Chapter 11: The Respiratory System

The respiratory system serves a number of functions within the body, the most notable being gas exchange. The majority of tissues of the body rely on aerobic metabolism to produce energy and so require a continuous supply of oxygen. This oxygen travels to these tissues by way of the blood stream. Carbon dioxide, a by-product of aerobic metabolism, is released from cells and is removed from their vicinity via the blood steam. The respiratory system is responsible for the acquisition of oxygen and the release of carbon dioxide to the external environment through a process of an exchange of these gases within the lungs. Fresh air, which has relatively high concentrations of oxygen and low concentrations of carbon dioxide is inspired into the lungs where it is brought into close proximity to capillaries. These pulmonary capillaries contain venous blood which has relatively low concentrations of oxygen and high concentrations of carbon dioxide. Gas exchange involves the transfer of oxygen from air to blood, and carbon dioxide from blood to air. The air, now enriched in carbon dioxide is expired from the lungs. Through its role in carbon dioxide excretion, the respiratory system also functions in acid-base balance; body sensors of carbon dioxide levels send input to the regions of the central nervous system involved with the control of breathing. Other functions of the respiratory system include sound production (phonation) and a number of biochemical reactions that affect body functions take place in the lungs. Finally, because of its exposure to the external environment, the respiratory system is also provided with a number of defense mechanisms to prevent the deleterious effects of environmental hazards.

The respiratory system consists of many different tissues and organs that are subdivided into three morphological and functional divisions. There is a **conducting portion** that includes the nasal cavities, paranasal air sinuses, pharynx, larynx, trachea, and a series of branching airways which include primary bronchi, lobar bronchi, segmental bronchi and terminal bronchioles (Fig. 11-1). The conducting portion functions to warm, moisten, and filter the incoming air. From the conducting system the air reaches the **respiratory portion** which includes the respiratory bronchioles, alveolar ducts and alveoli. Here gas exchange between alveolar air and the blood stream occurs by diffusion. The third component is the **ventilation system** which includes: the rib cage; the external and internal intercostal muscles and the muscular diaphragm which are the main muscles of respiration; the lining of the chest wall (pleura); and the elastic connective tissue component of the lungs. In addition there are other muscles that are involved in respiration such as several abdominal muscles as well as the sternocleidomastoid and scalenus muscles. The components of the ventilating system will not be discussed in this lab, other than to point out that each lung is encased in a pleural sac consisting of two layers called the parietal pleura and the visceral pleura. The **parietal pleura** is a thin serous membrane that lines the thoracic wall and mediastinum. It is reflected onto the surface of each lung where it is called the **visceral pleura**, which can be seen in tissue sections as a single layer of mesothelium that lies on the surface of the outer connective tissue covering the lung. Between these two layers is a potential space called the **pleural cavity**.

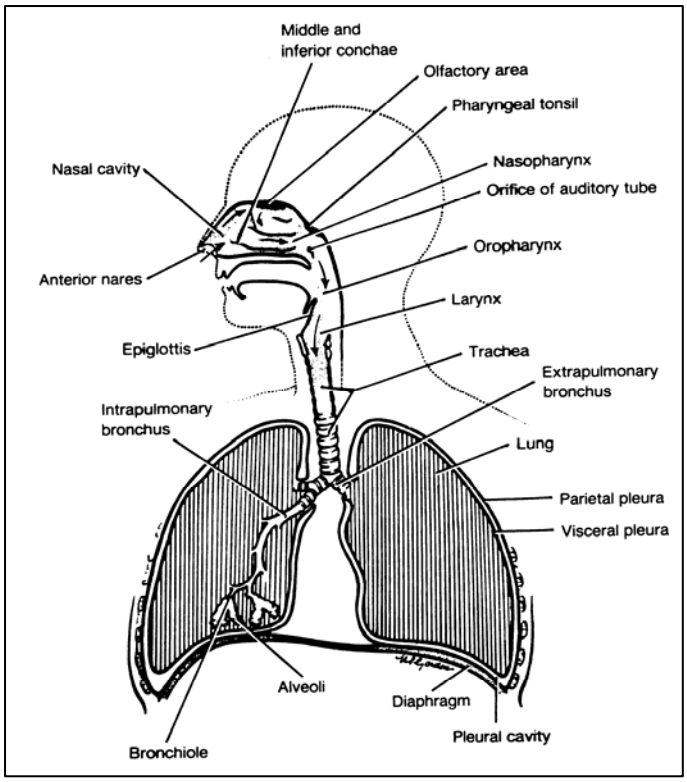

Figure 11-1: Overview to the Respiratory System

I. The Larynx

The larynx is the organ that connects the pharynx with the trachea and as such, serves as the direct opening into the respiratory system proper. Its walls are kept from collapsing during inspiration/expiration by a number of cartilages present within its wall. The three major unpaired cartilages that compose the larynx are the thyroid, cricoid, and epiglottic cartilage which form the core of the epiglottis (Fig. 11-2). In addition, there are three smaller paired cartilages called the arytenoid, corniculate, and cuneiform cartilages. Besides providing for phonation, the larynx serves as: (l) a valve to prevent contamination of the respiratory system from the oro- and nasopharynx; (2) a rigid wall to keep the entryway into the respiratory system patent; (3) a point of fixation for the thoracic cage by virtue of its muscular connection with the hyoid bone, mandible, clavicle and sternum; and (4) a valve (closure of true and false vocal folds) for increasing intra-abdominal pressures necessary for micturition, defecation, vomiting, parturition, coughing and sneezing.

