

Chapter 2

The Human Respiratory System

2.1 Introduction

Before delving into the computational methods of reconstructing the respiratory models, we first discuss the respiratory system from a functional point of view. In addition, descriptions, locations, geometry, and naming conventions for the anatomical parts are discussed in order to establish a basis for decision-making when reconstructing the model. This chapter provides the fundamentals of the anatomy and physiology of the respiratory system and may be skipped if the reader has an established background in this field.

The primary function of the respiratory system is gas exchange. Oxygen (which we need for our cells to function) from the external environment is transferred into our bloodstream while carbon dioxide (a waste product of cellular function) is expelled into the outside air. The billions of tissue cells in our body lie too far from the inhaled air to exchange gases directly, and instead blood circulates the oxygen to the cells. This occurs during each breath we take where oxygen first enters the nose or mouth during inhalation. The air passes through the larynx and the trachea which then splits into two bronchi. Each bronchus bifurcates into two smaller branches forming bronchial tubes. These tubes form a multitude of pathways within the lung and terminating at the end with a connection to tiny sacs called alveoli. The exchange of gases takes place at the alveoli, where oxygen (O_2) diffuses into the lung capillaries in exchange for carbon dioxide (CO_2). Exhalation begins after the gas exchange and the air containing CO_2 begins the return journey through the bronchial pathways and back out to the external environment through the nose or mouth. Secondary functions of the respiratory system include filtering, warming, and humidifying the inhaled air. This includes the vocal cords in the larynx for sound production, lungs for control (or homeostasis) of body pH levels, and the olfactory bulbs in the nose for smell.

The respiratory system can be separated into regions based on function or anatomy (Fig. 2.1). Functionally there is the conducting zone (nose to bronchioles), which consists of the respiratory organs that form a path to conduct the inhaled air into the deep lung region. The respiratory zone (alveolar duct to alveoli) consists of the alveoli and the tiny passageways that open into them where the gas exchange takes

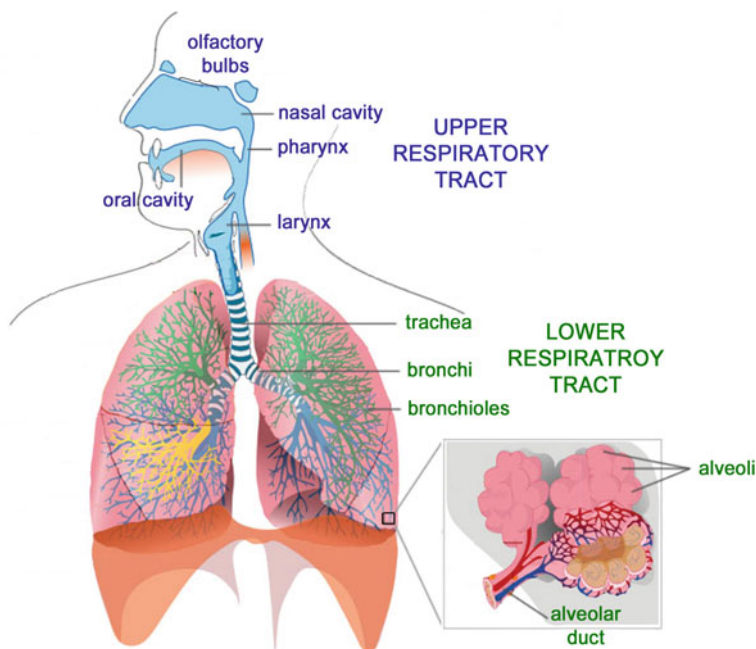


Fig. 2.1 Schematic of the respiratory system displayed by the upper and lower respiratory tract region

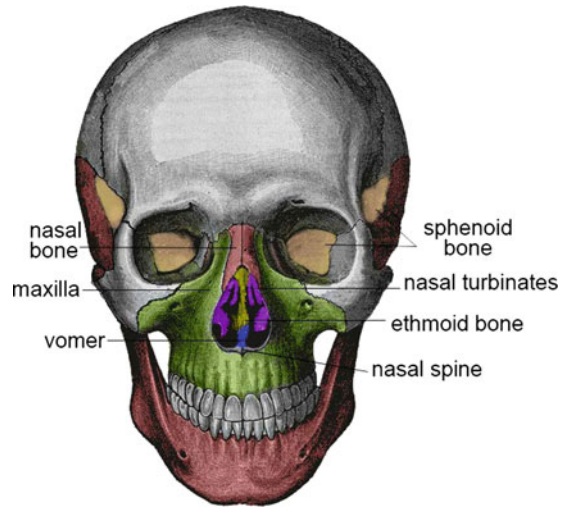
place. Anatomically, the respiratory system can be divided into the upper and lower respiratory tract. The upper respiratory tract includes the organs located outside of the chest cavity (thorax) area (i.e. nose, pharynx, larynx), whereas the lower respiratory tract includes the organs located almost entirely within it (i.e. trachea, bronchi, bronchiole, alveolar duct, alveoli). In the next section, the individual respiratory organs are discussed.

2.2 Nose and Nasal Cavity

2.2.1 Anatomy of the Nose and Nasal Cavity

The human nose differs in its anatomy and morphology between different racial and ethnic groups. Therefore, the following anatomical description is a generalisation and inter-racial variations exist. For completeness, structures that have synonyms are followed by their alternate names in parentheses and italicised. Structurally the nose can be divided into the external portion which is in fact termed as the nose and the internal portions being the nasal cavities (*nasal fossae; cavum nasi*). The nose is the only visible part of the respiratory system, protruding from the face, and lying

Fig. 2.2 Skeletal structure of the human skull showing the nasal cavity and the supporting facial bones



in between the forehead and the upper lip. It is made up of a bony section and a cartilaginous section. The bony section is located in the superior half and contains a pair of nasal bones sitting together side by side, separated in the middle and fused posteriorly by the medial plates of the cheekbones (*maxilla bones*) (Fig. 2.2).

The cartilaginous section is located in the inferior half, consisting of flexible cartilages in the anterior, caudal portion of the nose (Fig. 2.3). The cartilages are connected to each other and to the bones by a tough fibrous membrane. At the base

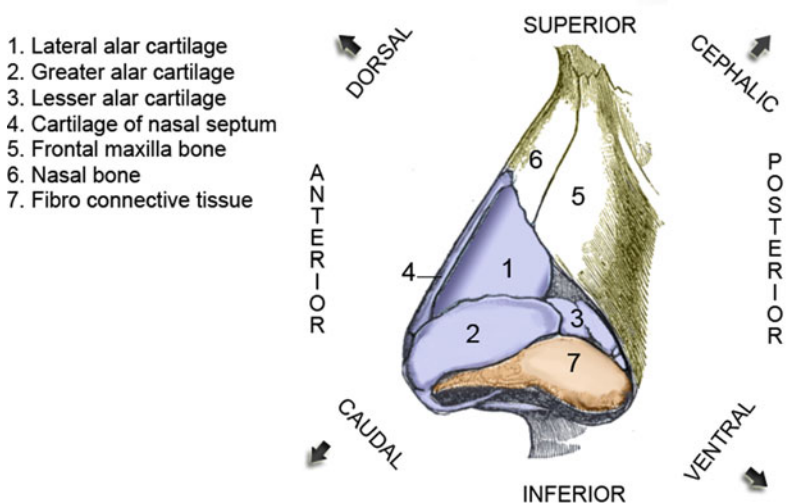


Fig. 2.3 Lateral view of the external nose showing the cartilage and bone structure. Terminology for the anatomical directions is also given

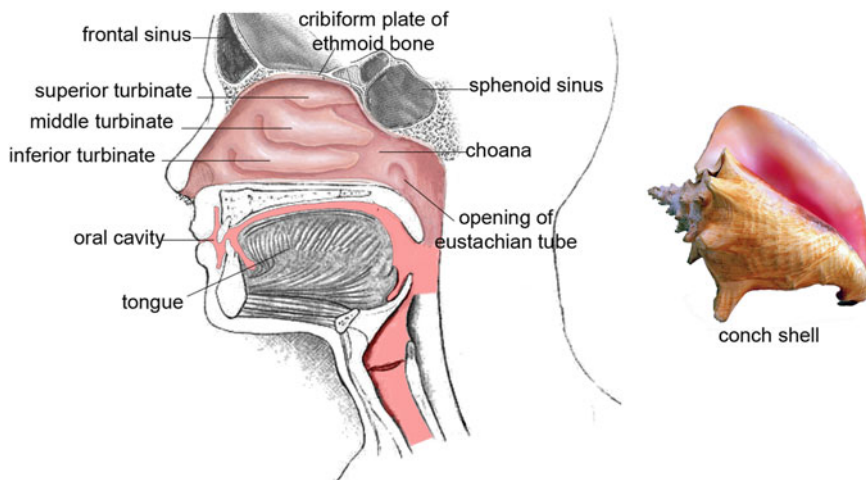


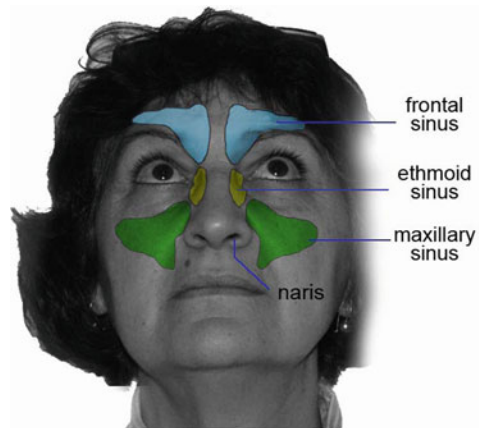
Fig. 2.4 Structure of the internal nasal cavity. The turbinates are also referred to as concha because of its resemblance to a conch shell

of the nose are two openings called the nostrils (*anterior nares*, sing. *naris*) and are separated by nasal septum cartilage (*columna*). The nostrils are a portal for air and particulates to enter the nasal cavity. Its shape can be very elliptical to circular varying between people from different ethnicity and race.

