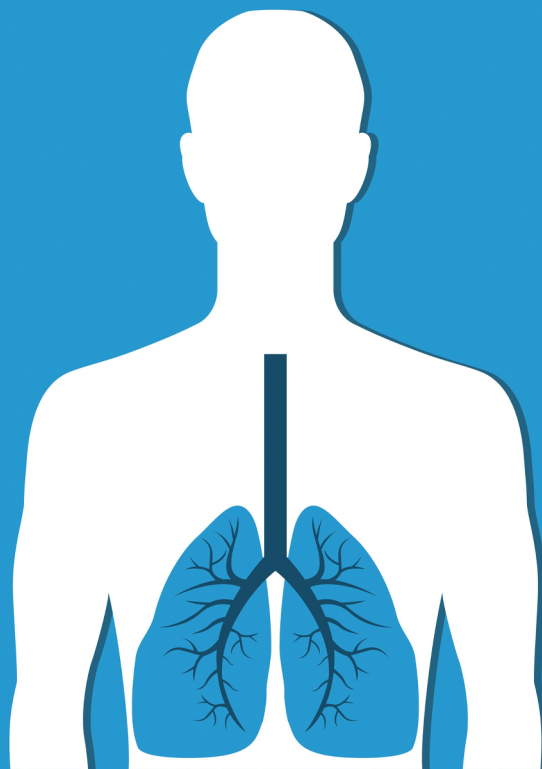


Blood and the respiratory system



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Introduction

At some point in your life, you have probably tried to see how long you could hold your breath. It most likely took about 30 seconds before you felt the need to breathe. Free-divers, people who descend deep underwater without any breathing equipment, can hold their breath for much longer. In July 2016, William Trubridge set a world record in unassisted free-diving by going down 102 metres (334 feet) into Dean's Blue Hole, a large marine sinkhole in the Bahamas. He did so on a single breath that he held for more than 4 minutes, as you can see in the following video. (Make sure to open the link in a new window/tab so you can easily navigate back to this page.)

[Link to Video 1 – William Trubridge's record free-diving descent.](#)

Exchange of gases between the body and the atmosphere involves a complex and finely tuned series of mechanical and cellular events.

In this free course, *Blood and the respiratory system*, you will learn about the structure of the respiratory system, how the lungs contract and expand, as well as the factors that affect pulmonary ventilation. In addition, you will explore how gases are transported between the lungs and other tissues, how the respiration rate is controlled and look at examples of genetic diseases that affect respiration.

This OpenLearn course is an adapted extract from the Open University course [SK299 Human biology](#).

Learning Outcomes

After studying this course, you should be able to:

- describe and illustrate the main anatomical structures of the respiratory system and the mechanics of inspiration and expiration
- discuss the factors that affect pulmonary ventilation
- outline the mechanisms of O₂ and CO₂ transport in the blood
- describe diseases resulting from mutations in haemoglobin
- demonstrate an understanding of the control of the respiration rate.

1 Respiratory structures and ventilation

Oxygen (O_2) is a critical component for human life and is needed for the homeostatic maintenance of all the body's tissues and organs.

Cellular respiration, the process by which energy is made, is dependent on a constant supply of O_2 . At the same time, this process generates the waste product carbon dioxide (CO_2), which must be continuously removed. The process by which O_2 and CO_2 are exchanged between the body and the environment is termed **external respiration**. On average, an adult takes between 12 and 18 breaths a minute at rest, exchanging more than 8000 litres of air per day.

Using the glossary

This course includes a glossary, as demonstrated by the terms 'cellular respiration' and 'external respiration' highlighted in the paragraph above. You can hover over these for a preview, and click on the words to be taken to the full definition in the glossary.

Over the course of this section, you will learn how physical forces such as pressure, surface tension, resistance and compliance determine the amount of airflow through the respiratory and conduction zones of the respiratory system.

1.1 Structure of the respiratory system

Pulmonary ventilation, the movement of air into and out of the lungs, involves the main structures of the respiratory system (Figure 1). They include:

- the lungs
- a system of airways that deliver the air to the blood vessels of the lungs
- the musculoskeletal system that ventilates the lungs
- the central and peripheral nervous system that controls the rate and depth of breathing.

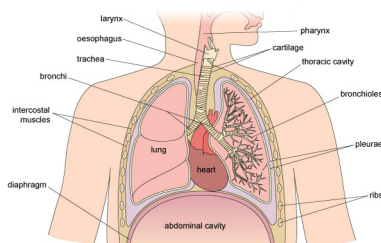


Figure 1 Cross-section through the structures of the respiratory system.

1.1.1 Upper respiratory tract

Air enters the body through the nostrils and passes into the **nasal cavities** (Figure 2). Cilia (hair-like organelles) within the nasal mucosa provide a continuous beating movement to move air particles along the nasal cavities, where they are warmed and moistened. This action helps in the detection of smells and traps potentially harmful particles, preventing them from entering the rest of the respiratory system.

From the nasal cavities, the air passes to the **pharynx** (throat) at the back of the mouth where it is joined by air that has entered the system through the mouth.

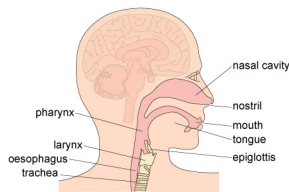


Figure 2 Structures of the upper respiratory tract.

At the base of the pharynx are two openings:

- One leads to the larynx (which contains the voice box and Adam's apple), from which air passes into the **trachea** or windpipe, a hollow tube kept permanently open by rings of cartilage (Figure 2).
- The other opening is to the entrance of the oesophagus, near the beginning of the digestive tract.

Food is normally prevented from getting into the trachea by the movement of the epiglottis, a small flap of tissue that closes the larynx during swallowing. If you have ever had food go down 'the wrong pipe' (i.e. into the respiratory system), you know that the immediate response is to cough in an effort to expel the foreign material from the lungs.

Question 1 A situation

John and Mary are celebrating their 25th wedding anniversary with a roast chicken dinner. Halfway through the meal, John begins choking on a piece of chicken and is rushed to hospital. Airflow to the lungs must be re-established as quickly as possible. Which of the respiratory tract structures shown in Figure 2 (above) should doctors target to do so?

- ☐ trachea
- ☐ nasal cavity
- ☐ mouth
- ☐ pharynx
- ☐ oesophagus

Answer

The chicken is likely to be stuck in John's trachea and is obstructing the air in the pharynx from reaching the lungs. Targeting the nasal cavity, mouth or pharynx will not help to restore airflow because these structures are all upstream of the trachea. Doctors will attempt to remove the obstruction and if unsuccessful, will probably make a small hole in the trachea below the obstruction (a procedure called a tracheotomy) and insert a tube that will allow air to flow directly into the lungs.

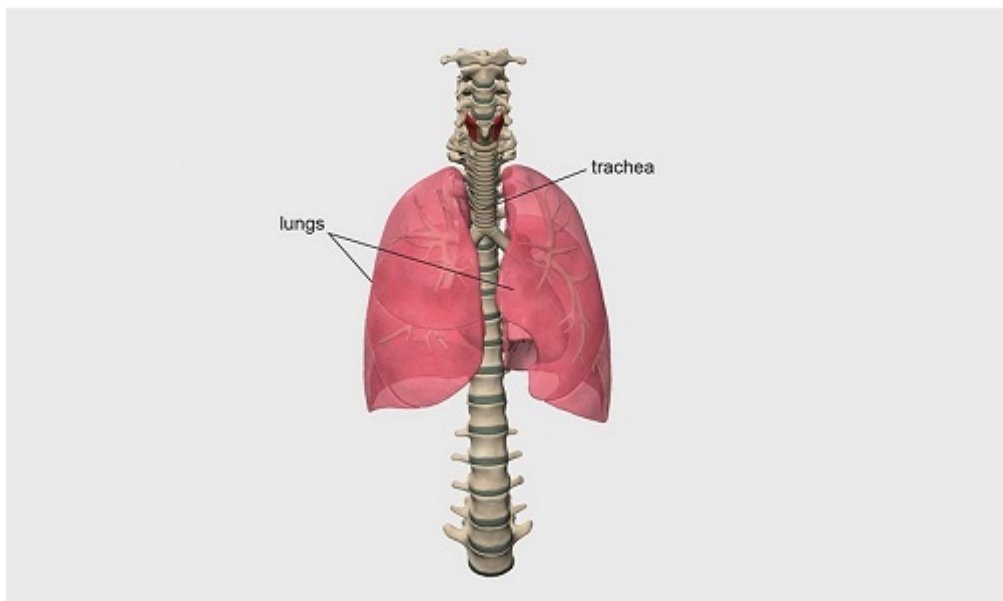
The nasal cavities, pharynx and larynx form the upper respiratory tract and are the areas that are usually affected by the common cold virus.

1.1.2 Lower respiratory tract

The trachea divides into two branches called **bronchi** (Video 2). These serve the left and right lungs. Like the trachea, the walls of the bronchi contain cartilage, which prevents their collapse. Each main bronchus divides into smaller and smaller tubes, finally ending in terminal bronchioles. Bronchioles also contain cilia that help to keep the airways clean by moving mucus and particles from the lower respiratory tract up to the pharynx to be expelled.

Video content is not available in this format.

Video 2 3D model of the trachea, bronchi and bronchioles. (Please note, this video has no audio.)



The **lungs** are organised into lobes (the left lung comprises two lobes and the right lung has three lobes). Two thin membranes, the visceral and parietal **pleura**, cover the lungs and keep them attached to the thoracic wall. The base of each lung is concave and rests on the diaphragm (more on that in Section 1.2), whereas the heart sits within the cardiac impressions, or grooves, in each lung (Figure 1, repeated).

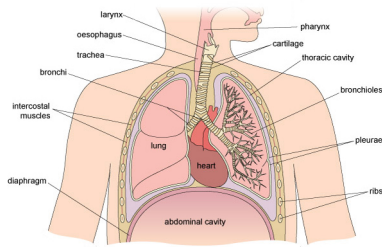


Figure 1 (repeated) Components of the respiratory system.

Because they act as a conduit for air to move into and out of the lungs, the nasal passages, pharynx, larynx, bronchi and bronchioles are collectively referred to as the **conduction zone** of the respiratory system.

Air then passes into progressively smaller structures deep in the lungs where gas exchange actually takes place in the respiratory zone, which you will explore in the next section.

1.1.3 Respiratory zone

The terminal bronchioles each divide a further seven times into respiratory bronchioles, then alveolar ducts and finally into **alveolar sacs** (alveoli; singular, alveolus) that contain holes in their walls called alveolar pores (Figure 3).

