Chapter 12
Respiratory System

12.1. Basic Structure

The respiratory system provides the body with oxygen and rids the body of carbon dioxide, the waste product of metabolism. The circulatory system works in close association with the respiratory system by providing a medium for the transport of these gases throughout the body.

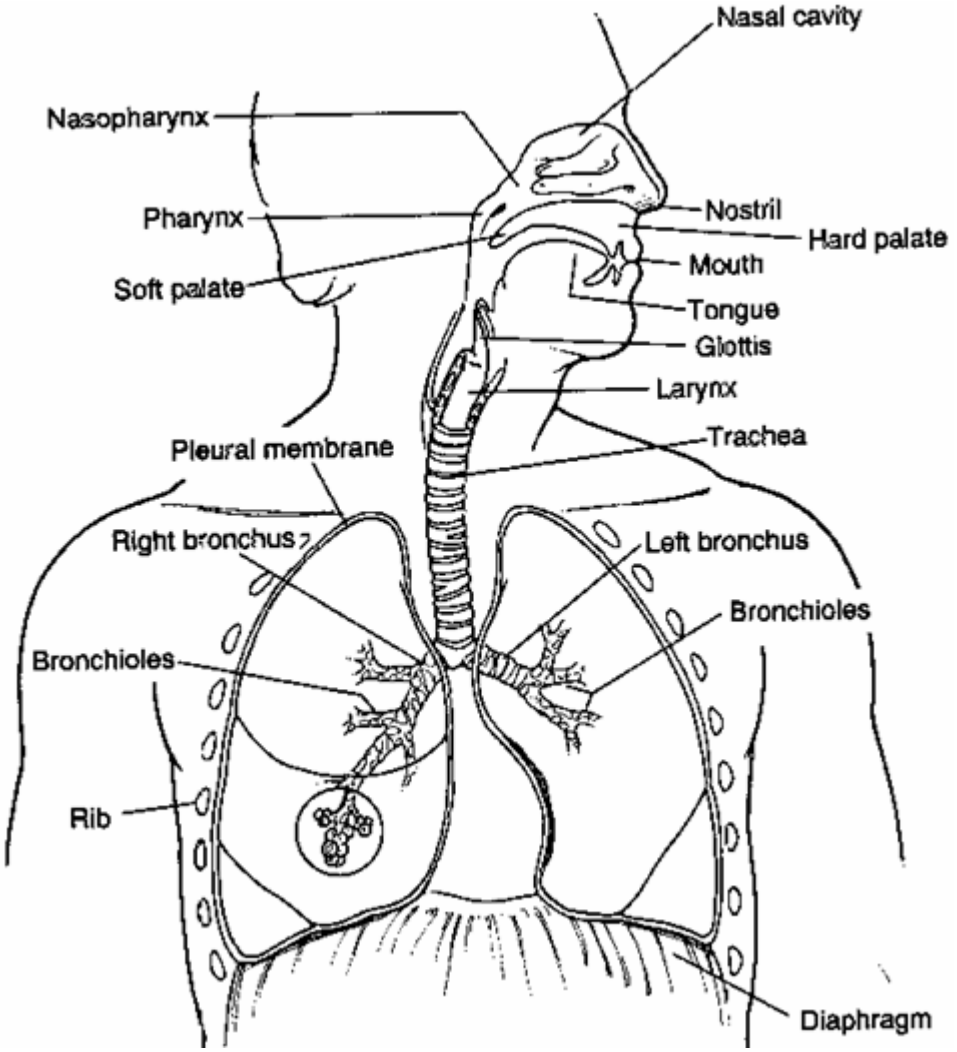

Fig.12.1. Respiratory System

The respiratory system proper can be divided into two portions:

a) The Conducting Portion: The conducting portion consists of the nasal cavity, pharynx, larynx, trachea, and the bronchial tree. It serves to conduct air from the environment to the respiratory portion of the lungs.

b) The Respiratory Portion: The respiratory portion consists of the alveoli. The alveoli

arise off of branches of the bronchial tree called bronchioles. Due to their extremely thin walls it is the alveoli which serve as the site of external respiration. External respiration is the exchange of gases between the lungs and the blood.In addition to the conducting and respiratory portions, the respiratory system also has a ventilation system designed to move air through the respiratory system proper. This ventilation system is composed of the walls of the thoracic cavity and the diaphragm.

