratory mucosa. Top: Most of the surface is covered with cilia. G, goblet cells. Bottom: Subsurface accumulations of mucus are evident in the goblet cells (thin arrows). Thick arrowheads indicate brush cells.

Nasal Cavity Properties

The **nasal cavity** is the inner space of the nose (**Figure 5**).

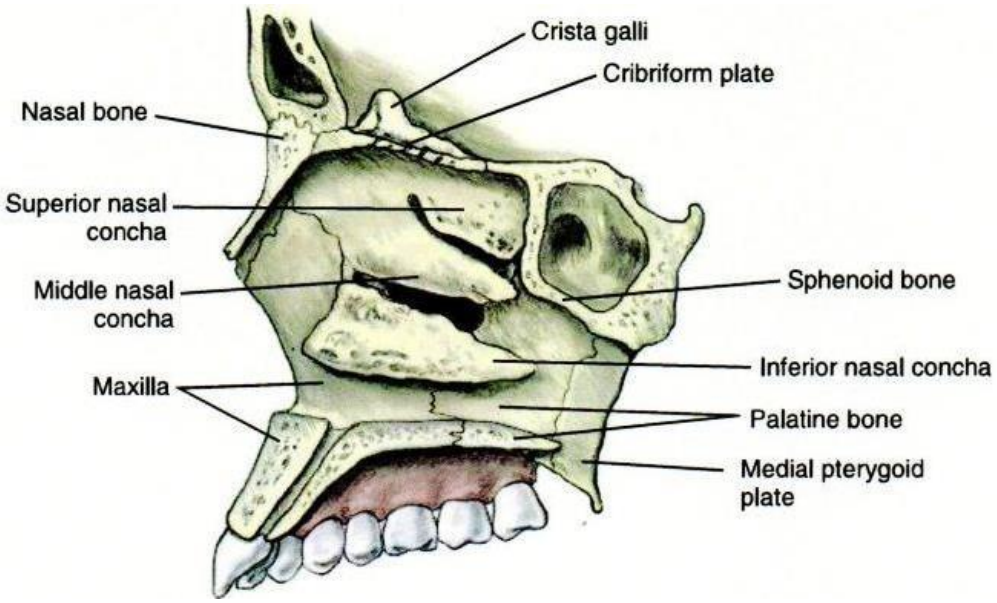


Figure 5. Nasal cavity and its nasal conchae.

It communicates with the exterior by two nares. The nares are separated by the midline nasal septum, which consists of both bone and cartilage. The nasal septum also divides the internal nasal cavity into two parts.

Each lateral wall of the nasal cavity has three projecting structures, or **nasal conchae**, which extend inward. 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**. Beneath each concha are openings through which the paranasal sinuses or nasolacrimal ducts communicate with the nasal cavity. The posterior part of the nasal cavity communicates with the nasopharynx and then with the rest of the respiratory system.

Nasal Cavity Histology

The nasal cavity is lined by a respiratory mucosa like the rest of the respiratory system. **Respiratory mucosa** is different from oral mucosa lining the oral cavity but similar to that lining the trachea and bronchi. It consists of ciliated pseudostratified columnar epithelium (**Figure 6**).

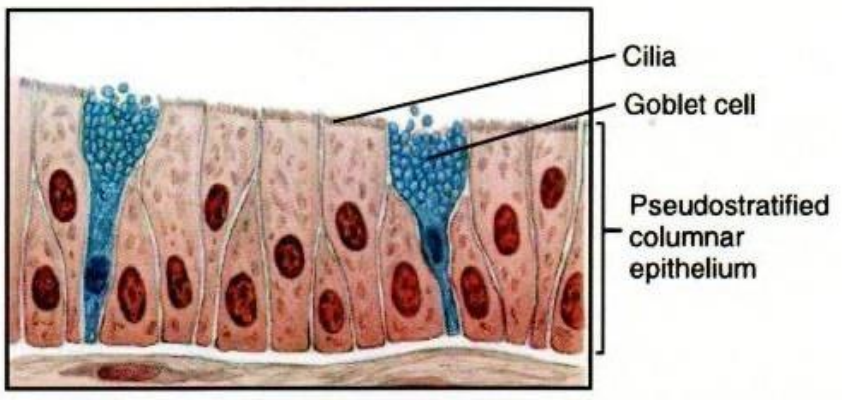


Figure 6. Histology of the respiratory mucosa lining the nasal cavity.

Within the epithelium, and surrounded by mucous and serous glands,are **goblet cells**, which rest on the basement membrane. Fluids or mucus from the goblet cells and glands keep this mucosa moist, provide humidity, and trap any foreign materials from the inspired air.

The moist mucus forms a superficial coating on the respiratory mucosa. This coating is moved by ciliary action posteriorly to the nasopharynx, where it is either expectorated or swallowed. In this manner, foreign materials are trapped and removed. Because the lamina propria of the mucosa is extremely vascular, it also warms the incoming breathed air.

Smell (Olfaction)

The olfactory chemoreceptors are located in the **olfactory epithelium**, a specialized area of the mucous membrane covering thesuperior conchae at the roof of the nasal cavity. In adult humans, it is about $10cm^2$ in area and up to 100µm in thickness. This thick, pseudostratified columnar epithelium has three major cells (**Figure 7**):

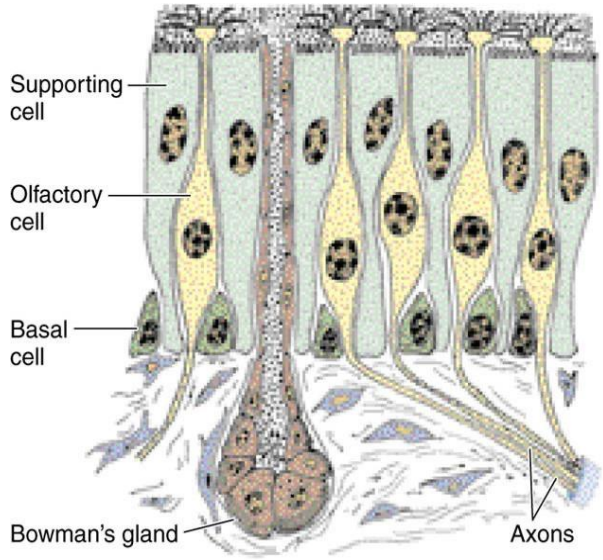


Figure 7. Olfactory mucosa showing the 3 cell types (supporting, olfactory, and basal) and a Bowman's gland.

1. **The Supporting Cells:** Have broad, cylindrical apexes and narrower bases. On their free surface are microvilli submerged in a fluid layer. Well-developed junctional complexes bind the supporting cells tothe adjacent olfactory cells. The cells contain a light yellow pigment that is responsible for the color of the olfactory mucosa.
2. **The Basal Cells:** Are small; they are spherical or cone-shaped and form a single layer at the base of the epithelium.
3. **The Olfactory Cells:** Are located between the basal cells and the supporting cells, bipolar neurons distinguished from the supporting cells by the position of their nuclei, which lie below the nuclei of the

supporting cells. The nucleus of the cell is spherical. Their apexes (dendrites) possess elevated and dilated areas from which arise6-8 cilia. These cilia are very long, nonmotile (see Figure 7), and respond to odoriferous substances by generating a receptor potential. They increase the receptor surface considerably. The afferent axons of these bipolar neurons unite in small bundles directed toward the central nervous system, where they synapse with neurons of the brain **olfactory lobe**. The lamina propria of the olfactory epithelium possesses the glands of Bowman. Their secretion produces a fluid environment around the olfactory cilia that may clear the cilia, facilitating the access of new odoriferous substances.