The inner wall of the larynx is covered by a mucous membrane continuous with that of the pharynx above and the trachea below. The mucous membrane is modified in two areas to form four folds that span from the thyroid cartilage anteriorly to the arytenoid cartilages posteriorly. The upper pair are called the vestibular or false vocal folds and the lower pair are the true vocal folds. The vestibular folds are largely protective in function and are not involved in phonation, although their closure is involved in trapping air making possible increases in intra-thoracic and intra-abdominal pressure. Phonation involves the narrowing of the space between the two true vocal folds which is called the rima glottidis. The term glottis refers to the combination of vocal folds, processes, and the rima glottidis.

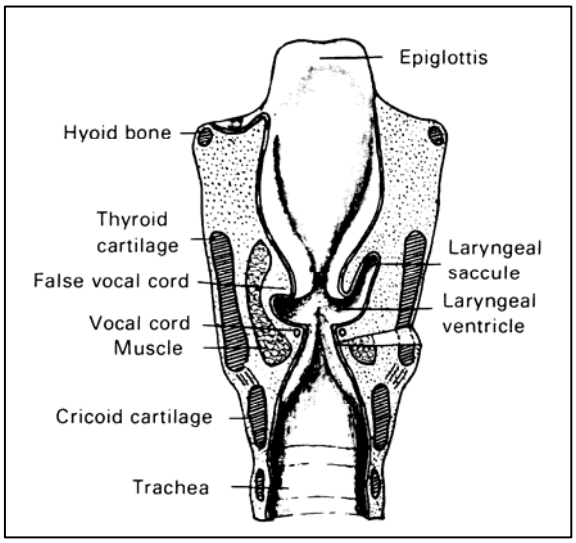

Figure 11-2: The larynx cut in a coronal section showing the posterior aspect of the anterior half.

The ovoid space between these folds is called the laryngeal ventricle which continues upward anteriorly to form a blind-ended space called the laryngeal saccule. In Fig. 11-2, the right side of the image is taken from a coronal section taken relatively more anteriorly than that shown on the left so as to show the saccule. The larynx is connected by muscles to bony structures located above, below and behind in the neck. These muscles raise, lower and change the laryngeal axis in the neck.

1. **The Epiglottis** (**Slides 40 and 41**): The epiglottis is a cartilage-containing flap attached to the posterior aspect of the thyroid cartilage, which projects over and covers the glottis tightly during swallowing (**Image 11-1**). Two surfaces can be distguished, the anterior and posterior, both of which consist of an epithelium, lamina (tunica) propria, and submucosa (**Image 11-2**). In the central portion of the epiglottis, there is a cartilage consisting of the tissue type, elastic cartilage.

a. **The anterior surface**. On the side of the epiglottis facing the tongue, the mucosa consists of an incompletely keratinized stratified squamous epithelium with a thin tunica propria of fine, dense irregular FECT (**Image 11-3**). Many blood and lymphatic capillary plexuses occur in the tunica propria. The submucosa also consists of dense irregular FECT, but the collagen fibers are thicker and more densely packed than the lamina propria. This connective tissue is continuous with the perichondrium. Few glands occur high on the anterior surface of the epiglottis but near its base and laterally there are numerous compound tubuloalveolar glands. Often they are embedded in notches or perforations in the cartilage where they intermingle with glands of the posterior surface.

b. **The posterior surface**: The posterior surface of the epiglottis is also normally covered with a stratified squamous epithelium except for the inferior portion at the entrance into the larynx, where the epithelium becomes pseudostratified columnar and possesses motile cilia and goblet cells (**Image 11-5**). The lamina propria is also thin and often contains areas of lymphocytic infiltration. The submucosa is the thicker layer, and in the lower portion of the posterior surface, there are numerous compound tubuloalveolar glands composed of both mucous and serous acini (**Image 11-4**). With regard to distinguishing the posterior surface from the anterior surface, besides the transition in epithelium, the posterior surface usually tends to have higher concentrations of glands.

c. **Elastic Cartilage**: At the center of the epiglottis is a region of elastic cartilage, which imparts elasticity to the entire epiglottis (**Image 11-6**). Elastic cartilage, a specialized connective tissue, consists of cells called chondrocytes embedded in a dense matrix consisting largely of collagen type II fibrils with the remaining space filled with proteoglycan aggregates and water. The proteoglycan aggregates consist of many proteoglycan molecules attached to a single hyaluronic acid molecule. The entire complex is very large (i.e., 10^8 daltons) and highly polyanionic. The cells, the chondrocytes, lie in spaces called **lacunae**. At the edges of the cartilage, there is a layer of FECT called the **perichondrium**, which completely surrounds the cartilage. In adults, this layer consists only of fibroblasts. No blood vessels or nerves develop within the perichondrium; thus cartilage is an avascular tissue. Elastic cartilage differs from the other cartilage types (hyaline and fibrocartilage) by possessing elastic fibers within the extracellular matrix in addition to the collagen type II fibrils. These elastic fibers impart a fibrous-looking appearance to the matrix because unlike the collagen fibrils, the elastic fibers are of sufficient size to be visible in the light microscope (**Image 11-7**). When stained with aldehyde fuchsin, the elastic fibers are even more prominent (**Image 11-8**).

