Anatomy and Physiology of the Respiratory System

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The primary function of the respiratory system is to facilitate the entry of oxygen into the bloodstream and allow the coincidental loss of carbon dioxide from that system. The respiratory system has to have the ability to respond quickly to demands of the body and plays a critical role in the restoration and preservation of homeostasis in the tissues. The anatomy and morphology of the respiratory system has not only evolved to support its primary function, but in addition has also evolved to support other functions that are vital in maintaining the body's integrity. Such important and crucial roles include: aiding in the maintenance of the body's acid–base balance; metabolism of specific compounds; filtering unwanted materials from the circulation; prevention and reduction of infection and acting as a reservoir for blood (West 2000).

The main aim of this chapter is to examine the premise that the major purpose of the respiratory system is to provide the opportunity for inspired air to come into close proximity with the circulating blood thus allowing diffusion to occur (Bourke 2003). The rate of that diffusion will be in accord with Fick's law of diffusion (see Table 1.1).

It can be seen that Fick's law defines the essential morphology and physiology of the lung. Thus it is predictable that the region of the respiratory system which allows gas exchange to occur will have a thin sheet of tissue between the inspired air and the circulating blood. These regions within the lungs are known as alveoli.

This chapter aims to:

- ❑ Provide an overview of the gross anatomy of the respiratory system.
- ❑ Review the key physiological principles of the respiratory system and related aspects of the cardiovascular system including: ventilation; perfusion; mechanics of breathing; the control of breathing; the transport of gases within the cardiovascular system.

STRUCTURE OF THE RESPIRATORY SYSTEM

The major components of the respiratory system are two lungs set within the thoracic cage. The right lung is divided into three lobes, upper middle and lower, and the left lung into two lobes.

Table 1.1 Fick's law of diffusion.

Solutes and ions move randomly in all directions and the consequence is that in a non-homogeneous solution such random movement will result in a net movement of solute from regions of high concentration towards regions of lower concentration, i.e. the effective net movement is down a concentration gradient.
Molecules of a gas also move randomly and will thus tend to distribute themselves equally in an enclosed space. The net movement of molecules will be from regions of high partial pressure towards regions with a lower partial pressure, i.e. net movement is dependent on a partial pressure difference. The rate of diffusion of a specific gas through any gas is very much greater than the rate of diffusion through a liquid. It is often quoted that the rate of diffusion of CO_2 through air is 10 000 times greater than its diffusion rate through water. Even so because of the constant collisions between gas molecules they do not move directly, taking minutes or hours to move across an average room.
The rates of diffusion of gasses through a 'porous body' are inversely proportional to the square root of their molecular weights (Graham's law).
Thus molecules of hydrogen (H_2) will diffuse at 4× the rate of oxygen molecules (O_2).
Fick's first law of diffusion states that the amount of gas (J_{net}) that moves across a sheet of tissue is proportional to the partial pressure gradient of the gas (C) and the area of the sheet (A) but inversely proportional to its thickness (Δx).
$J_{net} = -D.A.\Delta C/\Delta x$
Where D is the diffusion coefficient (m^2sec^{-1})

Vessels, nerves and lymphatics enter the lungs on their medial surfaces at a point known as the hilum (Cotes 1993). Each lobe is divided into a number of wedge-shaped bronchopulmonary segments with their apices at the hilum and their bases at the lung surface. Each bronchopulmonary segment can be removed surgically with little bleeding or air leakage from the remaining lung (Selby 2002).

Each lung is lined by a thin membrane, the visceral pleura that is continuous with the parietal pleura lining the chest wall, diaphragm, pericardium and mediasturnum. The space between the parietal and visceral layers is very thin in health and lubricated with pleural fluid (Ward *et al.* 2002).

Figure 1.1 illustrates the gross anatomical features of the respiratory system. The upper respiratory tract comprises the nose, pharynx and larynx. The lower respiratory tract commences with the trachea and comprises the remaining sections of respiratory tract (Ward *et al.* 2002).