Air enters the nasal cavity through the nostrils, which opens with a slight dilation into an enclosed area called the vestibule. It is enclosed by the greater alar cartilage and extends as a small recess toward the apex of the nose. The two nostril openings and consequently the two vestibules leading to two nasal chambers or cavities are separated by the septum. The anterior septum is primarily made of cartilage (*hyaline cartilage*) but posteriorly is composed of the vomer bone and the perpendicular plate of the ethmoid bone. It is a common occurrence for the septum to be deviated and in severe cases this can lead to nasal dysfunction requiring surgical procedures. The top of the nasal cavity is divided from the anterior cranial cavity by the cribriform plate of the ethmoid bone and the sphenoid bone. The cribriform plate is perforated with many small openings that allow the olfactory nerve branches that are responsible for the sense of smell to extend through to the brain. The lateral walls abut on either side with the maxillary bones, and the floor of the nasal cavity is separated from the top of the mouth by the palatal bones.

From the vestibule the air passes through a constricted cross-sectional area which has been termed the anterior nasal valve, before entering the main nasal passage. In each cavity there are three passageways (superior, middle, and inferior meati; singular, *meatus*) within the main nasal passage, formed by three corresponding curled bony plates that project medially into the main passage way from the septum wall, called the superior, middle and inferior nasal turbinates or conchae (so-called as they are shaped like a conch seashell, Fig. 2.4). At the posterior end of the main nasal

Fig. 2.5 Frontal view of a human face showing the locations of the paranasal sinuses: frontal, ethmoid, and maxillary sinuses



passage are the oval-shaped orifices of the posterior nares, (*choanae*) approximately 1.5–3.0 cm in diameter. The choanae are openings that allow air to pass from the main nasal passage, into the nasopharynx. Once air has passed through the posterior nares, it has left the nasal cavity and enters the next major segment of the upper respiratory tract—the pharynx (Fig. 2.5).

The paranasal sinuses are four pairs of empty air spaces that open or drain into the nasal cavity. They are located in the frontal, sphenoid, ethmoid, and maxillary bones and as such their names are taken from where they are located. The frontal sinuses are located just above the orbit (eye sockets) and don't develop until around the age of seven. The maxillary, the largest of the sinuses extends laterally (into the maxilla) on either side of the nose and is present at birth and grows with the body's development. The sphenoid sinuses lie in the body of the sphenoid bone, deep in the face just behind the nose. This sinus does not develop until adolescence. The ethmoid sinuses are not single large cavities but rather a collection of small air pockets, located around the area of the bridge of the nose. This sinus is also present at birth, and grows with development.

2.2.2 *Physiology of the Nose and Nasal Cavity*

The nose and its internal nasal cavity provides a passageway for the air to pass through to the lungs, warms and moistens (humidifies) the inhaled air, filters and cleans the inhaled air from any foreign particles, resonates sounds for speech, and houses the olfactory receptors for smell. At the entrance of the nasal cavity in the vestibule region, the surface wall is made up of stratified squamous epithelium (same as the external skin) which contains sebaceous glands, and nose hairs (*vibrissae*), serving to filter out inhaled particulates. In the main nasal passage the walls are lined with **respiratory mucosa**. This is made up of a pseudo stratified ciliated

columnar epithelium surface containing interspersed goblet cells that sits atop a lamina propria. The serous glands produce and deliver to the surface a watery fluid containing anti-bacterial enzymes while the mucous glands and goblet cells secrete a slimy, semi-sticky liquid called mucous. Approximately 125 mL of respiratory mucous (*sputum*) is produced daily which forms a continuous sheet called a 'mucous blanket'. The mucous traps any inhaled particulates such as dust, and bacteria, while the antibacterial enzymes destroy the particulates. The ciliated epithelium cells have cilia on their surface which are fine microscopic hair-like projections. These cilia move back and forth in a rhythmical movement (*mucociliary action*) which transport the secreted mucous blanket from the nasal cavity to the throat where it is swallowed into the digestive system. This movement occurs at a rate of about 1–2 cm/h. The respiratory mucosa in the turbinates has a thick, vascular and erectile glandular tissue layer which is subject to tremendous erectile capabilities of nasal congestion and decongestion, in response to the climatic conditions and changing needs of the body. This affects the flow resistance due to the airway passages narrowing or expanding. Near the roof of the nasal cavity in the region from the superior nasal concha and the opposed part of the septum at the olfactory region, the mucosa changes, having a yellowish colour and the epithelial cells are columnar and non-ciliated. This surface is referred to as the **olfactory mucosa** and it contains the sensory receptor cells for smell detection. The cells form the nerves that then pass through the cribiform plate to the olfactory centres within the brain.

Heating and conditioning of the inspired air occurs through a network of thin-walled veins that sits under the nasal epithelium. The superficial location and abundance of the blood vessels causes a natural heat transfer process to the colder inspired air. The turbinates that protrude into the main passage increases the mucosal surface area to enhance the heating and conditioning of the inspired air. The mucous walls are also supplied with sensory nerve endings, which trigger a sneeze reflex when it comes into contact with inhaled particles. The nose is also supplied by nerves capable of detecting pain, temperature and pressure. The surrounding sinuses lighten the skull, and also act as resonating chambers for speech. Each paranasal sinus is lined with the same respiratory mucosa found in the main nasal passage and therefore has the same heating and air conditioning capabilities. Particles can also be trapped by the mucous secretions produced in the sinuses which continually flow into the nose by the ciliated surface. In addition blowing of the nose helps to drain the sinuses.

Smell is another function of the nose. Sensory activity is transmitted via branches of the olfactory nerve, which cross the roof of the nasal cavity through the cribiform plate of the ethmoid bone. During the course of breathing the nasal cavity geometry can be affected by the **nasal cycle**. This physiologic phenomenon which has been reported in more than 80 % of normal individuals (Keay et al. 1987), is an important consideration when a patient undergoes a CT or MRI scan since the scan is an instant snapshot in time of the nasal cavity's physiological state. It also has a significant effect on the airflow through the nasal passage. The nasal cycle is defined

as a cyclic fluctuation in congestion and decongestion of the nasal venous sinusoids ranging over a period of 30 min to 6 h. Airflow through the nasal cavity is normally asymmetrical, where one nasal passage (left or right) is dominant. This asymmetry is referred to as the nasal cycle which is a result of congestion (swelling) of the erectile tissue (cavernous tissues of the mucosa) in one nasal cavity while at the same time decongestion (shrinking) occurs to the erectile tissue in the other cavity. The airflow through the each nasal cavity is then governed by the resistance caused by the cross-sectional area of each airway. The changes in nasal resistance associated with the nasal cycle are not always regular, and the term nasal cycle may be a misnomer, as there is little evidence to indicate a regular periodicity to the changes in nasal resistance (Eccles 1996). The functional role of the nasal cycle is not exactly known but some hypothesis include: a contribution towards respiratory defence during nasal infection (Eccles 1996); and increased contact of inspired air with the mucosa since there is increased airflow through a decongested airway which provides increased levels of turbulence (Lang et al. 2003).