2. **The False Vocal Fold**: In coronal sections of the larynx, it is possible to see both true and false vocal folds (**Image 11-9**). Located superior to the true vocal fold (see Fig. 11-2), the false vocal fold is identified based on its epithelium and the presence of glands (**Image 11-10**). Note that the epithelium lining the false vocal fold as well as the ventricle is predominantly pseudostratified columnar with cilia and goblet cells, with occasional patches of incompletely keratinized stratified squamous epithelium. Deep to the epithelium, adipose tissue and tubuloalveolar glands are embedded in dense irregular FECT. These glands are described as mixed, meaning that serous and mucous acini are present in each gland. They drain to the lumen via a series of ducts (**Image 11-11**)

3. **The True Vocal Fold**: The true vocal folds are thin shelf-like projections which lie nearer a median plane through the larynx than do the false vocal folds. Their inner margins are often called the vocal lips since they constitute the sound-producing elements of the larynx. *In vivo,* they appear pearly white except anteriorly near the thyroid cartilage where they are yellowish due to their elastin content. The true vocal cord is covered by pseudostratified columnar epithelium with cilia and goblet cells except over the vocal ligament where it is incompletely keratinized stratified squamous epithelium (**Image 11-12**). The location of this transition is somewhat variable. The lamina propria near the free margin of the vocal cord is less cellular than comparable regions elsewhere in the respiratory system. Collagen fibers are the predominant element here and are small in diameter and closely packed (**Image 11-13**). However, contained within the lamina propria is the **vocalis ligament**, a structure that despite its name actually consists of elastic connective tissue. Found in each true vocal fold, the vocalis ligament represents a portion of the cricothyroid ligament which connects the cricoid, thyroid, and the vocal processes of the arytenoid cartilages, and as such is rather extensive. There is a portion, however that extends upward from the cricoid cartilage to the true vocal fold which is called the conus elasticus, named for its abundant elastic fiber content. Thus, the upper border of the conus elasticus is seen as a region of elastic tissue located within the lamina propria which is called the vocalis ligament. The cells comprising the vocalis ligament can often undergo cellular transformation such that it is possible to see what appears to be cartilage that in later life can calcify. Deep to this structure there are isolated bundles of skeletal muscle that course from the body of the thyroarytenoid muscle and insert into the tunica propria of the true vocal fold along its length. Collectively these muscle bundles are called the **vocalis muscle**. They serve to change not only the tension on the cord but also its vibrational length and mass. There is no submucosa within the true vocal fold, but instead this region is occupied by the main

mass of the thyroarytenoid muscle. Laryngeal glands are also absent from the true vocal folds. Deep to the muscle are the laryngeal cartilages.

4. **The Laryngeal Cartilages**: The larynx is composed of several named cartilages. We have already discussed the epiglottic cartilage. In addition there are the thyroid, cricoid, the paired arytenoid cartilages, and other smaller cartilages. Unlike the epiglottic cartilage, the thyroid, cricoid, and arytenoid cartilages are composed of the tissue type hyaline cartilage (**Image 11-14**). Hyaline cartilage shares many of the same features described above for elastic cartilage, but lacks elastic fibers. In addition, note how the chondrocytes are clustered into groups consisting of 2-5 cells (**Image 11-15**). Each of these cell clusters is called an **isogenous group**. Isogenous groups represent the cloned progeny of a single chondrocyte whose offspring subsequently partition the original lacuna to form lacunae of their own. Also notice how the matrix close to the cells stains darker compared to that further away. The matrix close to the cells is called the **territorial matrix** to distinguish it from that lighter stained matrix further away called the **interterritorial matrix**. The difference in staining is presumably related to the concentration of sulfated proteoglycans. The thyroid cartilage lies at the level of the vocal folds (in a superior-inferior plane), whereas the cricoid cartilage lies below.

II. The Trachea

The trachea is a hollow tube starting at the base of the larynx and ending at its bifurcation into the two primary bronchi. Along its length, its walls are supported by a series of 16-20 horseshoe-shaped cartilages oriented so that their open ends face posteriorly. Posteriorly, where there is no cartilage, the tracheal wall consists of smooth mucles bundles (called the trachealis muscle) and connective tissue. Anteriorly, the successive cartilage rings are interconnected by dense irregular FECT which blends into the perichondrium surrounding each cartilage. Besides providing strength and protection to the enclosed airway, the trachea is also quite elastic, undergoing considerable stretching during deep inspiration and flexion-extension of the neck. Specializations of the mucosa enable the trachea to condition the air by warming, humidifying, and filtering out dust and other airborne particles as the air is conveyed to the lungs.

Starting from the lumen, the trachea is lined by the following concentric layers: a mucosa (in this case consisting of the epithelium); lamina propria; submucos; and then the hyaline cartilage (**Image 11-16**). The tissue located exterior to the cartilage is called either the adventitia or the posterior fibromuscular wall depending on location.