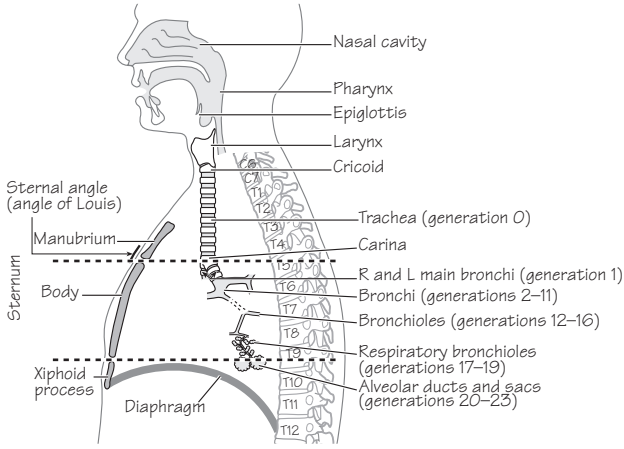

Fig. 1.1 Gross anatomical features of respiratory system. With permission from Blackwell Publishing (Ward *et al* 2002).

In fit healthy and well adults inspired air enters the respiratory tract usually via the nostrils. The mouth is an alternative route of entry but it is not usually the principal entrance for inspired air. During its passage through the respiratory airways the air is warmed and saturated with water vapour (Ganong 1993).

The inhaled air is first filtered by the nose and then any large sized inhaled particulate that remain are removed from the inspired air and deposited on the mucus coated walls of the respiratory airways. The walls of the respiratory tract are composed of ciliated columnar epithelium, mucus glands and goblet cells. The mucus glands and goblet cells secrete mucus and the cilia beat together sending waves of contraction passing in an organised manner from cell to cell. Any particles trapped in the sticky mucus layer are moved upwards and out of the lungs. This is known as the mucociliary escalator, and is an important component in the respiratory system's defence against infection (Cotes 1993). The beating of the cilia can be inhibited by the inhalation of toxins, for example tobacco smoke. The alveoli have no ciliated cells and any particles that reach this region of the lung will be removed by macrophages (cells of the immune system) and exported out of the lungs via the lymphatic system or the blood flow (Margereson 2002).

The first airway that the inspired air enters is known as the trachea. This divides into two at the level of the fifth cervical vertebrae to form the right and left bronchus (see Fig. 1.2) The right and left bronchus further subdivide into small and even smaller airways, known as bronchi and then bronchioles. Bronchi are airways with cartilage in their walls, and there are about ten divisions of such airways. The smaller airways without cartilage in their walls are the bronchioles (Ward *et al.* 2002). Bronchi make up the conducting airways of the respiratory system. No gas exchange takes place in these regions and thus they are often referred to as the anatomical dead space. The volume of air in this region is *circa* 150 mL (West 2000).

The bronchioles further lead into alveolar ducts which are completely lined with alveoli. This is the region of the lung where 'gas exchange' can occur and is known as the respiratory zone.

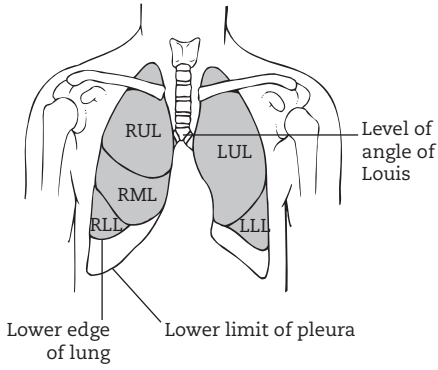

Fig. 1.2 Surface anatomy of the lungs. Anterior view. LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe. With permission from Blackwell Publishing (Bourke 2003).

Name	Zone number
Trachea	0
Bronchi	2
Bronchioles	4
Terminal Bronchioles	5–16
Respiratory Bronchioles	17
Alveolar ducts	20
Alveolar sacs	23

Conducting zone = anatomical dead space

Transitional and respiratory zones

Fig. 1.3 Generation of the respiratory system.

Figure 1.3 illustrates the generation of the respiratory tract and outlines the conducting airways and the airways involved directly in gas exchange.