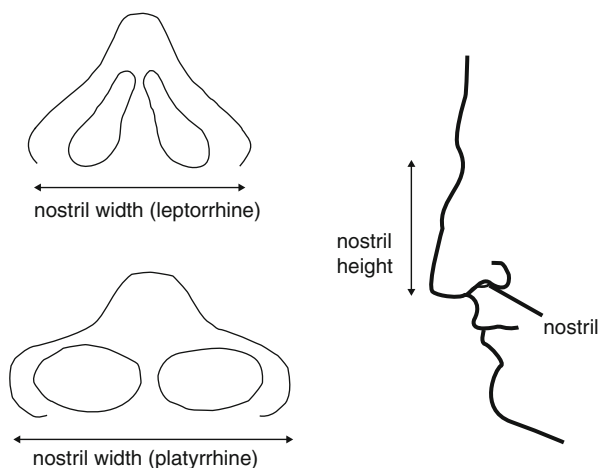
2.2.3 Nasal Cavity Variations and Diseases

Variations and diseases in the human anatomy are vast and this section introduces the reader to some of the possible variations to the nasal cavity that has an effect on the air and particle respiration. This theme is carried throughout the subsequent sections on variations and diseases of the other parts of the respiratory pathway (pharynx, larynx, and tracheobronchial and lung airway).

There have been a large number of studies indicating that morphological variation of the human nose is found among populations from different eco-geographical locations through adaptation to climate (Franciscus and Long 1991a). For example, in cold or dry environments the nose has a large external protrusion, small constricted nostrils, and is tall and narrow (*leptorrhine nose*). The nasal cross-sectional area is smaller to facilitate heat and moisture exchange (Carey and Steegmann 1981). For hot or moist environments, the nose has a small external protrusion, large flaring nostrils, and is short and broad (*platyrrhine nose*) in comparison to leptorrhine noses. The cross-sectional area is greater which reduces the heat transfer during exhalation (Seren and Seren 2009). The nasal index, which compares the width of the base of the nose with the height of the nose, (e.g. $\text{Index} = (\text{width} \times 100)/\text{height}$) is used as a way to determine the nose type. A low index (< 70) indicates a narrow nose and is considered as leptorrhine, and a high index > 85 is considered platyrrhine. In between 70 and 85 the nose is considered mesorrhine. Other morphological differences include differences between males and females, and also one's age (child, adult, elderly) (Fig. 2.6).

Nasal obstruction is the term used for any increased resistance to the airflow that is experienced by a person. The sensation is subjective and can occur from the

Fig. 2.6 Nasal width and height definition used for the nasal index definition. Typical nostril shape for leptorrhine and platyrrhine shaped nostrils are also shown



natural nasal cycle or by sinonasal pathologies. Some common sino-nasal pathologies include:

- deviated septum—where the septum has severely deviated from the midline;
- nasal polyps—abnormal growth of tissues projecting from the mucous membrane in the nasal sinus;
- turbinate/mucosa hypertrophy—increase in the volume of the turbinate/mucosa due to inflammation or abnormal development.

On the other hand atrophic rhinitis is a disease that causes an increase in the nasal airway passageway due to the destruction of the nasal structures such as the nasal mucosa, turbinate bones, and any nerve endings attached to the nose, from a decreased blood supply. A similar occurrence, but caused by human intervention, is empty nose syndrome in which there is an increase in the nasal passageway caused by the over-zealous resection of the turbinates during surgery (Fig. 2.7).

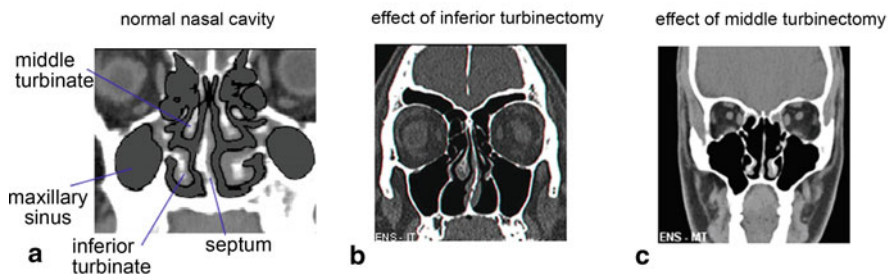


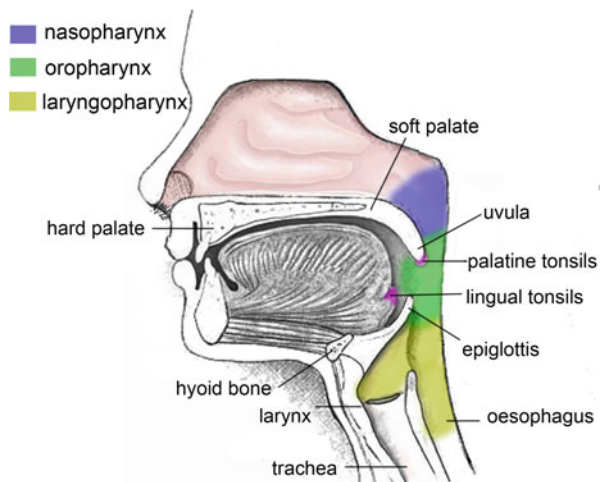
Fig. 2.7 Coronal slice of a CT scan showing **a** nasal cavity without any abnormalities **b** a nasal cavity after having an inferior turbinectomy **c** nasal cavity with the effect of middle turbinectomy. Large empty spaces are evident which contribute towards complaints of *empty nose syndrome*

2.3 Pharynx

2.3.1 Anatomy of the Pharynx

The pharynx (*throat*) is a tubelike structure about 12.5 cm long that connects the posterior nasal and oral cavities to the larynx and oesophagus. It extends from the base of the skull to the level of the sixth cervical vertebrae. Structurally the pharynx can be divided into three anatomical parts according to its location as shown in Fig. 2.8, which are the nasopharynx (posterior to the nasal chambers), the oropharynx (posterior to the mouth), and the laryngopharynx (posterior to the pharynx).

Fig. 2.8 The pharynx and its subdivisions into the nasopharynx, oropharynx, and laryngopharynx



The **nasopharynx** is located between the internal nares and the soft palate and lies superior to the oral cavity. At the base of the nasopharynx are the soft palate and the uvula. At the wall of the nasopharynx are the auditory (Eustachian) tubes connected to the middle ear. The pharyngeal tonsils (adenoids) are located in the nasopharynx on its posterior wall opposite the posterior internal nares. The **oropharynx** is located posterior to the mouth, inferior from the soft palate, and superior to the level of the hyoid bone. At this location the mouth leads into the oropharynx and both food and inhaled air pass through it. The palatine (*faucial*) tonsils lie in the lateral walls of the fauces. The **laryngopharynx** (*hypopharynx*) extends from the hyoid bone to the oesophagus. It is inferior to the epiglottis and superior to the junction where the airway splits between the larynx and the esophagus. The lingual tonsils are found at the posterior base of the tongue which is near the opening of the oral cavity.

2.3.2 Physiology of the Pharynx

The pharynx serves to provide a passageway for both the digestive system and respiratory system since food and air pass through it. The food or air is directed down the

correct passageway, either the oesophagus or the trachea, by being controlled by the epiglottis. The epiglottis is a flap of elastic cartilage tissue that acts as a lid to cover the trachea when food is swallowed in order to prevent objects entering the larynx (see later Sect. 2.4 Larynx). During swallowing, the soft palate and its uvula point upwards closing the nasopharynx so that neither air nor food can pass through it, thus breathing is momentarily stopped. The connection opens and closes to equalise the air pressure in the middle ear to that of the atmosphere for the conduction of sound. The surface of the nasopharynx is covered by pseudo-stratified columnar epithelium. This is the same epithelium found in the nasal cavity and similarly the same mechanism of mucous secretion from goblet cells in the epithelium to filter, warm, and humidify the inhaled air occurs here. In the oropharynx and laryngopharynx, the surface is lined with non-keratinizing stratified squamous epithelium which is needed as it is exposed to food moving through the passageway.

2.3.3 *Variations and Disease of the Pharynx*

Some disease of the pharynx that may have an effect on the airway geometry and airflow includes:

- **Pharyngitis**—Inflammation of the pharynx, which can be acute or chronic with many different causes such as bacteria or viruses. This can result in swelling and redness of the oropharynx and enlarged tonsils, restricting the passageway for breathing and swallowing.
- **Tonsillitis**—Inflammation of the tonsils, which is commonly caused by viral or bacterial infection. The tonsils become enlarged and this restricts the airway opening from the oral cavity to the oropharynx, causing breathing and swallowing problems.
- **Pharyngeal Cancer**—Cancer arising in the pharynx from the squamous epithelial cells can restrict the airway, altering the natural flow of air in the pharynx.