Paranasal Sinuses Properties

The **paranasal sinuses** are paired air-filled cavities in bone that include the frontal, sphenoidal, ethmoidal, and maxillary sinuses (**Figure 8**). The sinuses communicate with the nasal cavity through small openings in the lateral nasal wall. The sinuses serve to lighten the skull bones, act as sound resonators, and provide mucus for the nasal cavity.

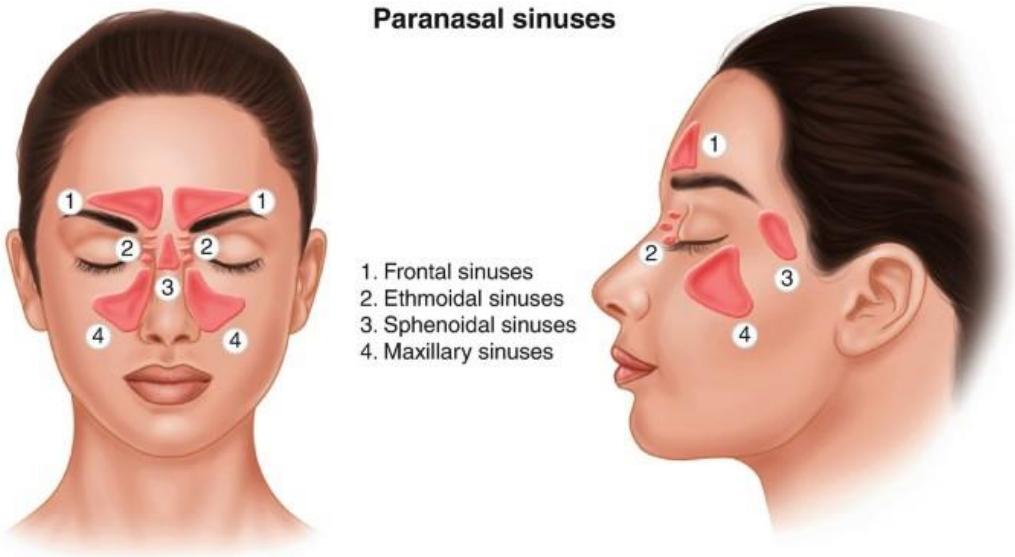


Figure 8. Paranasal sinuses: frontal, ethmoidal, maxillary, and sphenoidal sinuses

Paranasal Sinuses Histology

The sinuses are lined with respiratory mucosa continuous with the epithelial lining of the nasal cavity (see Figure 6). The epithelium of the sinuses, althoughit is similar to that of the nasal cavity, is thinner and contains fewergoblet cells. The respiratory mucosa of the sinuses also shows a thinner underlying lamina propria that is continuous with the deeper periosteum of the bone. It also has fewer associated glands, and no erectile tissue is present in the sinuses.

Medical Application

Sinusitis is an inflammatory process of the sinuses that may persist for long periods of time, mainly because of obstruction of drainage orifices. Chronic sinusitis and bronchitis are components of immotile cilia syndrome, which is characterized by defective ciliary action.

Nasopharynx

The nasopharynx is the first part of the pharynx. It is lined by a respiratory epithelium, whereas the oral and laryngeal regions are lined by a stratified squamous epithelium.

Larynx

The larynx, or voice box, is responsible for phonation and for preventing the entry of food and fluids into the respiratory system

during swallowing. It connects the pharynx to the trachea. It is cylindrical tube 4 cm in length and approximately 4 cm in diameter (**Figure 9**). Within the lamina propria lie a number of laryngeal cartilages.

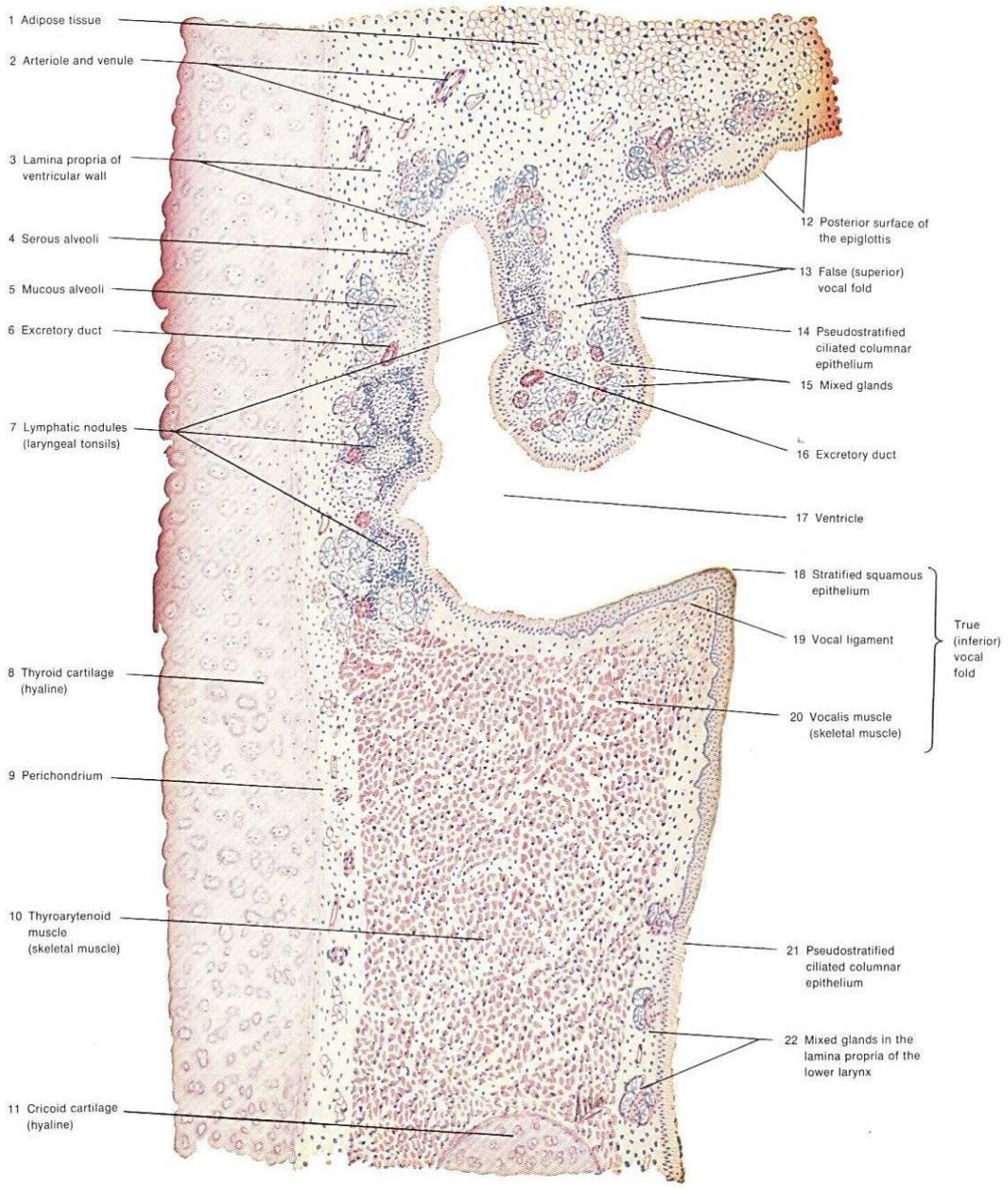


Figure 9. Larynx (frontal section).