12.2. The Conducting Portion

The conducting portion, which extends from the nasal cavity to the bronchi, is characterized by a lining of pseudostratified, ciliated columnar epithelium with goblet cells sitting on a lamina propria rich in lymphoid cells and seromucus glands. As the conducting passageways branch into smaller branches there are some changes which occur: The seromucus glands gradually disappear. The height of the epithelium decreases to a ciliated simple columnar and eventually to a simple cuboidal epithelium. The lining of the conducting portion is designed to perform three actions on air entering the respiratory system: warm, filter, and moisten. Secretions of the seromucus glands provide the first line of defense against pathogens, humidify the air, and detoxify soluble gases.. Their secretions coat the surface of the epithelium and so can trap contaminants. These debris laden mucus us removed by means of Mucociliary Clearance. The cilia of the columnar cells beat and move the debris laden mucus towards the pharynx for elimination. The lamina propria is well vascularized. These blood vessels will radiate heat so as to warm the nasal cavity and thereby the air.The lamina propria is also rich in lymphoid cells. These lymphoid cells form diffuse aggregates which can often permeate the above lying epithelium. Some of these lymphoid cells will produce IgA which will be transported across the epithelium to kill bacteria and viruses.

Changes in air pressure occur within the conducting portion during inspiration and expiration. Bone and cartilage will provide a degree of rigidity so as to withstand pressure differences. The bone is found in the walls of the nasal cavity. The cartilage is found in the larynx, trachea, bronchi, and bronchioles. Elastic fibers provide a degree of flexibility to allow for changes in the lengths of conducting tubes during breathing. Smooth muscle in the walls of bronchial tree will provide for the regulation of aeration volume in response to the body's needs. Parasympathetic stimulation causes the muscle to contract which decreases lumenal diameter. Sympathetic stimulation causes the muscle to relax which increases lumenal diameter.

12.2.1.The Nasal Cavity

a) General Comments

The nasal cavity is divided into the right and left nasal cavity by the nasal septum. The right and left nasal cavities are further divided into three groove-like passageways, called the nasal meatuses, by bony projections called conchae. The nasal cavity is separated from the oral cavity by the hard and soft palates. The nasal cavity communicates with the external environment by the External Nares and with the pharynx by the Internal Nares. The nasal cavity is lined by two types of mucosa: respiratory mucosa and olfactory mucosa.

b) The Respiratory Mucosa

The respiratory mucosa lines the bulk of the internal nasal cavity. The respiratory mucosa is composed of pseudostratified, ciliated columnar epithelium with goblet cells sitting on

a well developed lamina propria. The goblet cells are abundant and randomly distributed throughout the epithelium. Numerous branched, tubuloalveolar seromucus glands extend into the lamina propria. These glands will resemble small seromucus salivary glands. Small blood vessels are abundant in the lamina propria. These blood vessels will warm the inhaled air and allow for the passage and transport of various leucocytes. The network of capillaries directly beneath the epithelium is made up of fenestrated capillaries so as to allow for the rapid diffusion of materials. This is generally the case throughout much of the respiratory passageways. Veins and arteries are in close association and atriovenous anastomoses are common in this region. Lymphatic drainage is well developed.

c) The Olfactory Mucosa

The olfactory mucosa is limited in humans to the roof of the nasal cavity and a small portion of the superior septum. The glands of the olfactory mucosa are only serous. The serous fluid serves as a solvent for olfactory chemicals. Olfaction is chemoreceptive sense and requires the chemicals to be in solution for detection. The pseudostratified, ciliated columnar epithelium of this region is thicker than it is in respiratory mucosa. The specialized cells of the olfactory mucosa are the Olfactory Cells. Olfactory cells are bipolar neurons which will detect olfactory stimuli. The dendrite extends to the surface of the epithelium and terminates in a swollen structure called the Olfactory Knob. Several long stereocilia will extend from the knob onto the surface of the epithelium so as to pick up olfactory stimuli. The axon will extend basally and penetrate the basement membrane into the lamina propria. In the lamina propria axons will join together to form fascicles. In turn, these fascicles will join forming about 20 bundles of olfactory nerves called the Filia Olfactoria. The filia olfactoria will pass through the olfactory foramina of the cribiform plate to enter the brain.

Surrounding the olfactory cells are ciliated columnar epithelial cells called Sustentacular/Supporting Cells. These cells have apically oriented nuclei. The olfactory mucosa possess a third type of cell, the Basal Cell. Basal cells are short, round cells located at the basal lamina. Basal cells are undifferentiated and can give rise to ciliated columanr cells of goblet cells.