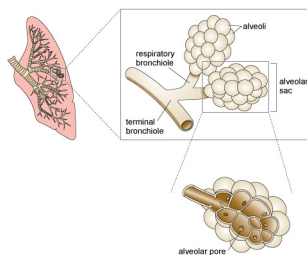


Figure 3 Terminal bronchioles further divide within the lungs.

Similar to other organs in the body, the organisation of the bronchioles and alveoli allows a large surface area of cells to be contained within the tight space of the thoracic (chest) cavity. This large respiratory surface, which is about 140 m² in the adult human (roughly the size of a tennis court), enhances the lungs' capacity to exchange CO₂ for O₂. This exchange occurs in the respiratory bronchioles, alveolar ducts and alveoli, which collectively form the **respiratory zones** deep in the lungs.

Alveoli are surrounded by a network of pulmonary capillaries that carry the blood (Video 3). Deoxygenated, CO₂-rich blood coming into the lungs from the heart exchanges CO₂ for O₂ by diffusion, and oxygenated blood then leaves the lungs, returning to the heart to be pumped around the body. The walls of an alveolus and a pulmonary capillary are each only one cell thick, which allows diffusion of O₂ and CO₂ to occur very quickly (Figure 4).

Because haemoglobin, the molecule that carries O₂ in the blood (explored further in Section 4.2), changes colour when bound by O₂, oxygenated blood is often depicted as bright red, whereas deoxygenated blood is shown as blue in colour. This course doesn't explore how blood circulates around the body, but it is important to note that the lungs differ from other organs in that deoxygenated blood is carried to the lungs via arterioles (and larger arteries), whereas oxygenated blood leaves the lungs along venules (and larger veins).

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Video 3 Exchange of CO_2 and O_2 carried by blood in the pulmonary capillaries within the alveoli of the lungs. (Please note, this video has no audio.)

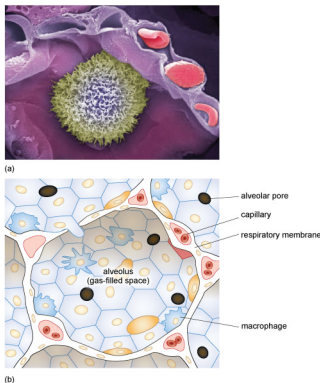
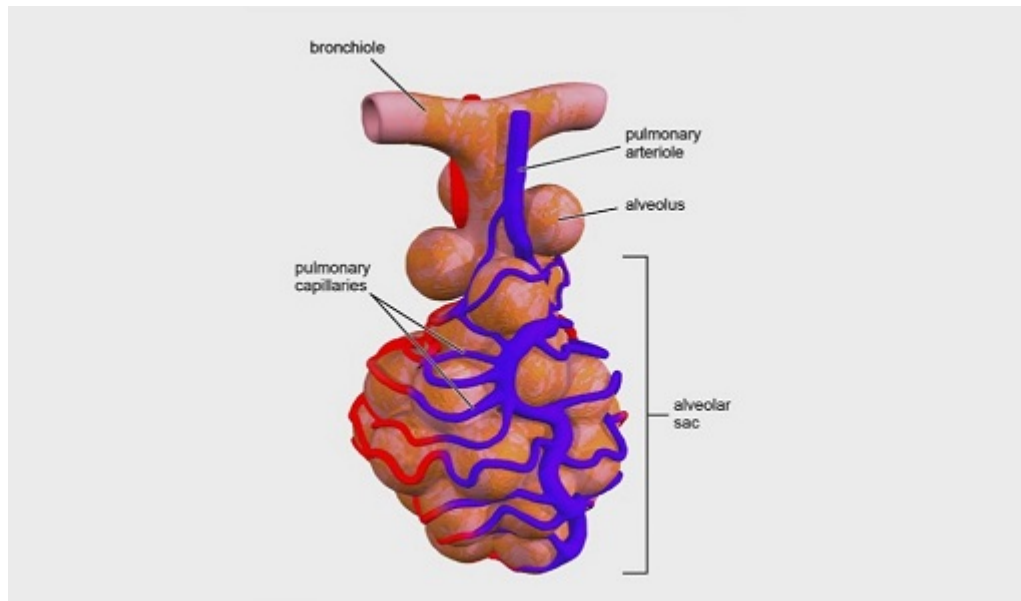


Figure 4 (a) Electron micrograph and (b) schematic showing a cross-section of an alveolus (purple), with red blood cells (red) in the surrounding intertwinning capillaries and a pulmonary macrophage (green) inside the alveolus.

Activity 1 Ordering the air flow

Allow about 5 minutes

To test your understanding so far, order the steps involved in the flow of air from the conduction zone through to the respiration zone.

Air is taken in through the nasal cavities.

Air passes down the back of the pharynx, past the epiglottis and into the larynx.

From the larynx, air travels into the trachea, and into the bronchi.

Air moves through the terminal bronchioles and into the respiratory bronchioles.

Air passes into the alveolar ducts and into the alveolar sacs.

Match each of the items above to an item below.

- 1
- 2
- 3
- 4
- 5

In the next section, you will explore the muscles that are involved in the expansion and contraction of the lungs.

1.2 Muscles of ventilation

The expansion and contraction of the lungs is controlled mechanically by the diaphragm and the intercostal muscles (Figure 1, repeated).

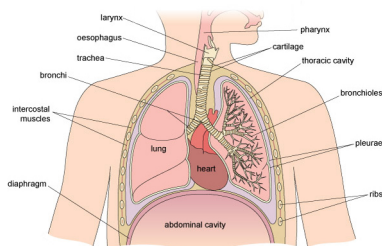


Figure 1 (repeated) Components of the respiratory system.

- The **diaphragm** is a dome-shaped muscle that sits underneath the lungs and separates the thoracic cavity from the abdominal cavity. It is innervated by the **phrenic nerve**, which originates in the medullary respiratory centre in the medulla of the brain.
- The **intercostal muscles** are located in the ribcage. They receive neuronal inputs from **intercostal nerves** that arise from the thoracic nerves of the spinal cord.

The bronchi and bronchioles are also surrounded by smooth muscle cells that contract and dilate to regulate the amount of air that passes down to the alveoli.

Activity 2 Diaphragm and intercostal muscles

Allow about 20 minutes

Part 1

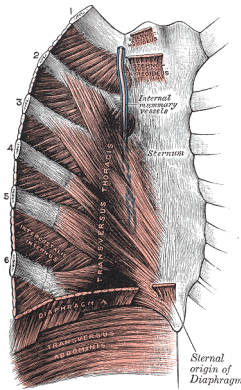


Figure 5 Diaphragm and intercostal muscles.

To explore the location and function of the diaphragm and intercostal muscles, take a look at the anatomical information and diagrams on this site (open the links in a new tab/window so you can easily return to this page):

[Diaphragm](#)

[Intercostal muscles](#)

Provide your answer...

Part 2

Now try matching each of these statements with the correct muscles.

flatten(s) when contracted to expand the size of the thoracic cavity and decrease the size of the abdominal cavity, generating a pressure gradient within the thoracic cavity

draw(s) the ribs upwards and outwards; most active during inhalation

draw(s) the ribs downwards and inwards; most active during forced exhalation

stiffen(s) the chest wall during respiration; most active during forced exhalation

Match each of the items above to an item below.

diaphragm

external intercostal muscles

internal intercostal muscles

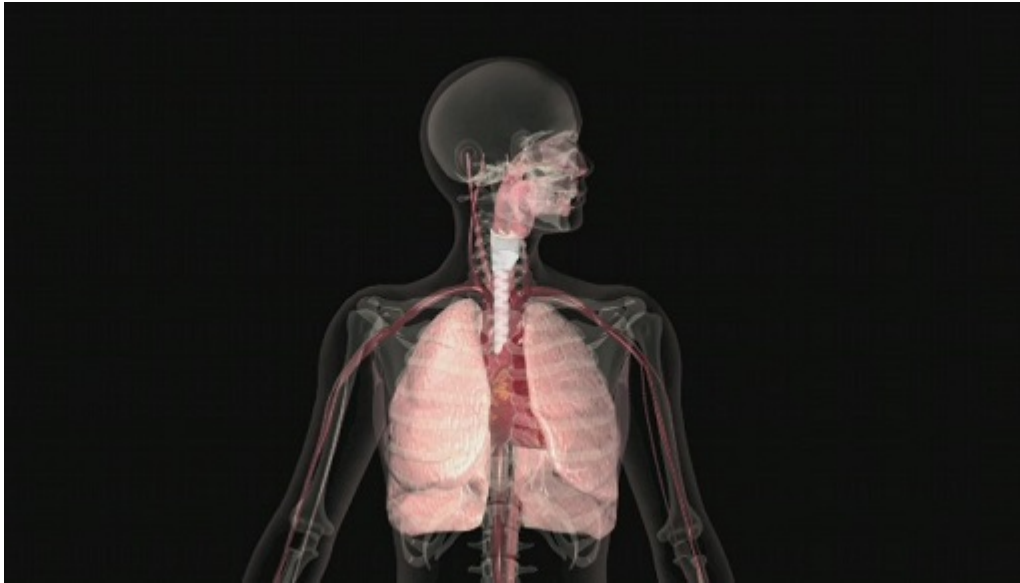
innermost intercostal muscles

1.3 Mechanics of inhalation and expiration

Movement of the diaphragm and intercostal muscles acts to expand and decrease the size of the thoracic cavity, creating pressure gradients that draw air into and force air out of the lungs, as described in Video 4.

Video content is not available in this format.

[Video 4 Mechanics of inhalation and expiration.](#)



Expiration is generally a passive event brought about by relaxation of the diaphragm and external intercostal muscles. The ribcage, diaphragm and lung tissue itself return by elastic recoil to their original pre-inspiratory positions. The consequent retraction of the chest wall forces air out of the lungs. Forced expiration is mainly achieved by contraction of the internal intercostal muscles, aided to some extent by contraction of the abdominal muscles.

Most of the time, you will be unaware of the contraction and relaxation of the muscles that control respiration. They become much more noticeable when you cough or develop a bout of hiccups. In fact, hiccups are caused by a spasm of the diaphragm and intercostal muscles in response to increased activity of the phrenic nerve and vagus nerve (which innervates the muscles of the abdomen). The spasms cause the floor of the thoracic cavity to drop suddenly, which pulls air quickly and forcefully into the airways. Movement of the air past the closed vocal cords creates the characteristic 'hic' sound.