2.4 Larynx

2.4.1 *Anatomy of the Larynx*

The larynx is commonly known as the **voice box** as it houses the vocal folds that are responsible for sound production (*phonation*). It serves as a sphincter in transmitting air from the oropharynx to the trachea and also in creating sounds for speech. It is found in the anterior neck, connecting the hypopharynx with the trachea, which extends vertically from the tip of the epiglottis to the inferior border of the cricoid cartilage (Fig. 2.9). At the top of the larynx is the epiglottis which acts as a flap that

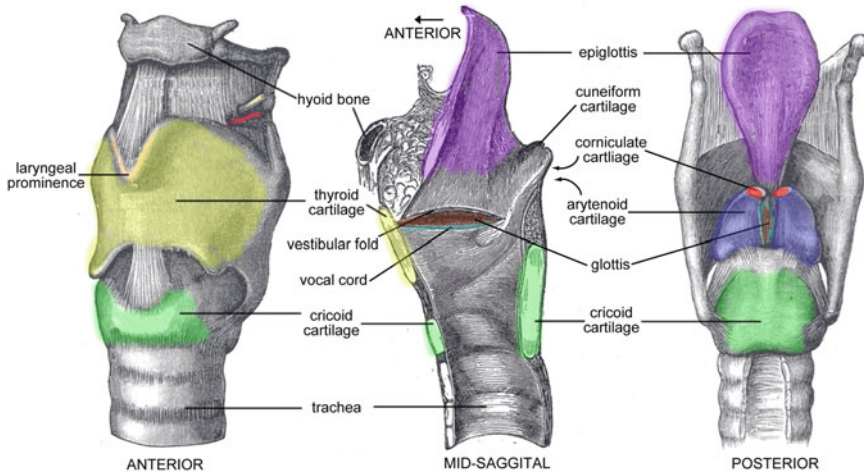


Fig. 2.9 Anterior, mid-sagittal (cut-away) and posterior views of the larynx

closes off the trachea during the act of swallowing to direct food into the oesophagus instead of the trachea. The laryngeal skeleton consists of nine cartilages, three single (thyroid, cricoid, and epiglottis) and three paired (arytenoid, corniculate, and cuneiform), connected by membranes and ligaments. The hyoid bone is connected to the larynx but is not considered part of the larynx. The single laryngeal cartilages are:

- The **epiglottis**—a leaf-shaped piece of elastic cartilage located at the top of the larynx. It is inferiorly anchored at one end between the back of the tongue and the anterior rim of the thyroid cartilage. The free superior end bends up and down like a flap to open and close the opening into the larynx.
- The **thyroid cartilage** (*Adam's apple*)—formed by the fusion of two cartilage plates and is the largest cartilage of the larynx. It is shaped like a triangular shield and is usually larger in males than in females due to male sex hormones stimulating its growth during puberty.
- The **cricoid cartilage**—a signet ring shaped cartilage so-called because the signet end forms part of the posterior wall of the larynx. It is attached to the top of trachea and is the most inferiorly placed of the nine cartilages.

The paired laryngeal cartilages form part of the lateral and posterior walls of the larynx, which are:

- The **arytenoid cartilages**—two upward protrusions located at the back of the larynx. The arytenoid cartilages are attached to the cricoarytenoid muscles, anchored by the cricoid cartilage and attached to the vocal cords. They are the most important because they influence the position and tension of the vocal folds.
- The **corniculate cartilages**—small and cone-shaped hyaline cartilages that sit on top of each of the arytenoid cartilages. During swallowing of food, the epiglottis

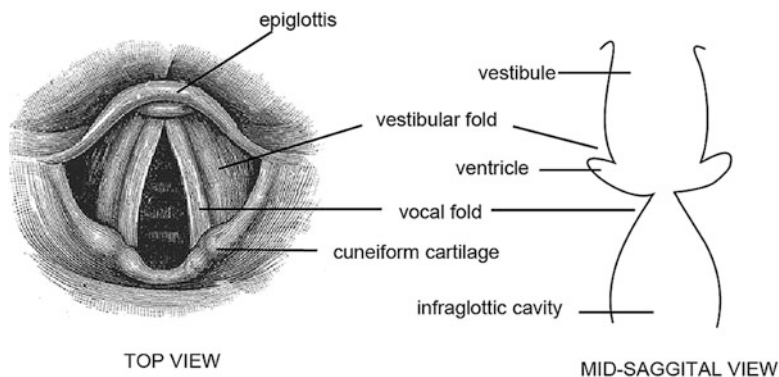


Fig. 2.10 Larynx opening at the glottis, showing the vocal and vestibular folds that separate the region into sub-cavities

bends down and meets the corniculate cartilages to close off the pathway to the trachea.

- The **cuneiform cartilages**—small elongated rod-like elastic cartilages located at the apex of each arytenoid cartilage, and at the base of the epiglottis above and anterior to the corniculate cartilage.

The airway cavity of the larynx extends from a triangular shaped inlet at the epiglottis to a circular outlet inferior to the cricoid cartilage where it is continuous with the lumen of the trachea. Two pairs of mucous membrane foldings stretch inward and horizontally across the larynx. The upper pair of folds are the vestibular folds (*ventricular or false folds*) which only play a minimal role in phonation but protect the more delicate folds below. The lower pair of folds are the true vocal folds, which form a slit-like opening called the glottis. This is the narrowest part of the larynx. The vestibular and vocal folds divide the larynx into (1) the vestibule (upper chamber), located above the vestibular folds; (2) the ventricle, the small middle chamber located between the vestibular and vocal folds; and (3) the infraglottic cavity, which extends from the vocal folds to the lower border of the cricoid cartilage (Fig. 2.10). The vocal cords, are flat triangular bands and white in colour because of their lack of blood supply (avascular) nature. They are attached posteriorly to the arytenoid cartilages, and anteriorly to the thyroid cartilage. The interior surface of the superior portion of the larynx is made up of stratified squamous epithelium which is an area that is subject to food contact. Below the vocal folds the epithelium is pseudo stratified ciliated columnar. Here mucociliary action directs mucous movement upward towards the pharynx, so that the mucous is continually being moved away from the lungs.

2.4.2 Physiology of the Larynx

The ciliated mucous lining of the larynx further contributes towards the respiratory system's ability to remove foreign particles and to warm and humidify the inhaled air

(the same physiological feature as the nasal cavity). During intentional swallowing the back of the tongue that is joined to the top of the larynx, pushes upwards, forcing the epiglottis to close over the glottis, preventing food or foreign objects to enter the larynx. If the items do enter the larynx and contact the vocal folds, stimulation of the larynx muscles causes a cough reflex to try and expel the items in order to prevent choking. The other important function of the larynx is sound generation (*phonation*), where the pitch and volume of sounds are manipulated by the body. Sounds generated at the larynx are caused by the expired air released from the lungs that pass through the glottis and hence the vocal cords. By flexing and reflexing muscles in the larynx, the arytenoid cartilages are forced to pivot at its base (i.e. at the cricoid cartilage) to bring together or separate the vocal cords for speech or breathing respectively. The vocal and cricothyroid muscles then control their length and tension. This variable tension in the vocal cords allows a wide range of pitch and tones to be produced. Generally the tenser the vocal cords, the faster they vibrate and the higher the pitch. As young boy's experience puberty, the larynx enlarges which produces thicker and longer vocal cords. This leads to the cords, vibrating more slowly and his voice becomes deeper. Louder sounds can be achieved through greater exhalation force from the diaphragm, creating stronger vibrations of the vocal cords. Just like guitar strings the vocal cords produce a vibrating buzzing sound and the final sound produced is dependent on the surrounding resonating chambers of the pharynx, mouth, and nose and also the geometry of the tongue and lips.

2.4.3 *Variations and Diseases of the Larynx*

One obvious variation of the larynx is the laryngeal prominence (*Adam's apple*) which is typically larger in men than in women. This protrusion is formed by the angle of the thyroid cartilage, which develops during puberty, protruding out the front of the neck more noticeably. Sound production in males is also usually lower pitched than in women as the male vocal cords are larger than female vocal cords. At birth the larynx is located more superiorly and is further forward (anteriorly) relative to its position in the adult body. As the child grows the larynx shifts downward. Some diseases of the larynx that may have an effect on the airway geometry and airflow includes:

- Laryngitis (acute and chronic)—inflammation and swelling of the larynx caused by the viruses, dust contaminated air, or by excessive shouting.
- Presbylarynx—a condition involving age-related atrophy of the vocal fold tissues of the larynx, resulting in a weak voice and restricted vocal range and stamina.
- Laryngomalacia—a common condition during infancy, where soft, immature cartilage of the upper larynx collapses inward during inhalation, causing airway obstruction.

2.5 Tracheobronchial Tree and Deep Lung Airways

2.5.1 Anatomy of the Tracheobronchial Tree and Lung Airways

The **tracheobronchial tree** is the structure from the trachea, bronchi, and bronchioles that forms the upper part of the lung airways. It is referred to as a tree because the trachea splits into the right and left main bronchi, which further bifurcates or branches out into more progressively smaller airways. It is an asymmetric dichotomous (splitting of a whole into exactly two non-overlapping parts) branching pattern, with the daughter bronchi of a parent bronchus varying in diameter, length, and the number of divisions. The bronchial generation is normally referred to by a number, indicating the number of divisions from the trachea, which is assigned as generation number 0 or 1 as found in the literature.