Alveoli are between 0.1 and 0.2 mm in diameter and are lined by a thin layer of cells. Two types of cells exist: type I pneumocytes and type II pneumocytes. The latter produce surfactant which is essential in reducing the surface tension of the alveoli and helps in maintaining their stability. The reduction or absence of surfactant can lead to the large forces that develop within the alveoli causing their collapse and thus their removal from gas exchange (Fig. 1.4).

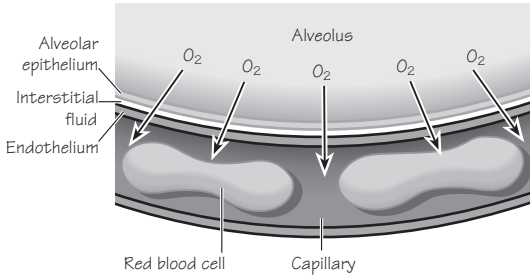

Fig. 1.4 Alveoli structure. With permission from Blackwell Publishing (Ward *et al* 2002).

MECHANICS OF BREATHING

During inspiration the volume of the thoracic cavity increases and air is drawn into the lung. The increase in volume is brought about partly by contraction of the diaphragm, which causes it to descend, and partly by the action of the intercostal muscles which raise the ribs thus increasing the cross-sectional area of the thorax (see Fig. 1.5). Inspired air flows down to about the terminal bronchioles by bulk flow. Beyond that point the combined cross sectional area of the airways is vast, such that the forward velocity of the gas becomes small. Diffusion of the gas within the airways then takes over as the dominant mechanism of ventilation within the respiratory zone.

The lung is elastic and during resting breathing, expiration occurs as it returns passively to its pre-inspiratory volume (West 2000).

Vigorous exercise, dyspnoea and other factors can result in the accessory muscles associated with breathing becoming recruited into use. These include the abdominal, sternocleidomastoid and pectoral muscles.

CONTROL OF BREATHING

Two distinct neural mechanisms regulate respiration (Bouhuys 1977). One is responsible for voluntary control, the other for

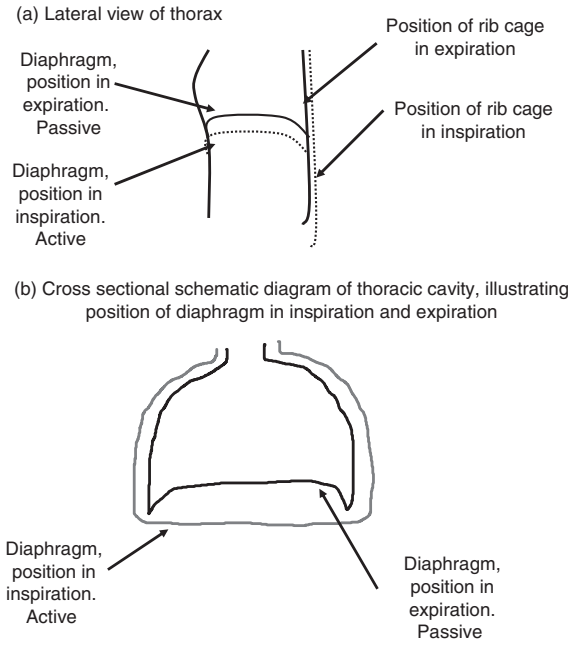

Fig. 1.5 Mechanics of breathing.

automatic control. The voluntary control system is located within the cerebral cortex, whereas the automatic system is located within the pons and medulla. The motor neurons to the expiratory muscles are inhibited when those supplying the inspiratory muscles are active and vice versa (Ganong 1993).

The automatic system generates a rhythmic discharge of neurons within the brain, producing the stimuli which control automatic respiration. Expiration during quiet breathing is passive, thus any control of expiration from the automatic neural system only becomes significant during fast laboured breathing.