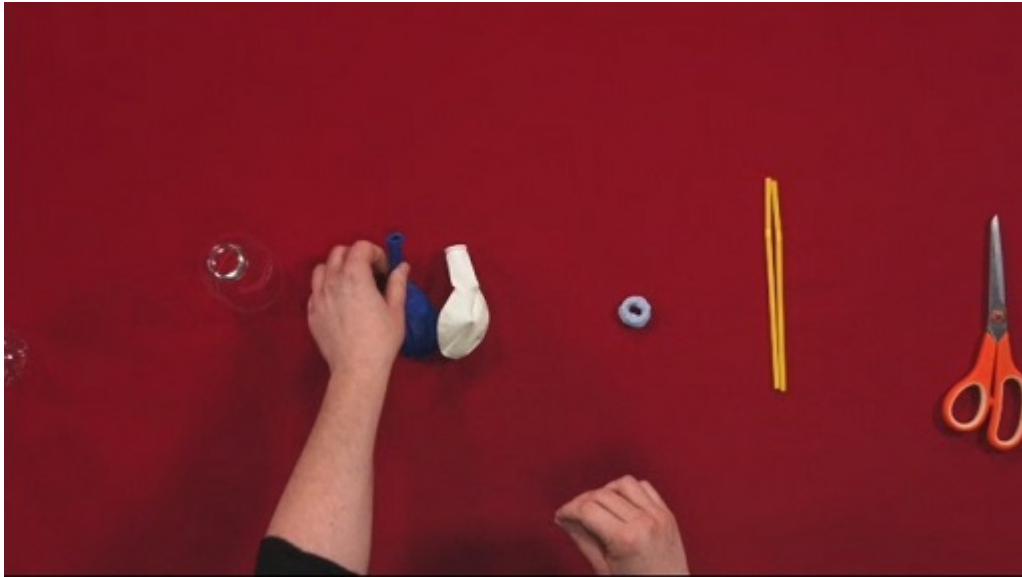
Activity 3 Lung in a bottle

Allow about 1 hour

You can explore the relationship between movement of the diaphragm and lung volume directly by making your own 'lung in a bottle' as shown in Video 5.

Video content is not available in this format.

[Video 5 'Lung in a bottle' experiment.](#)



According to the video, what factors are responsible for the inflation and deflation of the balloon 'lung' inside the bottle?

Provide your answer...

Answer

Pulling down on the blue balloon 'diaphragm' caused the air pressure in the ribcage to drop lower than the air pressure in the atmosphere. This drove air to flow down its pressure gradient into the balloon, causing it to inflate. Pressing up on the diaphragm increased the air pressure in the ribcage, driving air out of the balloon lung and causing it to collapse.

1.4 Non-respiratory functions

The respiratory system also performs important non-respiratory functions, for example:

- Vocalisation including speech and singing. The two bands of elastic tissue that lie across the opening of the larynx, called the vocal cords, can be stretched and positioned into different shapes by the laryngeal muscles. As air is passed over the vocal folds, they vibrate to produce characteristic patterns of sound.
- Detection of smells from airborne chemicals.
- Water loss and heat elimination. Inspired atmospheric air can be humidified and warmed by the respiratory airways; this is essential to prevent the alveolar membranes from drying out, which would significantly reduce diffusion of O_2 and CO_2 .
- Facilitation of blood flow around the body. During inspiration, there is a fall in pressure in the chest cavity, which reduces the resistance of blood vessels. In a

similar way, respiratory movements also aid the movement of lymph through the lymphatic system.

- Defence against foreign particulates or airborne infectious diseases via nasal hair and cilia lining the airways, and mechanisms including coughing and sneezing.

2 Factors affecting pulmonary ventilation

The previous section outlined the anatomical structures that are involved in ventilation. In this section, you will examine the factors that regulate pulmonary ventilation, including pressure gradients, surface tension, airway resistance and compliance of the lungs.

2.1 Atmospheric pressure

If you have recently taken a flight on a commercial airline, you will be familiar with the instructions that are given in the event of a change in cabin pressure, such as in Video 6 below.

Video content is not available in this format.

[Video 6 An Open University airline safety video.](#)



These safety measures highlight the importance of pressures for gas exchange in the lungs. To understand this relationship, it is helpful to use Boyle's law, which states that at a constant temperature (k), an increase in pressure (P) causes a proportional decrease in volume (V). Watch Boyle's law in action in Video 7 below. (Make sure to open the link in a new window/tab so you can easily navigate back to this page.)

[Link to Video 7 – The effect of increasing pressure on volume.](#)

Question 2 Increasing pressure

By how much did the volume of air in the cylinder decrease when the surrounding water pressure increased from 1 bar to 2 bar?

- ☐ it did not change
- ☐ by $\frac{1}{4}$
- ☐ by $\frac{1}{2}$

- by $\frac{3}{4}$

Answer

As the pressure increased by a factor of 2, the volume of the air decreased by $\frac{1}{2}$, from 1 litre to 0.5 litre.

In physiology, the unit of pressure is conventionally measured as millimetres (mm) of mercury (Hg). 'Millimetres of mercury' (mmHg) refers to the height of a column of mercury attached to an instrument that detects pressure (e.g. a sphygmomanometer). Other units of pressure, such as that used in Video 7, include bar, pounds per square inch (psi) and pascals (Pa). All units of pressure can be interconverted, so 1 bar = 14.5 psi, 1 psi = 51.7 mmHg and 1 mmHg = 133 Pa.

At sea level, the atmospheric pressure (i.e. the pressure exerted by the gases in the Earth's atmosphere) is about 760 mmHg. During inhalation, the volume of the lungs increases and the pressure inside the lungs decreases below that of atmospheric pressure. This creates a pressure gradient that draws air into the lungs. During exhalation, the lungs return to their original size, pressure in the lungs rises compared with the atmospheric pressure and air moves out.

Question 3 Boyle's law

Boyle's law is described by the following formula:

$$PV = k.$$

Part 1

How would you rewrite the formula to calculate pressure (P)?

Provide your answer...

Answer

$P = k/V$. To calculate pressure (P), divide the constant (k) by the volume (V).

Part 2

i) If $k = 1$, what will be the pressure of the gases if the volume of the lungs is 6 litres?

- ☐ 0.167 mmHg
- ☐ 6 mmHg
- ☐ 16 mmHg

Part 3

ii) If $k = 1$, what will be the pressure if the volume is 3 litres?

- ☐ 0.333 mmHg
- ☐ 3 mmHg

- ☐ 13 mmHg

Part 4

Is the pressure in the lungs higher during exhalation or inhalation?

- ☐ Exhalation
- ☐ Inhalation
- ☐ Neither, it is constant

Answer

As the volume of the lungs shrinks during exhalation, the pressure in the lungs increases above that of atmospheric pressure and air moves out of the lungs down the pressure gradient.

If you are unfamiliar with rearranging equations you might find our [Mathematics for science and technology](#) course helpful for brushing up.

Returning to the example of the aeroplane, the atmospheric pressure at cruising altitude (e.g. 243 mmHg at 30 000 feet or 9100 metres) is much lower than that at sea level (760 mmHg). If you were exposed to that same pressure as a passenger, the pressure in your lungs would be greater than that of the atmosphere, and you would be unable to draw a breath.

In the next section, you will learn how differences in pressures of gases in the atmosphere versus pressures of those gases in the lungs also drive O_2 and CO_2 exchange.

2.2 Partial pressure

Pressure is an important factor in O_2 and CO_2 exchange in the alveoli. The pressure of each individual gas in the atmosphere is described as its **partial pressure**.

Partial pressure is calculated by multiplying the percentage of the particular gas in the atmosphere by the total atmospheric pressure. For example, O_2 accounts for about 21% of the Earth's atmosphere so the partial pressure of O_2 (PO_2) in the atmosphere is $0.21 \times 760 \text{ mmHg} = 160 \text{ mmHg}$. CO_2 is present only in trace amounts, so the partial pressure of CO_2 (PCO_2) in the atmosphere is roughly 0.3 mmHg.

Question 4 Nitrogen

Nitrogen (N_2) comprises 78% of the Earth's atmosphere. What is the partial pressure of nitrogen (PN_2)?

Provide your answer...

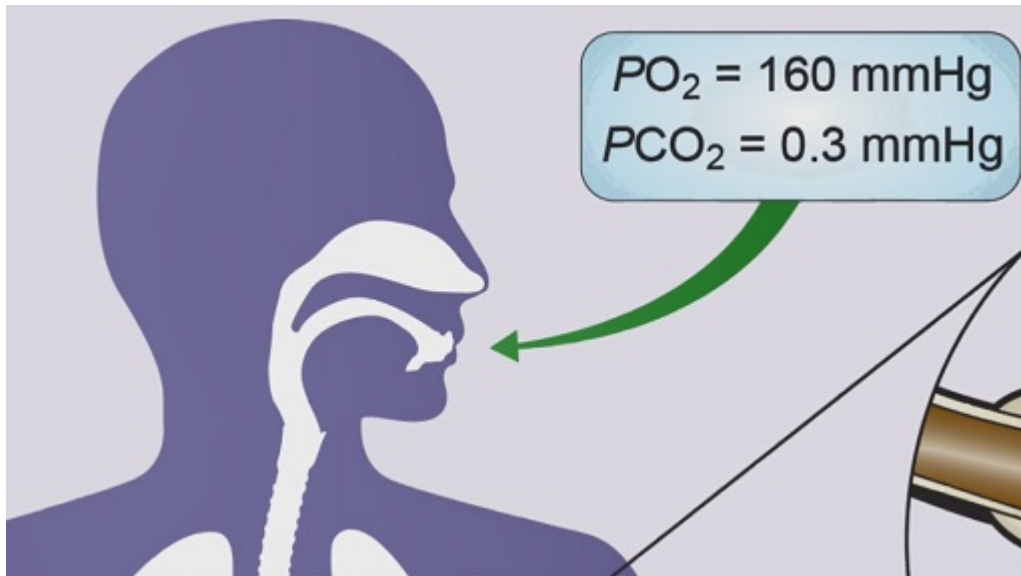
Answer

The PN_2 in the atmosphere is $0.78 \times 760 \text{ mmHg} = 593 \text{ mmHg}$.

The difference in PO_2 and PCO_2 between fresh air and the blood drives the diffusion of O_2 and CO_2 down their respective concentration gradients, as described in Video 8.

Video content is not available in this format.

Video 8 PO_2 and PCO_2 in lung and tissues.



Activity 4 O_2 movement

Allow about 5 minutes

Interactive content is not available in this format.

2.3 Decompression sickness

If you think back to William Trubridge and his free-diving record in the Introduction, you will recall that he swam up from a depth of 102 metres in just over 2 minutes, a rate of 51 m min^{-1} , without suffering any ill effects on his return to the surface. By contrast, scuba divers are advised not to ascend faster than 9 m min^{-1} to avoid developing decompression sickness ('the bends').