The larger cartilages (thyroid, cricoid, and most of the arytenoids) are hyaline. The smaller cartilages (epiglottis, cuneiform, corniculate, and the tips of the arytenoids) are elastic cartilages. These cartilages are

connected to one another by ligaments. In addition to their supporting role (maintenance of an open airway), these cartilages serve as a valve to prevent swallowed food or fluid from entering the trachea. They also participate in producing sounds for 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. Its upper, or lingual, surface has stratified squamous epithelium; at variable points on its laryngeal surface this epithelium undergoesa transition to ciliated pseudostratified columnar (respiratory) epithelium. Mixed mucous and serous glands are found in the lamina propria beneath the epithelium.

Below the epiglottis and laryngeal vestibule, the mucosa projectsinto the lumen bilaterally with two pairs of folds separated by a narrow space or ventricle. The upper pair, the immovable **vestibular folds**, is partly covered with typical respiratory epithelium overlying numerous seromucous glands and occasional lymphoid nodules. 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 **vocalis muscle**.

The vestibular folds and ventricles, along with other structures and spaces higher in the respiratory tract, contribute to the resonance of sound produced in the larynx. Speech is produced when sounds made in the

larynx are modified by movements of the pharynx, tongue, and lips. The larynx is larger in males than in females after puberty, causing men's voices to be typically deeper than women's voices.

Medical Application

Laryngitis: Inflammation of the laryngeal tissues including the vocal folds, prevents the vocal folds from vibrating freely. Persons suffering from laryngitis sound hoarse or can only whisper.

Trachea

The wall of the trachea consists of mucosa, submucosa, hyaline cartilage, and adventitia. The trachea (10 to 12 cm long in adults) is kept patent (open) by C-shaped **hyaline cartilage** rings. Hyaline cartilage is surrounded by the dense connective tissue **perichondrium**, which merges with the **submucosa** on one side and the **adventitia** on the other. Numerous **nerves, blood vessels**, and **adipose tissue** are located in the adventitia.

The gap between the posterior ends of the hyaline cartilage is filled by the smooth **trachealis muscle**. The trachealis muscle lies in the connective tissue deep to the **elastic membrane** of the mucosa. Most of the trachealis muscle fibers insert into the perichondrium that covers the hyaline cartilage.

The trachealis muscle (a bundle of smooth muscle) relaxes during swallowing to facilitate the passage of food by allowing the esophagus to bulge into the lumen of the trachea, with the elastic layer preventing excessive distention of the lumen. The muscle strongly contracts in the cough reflex to narrow the tracheal lumen and provide for increased

velocity of the expelled air and better loosening of material in the air passage.

The lumen of the trachea is lined with a **pseudostratified ciliated columnar epithelium** with goblet cells.

The mucosa exhibits **mucosal folds** along the posterior wall of the trachea where the hyaline cartilage is absent.

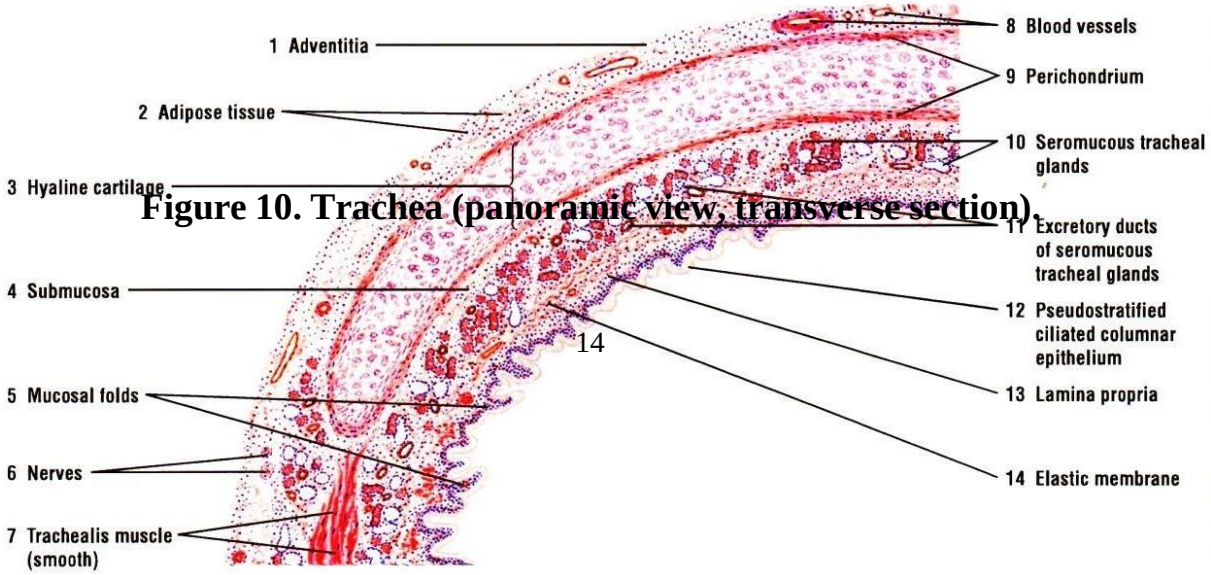


Figure 10. Trachea (panoramic view, transverse section).

Major features of all upper respiratory tract structures are summarized in Table 1.

Table 1. Histologic features of the upper respiratory tract, larynx, and trachea.

Region	Epithelium	Glands	Musculoskeletal Support	Other Features and Major Functions
Vestibules of nasal cavities	Stratified squamous, keratinized to nonkeratinized	Sebaceous and sweat glands	Hyaline cartilage	Vibrissae (stiff hairs) and moisture both filter and humidify air
Most areas of nasal cavities	Respiratory	Seromucous glands	Bone and hyaline cartilage	Rich vasculature and glands warm, humidify, and clean air
Superior areas of nasal cavities	Olfactory, with bipolar neurons	Serous (Bowman) glands	Bone (ethmoid)	Solubilize and detect odorant molecules in ai
Nasopharynx and posterior oropharynx	Respiratory and stratified squamous	Seromucous glands	Bone and skeletal muscle	Conduct air to larynx; pharyngeal and palatine tonsils
Larynx	Respiratory and stratified squamous	Mucous glands, smaller seromucous glands	Elastic and hyaline cartilage,ligaments, skeletal muscle	Site for phonation; epiglottis closes while swallowing
Trachea	Respiratory	Mainly mucous glands, some serous or mixed glands	C-shaped rings of hyaline cartilage, with smooth (trachealis) muscle in posterior opening of each	Conduct air to primary bronchi entering lungs; some MALT

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 course downward and outward, giving rise 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 (segmental) bronchi**. Each of the tertiary bronchi, together with the smaller branches it supplies, constitutes a **bronchopulmonary segment**—approximately 10% to 12% of each lung with its own connective tissue capsule and blood supply.