REGULATION OF THE RESPIRATORY CENTRE

In fit healthy humans the normal stimulus to breathe is associated with a rising level of CO_2 within the blood. The concentration of CO_2 within the blood is detected within the body by central chemoreceptors, whose exact location within the brain is not known. These central chemoreceptors are stimulated when there is a rise in CO_2 that has diffused across the cerebral spinal fluid. The increase in the molar concentration of CO_2 changes the equilibria and results in a consequential increase in the concentrations of bicarbonate ions and hydrogen ions (i.e. a pH shift).

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

The hydrogen ions stimulate the neuronal control of the respiratory centre and the resulting impulses cause the muscles involved in the respiratory processes to contract thereby increasing the respiration rate (Levitzky 1999).

The second stimulus to breathe is a decrease in PO_2, i.e. a fall in oxygen concentration within the blood. This is detected by the carotid bodies (located near the carotid bifurcation) and the aortic bodies (located near the aortic arch). This stimulus often becomes the main driving mechanism in type II respiratory failure. This is sometimes referred to as the 'hypoxic drive' to breathe. Figure 1.6 summarises the main control mechanisms of respiration (West 2000, Ward *et al.* 2002).

Of course other factors can influence respiration: these include painful stimuli, inflation receptors in the lungs, triggers for sneezing, coughing, exercise, etc.

Table 1.2 illustrates the key events that occur during normal quiet inspiration and expiration.

THE WORK OF BREATHING

Energy expenditure during quiet breathing is normally less than 5% of the total body oxygen uptake, although this may increase up to 30% or more during vigorous exercise or respiratory distress (Levitzky *et al.* 1990).

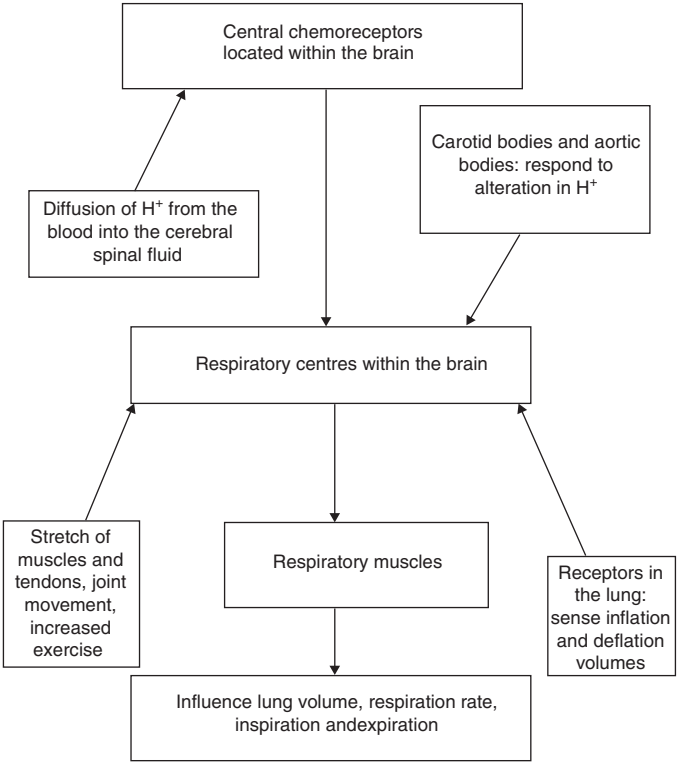

Fig. 1.6 Main control mechanisms of respiration.

Table 1.2 Key events in normal breathing.

Inspiration	**Expiration**
Increase CO_2 conc. within blood	Neuronal stimulation by automatic centre ceases
Stimulation of respiratory centre	Inspiratory muscles relax
Stimulation of diaphragm	Thoracic volume decreases
Increase in thoracic volume	Elastic recoil of lungs
Alveoli pressure decreases	Alveolar pressure increases
Air enters via bulk flow	Air flows out of lungs

MAINTENANCE OF AIRWAY TONE

Hormones, peptides and neurotransmitters can affect the smooth muscle lining the respiratory airway. There is a complex interplay between these factors, which minute to minute result in variations in the respiratory airway size.