This discrepancy between free-divers and scuba divers lies in the differences in partial pressures of gases that are inhaled under atmospheric pressure and under compression. When you breathe from a scuba tank, the air has the same pressure as the pressure of water at that depth. The pressure of water is much higher than air; for example, at 20 m below the surface of the water, the pressure exerted by water on the body is about three times that experienced on dry land.

The high pressure can cause some of the N_2 gas in the air to dissolve into the blood. As the diver swims back up to the surface, the PN_2 in the blood is higher than in the surrounding water, so N_2 will be released from the blood and into the alveoli to be exhaled. If the change in pressure happens too quickly, the N_2 will not have time to be exhaled and instead will form air bubbles (similar to what happens when you open a shaken can of

fizzy drink). These bubbles can cause severe pain in joints and muscles and in extreme cases, death due to embolism.

Free-divers experience the same effects of PN_2 as scuba divers at deep depths. However, because free-divers are not breathing pressurised air as they dive, their lungs actually get compressed (down to a quarter of their original size) by the high pressure of the water. As the divers ascend, their lungs will slowly expand back to their original volume.

Question 5 Pressure in the lungs

According to Boyle's law, what will happen to the pressure in the lungs as the free-divers ascend (see Section 2.1)

- ☐ it will increase
- ☐ it will stay the same
- ☐ it will decrease

Answer

It will decrease. According to Boyle's law, $P = k/V$, so as the volume gets bigger, the pressure gets smaller.

So, as the divers return to the surface, the PN_2 in the lungs decreases relative to the PN_2 in the blood and N_2 diffuses into the alveoli, thereby decreasing the chances that it will form bubbles in the tissue.

2.4 Surface tension

In the previous section, you saw how partial pressure gradients drive the exchange of O_2 and CO_2 between the blood and the alveoli. Diffusion of the gases at this air-liquid interface is facilitated by a thin layer of water that coats the inner surface of the alveoli. Condensation of the water vapour that is exhaled when you breathe out is the reason why you 'see' your breath in cold weather.

Individual molecules of water (H_2O) bind together because hydrogen and oxygen atoms are strongly attracted to each other. This is why your hair sticks together when it's wet. This force is called hydrogen bonding.

Because hydrogen bonds are quite strong, when water molecules come into contact with each other, they will be held together tightly. This tight packing creates a **surface tension** in the water that forces it to adopt the smallest shape possible (e.g. a droplet) (Figure 6).

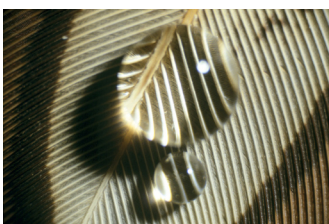


Figure 6 Surface tension of water holds it in a droplet form.

However, because the alveoli are round in shape, the surface tension that holds the water molecules together also puts an inward pressure on the inside of the alveolus (Figure 7).

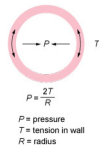


Figure 7 Surface tension (T) created by hydrogen bonding of water puts pressure on the inside of the alveoli, which have a small diameter or radius (R).

As you have just learnt, if the pressure in the alveolus is higher than the atmospheric pressure, air from the atmosphere will not enter and the alveolus will collapse (a medical condition called atelectasis). How does the lung combat the surface tension of water to ensure that the alveoli can expand with each breath? Cells within the alveoli secrete **surfactant**, a substance that attaches to the water molecules and prevents them from interacting with each other. This reduces the surface tension in the alveolus to near-zero levels. This effect is nicely demonstrated in Video 9. Why not try this experiment yourself at home?

Video content is not available in this format.

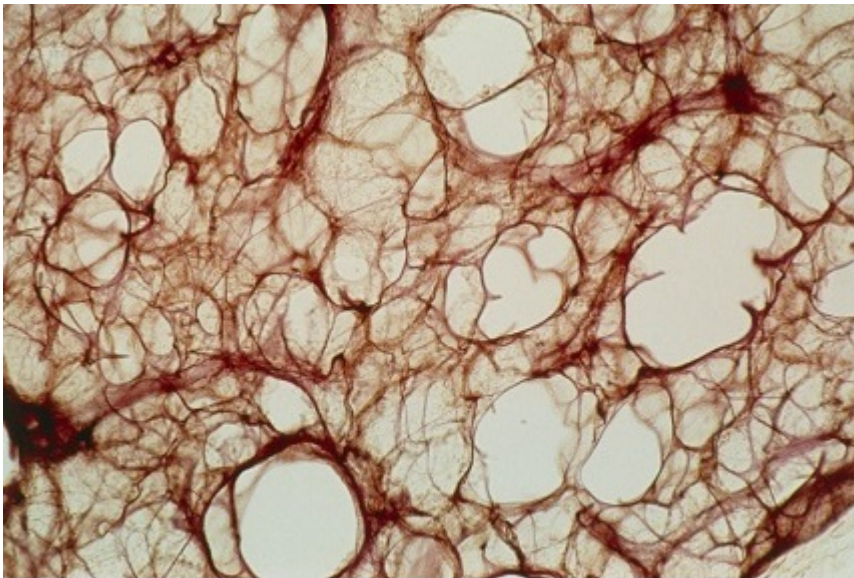
Video 9 Surface tension broken by surfactant.



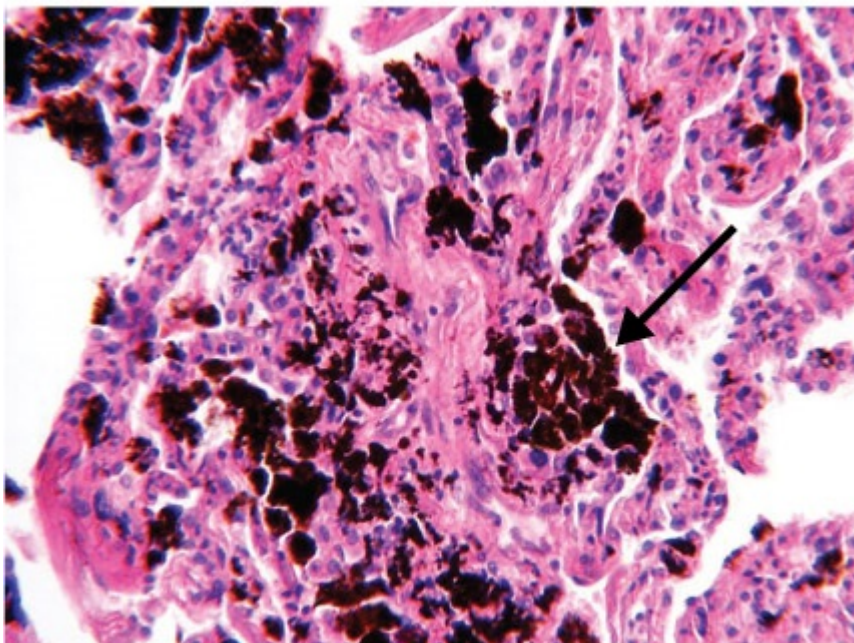
Surfactant also serves to prevent the collapse of the alveoli of newborn babies when they take their first breaths. Premature babies born before their surfactant production system is fully functional suffer from respiratory distress syndrome (RDS). Surface tension in the lungs of these babies is high and many alveoli fail to expand. Failure to produce enough surfactant may also be a problem in adult life; for example, surfactant production in the lungs of smokers is greatly reduced, increasing the likelihood of breathing difficulties compared to non-smokers.

2.5 Compliance and airway resistance

The ease with which the lungs and pleura expand and contract based on changes in pressure is called **compliance**. Low lung compliance means that the lungs and alveoli are 'stiff', so a higher-than-normal pressure gradient is needed to get the lungs to expand and contract. It can result from insufficient amounts of surfactant or fibrosis of the lungs due to prolonged inhalation of small particles such as asbestos or coal (e.g. black lung) (Figure 8).



(a)



(b)

Figure 8 (a) Cross-section through a healthy lung showing the air-filled alveoli. (b) Cross-section of a diseased lung showing deposits of coal particles (arrow).

High compliance results when the lungs are too pliable and move in response to small changes in pressure. This makes exhalation difficult because the elastic recoil of the lungs

(i.e. their ability to 'snap back' after inhalation) is decreased. High lung compliance is a characteristic of chronic obstructive pulmonary disease (COPD), a general term for a collection of diseases that are associated with lung damage, such as emphysema and chronic bronchitis, which are often associated with smoking (Figure 9).

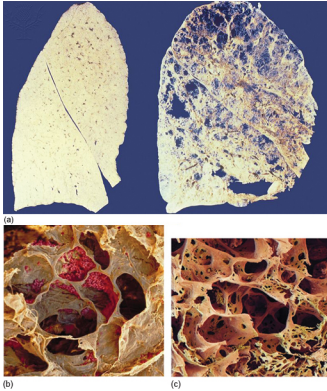


Figure 9 (a) Cross-section through a healthy lung (left) and a lung from a smoker (right). (b) and (c) Scanning electron microscope images showing alveoli in the lungs of (b) a healthy individual and (c) a person with COPD.

Activity 5 Comparing tissues

Allow about 10 minutes

Compare the tissue sections in Figure 9. List the differences you observe between:

1. the healthy lung versus the smoker's lung

Provide your answer...

Answer

The tissue from the healthy lung is uniform and pale in colour throughout. The lung from the smoker is bigger and contains large holes and has black-brown discolourations (probably due to tar and other particulates contained in cigarette smoke).

2. the healthy alveoli versus the COPD alveoli

Provide your answer...

Answer

The alveoli in the healthy lung are well defined and interconnected. The alveoli in the lung affected by COPD have incomplete and thinner walls, do not make as many connections with other alveoli and have larger air spaces that reduce the respiratory surface.

Pulmonary ventilation is also affected by the **resistance** of the airways to the flow of air. This resistance is caused by the friction that is generated when the air passes along the structures in the conduction and respiratory zones. Because the airways are made up of a series of tubes, resistance is largely affected by the diameter of the trachea, bronchi and bronchioles. Resistance is inversely proportional to radius, so structures with a small diameter have a higher resistance.

Question 6 Airflow resistance

Is the airflow resistance in a bronchiole higher or lower than in a bronchus?

- ☐ higher
- ☐ lower
- ☐ neither, they are the same

Answer

The radius of a bronchiole is smaller than that of a bronchus. A smaller radius results in higher resistance. Therefore, the resistance to airflow is higher in the bronchiole compared with the bronchus.

