

## 9 Gaseous exchange and smoking

The gas exchange system is responsible for the uptake of oxygen into the blood and excreting carbon dioxide. An understanding of this system shows how cells, tissues and organs function together

to exchange these gases between the blood and the environment. The health of this system and of the cardiovascular system is put at risk by smoking.

### 9.1 The gas exchange system

The gas exchange surface in the lungs is extensive, very thin, well supplied with blood and well ventilated. The trachea and bronchi provide little resistance to the movement of air to and from the alveoli.

By the end of this section you should be able to:

- describe the gross structure of the human gas exchange system
- observe and draw plan diagrams of the structure of the walls of the trachea, bronchi, bronchioles and alveoli indicating the distribution of cartilage, ciliated epithelium, goblet cells, smooth muscle, squamous epithelium and blood vessels
- describe the functions of cartilage, cilia, goblet cells, mucous glands, smooth muscle and elastic fibres and recognise these cells and tissues in prepared slides, photomicrographs and electron micrographs of the gas exchange system
- describe the process of gas exchange between air in the alveoli and the blood

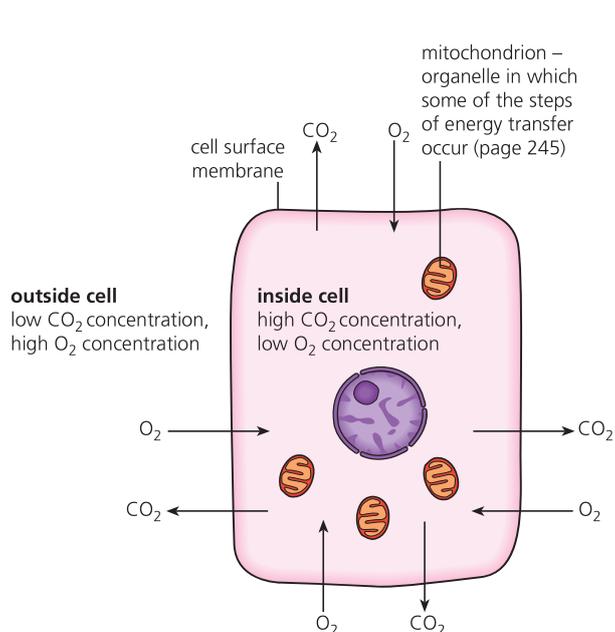


Figure 9.1 Gas exchange in an animal cell

#### Gaseous exchange – meeting the needs of respiration

Living things need energy to build, maintain and repair body structures and also for activities such as metabolism, excretion, and movement. Respiration is the process that transfers that energy. Respiration occurs continuously in living cells, largely in the mitochondria (Topic 1). Most respiration is aerobic and requires oxygen to transfer energy from carbohydrates and lipids. Respiration results in the formation of ATP which is the energy-transferring molecule used in metabolic processes in cells. Carbon dioxide is released as a waste product. This gas exchange in cells occurs by **diffusion**. For example, in a cell respiring aerobically there is a higher concentration of oxygen outside the cells than inside and so there is a net inward diffusion of oxygen (Figure 9.1).

#### Respiratory systems in large animals

In larger animals most if not all of their cells are too far from the surface of the body to receive enough oxygen by diffusion alone. Remember, the surface area to volume ratio decreases as the size of an organism increases. In addition, many of these animals have developed an external surface that provides protection for the body. This is true of water-tight (impervious) outer coverings and tough or hardened skins. These

### Questions

- List three factors affecting the rate of diffusion across a surface and explain why each is significant. (You may need to refer to Table 4.1, page 79.)
- Due to the presence of haemoglobin, about  $20 \text{ cm}^3$  of oxygen is carried per  $100 \text{ cm}^3$  of blood. By contrast, the solubility of oxygen in water is only  $0.025 \text{ cm}^3$  per  $\text{cm}^3$  under the same conditions. How much more oxygen is carried by a litre ( $1000 \text{ cm}^3$ ) of blood compared with the same quantity of water?

outer surfaces are no longer suitable for gas exchange and the organism requires an alternative **respiratory surface**. Active organisms have an increased metabolic rate, too, and the demand for oxygen in their cells is higher than in slow-moving or inactive organisms. So we find that, for many reasons, larger active animals have specialised organs for gas exchange.

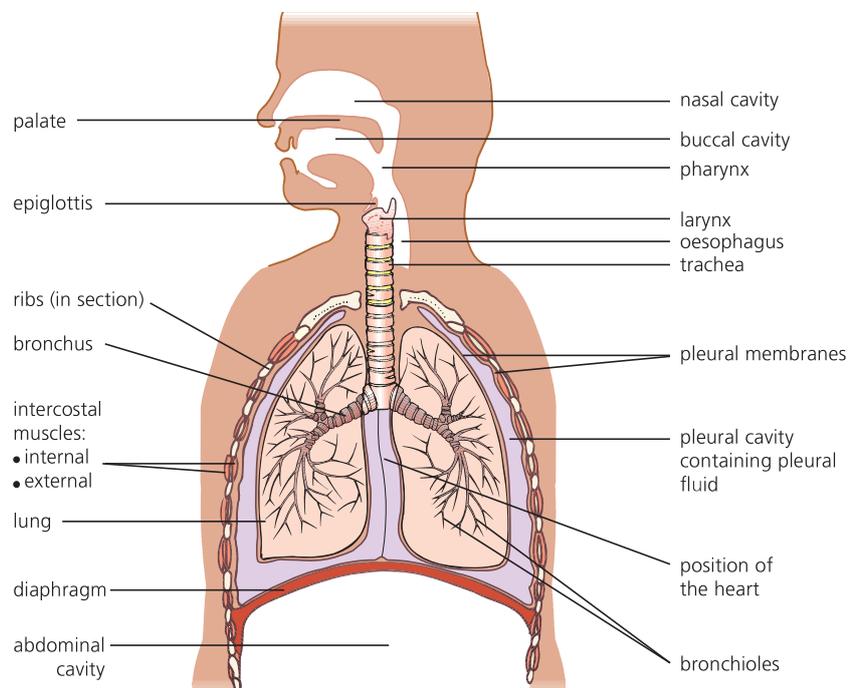
Efficient respiratory surfaces in animals take various forms, such as the gills of fish, the lungs of mammals, the tubular system of many insects that carries air to the most actively respiring organs. All these systems provide a large thin surface area, suitable for gas exchange. In addition, conditions for diffusion are often improved by three refinements.

- A ventilation mechanism** – a pumping mechanism that moves the respiratory medium (water or air) over the gills or into and out of the lungs or tubes. This maintains the concentration gradient for diffusion.
- A blood circulation system** – a means of speeding up the transport of dissolved oxygen from the respiratory surface as soon as it has diffused in. This, too, maintains the concentration gradient.
- A haem protein**, such as haemoglobin, that can associate with oxygen and so increase the gas-carrying ability of the blood. For example, we have seen that our blood contains red blood cells packed with the **respiratory pigment** haemoglobin (Figure 8.10, page 160).

### The lungs of mammals

We can now consider the human lungs as structures adapted for rapid gas exchange. The structure of the human thorax is shown in Figure 9.2.

The lungs are housed in the **thorax**, an air-tight dome-shaped chamber formed by the **rib cage** and its muscles (**intercostal muscles**) and with a domed floor, the **diaphragm**. The diaphragm is a sheet of muscle attached to the body wall at the base of the rib cage, separating the thorax from the abdomen. The internal surfaces of the thorax are lined by the **pleural membrane**, which secretes and maintains pleural fluid. Pleural fluid is a lubricating liquid made from the blood plasma. This fluid provides the surface tension that holds the lungs to the rib cage and protects the lungs from friction during breathing movements.