1. **The Mucous Membrane**: The airway is lined by a pseudostratified columnar epithelium, which has a very prominent basement membrane. By way of review from Chapter 5, four cell types can be distinguished within this epithelium (**Image 5-10**).

a. **Ciliated cells**: are the most numerous, and are named on the basis of their motile cilia that beat synchronously in waves toward the larynx. There are approximately 200-300 cilia per cell. The cilia extend from the apical surface of the cells through a fluid (serous) layer and their tips impinge on a more viscous superficial mucous layer. As the cilia beat, the mucus with its trapped particulate and cellular debris is moved toward the larynx at rates of l0-40 mm per minute. The beating of the cilia requires ATP, and accordingly these cells are enriched in mitochondria.

b. **Goblet cells**: are easily identified on the basis of their lightly stained, "goblet-shaped" apical cytoplasm. Goblet cells secrete mucus, a glycoprotein whose protein moiety is synthesized in the RER which is subsequently glycosylated here and in the Golgi. The resulting

glycoprotein molecules are stored in secretory vesicles, which collectively form what appears to be one large droplet in the apical cytoplasm. The secreted mucus is released from the cells where it contributes to the mucous layer covering the respiratory epithelium which functions to trap foreign material. The number of goblet cells varies in regions along the trachea. They are more numerous in regions of abrasion and increase in number in response to such irritants as smoke. The reduced number of ciliated cells in such a region and the increased viscosity of the mucous produced in response to irritation impedes the clearance of the mucous layer.

c. **"Brush" cells**: are the least common cell type and most difficult to identify. Like ciliated and goblet cells, brush cells reach the lumen but lack cilia and mucus droplets. Instead their apical surfaces contain microvilli and tend to bulge somewhat into the lumen. Although the function of these cells is not known with certainty, they are thought to be a form of sensory receptor (chemoreceptor) based on the observation that they are frequently found in close association with afferent nerve endings.

d. **Basal cells**: These cells lie along the surface of the basement membrane and do not extend to the apical surface. Often their ovoid nuclei are oriented parallel, rather than perpendicular to the basement membrane. The basal cell is mitotically active and gives rise to cells that differentiate into ciliated cells or goblet cells. Basal cells are sensitive to irritants such as those found in cigarette smoke, and may proliferate to form a thick stratified layer of cuboidal cells underlying the differentiated surface cells.

2. **The Lamina Propria**: The lamina propria is a relatively thin layer of loose FECT located just subjacent to the epithelium (**Image 11-17**). It contains numerous elastic fibers (which may be difficult to identify in H&E) along with fine, but densely packed collagen fibers. It is highly vascular, and many small nerves can often be found (**Image 11-18**). The lamina propria is also strikingly cellular throughout the length of the trachea, containing many lymphocytes, macrophages, plasma cells and mast cells.

3. **The Submucosa**: Subjacent to the tunica propria is a layer that has less elastic fibers, and the collagen fibers are coarser but more loosely packed. This layer is the called the submucosa, which is also identified as the layer containing the secretory portions of the numerous exocrine glands that drain to the tracheal lumen (**Image 11-17**). These glands are mixed, consisting of both serous and mucous acini along with structures called mucous acini with serous demilunes (**Image 11-19**). Surrounding these acini are myoepithelial cells, which as their name suggests, contain contractile proteins that function to squeeze the acinar contents to the duct system. These acini are also surrounded by an abundance of blood vessels, nerves, and wandering cells. Especially important are the large numbers of plasma cells that secrete IgA. These IgA molecules are taken up by serous acinar cells, where they are dimerized and complexed with a protein called secretory component. The entire complex is then released to the acinar lumen where it ends up on the epithelial surface. The exocrine glands are drained by a series of ducts, and are largely responsible for the serous and mucous layers that lie on the epithelial surface. The submucosa ends by blending into the perichondrium of the tracheal cartilage.

4. **The C-shaped Rings of the Trachea**: composed of the tissue type hyaline cartilage. You should be able to identify the same structures described above for the thyroid and cricoid cartilages of the larynx (**Image 11-20**).

5. **Posterior Fibromuscular Wall**: This membranous portion of the tracheal wall consisting of connective tissue and the trachealis muscle accommodates changes in the diameter of the esophagus during the swallowing of a bolus of food or drink.

III. The Bronchi

At its inferior end, the trachea bifurcates into two bronchi, each called a **primary bronchus,** that supply the right and left lungs. The initial portion of each primary bronchus is referred to as the extrapulmonary portion. At the hilum of the lung, each primary bronchus becomes associated with blood vessels, lymphatics, and nerves, all of which are embedded in a mass of connective tissue. Taken together, all of these structures form what is called the root of the lung. The left primary bronchus is smaller in diameter (l0 to l4 mm) than the right (l2 to l6 mm), giving a total cross-sectional area greater than that of the trachea. (This increase in total cross-sectional area is found at all further divisions of the conducting system.) Within the lung, each primary bronchus branches giving rise to bronchi that supply each lobe. These bronchi are called **lobar bronchi** and accordingly, there are 3 lobar bronchi in the right lung and 2 in the left. Each lobar bronchus then branches to form **segmental bronchi**, each of which supplies one bronchopulmonary segment (10 in the right lung and 8 in the left lung). These segmental bronchi are actually referred to as first generation segmental bronchi, because they continue to branch to form successive generations of smaller bronchi that are also referred to as segmental bronchi. Although these different classes of bronchi are anatomically distinct, they all share a similar histological appearance and so we describe them together (**Image 11-21**).

l. **The Mucous Membrane**: The epithelial lining of the primary, lobar, and segmental bronchi is similar to that described for the trachea (**Image 11-22**). The epithelium varies in height along a segmental bronchus, decreasing in height with successive branching to become a simple columnar epithelium at the point in which the last generation segmental bronchus branches to form a terminal bronchiole. .