The autonomic nervous system is perhaps the key player in regulating the contraction and relaxation of airway smooth muscle. Parasympathetic nerves release acetylcholine which acts upon muscarinic receptors within the smooth muscle, causing smooth muscle contraction and an increase secretion of mucus. Drugs which mimic these effects are sometimes given in bronchial challenges, e.g. metacholine. However drugs that inhibit these effects are frequently given in respiratory medicine and these include atropine and ipratropium bromide (Margareson 2002).

Sympathetic nerves release noradrenaline and their effects are also mediated by adrenaline. Smooth airway muscles have β_2 receptors which respond to adrenaline by causing relaxation of the smooth muscle. However their activation may not be as a direct response of stimulation from the sympathetic system. Recent research suggests that sympathetic nerves do not play a primary regulatory role in the relaxation of smooth muscle (Barnes 1986, 1993, 1998). Rather the circulating blood levels of adrenaline and noradrenaline are more important in causing airway smooth muscle relaxation.

Drugs that stimulate the β_2 receptors, thus initiating smooth muscle relaxation, are called β_2 agonists and include salbutamol and terbutaline.

PULMONARY CIRCULATION

The pulmonary vascular system is described as a high-volume low-pressure system (Brewis & White 1995). Resistance within the pulmonary vascular system is mainly within the arterioles and capillaries, and these can alter their dilation rapidly. Thus in the regions of the lung that become poorly oxygenated, the capillaries supplying them will constrict and divert blood to those areas that have a greater supply of oxygen. Detailed anatomy of the pulmonary circulation is outside the scope of

this chapter. More information can be found in any good standard textbook of anatomy.

Pulmonary arterioles may also constrict in response to localised hypoxia. In chronic lung disease this may result in long term vasoconstriction, increased cardiac output resulting in right ventricular failure (cor pulmonale) and in many cases death (Ferguson & Cherniack 1993).

COMPOSITION OF INSPIRED AIR

Inspired atmospheric air at sea level is comprised of a number of gases. Of particular importance in respiration are:

- Nitrogen (N_2) 76%.
- Oxygen (O_2) 20.98%.
- Carbon dioxide (CO_2) 0.04%.

The balance is made up by the inert gases.

The partial pressure of water vapour is variable, usually in the range 0.2 to 2.0 kPa.

Each gas exerts a pressure (partial pressure). The sum or total of all the partial pressures of gases and partial pressure of the water vapour within the atmosphere exert a pressure known as atmospheric pressure, or barometric pressure (Dalton's law). At sea level the 'standard' atmospheric pressure is usually defined as 101 kPa.

Thus the partial pressure of nitrogen is:

$$\frac{76}{100} \times 101\,\text{kPa} = 76.76\,\text{kPa}$$

Oxygen's partial pressure is:

$$\frac{20.98}{100} \times 101\,\text{kPa} = 21.19\,\text{kPa}$$

With increasing altitude the partial pressure that each gas exerts decreases and the total atmospheric pressure falls. Roughly every rise in altitude of 550 m will halve the atmospheric pressure. Consequently those people who undertake climbing Everest (circa 8850 m) will experience a significant decrease in

atmospheric pressure and an associated decrease in the partial pressure of inspired oxygen. This reduction in the amount of oxygen inspired combined with the effect of the smaller diffusion pressure gradient existing within the lungs will contribute to the risk of developing altitude sickness.

Those who engage in aeroplane travel might consider the advantages they enjoyed by being in a pressured cabin while flying at 10 000–12 000 m. Aeroplane cabins are usually pressurised to remain at the equivalent of the atmospheric pressure found at 2000–3000 m irrespective of the actual altitude of the flight. This 'simulated altitude' would usually have little effect upon the respiratory system of a fit and healthy adult; however those with abnormal or immature respiratory systems can be affected by aeroplane flight as can those who require oxygen therapy at home. Consequently guidelines have been written to aid in decisions concerning the fitness for flight and the possible consequences of aeroplane travel (British Thoracic Society (BTS) 2002).