**Figure 9.2** The structure of the human thorax

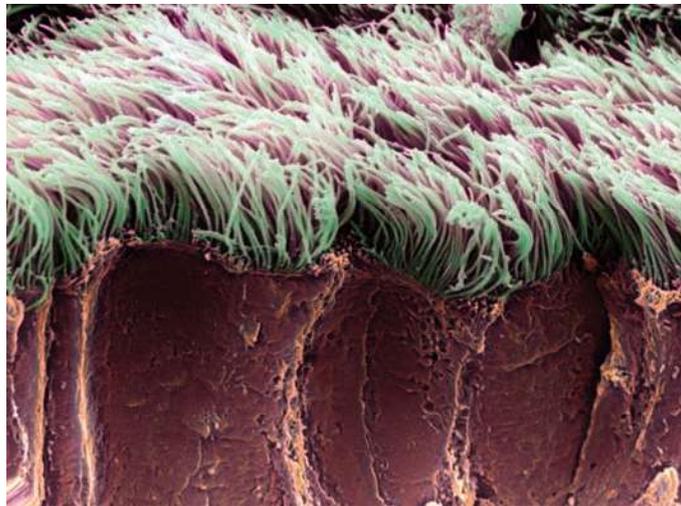
The lungs connect with the pharynx at the rear of the mouth by the **trachea**. Air reaches the trachea from the mouth and nostrils, passing through the larynx ('voice box'). Entry into the larynx is via a slit-like opening, the glottis. Above it is a cartilaginous flap, the **epiglottis**. Glottis and epiglottis work to prevent the entry of food into the trachea.

The trachea then divides into two **primary bronchi**, one to each lung. Within the lungs the primary bronchi divide into **secondary bronchi** and these continue to divide into smaller bronchi, a branching system referred to as the 'bronchial tree'. The smallest bronchi themselves divide into **bronchioles**. The finest bronchioles, the **terminal bronchioles**, end in air sacs – the **alveoli**.

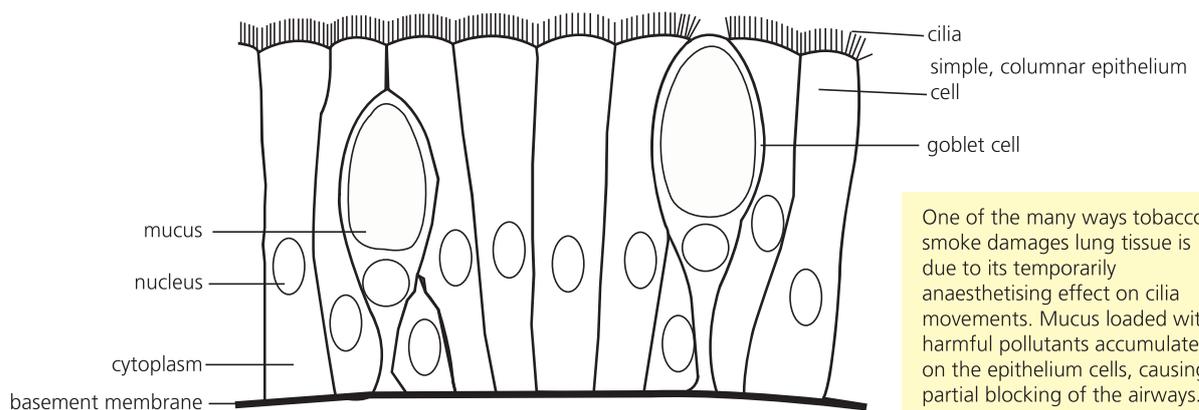
### Trachea, bronchi and bronchioles – structure in relation to function

To protect the delicate lining of the alveoli, the air reaching them needs to be warmed (preferably to body temperature), to be moist and to be as free of dust particles and other foreign bodies as possible. In the nostrils, hairs trap and filter out large dust particles from the incoming air stream. Superficial blood vessels in the nostrils start to warm the incoming air. The trachea and bronchi are lined with a **ciliated epithelium** with numerous **goblet cells** (Figure 9.3). The sticky mucus produced here moistens the incoming air and traps finer dust particles. The ciliated epithelium beats the mucus stream up into the buccal cavity, where it is swallowed.

**SEM showing that the lining of the bronchioles is of simple, ciliated columnar epithelium, with mucus secreted by goblet cells (x6 000)**



a drawing of the ciliated epithelium cells with goblet cells (HP)



One of the many ways tobacco smoke damages lung tissue is due to its temporarily anaesthetising effect on cilia movements. Mucus loaded with harmful pollutants accumulates on the epithelium cells, causing partial blocking of the airways.

**Figure 9.3** Ciliated epithelium with goblet cells

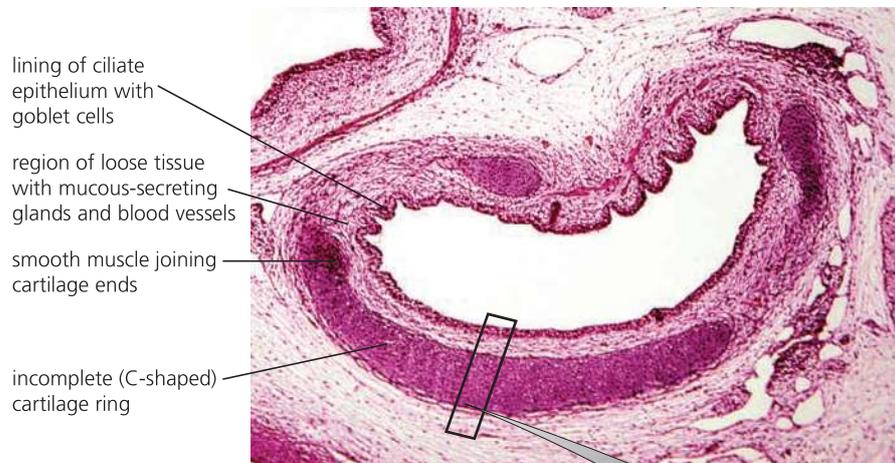
The trachea lies beside and in front of the oesophagus (the 'food tube'). Any hard mass of food passing down the oesophagus might interrupt the air supply to the lungs. Incomplete **rings of cartilage** in the trachea wall prevent collapse under pressure from a large bolus passing down the oesophagus (Figure 9.4).

The walls of the bronchi and larger bronchioles, in addition to rings or tiny plates of cartilage, also contain **smooth muscle**. At each division of the bronchial tree the amount of cartilage decreases and the amount of smooth muscle increases. Together they prevent collapse of these tubes – collapse might be triggered by the sudden reduction in pressure that occurs with powerful inspirations of air, for example. The smooth muscles also regulate the size of the smaller airways as the muscle fibres contract or relax.