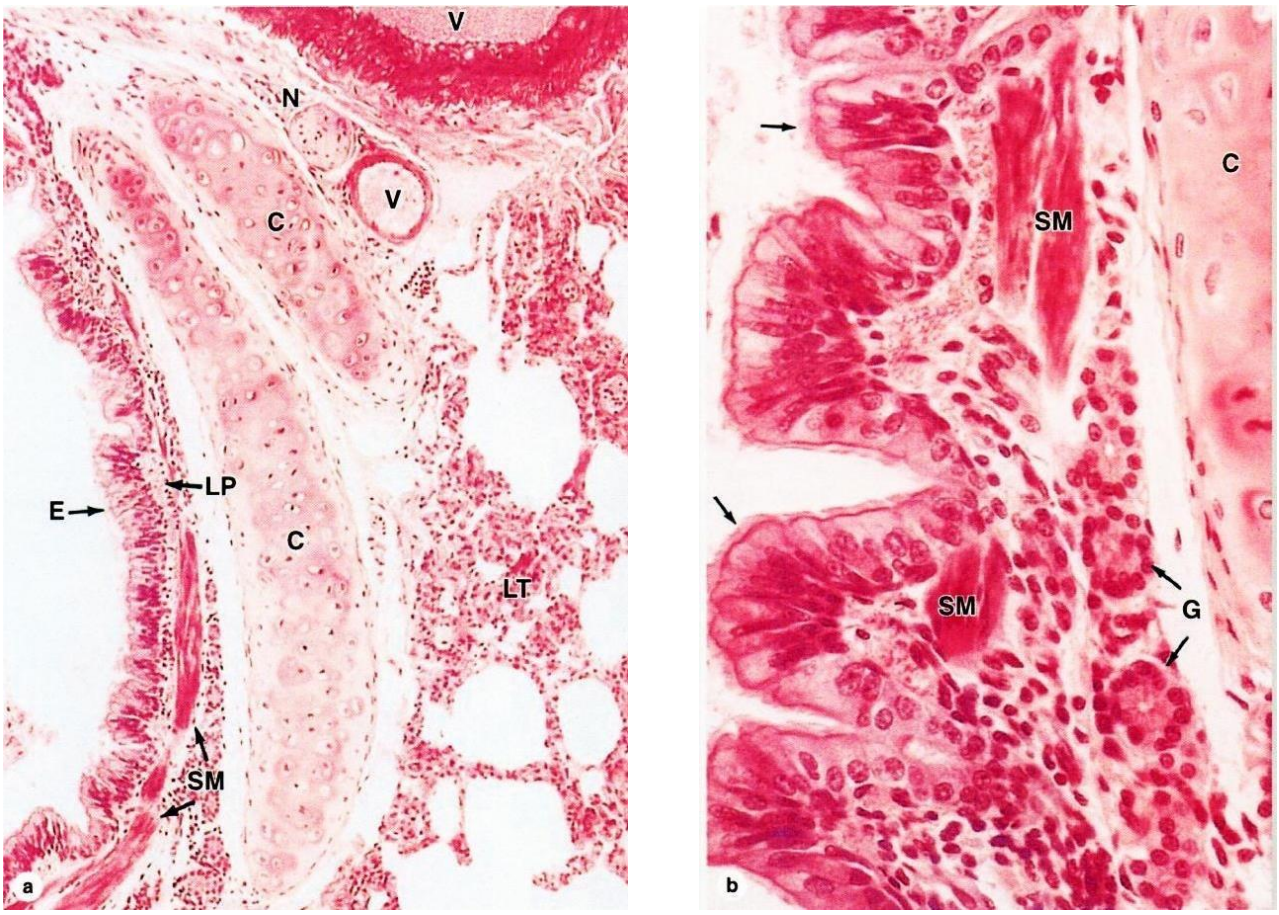
The existence of such lung segments facilitates the specific surgical resection of diseased lung tissue without affecting nearby healthy tissue.

The tertiary bronchi give rise to smaller and smaller bronchi, whose terminal branches are called **bronchioles**. Each bronchiole entersa pulmonary lobule, where it branches to form five to seven **terminal bronchioles**.

Bronchi

Each primary bronchus branches repeatedly, with each branch becoming progressively smaller until it reaches a diameter of 1 to 2 mm. 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, butas 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 also contains crisscrossing bundles of spirally arranged smooth muscle and elastic fibers (**Figure 11**), which become more prominent in the smaller bronchial branches.



Figures 11. Bronchial wall.

a) The epithelial lining (E) of bronchi is mainly pseudostratified ciliated columnar cells with a few goblet cells. The lamina propria (LP) contains the distinct layer of smooth muscle (SM) surrounding the entire bronchus. The submucosa is the site of the supporting cartilage (C) and the adventitia includes blood vessels (V) and nerves (N). Lung tissue (LT) directly surrounds the adventitia of bronchi.

b) In the smaller bronchi the epithelium is primarily of columnar cells with cilia (arrows), with fewer goblet cells. The lamina propria has both smooth muscle (SM) and small serous glands (G) near cartilage (C).

Contraction of this muscle layer is responsible for the folded appearance of the bronchial mucosa observed histologically in cross sections.

Bronchioles and Terminal Bronchioles

Bronchioles are typically designated as the intralobular airways with diameters of 1 mm or less, formed after about the 10th generation of branching; they lack both mucosal glands and cartilage, although dense connective tissue is associated with the smooth muscle (**Figure 12**).

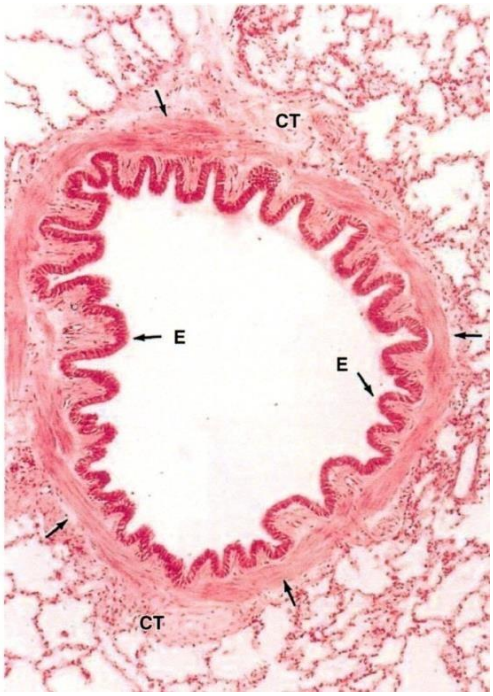


Figure 12. Bronchiole.

The smallest branches of the bronchial tree are the bronchioles, which lack supporting cartilage and glands. The figure illustrates a large bronchiole which has the characteristically folded respiratory epithelium (E) and prominent smooth muscle (arrows), but it is supported only by fibrous connective tissue (CT).