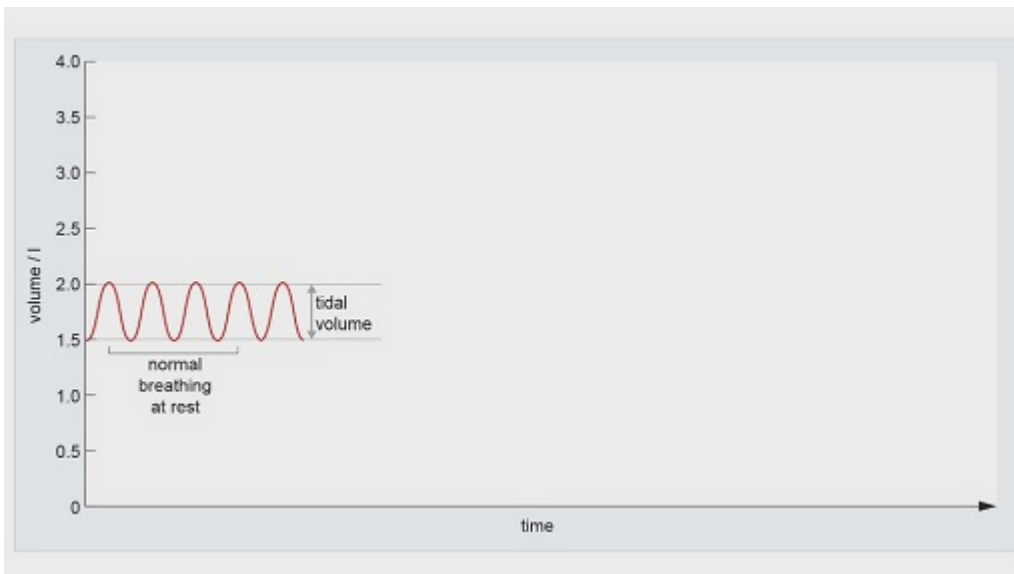
During an asthma attack, the airway resistance increases because the bronchial smooth muscle cells contract and reduce the diameter of the bronchi and bronchioles. This results in the characteristic wheezing, coughing and shortness of breath. Fast-acting reliever inhalers release drugs that relax the smooth muscle cells and thereby increase airflow. In the next section, you will see how lung capacity and function are measured and used as a guide for overall lung health.

3 Lung function

Changes in the compliance and resistance of the lungs can affect the capacity of the lungs to hold and exchange air. Lung capacity is calculated from the volume of air that is exchanged during normal and forceful breathing. The volumes that are used to calculate total lung capacity are described in Video 10.

Video content is not available in this format.

[Video 10 Calculating lung capacity.](#)



Activity 6 Lung capacity

Allow about 10 minutes

Part 1

Match the volume with the corresponding definition:

- expiratory reserve volume
- inspiratory reserve volume
- residual volume
- tidal volume

Match each of the items above to an item below.

- extra volume breathed out during forceful exhalation
- extra volume breathed in during forceful inhalation
- amount of air left in the lungs in addition to the expiratory reserve volume
- amount of air entering or leaving the lungs in a single resting breath

Part 2

Which of the volumes are NOT used to calculate the vital capacity of the lungs? Select all that apply.

- ☐ tidal volume
- ☐ inspiratory reserve volume
- ☐ residual volume

Correct. The vital capacity is the sum of the tidal volume, inspiratory reserve volume and expiratory reserve volume.

- ☐ expiratory reserve volume

3.1 Spirometry

Lung function can be measured using **spirometry**. A typical test involves blowing out into a spirometer as hard as possible until the lungs are empty (Figure 10). The **forced vital capacity** (FVC) is calculated as the total volume of air that can be forcefully blown out. **Peak expiratory flow** (PEF) measures the maximum speed at which air is forcefully expired (litres per second). The **forced expiratory volume 1** (FEV₁) is the amount of air that is forcibly blown out within the first second of the test.

Plotting the FVC and PEF values generates a spirograph similar to the one shown in Video 7. The FEV₁/FVC ratio (also calculated as a percentage) is used to evaluate lung function. In healthy individuals, the FEV₁/FVC ratio is approximately 0.8, meaning that 80% of total volume of air is blown out within the first second.



Figure 10 Portable spirometer used to measure lung function.

It is important to note that normal lung function is dependent on an individual's age, height, sex, ethnicity and general fitness. An example of the predicted FEV₁/FVC ratios for particular groups of men and women is shown in Table 1.

Table 1 Predicted FEV₁/FVC ratios for asymptomatic, lifelong non-smoker Caucasian men and women over the lifespan.

FEV ₁ /FVC (%) Male													
Age	20	25	30	35	40	45	50	55	60	65	70	75	80
All heights	83.9	82.9	81.9	80.8	79.8	78.8	77.7	76.7	75.7	74.6	73.6	72.6	71.5
FEV ₁ /FVC (%) Female													
Age	20	25	30	35	40	45	50	55	60	65	70	75	80
All heights	86.6	85.5	84.4	83.4	82.3	81.2	80.2	79.1	78.1	77.0	75.9	74.9	73.8

Question 7 Lung function across ages

Looking at Table 1, what happens to lung function with age in both men and women?

- ☐ It stays the same across all ages.
- ☐ It increases with age.
- ☐ It decreases with age.

Answer

Correct. Lung function, as measured by the FEV₁/FVC percentage, decreases with age in both men and women.

3.2 Lung function impairment

When lung function is impaired, the PEF, FEV₁, FVC and FEV₁/FEC values can be used to help determine the cause of the dysfunction; for example, decreased lung volume due to fibrosis or increased airway resistance due to asthma.

Activity 7 Spirometry experiment

Allow about 2 hours

In this activity, you will use the spirometer application in the Open Science Laboratory to measure changes in FEV₁/FEC over time between smokers and non-smokers. Here's the link to the application – open it in a new window or tab, so you can return to this page easily.

[Link to Spirometer application](#)

Before you begin collecting data, watch the video in the Introduction tab of the spirometer to familiarise yourself with the application.

Research studies that look at relationships between different groups of people can be categorised into cross-sectional or longitudinal studies. Cross-sectional studies compare different groups of people at one moment in time. Longitudinal studies analyse the same group of people across different points in time.

Now go to the Spirometer tab in the application and set the following parameters:

- age: 20

- male
 - height: 180 cm
 - non-smoker
1. Start the measurement and record the output of the FEV_1 , FVC and FEV_1/FVC (%) using the 'Record data' button. Repeat this measurement three times, remembering to record the data each time.
 2. Repeat the data collection for the same male individual at ages 40 and 80. Repeat both measurements three times, remembering to record the data each time.
 3. Then select the same parameters for age, sex and height, but choose 'smoker'. This group smoked one pack of 20 cigarettes each day from the age of 20. Collect data for three ages – 20, 40 and 80 – repeating and recording the measurement three times.
 4. Select the 'Export data' button then copy and paste the results into a spreadsheet program such as Excel.
 5. Determine the mean (average) of the three values that you collected of FEV_1/FVC (%) at each age for the non-smoker and smoker conditions.
 6. Plot a computer-generated x - y graph showing the mean FEV_1/FVC (%) of the smoker and non-smoker at 20, 40 and 80 years of age. Make sure to plot this in chronological order.

4 Gas exchange

In this section, you will examine the chemical changes that underlie exchange of O_2 and CO_2 between peripheral tissues and the lungs. You will also learn about genetic mutations of haemoglobin and how the body senses and responds to changes in O_2 and CO_2 levels to maintain homeostasis.

4.1 O_2 and CO_2 transport in the blood

You've seen how gradients between PO_2 and PCO_2 drive gas exchange in the alveoli. But how are these gases carried in the blood? Small amounts of O_2 (~0.3%) and CO_2 (~3%) dissolve directly into the plasma. However, such concentrations are not sufficient to fulfil the metabolic demands of the body. The main transport of O_2 and CO_2 in the blood is mediated via haemoglobin molecules and bicarbonate ions, respectively.

4.2 Haemoglobin

Most O_2 is carried in the blood by erythrocytes (red blood cells) which contain **haemoglobin** (Hb). In adults, Hb is a protein formed of four polypeptide chains, called globins – there are two alpha and two beta chains (Figure 11). Attached to the interior of each globin chain is a small non-protein structure known as a haem group. The haem group has at its centre an iron ion (Fe^{2+}) that binds to one O_2 molecule. As there are four globin chains and four haem groups, each with one Fe^{2+} , one Hb molecule can carry four O_2 molecules.

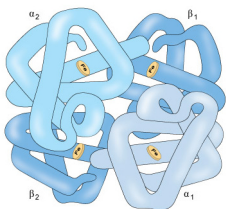


Figure 11 Schematic of the haemoglobin protein, comprising two alpha and two beta chains and four haem groups.

When O_2 is bound to Hb, the Hb is said to be oxygenated and the complex formed is called **oxyhaemoglobin**. Oxygenation occurs where there is a plentiful supply of O_2 ; that is, in the capillaries surrounding the alveoli of the lungs.

O_2 binding to Hb is governed by positive cooperativity, meaning that once one haem group binds O_2 , it becomes progressively easier for the other haem groups to also bind O_2 . This ensures that the Hb molecule can become quickly saturated (i.e. with four O_2 molecules bound). Oxygen saturation levels ('sats') are used by doctors to detect respiratory distress or illness.

Binding of O_2 to Hb is reversible, meaning that when oxyhaemoglobin reaches the capillaries within the tissues, where O_2 is being consumed and the PO_2 is low, the O_2 is released and diffuses into the tissues. Hb that is not bound to O_2 is termed **deoxyhaemoglobin**.

Question 8 Pulmonary arteries

Which form of Hb is predominant in the blood carried by the pulmonary arteries? (see Section 1.1.3)

- ☐ oxyhaemoglobin
- ☐ deoxyhaemoglobin

Answer

Pulmonary arteries carry blood coming from the peripheral organs into the lungs where CO_2 will be exchanged for O_2 , so they carry CO_2 -rich blood. Therefore, the predominant form of Hb in the pulmonary arteries will be deoxyhaemoglobin.

The binding and dissociation of O_2 to and from haemoglobin is dependent on the PO_2 . This is not surprising, because as you saw in Section 2.2, differences in partial pressures between tissue capillaries and pulmonary capillaries drive the exchange of O_2 and CO_2 . However, if you look at the **oxygen–haemoglobin dissociation curve** in Activity 8, you will see that O_2 binding to haemoglobin is not a linear relationship. Rather, the amount of Hb bound to O_2 over a range of PO_2 has a sigmoidal 'S'-shaped curve.

Activity 8 Oxygen–haemoglobin dissociation curve

Allow about 5 minutes

Take a look at this dissociation curve, then place the marker as directed and click 'Enter answer'. If you place it correctly, one more question will then be posed to you.

