

## Respiratory system

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### Components

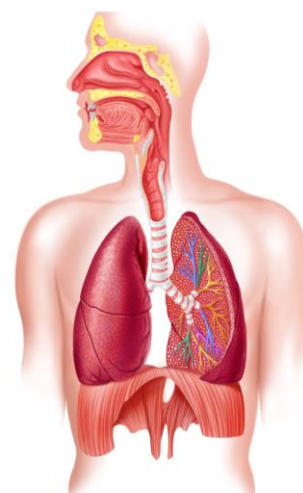
The respiratory system is made up of the nasal cavity, nasopharynx, epiglottis, larynx, trachea, bronchi, lungs (containing bronchioles and alveoli), pleural membranes, diaphragm, ribs and intercostal muscles.

It has its own circulatory system *via* the right side of the heart and the pulmonary arteries and veins.

### Functions

Cells in the body need oxygen for aerobic respiration, a process that releases energy stored in glucose and other molecules. The respiratory system obtains oxygen from and eliminates carbon dioxide to the external environment through the alveoli (air sacs) in the lungs. This involves breathing and gaseous exchange, a process called external respiration.

Oxygen for use in cell respiration is transferred from air into the blood. Carbon dioxide produced in respiration is removed from the blood and excreted into the atmosphere.



**Figure 1** The respiratory system.

### Key mechanisms

#### Ventilation of the lungs / blood circulation

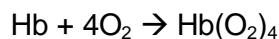
The rate of diffusion of oxygen and carbon dioxide (gaseous exchange) is maximised by:

- a large surface area for gaseous exchange (the lungs contain numerous air sacs or alveoli and numerous blood capillaries in contact with the alveoli);
- the epithelium of the alveoli and the endothelium of the capillaries are extremely thin to keep diffusion distances short;
- a concentration gradient is maintained between the alveoli of the lungs and the blood plasma; the lungs are ventilated by the action of respiratory muscles between the ribs and around the periphery of the diaphragm, causing expansion of the thorax and intake of about 500 cm<sup>3</sup> of air, and blood is pumped to the lungs by the heart;
- deoxygenated blood travelling to the lungs from the right side of the heart under high pressure through the pulmonary artery, while oxygenated blood is returned to the left side of the heart by the pulmonary vein;
- high pressure restored, so that the oxygenated blood is pumped through the aorta to all parts of the body other than the lungs, and deoxygenated blood is returned to the heart by the vena cava.

#### Oxygen transport

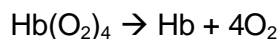
Oxygen that diffuses into blood binds to haemoglobin molecules packed into red blood cells and is moved around the body.

Haemoglobin is a globular protein with four haem molecules held in it by intermolecular bonds. In the concentrations of oxygen found in the lungs, oxygen molecules bond to the iron(II) ions in the haem molecules to form oxyhaemoglobin.



One haemoglobin molecule carries four oxygen molecules. About 98.5% of the oxygen in blood is transported as oxyhaemoglobin.

In the lower concentrations of oxygen found in respiring tissues, the oxyhaemoglobin dissociates to release oxygen.

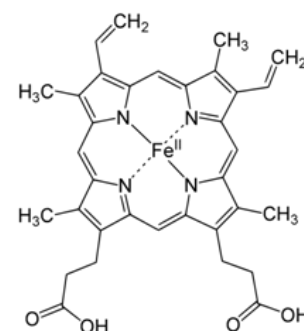


Cells that have higher respiratory rates liberate the extra oxygen that they need. In respiring tissues the dissociation of oxyhaemoglobin is driven by:

- a rise in temperature caused by the release of energy;
- liberation of carbon dioxide, which lowers blood pH.

Haemoglobin has a greater affinity for oxygen in the lungs (forming oxyhaemoglobin) than it does in respiring tissues.

- The lung environment is cooler.
- Carbon dioxide is removed, raising blood pH.

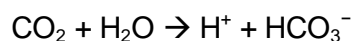


**Figure 2** A haem molecule can bind reversibly with an oxygen molecule to form oxyhaemoglobin.

### Carbon dioxide transport

Carbon dioxide is transported in three ways.

- About 5-10% dissolves in its molecular form in blood plasma.
- About 70-80% is converted into hydrocarbonate ions in red blood cells, catalysed by the enzyme carbonic anhydrase.



Hydrogencarbonate ions,  $\text{HCO}_3^-$ , diffuse out of red blood cells, but hydrogen ions,  $\text{H}^+$ , are held in the cells. The resulting electrochemical gradient causes chloride ions,  $\text{Cl}^-$ , to diffuse into red blood cells to restore the balance. The retained hydrogen ions displace oxygen from oxyhaemoglobin and bind to haemoglobin. This enhances the release of oxygen from oxyhaemoglobin in respiring tissues that are producing carbon dioxide (known as the Bohr Effect).