The **trachea** (*windpipe*) is a hollow tube about 11–14 cm long connecting from the cricoid cartilage in the larynx to the primary bronchi of the lungs. Its cross-sectional diameter in normal human adult males is 1.3–2.5 cm in the coronal plane and 1.3–2.7 cm in the sagittal plane, while for females the diameters are slightly smaller (1.0–2.1 cm and 1.0–2.3 cm for coronal and sagittal diameters respectively) (Breatnach et al. 1984). The variation in the trachea cross-section between the coronal and sagittal plane is due to its shape being a horse-shoe where the anterior side is made up of C-shaped cartilaginous rings, and posteriorly by a flat band of muscle and connective tissue called the posterior tracheal membrane, closing the C-shaped rings. There are 16–20 tracheal rings, which hold and support the trachea preventing it from collapsing in on itself but also provides some flexibility for any neck movement. Further downstream, along subsequent bronchi, the cartilage support becomes progressively smaller and less complete. The tracheal mucosa consists of pseudo stratified, ciliated columnar epithelium, while its submucosa contains cartilage, smooth muscle, and seromucous glands.

The trachea divides into the **main bronchi** (*primary bronchi*) at the carina, with the right bronchus wider, shorter and more vertical than the left bronchus (Moore and Dalley 2006) (mean lengths of ~ 2.2 cm and ~ 5 cm respectively). This leads to increased chances of inhaled foreign particles depositing within the right bronchus. The right main bronchus bifurcates posterior and inferiorly into the right upper lobe bronchus and an intermediate bronchus. This bifurcation occurs earlier on the right than on the left lung in all models.

The left bronchus passes inferolaterally at a greater angle from the vertical axis than the right bronchus. It is located anterior to the oesophagus and thoracic aorta and inferior to the aortic arch. Each main bronchi leads into the lung on its respective side (Fig. 2.11). The right main bronchus subdivides into three lobar (*secondary*) bronchi (right upper lobe bronchus, right middle lobe bronchus, and right lower lobe bronchus) while the left main bronchus divides into two (left upper lobe bronchus and left lower lobe bronchus). Each lobar bronchus serves as the airway to a specific lobe of the lung.

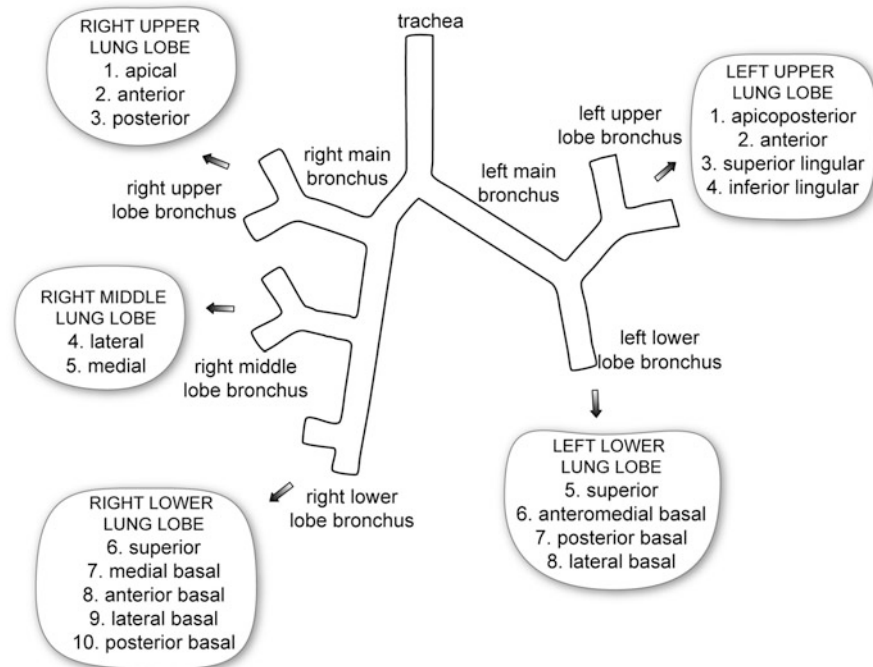


Fig. 2.11 Schematic of the tracheobronchial airway showing the subdivisions in the first three generations and where the branches lead into the segments of the lung, subsequently called the bronchopulmonary segments. The right lung has three lobes and approximately ten segments. The left lung has two lobes and approximately eight segments

The lobar bronchi further divide into segmental bronchi (*tertiary bronchi*), which supply the bronchopulmonary segments of each lobe. Figure 2.12 and 2.13 show the first three generations of the tracheobronchial tree in the left and right lung respectively. A bronchopulmonary segment may be defined as an area of distribution of any bronchus (Jackson and Huber 1943). Technically there are ten bronchopulmonary segments in each lung, however in the left lung some of these segments fuse and there are as few as eight bronchopulmonary segments. The bronchi continually divide into smaller and smaller bronchi up to about 23–24 generations of divisions from the main bronchi. As the bronchi become smaller, their structure changes:

- the cartilaginous rings that support the branches turn into irregular plates of cartilage and eventually disappear by the time bronchioles are reached (~ 1 mm in diameter). When the bronchi eventually lose all support (usually between generations 12–15) the airways are then referred to as bronchioles (Vanpeperstraete 1974);
- the epithelium changes from pseudo stratified columnar to columnar and then to cuboidal in the terminal bronchioles. There are no cilia or mucous producing cells