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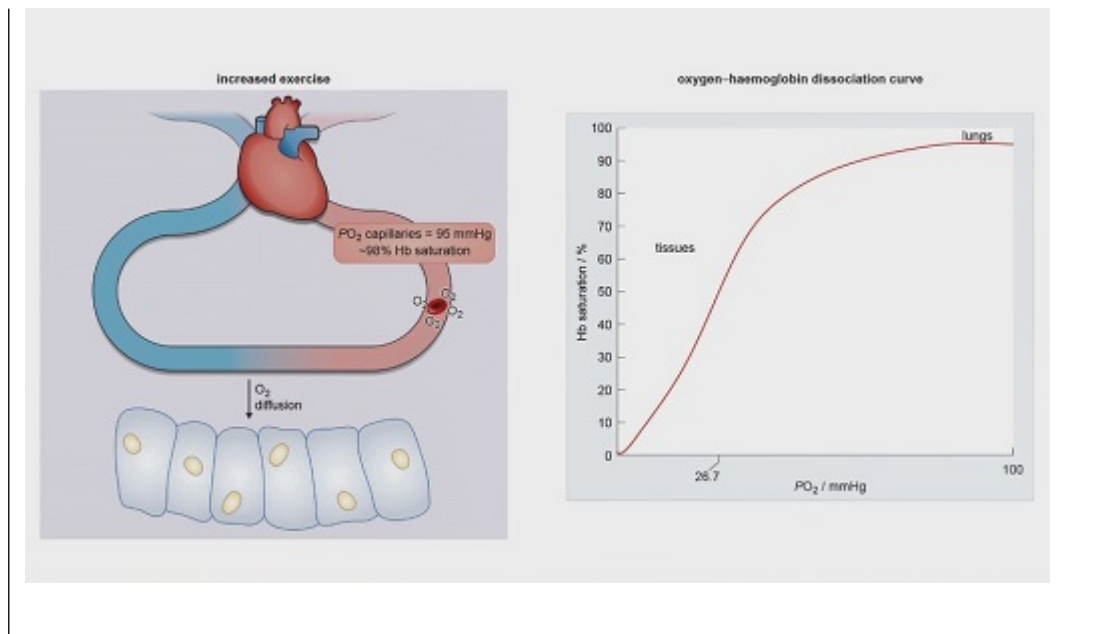
4.2.1 Influencing the curve

A number of biological factors influence the oxygen–haemoglobin dissociation curve and shift it to the right or left. These factors are summarised in the following video.

The term 'affinity' refers to the strength of binding between two particles or proteins. Low affinity means that the binding is weak and the particles can be easily separated. High affinity means that the binding is strong. In the context of Hb and O_2 , low affinity means that the O_2 binds weakly to the Hb and is therefore easily transferred to the tissues.

Video content is not available in this format.

[Video 11 Factors influencing the oxygen–haemoglobin dissociation curve.](#)



Question 9 Biological factors

Having watched Video 11, note down the biological factors that affect the affinity of Hb binding of O₂.

Provide your answer...

Answer

- CO₂
- acidity
- 2,3-DPG
- exercise
- temperature

4.3 Bicarbonate

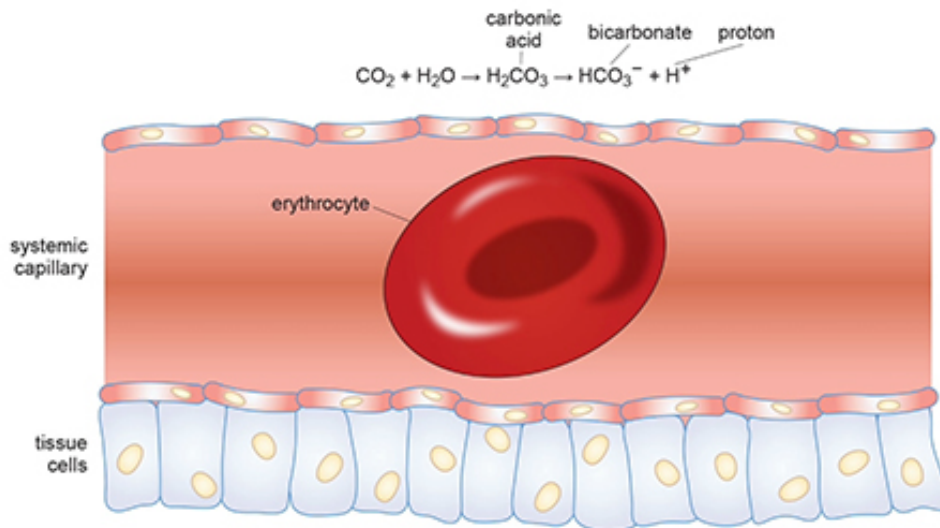
In the previous section, you saw how the affinity of Hb for O₂ decreases in the presence of elevated CO₂ and acidity. This is known as the **Bohr effect**. This is due to the chemical reaction that takes place between CO₂ and water (H₂O) to generate bicarbonate (HCO₃⁻) and protons (H⁺). This reaction is represented by the equation:

In chemistry, the \rightleftharpoons arrow represents a reversible reaction, meaning it can go in the right or the left direction. In this case, adding more CO₂ will push the reaction to the right and generate more H⁺ and HCO₃⁻ ions. H⁺ ions decrease the pH of a solution (make it more acidic) whereas HCO₃⁻ ions increase the pH and make it more basic.

The reversible nature of this reaction is critical in allowing the body to transport CO_2 from the tissues and be exhaled in the lungs. This process is detailed in Video 12.

Video content is not available in this format.

[Video 12 Bicarbonate buffering.](#)



In Video 12, you saw that protons (H^+) generated during bicarbonate buffering of CO_2 bind to Hb in the erythrocytes to form protonated haemoglobin (HbH^+). This binding decreases the affinity of Hb for O_2 , thereby facilitating O_2 diffusion into tissues, as described by the following equation:

At the same time, CO_2 that has not been converted into HCO_3^- (~30% of total CO_2 in the blood) binds with high affinity to deoxyhaemoglobin to form **carbaminohaemoglobin** (HbCO_2). This complex is then carried to the lungs (Figure 12).

In the alveoli, binding of O_2 to HbH^+ results in the release of free H^+ ions.

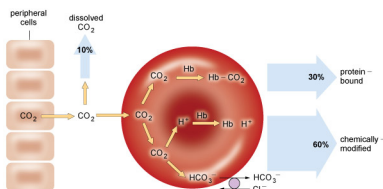


Figure 12 Mechanisms by which CO_2 is carried in the blood.

Question 10 Higher H^+

In what direction will the higher concentration of H^+ push the equilibrium reaction?

- ☐ left, towards increased CO_2 production

- right, towards HCO_3^- production
- neither, the reaction will stay in equilibrium

Answer

The answer is left. It will help drive the diffusion of CO_2 out of the blood and into the alveoli to be exhaled.

In parallel, carbaminohaemoglobin loses its affinity for CO_2 as it becomes reoxygenated. Collectively, these actions increase the PCO_2 at the alveoli. The phenomenon by which O_2 influences CO_2 concentrations is known as the **Haldane effect**.

The capacity of the blood to carry O_2 is also greatly reduced by carbon monoxide (CO), a gas emitted by car exhausts and faulty gas appliances. CO competes with O_2 for binding to Hb. Because the affinity of Hb for CO is higher than its affinity for O_2 , CO molecules will bind preferentially and irreversibly to form carboxyhaemoglobin (HbCO), which is cherry red in colour. Inhaling CO will therefore progressively reduce the amount of Hb available to bind O_2 and lead to CO poisoning. If the source of CO is not removed, death could result due to the total lack of oxygen (asphyxiation).

5 Inherited disorders of haemoglobin

In the previous section, you saw that erythrocytes and the haemoglobin they contain play a crucial role in mediating exchange of both O_2 and CO_2 between the tissues and the lungs. This section will use two examples, sickle cell anaemia and thalassaemia, to illustrate how genetic disorders of haemoglobin can affect gas transport and exchange in the body.

5.1 Sickle cell anaemia

Sickle cell anaemia gets its name from the abnormal shape of the erythrocytes, which resemble that of an old farming tool, the sickle (Figure 13). This shape is due to a single nucleotide substitution (A to T) that converts a glutamic acid codon (GAG) into a valine codon (GUG) in the beta chains of Hb.

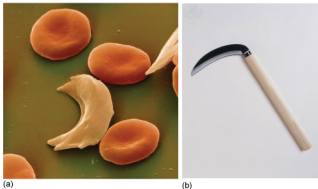


Figure 13 Sickle cell erythrocytes.

Activity 9 RNA codon wheel

Allow about 15 minutes

Take a look at this interactive RNA codon wheel. If you click on an amino acid, the diagram will highlight the corresponding nucleotides. You can view some further information and chemical structures for each amino acid. When you've done this, use the diagram to answer the question underneath.

Interactive content is not available in this format.

Which nucleotide substitution would still result in a functional Hb protein?

- ☐ GAG → GCG

Incorrect. Substitution of A by C will produce the codon GCG which codes for the amino acid alanine.

- ☐ GAG → GAA

Correct. Both GAG and GAA are codons for glutamic acid. Therefore, substitution of G by A will still produce a functional Hb protein.

- ☐ GAG → CAG

Incorrect. Substitution of G by C will produce the codon CAG which codes for the amino acid glutamine.

Sickle Hb is denoted as HbS. Because glutamic acid is negatively charged, these amino acids would normally repel each other and help the Hb retain its shape. However, these repulsive forces are absent in the HbS because valine is uncharged.

HbS is able to bind O₂ normally in the lungs and carry it to the tissues. However, as the HbS becomes deoxygenated, the valine amino acids are exposed and start to bind to each other, forming long chains of deoxyHbS. These chains distort the cell and cause it to bend out of shape. As more and more deoxyHbS molecules come in contact with each other, they can result in the formation of a chain of sickled erythrocytes, which clump together and get stuck in the capillaries (Figure 14).

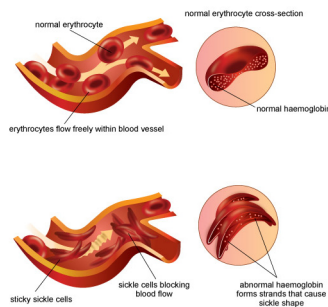


Figure 14 Misshapen erythrocytes carrying the HbS mutation can aggregate and get stuck in tissue capillaries.

Sickled erythrocytes that return to the alveoli will regain their biconcave disc shape as they once again become oxygenated. Note that erythrocytes carrying normal Hb maintain this biconcave shape regardless of their O₂ saturation levels.

The repeated episodes of polymerisation and depolymerisation of HbS as it travels between the lungs and tissues damages both the haemoglobin molecules and the erythrocyte itself, making it rigid and unable to move through the small-diameter capillaries.

Amplified many times, blockage of the capillaries can produce tissue hypoxia (i.e. low levels of oxygen), resulting in tissue pain and damage. In addition, the sickled erythrocytes are more fragile and die on average after 20 days in circulation, compared with normal erythrocytes that live for 120 days. Loss of erythrocytes leads to the anaemia (low red blood cell count) of sickle cell disease.