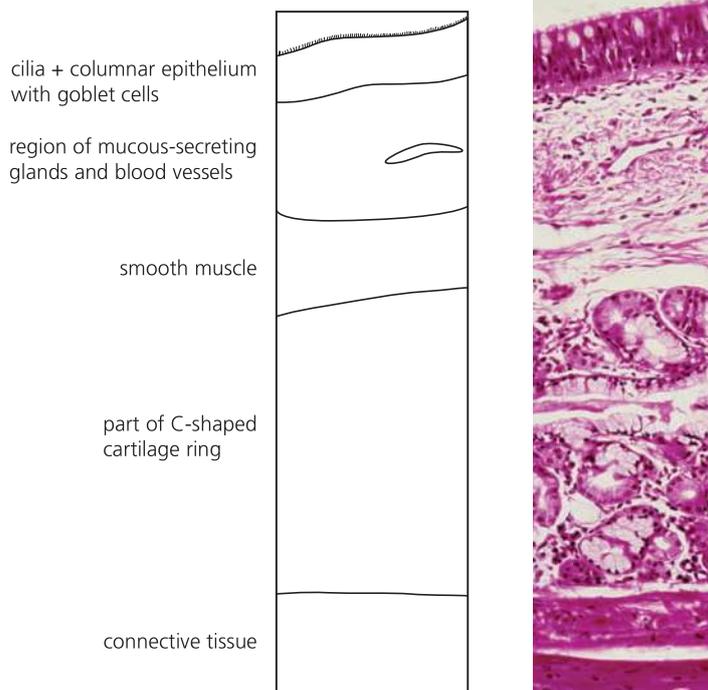
The walls of the smaller **bronchioles** are without cartilage (Figure 9.5). These tubes, the narrowest of the airways serving the alveoli, branch repeatedly and, as they do so, become progressively narrower. Here, smooth muscle is the major component of their walls and the lining of columnar epithelium contains only very occasional goblet cells.

So the air sacs are supplied with warm moist clean air for gaseous exchange, but of course the lungs cannot prevent some water loss during breathing – a significant issue for most terrestrial organisms (Figure 9.6).

**photomicrograph of trachea in TS (x 10)**



**photomicrograph of part of wall of trachea, HP (x 50) with interpretive drawing**



**Figure 9.4** The structure of the trachea

photomicrograph of a trachiole HP (x 000)

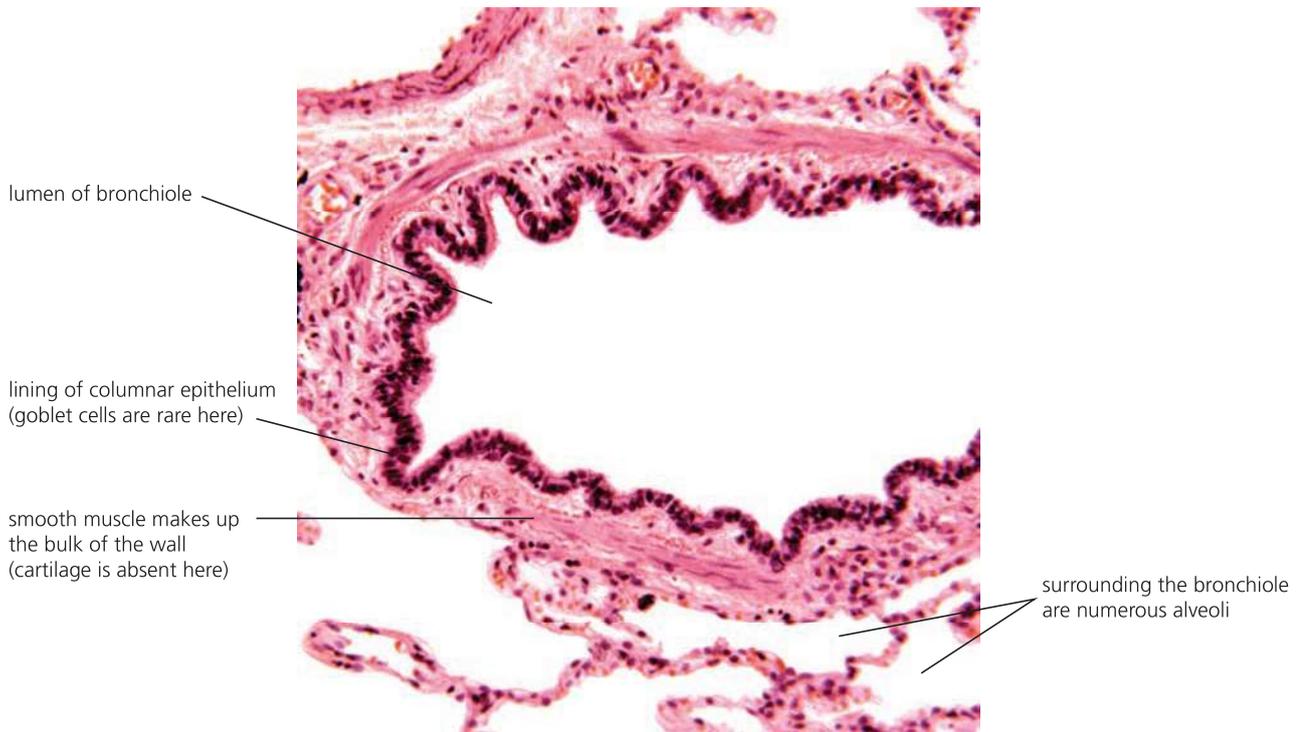


Figure 9.5 The structure of a small bronchiole

Questions

- 3 Draw and label a low-power plan of a representative part of the wall of the bronchiole, as see under high power magnification in Figure 9.5.
- 4 What percentage of our total daily water loss occurs from the lungs? Explain why this happens.

**Exhaled air is saturated with water vapour**, an invisible component except in freezing weather or when breathed onto a very cold surface.

**The water balance of the body:**

- about 3 litres is taken in and lost daily
- about 10–15% of this total is lost from the lungs.

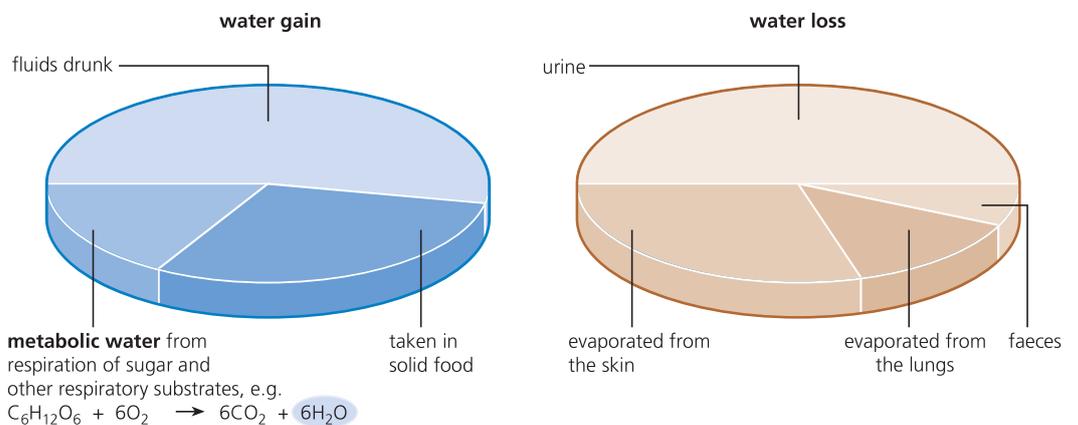


Figure 9.6 Water loss during gas exchange in humans

## Extension

## Bronchiole structure and asthma



**Figure 9.7** Asthma patient using an inhaler

**Asthma** is a disease of the airways of the lungs. In an asthma attack, the bronchioles are narrowed by excessive contraction of the smooth muscle in their walls. Immediately, getting air into and out of the lungs becomes difficult. Also, extra mucus is produced, exaggerating the symptoms. Breathing can become very difficult indeed.

Asthma attacks may be started by the arrival of irritants like pollen, dust from pets or droppings from house dust mites. Certain viruses and the oxides of nitrogen present in vehicle exhaust fumes may also be triggers.

During times of physical activity our involuntary nervous system naturally releases hormones that relax the smooth muscles of the bronchioles, dilating them so that air reaches the alveoli more quickly. Medical treatments for asthma sufferers seek to trigger this relaxation, too (Figure 9.7).

