SECTION 3

Intake of raw materials and elimination of waste

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CHAPTER 10

The respiratory system

ANIMATIONS

This chapter describes the structure and functions of the respiratory system.

The cells of the body need energy for all their metabolic activities. Most of this energy is derived from chemical reactions, which can only take place in the presence of oxygen (O_2). The main waste product of these reactions is carbon dioxide (CO_2). The respiratory system provides the route by which the supply of oxygen present in the atmospheric air enters the body, and it provides the route of excretion for carbon dioxide.

The condition of the atmospheric air entering the body varies considerably according to the external environment, e.g. it may be dry or moist, warm or cold, and carry varying quantities of pollutants, dust or dirt. As the air breathed in moves through the air passages to reach the lungs, it is warmed or cooled to body temperature, saturated with water vapour and 'cleaned' as particles of dust stick to the mucus which coats the lining membrane. Blood provides the transport system for O_2 and CO_2 between the lungs and the cells of the body. Exchange of gases between the blood and the lungs is called *external respiration* and that between the blood and the cells *internal respiration*. The organs of the respiratory system are:

- nose
- pharynx
- larynx
- trachea
- two bronchi (one bronchus to each lung)
- bronchioles and smaller air passages
- two lungs and their coverings, the pleura
- muscles of breathing – the intercostal muscles and the diaphragm.

Figure 10.1 shows the organs of the respiratory system and associated structures. **10.1, 10.2**

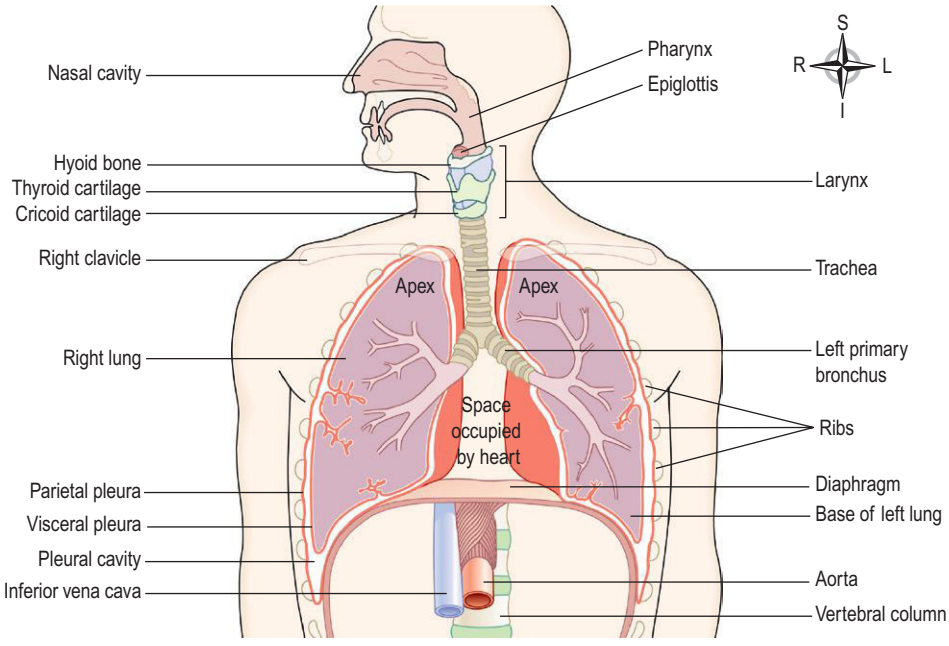


Figure 10.1 Structures associated with the respiratory system.

The effects of ageing on respiratory function are described on p. 261, and important respiratory disorders on p. 262.

Nose and nasal cavity

Learning outcomes

After studying this section, you should be able to:

- describe the location of the nasal cavities
- relate the structure of the nasal cavities to their function in respiration
- outline the physiology of smell.

Position and structure

The nasal cavity is the main route of air entry, and consists of a large irregular cavity divided into two equal passages by a *septum*. The posterior bony part of the septum is formed by the perpendicular plate of the ethmoid bone and the vomer. Anteriorly, it consists of hyaline cartilage (Fig. 10.2).

The roof is formed by the cribriform plate of the ethmoid bone and the sphenoid bone, frontal bone and nasal bones.

The floor is formed by the roof of the mouth and consists of the hard palate in front and the soft palate behind. The hard palate is composed of the maxilla and palatine bones and the soft palate consists of involuntary muscle.

The medial wall is formed by the septum.

The lateral walls are formed by the maxilla, the ethmoid bone and the inferior conchae (Fig. 10.3).

The posterior wall is formed by the posterior wall of the pharynx.

Lining of the nasal cavity 10.3

The nasal cavity is lined with very vascular *ciliated columnar epithelium* (ciliated mucous membrane, see Fig. 10.12, respiratory mucosa) which contains mucus-secreting goblet cells (p. 249). At the anterior nares this blends with the skin and posteriorly it extends into the nasal part of the pharynx (the nasopharynx).

Openings into the nasal cavity

The anterior nares, or nostrils, are the openings from the exterior into the nasal cavity. Nasal hairs are found here, coated in sticky mucus.

The posterior nares are the openings from the nasal cavity into the pharynx.

The paranasal sinuses are cavities in the bones of the face and the cranium, containing air. There are tiny openings between the paranasal sinuses and the nasal cavity. They

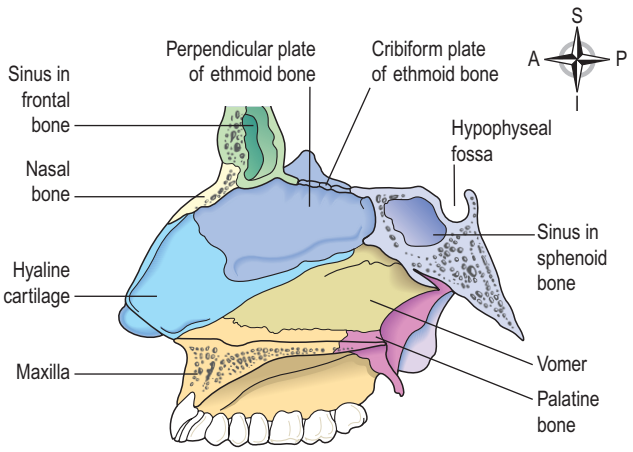


Figure 10.2 Structures forming the nasal septum.

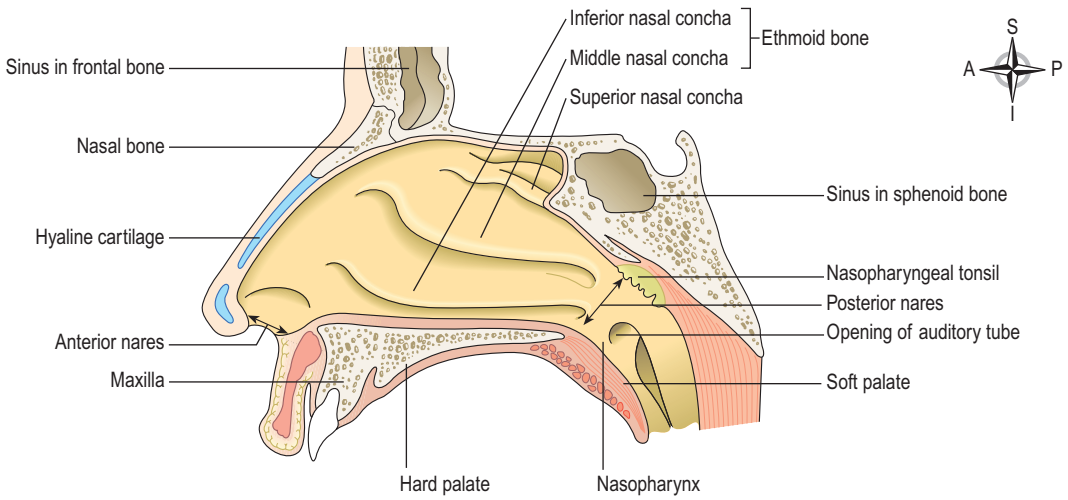


Figure 10.3 Lateral wall of right nasal cavity.

are lined with mucous membrane, continuous with that of the nasal cavity. The main sinuses are:

- maxillary sinuses in the lateral walls
- frontal and sphenoidal sinuses in the roof (Fig. 10.3)
- ethmoidal sinuses in the upper part of the lateral walls.

The sinuses are involved in speech (p. 248) and also lighten the skull. *The nasolacrimal ducts* extend from the lateral walls of the nose to the conjunctival sacs of the eye (p. 204). They drain tears from the eyes.

Respiratory function of the nose

The nose is the first of the respiratory passages through which the inspired air passes. In the nasal cavity, air is warmed, moistened and filtered. The three projecting *conchae* (Figs 10.3 and 10.4) increase the surface area and cause turbulence, spreading inspired air over the whole nasal surface. The large surface area maximises warming, humidification and filtering.

Warming. The immense vascularity of the mucosa permits rapid warming as the air flows past. This also explains the large blood loss when a nosebleed (epistaxis) occurs.

Filtering and cleaning. Hairs at the anterior nares trap larger particles. Smaller particles such as dust and bacteria settle and adhere to the mucus. Mucus protects the underlying epithelium from irritation and prevents drying. Synchronous beating of the cilia wafts the mucus towards the throat where it is swallowed or coughed up (expectorated).

Humidification. As air travels over the moist mucosa, it becomes saturated with water vapour. Irritation of the nasal mucosa results in *sneezing*, a reflex action that forcibly expels an irritant.

The sense of smell

The nose is the organ of the sense of smell (*olfaction*). Specialised receptors that detect smell are located in the roof of the nose in the area of the cribriform plate of the ethmoid bones and the superior conchae (Figs 10.4 and 8.23A). These receptors are stimulated by airborne odours. The resultant nerve signals are carried by the *olfactory nerves* to the brain where the sensation of smell is perceived (p. 206).

Pharynx

Learning outcomes

After studying this section, you should be able to:

- describe the location of the pharynx
- relate the structure of the pharynx to its function.

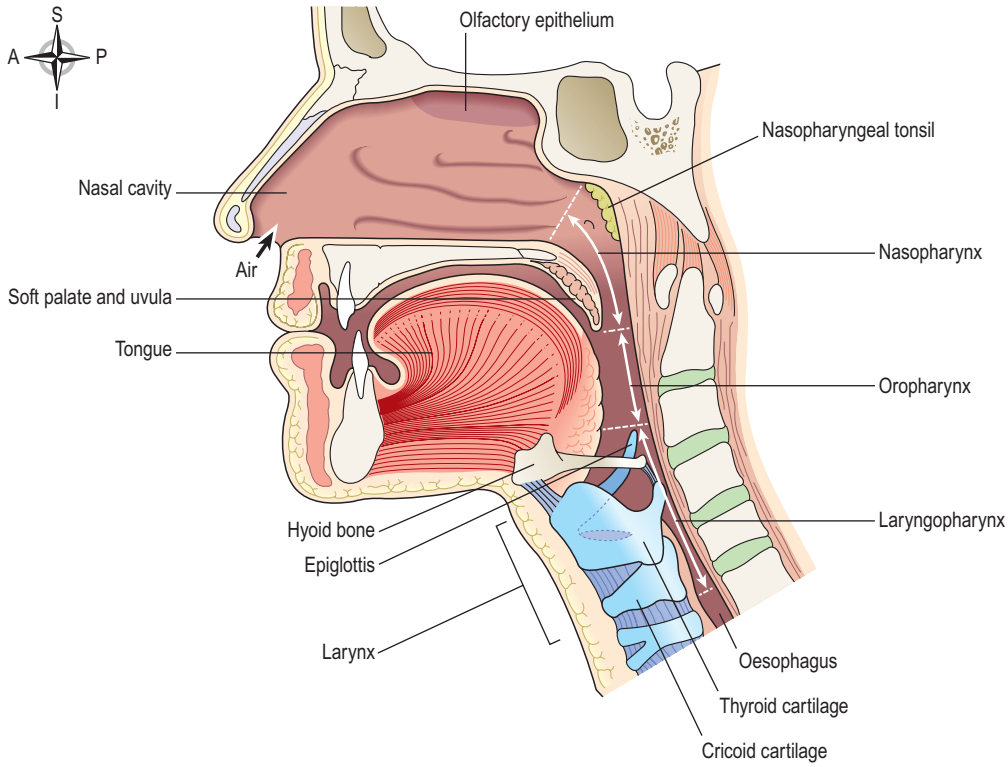


Figure 10.4 The pathway of air from the nose to the larynx.

Position

The pharynx (throat) is a passageway about 12–14 cm long. It extends from the posterior nares, and runs behind the mouth and the larynx to the level of the 6th thoracic vertebra, where it becomes the oesophagus.

Structures associated with the pharynx

Superiorly – the inferior surface of the base of the skull
Inferiorly – it is continuous with the oesophagus
Anteriorly – the wall is incomplete because of the openings into the nose, mouth and larynx
Posteriorly – areolar tissue, involuntary muscle and the bodies of the first six cervical vertebrae.

For descriptive purposes the pharynx is divided into three parts: *nasopharynx, oropharynx* and *laryngopharynx*.

The nasopharynx

The nasal part of the pharynx lies behind the nose above the level of the soft palate. On its lateral walls are the two openings of the *auditory tubes* (p. 193), one leading to each middle ear. On the posterior wall are the *pharyngeal tonsils* (adenoids), consisting of lymphoid tissue. They are most prominent in children up to approximately 7 years of age. Thereafter they gradually atrophy.

The oropharynx

The oral part of the pharynx lies behind the mouth, extending from below the level of the soft palate to the level of the upper part of the body of the 3rd cervical vertebra. The lateral walls of the pharynx blend with the soft palate to form two folds on each side. Between each pair of folds is a collection of lymphoid tissue called the *palatine tonsil*.

When swallowing, the soft palate and uvula are pushed upwards, sealing off the nasal cavity and preventing the entry of food and fluids.

The laryngopharynx

The laryngeal part of the pharynx extends from the oropharynx above and continues as the oesophagus below, with the larynx lying anteriorly.

Structure

The walls of the pharynx contain several types of tissue.

Mucous membrane lining

The mucosa varies slightly in the different regions. In the nasopharynx it is continuous with the lining of the nose and consists of ciliated columnar epithelium; in the oropharynx and laryngopharynx it is formed by tougher stratified squamous epithelium, which is continuous with the lining of the mouth and oesophagus. This lining protects underlying tissues from the abrasive action of foodstuffs passing through during swallowing.

Submucosa

The layer of tissue below the epithelium (the submucosa) is rich in mucosa-associated lymphoid tissue (MALT, p. 139), involved in protection against infection. Tonsils are masses of MALT that bulge through the epithelium. Some glandular tissue is also found here.

Smooth muscle

The pharyngeal muscles help to keep the pharynx permanently open so that breathing is not interfered with. Sometimes in sleep, and particularly if sedative drugs or alcohol have been taken, the tone of these muscles is reduced and the opening through the pharynx can become partially or totally obstructed. This contributes to snoring and periodic wakenings, which disturb sleep.

Constrictor muscles close the pharynx during swallowing, pushing food and fluid into the oesophagus.

Blood and nerve supply

Blood is supplied to the pharynx by several branches of the facial artery. The venous return is into the facial and internal jugular veins.

The nerve supply is from the pharyngeal plexus, and includes both parasympathetic and sympathetic nerves. Parasympathetic supply is by the *vagus* and *glossopharyngeal* nerves. Sympathetic supply is by nerves from the *superior cervical ganglia* (p. 174).

Functions

Passageway for air and food

The pharynx is involved in both the respiratory and the digestive systems: air passes through the nasal and oral sections, and food through the oral and laryngeal sections.

Warming and humidifying

By the same methods as in the nose, the air is further warmed and moistened as it passes towards the lungs.

Hearing

The auditory tube, extending from the nasopharynx to each middle ear, allows air to enter the middle ear. This leads to air in the middle ear being at the same pressure as the outer ear, protecting the tympanic membrane (eardrum, p. 193) from any changes in atmospheric pressure.

Protection

The lymphatic tissue of the pharyngeal and laryngeal tonsils produces antibodies in response to swallowed or inhaled antigens (Ch. 15). The tonsils are larger in children and tend to atrophy in adults.

Speech

The pharynx functions in speech; by acting as a resonating chamber for sound ascending from the larynx, it

helps (together with the sinuses) to give the voice its individual characteristics.

Larynx

Learning outcomes

After studying this section, you should be able to:

- describe the structure and function of the larynx
- outline the physiology of speech generation.

Position

The larynx or 'voice box' links the laryngopharynx and the trachea (Figs 10.1 and 10.4). It lies in front of the laryngopharynx and the 3rd, 4th, 5th and 6th cervical vertebrae. Until puberty there is little difference in the size of the larynx between the sexes. Thereafter, it grows larger in the male, which explains the prominence of the 'Adam's apple' and the generally deeper voice.

Structures associated with the larynx

Superiorly – the hyoid bone and the root of the tongue
Inferiorly – it is continuous with the trachea
Anteriorly – the muscles attached to the hyoid bone and the muscles of the neck
Posteriorly – the laryngopharynx and 3rd–6th cervical vertebrae
Laterally – the lobes of the thyroid gland.