Symptoms of sickle cell anaemia include episodes of pain (called sickle cell crises) in tissues and bones, swelling of hands and feet, frequent infections, delayed growth and problems with vision. In addition, chronic pulmonary complications are common in individuals with sickle cell disease, including asthma, pulmonary fibrosis, decreased FEV₁ values and sleep apnoea (which is further explored later in the course).

Sickle cell anaemia is a recessive disorder, meaning that in order for an individual to develop the disease, they must inherit two *HbS* alleles.

5.2 Thalassaemia

Thalassaemias are a group of inherited autosomal recessive disorders that cause anaemia because of the decreased or absent synthesis of a globin chain (Muncie and Campbell, 2009). Alpha thalassaemia is the result of either deficient or absent production of the alpha globin chain, which is then replaced by extra beta globin chains. Production of the alpha globin protein is slightly more complicated because it is controlled by two genes,

both located on chromosome 16. This means that disease susceptibility is dependent on the inheritance pattern of four alleles – two inherited from the mother and two from the father. Alpha thalassaemia is usually due to the deletion of one of these alleles and the severity of the disease corresponds to the number of deletions:

- one deletion is silent and asymptomatic
- two deletions result in mild anaemia
- three deletions cause haemoglobin H disease and moderate to severe anaemia
- four deletions cause alpha thalassaemia major, a fatal condition.

Activity 10 Inheritance pattern of alpha thalassaemia

Allow about 20 minutes

In this activity, you will predict the phenotype and pattern of inheritance of alpha globin genes in a family affected by alpha thalassaemia. Click below to reach the full activity.

Interactive content is not available in this format.

Beta thalassaemia results from deficient or absent production of the beta globin chains, leading to excess alpha chains in the Hb molecules (Figure 15).

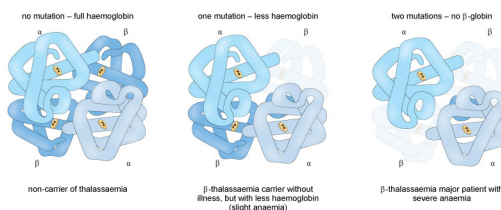


Figure 15 The severity of disease related to beta thalassaemia is dependent on the number of beta globin chains that are functional.

Unlike alpha thalassaemia, beta thalassaemia is usually due to a point mutation (more than 200 of which have been identified to date) in the gene that codes for beta globin. Again, the degree of disease symptomology is dependent on how many beta globin chains are functional. Beta thalassaemia minor is asymptomatic whereas beta thalassaemia major causes growth retardation, skeletal abnormalities and jaundice, and requires lifelong blood transfusions to treat.

The overall effect of either alpha or beta thalassaemia is haemolysis, the rupture and destruction of the erythrocytes. Because of this, people with thalassaemia are at risk of developing pulmonary hypertension, a higher than normal pressure in the arteries that carry blood to and from the lungs. This can cause dizziness, shortness of breath and damage to the heart.

Question 11 Hb mutations

Why do you think Hb mutations that cause potentially fatal anaemias continue to exist in the human genome?

Provide your answer...

Answer

The rates of both sickle cell anaemia and thalassaemias are higher in people of African, Southeast Asian and Mediterranean descent. It is not a coincidence that these are also regions where the malaria parasite is highly prevalent. Heterozygous carriers of the *HbS* gene or thalassaemia mutations are less likely to be infected with the *Falciparum malaria* parasite than people with the normal copies of those genes. Malaria can cause serious illness and over one million people die from the infection every year. Therefore, mutations in Hb lead to a trade-off between increased risk of anaemia and decreased risk of death from malaria. Malaria is a good example of how parasites (and other infectious organisms) exert evolutionary pressure on the human genome to adopt multiple polymorphisms that protect against severe disease.

6 Control of respiration

Generally, respiration is an involuntary, automatic event. You are probably not aware it is happening unless you exert voluntary control over it by holding your breath, or breathing deeply. The rate and depth of your respiration adjusts automatically according to the metabolic needs of the tissues in the body. For example, athletes will breathe much more quickly and deeply during bouts of exercise to accommodate increased aerobic activity of their muscles, as discussed from 2:13 onwards in this video about Olympic rowing. (Make sure to open the link in a new window/tab so you can easily navigate back to this page.)

[Link to Video 13 – Anatomy of a rower.](#)

How does the body sense and respond to changes in metabolic rate? This function is mediated by **peripheral chemoreceptors** in the blood vessels and heart, and **central chemoreceptors** in the brain that detect changes in O_2 and CO_2 levels in the blood. Although changes in the partial pressures of both gases are involved in the regulation of respiration, alteration in PCO_2 is the principal driver of respiration rate in humans.

6.1 Central chemoreceptors

Changes in PCO_2 , and therefore in pH, are detected largely by chemoreceptors within the **respiratory centres** of the brain (Figure 16). During increased metabolic activity, such as exercise, the PCO_2 in the arterial blood increases.

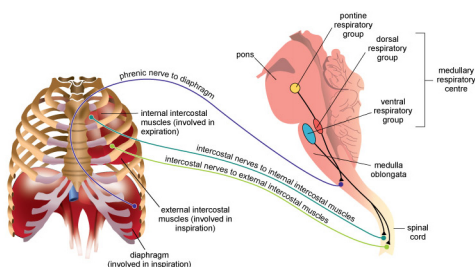


Figure 16 Neurons in the pontine and medullary respiratory centres of the brain synapse onto the diaphragm and intercostal muscles to regulate breathing rate.

Question 12 Increased exercise

What happens to the P_{50} (the PO_2 at which 50% of Hb molecules are saturated with O_2) of the oxygen–haemoglobin dissociation curve during increased exercise? (see Section 4.2)

- ☐ it increases
- ☐ it decreases
- ☐ it stays the same

Answer

Increasing exercise will shift the oxygen–haemoglobin dissociation curve to the right, so the P_{50} will increase.

As CO_2 -rich blood reaches the brain, CO_2 diffuses across the blood–brain barrier into the interstitial fluid and cerebrospinal fluid that surrounds the medulla.

Activity 11 Reaction components

Allow about 10 minutes

Part 1

Enter the components represented by x and y that complete the formula below.

There are superscript and subscript buttons in the formatting bar. Make sure to use these to enter the correct chemical formula, including the associated positive and negative charges:

x = y =

Answer

giving:

Part 2

Using the completed formula above, what will happen to levels of H^+ in the brain as CO_2 -rich blood reaches the medulla?

- ☐ levels of H^+ will increase
- ☐ levels of H^+ will decrease
- ☐ levels of H^+ will stay the same

Answer

Adding more CO_2 will increase the production of H^+ and HCO_3^- . Increased H^+ will make the tissue more acidic, meaning that the pH will decrease.

Neurons within the medullary and pontine respiratory centres will fire action potentials in response to the change in pH, via activation of receptors that are sensitive to protons (Guyenet and Bayliss, 2015). These neurons synapse onto the phrenic and intercostal nerves which innervate the diaphragm and intercostal muscles (see Section 1.2) and stimulate increased breathing (Figure 16).

As the pH returns to homeostatic levels, the chemoreceptors stop being activated and the breathing rate returns to normal. Therefore, the respiratory centres act as the

'pacemakers' of respiration during both resting and stimulated conditions, via communication with the muscles that control the expansion and contraction of the lungs (McKay et al., 2003). Fine-tuning of the breathing pattern is controlled by inputs from the pontine respiratory group (Figure 16). Information from stretch receptors in the lungs is also used by the respiratory centres to determine when the lungs have expanded to full capacity. Some neurodegenerative diseases, such as motor neurone disease, are characterised by respiratory problems that are caused by the gradual loss of innervation to the diaphragm and intercostal muscles, despite the fact that the respiratory centres are intact. In other cases, when the respiratory centres of the medulla are damaged, individuals may require artificial ventilation of the lungs to regulate their breathing rate.

6.2 Peripheral chemoreceptors

Before the blood reaches the chemoreceptors in the brain, changes in PO_2 are detected by specialised cells – called type 1 glomus cells – that are located in the carotid artery (carotid bodies) and aorta (aortic bodies) of the heart.

Glomus cells are derived from the same tissue as neurons and therefore have similar properties, including electrical excitability and release of neurotransmitters. The cells express O_2 -sensitive potassium channels; when the PO_2 falls, the K^+ channels close and the resting potential of the cell becomes less negative.

Glomus cells release dopamine across the neuromuscular junction, which causes the postsynaptic sensory neurons to send an afferent signal to the medullary respiratory centres. The respiratory centres will then send action potentials to the phrenic and intercostal nerves to increase the respiration rate.

6.3 Additional neuronal control

The lungs also receive innervation from the autonomic nervous system (Figure 17). The sympathetic innervation originates from the thoracic portion of the spinal cord and synapses onto the bronchiolar smooth muscle. Stimulation of these nerves causes bronchodilation.

Question 13 Bronchodilation

What happens to airway resistance during bronchodilation?

- ☐ it increases
- ☐ it decreases
- ☐ it stays the same

Answer

It decreases. Dilation will increase the diameter of the bronchioles, so the resistance to airflow will decrease.

In parallel, the vagus nerves (or cranial nerve X) synapse onto the bronchi and pulmonary blood vessels as part of the parasympathetic innervation. Activity of these neurons counterbalances the sympathetic response by stimulating constriction of the bronchi. Activation of these pathways is involved in the 'fight or flight' response.

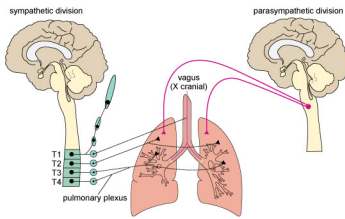


Figure 17 Innervation of the lungs by the autonomic nervous system.

Question 14 Hyperventilation

Sarah has a panic disorder and frequently experiences panic attacks that cause her to hyperventilate (i.e. breathe more rapidly than normal) and feel dizzy. What branch of the autonomic nervous system is activated during the panic attack?

- ☐ parasympathetic
- ☐ sympathetic
- ☐ enteric

Answer

Activation of the sympathetic nervous system will cause the bronchioles to dilate to meet the demands of increased inspiration and expiration.

What will happen to the PCO_2 levels in the alveoli during hyperventilation?

- ☐ they will drop
- ☐ they will increase
- ☐ they will stay the same

Answer

They will drop. The rapid breathing causes more CO_2 to be expired, so the PCO_2 in the alveoli will be lower than normal.

Sarah finds that if she breathes into a paper bag during hyperventilation, her breathing returns to normal more quickly than when she just waits for the attack to pass. Why do you think this is?