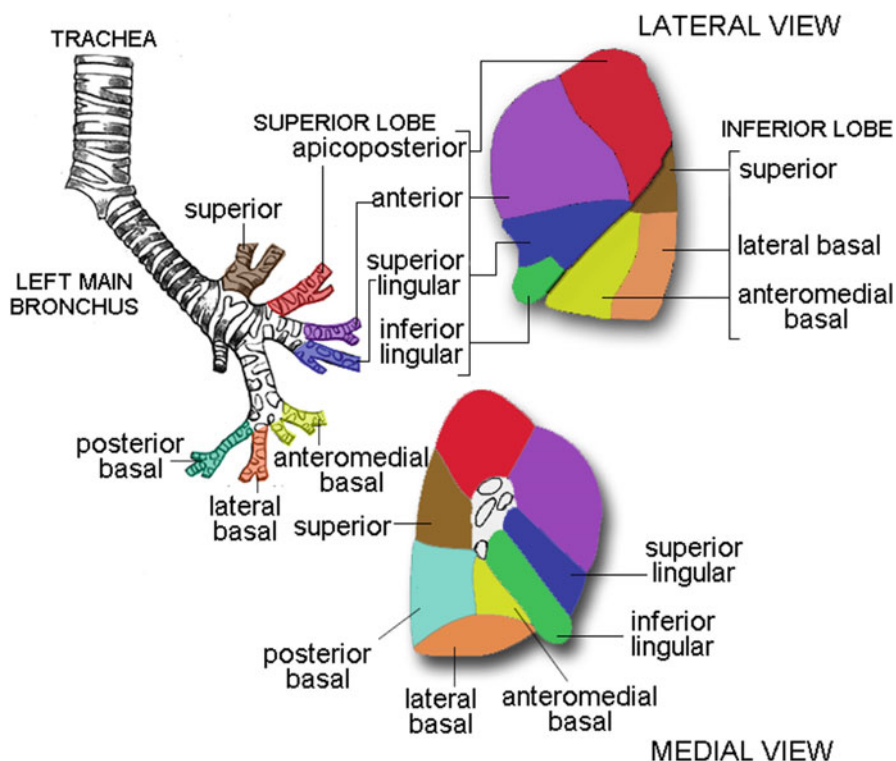


Fig. 2.12 Left segmental bronchi and its attachment to the left lung segments

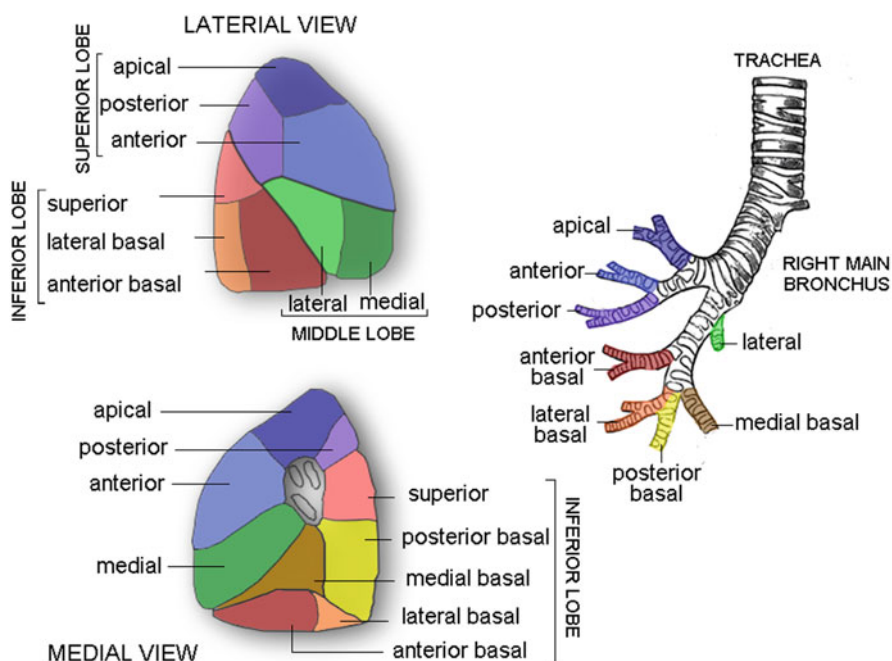
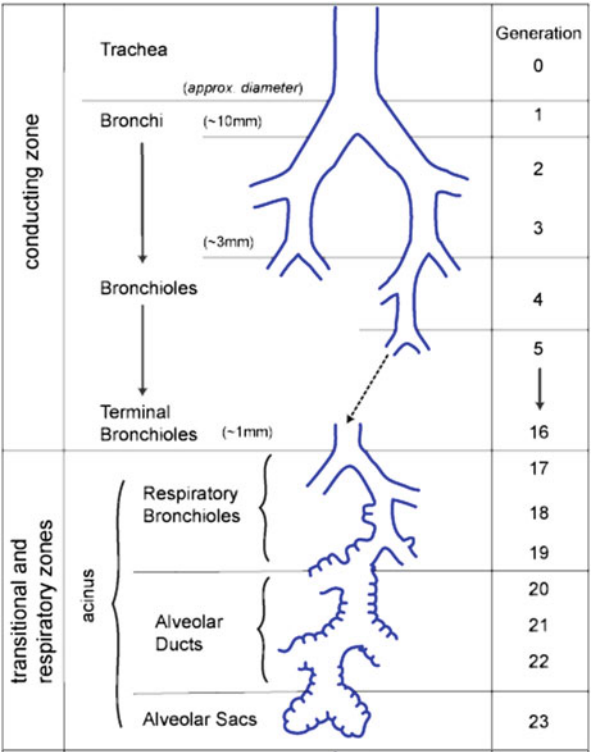


Fig. 2.13 Right segmental bronchi and its attachment to the right lung segments

- in the bronchioles and foreign particles are removed by macrophages located in the alveoli instead of mucociliary action;
- The amount of smooth muscle in the tube walls increases as the passageways become smaller.

The passageway from the trachea, bifurcating into the right and left main bronchi, which further divide into lobar, then segmental bronchi and continues this bifurcating process down to the terminal bronchioles (which are the smallest airways without alveoli) is called the *conducting airways* (Fig. 2.14). In this area, gas exchange does not take place because no alveoli are present, and it contributes to the *anatomic dead space* which takes up approximately 150 mL in volume.

Fig. 2.14 Schematic of the airway generations in the human adult lung. On average, a total of 21–25 generations are found between the trachea and the alveoli. (Redrawn from Weibel 1963)



The terminal bronchioles that divide into respiratory bronchioles are also called transitional bronchioles as they have occasional alveoli present at the walls. The respiratory bronchioles further divide into alveolar ducts which are completely lined with alveoli. This region is the *acinus* (meaning berry in Latin) region because of the cluster of cells that resemble a knobby berry, like a raspberry. It includes all parts distal to a single terminal bronchiole and on average is beyond the sixteenth generation (Haefeli-Bleuer and Weibel 1988). The acinus is therefore comprised of respiratory airways and forms the functional tissue of the lung, or, the lung parenchyma. It extends only a few millimetres for about eight generations with the first three

generations consisting of respiratory bronchioles (Sznitman 2008). In total the respiratory zone makes up most of the lung, with its volume being about 2.5–3 litres during rest (West 2008) in comparison to the conducting airways that make up 150 mL (anatomic dead space). The alveolar ducts are short tubes that are supported by a rich matrix of elastic and collagen fibres. The distal end of the alveolar duct opens into the alveolar sac, which is made up of an atrium and the alveoli (Fig. 2.15). The walls between adjacent alveoli have tiny holes known as *pores of Kohn* that serves as additional ventilation by allowing in air between the alveoli. This is the terminating end of all airway passages in the respiratory system. Because exchange takes place in the acinus, the area is surrounded by a rich network of blood capillaries. It has been estimated that each adult lung has about 300 million alveoli, with a total surface area for gas exchange of 70–80 m².

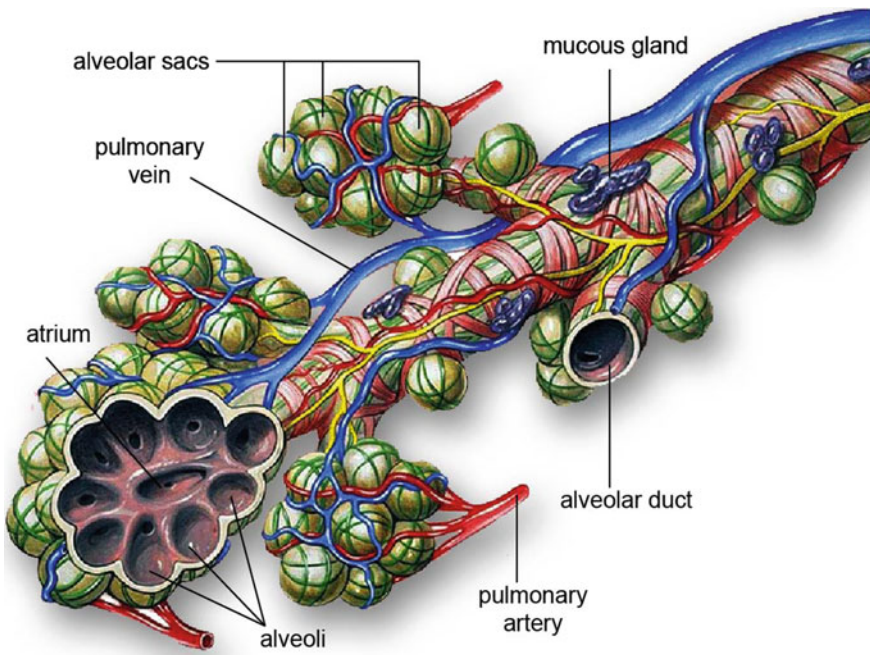


Fig. 2.15 Acinus region showing the alveolar ducts, and a cutaway of the alveolar. (Original drawing courtesy of Patrick J. Lynch, medical illustrator)

2.5.2 Physiology of the Tracheobronchial Tree and Lung Airways

The tracheobronchial tree conducts the inspired air to and from the alveoli. During inhalation the distal end and bifurcation of the trachea are displaced downwards, which is important for facilitating inspiration (Harris 1959). The epithelial changes in the bronchi reflect the physiological functions of the airway. For example the ciliated columnar epithelium in the early branch generations allow for both heating

and conditioning of the air as well as filtering through mucociliary action to remove mucous secretions in an upward motion towards the oesophagus. In the distal branches, the epithelium becomes cuboidal to allow for gas exchange. The cartilage support around the trachea and early branches also changes, progressively diminishing in order to maintain patency of the smaller airways. During gas exchange oxygen is brought into the body and is exchanged with carbon dioxide that is produced from cell metabolism. This occurs in the alveolar-capillary network which consists of a dense mesh-like network of the respiratory bronchioles, the alveolar ducts, the alveoli, and the pulmonary capillary bed. At the gas exchange surface of the alveoli is a lining that is 1–2 μm thick where O_2 and CO_2 passively diffuse across and into plasma and red blood cells. The diffusion occurs between the alveolar gas and blood in the pulmonary capillaries within less than one second.