Structure

Cartilages

The larynx is composed of several irregularly shaped cartilages attached to each other by ligaments and membranes. The main cartilages are:

- 1 thyroid cartilage
- 1 cricoid cartilage
- 2 arytenoid cartilages } hyaline cartilage
- 1 epiglottis — elastic fibrocartilage.

Several ligaments attach the cartilages to each other and to the hyoid bone (Figs 10.5, 10.6 and 10.8).

The thyroid cartilage (Figs 10.5 and 10.6)**.** This is the most prominent of the laryngeal cartilages. Made of hyaline cartilage, it lies to the front of the neck. Its anterior wall projects into the soft tissues of the front of the throat, forming the *laryngeal prominence* or Adam's apple, which is easily felt and often visible in adult males. The anterior wall is partially divided by the *thyroid notch*. The cartilage is incomplete posteriorly, and is bound with ligaments to the hyoid bone above and the cricoid cartilage below.

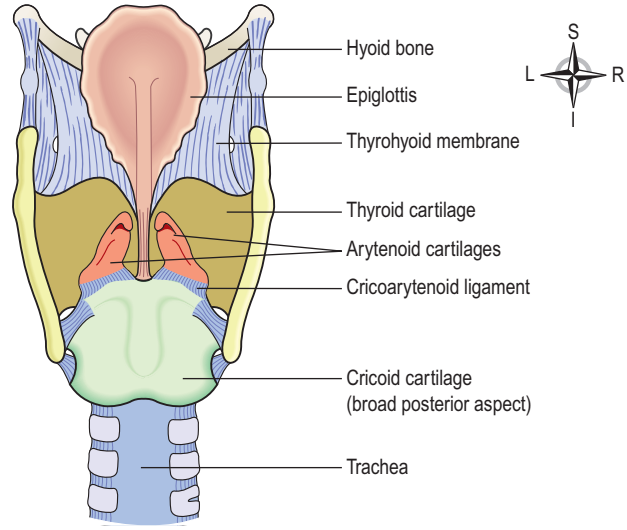


Figure 10.5 Larynx. Viewed from behind.

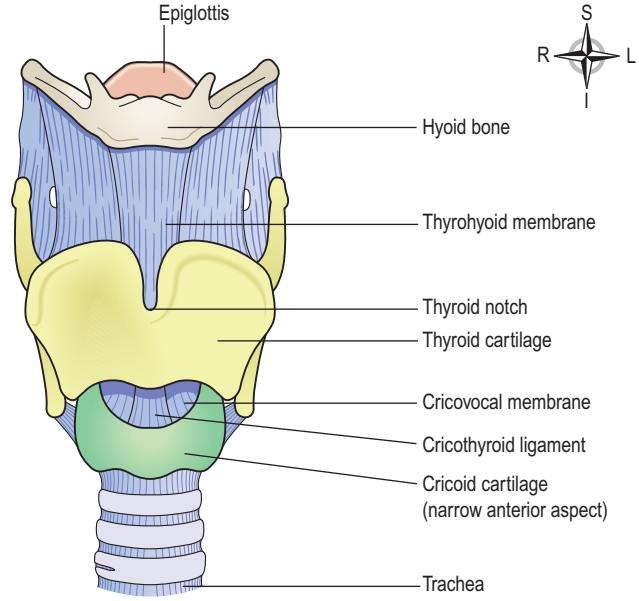


Figure 10.6 Larynx. Viewed from the front.

The upper part of the thyroid cartilage is lined with stratified squamous epithelium like the larynx, and the lower part with ciliated columnar epithelium like the trachea. There are many muscles attached to its outer surface.

The thyroid cartilage forms most of the anterior and lateral walls of the larynx.

The cricoid cartilage (Fig. 10.7)**.** This lies below the thyroid cartilage and is also composed of hyaline cartilage. It is shaped like a signet ring, completely encircling the larynx with the narrow part anteriorly and the broad part posteriorly. The broad posterior part articulates with the arytenoid cartilages and with the thyroid cartilage. It is lined with ciliated columnar epithelium and there are

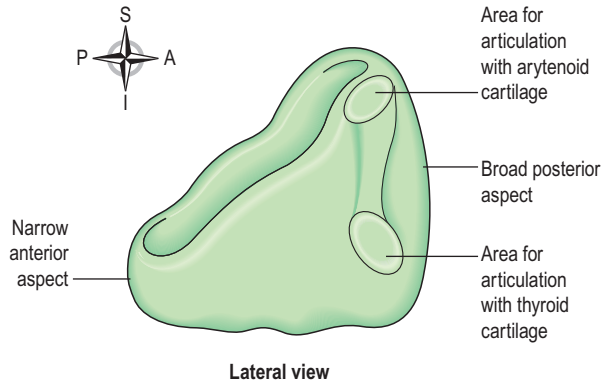


Figure 10.7 The cricoid cartilage.

muscles and ligaments attached to its outer surface (Fig. 10.7). The lower border of the cricoid cartilage marks the end of the upper respiratory tract.

The arytenoid cartilages. These are two roughly pyramid-shaped hyaline cartilages situated on top of the broad part of the cricoid cartilage forming part of the posterior wall of the larynx (Fig. 10.5). They give attachment to the vocal cords and to muscles and are lined with ciliated columnar epithelium.

The epiglottis (Figs 10.4–10.6 and 10.8)**.** This is a leaf-shaped fibroelastic cartilage attached on a flexible stalk of cartilage to the inner surface of the anterior wall of the thyroid cartilage immediately below the thyroid notch. It rises obliquely upwards behind the tongue and the body of the hyoid bone. It is covered with stratified squamous epithelium. If the larynx is likened to a box then the epiglottis acts as the lid; it closes off the larynx during swallowing, protecting the lungs from accidental inhalation of foreign objects.

Blood and nerve supply

Blood is supplied to the larynx by the superior and inferior laryngeal arteries and drained by the thyroid veins, which join the internal jugular vein.

The parasympathetic nerve supply is from the superior laryngeal and recurrent laryngeal nerves, which are branches of the vagus nerves. The sympathetic nerves are from the superior cervical ganglia, one on each side. These provide the motor nerve supply to the muscles of the larynx and sensory fibres to the lining membrane.

Interior of the larynx (Fig. 10.8)

The *vocal cords* are two pale folds of mucous membrane with cord-like free edges, stretched across the laryngeal opening. They extend from the inner wall of the thyroid prominence anteriorly to the arytenoid cartilages posteriorly.

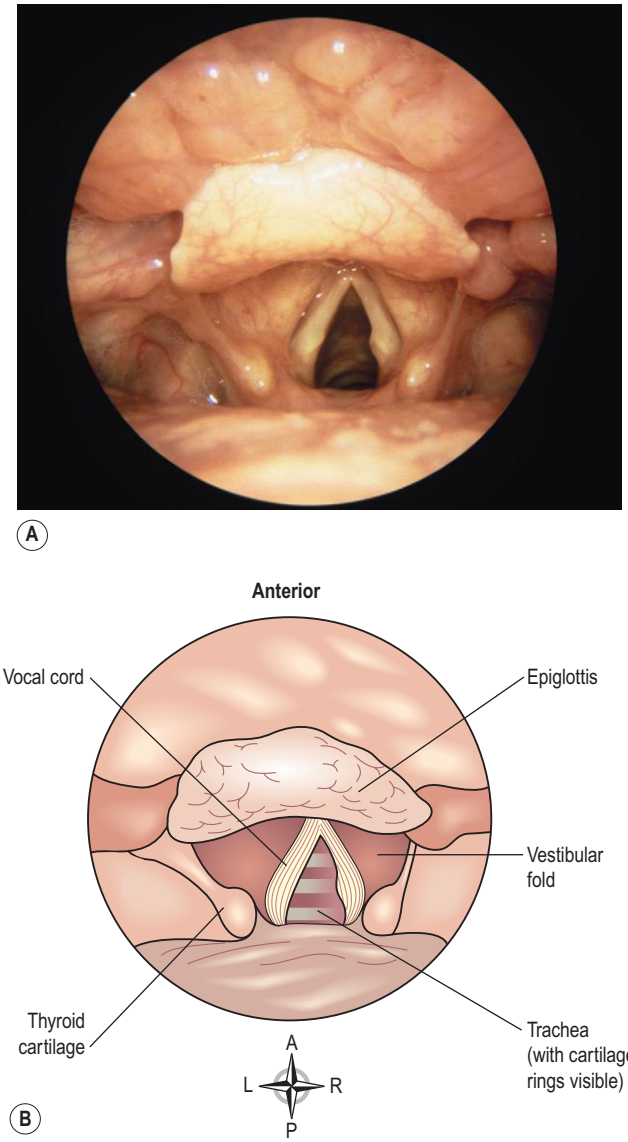


Figure 10.8 Vocal cords. A. Bronchoscopic image of the open (abducted) vocal cords. **B.** Diagram of the vocal cords showing the principal structures.

When the muscles controlling the vocal cords are relaxed, the vocal cords open and the passageway for air coming up through the larynx is clear; the vocal cords are said to be *abducted* (open, Fig. 10.9A). Vibrating the vocal cords in this position produces low-pitched sounds. When the muscles controlling the vocal cords contract, the vocal cords are stretched out tightly across the larynx (Fig. 10.9B), and are said to be *adducted* (closed). When the vocal cords are stretched to this extent, and are vibrated by air passing through from the lungs, the sound produced is high pitched. The pitch of the voice is therefore determined by the tension applied to the vocal cords by the appropriate sets of muscles. When not in use, the vocal cords are adducted. The space between the vocal cords is called the *glottis*.

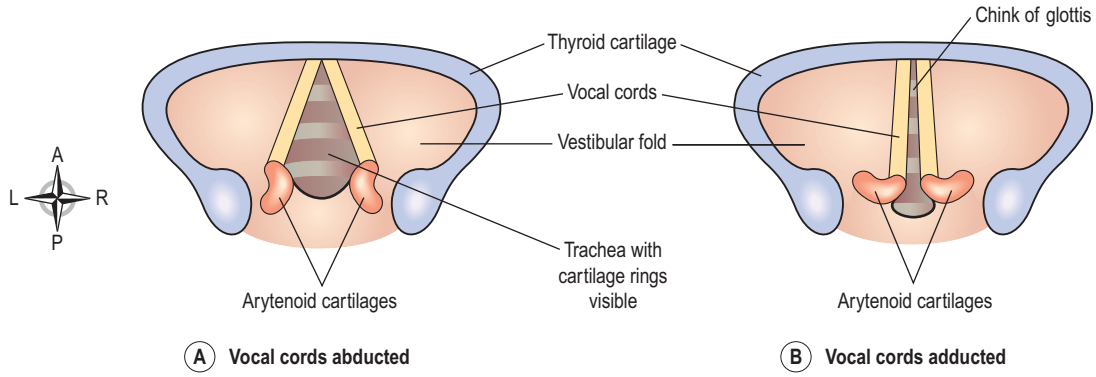


Figure 10.9 The extreme positions of the vocal cords. A. Abducted (open). **B.** Adducted (closed).

Functions

Production of sound. Sound has the properties of *pitch*, *volume* and *resonance*.

- Pitch of the voice depends upon the *length* and *tightness* of the cords. Shorter cords produce higher pitched sounds. At puberty, the male vocal cords begin to grow longer, hence the lower pitch of the adult male voice.
- Volume of the voice depends upon the *force* with which the cords vibrate. The greater the force of expired air, the more strongly the cords vibrate and the louder the sound emitted.
- Resonance, or tone, is dependent upon the shape of the mouth, the position of the tongue and the lips, the facial muscles and the air in the paranasal sinuses.

Speech. This is produced when the sounds produced by the vocal cords are amplified and manipulated by the tongue, cheeks and lips.

Protection of the lower respiratory tract. During swallowing (p. 297) the larynx moves upwards, blocking the opening into it from the pharynx. In addition, the hinged epiglottis closes over the larynx. This ensures that food passes into the oesophagus and not into the trachea.

Passageway for air. The larynx links the pharynx above with the trachea below.

Humidifying, filtering and warming. These processes continue as inspired air travels through the larynx.

Trachea

Learning outcomes

After studying this section, you should be able to:

- describe the location of the trachea
- outline the structure of the trachea
- explain the functions of the trachea in respiration.

Position

The trachea or windpipe is a continuation of the larynx and extends downwards to about the level of the 5th thoracic vertebra where it divides at the *carina* into the right and left primary bronchi, one bronchus going to each lung. It is approximately 10–11 cm long and lies mainly in the median plane in front of the oesophagus (Fig. 10.10).

Structures associated with the trachea

(Fig. 10.10)

Superiorly – the larynx
Inferiorly – the right and left bronchi
Anteriorly – upper part: the isthmus of the thyroid gland; lower part: the arch of the aorta and the sternum
Posteriorly – the oesophagus separates the trachea from the vertebral column
Laterally – the lungs and the lobes of the thyroid gland.

Structure

The tracheal wall is composed of three layers of tissue, and is held open by between 16 and 20 incomplete (C-shaped) rings of hyaline cartilage lying one above the other. The rings are incomplete posteriorly where the trachea lies against the oesophagus (Fig. 10.11). The cartilages are embedded in a sleeve of smooth muscle and connective tissue, which also forms the posterior wall where the rings are incomplete.

Three layers of tissue 'clothe' the cartilages of the trachea.

- The outer layer contains fibrous and elastic tissue and encloses the cartilages.
- The middle layer consists of cartilages and bands of smooth muscle that wind round the trachea in a helical arrangement. There is some areolar tissue, containing blood and lymph vessels and autonomic nerves. The free ends of the

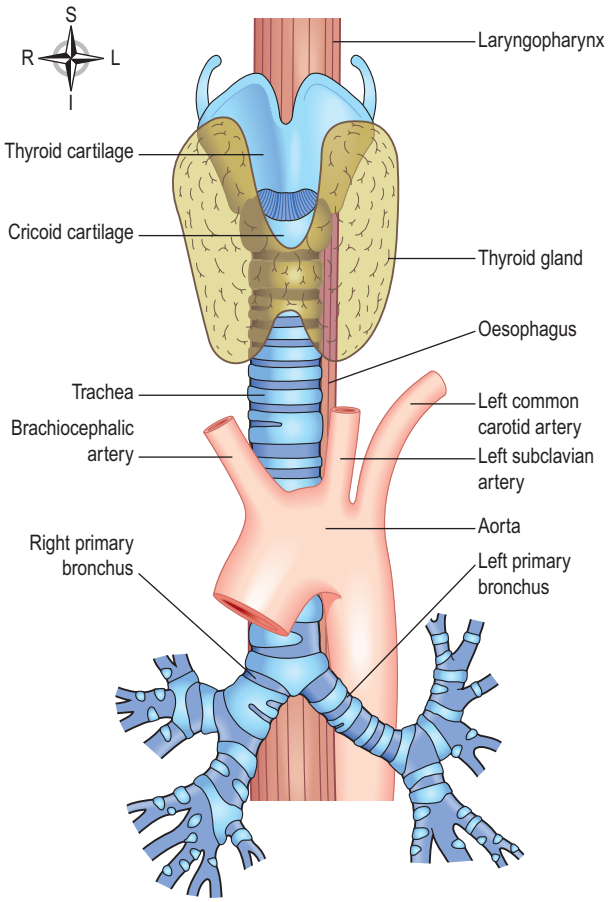


Figure 10.10 The trachea and some of its related structures.

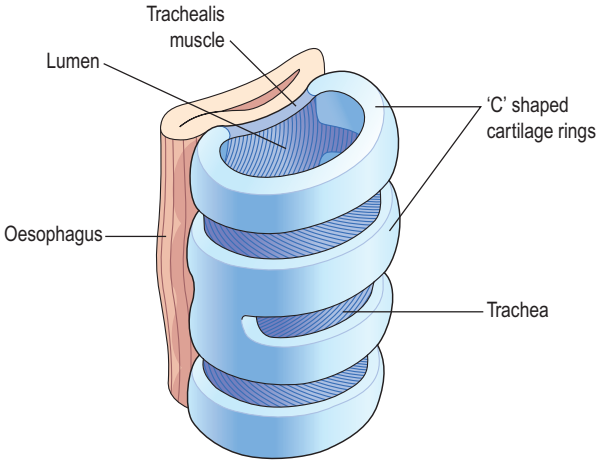
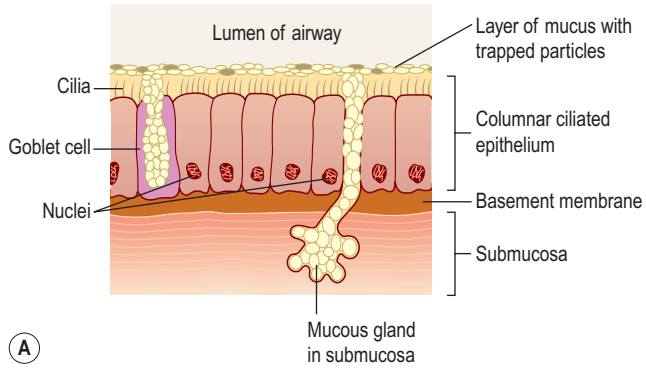


Figure 10.11 The relationship of the trachea to the oesophagus.

incomplete cartilages are connected by the trachealis muscle, which allows for adjustment of tracheal diameter.