2. **The Tunica Propria**: The tunica propria of the primary, lobar and segmental bronchi consists of fine dense fibroelastic connective tissue. The layer is very cellular, with numerous lymphocytes, plasma cells and macrophages.

3. **The Submucosa**: The submucosa consists of loose to dense irregular FECT (**Image 11-23**). It exhibits great mobility during inspiration and expiration. It contains numerous compound tubuloalveolar glands with nearly equal numbers of mucous and serous acini. In the primary and lobar bronchi the secretory portions of the glands lie external to the tunica muscularis and may even extend into the peribronchial connective tissue between the bronchial cartilages. The glands are most numerous in early generations of segmental bronchi (approximately l gland per mm) and more commonly lie in the submucosa inside the muscularis. In later generations, the glands gradually diminish in number and are absent in the smallest segmental bronchi.

4. **The Tunica Muscularis**: Beginning in the lobar bronchus bundles of smooth muscle extend from their attachment to the surrounding bronchial cartilages into the submucosa. They run in a helical course with a steep pitch and so do not form a continuous layer. In the segmental bronchi, muscle bundles are no longer attached to the surrounding cartilaginous plates but instead form a nearly continuous layer demarcating the submucosa from the lamina propria (**Image 11-23**). Contraction of the tunica muscularis upon fixation of the tissue results in characteristic longitudinal folds of the mucosa seen in histological sections.

5. **Bronchial Cartilages and Fibroelastic Membrane**: The primary, lobar and segmental bronchi all contain hyaline cartilage (**Image 11-24**), but unlike the horse-shoe shape of the

tracheal cartilage, the bronchi contain cartilages that decrease in size with successive branching to form cartilage plates. These plates are bound together by dense irregular FECT which is continuous with the perichondrium. By the last generation segmental bronchi, the cartilage plates are either very small or not present at all.

6. **Functional Correlations**: As described above, the conducting portion of the respiratory system functions to modify the incoming air by heating it, increasing its relative humidity, and cleansing it of particulate material. Heating the incoming air occurs through the proximity of the rich vasculature of the airway walls. These other processes are accomplished by the presence of a system called the "mucociliary escalator" which refers to the mucous and serous layers that overly the epithelium and the cilia that move it toward the pharynx. In immediate contact with the apical surface of the epithelium is a serous layer which is mostly water with some dissolved proteins and other molecules. Sitting on the surface of the serous layer is the mucous layer, a more viscous layer formed mostly of mucus secreted from goblet cells and the exocrine glands. It is this mucous layer which traps the particulate material and humidifies the air. The cilia, through synchronized motion, move this blanket of mucus along out of the respiratory system. The importance of this system is seen by consideration of some clinical disorders such as immotile cilia syndromes. In these individuals, there are genetic defects involved with the nonexpression of functionally important components such as dynein or other proteins involved with ciliary action. Lack of normal ciliary activity results in impaired clearance of the mucous layer and is associated with chronic respiratory diseases. Similarly, cystic fibrosus is a pediatric disorder involving abnormally thick and viscous mucus that tends to obstruct airways.

IV. The Terminal Bronchiole

The terminal bronchiole is the last segment of the conducting portion of the respiratory system, and differs in structure from bronchi in the following respects. First the epithelium is no longer pseudostratified columnar with goblet cells, but instead is a simple columnar epithelium with ciliated and non-ciliated cells. Secondly, terminal bronchioles do not possess goblet cells nor exocrine glands so the ability to produce a mucous layer is no longer present. Any mucus that may have migrated beyond the segmental bronchi is removed from the bronchiole by the action of the ciliated cells. Finally, terminal bronchioles no longer possess cartilage in their walls. Each terminal bronchiole formed by the dividing of a segmental bronchus supplies a unit of the lung called a lung lobule (Fig. 11-3). The lung lobule is the basic functional unit of the lung, and

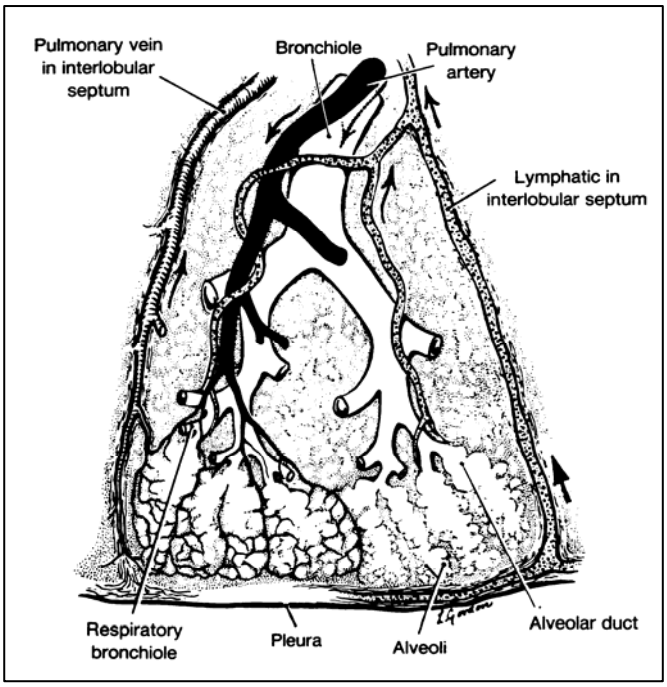

Figure 11-3: Schematic representation of a lung lobule. Note the dissociation of pulmonary arteries from the veins and lymphatics within the lobule.