12.2.2. The Pharynx

The pharynx is divided into three portions: nasopharynx, oropharynx, and laryngeopharynx.

a) Nasopharynx

The nasopharynx extends from the internal nares to the soft palate. Unlike the other two portions of the pharynx, the nasopharynx is (normally) only a respiratory passageway and it's histology reflects that fact: The mucosa of the nasopharynx is similar to the respiratory mucosa of the nasal cavity. It is a pseudostratified, ciliated columnar epithelium with numerous goblet cells sitting on a lamina propria rich in lymphoid cells and seromucus glands.

b) Oropharynx

The oropharynx extends from the level of the soft palate to the level of the hyoid bone. It serves as both a passageway for air and for ingested foods. The oropharynx will communicate with the oral cavity through the fauces. Due to it's dual role, the oropharynx has a lining more similar to that of the oral cavity. It is lined by a stratified squamous, nonkeratinized, epithelium sitting on a lamina propria rich in lymphoid cells. It will also have associated mucus glands.

c) Laryngeopharynx

The laryngeopharynx extends from the level of the hyoid bone to the opening into the larynx, the Glottis. It also serves as both a passageway for air and for ingested foods and so it's histology is identical to that of the oropharynx.

12.2.3. The Larynx

The larynx serves a purely respiratory role and is located anterior to the upper esophagus. The larynx is a hollow, bilaterally symmetrical structure formed by plates of cartilage and by muscle. The cartilage component is made up of nine pieces, three singular and three paired. The singular cricoid cartilage attaches the larynx to the trachea by means of the cricoid ligament. The thyroid cartilage is quite large and makes up most of the anterior wall. The paired arytenoid, corniculate, and cuneiform cartilages are held together by skeletal muscle. The epiglottis is the most specialized of the laryngeal cartilages. It guards the opening into the respiratory tree, the glottis. It is composed of elastic cartilage covered by loose connective tissue and an epithelium which varies based on location. On the external surface, where abrasion may come from food, the epithelium is a stratified squamous nonkeratinized. On the internal surface, which should come in contact only with air, the epithelium is a pseudostratified, ciliated columnar epithelium with numerous goblet cells. The muscular component is divided into extrinsic and intrinsic muscles. The intrinsic muscles, along with dense connective tissue, attach the paired cartilages together. The extrinsic muscles attache the larynx to other structures of the throat. They are skeletal muscles of pharyngeal arch derivation.

The laryngeal mucosa is arranged into three pairs of lateral folds, reinforced by dense connective tissue cores, which project into the lumen. The three pairs of folds are:

1] Aryepiglottic Folds : They are the superiormost pair.

2] Ventricular Folds: They are the middle pair and are often referred to as the "false vocal cords".

3] True Vocal Cords: These are the inferiormost pair and have a core of skeletal muscle, along with dense connective tissue, so as to vary the size and shape of the passage.

Between the true and false vocal cords is a recess called the Laryngeal Ventricles. The mucosa is primarily a pseudostratified, ciliated columnar epithelium with numerous goblet cells sitting on top of a lamina propria rich in lymphoid cells. However there are some areas where it is a stratified squamous nonkeratinized epithelium sitting on top of a lamina propria rich in lymphoid cells. These areas are the external surface of the epiglottis and the aryepiglottic folds.

12.2.4. The Trachea

The Trachea is a rigid tube composed of 16 to 20 segments, each segment containing a c-shaped piece of hyaline cartilage. The cartilage free regions are on the posterior trachea, facing the esophagus. The cartilages are joined to one another by bands of smooth muscle called the Trachealis Muscle. Also joining the cartilaginous rings together is the Intersegmental Dense Connective Tissue composed of dense regular connective tissue rich in collagen and elastic fibers. These collagen fibers are continuous with the perichondrium of the rings. The trachea will extend from the larynx into the thoracic cavity where it will branch. The two branches coming off of the trachea are the right and left primary bronchi. The branching point is called the carina.

Histologcally, the trachea is made up of three tunics, the tunica mucosa, the tunica submucosa, and the tunica adventitia.

a) Tunica Mucosa - the tunic in contact with the tracheal lumen

The mucosa has a pseudostratified, ciliated columnar epithelium with numerous goblet cells resting on a thick basement membrane. There are actually five cell types in the tracheal epithelium (three are observable under light microscopy, two are observable only under electron microscopy): ciliated columnar cells, goblet cells, basal cells, Brush Cells. Unlike ciliated columnar cells brush cells possess microvillae. They may be immature columanr cells or degraded goblet cells. A small number of brush cells may even serve as sensory receptors. These cells are synapsed with the dendrites of sensory neurons. The 5th type of cells is the Granule Cells which are small cells, basally oriented cells filled with numerous small granules. There are two classes of granule cells recognized based on histochemical properties:

1. Neurosecretory Granule Cells - produce catecohlamines such as epinepherine and norepinepherine.
2. Protein-Hormone Secreting Cells - produce hormones.