- The lining is ciliated columnar epithelium, containing mucus-secreting goblet cells (Fig. 10.12).



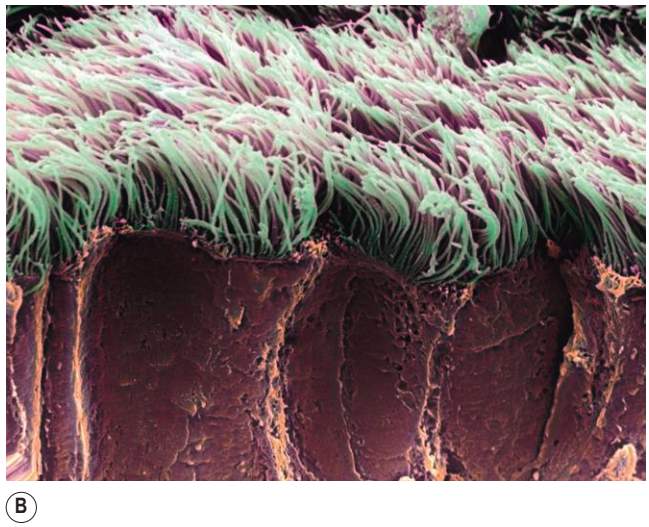


Figure 10.12 Cells lining the trachea. A. Ciliated mucous membrane. **B.** Coloured scanning electron micrograph of bronchial cilia.

Blood and nerve supply, lymph drainage

Arterial blood supply is mainly by the inferior thyroid and bronchial arteries and venous return is by the inferior thyroid veins into the brachiocephalic veins.

Parasympathetic nerve supply is by the recurrent laryngeal nerves and other branches of the vagi. Sympathetic supply is by nerves from the sympathetic ganglia. Parasympathetic stimulation constricts the trachea, and sympathetic stimulation dilates it.

Lymph from the respiratory passages drains through lymph nodes situated round the trachea and in the carina, the area where it divides into two bronchi.

Functions

Support and patency. Tracheal cartilages hold the trachea permanently open (patent), but the soft tissue bands in between the cartilages allow flexibility so that the head and neck can move freely without obstructing or kinking the trachea. The absence of cartilage posteriorly permits the oesophagus to expand comfortably during swallowing. Contraction or relaxation of the trachealis muscle, which links the free ends of the

C-shaped cartilages, helps to regulate the diameter of the trachea.

Mucociliary escalator. This is the synchronous and regular beating of the cilia of the mucous membrane lining that wafts mucus with adherent particles upwards towards the larynx where it is either swallowed or coughed up (Fig. 10.12B).

Cough reflex. Nerve endings in the larynx, trachea and bronchi are sensitive to irritation, which generates nerve impulses conducted by the vagus nerves to the respiratory centre in the brain stem (p. 160). The reflex motor response is deep inspiration followed by closure of the glottis, i.e. closure of the vocal cords. The abdominal and respiratory muscles then contract causing a sudden and rapid increase of pressure in the lungs. Then the glottis opens, expelling air through the mouth, taking mucus and/or foreign material with it.

Warming, humidifying and filtering. These continue as in the nose, although air is normally saturated and at body temperature when it reaches the trachea.

Lungs

Learning outcomes

After studying this section, you should be able to:

- name the air passage of the bronchial tree in descending order of size
- describe the structure and changing functions of the different levels of airway
- describe the location and gross anatomy of the lungs
- identify the functions of the pleura
- describe the pulmonary blood supply.

Position and gross structure (Fig. 10.13)

There are two lungs, one lying on each side of the midline in the thoracic cavity. They are cone-shaped and have an *apex*, a *base*, a *tip*, *costal surface* and *medial surface*.

The apex This is rounded and rises into the root of the neck, about 25 mm above the level of the middle third of the clavicle. It lies close to the first rib and the blood vessels and nerves in the root of the neck.

The base This is concave and semilunar in shape, and lies on the upper (thoracic) surface of the diaphragm.

The costal surface This is the broad outer surface of the lung that lies directly against the costal cartilages, the ribs and the intercostal muscles.

The medial surface The medial surface of each lung faces the other directly across the space between the lungs, the *mediastinum*. Each is concave and has a roughly triangular-shaped area, called the *hilum*, at the level of the 5th, 6th and 7th thoracic vertebrae. The primary bronchus, the pulmonary artery supplying the lung and the two pulmonary veins draining it, the bronchial artery and veins, and the lymphatic and nerve supply enter and leave the lung at the hilum (Fig. 10.14).

The mediastinum contains the heart, great vessels, trachea, right and left bronchi, oesophagus, lymph nodes, lymph vessels and nerves.

The right lung is divided into three distinct lobes: superior, middle and inferior. The left lung is smaller because the heart occupies space left of the midline. It is divided into only two lobes: superior and inferior. The divisions between the lobes are called *fissures*.

Pleura and pleural cavity

The pleura consists of a closed sac of serous membrane (one for each lung) which contains a small amount of serous fluid. The lung is pushed into this sac so that it forms two layers: one adheres to the lung and the other to the wall of the thoracic cavity (Figs 10.1 and 10.15).

The visceral pleura

This is adherent to the lung, covering each lobe and passing into the fissures that separate them.

The parietal pleura

This is adherent to the inside of the chest wall and the thoracic surface of the diaphragm. It is not attached to other structures in the mediastinum and is continuous with the visceral pleura round the edges of the hilum.

The pleural cavity

This is only a potential space and contains no air, so the pressure within is negative relative to atmospheric pressure. In health, the two layers of pleura are separated by a thin film of serous fluid (pleural fluid), which allows them to glide over each other, preventing friction between them during breathing. The pleural fluid is secreted by the epithelial cells of the membrane. The double membrane arrangement of the pleura is similar to the serous pericardium of the heart (p. 87).

The two layers of pleura, with pleural fluid between them, behave in the same way as two pieces of glass separated by a thin film of water. They glide over each other easily but can be pulled apart only with difficulty, because of the surface tension between the membranes and the fluid. This is essential for keeping the lung inflated against the inside of the chest wall. The airways and the alveoli of the lungs are embedded in elastic tissue, which constantly pull the lung tissues towards the hilum, but

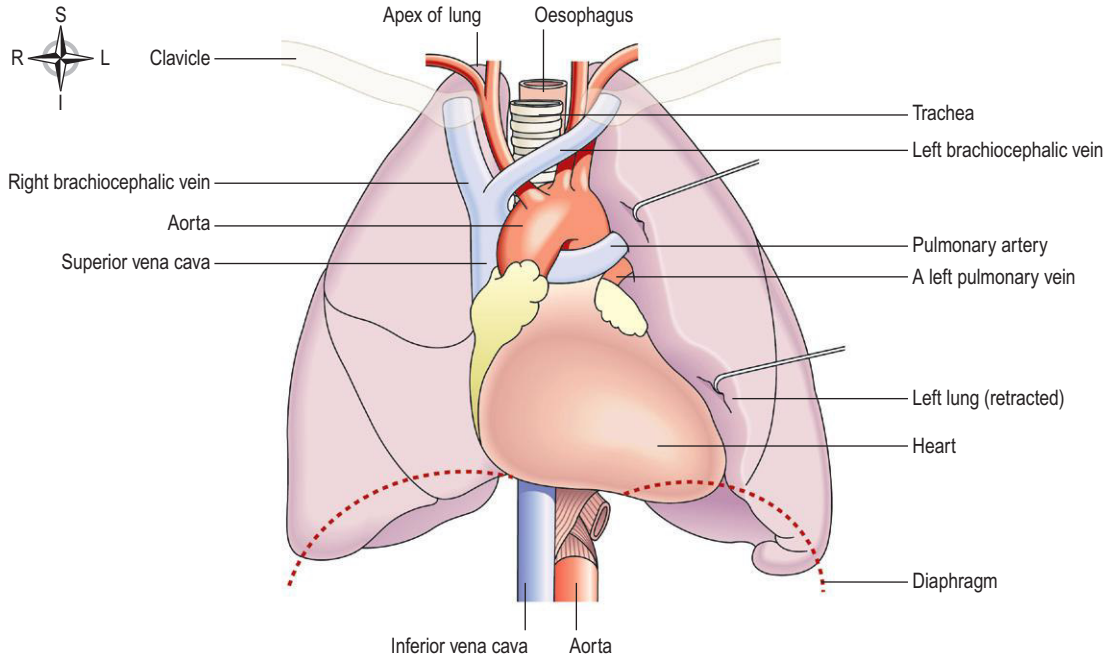


Figure 10.13 Organs associated with the lungs.

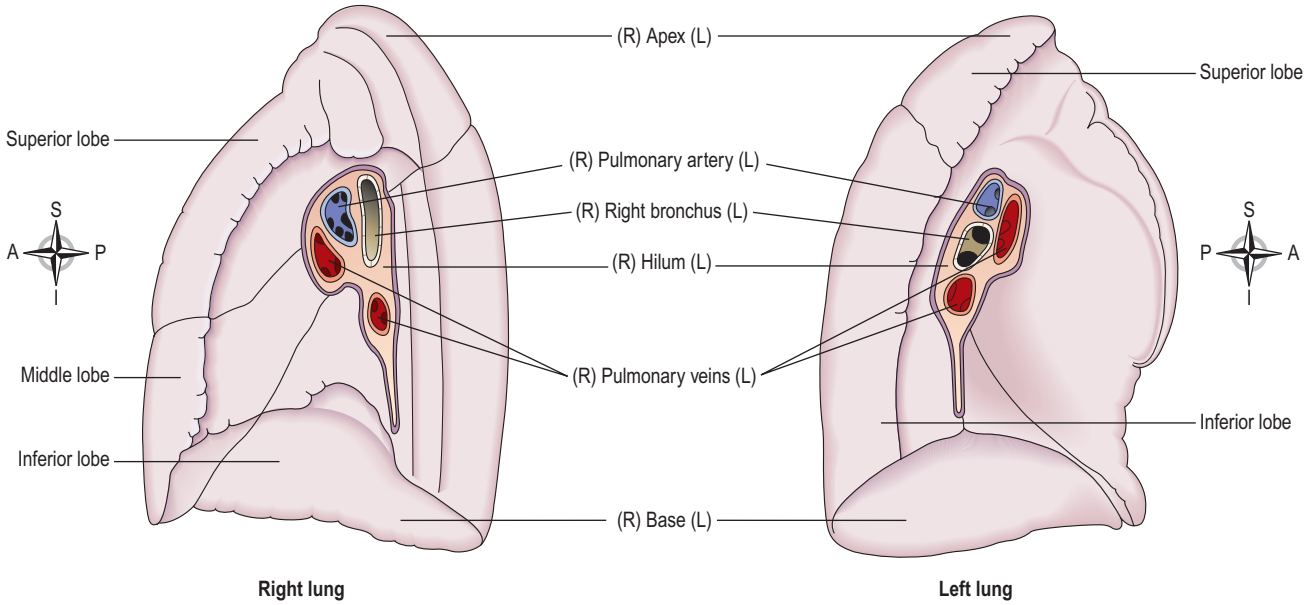


Figure 10.14 The lobes of the lungs and vessels/airways of each hilum. Medial views.

because pleural fluid holds the two pleura together, the lung remains expanded. If either layer of pleura is punctured, air is sucked into the pleural space and part or all of the entire underlying lung collapses.

Interior of the lungs

The lungs are composed of the bronchi and smaller air passages, alveoli, connective tissue, blood vessels, lymph vessels and nerves, all embedded in an elastic connective tissue matrix. Each lobe is made up of a large number of *lobules*.

Pulmonary blood supply (Fig. 10.16)

The *pulmonary trunk* divides into the right and left pulmonary arteries, carrying deoxygenated blood to each lung. Within the lungs each pulmonary artery divides into many branches, which eventually end in a dense capillary network around the alveoli (see Fig. 10.18). The walls of

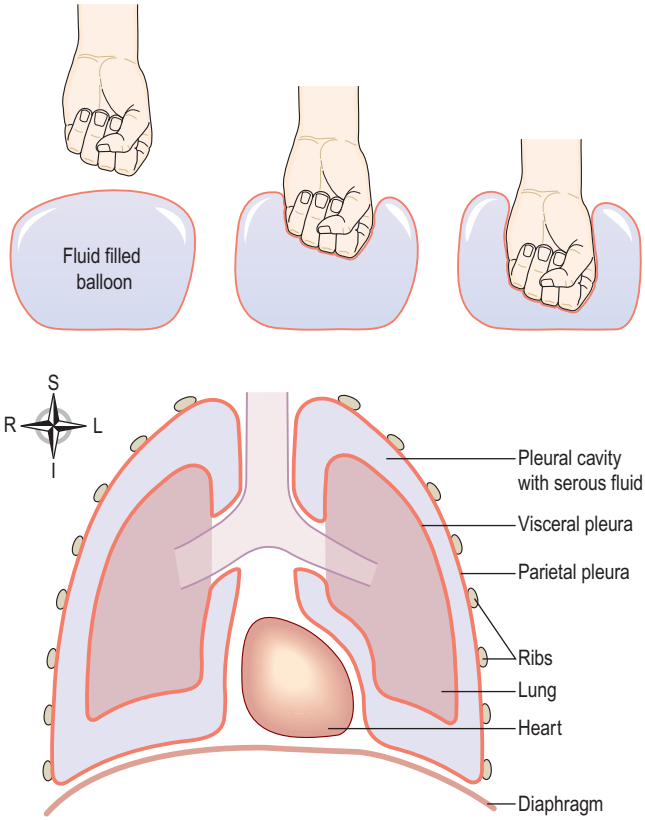


Figure 10.15 The relationship of the pleura to the lungs.

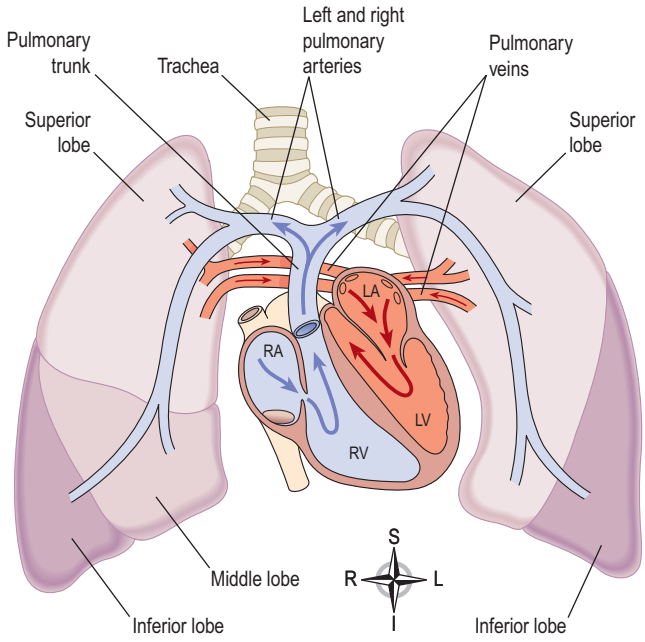


Figure 10.16 The flow of blood between heart and lungs.

the alveoli and the capillaries each consist of only one layer of flattened epithelial cells. The exchange of gases between air in the alveoli and blood in the capillaries takes place across these two very fine membranes (together called the *respiratory membrane*). The pulmonary capillaries merge into a network of pulmonary venules, which in turn form two pulmonary veins carrying oxygenated blood from each lung back to the left atrium of the heart.

The blood supply to the respiratory passages, lymphatic drainage and nerve supply is described later (p. 253).

Bronchi and bronchioles

The two primary bronchi are formed when the trachea divides, at about the level of the 5th thoracic vertebra (Fig. 10.17).

The right bronchus. This is wider, shorter and more vertical than the left bronchus and is therefore more likely to become obstructed by an inhaled foreign body. It is approximately 2.5 cm long. After entering the right lung at the hilum it divides into three branches, one to each lobe. Each branch then subdivides into numerous smaller branches.

The left bronchus. This is about 5 cm long and is narrower than the right. After entering the lung at the hilum it divides into two branches, one to each lobe. Each branch then subdivides into progressively smaller airways within the lung substance.

Structure 10.4

The bronchial walls contain the same three layers of tissue as the trachea, and are lined with ciliated columnar epithelium. The bronchi progressively subdivide into bronchioles (Fig. 10.17), terminal bronchioles, respiratory bronchioles, alveolar ducts and finally, alveoli. The wider passages are called *conducting airways* because their function is to bring air into the lungs, and their walls are too thick to permit gas exchange.

Structural changes in the bronchial passages

As the bronchi divide and become progressively smaller, their structure changes to match their function.

Cartilage. Since rigid cartilage would interfere with expansion of lung tissue and the exchange of gases, it is present for support in the larger airways only. The bronchi contain cartilage rings like the trachea, but as the airways divide, these rings become much smaller plates, and at the bronchiolar level there is no cartilage present in the airway walls at all.

Smooth muscle. As the cartilage disappears from airway walls, it is replaced by smooth muscle. This allows the diameter of the airways to be increased or decreased through the influence of the autonomic nervous system, regulating airflow within each lung.

Epithelial lining. The ciliated epithelium is gradually replaced with non-ciliated epithelium, and goblet cells disappear.