By the time the inspired air reaches the alveoli it is fully saturated with water vapour: saturated water vapour at sea level would have a partial pressure of about 6 kPa. Thus to calculate the partial pressure of oxygen within the alveoli the partial pressure of water vapour must first be subtracted from the atmospheric pressure. Thus the pressure of oxygen within the alveoli of fit healthy individuals is usually estimated to be circa 13 kPa (Ganong 1993).

TRANSPORT OF GASES

It has been shown above that the partial pressure of oxygen within the alveoli is circa 13 kPa, while the blood returning from the right side of the heart in the pulmonary artery has a pO_2 of circa 5.7 kPa. Thus the pressure difference for oxygen within the respiratory system is such that diffusion (movement of molecules from regions of high concentration to a region of low concentration) will ensure oxygen moves from the alveoli into the blood. Conversely the concentration of CO_2 within the inspired air is lower than in the blood so that diffusion will ensure CO_2 moves from the blood into the alveoli and is then expired.

In fit healthy individuals this is usually achieved within 0.25 seconds (Riley & Cournard 1949, Sykes *et al.* 1976). Factors that influence this diffusion process are:

- Thickness of membrane which separates the gases.
- Surface area of membrane (alveoli).
- Solubility of gases.
- Partial pressure gradient of gases.
- Ventilation of alveoli.
- Perfusion of the alveoli capillaries.

Lung diseases can influence many of the above factors, for example: mucus plugging associated with asthma will reduce the ventilation of alveoli; the effective surface area of alveoli decreases in emphysema. Other co-morbidities can also influence the diffusion time and process (West 2000).

Oxygen, once it has diffused across the alveolar capillary membrane, is carried within the blood by two methods. Some 3% of the oxygen is dissolved in the plasma; the remaining 97% is bound to haemoglobin in the red blood cells to form oxyhaemoglobin. Oxygen readily combines with haemoglobin and this reaction is fully reversible. Four molecules of oxygen can combine with one haemoglobin molecule.

The percentage of haemoglobin combined with oxygen is dependent upon the concentration of oxygen available, i.e. the partial pressure of oxygen. In the regions of the body with a high partial pressure of oxygen most of the haemoglobin will be bound with oxygen. However in regions of the body with low partial pressure of oxygen, oxygen will dissociate from the haemoglobin following the laws of diffusion (Baumann *et al.* 1987). In cases of anaemia all the available haemoglobin may be bound with oxygen within the lungs but the total oxygen carrying capacity of the blood will be insufficient to meet the body's demands. This demonstrates the principle that concentration of haemoglobin within the body significantly influences the oxygen carrying capacity of the blood. Each 1 g of fully saturated haemoglobin molecule can 'hold' 1.39 cm^3 of oxygen. Thus if the haemoglobin concentration of blood is 15 g/dL then

it can be estimated that the total oxygen carrying capacity for each 100 cm^3 of blood is $15 \times 1.39 = 20\,cm^3$ plus the oxygen dissolved within the plasma (Hsia 1998).

Factors which influence the oxygen concentration within the blood are manifold. However the commonest are: anaemia; the partial pressure of the oxygen in the alveoli; the rate of ventilation; the rate of perfusion of the alveoli; the presence of other gases (e.g. carbon monoxide which will bind to haemoglobin in favour of oxygen); temperature; and pH.

OXYHAEMOGLOBIN DISSOCIATION CURVE

The oxyhaemoglobin dissociation curve is a sigmoid (S-shaped) curve (see Fig. 1.7). If oxygen partial pressure remains above 10 kPa and below 13 kPa the saturation of haemoglobin with oxygen remains high. However once the oxygen partial pressure falls below circa 8 kPa, the saturation of haemoglobin with oxygen rapidly falls. This has a catastrophic influence upon the normal functioning of the body.