2.5.3 Variation and Disease of the Tracheobronchial Tree and Lung Airways

The cross-section of the trachea typically has a coronal-to-sagittal diameter ratio of 0.6:1.0, and narrowing of the coronal diameter producing a coronal/sagittal ratio of <0.6 is then termed a sabre sheath trachea and is seen in patients with chronic obstructive pulmonary disease (Brant and Helms 2007). A slight tracheal deviation to the right after entering the thorax can be a normal radiographic finding and in some instances, the presence of the aortic arch can lead to the left lateral wall of the distal trachea being indented by the transverse portion of the aortic arch. In younger individuals the trachea is elastic and extensible, while in older people it is more rigid or even sometimes ossified, so that it is less distensible (Franciscus and Long 1991b). There are many reported diseases of the lung airways (*pulmonary disease*) ranging from the common cold to life-threatening examples such as bacterial pneumonia or cancer, and include:

- Chronic Obstructive Pulmonary Disease (COPD)—One of the most common pulmonary diseases (e.g. bronchitis, emphysema and asthma), resulting in the inflammation of the airways which in turn causes narrowing and obstruction of the airways, seriously affecting the capacity for normal respiratory function.
- Restrictive lung disease (*interstitial lung disease*)—is a disease of the lung parenchyma (covering layer of the lungs), and the connective tissue that hold the air sacs together. This results in a decreased ability to breathe in because of incomplete lung expansion and increased lung stiffness.
- Respiratory tract infection—any infection that can affect any part of the respiratory system such as viral or bacterial. This is normally categorised as an upper respiratory tract infection (nose, sinus, pharynx, larynx) or a lower respiratory tract infection. The most common lower respiratory tract infection is pneumonia.
- Lung cancer—is a disease of uncontrolled cell growth in tissues of the lung. The collection of these cells forms a tumour which is either malignant or benign. The

spread of the disease to other tissues in the lung and even other body organs has serious health effects and from a respiratory perspective results in a decline in all aspects of respiratory function.

2.6 Respiration Physiology

2.6.1 Lung Volumes and Capacity

The lungs can be measured for different lung volumes and its value is important when deciding on what flow rates and conditions are needed for CFPD settings. Normally lung volumes are measured with a spirometer, and its lung capacity is then inferred from the measurements. Figure 2.16 shows a typical tracing measured from a spirometer. There are five volumes and four capacities used to define the lung space. They are:

- Tidal Volume (TV) is the amount of volume that is inspired and exhaled during normal quiet breathing. 7–9 mL/kg of ideal body weight $\sim 8\text{--}10\%$ of TLC
- Inspiratory Reserve Volume (IRV) is the maximum volume that can be inhaled above the tidal volume.
- Expiratory Reserve Volume (ERV) is the maximum volume that can be expired after the expiration of a tidal volume.
- Residual Volume (RV) is the volume left in the lungs after maximum expiration.
- Functional Residual Capacity (FRC) is the volume of air left in the lungs that can be exhaled after normal expiration.
- Inspiratory Capacity (IC) is the volume of maximum inhalation.
- Vital Capacity (VC) is the volume of maximum inhalation and exhalation.
- Total Lung Capacity (TLC) is the maximum volume in the lungs.

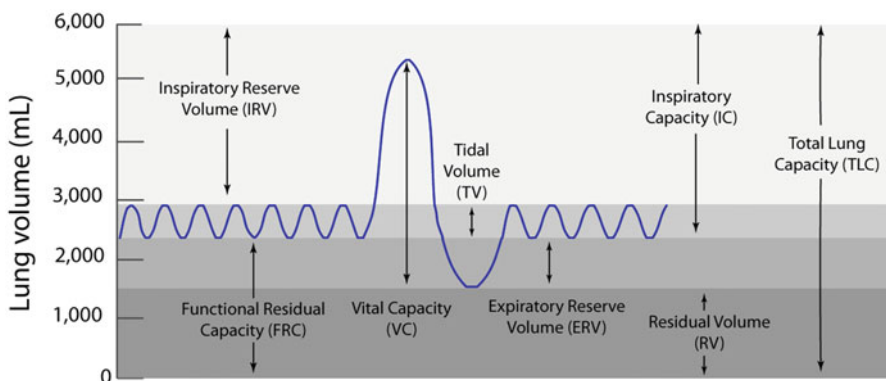


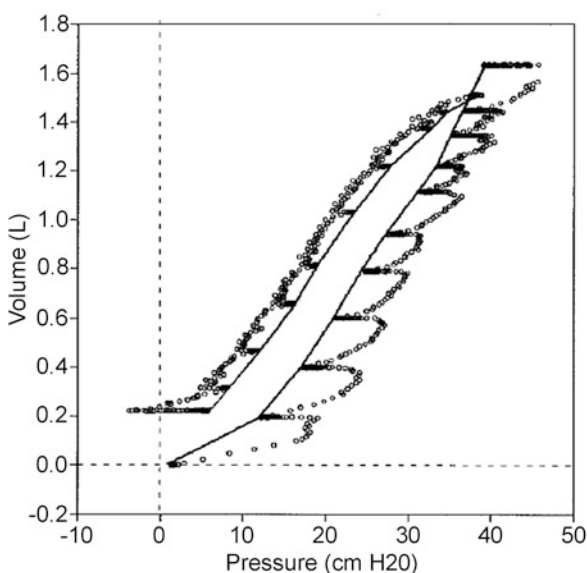
Fig. 2.16 Static lung volumes and capacity tracing measured by a spirometer. The vertical axis is the volume and the horizontal axis is time

2.6.2 Mechanics of Breathing

Inhalation is initiated by the contraction of the diaphragm which contracts and descends about 1 cm during normal breathing and up to 10 cm on forced breathing. The diaphragm lines the lower part of the thorax, sealing it off air-tight from the abdominal cavity below. Its contraction causes muscles in the thorax to pull the anterior end of each rib up and outwards enlarging its volume. As a result, the pressure inside the thorax (intrathoracic pressure) and inside the lungs (intrapulmonary pressure) decreases relative to the outside atmospheric air pressure. The pressure difference induces the inhaled air from a higher pressure to a lower pressure in order to equalise the pressure. During exhalation the lung and chest wall return to its equilibrium position and shape. The thoracic cavity volume is reduced and the pressure builds up to release the air from the lungs. In quiet breathing only the elastic recoil of the lung and chest walls is needed to return the thorax to equilibrium (a passive process). However in forceful expiration additional muscles (intercostals) in the thorax and abdomen are also used to further increase the pressure.

A pressure-volume curve can be used to obtain information about how the lung deforms during breathing. It can describe the mechanical behaviour of the lungs and chest walls such as the elasticity of the lung, and its ability to expand and stretch (distensibility) through the slope of the pressure-volume curve. This is referred to as lung compliance (C_L) and has units of mL/cm H₂O to reflect the change in lung volume (ΔV) as a result of a change in the pressure (ΔP) of the lung (e.g. $C_L = \Delta V / \Delta P$). A pressure-volume curve from the literature (Harris 2005) is shown in Fig. 2.17. A high compliance value refers to a lung that is easily distended and is reflected with a steep pressure-volume curve. A low compliance means that

Fig. 2.17 Pressure-volume curve taken from Harris (2005) acquired with the super-syringe method. The open circles are the data points plotted continuously during the maneuver. The solid lines show the quasi-static points connected to form a smooth P-V curve. The inflation and deflation points are not connected, because they were performed separately in this example



the lung is ‘stiff’, and is not easily distended with a flat pressure-volume curve. When reading the compliance slope the lung volume must be considered, since at low lung volumes the lung distends easily, but at high lung volumes large changes in pressure only produce small changes in lung volume. This is because at high lung volumes the all alveolar and airways have been maximally stretched. To account for the variations in volume, specific compliance (compliance divided by the lung volume usually FRC) is used.

2.6.3 Airflow Dynamics and Resistance

Airflow through the respiratory system is driven by the pressure difference from one end to the other. During respiration, the glottis at the larynx opens allowing gas flow to enter from the upper respiratory tract into the lung airways. The flow in the airway can be defined as laminar or turbulent. Laminar flows are characterised by smooth streamlines while turbulent flows have eddies and fluctuations within the flow. In straight tubular or pipe flows this flow regime can be defined by the Reynolds number,

$$\text{Re} = \frac{\rho DU}{\mu} \quad (2.1)$$

where ρ is the density, D is the hydraulic diameter, U is the average velocity, and μ is the dynamic viscosity. For a given fluid with constant density and viscosity, increases in the flow velocity contributes to the flow becoming turbulent. While in the smaller airway bronchi and even bronchioles, the small diameters will essentially damp out the inertial effects and contribute towards a laminar flow. Fluid flow regimes are discussed in further detail in Sect. 5.3.

Airflow resistance in the respiratory airways is a concept that describes the opposition to air flow from its inhalation point to the alveoli, caused by frictional forces. It has the unit $\text{cm H}_2\text{O s/L}$ and is defined as the ratio of the driving pressure to the flow rate,

$$R = \frac{\Delta P}{\dot{V}} \quad (2.2)$$

where \dot{V} is the flow rate given in L/s. For a laminar flow, the flow rate can be estimated through Poiseuille’s law by:

$$\dot{V} = \frac{\Delta P \pi r^4}{8 \mu L} \quad (2.3)$$

where r is the radius, and L is the airway length. It is therefore apparent that the resistance is inversely proportional to the fourth power of the radius and that a change in the airway geometry will have a greater effect in comparison to the other

variables. Therefore airway resistance decreases as lung volume increases because the airways distend as the lungs inflate, and wider airways have lower resistance. For turbulent flow, resistance is relatively large because a larger driving pressure is needed to produce the same flow rate in comparison with a laminar flow. There is no simple resistance relationship for turbulent flow since the pressure-flow relationship ceases to be linear.