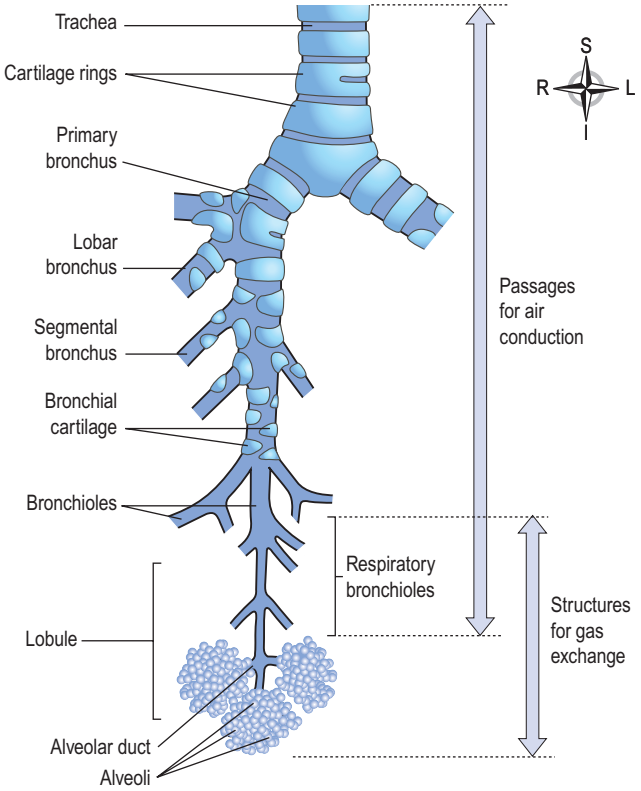


Figure 10.17 The lower respiratory tract.

Blood and nerve supply, lymph drainage

The arterial supply to the walls of the bronchi and smaller air passages is through branches of the right and left bronchial arteries and the venous return is mainly through the bronchial veins. On the right side they empty into the azygos vein and on the left into the superior intercostal vein (see Fig. 5.29, p. 104).

The vagus nerves (parasympathetic) stimulate contraction of smooth muscle in the bronchial tree, causing bronchoconstriction, and sympathetic stimulation causes bronchodilation (see below).

Lymph is drained from the walls of the air passages in a network of lymph vessels. It passes through lymph nodes situated around the trachea and bronchial tree then into the thoracic duct on the left side and right lymphatic duct on the other.

Functions

Control of air entry. The diameter of the respiratory passages is altered by contraction or relaxation of the smooth muscle in their walls, regulating the speed and volume of airflow into and within the lungs. These changes are controlled by the autonomic nerve supply: parasympathetic stimulation causes constriction and sympathetic stimulation causes dilation (p. 176).

The following functions continue as in the upper airways:

- warming and humidifying
- support and patency
- removal of particulate matter
- cough reflex.

Respiratory bronchioles and alveoli 10.5

Structure

Within each lobe, the lung tissue is further divided by fine sheets of connective tissue into *lobules*. Each lobule is supplied with air by a terminal bronchiole, which further subdivides into respiratory bronchioles, alveolar ducts and large numbers of alveoli (air sacs). There are about 150 million alveoli in the adult lung. It is in these structures that the process of gas exchange occurs. As airways progressively divide and become smaller and smaller, their walls gradually become thinner until muscle and connective tissue disappear, leaving a single layer of simple squamous epithelial cells in the alveolar ducts and alveoli. These distal respiratory passages are supported by a loose network of elastic connective tissue in which macrophages, fibroblasts, nerves and blood and lymph vessels are embedded. The alveoli are surrounded by a dense network of capillaries (Fig. 10.18). Exchange of gases in the lung (external respiration) takes place across a membrane made up of the alveolar wall and the capillary wall fused firmly together. This is called the *respiratory membrane*.

On microscopic examination, the extensive air spaces are clearly seen and healthy lung tissue has a honeycomb appearance (Fig. 10.19). **10.6**

Lying between the squamous cells are *septal* cells that secrete *surfactant*, a phospholipid fluid which prevents the alveoli from drying out and reduces surface tension preventing alveolar collapse during expiration. Secretion of surfactant into the distal air passages and alveoli begins about the 35th week of fetal life. Its presence in newborn babies permits expansion of the lungs and the establishment of respiration immediately after birth. It may not be present in sufficient amounts in the immature lungs of premature babies, causing serious breathing problems.

Nerve supply to bronchioles

Parasympathetic stimulation, from the vagus nerve, causes bronchoconstriction. The absence of supporting cartilage means that small airways may be completely closed off by constriction of their smooth muscle. Sympathetic stimulation relaxes bronchiolar smooth muscle (bronchodilation).

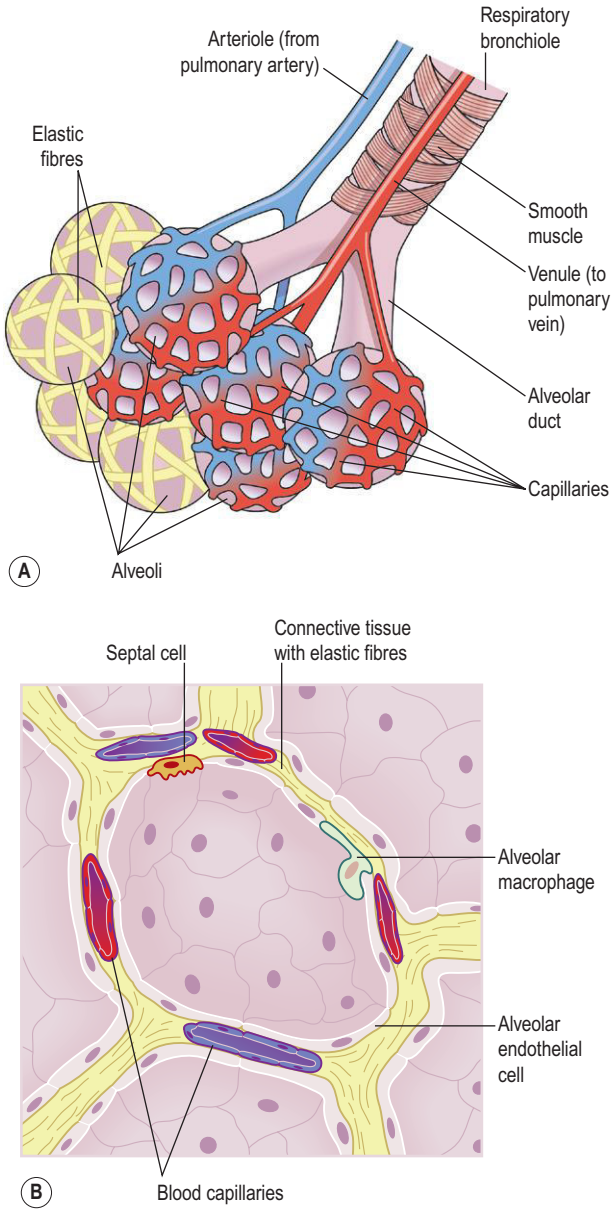


Figure 10.18 The alveoli and their capillary network.
A. A group of intact alveoli. **B.** Section through an alveolus.

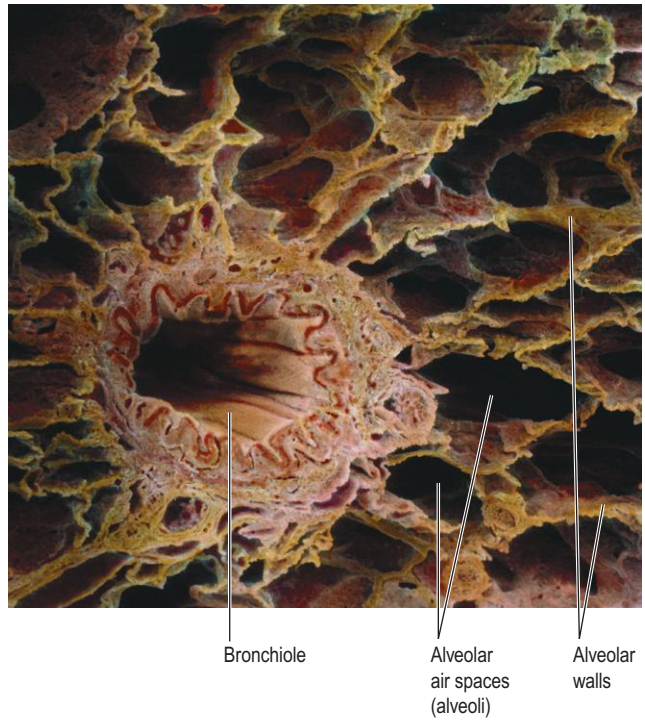


Figure 10.19 Coloured scanning electron micrograph of lung alveoli and a bronchiole.

Functions

External respiration. (See p. 259.)

Defence against infection. At this level, ciliated epithelium, goblet cells and mucus are no longer present, because their presence would impede gas exchange and encourage infection. By the time inspired air reaches the alveoli, it is usually clean. Defence relies on protective cells present within the lung tissue. These include lymphocytes and plasma cells, which produce antibodies, and phagocytes, including alveolar macrophages. These cells are most active in the distal air passages where ciliated epithelium has been replaced by squamous (flattened) cells.

Warming and humidifying. These continue as in the upper airways. Inhalation of dry or inadequately humidified air over a period of time irritates the mucosa and encourages infection.

Respiration

Learning outcomes

After studying this section, you should be able to:

- describe the actions of the main muscles involved in breathing
- compare and contrast the mechanical events occurring in inspiration and expiration
- define the terms compliance, elasticity and airflow resistance
- describe the principal lung volumes and capacities
- compare the processes of internal and external respiration, using the concept of diffusion of gases
- describe O_2 and CO_2 transport in the blood
- explain the main mechanisms by which respiration is controlled.

The term respiration means the exchange of gases between body cells and the environment. This involves two main processes.

Breathing (pulmonary ventilation). This is movement of air into and out of the lungs.

Exchange of gases. This takes place:

- in the lungs: external respiration
- in the tissues: internal respiration.

Each of these will be considered later in this section.

Breathing

Breathing supplies oxygen to the alveoli, and eliminates carbon dioxide.

Muscles of breathing

Expansion of the chest during inspiration occurs as a result of muscular activity, partly voluntary and partly involuntary. The main muscles used in normal quiet breathing are the *external intercostal muscles* and the *diaphragm*.

Intercostal muscles

There are 11 pairs of intercostal muscles occupying the spaces between the 12 pairs of ribs. They are arranged in two layers, the external and internal intercostal muscles (Fig. 10.20).

The external intercostal muscles These extend downwards and forwards from the lower border of the rib above to the upper border of the rib below. They are involved in inspiration.

The internal intercostal muscles These extend downwards and backwards from the lower border of the rib above to the upper border of the rib below, crossing the external intercostal muscle fibres at right angles. The internal intercostals are used when expiration becomes active, as in exercise.

The first rib is fixed. Therefore, when the external intercostal muscles contract they pull all the other ribs towards the first rib. The ribcage moves as a unit, upwards and outwards, enlarging the thoracic cavity. The intercostal muscles are stimulated to contract by the *intercostal nerves*.

Diaphragm 10.7

The diaphragm is a dome-shaped muscular structure separating the thoracic and abdominal cavities. It forms the floor of the thoracic cavity and the roof of the abdominal cavity and consists of a central tendon from which muscle fibres radiate to be attached to the lower ribs and sternum and to the vertebral column by two crura. When the diaphragm is relaxed, the central tendon is at the level of the 8th thoracic vertebra (Fig. 10.21). When it contracts, its muscle fibres shorten and the central tendon is pulled downwards to the level of the 9th thoracic vertebra, lengthening the thoracic cavity. This decreases pressure in the thoracic cavity and increases it in the abdominal and pelvic cavities. The diaphragm is supplied by the *phrenic nerves*.

Quiet, restful breathing is sometimes called *diaphragmatic breathing* because 75% of the work is done by the diaphragm.

During inspiration, the external intercostal muscles and the diaphragm contract simultaneously, enlarging the thoracic cavity in all directions, that is from back to front, side to side and top to bottom (Fig. 10.22).

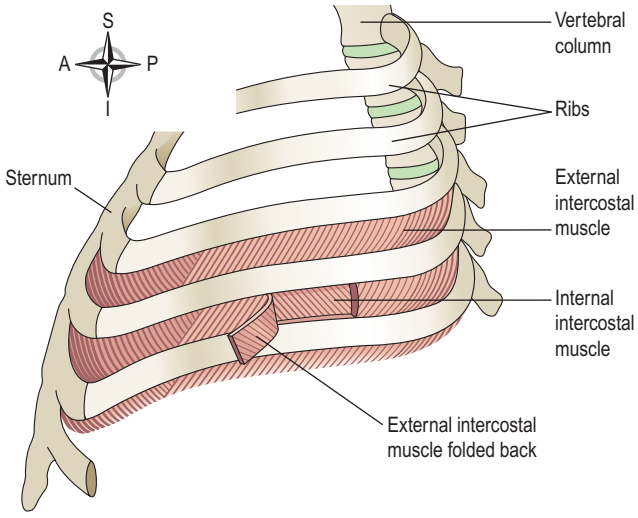


Figure 10.20 The intercostal muscles and the bones of the thorax.

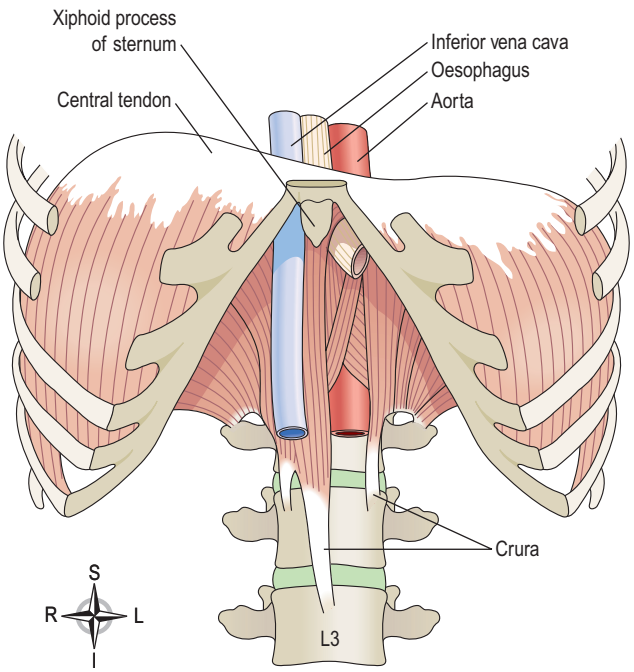


Figure 10.21 The diaphragm.

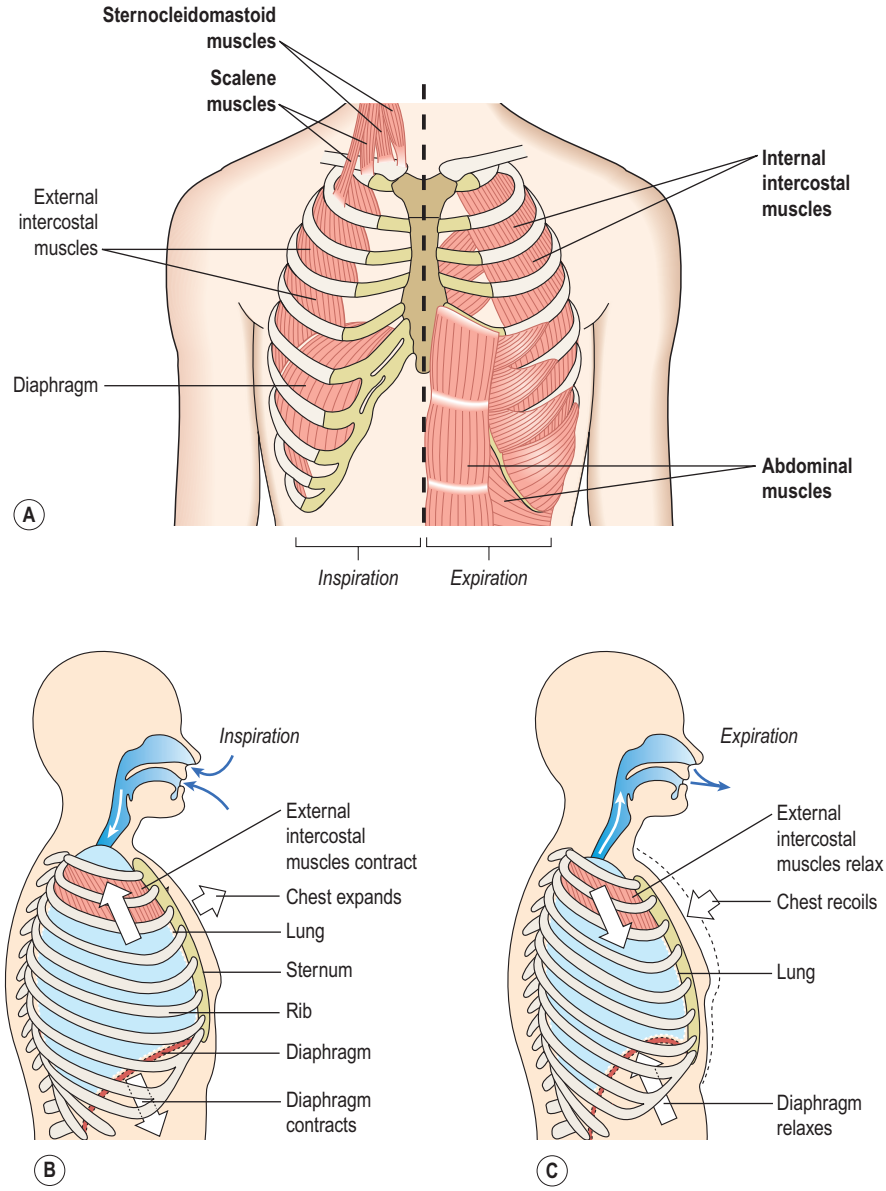


Figure 10.22 Changes in chest size during inspiration. A. Muscles involved in respiration (accessory muscles labelled in bold). **B, C.** Changes in chest volume.