## Question

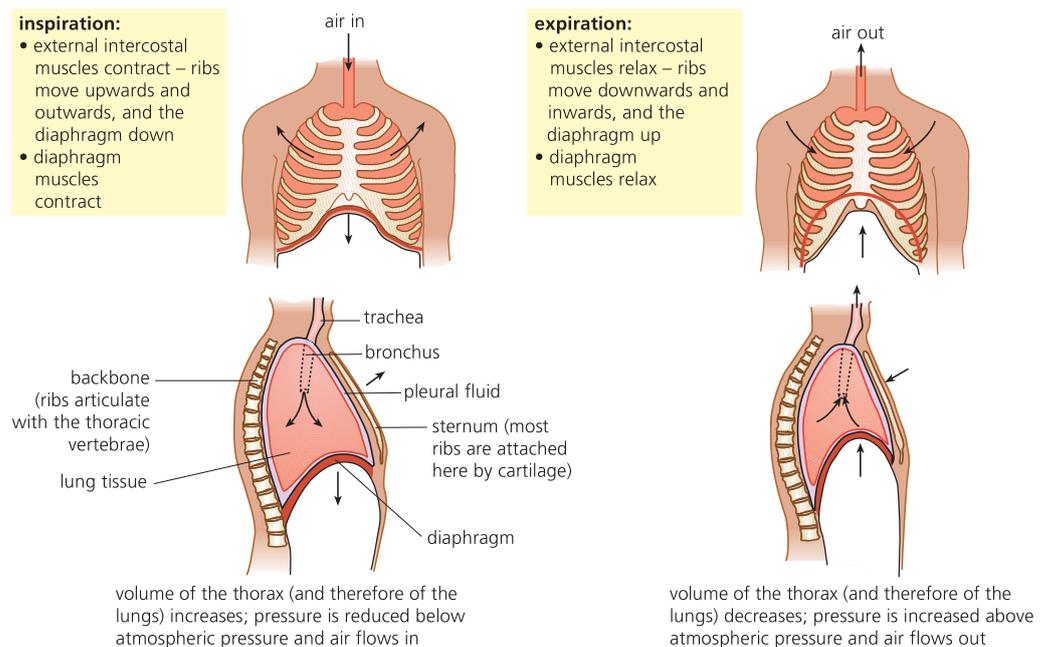
- 5 Explain the difference between gas exchange and cellular respiration.

## Ventilation of the lungs

Air is drawn into the alveoli when the air pressure in the lungs is lower than atmospheric pressure and it is forced out when the pressure is higher than atmospheric pressure. Since the thorax is an air-tight chamber, pressure changes in the lungs occur when the volume of the thorax changes (Figure 9.8).

The volume of the thorax is increased when the ribs are moved upwards and outwards, and the diaphragm dome is lowered. These movements are brought about by contraction of the diaphragm and external intercostal muscles.

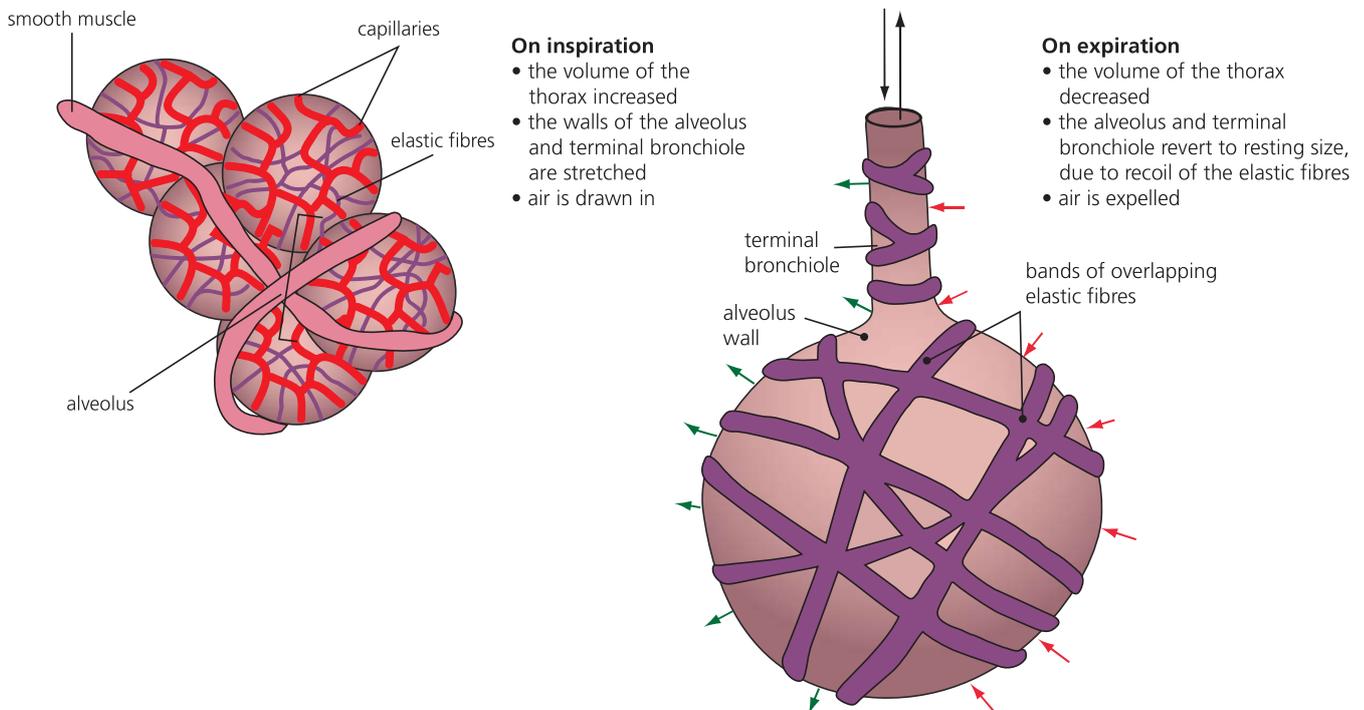
The volume of the thorax is decreased by the diaphragm muscles relaxing and the diaphragm becoming more dome shaped by pressure from below (the natural elasticity of the stomach and liver mean that they can be displaced and stretched at inspiration). The ribs move down and inwards, largely brought about by the elastic recoil of the lungs and the weight of the rib cage, as the external intercostal muscles relax.



**Figure 9.8** Ventilation of the lungs in quiet breathing

### Alveolar structure and gaseous exchange

The lung tissue consists of the alveoli, arranged in clusters, each served by a tiny terminal bronchiole. Alveoli and the terminal bronchioles have **elastic connective tissue** as an integral part of their walls. These fibres are stretched during inspiration, when the alveoli are caused to expand, but recoil during expiration, aiding the expulsion of air as the alveoli return to their resting condition (Figure 9.9).