High resistance that causes problems in respiration function may be a sign of obstructed pulmonary diseases such as asthma. While it is not applicable to control the airway geometry, other variables such as the inhaled gas mixture can be controlled for certain applications. It has been shown in clinical and theoretical studies (Jaber 2001; Sandeau et al. 2010) that there are benefits of helium–oxygen gas mixtures to improve respiratory assistance because the helium–oxygen gas mixture has a smaller density and higher viscosity in comparison to air. This can result in a lowering of respiratory effort, and assist in breathing for patients with obstructive lung diseases.

2.6.4 Gas Exchange

Gas exchange during the respiration process takes place in the alveolus at its surface that separates the alveolus with the capillary. In addition each alveolus is smaller than a grain of salt, in which there are approximately 300 million of them in the lungs. Each alveolus is optimised for gas exchange by having a thin moist surface and a very large total surface area in total. The surfaces of the alveoli are covered with a network of capillaries which are narrow blood vessels. Oxygen is passed from the alveoli into the surrounding capillaries that contains oxygen deprived, carbon dioxide rich blood passed from the heart. Gas exchange takes place where the oxygen is dissolved in the water lining of the alveoli before it diffuses into the blood while carbon dioxide is removed from the blood and into the alveoli where it leaves the body during exhalation. After leaving the lungs, the refreshed blood is now oxygen-rich and returns back to the heart before it is redistributed to tissues in the human body (Fig. 2.18).

The exchange of O_2 and CO_2 occurs through diffusion which is the net movement of gas molecules from a region that has a higher partial pressure to another region that has a lower partial pressure. For example the partial pressure of oxygen in the inspired air within the alveolar spaces in the lung is greater than the partial pressure of oxygen in the blood which enables oxygen to diffuse into the red blood cells. The diffusion process is defined by Fick's law of diffusion which states that the diffusion of a gas across a boundary is directly related to its surface area (A), the diffusion constant of the specific gas (D), and the partial pressure difference of the gas on each side of the boundary ($P_1 - P_2$), and inversely related to the boundary thickness (T):

$$\text{Diff} \propto \frac{AD(P_1 - P_2)}{T} \quad (2.4)$$

Because the process is at a molecular level, the gas moves randomly in the direction of the partial pressure gradient, and is temperature dependent. This occurs until there

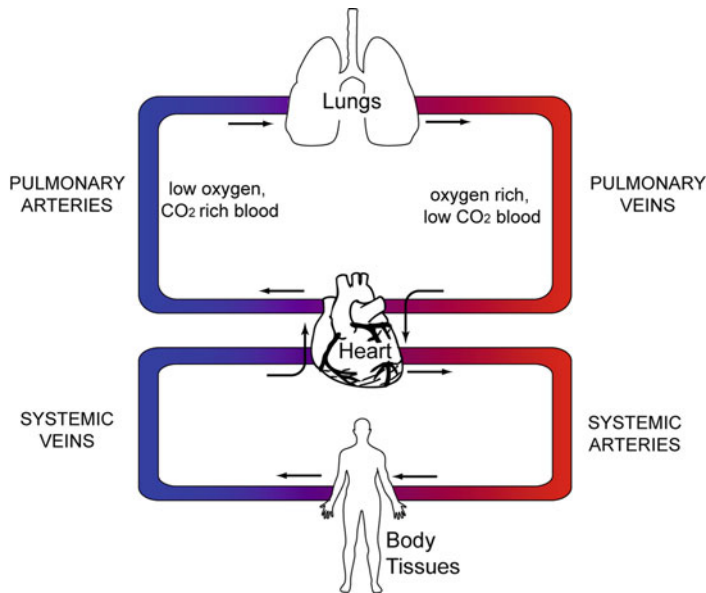


Fig. 2.18 Schematic of blood flow from the body through the heart and lungs. Gas exchange takes place in the lungs which changes the state of the blood from being low in oxygen to highly rich in oxygen

is equilibrium and there is no longer a pressure gradient. As the gas enters the alveoli, it is slowed down due to an increased in cross-sectional area of the alveolar sacs. This lack of inertia assists in the gas moving across the $1\ \mu\text{m}$ alveolus-capillary interface by diffusion (Fig. 2.19).

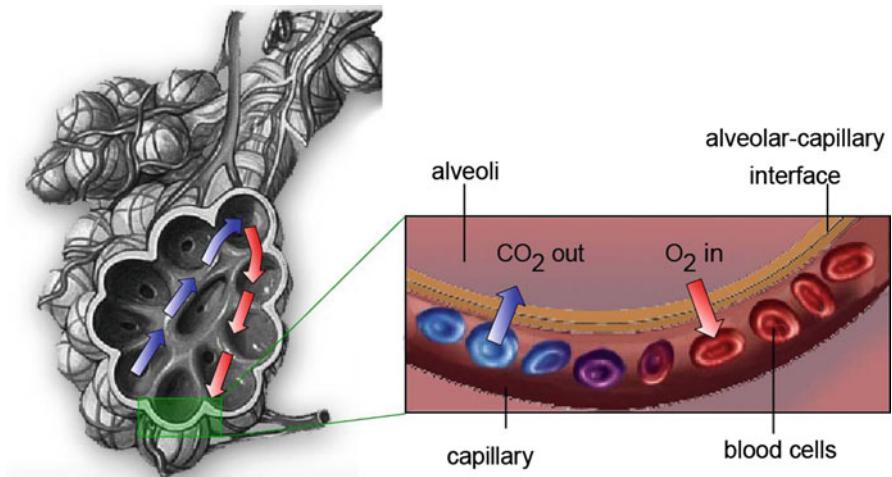


Fig. 2.19 Oxygen and carbon dioxide gas exchange taking place at the alveolar-capillary interface in the deep lung airways

2.7 Summary

The primary function of the respiratory system is to supply the body with oxygen and remove carbon dioxide. During inspiration outside air is inspired into the body which travels from either the nose or mouth down to the lungs. The organs of the respiratory system can be divided functionally into the conducting zone and the respiratory zone. The conducting zone is the airway from the nose or mouth down to the bronchioles and is significant for CFPD as its anatomy and physiology is responsible for transporting air and any foreign particles. The respiratory zone includes the respiratory bronchioles down to the alveoli, where gas exchange takes place through a diffusion process.

The primary aim of this chapter is to summarise the important features of respiration by presenting the anatomy and physiology of the respiratory system. It by no means is a replacement for comprehensive anatomy and physiology study. However it is hoped that the reader has gained enough understanding of the anatomy and physiology of the respiratory system, and the mechanics of breathing, in order to reconstruct any section of the respiratory airway. Furthermore the physiology, variations and diseases of the respiratory organs should be taken into account as it influences many settings for computational modelling. Now that some theory of the respiratory system has been covered, the first step in CFPD, reconstruction of the airways, is presented in the next chapter. Techniques in extraction of data from CT or MRI scans and how to create the 3D model will be given.

2.8 Review Questions

1. What organs make up the upper and lower respiratory system?
2. What parts of the respiratory system does the *conducting airway* consist of?
3. The left and right chambers of the nasal cavity are separated by what bone? What material is it made of?
4. Based on the human nasal cavity geometry, describe in general the path inhaled air may take?
5. Which physiological functions of the nose may need to be considered when modelling the inhalation process in CFPD?
6. What factors can influence the nasal cavity geometry?
7. What are the anatomical parts that make up the pharynx? Of these three, which one connects to the nasal cavity, and which one connects to the oral cavity?
8. What physiological function does the pharynx serve, and how do you think this would be modelled in CFPD?
9. Draw a mid-sagittal plane view schematic of the larynx. Do you think the flow entering into the infraglottic cavity will be fast or slow? Why?
10. Describe the geometry of the trachea—what kind of shape surrounds it? If a smooth pipe was used instead, do you think more or less particles will deposit in the trachea?

11. Name the subregions or lung lobes that make up the lungs.
12. What is supporting structure that holds the early bronchi such as the primary bronchus, in place? When does this support disappear?
13. In most CFPD models, the respiratory walls are smooth and rigid. Describe the surface of a realistic tracheobronchial airway walls. What considerations would you need to make when reviewing the CFPD flow and particle results?
14. In the physiology of respiration, describe the difference between Tidal Volume and Total Lung Capacity.
15. Discuss in the terms of pressure difference, how respiration occurs within the lungs.
16. Referring to the Reynolds number, do you think the bronchiole airways will increase or decrease the inertial effects of the flow in comparison with the primary bronchi?
17. What is the transport process that allows the exchange of O_2 and CO_2 gas and in which anatomy does this occur?

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