These five types of cells are also found in other portions of the respiratory mucosa. Due to their similarities, the epithelial of the larynx, trachea, and bronchi are collectively called Laryngobronchial Epithelium. The lamina propria of the mucosa will be the typical loose connective tissue rich in lymphoid cells having reticular and elastic fibers. An elastic membrane separates the tunica mucosa from the tunica submucosa. This elastic membrane extends into the primary bronchi. At the distal portion of the primary bronchus it is replaced by the Muscularis Mucosa a ring of smooth muscle.

b) Tunica Submucosa - the middle tunic

The submucosa is a loose connective tissue tunic containing numerous seromucus glands. These seromucus glands are called Submucosal Glands. The ducts of these submucosal glands will pass through the submucosa and mucosa to open up in the lumen. Myoepithelial cells are associated with the acini and with certain ducts of these glands.

c) Tunica Adventitia - the outermost tunic

The adventitia consists of the cartilaginous rings, the trachealis muscle, and the intersegmental dense connective tissue. In the cartilage free posterior surface of the trachea the submucosal glands will partially penetrate into the adventitia and be interspersed with smooth muscle fibers of the trachealis.

12.2.5. The Lungs

The lungs are paired conical shaped organs located in the pleural cavities of the thorax. The lungs are covered by a thick, elastic serous membrane called the Visceral Pleura. The visceral pleura produces pleural fluid. The visceral pleura is contiguous with the serous, inner layer of the parietal pleura. The connective tissues within the lungs is rich in elastic fibers and smooth muscle cells to allow for the expansion and reduction of the lungs during breathing. The mediastinal surface of each lung has a concave depression called the hilus. The hilus is the point where the pulmonary vessels and the primary bronchus enters the lung. The lung is divided into Lobes. The right lung has three lobes and the left lung has two lobes. The primary bronchus will send a branch into each lobe. These branches are called Lobar/Secondary Bronchi. Each lobe will be further divided into Segments. The segments are each separated from one another by a connective tissue septum containing blood vessels. Smaller branches come off of the secondary bronchi to service each segment called Tertiary/Segmental Bronchi. The segments are divided into Subsegments. The subsegments are divided into Lobules. Each lobule is separated

from the adjacent lobules by a connective tissue septum. The internal structure of the lung consists of a branching system of conducting passages called the Bronchial tree.

a) The Primary Bronchi

There are two primary bronchi, one going into each lung at the hilus. The primary bronchus is almost identical to the trachea in it's histology, particularly in the proximal portions. The major difference is that the hyaline cartilage rings are complete circles; they are not c-shaped.

b) The Secondary/Lobar Bronchi

The secondary bronchi branch off of the primary bronchi. One secondary bronchus will enter each lobe of the lung. Since they are actually within the lung, secondary bronchi could be considered to be the first of the intrapulmonary conducting passageways. The previously mentioned structures are part of the extrapulmonary conducting system. Secondary bronchi are histologically quite similar to primary bronchi. One major difference is that, instead of having a continuous piece of cartilage, they have a cartilaginous ring composed of several smaller discontinuous plates. Another difference is that where the secondary bronchus lacks plates the submucosal glands will bulge outwards, obscuring the boundary between the adventitia and the submucosa. Also, the elastic membrane is lacking having been replaced by the muscularis mucosa. This will be the case in the smaller branches as well. It will increase in thickness in the smaller branches. The smooth muscle cells of the muscularis mucosa will be interspersed with some elastic fibers. When the muscularis mucosa contracts the mucosa displays longitudinal folding. The secondary bronchi will have a pseudostratified, ciliated columnar epithelium but as the bronchial tree continues to branch this epithelium will diminish in height. The lamina propria is rich in lymphoid cells and has all three fiber types.

c) Tertiary/Segmental Bronchi

Tertiary bronchi will branch off of the secondary bronchi and enter into each segment. They will travel in the connective tissue of the intersegmental septa. These smaller vessels show some modifications from secondary bronchi: They show decreasing cartilaginous plates. They show decreasing epithelial height (although its the same type). They show an increase in the muscularis mucosa.