Accessory muscles of respiration (Fig. 10.22A)

When extra respiratory effort is required, additional muscles are used. Forced inspiration is assisted by the *sternocleidomastoid* muscles (p. 425) and the *scalene* muscles, which link the cervical vertebrae to the first two ribs, and increase ribcage expansion. Forced expiration is helped by the activity of the internal intercostal muscles and sometimes the abdominal muscles, which increase the pressure in the thorax by squeezing the abdominal contents.

Cycle of breathing 10.8

The average respiratory rate is 12–15 breaths per minute. Each breath consists of three phases: inspiration, expiration and pause.

The visceral pleura is adherent to the lungs and the parietal pleura to the inner wall of the thorax and to the diaphragm. Between them is a thin film of pleural fluid (p. 250).

Breathing depends upon changes in pressure and volume in the thoracic cavity. It follows the underlying physical principle that increasing the volume of a container decreases the pressure inside it, and that decreasing the volume of a container increases the pressure inside it. Since air flows from an area of high pressure to an area of low pressure, changing the pressure inside the lungs determines the direction of airflow.

Inspiration

Simultaneous contraction of the external intercostal muscles and the diaphragm expands the thorax. As the

parietal pleura is firmly adhered to the diaphragm and the inside of the ribcage, it is pulled outward along with them. This pulls the visceral pleura outwards too, since the two pleura are held together by the thin film of pleural fluid. Because the visceral pleura is firmly adherent to the lung, the lung tissue is, therefore, also pulled up and out with the ribs, and downwards with the diaphragm. This expands the lungs, and the pressure within the alveoli and in the air passages falls, drawing air into the lungs in an attempt to equalise atmospheric and alveolar air pressures.

The process of inspiration is *active*, as it needs energy for muscle contraction. The negative pressure created in the thoracic cavity aids venous return to the heart and is known as the *respiratory pump*.

At rest, inspiration lasts about 2 seconds.

Expiration

Relaxation of the external intercostal muscles and the diaphragm results in downward and inward movement of the ribcage (Fig. 10.22) and elastic recoil of the lungs. As this occurs, pressure inside the lungs rises and expels air from the respiratory tract. At the end of expiration, the lungs still contain some air, and are prevented from complete collapse by the intact pleura. This process is *passive* as it does not require the expenditure of energy.

At rest, expiration lasts about 3 seconds, and after expiration there is a pause before the next cycle begins.

Physiological variables affecting breathing

Elasticity. Elasticity is the ability of the lung to return to its normal shape after each breath. Loss of elasticity, e.g. in emphysema (p. 263), of the connective tissue in the lungs necessitates forced expiration and increased effort on inspiration.

Compliance. This is the stretchability of the lungs, i.e. the effort required to inflate the alveoli. The healthy lung is very compliant, and inflates with very little effort. When compliance is low the effort needed to inflate the lungs is greater than normal, e.g. when insufficient surfactant is present. Note that compliance and elasticity are opposing forces.

Airway resistance. When this is increased, e.g. in bronchoconstriction, more respiratory effort is required to inflate the lungs.

Lung volumes and capacities (Fig. 10.23)

In normal quiet breathing there are about 15 complete respiratory cycles per minute. The lungs and the air passages are never empty and, as the exchange of gases takes place only across the walls of the alveolar ducts and alveoli, the remaining capacity of the respiratory passages is called the *anatomical dead space* (about 150 mL).

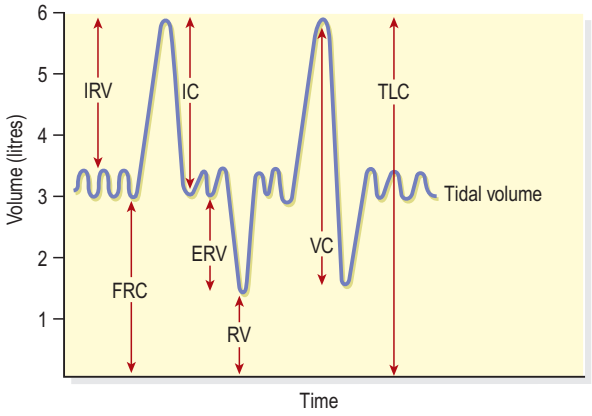


Figure 10.23 Lung volumes and capacities. IRV: inspiratory reserve volume; IC: inspiratory capacity; FRC: functional residual capacity; ERV: expiratory reserve volume; RV: residual volume; VC: vital capacity; TLC: total lung capacity.

Tidal volume (TV). This is the amount of air passing into and out of the lungs during each cycle of breathing (about 500 mL at rest).

Inspiratory reserve volume (IRV). This is the extra volume of air that can be inhaled into the lungs during maximal inspiration, i.e. over and above normal TV.

Inspiratory capacity (IC). This is the amount of air that can be inspired with maximum effort. It consists of the tidal volume (500 ml) plus the inspiratory reserve volume.

Functional residual capacity (FRC). This is the amount of air remaining in the air passages and alveoli at the end of quiet expiration. Tidal air mixes with this air, causing relatively small changes in the composition of alveolar air. As blood flows continuously through the pulmonary capillaries, this means that exchange of gases is not interrupted between breaths, preventing moment-to-moment changes in the concentration of blood gases. The functional residual volume also prevents collapse of the alveoli on expiration.

Expiratory reserve volume (ERV). This is the largest volume of air which can be expelled from the lungs during maximal expiration.

Residual volume (RV). This cannot be directly measured but is the volume of air remaining in the lungs after forced expiration.

Vital capacity (VC). This is the maximum volume of air which can be moved into and out of the lungs:

$$VC = \text{Tidal volume} + IRV + ERV$$

Total lung capacity (TLC). This is the maximum amount of air the lungs can hold. In an adult of average build, it is normally around 6 litres. Total lung capacity represents

the sum of the vital capacity and the residual volume. It cannot be directly measured in clinical tests because even after forced expiration, the residual volume of air still remains in the lungs.

Alveolar ventilation. This is the volume of air that moves into and out of the alveoli per minute. It is equal to the tidal volume minus the anatomical dead space, multiplied by the respiratory rate:

Alveolar ventilation = TV – anatomical dead space × respiratory rate
= (500 – 150) mL × 15 per minute
= 5.25 litres per minute

Lung function tests are carried out to determine respiratory function and are based on the parameters outlined above. Results of these tests can help in diagnosis and monitoring of respiratory disorders.

Exchange of gases

Although breathing involves the alternating processes of inspiration and expiration, gas exchange at the respiratory membrane and in the tissues is a continuous and ongoing process. Diffusion of oxygen and carbon dioxide depends on pressure differences, e.g. between atmospheric air and the blood, or blood and the tissues.

Composition of air

Atmospheric pressure at sea level is 101.3 kilopascals (kPa) or 760 mmHg. With increasing height above sea level, atmospheric pressure is progressively reduced and at 5500 m, about two-thirds the height of Mount Everest (8850 m), it is about half that at sea level. Under water, pressure increases by approximately 1 atmosphere per 10 m below sea level.

Air is a mixture of gases: nitrogen, oxygen, carbon dioxide, water vapour and small quantities of inert gases. The percentage of each in inspired and expired air is listed in Table 10.1. Each gas in the mixture exerts a part of the total pressure proportional to its concentration, i.e. the *partial pressure* (Table 10.2). This is denoted as, e.g. PO_2, PCO_2.

Alveolar air

The composition of alveolar air remains fairly constant and is different from atmospheric air. It is saturated with water vapour, and contains more carbon dioxide and less oxygen. Saturation with water vapour provides 6.3 kPa (47 mmHg) thus reducing the partial pressure of all the other gases present. Gaseous exchange between the alveoli and the bloodstream (*external respiration*) is a continuous process, as the alveoli are never empty, so it is independent of the respiratory cycle. During each inspiration only some of the alveolar gases are exchanged.

Diffusion of gases

Exchange of gases occurs when a difference in partial pressure exists across a semipermeable membrane. Gases move by diffusion from the higher concentration to the lower until equilibrium is established (p. 29). Atmospheric nitrogen is not used by the body so its partial pressure remains unchanged and is the same in inspired and expired air, alveolar air and in the blood.

These principles govern the diffusion of gases in and out of the alveoli across the respiratory membrane

Table 10.1 The composition of inspired and expired air

	Inspired air %	Expired air %
Oxygen	21	16
Carbon dioxide	0.04	4
Nitrogen	78	78
Water vapour	Variable	Saturated

Table 10.2 Partial pressures of gases

	Alveolar air		Deoxygenated blood		Oxygenated blood	
Gas	*kPa*	*mmHg*	*kPa*	*mmHg*	*kPa*	*mmHg*
Oxygen	13.3	100	5.3	40	13.3	100
Carbon dioxide	5.3	40	5.8	44	5.3	40
Nitrogen	76.4	573	76.4	573	76.4	573
Water vapour	6.3	47				
Total	101.3	760				

(*external respiration*) and across capillary membranes in the tissues (*internal respiration*).

External respiration (Fig. 10.24A) 10.9

This is exchange of gases by diffusion between the alveoli and the blood in the alveolar capillaries, across the respiratory membrane. Each alveolar wall is one cell thick and is surrounded by a network of tiny capillaries (the walls of which are also only one cell thick). The total area of respiratory membrane for gas exchange in the lungs is about equivalent to the area of a tennis court. Venous blood arriving at the lungs in the pulmonary artery has travelled from all the tissues of the body, and contains high levels of CO_2 and low levels of O_2. Carbon dioxide diffuses from venous blood down its concentration gradient into the alveoli until equilibrium with alveolar air is reached. By the same process, oxygen diffuses from the alveoli into the blood. The relatively slow flow of blood through the capillaries increases the time available for gas exchange to occur. When blood leaves the alveolar capillaries, the oxygen and carbon dioxide concentrations are in equilibrium with those of alveolar air (Fig. 10.24A).

Internal respiration (Fig. 10.24B) 10.10

This is exchange of gases by diffusion between blood in the capillaries and the body cells. Gas exchange does not occur across the walls of the arteries carrying blood from the heart to the tissues, because their walls are too thick. PO_2 of blood arriving at the capillary bed is therefore the same as blood leaving the lungs. Blood arriving at the tissues has been cleansed of its CO_2 and saturated with O_2 during its passage through the lungs, and therefore has a higher PO_2 and a lower PCO_2 than the tissues. This creates concentration gradients between capillary blood and the tissues, and gas exchange therefore occurs (Fig. 10.24B). O_2 diffuses from the bloodstream through the capillary wall into the tissues. CO_2 diffuses from the cells into the extracellular fluid, then into the bloodstream towards the venous end of the capillary.

Figure 10.25 summarises the processes of internal and external respiration. 10.11

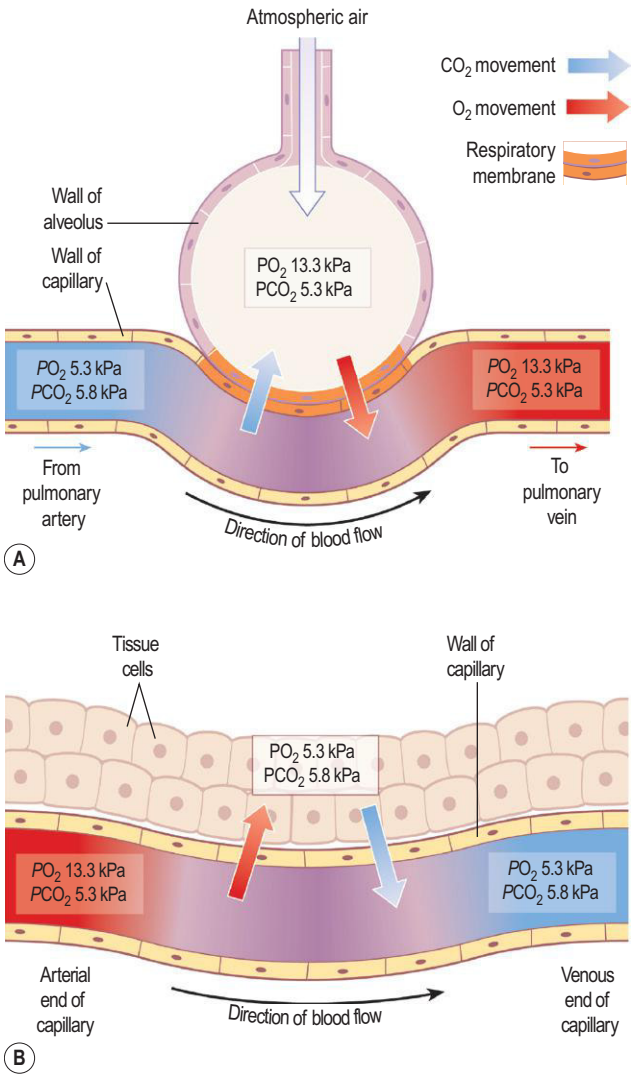


Figure 10.24 Respiration. A. External respiration. **B.** Internal respiration.

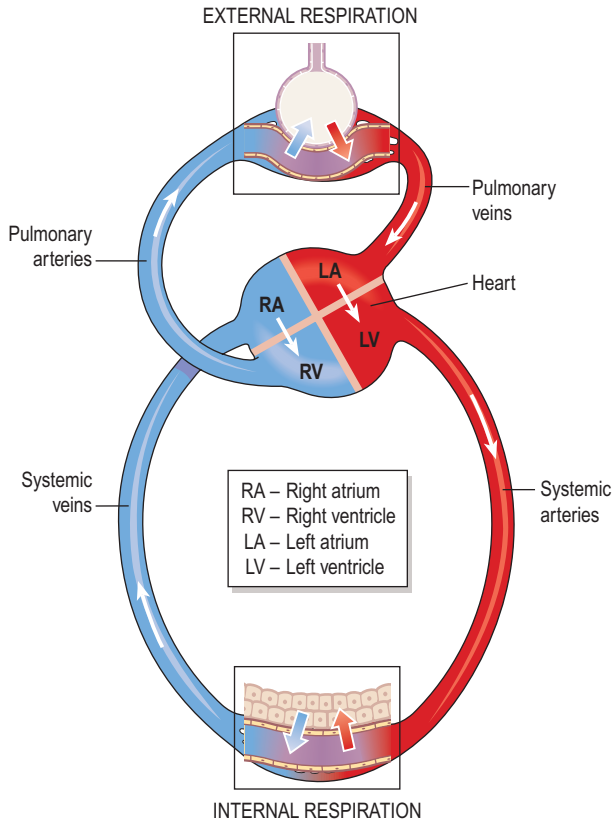


Figure 10.25 Summary of external and internal respiration.

Transport of gases in the bloodstream

Oxygen and carbon dioxide are carried in the blood in different ways.

Oxygen

Oxygen is carried in the blood in:

- chemical combination with haemoglobin (see Fig. 4.6, p. 66) as *oxyhaemoglobin* (98.5%)
- solution in plasma water (1.5%).

Oxyhaemoglobin is unstable, and under certain conditions readily dissociates releasing oxygen. Factors that increase dissociation include low O_2 levels, low pH and raised temperature (see Ch. 4). In active tissues there is increased production of carbon dioxide and heat, which leads to increased release of oxygen. In this way oxygen is available to tissues in greatest need. Whereas oxyhaemoglobin is bright red, deoxygenated blood is bluish-purple in colour.

Carbon dioxide

Carbon dioxide is one of the waste products of metabolism. It is excreted by the lungs and is transported by three mechanisms:

- as bicarbonate ions (HCO_3^-) in the plasma (70%)
- some is carried in erythrocytes, loosely combined with haemoglobin as *carbaminohaemoglobin* (23%)
- some is dissolved in the plasma (7%).

Carbon dioxide levels must be finely managed, as either an excess or a deficiency leads to significant disruption of acid-base balance. Sufficient CO_2 is essential for the bicarbonate buffering system that protects against a fall in body pH. Excess CO_2 on the other hand reduces blood pH, because it dissolves in body water to form carbonic acid.

Regulation of air and blood flow in the lung

During quiet breathing, only a small portion of the lung's total capacity is ventilated with each breath. This means that only a fraction of the total alveolar numbers are being ventilated, usually in the upper lobes, and much of the remaining lung is temporarily collapsed. Airways supplying alveoli that are not being used are constricted, directing airflow into functioning alveoli. In addition, the pulmonary arterioles bringing blood into the ventilated alveoli are dilated, to maximise gas exchange, and blood flow (perfusion) past the non-functioning alveoli is reduced.