In the larger bronchioles (see Figure 12), 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. The ciliated epithelial lining of bronchioles begins the **mucociliary apparatus** or escalator, important in clearing debris and mucus by moving it upward along the bronchial tree and trachea.

Most numerous in the cuboidal epithelium of terminal bronchiolesare **Clara cells**, or **exocrine bronchiolar cells**, which have nonciliated, dome-shaped apical ends with secretory granules (**Figure 13**).

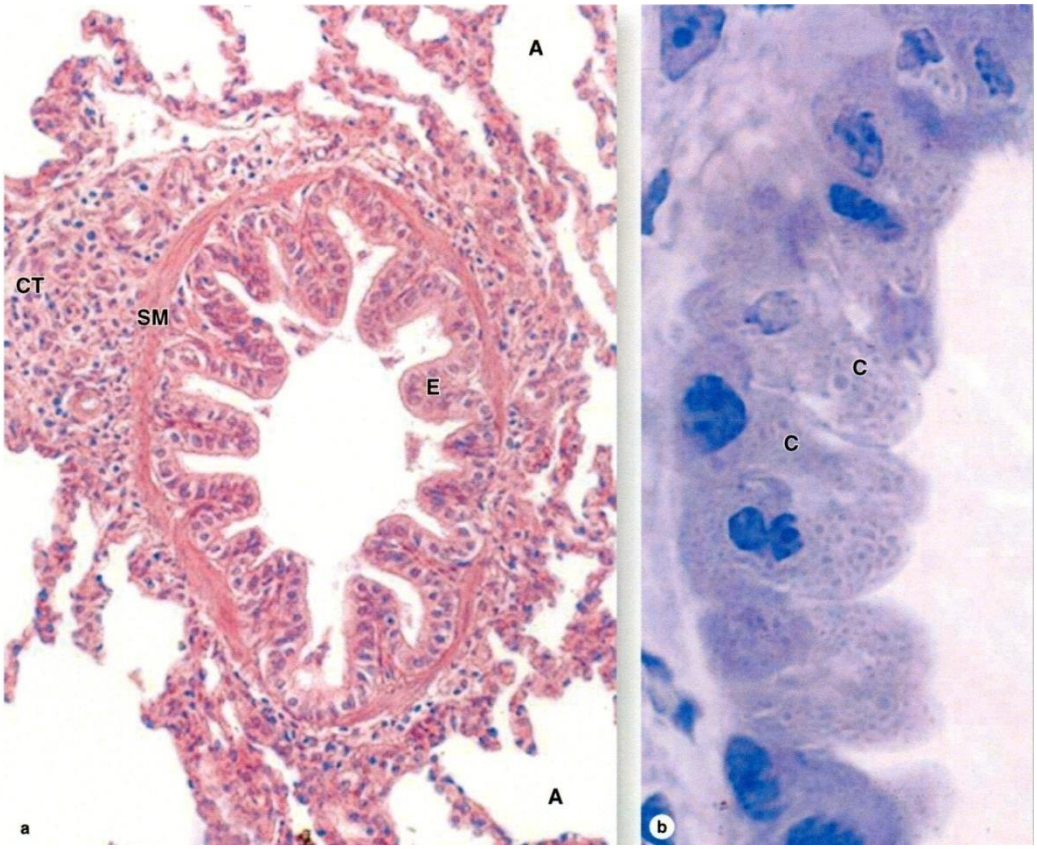


Figure 13. Terminal bronchiole and Clara cells.

The last parts of the air conducting system before the sites of gas exchange appear are called the terminal bronchioles. (a) A terminal bronchiole has only one or two layers of smooth muscle (SM) cells

surrounded by connective tissue (CT). The epithelium (E) contains ciliated cuboidal cells and many low columnar nonciliated cells. Alveoli (A) are seen in the surrounding lung tissue.

(b) The nonciliated Clara cells (C) with bulging domes of apical cytoplasm contain granules, as seen better here in a plastic section. Named after Dr. Max Clara, the histologist who first described them in 1937, these cells have several important functions. They secrete components of surfactant (liporoteins and mucins) in the fluid layer which reduces surface tension and helps prevent collapse of the bronchioles. Detoxification of inhaled xenobiotic compounds by enzymes of the SER. Secretion of antimicrobial peptides and cytokines for local immune defense. Also included among Clara cells are the occasional stem cells that give rise to all of the cells within the bronchiolar epithelium.

The bronchiolar lamina propria still contains elastic fibers and smooth muscle, producing folds in the mucosa. Muscular contraction in both the bronchi and the bronchioles is controlled primarily by nerves of the autonomic nervous system.

Lecture 6

General Histology

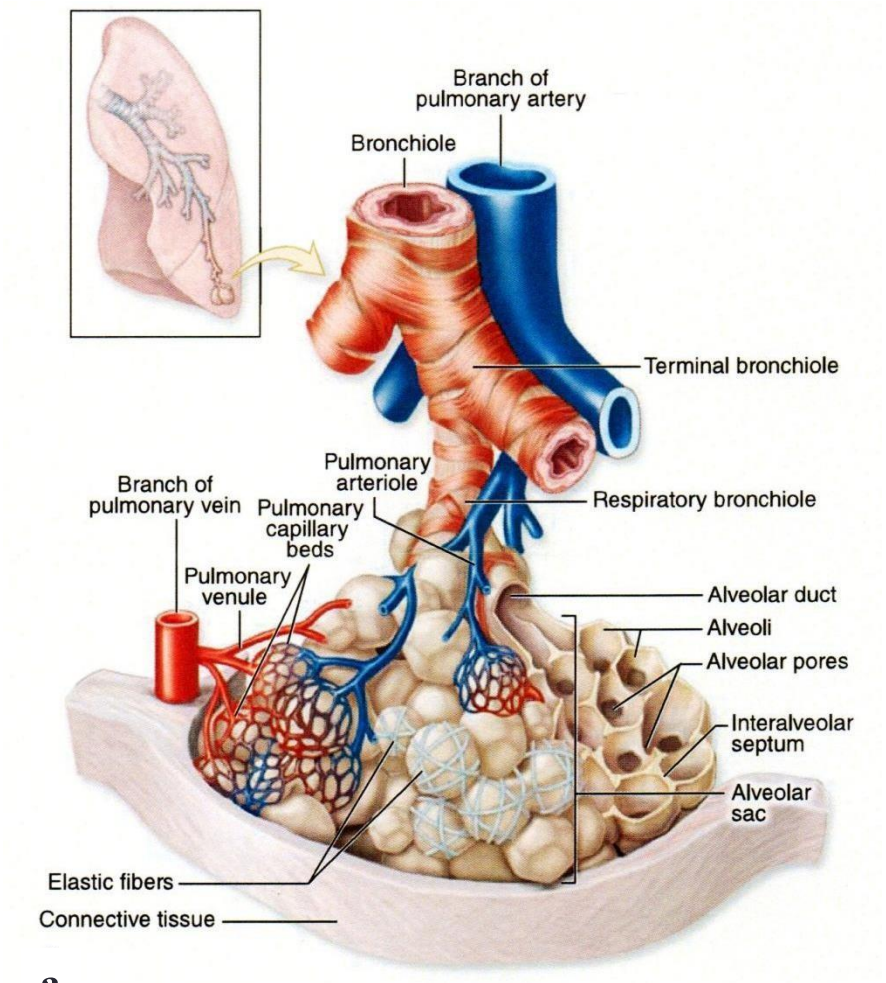
Second Grade/ College of Dentistry/

University of Baghdad

2. The Respiratory Portion of the Respiratory System

Respiratory Bronchioles

Each terminal bronchiole subdivides into two or more **respiratory bronchioles** that include saclike **alveoli** and represent, therefore, the first-part respiratory region of this organ system (**Figure 14**).