is roughly shaped like a pyramid. Their bases, which measure 1-2 cm, are distinguishable as polygonal areas beneath the pleura (**Image 11-25**). As shown in Fig. 11-3, adjacent lobules are partially subdivided by fibrous septa, which contain lymphatics and the pulmonary venules. Thus within a pulmonary lobule, the pulmonary arteries and veins no longer run side by side but instead dissociate. Each terminal bronchiole proceeds to branch 5-9 times, but ultimately gives rise to a respiratory bronchiole. Terminal bronchioles are surrounded by alveoli and other lung structures (**Image 11-26**).

l. **The Mucous Membrane**: The lining epithelium of the terminal bronchiole varies from simple columnar near the segmental bronchus to cuboidal where the terminal bronchioles join the respiratory bronchioles. The epithelium contains at least two cell types: ciliated cells and cells with microvilli (**Image 11-28**). Goblet cells occur only infrequently in the beginning segments of the terminal bronchioles but are absent in segments of the second or third generation.

2. **The Tunica Propria**: This layer is exceedingly thin and consists of fibroelastic connective tissue containing reticular, collagenous, and elastic fibers with only an occasional fibroblast or wandering cell (**Image 11-27**).

3. **The Tunica Muscularis**: An incomplete layer of helically-arranged smooth muscle bundles separates the mucosa from the peribronchiolar connective tissue. Contraction of this smooth muscle upon fixation gives terminal bronchioles their characteristic star-shaped luminal appearance (**Image 11-28**).

4. **The Peribronchiolar Tissue**: This tissue varies in thickness along the length of the terminal bronchiole and its branches. It is composed of fibroelastic connective tissue with about equal proportions of reticular, collagenous and elastic fibers that are continuous with similar fibers in and around the surrounding alveolar walls. This region is strikingly cellular with many

lymphocytes, macrophages and plasma cells. Arterial branches of the pulmonary artery are located in or near this layer.

V. The Respiratory Bronchiole

Respiratory bronchioles arise as the last branches of terminal bronchioles. They divide into further respiratory bronchioles or directly into alveolar ducts. Respiratory bronchioles vary in length from l to 4 mm and are about 0.5 to l.0 mm in diameter. Respiratory bronchioles are considered as part of the respiratory portion of the respiratory system because of the presence of respiratory alveoli which project from their walls. Respiratory bronchioles are accompanied by a branch of the pulmonary artery (**Image 11-29**).

l. **The Mucous Membrane**: These bronchioles are lined by a simple cuboidal to squamous epithelium. In respiratory bronchioles of the first order the epithelium may contain ciliated cells similar to those of conducting portions of the lung. No goblet cells are present. Where alveoli exit from the wall of the respiratory bronchiole the epithelium becomes squamous and is continuous with that lining the alveolus (**Image 11-30**).

2. **The Tunica Propria**: This layer is exceedingly thin and consists of fibroelastic connective tissue containing reticular and elastic fibers and only an occasional fibroblast and wandering cell. Elastic fibers are oriented mostly parallel to the axis of the bronchiole; they also form loops or rings around the entrances into alveoli and extend into the adjacent interalveolar septa of the surrounding parenchyma.

3. **The Tunica Muscularis**: Small bundles of smooth muscle are arranged in open helices around the axis of the bronchiole and so do not form a complete layer. Like elastic fibers, they form loops around the entrances to alveoli from the bronchiolar wall.

4. **The peribronchiolar tissue**: This layer is very thin; usually few cells are present.

VI. The Alveolar Duct and Alveolar Sac

Alveolar ducts begin at the termination of the last order of respiratory bronchioles. Alveolar ducts further ramify to give 2 to 11 generations of alveolar ducts that are about 0.5 mm in diameter and 0.5 to 1 mm in length. While alveoli on respiratory bronchioles are

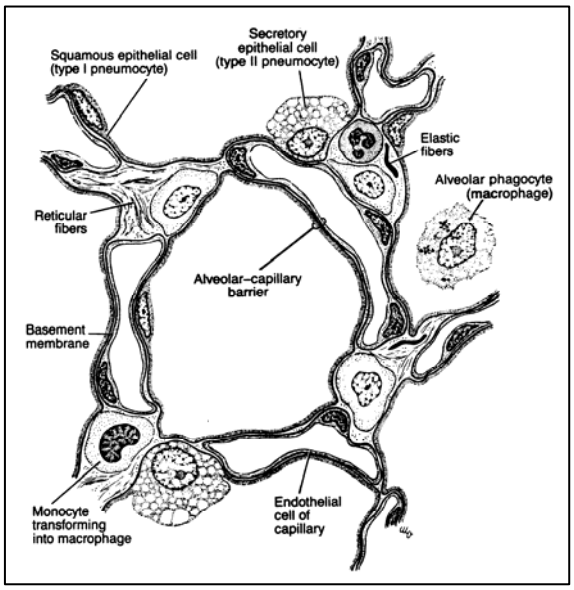

Figure 11-4: Schematic representation of the interalveolar septum

irregularly spaced those on alveolar ducts are so closely spaced as to make the wall of the alveolar duct simply a series of openings into the alveoli (**Image 11-31**). Often alveolar ducts end with a structure called the alveolar sac, a blind-ending space that gives rise to several alveoli, much as a houses within a cul-de-sac.