When respiratory requirements are increased, e.g. in exercise, the increased tidal volume expands additional alveoli, and the blood flow is redistributed to perfuse these too. In this way, air flow (ventilation) and blood flow (perfusion) are matched to maximise the opportunity for gas exchange.

Control of respiration

Effective control of respiration enables the body to regulate blood gas levels over a wide range of physiological, environmental and pathological conditions, and is normally involuntary. Voluntary control is exerted during activities such as speaking and singing but is overridden if blood CO_2 rises (hypercapnia).

The respiratory centre

This is formed by groups of nerves in the medulla, the *respiratory rhythmicity centre*, which control the respiratory pattern, i.e. the rate and depth of breathing (Fig. 10.26). Regular discharge of *inspiratory neurones* within this centre set the rate and depth of breathing. Activity of the respiratory rhythmicity centre is adjusted by nerves in the pons (the *pneumotaxic centre* and the *apneustic centre*), in response to input from other parts of the brain.

Motor impulses leaving the respiratory centre pass in the *phrenic* and *intercostal nerves* to the diaphragm and intercostal muscles respectively to stimulate respiration.

Chemoreceptors

These are receptors that respond to changes in the partial pressures of oxygen and carbon dioxide in the blood and cerebrospinal fluid. They are located centrally and peripherally.

Central chemoreceptors. These are located on the surface of the medulla oblongata and are bathed in cerebrospinal fluid. When arterial PCO_2 rises (hypercapnia), even slightly, the central chemoreceptors respond by stimulating the respiratory centre, increasing ventilation of the lungs and reducing arterial PCO_2. The sensitivity of the central chemoreceptors to raised arterial PCO_2 is the most important factor in controlling normal blood gas levels. A small reduction in PO_2 (hypoxaemia) has the same, but less pronounced effect, but a substantial reduction depresses breathing.

Peripheral chemoreceptors. These are situated in the arch of the aorta and in the carotid bodies (Fig. 10.26). They respond to changes in blood CO_2 and O_2 levels, but are much more sensitive to carbon dioxide than oxygen. Even a slight rise in CO_2 levels activates these receptors, triggering nerve impulses to the respiratory centre via the glossopharyngeal and vagus nerves. This stimulates an immediate rise in the rate and depth of respiration. An increase in blood acidity (decreased pH or raised $[H^+]$) also stimulates the peripheral chemoreceptors, resulting in increased ventilation, increased CO_2 excretion and increased blood pH. These chemoreceptors also help to regulate blood pressure (p. 97).

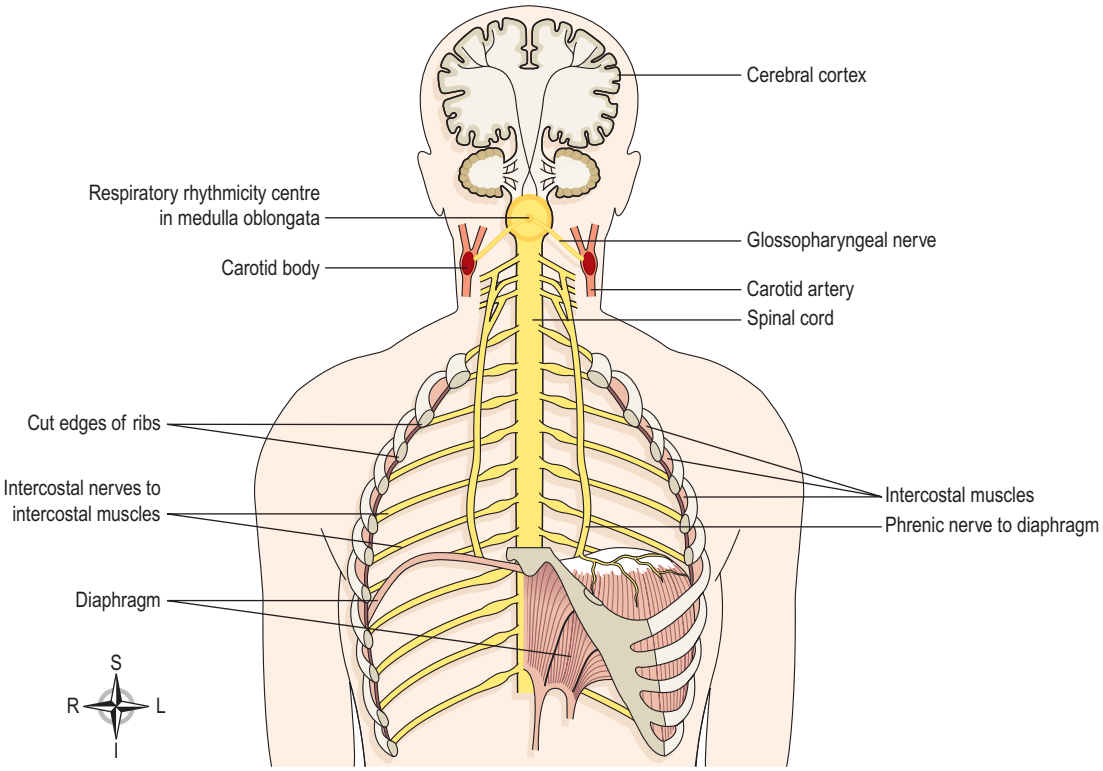


Figure 10.26 Some of the structures involved in control of respiration.

Exercise and respiration

Physical exercise increases both the rate and depth of respiration to supply the increased oxygen requirements of the exercising muscles. Exercising muscles produces higher quantities of CO_2, which stimulates central and peripheral chemoreceptors. The increased respiratory effort persists even after exercise stops, in order to supply enough oxygen to repay the 'oxygen debt'. This represents mainly the oxygen needed to get rid of wastes, including lactic acid.

Other factors that influence respiration

Breathing may be modified by the higher centres in the brain by:

- speech, singing
- emotional displays, e.g. crying, laughing, fear
- drugs, e.g. sedatives, alcohol
- sleep.

Body temperature influences breathing. In fever, respiration is increased due to increased metabolic rate, while in hypothermia respiration and metabolism are depressed. Temporary changes in respiration occur in swallowing, sneezing and coughing.

The Hering–Breuer reflex prevents overinflation of the lungs. Stretch receptors in the lung, linked to the respiratory centre by the vagus nerve, inhibit respiration when lung volume approaches maximum.

Ageing and the respiratory system

Learning outcome

After studying this section, you should be able to:

- describe the main consequences of ageing on respiratory structure and function.

Respiratory performance declines with age, beginning in the mid-20s. General loss of elastic tissue in the lungs increases the likelihood that small airways will collapse during expiration and decreases the functional lung volume. Varying degrees of emphysema (p. 263) are normal in older people, usually without symptoms. Cartilage in general becomes less flexible with age and there is an increased risk of arthritic joint changes. The ribcage therefore becomes stiffer which, along with the general age-related reduction in muscle function, reduces the respiratory minute volume.

The risk of respiratory infections rises because of age-related immune decline and loss of mucus production in the airways. The respiratory reflexes that increase respiratory effort in response to rising blood CO_2/falling blood O_2 levels become less efficient, so older people may respond less well to adverse changes in blood gases.

Age-related respiratory compromise is greatly enhanced in smokers.

Disorders of the upper respiratory tract

Learning outcome

After studying this section, you should be able to:

- describe the common inflammatory and infectious disorders of the upper respiratory tract.

Infectious and inflammatory disorders

Inflammation of the upper respiratory tract can be caused by inhaling irritants, such as cigarette smoke or air pollutants, but is commonly due to infection. Such infections are usually caused by viruses that lower the resistance of the respiratory tract to other infections. This allows bacteria to invade the tissues. Such infections are only life-threatening if they spread to the lungs or other organs, or if inflammatory swelling and exudate block the airway.

Pathogens are usually spread by droplet infection (tiny droplets containing pathogenic material suspended in the air), in dust or by contaminated equipment and dressings. If not completely resolved, acute infection may become chronic.

Viral infections cause acute inflammation of the mucous membrane, leading to tissue congestion and profuse exudate of watery fluid. Secondary bacterial infection is particularly likely in vulnerable people such as children and older adults.

Viral infections are most dangerous in infants, young children and the elderly.

Common cold and influenza

The common cold (coryza) is usually caused by the rhinoviruses and is a highly infectious, normally mild illness characterised mainly by a runny nose (rhinorrhoea), sneezing, sore throat and sometimes slight fever. Normally a cold runs its course over a few days. Influenza is caused by a different group of viruses and produces far more severe symptoms than a cold, including very high temperatures and muscle pains; complete recovery can take weeks and secondary bacterial infections are more common than with a simple cold. In healthy adults, most strains of influenza are incapacitating but rarely fatal unless infection spreads to the lungs.

Sinusitis

This is usually caused by spread of microbes from the nose and pharynx to the mucous membrane lining the paranasal sinuses. The primary viral infection is usually followed by bacterial infection. The congested mucosa may block the openings between the nose and the sinuses, preventing drainage of mucopurulent discharge. Symptoms include facial pain and headache. If there are repeated attacks or if recovery is not complete, the infection may become chronic.

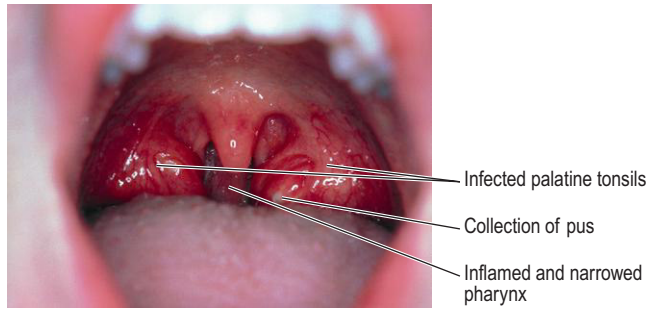


Figure 10.27 Streptococcal tonsillitis.

Tonsillitis

Viruses and *Streptococcus pyogenes* are common causes of inflammation of the palatine tonsils, palatine arches and walls of the pharynx (Fig. 10.27). Severe infection may lead to suppuration and abscess formation (*quinsy*). Occasionally the infection spreads into the neck causing cellulitis. Following acute tonsillitis, swelling subsides and the tonsil returns to normal but repeated infection may lead to chronic inflammation, fibrosis and permanent enlargement. Endotoxins from tonsillitis caused by *Streptococcus pyogenes* are associated with the development of rheumatic fever (p. 434) and glomerulonephritis (p. 350). Repeated infection of the nasopharyngeal tonsil (adenoids, Fig. 10.3) can leave them enlarged and fibrotic, and can cause airway obstruction, especially in children.

Pharyngitis, laryngitis and tracheitis

The pharynx, larynx and trachea may become infected secondary to other upper respiratory tract infections, e.g. the common cold or tonsillitis

Laryngotracheobronchitis (croup in children) is a rare but serious complication of upper respiratory tract infections. The airway is obstructed by marked swelling around the larynx and epiglottis, accompanied by wheeze and breathlessness (dyspnoea).

Diphtheria

This is a bacterial infection of the pharynx which may extend to the nasopharynx and trachea, caused by *Corynebacterium diphtheriae*. A thick fibrous membrane forms over the area and may obstruct the airway. The microbe produces powerful exotoxins that may severely damage cardiac and skeletal muscle, the liver, kidneys and adrenal glands. Where immunisation is widespread, diphtheria is rare.

Hay fever (allergic rhinitis)

In this condition, *atopic* ('immediate') hypersensitivity (p. 385) develops to foreign proteins (antigens), e.g. pollen, mites in pillow feathers, animal dander. The acute inflammation of nasal mucosa and conjunctiva causes

rhinorrhoea (excessive watery exudate from the nose), redness of the eyes and excessive tear production. Atopic hypersensitivity tends to run in families, but no single genetic factor has yet been identified; it is likely to involve multiple genes. Other forms of atopic hypersensitivity include childhood onset asthma (see below), eczema (p. 371) in infants and young children and food allergies.

Obstructive lung disorders

Learning outcomes

After studying this section, you should be able to:

- compare the causes and pathology of chronic and acute bronchitis
- discuss the pathologies of the main forms of emphysema
- discuss the causes and disordered physiology of asthma
- explain the main physiological abnormality in bronchiectasis
- describe the effect of cystic fibrosis on lung function.

Obstructive lung disorders are characterised by blockage of airflow through the airways. Obstruction may be acute or chronic.

Bronchitis

Acute bronchitis

This is usually a secondary bacterial infection of the bronchi, usually preceded by a common cold or influenza, which may also complicate measles and whooping cough in children. Viral infection depresses normal defence mechanisms, allowing pathogenic bacteria already present in the respiratory tract to multiply. Downward spread of infection may lead to bronchiolitis and/or bronchopneumonia, especially in children and in debilitated or older adults.

Chronic bronchitis

This is a common disorder that becomes increasingly debilitating as it progresses. Chronic bronchitis is defined clinically when an individual has had a cough with sputum for 3 months in 2 successive years. It is a progressive inflammatory disease resulting from prolonged irritation of the bronchial epithelium, often worsened by damp or cold conditions.

It is often a consequence of cigarette smoking, but can also follow episodes of acute bronchitis (often caused by *Haemophilus influenzae* or *Streptococcus pneumoniae*) and chronic exposure to airborne irritants such as urban fog, vehicular exhaust fumes or industrial pollutants.

It develops mostly in middle-aged men who are chronic heavy smokers and may have a familial predisposition. Acute exacerbations are common, and often associated with infection. The changes occurring in the bronchi include:

Increased size and number of mucus glands. The increased volume of mucus may block small airways, and overwhelm the ciliary escalator, leading to reduced clearance, a persistent cough and infection.

Oedema and other inflammatory changes. These cause swelling of the airway wall, narrowing the passageway and obstructing airflow.

Reduction in number and function of ciliated cells. Ciliated epithelium is progressively destroyed and replaced by a different type of epithelium with no cilia. This may precede neoplastic (cancerous) change. As ciliary efficiency is reduced, the problem of mucus accumulation is worsened, further increasing the risk of infection.

Fibrosis of the airways. Inflammatory changes lead to fibrosis and stiffening of airway walls, further reducing airflow.

Breathlessness (dyspnoea). This is worse with physical exertion and increases the work of breathing.

Ventilation of the lungs becomes severely impaired, causing breathlessness, leading to hypoxia, pulmonary hypertension and right-sided heart failure. As respiratory failure develops, arterial blood PO_2 is reduced (*hypoxaemia*) and is accompanied by a rise in arterial blood PCO_2 (*hypercapnia*). When the condition becomes more severe, the respiratory centre in the medulla responds to hypoxaemia rather than to hypercapnia. In the later stages, the inflammatory changes begin to affect the smallest bronchioles and the alveoli themselves, and emphysema develops (see below). The term *chronic obstructive pulmonary disease* (COPD) is sometimes used to describe this situation.

Emphysema (Figs 10.28, 10.29)

Pulmonary emphysema

Pulmonary emphysema, generally referred to simply as emphysema, usually develops as a result of long-term inflammatory conditions or irritation of the airways, e.g. in smokers or coal miners. Occasionally, it may be due to a genetic deficiency in the lung of an antiproteolytic enzyme, α_1 anti-trypsin. These conditions lead to progressive destruction of supporting elastic tissue in the lung, and the lungs progressively expand (barrel chest) because their ability to recoil is lost. In addition, there is irreversible distension of the respiratory bronchioles, alveolar

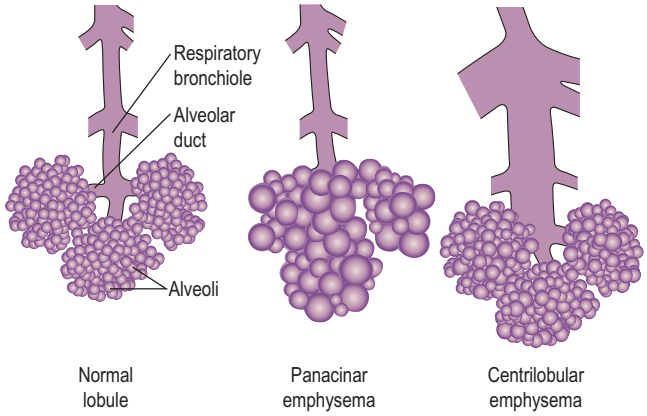


Figure 10.28 Emphysema.

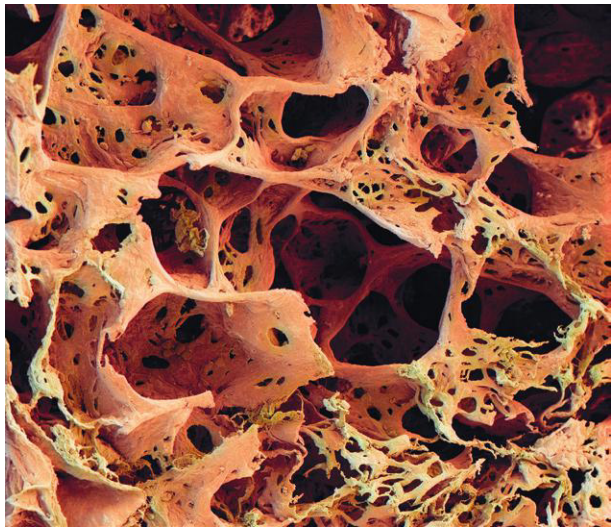


Figure 10.29 Coloured scanning electron micrograph of lung tissue with emphysema.

ducts and alveoli, reducing the surface area for the exchange of gases.