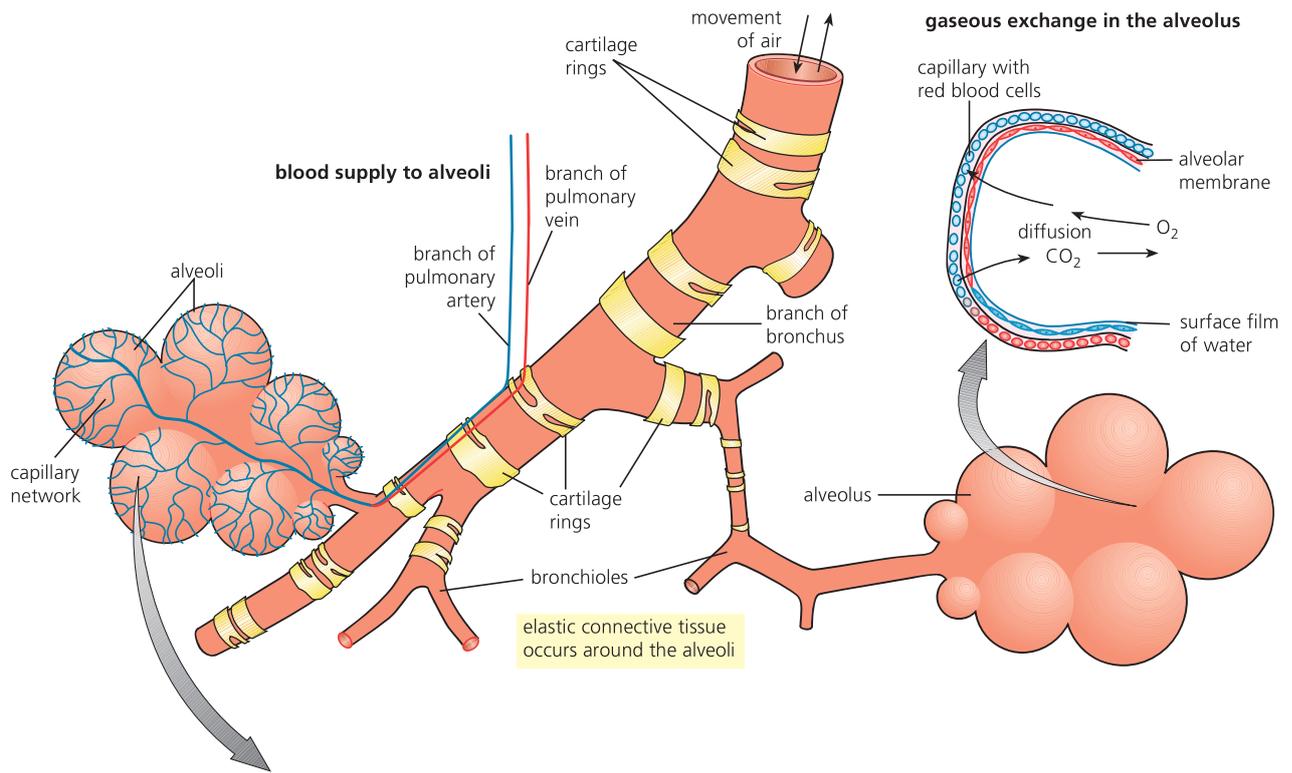
**Figure 9.9** The role of elastic fibres in the alveoli and bronchioles

A **capillary system** wraps around the clusters of alveoli. Each capillary is connected to a branch of the **pulmonary artery** and is drained by a branch of the **pulmonary vein** (Figure 9.10). The pulmonary circulation is supplied with deoxygenated blood from the right side of the heart and oxygenated blood is returned to the left side of the heart to be pumped to the rest of the body (page 165).

There are some 700 million alveoli present in our lungs, providing a surface area of about 70 m<sup>2</sup> in total. This is an area 30–40 times greater than that of the body's external skin. The wall of an alveolus is formed by pavement epithelium, one cell thick. An epithelium is a sheet of cells bound strongly together, covering internal or external surfaces of multicellular organisms. Lying very close is a capillary, its wall also just a single, flattened (endothelium) cell thick. The combined thickness of walls separating air and blood is typically 2–4 µm thick. The capillaries are extremely narrow, just wide enough for red blood cells to squeeze through, so red blood cells are close to or in contact with the capillary walls.

The extremely delicate structure of the alveoli is protected by two types of cell, present in abundance in the surface film of moisture (Figure 9.10).

- **Macrophages** (dust cells) are the main detritus-collecting cells of the body. They originate from bone marrow stem cells and are then dispersed about the body in the blood circulation. These amoeboid cells migrate into the alveoli from the capillaries. Here these phagocytic white blood cells ingest any debris, fine dust particles, bacteria and fungal spores present. They also occur lining the surfaces of the airways leading to the alveoli.
- **Surfactant cells** produce a detergent-like mixture of lipoproteins and phospholipid-rich secretion that lines the inner surface of the alveoli. This lung surfactant lowers surface tension, permitting the alveoli to flex easily as the pressure of the thorax falls and rises. It reduces a tendency of alveoli to collapse on expiration.



photomicrograph of TS alveoli, HP

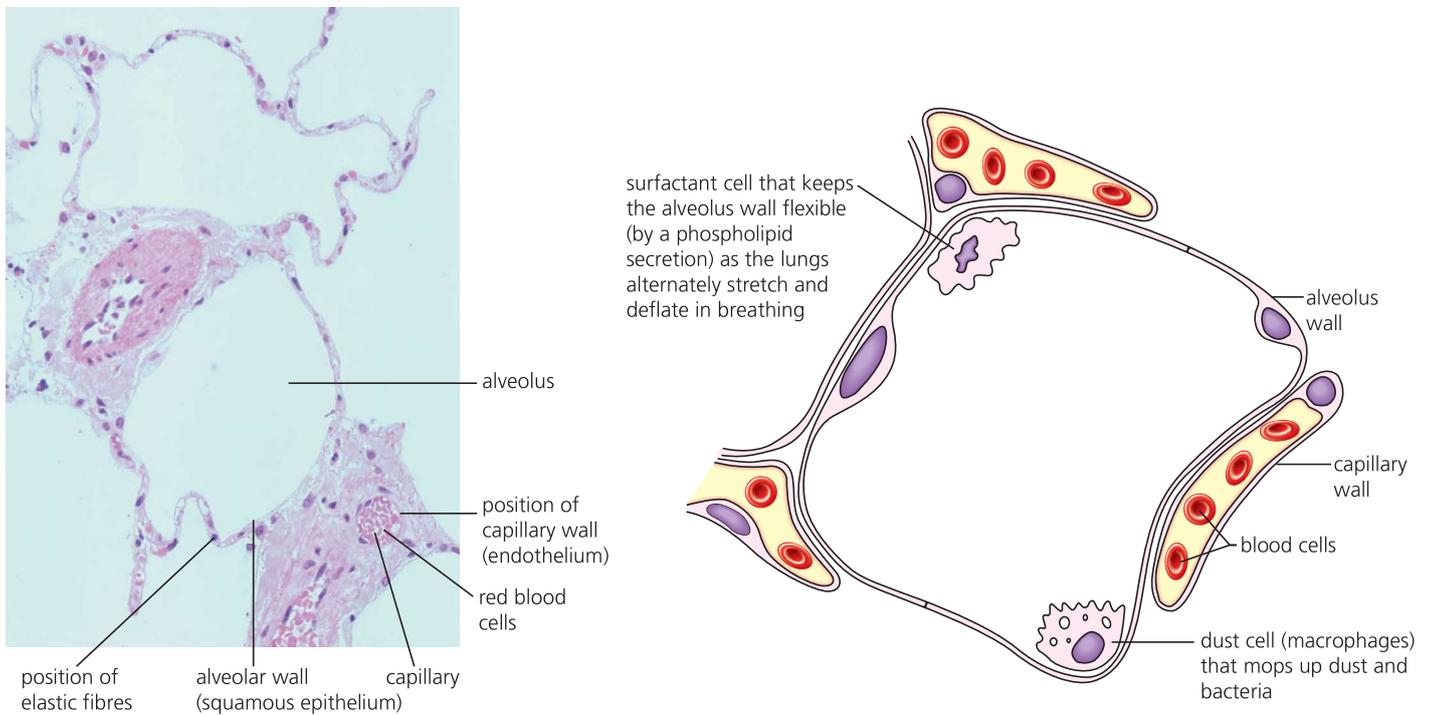


Figure 9.10 Gas exchange in the alveoli

## Questions

- 6 Explain how the macrophages remove foreign matter around them. (The discussion on page 222 in Topic 11 may help in the answering of this question.)
- 7 Create a table listing the main structural features of the air sacs (alveoli) and identifying the effects and consequence of each feature for gas exchange.
- 8 If the concentration of carbon dioxide were to build up in the blood of a mammal, why would this be harmful?