- The remainder binds to haemoglobin, but not to the same sites as the oxygen molecules.

### Role in homeostasis

Cells need a constant supply of oxygen for aerobic respiration, but it is even more important that the respiratory system removes the carbon dioxide that is formed from the body at the same rate that it is produced. This is because creation of carbon dioxide generates carbonic acid, potentially lowering pH. Cells can survive only within a very narrow pH range, since changes in pH affect protein structure and therefore the efficiency of enzymes, protein channels and carriers and other structures. The rate of carbon dioxide excretion is regulated through control of breathing rate.

The pH of arterial blood, which is low in dissolved carbon dioxide, is normally 7.45. That of venous blood, which is higher in carbon dioxide content, is 7.35. Acidosis is said to occur at  $\text{pH} < 7.35$ , alkalosis when  $\text{pH} > 7.45$ . Death occurs if arterial pH is outside the range 6.8-8.0 for more than a few seconds.

In particular,

- in the nervous system: lower pH depresses activity and higher pH increases activity;

- changes to pH affect enzyme structure altering the normal pattern of metabolic activity and accelerating some chemical processes while depressing others;
- changes in pH alter potassium ion,  $K^+$ , levels in the body which, for example, affects the function of the heart.

Control of lung ventilation is therefore mediated by hydrogen ion,  $H^+$ , concentration and not by oxygen or carbon dioxide concentrations.

## Drugs and the lungs

Anaesthetics are often delivered as gases inhaled into the lungs. The rate of uptake depends on a variety of factors, including the difference between the inspired partial pressure of the agent in the alveoli and its partial pressure in the blood, the rate of alveolar ventilation, the blood/gas solubility coefficient and cardiac output. The lungs are pharmacologically active. They can take up and retain or metabolise a wide range of drugs, and can delay drug release. Basic amines with  $pK_a$  values  $>8$  have significant pulmonary uptake. Many drugs used as anaesthetics are basic amines.

## Examples of what can go wrong

### Hay fever and asthma

Asthma is an example of an allergic response which is an inappropriate specific immune reaction to a substance that is usually harmless.

It results from an immediate allergic reaction caused by the activation of a B cell response by an allergen. The antibodies involved differ to those normally used against bacteria. They are found in mast cells which mainly occur in areas that come into contact with the external environment, including the linings of the respiratory system.

Binding of an allergen with the antibody attached to a mast cell stimulates it to release histamine.

If the reaction is limited to the upper respiratory tract, e.g. after the inhalation of grass pollen, the symptoms of hay fever may appear – localised oedema, sneezing and a runny nose due to increased mucus secretion.

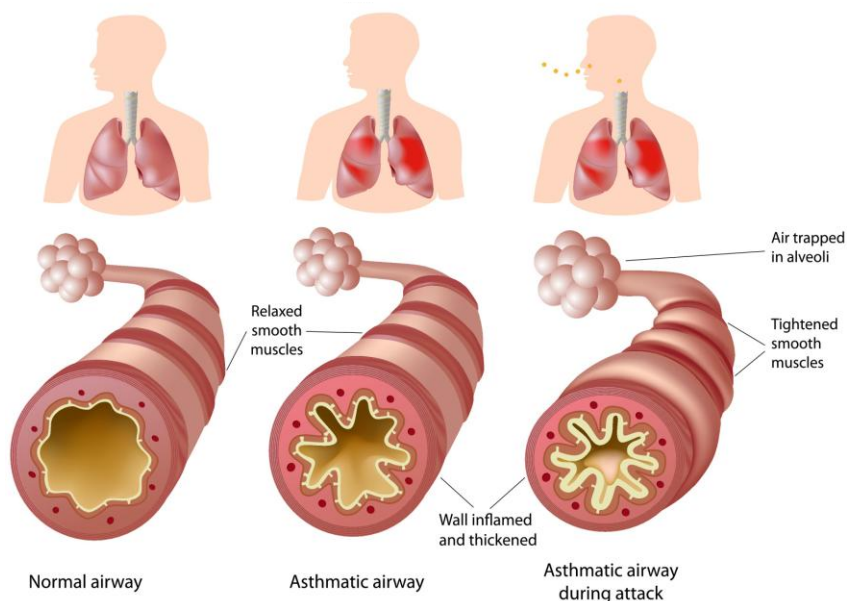
If the reaction concentrates in the bronchioles, asthma occurs – contraction of smooth muscle constricts the airways making breathing very difficult.

In the body the glucocorticoid cortisol is a steroid hormone that is thought to regulate immune responses to prevent them from overshooting. Glucocorticoid drugs are powerful anti-inflammatory drugs which suppress immune responses, including histamine release.

## Finding out

What is 'laughing gas', how was it discovered and what gases are used in modern anaesthetics?

Find examples of substances and materials that cause asthma.



**Figure 3** The pathology of asthma.