On microscopic examination, the lung tissue is full of large, irregular cavities created by the destruction of alveolar walls (Fig. 10.29, and compare with Fig. 10.19). There are two main types and both are usually present.

Panacinar emphysema

The walls between adjacent alveoli break down, the alveolar ducts dilate and interstitial elastic tissue is lost. The lungs become distended and their capacity is increased. Because the volume of air in each breath remains unchanged, it constitutes a smaller proportion of the total volume of air in the distended alveoli, reducing the partial pressure of oxygen. This reduces the concentration gradient of O_2 across the alveolar membrane, decreasing diffusion of O_2 into the blood. Merging of alveoli reduces the surface area for exchange of gases. In the early stages of the disease, normal arterial blood O_2 and CO_2 levels are maintained at rest by hyperventilation. As the disease progresses the combined effect of these changes may lead to hypoxia, pulmonary hypertension and eventually right-sided heart failure.

Centrilobular emphysema

In this form there is irreversible dilation of the respiratory bronchioles supplying lung lobules. When inspired air reaches the dilated area the pressure falls, leading to a reduction in alveolar air pressure, reduced ventilation efficiency and reduced partial pressure of oxygen. As the disease progresses the resultant hypoxia leads to pulmonary hypertension and right-sided heart failure.

Interstitial emphysema

Interstitial emphysema means the presence of air in the thoracic interstitial tissues, and this may happen in one of the following ways:

- from the outside by injury, e.g. fractured rib, stab wound
- from the inside when an alveolus ruptures through the pleura, e.g. during an asthmatic attack, in bronchiolitis, coughing as in whooping cough.

The air in the tissues usually tracks upwards to the soft tissues of the neck where it is gradually absorbed, causing no damage. A large quantity in the mediastinum may, however, limit heart movement.

It is important to distinguish between interstitial emphysema and pneumothorax (p. 271), where the air is trapped between the pleura.

Asthma (Fig. 10.30)

Asthma is a common inflammatory disease of the airways associated with episodes of reversible over-reactivity of the airway smooth muscle. The mucous membrane and muscle layers of the bronchi become thickened and the mucous glands enlarge, reducing airflow in the lower respiratory tract. The walls swell and thicken with inflammatory exudate and an influx of inflammatory cells, especially eosinophils. During an asthmatic attack, spasmodic contraction of bronchial muscle (*bronchospasm*) constricts the airways and there is excessive secretion of thick sticky mucus, which further narrows the airway. Only partial expiration is achieved, so the lungs become hyperinflated and there is severe dyspnoea and wheezing. The duration of attacks usually varies from a few minutes to hours. In severe acute attacks the bronchi may be obstructed by mucus plugs, blocking airflow and leading to acute respiratory failure, hypoxia and possibly death.

Non-specific factors that may precipitate asthma attacks include cold air, cigarette smoking, air pollution, upper respiratory tract infection, emotional stress and strenuous exercise.

There are two clinical categories of asthma, which generally give rise to identical symptoms and are

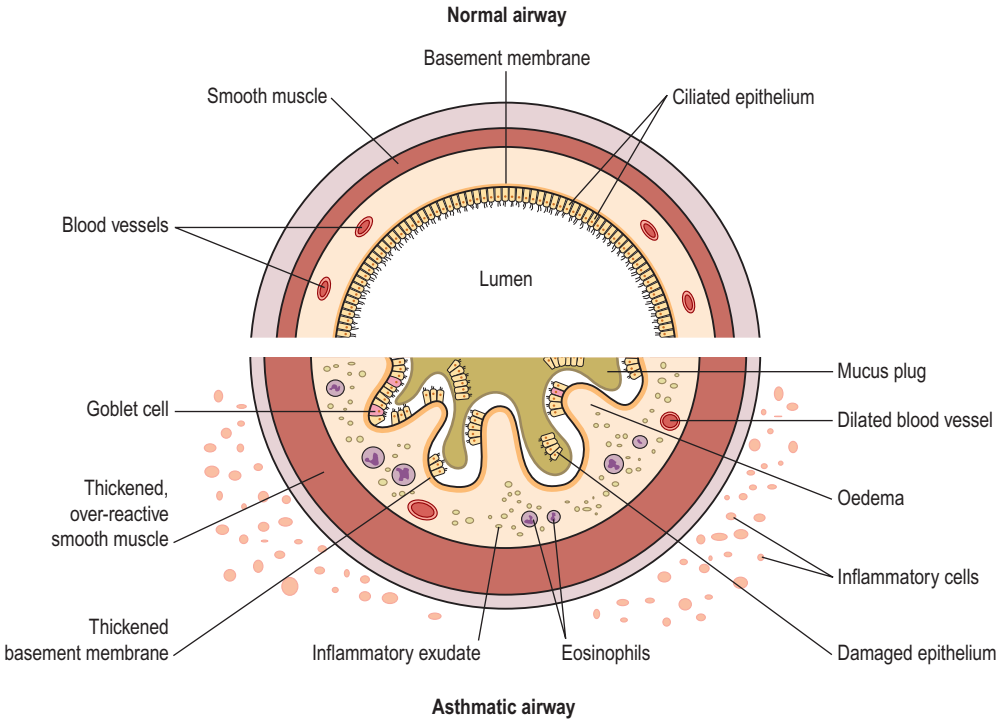


Figure 10.30 Cross-section of the airway wall in asthma.

treated in the same way. Important differences include typical age of onset and the contribution of an element of allergy. Asthma, whatever the aetiology, can usually be well controlled with inhaled anti-inflammatory and bronchodilator agents, enabling people to live a normal life.

Atopic (childhood onset, extrinsic) asthma

This occurs in children and young adults who have atopic (type I) hypersensitivity (p. 385) to foreign protein, e.g. pollen, dust containing mites from carpets, feather pillows, animal dander, fungi. A history of infantile eczema or food allergies is common and there are often close family members with a history of allergy.

As in hayfever, antigens (allergens) are inhaled and absorbed by the bronchial mucosa. This stimulates the production of IgE antibodies that bind to the surface of mast cells and basophils round the bronchial blood vessels. When the allergen is encountered again, the antigen/antibody reaction results in the release of histamine and other related substances that stimulate mucus secretion and muscle contraction that narrows the airways. Attacks tend to become less frequent and less severe with age.

Non-atopic (adult onset, intrinsic) asthma

This type occurs later in adult life and there is no history of childhood allergic reactions. It can be associated with chronic inflammation of the upper respiratory tract, e.g. chronic bronchitis, nasal polyps. Other trigger factors include exercise and occupational exposure, e.g. inhaled paint fumes. Aspirin triggers an asthmatic reaction in some people. Attacks tend to increase in severity over time and lung damage may be irreversible. Eventually, impaired lung ventilation leads to hypoxia, pulmonary hypertension and right-sided heart failure.

Bronchiectasis

This is permanent abnormal dilation of bronchi and bronchioles. It is associated with chronic bacterial infection, and sometimes with a history of childhood bronchiolitis and bronchopneumonia, cystic fibrosis, or bronchial tumour. The bronchi become obstructed by mucus, pus and inflammatory exudate and the alveoli distal to the blockage collapse as trapped air is absorbed. Interstitial elastic tissue degenerates and is replaced by fibrous adhesions that attach the bronchi to the parietal pleura. The pressure of inspired air in these damaged bronchi leads to dilation proximal to the blockage. The persistent severe coughing to remove copious purulent sputum causes intermittent increases in pressure in the blocked bronchi, leading to further dilation.

The lower lobe of the lung is usually affected. Suppuration is common. If a blood vessel is eroded, haemoptysis may occur, or pyaemia, leading to abscess formation elsewhere in the body, commonly the brain. Progressive fibrosis of the lung leads to hypoxia, pulmonary hypertension and right-sided heart failure.

Cystic fibrosis (mucoviscidosis)

This is one of the most common genetic diseases (p. 446), affecting 1 in 2500 babies. It is estimated that almost 5% of people carry the abnormal recessive gene which must be present in both parents to cause the disease.

The secretions of all exocrine glands have abnormally high viscosity, but the most severely affected are those of the lungs, pancreas, intestines, biliary tract, and the reproductive system in the male. Sweat glands secrete abnormally large amounts of salt during excessive sweating. In the pancreas, highly viscous mucus is secreted by the walls of the ducts and causes obstruction, parenchymal cell damage, the formation of cysts and defective enzyme secretion. In the newborn, intestinal obstruction may be caused by a plug of meconium (fetal faeces) and viscid mucus, leading to perforation of the alimentary canal wall and meconium peritonitis which is often fatal. In less acute cases there may be impairment of protein and fat digestion resulting in malabsorption, steatorrhoea and failure to thrive in infants. In older children, common consequences include:

- digestion of food and absorption of nutrients is impaired
- there may be obstruction of bile ducts in the liver, causing cirrhosis
- bronchitis, bronchiectasis and pneumonia may develop.

The life span of affected individuals is around 50 years; the main treatments offered are aimed at maintaining effective respiratory function and preventing infection. Chronic lung and heart disease are common complications.

Restrictive disorders

Learning outcomes

After studying this section, you should be able to:

- describe the main pneumoconioses
- outline the main causes and consequences of chemically induced lung disease.

Restrictive lung disorders are characterised by increasing stiffness (low compliance) of lung tissue, making it harder to inflate the lung and increasing the work of breathing. Chronic restrictive disease is often associated with progressive fibrosis caused by repeated and ongoing inflammation of the lungs.

Pneumoconioses

This group of lung diseases is caused by prolonged exposure to inhaled organic dusts, which triggers a generalised inflammation and progressive fibrosis of lung tissues. Inhalation of work-related pollutants was a major cause of lung disease prior to the introduction of legislation that limits workers' exposure to them. To cause disease, particles must be so small that they are carried in inspired air to the level of the respiratory bronchioles and alveoli, where they can only be cleared by phagocytosis. Larger particles are trapped by mucus higher up the respiratory tract and expelled by ciliary action and coughing. The risk increases with the duration and concentration of exposure, and in cigarette smokers.

Coal worker's pneumoconiosis

Inhalation of coal dust over a prolonged period leads to varying degrees of respiratory impairment; many miners develop little or no disease but others suffer massive progressive fibrosis that is ultimately fatal. The inhaled dust collects in the lung and is phagocytosed by macrophages, which collect around airways and trigger varying degrees of fibrosis. If the fibrosis remains restricted to these small collections of macrophages and there is no significant reduction in lung function, the disorder is referred to as *simple coal worker's pneumoconiosis*, and is unlikely to progress once exposure to dust stops. For reasons that are unclear, the fibrotic changes in the lungs progress much more aggressively in some people, with formation of large dense fibrotic nodules, destruction and cavitation of lung tissue and potentially fatal respiratory impairment.

Silicosis

This may be caused by long-term exposure to dust containing silicon compounds. High-risk industries include quarrying, mining of minerals, stone masonry, sand blasting, glass making and pottery production.

Inhaled silica particles accumulate in the alveoli and are ingested by macrophages to which silica is toxic. The inflammatory reaction triggered when the macrophages die causes significant fibrosis.

Silicosis appears to predispose to the development of tuberculosis, which rapidly progresses to tubercular bronchopneumonia and possibly miliary TB. Gradual destruction of lung tissue leads to progressive reduction in pulmonary function, pulmonary hypertension and right-sided heart failure.

Asbestosis

Asbestosis, caused by inhaling asbestos fibres, usually develops after 10–20 years' exposure, but sometimes after only 2 years. Asbestos miners and workers involved in making and using some products containing asbestos are at risk. There are different types of asbestos, but blue asbestos is associated with the most serious disease.

In spite of their large size, asbestos particles penetrate to the level of respiratory bronchioles and alveoli. Macrophages accumulate in the alveoli and ingest shorter fibres. The larger fibres form *asbestos bodies*, consisting of fibres surrounded by macrophages, protein material and iron deposits. Their presence in sputum indicates exposure to asbestos but not necessarily asbestosis. The macrophages that have engulfed fibres migrate out of the alveoli and accumulate around respiratory bronchioles and blood vessels, stimulating the formation of fibrous tissue. Lung tissue is progressively destroyed, with the development of dyspnoea, chronic hypoxia, pulmonary hypertension and right-sided heart failure. The link between inhaled asbestos and fibrosis is not clear. It may be that asbestos stimulates the macrophages to secrete enzymes that promote fibrosis or that it stimulates an immune reaction causing fibrosis. Asbestos is linked to the development of mesothelioma (p. 270).

Extrinsic allergic alveolitis

This group of conditions is caused by inhaling organic dusts, including those in Table 10.3. The contaminants act as antigens causing a type III hypersensitivity reaction in the walls of the alveoli.

Initially, the allergy causes bronchiolitis, dyspnoea, cough, accumulation of inflammatory cells and granuloma (collections of macrophages) formation. If the exposure is brief, the inflammatory response may resolve but on repeated exposures, pulmonary fibrosis develops.

Pulmonary toxins

Lung disease can be triggered by a range of toxins and drugs, including:

Paraquat. This weedkiller causes pulmonary oedema, irreversible pulmonary fibrosis and renal damage and ingestion can be fatal.

Drugs. The mechanism and severity of drug-induced pulmonary damage varies depending on the drug and the general condition of the patient. Some drugs used to treat cancer, including bleomycin and methotrexate, can trigger progressive fibrotic changes. Other common drugs, including angiotensin converting enzyme inhibitors (used in hypertension and other cardiovascular conditions), phenytoin (an anticonvulsant) and hydralazine (used in hypertension) can also have pulmonary side-effects.

High concentration oxygen therapy. Premature babies may require oxygen treatment while their lung function matures, but the high concentrations used can cause permanent fibrotic damage to the lungs, as well as to the retina of the eye (p. 212). People of any age who require high concentration oxygen therapy may also develop pulmonary fibrosis.

Table 10.3 Conditions caused by organic dusts

Disease	Contaminant
Farmer's lung	Mouldy hay
Bagassosis	Mouldy sugar waste
Bird handler's lung	Moulds in bird droppings
Malt worker's lung	Mouldy barley
Byssinosis	Cotton fibres

Lung infections

Learning outcome

After studying this section, you should be able to:

- describe the causes and effects of lung infection, including pneumonia, abscess and tuberculosis.

Pneumonia (Fig. 10.31)

Pneumonia means infection of the alveoli. This occurs when pulmonary defence mechanisms fail to prevent

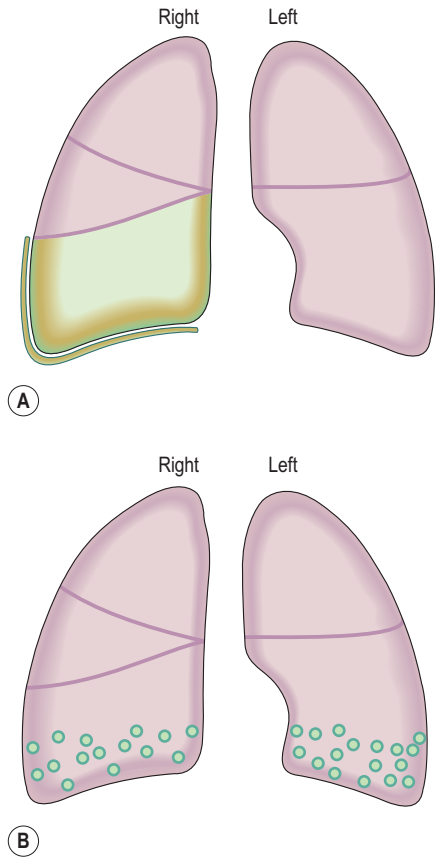


Figure 10.31 Distribution of infected tissue. A. Lobar pneumonia. **B.** Bronchopneumonia.

inhaled or blood-borne microbes reaching and colonising the lungs. The following are some predisposing factors.

Impaired coughing. Coughing is an effective cleaning mechanism, but if it is impaired or lost by, e.g., damage to respiratory muscles or the nerves supplying them, or painful coughing, then respiratory secretions may accumulate and become infected.

Damage to the epithelial lining of the tract. Ciliary action may be impaired or the epithelium destroyed by, e.g., tobacco smoking, inhaling noxious gases, infection.

Impaired alveolar phagocytosis. Depressed macrophage activity may be caused by tobacco smoking, alcohol, anoxia, oxygen toxicity.

Hospitalisation. Especially when mechanically assisted ventilation is required.

Other factors. The risk of pneumonia is increased in:

- extremes of age
- leukopenia
- chronic disease, e.g. heart failure, cancer, chronic renal failure, alcoholism
- suppression of immunity caused by, e.g. ionising radiation, corticosteroid drugs
- hypothermia.

Causative organisms

A wide variety of organisms, including bacteria, viruses, mycoplasma, protozoa and fungi, can cause pneumonia under appropriate conditions. The commonest pathogen, especially in lobar pneumonia, is the bacterium *Streptococcus pneumoniae*. Others include *Staphylococcus aureus* and *Haemophilus influenzae*. *Legionella pneumophila* spreads through water distribution systems, e.g. air conditioning systems, and is transmitted via droplet inhalation. *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are common causes of hospital-acquired pneumonia.