Blood arriving in the lungs is low in oxygen (it has a lower **partial pressure** of oxygen than the alveolar air – see Table 9.1) but high in carbon dioxide (it has a higher partial pressure of carbon dioxide than the alveolar air). As blood flows past the alveoli, gaseous exchange occurs by diffusion. Oxygen dissolves in the surface film of water, diffuses across into the blood plasma and into the red blood cells where it combines with haemoglobin to form oxyhaemoglobin. At the same time, carbon dioxide diffuses from the blood into the alveolus.

Air flow in the lungs of mammals is tidal in that air enters and leaves by the same route. Consequently there is a **residual volume** of air that cannot be expelled. Incoming air mixes with and dilutes the residual air. The effect of this is that air in the alveoli contains significantly less oxygen than the atmosphere outside (Table 9.1). Nevertheless, the lungs are efficient organs of gaseous exchange.

**Table 9.1** The composition of air in the lungs

	Inspired air	Alveolar air	Expired air
Oxygen	20%	14%	16%
Carbon dioxide	0.04%	5.5%	4.0%
Nitrogen	79%	81%	79%
Water vapour	variable	saturated	saturated

We have already noted that, in a mixture of gases, each component gas exerts a partial pressure in proportion to how much is present. The partial pressure of oxygen is written as  $pO_2$  and of carbon dioxide as  $pCO_2$ . At sea level, the atmospheric pressure is 101.3 kPa so, for example, the partial pressure of oxygen in the air at sea level is:

$$pO_2 = \frac{101.3}{100} \times 20 = 20.3 \text{ kPa.}$$

but in the alveolus the partial pressure of oxygen is only:

$$pO_2 = \frac{101.3}{100} \times 14 = 14.2 \text{ kPa.}$$

### Observing and drawing plan diagrams of the gas exchange system

You will be required to observe and draw plan diagrams of the structure of the walls of the trachea, bronchi, bronchioles and alveoli in which the distribution and roles of cartilage, ciliated epithelium, and blood vessels are identified by your annotations. Sources should include prepared slides observed by medium and high power, photomicrographs and electron micrographs.



**Figure 9.11** TEM of the air–blood barrier in an alveolus/capillary section

## 9.2 Smoking

Smoking is one of the major avoidable risk factors of chronic, life-threatening diseases of the gas exchange and circulatory systems.

### By the end of this section you should be able to:

- describe the effects of tar and carcinogens in tobacco smoke on the gas exchange system with reference to lung cancer and chronic obstructive pulmonary disease (COPD)
- describe the short-term effects of nicotine and carbon monoxide on the cardiovascular system

## Smoking and health

The cultivation and use of the tobacco plant (*Nicotiana glauca*) has origins in Central America. By the fifteenth century the tobacco leaf had reached Europe, mostly to be smoked in pipes or as cigars, but increasingly considered a 'cure-all' for many common conditions! Only with the mass production of cigarettes and the invention of the match in the 1800s did this form of smoking become available to many – it had become easy and affordable. In the twentieth century, cigarette smoking in the developed world was advanced hugely by the availability of cigarettes to the troops of two World Wars. Subsequent bold and aggressive advertising campaigns, persuasive product placement in films and the generous sponsorships of sporting and cultural events by cigarette manufacturers, all encouraged greater smoking by men, and persuaded women to take it up, too. Very slowly, the dangers of smoking became known but many people doubted the evidence. However, by the 1950s it started to be recognised just how dangerous cigarette smoking and the inhalation of cigarette smoke was.

### The composition of cigarette smoke

Analysis of cigarette smoke shows it contains a cocktail of harmful substances – more than 4000, in fact. These include acetone, ammonia, arsenic, butane, cadmium, hydrogen cyanide, methanol, naphthalene, toluene and vinyl chloride. However, to understand the danger to health that cigarette smoke poses we shall focus on the following components.

- Carcinogens in the 'tar' component**, of which there are at least twenty different types. Particularly harmful are certain polycyclic aromatic hydrocarbons and nitrosamines. Remember, a carcinogen is any agent that may cause cancer by damage to the DNA molecules of chromosomes. Such 'mistakes' or mutations of different types may build up in the DNA of body cells exposed to these substances.
- Nicotine**, a stimulating and relaxing drug which, on entering the blood stream, is able to cross the blood–brain barrier. In the brain it triggers the release of dopamine, the natural neurotransmitter substance (page 319) associated with our experience of pleasure. Long-term exposure to nicotine eventually comes to have the reverse effect, actually depressing the ability to experience pleasure. So more nicotine is needed to 'satisfy', and cigarettes become addictive; it is as addictive as heroin and cocaine, in fact. Smokers find it increasingly hard to quit the habit.
 

Nicotine also increases the heart rate and blood pressure. It decreases the blood flow, particularly in the hands and feet, and it makes blood clotting more likely. It can make platelets stick together.
- Carbon monoxide**, a gas that diffuses into the red blood cells and combines irreversibly with haemoglobin (page 160). In smokers, the blood is able to transport less oxygen. The strain this puts on the heart and circulation is most apparent during physical activity.
 

Carbon monoxide also promotes the release of damaging free radicals and makes platelets and neutrophils stick together.

Cigarette smoke reaches the smoker's lungs when it is drawn down the cigarette and inhaled, but it reaches other people, too, when it escapes from the glowing tip into the surrounding air. These latter fumes normally have a higher concentration of the toxic ingredients and it is this mixture that others inhale. **'Passive smoking'** has itself been shown to be dangerous, too.

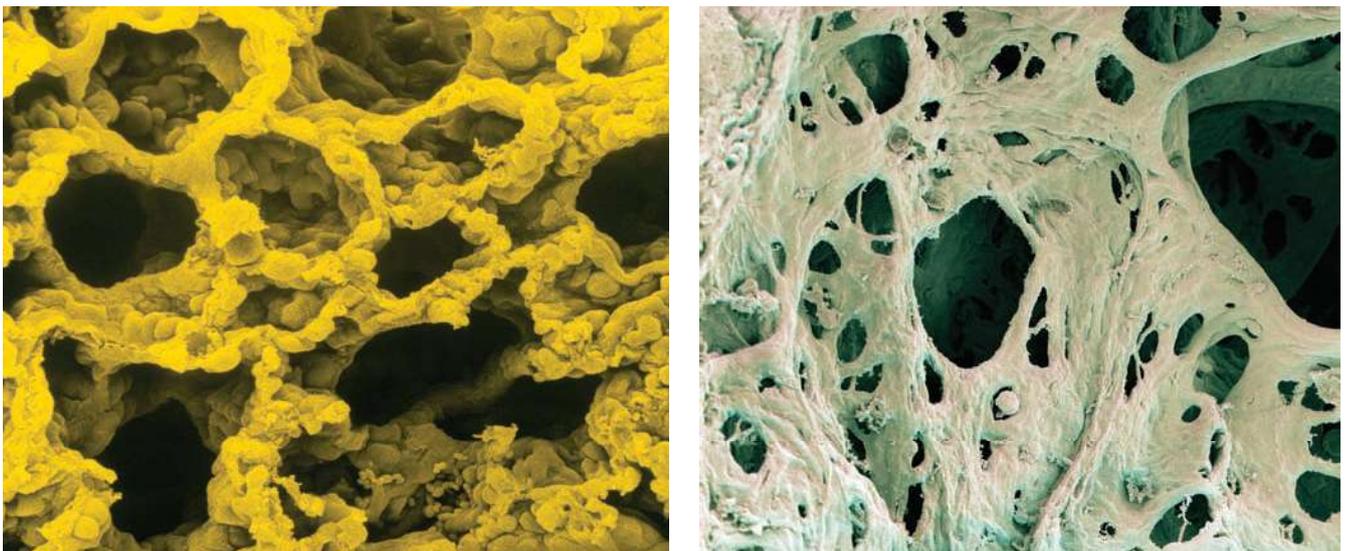
Two of the major diseases that are directly induced by cigarette smoke are **chronic obstructive pulmonary disease (COHD)** and **lung cancer**. We will review each in turn, focusing on the effects of tar and carcinogens in tobacco smoke as the causative agents.