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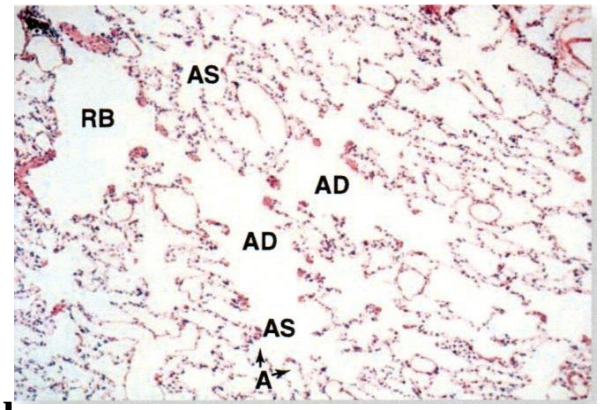

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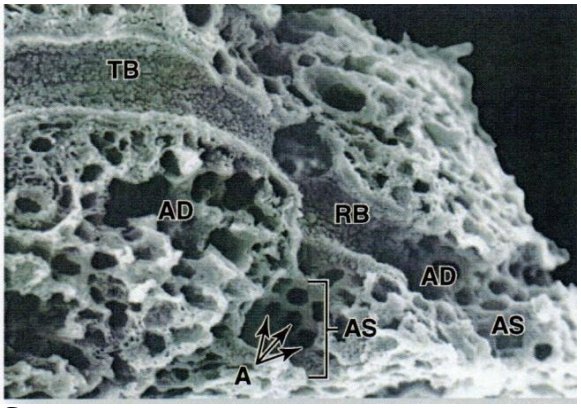

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Figure 14. Terminal bronchioles, respiratory bronchioles, and alveoli. Terminal bronchioles branch into respiratory bronchioles, which then branch further into alveolar ducts and individual alveoli. Respiratory bronchiole (RB), alveolar ducts (AD), alveolar sacs (AS), individual alveoli (A), and terminal bronchiole (TB).

The respiratory bronchiolar mucosa is structurally identical to thatof the terminal bronchioles, except for a few openings to the alveoli where gas exchange occurs. 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 (see Figure 14) and (**Figure 15**).

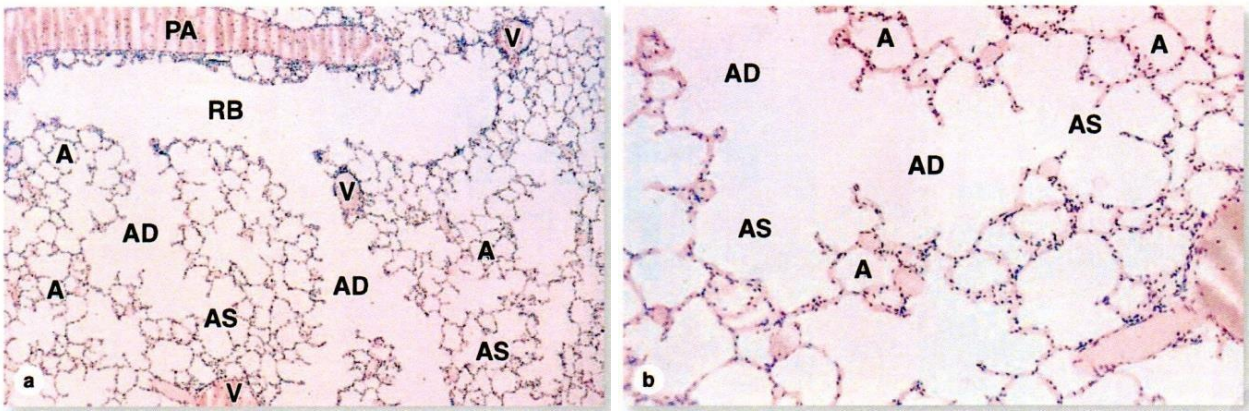

Figure 15. Respiratory bronchioles, alveolar ducts, and alveoli. Lung tissue has a spongy structure because of the abundant air passages and pockets called alveoli. Respiratory bronchioles (RB), and shows the branching continuity with alveolar ducts (AD), alveolar sacs (AS), alveoli (A), and pulmonary artery (PA), while branches of thepulmonary vein (V) course elsewhere in the parenchyma.

Both the alveolar ducts and the alveoli themselves are lined with extremely attenuated 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 andits alveoli.

Larger clusters of alveoli called **alveolar sacs** form the ends of alveolar ducts distally and occur occasionally along their length (see Figures 14 and 15). The lamina propria is now extremely thin, consisting

essentially of a network of **elastic** and **reticular fibers** that encircles the alveolar openings and closely surrounds each alveolus. Prominent in this sparse connective tissue, another network of **capillaries** also surrounds each alveolus.

Alveoli

Alveoli are saclike evaginations, each about 200 μm in diameter. Alveoli are responsible for the spongy structure ofthe lungs (see Figures 14 and 15). Each adult lung has approximately 200 million alveoli with a total internal surface area of $75m^2$. Each alveolus resembles a small rounded pouch open on one side to an alveolar duct or alveolar sac. Air in these structures exchanges O_2 and CO_2 with the blood in surrounding capillaries, through thin specialized alveolar walls that enhance diffusion between the external andinternal environments.

Between neighboring alveoli lie thin **interalveolar septa** consisting of scattered fibroblasts and sparse extracellular matrix (ECM), notably 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 interalveolar septa are vascularized with the richest capillary networks in the body (see Figure 14).

Air in the alveoli is separated from capillary blood by three components

referred to collectively as the respiratory membrane or **blood-air barrier** (**Figure 16**):

- two to three highly attenuated, thin cells lining the alveolus,
- the fused basal laminae of these cells and of the capillary endothelial cells, and
- the thin endothelial cells of the capillary.

The total thickness of these layers varies from 0.1 to 1.5µm. **Macrophages** and other **leukocytes** can also be found within the septa (see Figure 16) and (**Figure 17**).