Lobar pneumonia (Fig. 10.31A)

This is infection of one or more lobes, usually by *Streptococcus pneumoniae*, leading to production of watery inflammatory exudate in the alveoli. This accumulates and fills the lobule which then overflows into and infects adjacent lobules. It is of sudden onset and pleuritic pain accompanies inflammation of the visceral pleura. If not treated with antibiotics the disease follows its course and resolves within 2–3 weeks. This form of pneumonia is most common in previously healthy young adults.

Bronchopneumonia (Fig. 10.31B)

Infection spreads from the bronchi to terminal bronchioles and alveoli. As these become inflamed, fibrous exudate accumulates and there is an influx of leukocytes. Small foci of consolidation (fluid-filled alveoli) develop. There is frequently incomplete resolution with fibrosis. Bronchiectasis is a common complication leading to further acute attacks, lung fibrosis and progressive destruction of lung substance. Bronchopneumonia occurs most commonly in infancy and old age, and death is fairly common, especially when the condition complicates debilitating diseases. Predisposing factors include:

- debility due to, e.g., cancer, uraemia, cerebral haemorrhage, congestive heart failure, malnutrition, hypothermia
- lung disease, e.g. bronchiectasis, cystic fibrosis or acute viral infection
- general anaesthesia, which depresses respiratory and ciliary activity
- inhalation of gastric contents (*aspiration pneumonia*) in, e.g., unconsciousness, very deep sleep, following excessive alcohol consumption, drug overdose
- inhalation of infected material from the paranasal sinuses or upper respiratory tract.

Lung abscess

This is localised suppuration and necrosis within the lung substance.

Sources of infection

The abscess may develop from local infection:

- if pneumonia is inadequately treated
- as a result of trauma, e.g. rib fracture, stab wound or surgery
- of adjacent structures, e.g. oesophagus, spine, pleural cavity, or a subphrenic abscess.

Occasionally a lung abscess develops when infected material travelling in the bloodstream, a *septic embolus*, arrives and lodges in the lung. Such material usually originates from a thrombophlebitis (p. 123) or infective endocarditis (p. 128).

Outcomes

Recovery from lung abscess may either be complete or lead to complications, e.g.:

- chronic suppuration
- septic emboli may spread to other parts of the body, e.g. the brain, causing cerebral abscess or meningitis
- subpleural abscesses may spread and cause empyema and possibly bronchopleural fistula formation
- erosion of a pulmonary blood vessel, leading to haemorrhage.

Tuberculosis (TB)

TB is a major health problem worldwide, particularly in low-income countries that cannot afford effective prevention or treatment, and in countries where HIV disease is common. It is caused by one of two similar forms of

mycobacteria, the main one being *Mycobacterium tuberculosis*. Humans are the main host. The microbes are spread by inhalation, either by aerosol droplet infection from an individual with active tuberculosis, or in dust contaminated by infected sputum.

Less commonly in developed countries because of pasteurisation of milk, TB can be caused by *Mycobacterium bovis*, from cows.

Pulmonary tuberculosis

Primary tuberculosis

Initial infection usually involves the apex of the lung. Inflammatory cells, including macrophages and lymphocytes, are recruited in defence, sealing off the infected lesions in *Ghon foci*. The centres of Ghon foci are filled with a cheese-like necrotic material that may contain significant numbers of active bacteria that have survived inside macrophages. If infection spreads to the regional lymph nodes, the Ghon foci and these infected nodes together are called the *primary complex*. At this stage, the disease is likely to have caused few, if any, clinical symptoms and in the great majority of people progresses no further, although calcified primary complexes are clearly identifiable on X-ray. Exposure to the bacterium causes *sensitisation*, which leads to a strong T-cell mediated immune reaction (p. 380) if the infection becomes reactivated.

Secondary TB

This is usually due to reactivation of disease from latent bacteria surviving primary TB, and can occur decades after the initial exposure in response to factors such as stress, ageing, immunocompromise or malnutrition. The infection is now much more likely to progress than it was at the primary stage, with significant destruction and cavitation of lung tissues. Symptoms include fever, cough, malaise, haemoptysis, weight loss and night sweats. Nearly half of patients with secondary TB develop non-pulmonary involvement.

Non-pulmonary TB

Primary TB rarely affects tissues other than the lung, but non-pulmonary involvement in secondary TB is very common. Widely disseminated TB is nearly always fatal unless adequately treated.

Miliary TB

Blood-borne spread from the lungs leads to widespread dissemination of the bacilli throughout body tissues, and foci of infection can establish in any organ, including the bone marrow, liver, spleen, kidneys and CNS. Numerous tiny nodules develop in the lungs, which on X-ray look like sprinkled millet seeds (hence 'miliary'). Rapid treatment is essential to prevent further spread.

Lymph node TB

This is the second commonest site of infection after the lung. Lymph nodes in the mediastinum, neck, axilla and groin are most likely to be affected. Infection causes swelling and central necrosis of the node. It is usually painless.

Joint and bone TB

The intervertebral, hip and knee joints are most commonly affected, and in children are usually a consequence of primary TB. Infection of the intervertebral disc or synovial membrane of a synovial joint is followed by extensive destruction of cartilage and adjacent bone, which in turn can progress to tuberculous osteomyelitis.

Other affected tissues

The pericardium, skin and GI tract may all become involved. One in five people with extrapulmonary disease develop CNS infection, which requires urgent treatment and, if not fatal, can leave survivors with permanent neurological damage.

Lung tumours

Learning objective

After studying this section, you should be able to:

- describe the pathology of the common lung tumours.

Benign tumours of the lung are rare.

Bronchial carcinoma

Primary bronchial carcinoma is a very common malignancy. The vast majority of cases (up to 90%) occur in smokers or those who inhale other people's smoke (passive smokers). Other risk factors include exposure to airborne dusts and the presence of lung fibrosis. The primary tumour has usually spread by the time of diagnosis, and therefore the prognosis of this type of cancer is usually extremely poor.

The tumour usually develops in a main bronchus, forming a large friable mass projecting into the lumen, sometimes causing obstruction. Mucus then collects and predisposes to infection. As the tumour grows it may erode a blood vessel, causing haemoptysis.

Spread of bronchial carcinoma

This does not follow any particular pattern or sequence. Spread is by infiltration of local tissues and the transport of tumour fragments in blood and lymph. If blood or lymph vessels are eroded, fragments may spread while the tumour is still quite small. A metastatic tumour may, therefore, cause symptoms before the primary in the lung has been detected.

Local spread. This may be within the lung or to mediastinal structures, e.g. blood vessels, nerves, oesophagus.

Lymphatic spread. Tumour fragments spread along lymph vessels to successive lymph nodes in which they may cause metastatic tumours. Fragments may enter lymph draining from a tumour or gain access to a larger vessel if its walls have been eroded by a growing tumour.

Blood spread. Tumour cells can enter the blood if a blood vessel is eroded by a growing tumour. The most common sites of blood-borne metastases are the liver, brain, adrenal glands, bones and kidneys.

Pleural mesothelioma

The majority of cases of this malignant tumour of the pleura are linked with previous exposure to asbestos dust, e.g. asbestos workers and people living near asbestos mines and factories. Smoking multiplies the risk of mesothelioma several fold in people exposed to asbestos. Mesothelioma may develop after widely varying duration of asbestos exposure, from 3 months to 60 years, and is usually associated with crocidolite fibres (blue asbestos). The tumour involves both layers of pleura and as it grows it obliterates the pleural cavity, compressing the lung. Lymph and blood-spread metastases are commonly found in the hilar and mesenteric lymph nodes, the other lung, liver, thyroid and adrenal glands, bone, skeletal muscle and the brain. The prognosis is usually very poor.

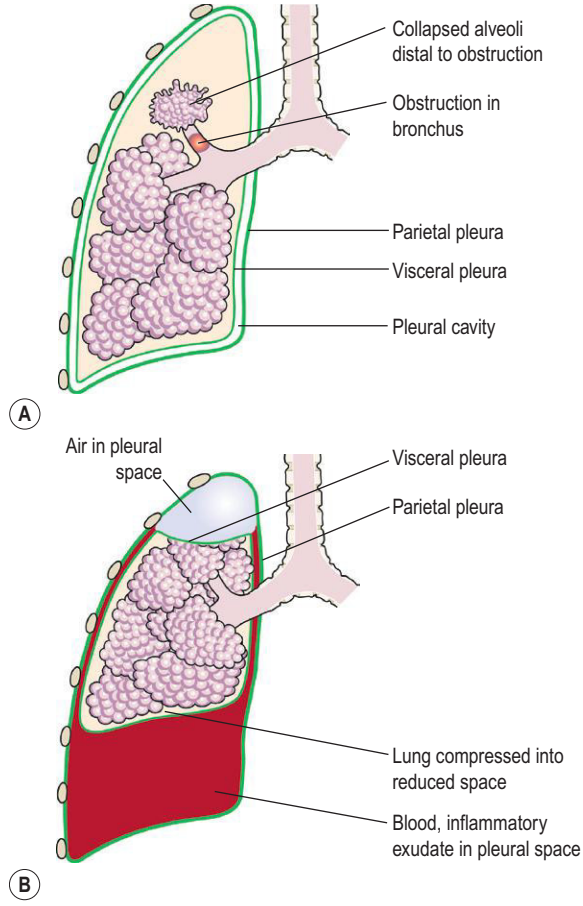


Figure 10.32 Collapse of a lung. A. Absorption collapse. **B.** Pressure collapse.

Lung collapse (Fig. 10.32)

Learning objectives

After studying this section, you should be able to:

- list the main causes of lung collapse
- describe the effects of lung collapse.

The clinical effects of collapse (*atelectasis*) of all or part of a lung depend on how much of the lung is affected. Fairly large sections of a single lung can be out of action without obvious symptoms. There are four main causes of this condition:

- obstruction of an airway (absorption collapse)
- impaired surfactant function
- pressure collapse
- alveolar hypoventilation.

Obstruction of an airway (absorption collapse, Fig. 10.32A)

The amount of lung affected depends on the size of the obstructed air passage. Distal to the obstruction air is trapped and absorbed, the lung collapses and secretions collect. These may cause infection, and sometimes abscess formation. Short-term obstruction is usually followed by reinflation of the lung without lasting ill-effects. Prolonged obstruction leads to progressive fibrosis and permanent collapse. Sudden obstruction may be due to inhalation of a foreign body (usually into the (R) primary bronchus, which is wider and more steeply angled than the left) or a mucus plug formed during an asthmatic attack or in chronic bronchitis. Gradual obstruction may be due to a bronchial tumour or pressure on a bronchus by, e.g., enlarged mediastinal lymph nodes, aortic aneurysm.

Impaired surfactant function

Premature babies, born before the 34th week, may be unable to expand their lungs by their own respiratory effort because their lungs are too immature to produce surfactant (p. 253). These babies may need to be mechanically ventilated until their lungs begin to produce surfactant. This is called *neonatal respiratory distress syndrome* (NRDS).

In *adult respiratory distress syndrome* (ARDS), dilution of surfactant by fluid collecting in the alveoli (pulmonary oedema) leads to atelectasis. These patients are nearly always gravely ill already, and collapse of substantial areas of lung contributes to the mortality rate of around one-third.

Pressure collapse

When air or fluid enters the pleural cavity the negative pressure becomes positive, preventing lung expansion. Fluids settle in the lung bases, whereas collections of air are usually found towards the lung apex (Fig. 10.32B). The collapse usually affects only one lung and may be partial or complete. There is no obstruction of the airway.

Pneumothorax

In this condition there is air in the pleural cavity. It may occur spontaneously or be the result of trauma.

Spontaneous pneumothorax. This may be either primary or secondary. *Primary spontaneous pneumothorax* is of unknown cause, often recurrent, and occurs in fit and healthy people, usually males between 20 and 40 years. *Secondary spontaneous pneumothorax* occurs when air enters the pleural cavity after the visceral pleura ruptures due to lung disease, e.g. emphysema, asthma, pulmonary tuberculosis, bronchial cancer.

Traumatic pneumothorax. This is due to a penetrating injury that breaches the pleura, e.g. compound fracture of rib, stab or gunshot wound, surgery.

Tension pneumothorax (Fig. 10.33)**.** This occurs as a complication when a flap or one-way valve develops between the lungs and the pleural cavity. Air enters the pleural cavity during inspiration but cannot escape on expiration and steadily, sometimes rapidly, accumulates. This expansion of the affected lung pushes the mediastinum towards the unaffected side, compressing its contents, including the unaffected lung and great vessels. Without prompt treatment, severe respiratory distress precedes cardiovascular collapse.

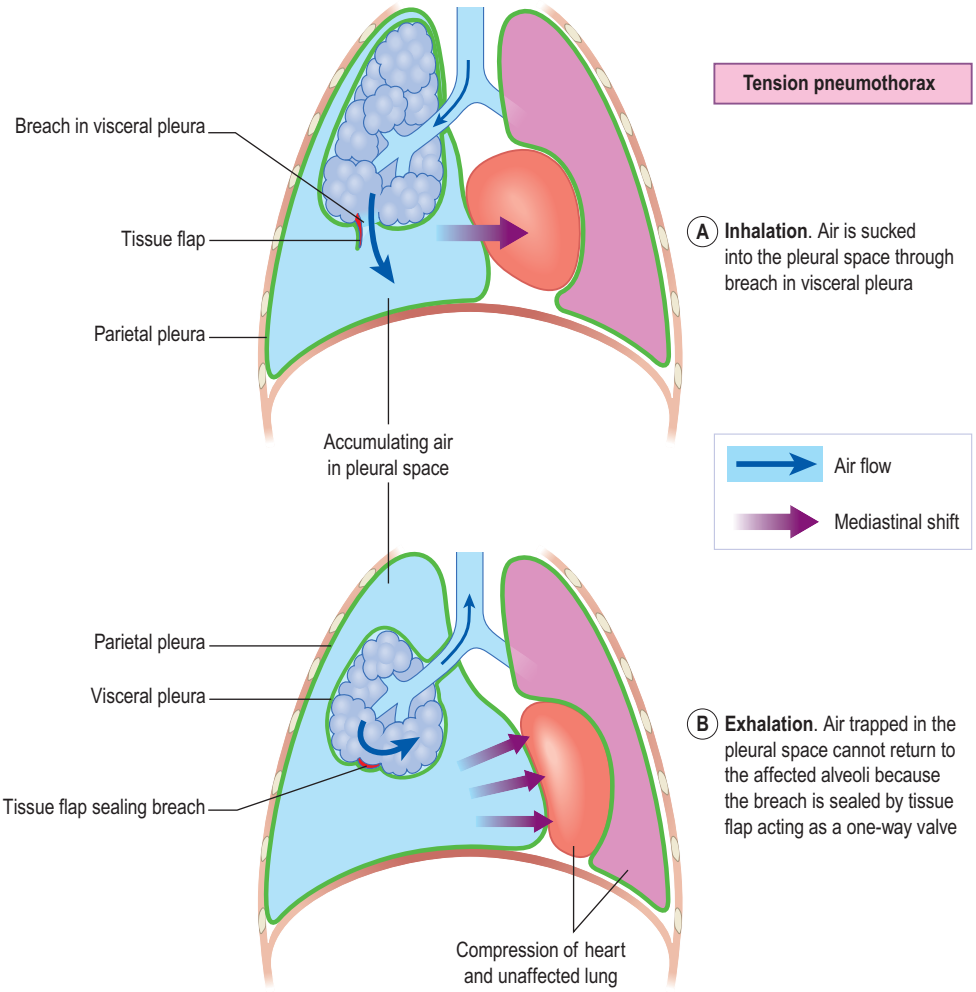


Figure 10.33 Tension pneumothorax.

Haemothorax

This is blood in the pleural cavity. It may be caused by:

- penetrating chest injury involving blood vessels
- ruptured aortic aneurysm
- erosion of a blood vessel by a malignant tumour.

Pleural effusion

This is excess fluid in the pleural cavity that may be caused by:

- increased hydrostatic pressure, e.g. heart failure (p. 126), increased blood volume
- increased capillary permeability due to local inflammation, e.g. lobar pneumonia, pulmonary tuberculosis, bronchial cancer, mesothelioma
- decreased plasma osmotic pressure, e.g. nephrotic syndrome (p. 351), liver cirrhosis (p. 334)
- impaired lymphatic drainage, e.g. malignant tumour involving the pleura.

Following haemothorax and pleural effusion, fibrous adhesions which limit reinflation may form between the layers of pleura.

Alveolar hypoventilation

In the normal individual breathing quietly at rest, there are always some collapsed lobules within the lungs because of the low tidal volume. These lobules re-expand without difficulty at the next deep inspiration. Non-physiological causes of hypoventilation collapse include post-operative collapse, particularly after chest and upper abdominal surgery, when pain restricts thoracic expansion. This predisposes to chest infections, because mucus collects in the underventilated airways and is not coughed up (expectorated).

For a range of self-assessment exercises on the topics in this chapter, visit Evolve online resources: https://evolve.elsevier.com/Waugh/anatomy/