1. **The Mucous Membrane**: The lining epithelium of the alveolar duct and alveolar sac is squamous, lacking any ciliated or goblet cells, and is continuous with the squamous epithelium of each alveolus. The epithelium rests on a thin basement membrane. The lamina propria is an exceedingly thin layer of reticular fibers with rare fibroblasts that is difficult to see in the light microscope.

2. **The Tunica Muscularis**: The wall of the alveolar duct consists of thin bundles of smooth muscle and elastic fibers that appear as knobs on either side of the entrance into an alveolus.

VII. The Respiratory Alveolus

The respiratory alveolus is the basic structural and functional unit of gas exchange. Alveoli are small air spaces, ranging in diameter from 200-250 μm, that open into alveolar sacs, alveolar ducts, or directly to a respiratory bronchiole. Adjacent alveoli share a common wall called the interalveolar septum which contains the capillary system of the pulmonary circulation. Adjacent alveoli also communicate by small apertures (i.e., <10 μm in diameter) within the interalveolar septa called alveolar pores. These pores allow some degree of collateral air circulation during normal respiratory function, and presumably become important in the event of bronchiolar obstruction. Although estimates vary somewhat, there are on the order of approximately 300 million alveoli between the two lungs, providing a total surface area for gas exchange of approximately 80 square meters.

1. **Interalveolar Septum**: refers to the tissue which separates adjacent alveoli (**Image 11-32**). It contains the extensive alveolar capillary plexus and thus represent the site where the diffusion of gases takes place between alveolar air and capillary blood (Fig. 11-4). The walls are supported by an extensive series of reticular fibers as well as some elastic fibers. These elastic fibers function in combination with other elastic components of the bronchial tree to impart elasticity to the respiratory system. During inspiration, these elastic components are stretched which then recoil upon expiration allowing the air to be expelled without muscle activity. The relative contributions of the various structural components of the respiratory system as a function of location in summarized in Fig. 11-5.

2. **Alveolar Cell Types**: Alveoli are lined by a continuous epithelium that is made up of several cell types:

a. **Type I Pneumocytes**: are very flat squamous cells that are so thin that their cytoplasm cannot be seen in the light microscope. The only indication of their presence is their nuclei which lie along the alveolar surface (**Image 11-34**). Apart from the perinuclear region, these cells are less than 0.2 μm thick which facilitates the diffusion of gases across their cytoplasm.

b. **Type II Pneumocytes**: are connected to the type I cells by tight junctions and are distinguished by their discernible cytoplasm and more rounded appearance (**Image 11-35**). Unlike type I cells, type II pneumocytes have a round nucleus and their cytoplasm tends to bulge somewhat into the lumen. These are secretory cells, whose major product is pulmonary surfactant. Besides the organelles needed for secretion, electron micrographs of these cells shows the presence of structures called lamellar bodies which contain phospholipids and other molecules for release to the alveolar lumen. The alveolar surface is actually covered by a thin layer of water. At any air-water interface, there are strong attractive forces between the water molecules (surface tension) that would lead to adherence of the opposing walls during expiration. This tendency is countered by the presence of surfactant which reduces these attractive forces. Actually a complex mixture of phospholipids, proteins, and carbohydrates, surfactant is released from the type II cell where it spreads along and across the aqueous layer.

c. **Alveolar Macrophages**: are large phagocytic cells that bulge into the lumen. Often they appear to be free in the lumen but are actually loosely attached to the epithelium (**Image 11-36**). They are derived from monocytes, which evidently leave alveolar capillaries where they intercalate themselves into the alveolar wall (see Fig. 11-4). There is also evidence that they remain mitotically active and that the resident macrophage population is to some extent self-propagating. Like other macrophages, these cells phagocytose material, in this case dust and debris that gain access to the alveoli. These cells are migratory, and eventually move to the bronchi where they are carried out of the lungs via the mucociliary escalator. Finally the lungs of smokers appear black because of the ingested carbon contained within the cytoplasm of these cells.

3. **Alveolar-Capillary Barrier**: Air within the alveolus is separated from capillary blood by the following structures: 1) cytoplasm of the type I pneumocyte; 2) the fused basement membranes of the alveolar epithelium and endothelium; 3) cytoplasm of the endothelial cell. Altogether, the distance that gas molecules must diffuse is between 0.2 and 2.0 μm.