## Chronic obstructive pulmonary disease (COPD)

Cigarette smoke reaching the lungs stimulates the secretion of viscous mucus by the goblet cells and, at the same time, inhibits the movements of the cilia (Figure 9.3, page 174) of the epithelium lining the airways. The result is that mucus, in which dust and carcinogenic chemicals are trapped, accumulates in the bronchioles. The smallest bronchioles may be blocked off. Also, irritation of the airways by the smoke results in inflammation and scarring in the lungs. The elasticity that permits the air sacs to expand and contract is progressively lost. The outcome may be chronic obstructive pulmonary disease, which takes two main forms.

**Chronic bronchitis**, the symptoms of which are a long-term cough with phlegm (mucus), has a gradual onset but is of long duration. The bronchi are inflamed and produce excess mucus which ultimately has to be coughed up, leading to recurring attacks of coughing. As the disease progresses the bronchioles narrow and breathing becomes difficult. The airways are narrowed by the mucus but, unlike asthma where the narrowing of the airways can be reversed, here the narrowing is progressive and not fully reversible. Cigarette smoking is the most important cause of chronic bronchitis but other forms of air pollution and some respiratory infections may be the cause in some cases.

**Emphysema** is a disease in which the walls of the alveoli lose their elasticity. It results in the destruction of the lung tissue with time. This is because such lungs now contain large numbers of macrophages, accumulated from the blood circulation (Figure 9.10). These phagocytic cells release a high level of the natural hydrolytic enzymes that break down elastic fibres of the alveolar walls. With failing elastic fibres, the air sacs are left over-inflated when air becomes trapped in them and they fail to recoil and expire air properly. Small holes also develop in the walls of the alveoli. These begin to merge, forming huge air spaces with drastically lowered surface area for gas exchange. The patient becomes permanently breathless. The destruction of air sacs can be halted by stopping smoking but any damage done to the lungs cannot be reversed.



**Figure 9.12** SEMs of Healthy human lung tissue (left) and human lung tissue showing advanced emphysema (right)

## Lung cancer

Persistent exposure of the bronchi to cigarette smoke results in damage to the goblet cells. These are then replaced by an abnormally thickened epithelium. With prolonged exposure to the carcinogens, permanent mutations may be triggered in the DNA of some of the cells that have replaced goblet cells. If this occurs in their proto-oncogenes or tumour-suppressing genes the result is loss of control over normal cell growth (page 104).

A single mutation is unlikely to be responsible for triggering lung cancer; it is the accumulation of mutations with time that causes a group of cells to divide by mitosis repeatedly, without control or regulation, forming an irregular mass of cells – the **tumour**. Tumour cells then emit signals promoting the development of new blood vessels to deliver oxygen and nutrients, all at the expense of the surrounding healthy tissues. Sometimes tumour cells break away and are carried to other parts of the body, forming a secondary tumour (a process called **metastasis**). Unchecked, cancerous cells ultimately take over the body, leading to malfunction and death.

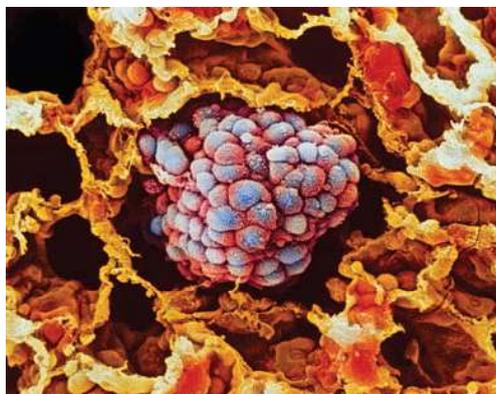
### Signs and symptoms of lung cancer

Lung cancer is dangerous because the symptoms are vague and only become severe when the disease is in its late stages. Lung cancer can be cured but only if it is detected early enough.

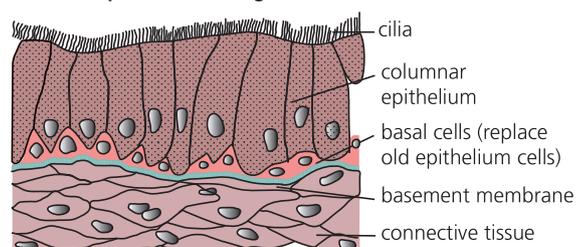
The symptoms of the disease are:

- frequent and severe coughing that persists for more than three weeks
- the coughing up of blood
- shortness of breath and a feeling of weakness or tiredness
- an unexpected and unexplained loss of weight
- pain in the rib cage and/or the shoulder areas
- chest infections that will not go away, even with antibiotics
- hoarseness of the voice and swelling of the face and neck.

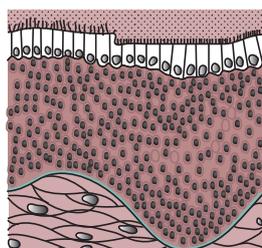
SEM of human lung tissue with cancer



ciliated epithelium lining the bronchial tree



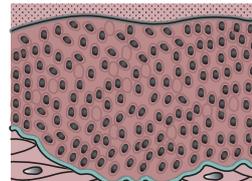
in response to continuing exposure to cigarette smoke



beating of cilia inhibited;  
excessive, abnormal  
proliferation of basal cells



ciliated epithelium  
replaced by squamous  
epithelium



mass of basal cells  
showing abnormal growth



accumulation of mutations  
in mass of abnormal cells;  
forms a tumour

**Figure 9.13** The development of a lung tumour

### Diagnosis and treatment of lung cancer

From the initial critical mutations until symptoms of the disease are evident typically takes 20–30 years. A diagnosis may be confirmed by chest X-ray, CT scan (a three-dimensional image of part of the body produced using X-rays) and ultimately, by bronchoscopy (where a device is used to see inside the lungs). The latter is combined with biopsy (the removal of a small piece of tissue for laboratory examination).

Treatment of lung cancer largely depends upon the general health of the patient, on what type of lung cancer has been contracted, and how far it has spread. Many of the tumours detected by early diagnosis may be removed by surgery or suppressed by radiotherapy (with X-rays or another form of radiation) – possibly followed in either case by chemotherapy using anti-cancer drugs. However, more than half of patients diagnosed currently die within a year because lung cancer is a deadly disease that is rarely diagnosed early enough. Incidentally, a person who gives up smoking may eventually achieve a life expectancy very similar to that of a non-smoker (Figure 9.14).