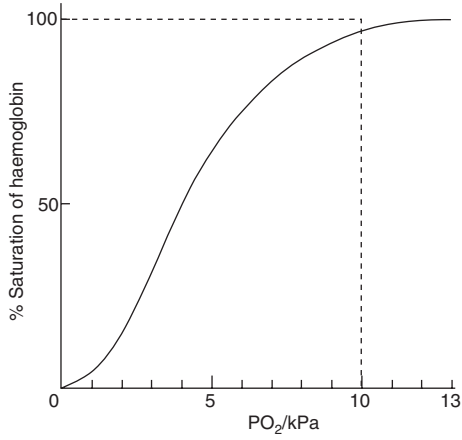

Fig. 1.7 Oxyhaemoglobin dissociation curve.

The oxyhaemoglobin dissociation curve can be influenced by a number of factors (see above). However the commonest factors which influence how haemoglobin binds with oxygen are temperature, pH and CO_2 concentration. These factors cause the curve to shift either to the left or the right (see Fig. 1.8). As can be noted by observation of this figure, a shift to the left of the oxyhaemoglobin curve will result in the haemoglobin remaining fully bound with oxygen at lower partial pressures of oxygen. Thus release of oxygen to the peripheral tissues is perhaps greater than normal; the uptake of oxygen by haemoglobin within the alveoli is reduced. A shift to the right results in oxygen unbinding from the haemoglobin at higher than usual

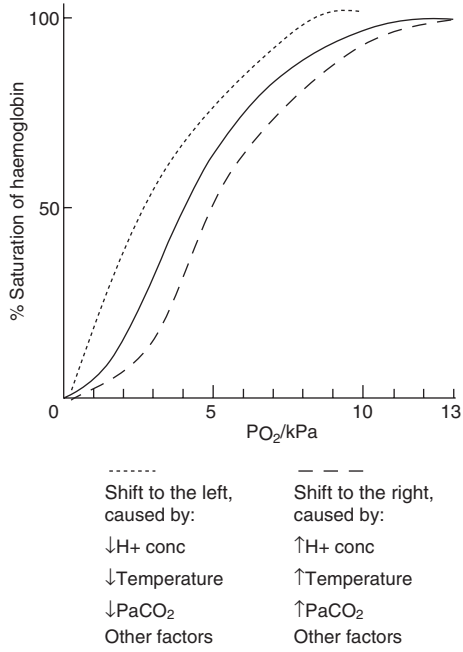

Fig. 1.8 Left and right shift oxyhaemoglobin.

partial pressure of oxygen, thus altering the amount of oxygen delivered to the peripheral tissues.

CARRIAGE OF CARBON DIOXIDE

Carbon dioxide is much more soluble in water or blood than oxygen. However although a significant amount of dissolved carbon dioxide exists in the plasma even at low pCO_2, most of the carbon dioxide transported is in the form of bicarbonate ions. Only small concentrations of the intermediate carbonic acid exist since it can rapidly dissociate to form bicarbonate and hydrogen ions (Klocke 1987).

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

Some 70% of the carbon dioxide entering the venous system is transported in the plasma, and the remaining 30% enters the red blood cells.

The carriage of carbon dioxide within the red blood cells is important. The enzyme carbonic anhydrase found within the red blood cells will considerably speed up the reaction converting the carbon dioxide and water molecules into carbonic acid molecules. As in the plasma this carbonic acid then speedily dissociates to form the bicarbonate and hydrogen ions. The overall reaction is quicker than the identical reactions that occur within the plasma.

In the red blood cells some of the carbon dioxide will also combine with amino groups of the proteins to form carbamino-CO_2. The concentration of hydrogen ions and bicarbonate ions will continue to increase in red blood cells as more carbon dioxide is unloaded from the metabolically active tissues into the veins. While bicarbonate anions will diffuse from the erythrocytes into the blood plasma the erythrocyte cell membrane is relatively impermeable to H^+ and other cations such as Na^+ or K^+. Some of the hydrogen ions will complex with the haemoglobin while chloride ions diffuse from the plasma in exchange for the bicarbonate ions and in effect balance the charges on remaining hydrogen cations. The number of osmotically active ions in the erythrocytes has thus increased as a result of the chain of reactions that followed the uptake of CO_2 into the

cells. Water molecules will now move into the cell, the consequential effects being the dilution of the molecular and ionic concentrations and a small increase in the volume of the erythrocytes.