12.2.6. The Bronchioles

The tertiary bronchioles give rise to several orders of smaller vessels collectively called bronchioles. The lumenal diameters of these passageways become progressively smaller and the walls become increasingly simplified. They lack cartilage plates and very few have seromucus glands in the submucosa. What remains is simply the mucosa surrounded by a bit of loose connective tissue making a up the adventitia. The bronchioles are named (in order of branching): Primary, Secondary, Tertiary, and Terminal Bronchioles. The terminal bronchioles will enter into the respiratory portion of the respiratory system proper.

Histologically, the epithelium is a simple ciliated columnar. It will have some goblet cells but the number of goblet cells will progressively diminish. The goblet cells will be replaced by Clara/Bronchiolar Secretory Cells. Clara cells are dome shaped secretory cells. Their secretions may reduce surface tension on the walls of more distal bronchioles. The muscularis mucosa reaches it's greatest thickness in the tertiary bronchioles and

begins to thin more distally. Bronchioles, especially terminal bronchioles, can alter their lumenal diameter.

12.3. The Respiratory Portion

12.3.1. The Passageways of the Respiratory Portion

The terminal bronchioles will give rise to two orders of Respiratory Bronchioles. Histologically respiratory bronchioles resemble the other types of bronchioles. The major difference is that they show thin walled outpocketings called Alveoli. The number of alveoli will increase with each branching. The portions that lack alveoli show: a simple cuboidal epithelium, a thin lamina propria, and a muscularis mucosa which is heavily laced with elastic fibers. The respiratory bronchioles will give rise to smaller passageways called Alveolar Ducts. The walls of the alveolar ducts have numerous alveoli. There are so many alveoli that there is little space between them and the portions of the walls between adjacent alveoli lack the simple cuboidal epithelium. Instead the wall is lined by a simple squamous epithelium (like that of the alveoli) resting on top of a thin connective tissue containing some smooth muscle fibers. The alveolar ducts terminate in Alveolar Sacs. Alveolar sacs are thin walled structures that contain elastic and reticular fibers. Alveolar sacs lack smooth muscle. It's epithelium is a simple squamous epithelium. Each alveolar sac is composed of several alveoli which will open into a common chamber called the Atrium.

12.3.2. The Alveoli

Alveoli are the site of external respiration. Alveoli are delicate, cup-shaped structures that are lined by an extremely attenuated simple squamous epithelium. A single wall, termed the Interalveolar Septum, is formed between two adjacent alveoli. The interalveolar septum is composed of the cells of the two alveoli and a thin connective tissue component between them. The connective tissue contains many elastic and reticular fibers, a few mast cells, leucocytes, fibroblasts, and an anastomizing capillary network. The interalveolar septum also contains a specialized cell called the Septal Cell. Septal cells superficially resemble fibroblasts. Septal cells contain bundles of actin and myosin which allow them to contract due to hypoxia. However, their function is still unknown. Alveoli communicate through openings called Alveolar Pores. Alveolar pores allow for the equilibration of air pressure within a lung lobule. The alveoli are lined by two cell types:

a) Alveolar Epithelial Cells/Type 1 Alveolar Cells

These are extremely attenuated squamous cells that form the bulk of the alveolar wall. Type 1 cells share a common basement membrane with the endothelial cells of the pulmonary capillaries. The fusion of type 1 cells and endothelial cells forms the Alveolar Membrane/Respiratory Membrane. This is an extremely thin structure (at 0.5 um in thickness) to maximize the diffusive exchange of gases. The pulmonary capillaries are continuous capillaries although they are very thin walled.

b) Secretory Cells/Type 2 Alveolar Cells

These are short, somewhat rounded cuboidal cells. They contain the normal host of organelles found in a secretory cell. Especially prominent are Cytosomes/ Multilamellar Bodies. These organelles produce surfactant a phospholipid rich secretion which reduces surface tension.

c) Local Defense Mechanisms of the Alveolus

Alveolar macrophages are commonly found in the interalveolar septum or on the alveolar cells. In respiratory passages these macrophages dispose of particulate matter and pathogens. Bacteria and viruses are also hindered by the fluids of the alveolus which will contain IgA and interferon. Alveolar macrophages will also play a role in augmenting specific immune reactions of the local lymphoid cell population and of regional lymph nodes. Regional lymph nodes are at their most abundant near the hilus. Both humoral and cell-mediated immunity play a prominent role in the lungs' defense against infection. B cells, T cells, macrophages, mast cells, and other leucocytes produce various antibodies, lymphokines, and other mediators that will promote and regulate inflammation and the immune response.