Provide your answer...

Answer

During hyperventilation, PCO_2 in the alveoli will be lower than normal. Decreased CO_2 , in combination with the decreased acidity of the blood, will shift the oxygen–haemoglobin dissociation curve to the left, increasing the affinity of Hb for O_2 and making it harder for O_2 to diffuse into the tissue (which partly explains why she feels dizzy).

Breathing into a bag concentrates the gases that are breathed out, including CO_2 . Re-breathing the expired, concentrated CO_2 will lower the pH, reduce the activity of the respiratory neurons and restore the homeostatic breathing rate.

Finally, if you play a musical wind instrument, you know that some aspects of breathing can be controlled voluntarily. This ‘override’ of the autonomic breathing system involves

the motor cortex, thalamus and cerebellum, which are also involved in breath control during speech and behavioural tasks that modify breathing by learning and experience.

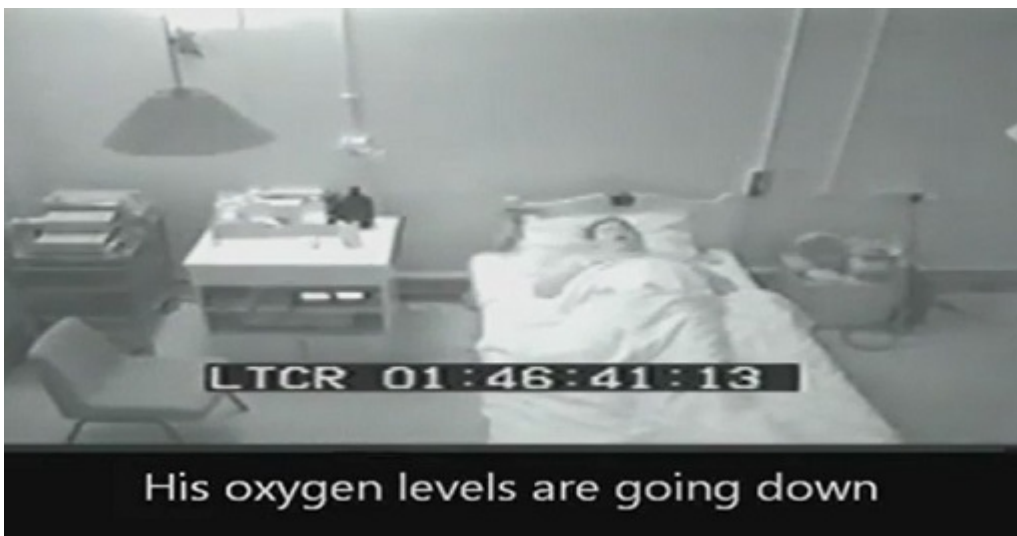
6.4 Sleep apnoea

Sleep apnoea occurs when airflow is disrupted during sleep. It can arise due to abnormalities in the medullary respiratory centres that result in a failure to regulate the contraction of the diaphragm and intercostal muscles (called central apnoea).

However, the most common form of sleep apnoea is caused by an obstruction of the pharynx (termed obstructive sleep apnoea) by the muscles and soft tissues in the throat, which relax during sleep. A reduction in airflow (due to increased airway resistance) is termed **hypopnoea**, whereas a complete blockage of airflow (interruption for more than 10 seconds) is called **apnoea**. Symptoms of obstructive sleep apnoea include snoring (caused by the vibration of the soft tissues in the pharynx), struggling to breathe (or cessation of breathing) during sleep, and fatigue or falling asleep in the daytime. An instance of apnoea is shown in Video 14 below.

Video content is not available in this format.

[Video 14 Obstructive sleep apnoea.](#)



Some people may be completely unaware that they stop breathing at night and therefore are only conscious of feeling very tired despite having slept 'well'. The fatigue occurs because during the apnoea, the response of the respiratory neurons to the rising PCO_2 of the blood causes the brain to come out of REM sleep. In people with severe obstructive sleep apnoea, such interruptions can occur more than 30 times in an hour, leading to very poor quality sleep.

Treatments for sleep apnoea typically involve lifestyle changes that result in physiological changes (e.g. weight loss, cessation of smoking), mandibular advancement mouthpiece devices that keep the jaw open, and wearing continuous positive airway pressure (CPAP) masks that push pressurised air into the airway (Figure 18).



Figure 18 Use of a CPAP device for treatment of sleep apnoea.

Conclusion

In Act 1, Scene 3 of William Shakespeare's *The Merchant of Venice*, Shylock asks Antonio:

... shall I bend low, and in a bondman's key with bated breath and whisp'ring humbleness say this: "Fair sir, you spet on me on Wednesday last... and for these courtesies I'll lend you thus much moneys"?

(Shakespeare, 1605, p.28)

Shylock is mockingly implying that he is holding his breath in eager anticipation of lending Antonio money. Although written many years before the physiology of respiration was understood, Shakespeare recognised that breathing is a dynamic process that responds to changes in the environment.

In this course, you have learnt how exchange of O_2 and CO_2 is mediated by physical factors such as pressure gradients and chemical changes such as bicarbonate buffering and pH. The airways, musculoskeletal system, lungs and nervous system act in concert to make sure that adequate levels of O_2 are maintained throughout the body.

Here is a summary of the main points that have been covered in this course:

- The respiratory system comprises structures that conduct air into and out of the lungs. The conduction zone includes the nasal passages, pharynx, larynx, bronchi and bronchioles. Gas exchange occurs in the respiration zone of the bronchioles, alveolar ducts and alveoli.
- Exchange of O_2 and CO_2 is influenced by pressure (atmospheric and partial), surface tension, lung compliance and airway resistance. These factors are altered by respiratory disorders such as asthma, smoking and COPD, which also influence lung capacity.
- The majority of O_2 is carried in the blood bound to haemoglobin that is present in erythrocytes. Most of the CO_2 is carried in the blood as bicarbonate, whereas a smaller percentage also binds to haemoglobin.
- Recessive polymorphisms in the haemoglobin genes can cause anaemias such as sickle cell anaemia and thalassaemia, but may confer protection against infectious disease.
- Changes in PCO_2 and PO_2 are detected by chemoreceptors located in the heart, blood vessels and brain. Respiratory centres in the medulla communicate via the peripheral nervous system with the muscles that control ventilation.

This OpenLearn course is an adapted extract from the Open University course [SK299 Human biology](#).

Glossary

alveolar sacs

Part of the respiratory zone structures, located at the end of the alveolar duct.

apnoea

A temporary cessation of breathing.

Bohr effect

Influence of CO₂ and acidity on the affinity of haemoglobin for oxygen.

bronchi

The two main branches of the windpipe or trachea, leading to the lungs (singular, bronchus).

carbaminohaemoglobin

Haemoglobin that is bound to carbon dioxide (HbCO₂).

cellular respiration

The metabolic process in which living cells obtain energy (in the form of adenosine triphosphate, ATP) from the breakdown of molecules, particularly glucose.

central chemoreceptors

Receptors located on neurons within the medullary and pontine respiratory centres of the brain that detect differences in blood pH.

compliance

The ease with which the lungs and pleura expand and contract based on changes in pressure.

conduction zone

The parts of the lungs that conduct gas to and from the external environment.

deoxyhaemoglobin

Haemoglobin that is not bound to oxygen.

diaphragm

A muscular wall involved in lung ventilation, separating the chest (thoracic) cavity from the abdominal cavity.

external respiration

Exchange of gases in the lung between the blood and the external environment.

forced expiratory volume 1

The amount of air that is forcibly blown out within the first second of a spirometry test.

forced vital capacity

Total volume of air that can be forcefully blown out.

haemoglobin

A globular iron-containing protein present in red blood cells, which binds oxygen at the lungs and transports it to the tissues. Some of the carbon dioxide transported from the tissues to the lungs is also carried by haemoglobin.

Haldane effect

Influence of oxygen on haemoglobin transport of carbon dioxide.

hypopnoea

Reduction in airflow.

intercostal muscles

External and internal muscles between the ribs that are involved in the movement of the ribcage during breathing.

intercostal nerves

Nerves that innervate the intercostal muscles.

lungs

The respiratory organs that are located in the chest cavity; consisting of two elastic sacs with branching airways that allow air to be drawn into the body and expelled by a combination of muscular action and elastic recoil. They provide a large surface area where gaseous exchange occurs between the blood and the air.

nasal cavities

Part of the upper respiratory tract by which air enters and leaves the body.

oxygen–haemoglobin dissociation curve

'S'-shaped curve that dictates how the affinity of haemoglobin for oxygen changes with different partial pressures of oxygen.

oxyhaemoglobin

Haemoglobin bound to oxygen molecules. Oxyhaemoglobin transports oxygen from blood vessels in the lungs to the cells in the rest of the body.

partial pressure

The pressure that one component of a mixture of gases would exert if it were alone in a container.

peak expiratory flow

The maximum rate at which air is forcefully expired (litres per second).

peripheral chemoreceptors

Receptors in the carotid artery (carotid bodies) and aorta (aortic bodies) of the heart that detect and respond to changes in partial pressure of oxygen.

pharynx

The opening at the back of the throat that serves as a common passageway for the digestive and respiratory systems.

phrenic nerve

Nerve originating in the medulla of the brain that innervates the diaphragm.

pleura

The thin membranes lining the fluid-filled cavity (the pleural cavity) between the lungs and the inside of the thoracic (chest) wall (singular, pleura).

resistance

The friction that is generated when the air passes along the structures in the conduction and respiratory zones.

respiratory centres

The areas of the medulla region in the brain that integrate sensory information from chemoreceptors monitoring the level of oxygen and carbon dioxide in the blood. The respiratory centres send out appropriate signals to regulate the rate of contraction of the respiratory muscles (including the diaphragm and intercostal muscles).

respiratory zones

Composed of the bronchioles, alveolar ducts and alveoli in which gas exchange takes place during respiration.

sickle cell anaemia

A genetic disorder linked to abnormal haemoglobin. A point mutation has replaced the amino acid glutamic acid with valine, disrupting the structure of haemoglobin. The abnormal haemoglobin crystallizes when deoxygenated, forming sickle-shaped red blood cells that tend to block capillaries.

spirometry

A test used to measure lung function.

surface tension

Chemical forces that hold liquids in their smallest surface area possible.

surfactant

A phospholipid substance that breaks surface tension of water by attaching to the water molecules and preventing them from interacting with each other.

thalassaemias

A group of inherited autosomal recessive disorders that cause anaemia because of the decreased or absent synthesis of a globin chain of haemoglobin.

trachea

A tube that connects the throat (pharynx) and voice box (larynx) to the lungs, allowing the passage of air. Also known as the windpipe.

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