It is generally regarded that the 'total CO_2 content of the blood' may be quantified as being equivalent to the sum of the dissolved carbon dioxide, plus the carbon dioxide that could be released from the bicarbonate and carbonate anions together with that transported as the carbamino-CO_2.

All the above reactions are fully reversible and in the lung they form a system which ensures that carbon dioxide is released from the arterial blood after entering the lung via the Pulmonary artery. The carbon dioxide released then moves by diffusion from the blood into the alveoli of the lungs.

Respiratory acidosis is said to occur when the total dissolved CO_2 is higher than its normal limits. Respiratory alkalosis is said to occur when the total dissolved CO_2 is too low. (Note the effect of CO_2 concentration on the equilibrium reached in the reactions given above, particularly with reference to the changes that would occur in H^+ concentration.)

ACID–BASE BALANCE

The body is continuously producing acids as a consequence of:

- the catabolism of carbohydrates, proteins and nucleic acids;
- the conversion of metabolically produced CO_2 to carbonic acid;
- the release of lactic and other acids formed during anaerobic catabolism (West 2000).

These organic acids will partially dissociate to increase the H^+ concentration of the blood.

The general metabolic activity of the body can adjust to maintain homeostasis and compensate for any further tendency to increase the concentration of hydrogen ions by utilising its capacity to produce hydrogen ion acceptors. In general those compounds within the body that act as hydrogen ion (H^+) acceptors will either tend to increase in concentration when the pH falls or decrease in concentration as the pH rises.

There are three major systems that exist to deal with this fluctuating situation:

1. The buffer base: for example bicarbonate, proteins and phosphates are compounds that are able to accept hydrogen ions to form weak acids. This mechanism is activated almost immediately.
2. The respiratory system: the lungs will either remove or retain CO_2 depending upon the 'need' to increase or decrease CO_2 concentration. This mechanism follows the changes in the buffer system fairly quickly. Thus a fall in blood pH (i.e. a rise in H^+) will drive the equilibria towards the left to increase the pCO_2. This increase in pCO_2 will in turn increase the respiration rate and thus remove more CO_2 from the blood until a new equilibrium is established. Hyperventilation and hypoventilation have rapid effects on concentration of carbon dioxide in the blood.
3. The renal system: the renal tubules are able to retain bicarbonate or hydrogen ions or secrete them. This system response is the slowest but it is the most efficient.

The respiratory systems have other important functions, such as defence against infection, metabolism of active compounds from the body, etc. Further information concerning these functions can be found in detailed texts on the physiology and immunology of the respiratory system.

SUMMARY

- ❏ The respiratory system's main function is to facilitate gas exchange thus ensuring that adequate oxygen and carbon dioxide tensions are maintained within the body.
- ❏ Other functions of the respiratory system include allowing speech to occur; defence against infection; blood storage; acid–base balance.
- ❏ The structure of the respiratory system in fit healthy individuals ensures that adequate gas exchange occurs.
- ❏ In quiet breathing inspiration is active, involving the use of the diaphragm to increase the thoracic volume, and expiration is passive.

- ❏ In dyspnoea, laboured breathing or during exercise, both inspiration and expiration are active energy dependent components of respiration.
- ❏ Control of breathing is via two mechanisms: one automatic, the other under voluntary control.
- ❏ The automatic control of breathing is based upon neural impulses that are generated rhythmically within the brain.
- ❏ Factors that influence the control of breathing via the autonomic system are the concentration of hydrogen ions and the partial pressure of oxygen.
- ❏ Carriage of carbon dioxide within the body occurs within the plasma, and red blood cells.
- ❏ Carriage of oxygen around the body is primarily affected by the oxygen being bound to haemoglobin within the red blood cells.
- ❏ The oxygen dissociation curve graphically represents unloading of oxyhaemoglobin in those regions of the body with a low partial pressure of oxygen.
- ❏ Factors that influence the unloading and loading of oxygen with haemoglobin are temperature, pH, and atmospheric pressure.

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