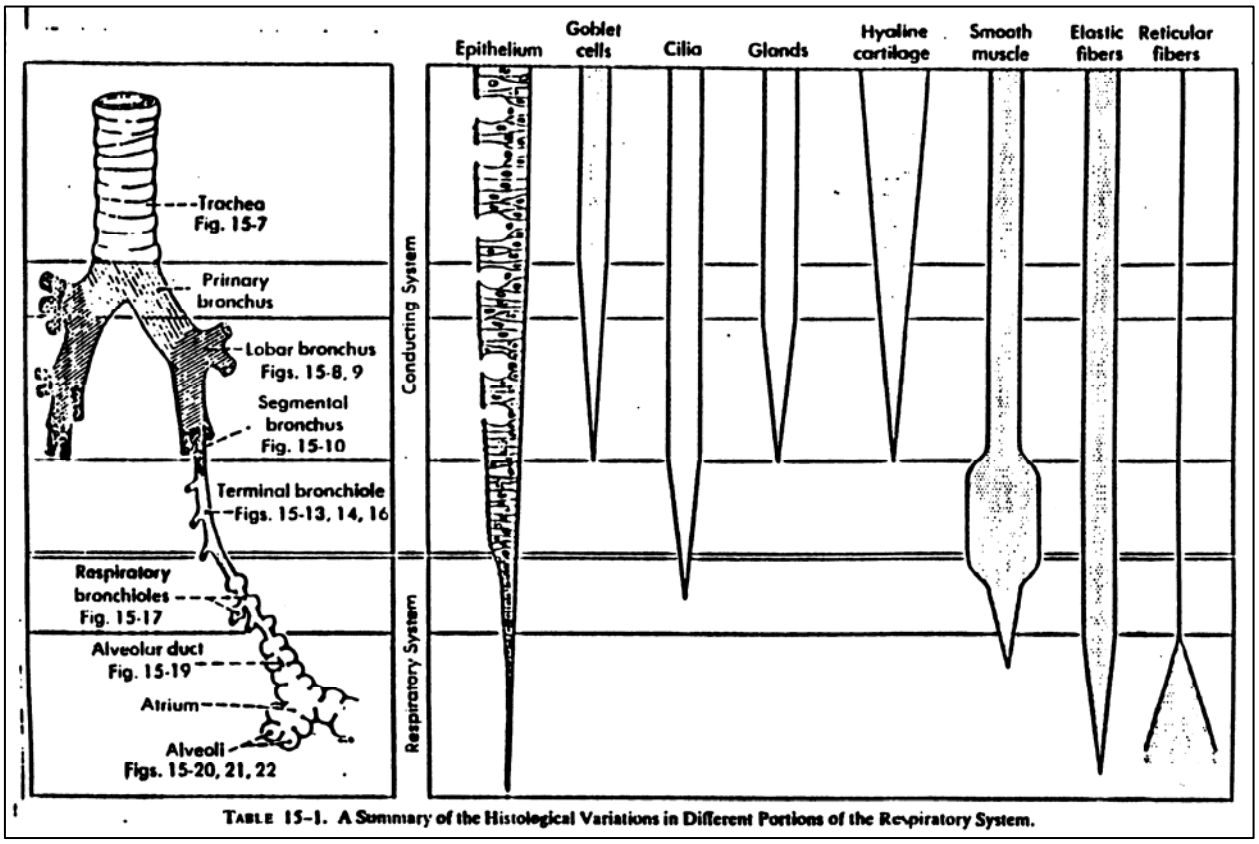

Figure 11.5: Summary of Histological Components of the Respiratory System.

VIII. The Blood Supply

The blood supply to the lung is from two sources: systemic and pulmonary. The conducting portion of the lung receives branches from the thoracic aorta. The parenchyma (respiratory portion) is supplied and drained by the pulmonary circuit. Pulmonary arteries run with the conducting portion of the lung and end as arterioles on the respiratory duct. Only capillaries occur among the alveoli. Pulmonary veins run in the connective tissue septa between lobules (**Image 11-33**). Arteries and veins are thus separated.

IX. Learning Objectives:

The following is a list of cell types, tissue types, and structures that you should be able to identify in images based on the morphological descriptions given above. In particular:

You Must be Able to Identify the Following:

Cell types:
Ciliated cells
Goblet cells
Brush cells

Basal cells
Fibroblasts
Lymphocytes
Macrophages
Plasma cells
Mast cells
Pneumocytes Type I and II
Alveolar macrophages
Endothelial cells
Neurons (postganglionic parasympathetic)
Schwann cells
Mucous and serous acinar cells
Myoepithelial cell
Chondrocytes
Smooth muscle cells

Structures:
Epiglottis
Basement membrane
Lacuna
Perichondrium
Elastic fibers
Collagen fibers
Vocal folds (true and false)
Vocal ligament
Vocalis muscle
Ventricle of larynx
Isogenous group
Territorial Matrix
Interterritorial matrix
Lamina propria
Submucosa
Tunica muscularis
Bronchi (primary, lobar, and segmental)
Bronchioles (terminal and respiratory)
Alveolar Ducts
Alveolar sacs
Alveoli
Alveolar pore
Glands (mucous and serous)
Secretory acini (mucous, serous, mucous acini with serous demilunes)
Parasympathetic ganglia
Perineureum

Organs:
Larynx
Trachea
Lung

You must be able to identify the component tissue types

XII. Sample Histology Problems

In order to assist you in applying the morphological descriptions that you have learned, a sample problem set covering this material has been constructed, along with explained answers. Note, although an attempt has been made to illustrate as many of the cell types and structures from the list above, this sample problem set is not comprehensive.

Respiratory Sample Problem Set

Respiratory Sample Problem Set Answers

XIII. Student Presentations: Nervous Tissue Histology Problem Set:

The following represents the problem set that you will be responsible for during the class session entitled “Histology Presentations: Muscle Tissue”.

Respiratory Histology Problem Set