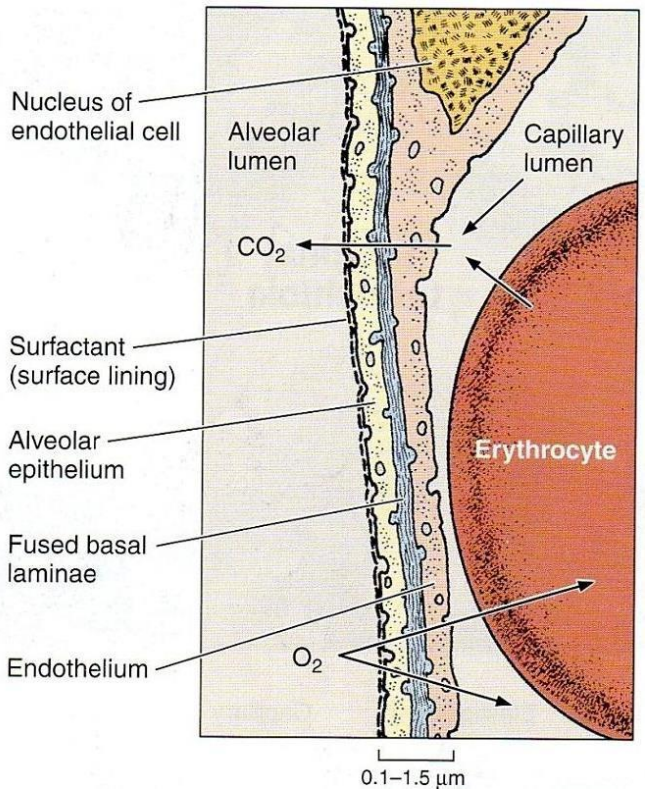

Figure 16. Portion of the interalveolar septum showing the blood-air barrier.

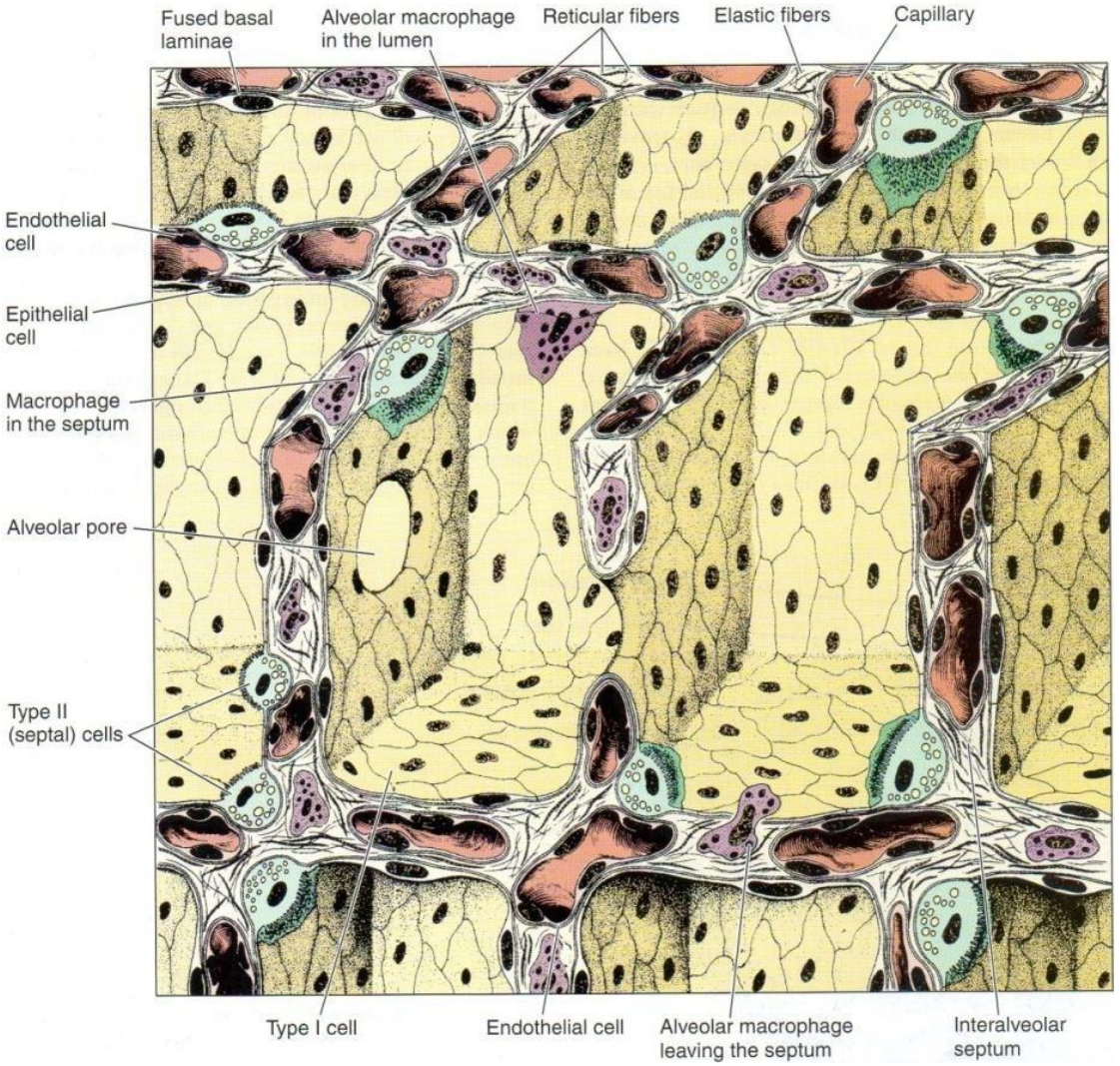

Figure 17. Pulmonary alveoli.

Alveolar pores (of Kohn), ranging 10-15 μm in diameter, penetrate the interalveolar septa (see Figure 17) and connect neighboring alveoli that open to different bronchioles. The pores equalize air pressure in these alveoli and permit collateral circulation of air when a bronchiole is obstructed.

O_2 from the alveolar air diffuses through the blood-air barrier into the capillary blood and binds **hemoglobin** in erythrocytes; CO_2 diffuses (in the opposite direction) into the alveolar air from the pulmonary blood. Most CO_2 arrives in the lungs as part of H_2CO_3 inside erythrocytes and is liberated through the action of enzyme **carbonic anhydrase** present in erythrocytes.

Walls of alveoli are composed of two types of cells:

1. **Type I alveolar cells (**or **type I pneumocytes**) are also extremely attenuated cells that line the alveolar surfaces. Type I cells which composed of simple squamous epithelium maintain the alveolar side of the blood-air barrier and cover about 95% of the alveolar surface; type II alveolar cells (see Figure 17) cover the remainder. **Pinocytotic vesicles** in the attenuated cytoplasm may play a role in the turnover of surfactant and the removal of small particulate contaminants from the outer surface. In addition to desmosomes, all type I epithelial cells have occluding junctions that prevent the leakage of tissue fluid into the alveolar air space.

2. **Type II alveolar cells (type II pneumocytes** or septal cells) are cuboidal cells that bulge into the air space, interspersed among the type I alveolar cells and bound to them with occluding junctions and desmosomes. Type II cells often occur in groups of two or three along at points where two or more alveolar walls unite (see Figure 17). These epithelial cells rest on the same basal lamina and have the sameorigin as the type I cells that line most of the alveolus. Type II cells divide to replace their own population after injury and to provide progenitor cells for the type I cell population. Type II cell nuclei are rounded and may have nucleoli, and their cytoplasm is typically lightly stained with many vesicles.

Many vesicles of type II alveolar cells are **lamellar bodies**, which about 1 to 2 μm in diameter. Lamellar bodies can be considered markers for type II cells. They contain various lipids, phospholipids, and proteins that are continuously synthesized and released at the apical cell surface. The secreted material spreads over the entire inner alveolar surface as

a film of complexed lipoproteins and water that acts as **pulmonary surfactant**. The surfactant film lowers alveolar surface tension, which helps prevent alveolar collapse at exhalation and allows alveoli to be inflated with less inspiratory force, easing the work of breathing.

Alveolar macrophages, also called **dust cells**, are found in alveoli and in the interalveolar septum (see Figure 17). Tens of millions of monocytes migrate daily from the microvasculature into the lung tissue, where they phagocytose erythrocytes lost from damaged capillaries and airborne particulate matter that has penetrated as far as the alveoli. Active macrophages in alveoli can often be distinguished from type II pneumocytes because they are slightly darker due to their content of dust and carbon from air and complexed iron (hemosiderin) from erythrocytes (see Figure 17). Filled macrophages have various fates: most migrate into bronchioles where they move up the mucociliary apparatus for removal in the pharynx; others exit the lungs in the lymphatic drainage; and some remain in the interalveolar septa connective tissue for years.

Alveolar lining fluids are also removed via the conducting passages as a result of ciliary activity. As the secretions pass up through theairways, they combine with bronchial mucus to form **bronchoalveolar fluid**, which helps remove particulate components from inspired air. The bronchoalveolar fluid is bacteriostatic, containing lysozyme and other protective agents produced by Clara cells, type II alveolar cells, and alveolar macrophages.

Medical Application

In congestive heart failure, the lungs become congested with blood, and erythrocytes pass into the alveoli, where they are phagocytized by

alveolar macrophages. In such cases, these macrophages are called **heart failure cells** when present in the lung and sputum; they are identified by a positive histochemical reaction for iron pigment (hemosiderin).

Regeneration in the Alveolar Lining

Inhalation of toxic gases or similar materials can kill types I and II cells lining pulmonary alveoli. Death of the first cells results in increased mitotic activity in the remaining type II cells, the progeny of which become both cell types. The normal turnover rate of type II cells is estimated to be 1% per day and results in a continuous renewal of both alveolar cells. With increased toxic stress, some Clara cells can also be stimulated to divide and give rise to alveolar cells.

Lung Nerves

Both parasympathetic and sympathetic autonomic fibers innervate the lungs and control reflexes regulating smooth muscle contractionswhich determine the diameters of the airways. The nerves are found primarily in the connective tissue surrounding the larger elements of the bronchial tree and exit the lung at the hilum.

Pleural Membranes

The lung's outer surface and the internal wall of the thoracic cavity are covered by a serous membrane called the **pleura** (**Figure 18)**.

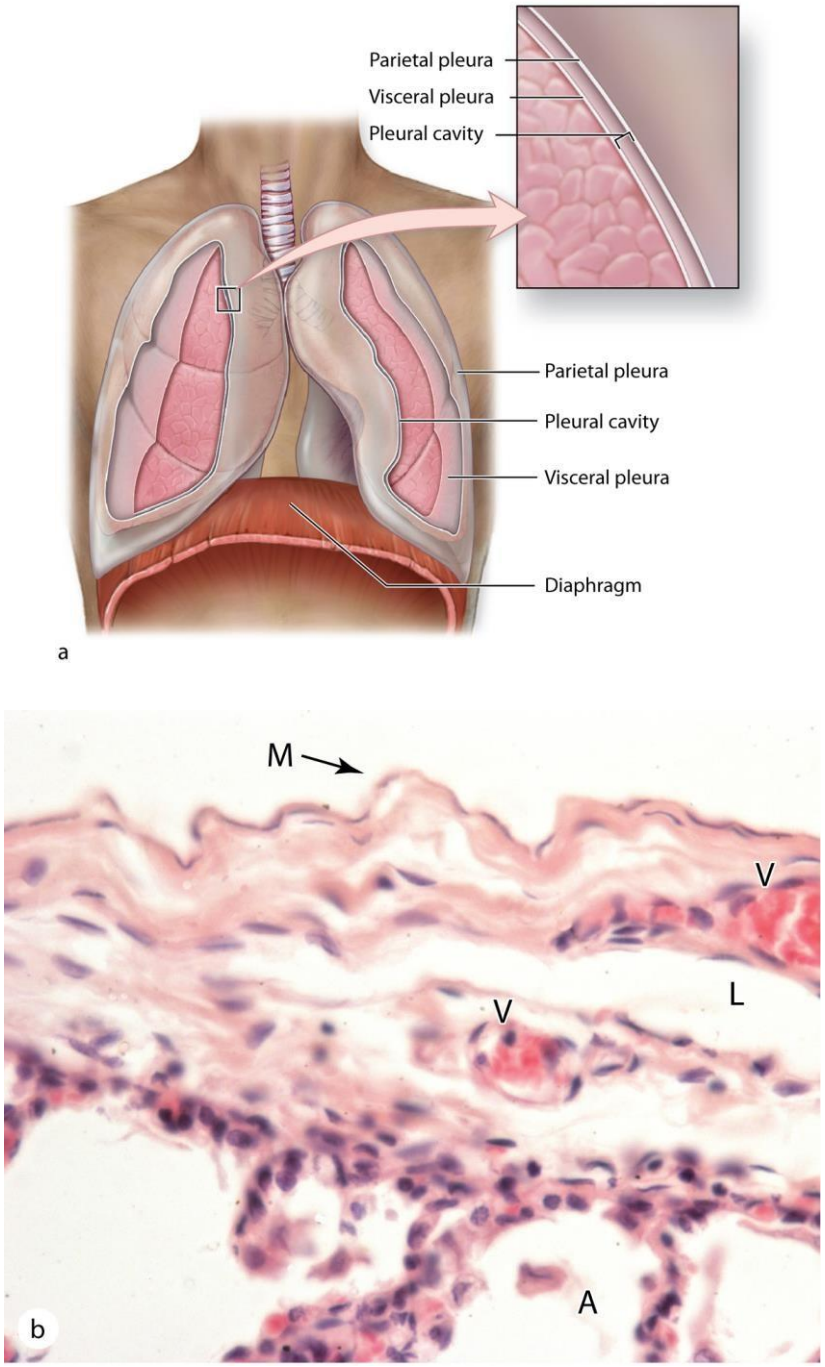

Figure 18. Pleura.
The pleura are serous membranes (serosa) associated with each lung and thoracic cavity. (a) The diagram shows the parietal pleura lining the inner surface of the thoracic cavity and the visceral pleura covering the outer surface of the lung. Between these layers is the narrow space of the pleural cavity. (b) Both layers are similar histogically and consist of a simple squamous mesothelium (M) on a thin layer of connective tissue, as shown here for visceral pleura covering alveoli (A). The connective tissue is rich in both collagen and elastic fibers and contains both blood vessels (V) and lymphatics (L).

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.

The narrow **pleural cavity** (see Figure 18) between the parietal and visceral layers is entirely lined with mesothelial cells that normally produce a thin film of serous fluid that acts as a lubricant, facilitating the smooth sliding of one surface over the other during respiratorymovements.

In certain pathologic states, the pleural cavity may contain liquid or air. Like the walls of the peritoneal and pericardial cavities, the serosa of the pleural cavity is water - permeable and fluid exuded from blood plasma commonly accumulates (as a pleural effusion) in this cavity during inflammation and other abnormal conditions.