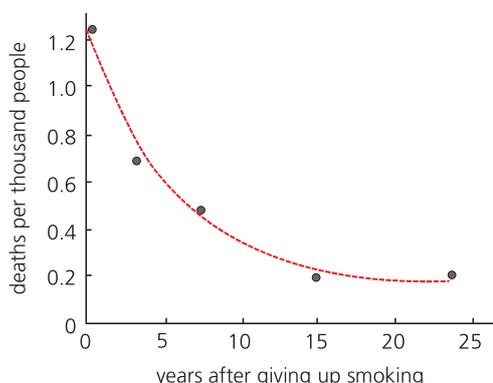


Figure 9.14 Death rates from cancer after giving up smoking

### Cigarette smoking causes lung diseases – the evidence

It was **epidemiology** (the study of the incidence and distribution of diseases and of their control and prevention) that first identified a likely causal link between smoking and disease. For example, a 1938 study of longevity in people who smoked lightly and heavily compared with those who did not smoke established that heavy smoking most shortened life expectancy (Table 9.2).

In 1950, an American study of over 600 smokers compared with a similar group of non-smokers found **lung cancer** was 40 times higher among the smokers. The risk of contracting cancer increased with the numbers of cigarettes smoked (Table 9.3).

Table 9.2 Longevity in smokers and non-smokers

Age	Number of people still alive at each age		
	Non-smokers	Light smokers	Heavy smokers
30	100 000	100 000	100 000
40	91 546	90 883	81 191
50	81 160	78 436	62 699
60	66 564	61 911	46 226
70	45 919	41 431	30 393
80	21 737	19 945	14 494

Table 9.3 Cancer rates and the number of cigarettes smoked per day

Number of cigarettes smoked per day	Incidence of cancer per 100 000 men
0	15
10	35
15	60
20	135
30	285
40	400

A survey of smoking in the UK was commenced in 1948, at which time 82 per cent of the male population smoked and of whom 65 per cent smoked cigarettes. This had fallen to 55 per cent by 1970 and continued to decrease. In same period the numbers of females who smoked remained just above 40 per cent until 1970, after which numbers also declined (Figure 9.15). Look carefully at the changing pattern in the incidences of lung cancer – figures are available since 1975.

Concerning smoking and **respiratory diseases**, the National Institute for Health and Clinical Excellence (NICE) reports that chronic obstructive pulmonary disease (COPD) accounts for 30 000 deaths per year in the UK, of which 85 per cent could be attributed to smoking – a figure approximately double the European average. The World Health Organisation (WHO) provides leadership on health matters for the United Nations by monitoring and reporting on the health of peoples and assessing health trends worldwide. The World Health Organisation predicts that by 2030, chronic obstructive pulmonary disease will be the third most common cause of death worldwide.

## Question

9 Look at Figure 9.15. Comment on the incidence of lung cancer in men and women between 1975 and 2007 in relation to the changing pattern of smoking since UK records began.

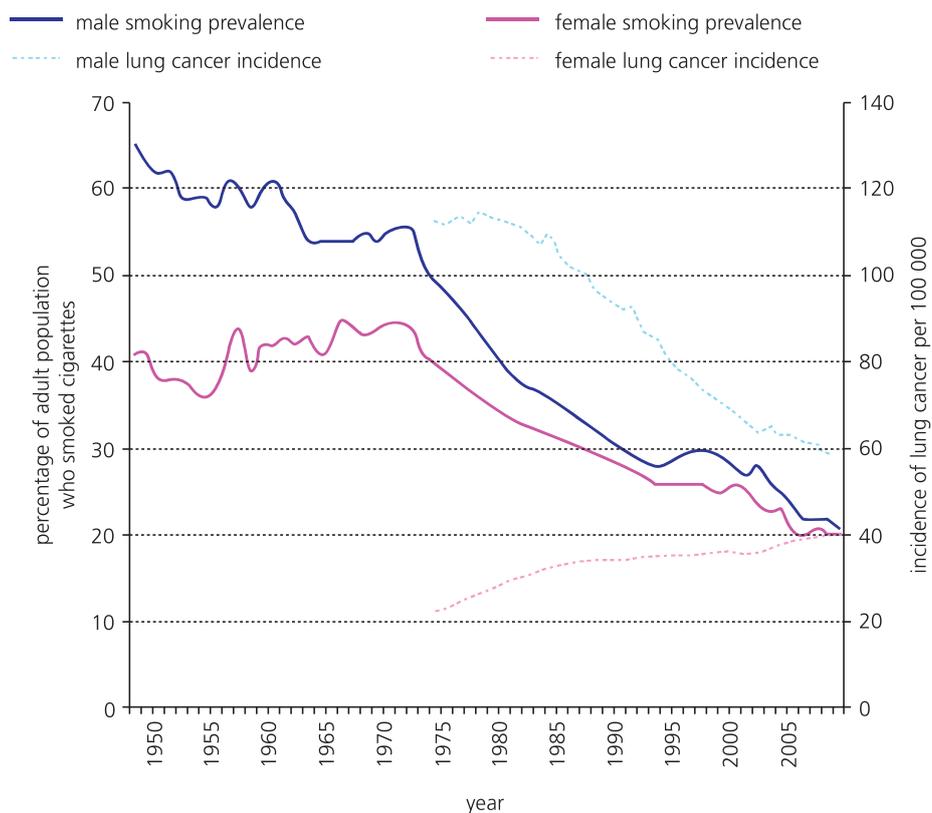


Figure 9.15 Lung cancer incidence and smoking trends in the UK, 1948–2007

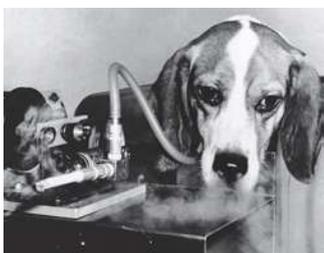


Figure 9.16 An animal experiment investigating the harmful effects of cigarette smoke

Meanwhile, experimental **laboratory-based investigations** have demonstrated *how* cigarette smoke causes disease. For example, experiments in which laboratory animals (mice, rats and dogs) were exposed to cigarette smoke (passive smoking) for an extended period resulted in damage and disease in their lungs identical to that often observed in the lungs of deceased human smokers. Additionally, cancers have been induced when components of cigarette smoke, mainly polycyclic aromatic hydrocarbons (PAHs), were applied in concentrated form to the exposed external skin of experimental mammals.

Most significantly, specific damage to DNA, induced by exposure to polycyclic aromatic hydrocarbons, has been identified. Firstly, labelled polycyclic aromatic hydrocarbons were added to cigarettes that were then smoked by human volunteers taking part in a clinical experiment. These labelled polycyclic aromatic hydrocarbons were shown to be absorbed into the bloodstream and quickly metabolised into substances that damaged DNA – within about 15–30 minutes of the cigarettes being smoked, in fact. Secondly, it was found that these substances actually reacted with specific points on the p53 gene. Remember, this gene in an un-mutated state restricts unlimited cell division (a feature of cancerous cells) and it stimulates repair of damaged DNA. Further, the p53 gene has been shown to be inactivated in the majority of people suffering from lung cancers. The inescapable conclusion of these studies is that specific chemicals in cigarette smoke directly trigger lung cancer.

Experiments have been supported by **clinical investigations** of the biochemical and structural changes that cigarette smoke induces in patients. Further, **intervention studies** with vulnerable groups of patients who were persuaded to change their habits established how smoking-related diseases were reduced in them compared with rates in other patients who did not change their habits. These others were, in effect, a **control group**.

## Question

10 Explain what is meant by a 'control group' in a medical investigation.

## Short-term effects of nicotine on the cardiovascular system

The short-term effects that the nicotine in tobacco smoke has on the cardiovascular system are all profoundly harmful. Examining these in turn, they are:

### 1 As an addictive, psychoactive drug.

Smoking a single cigarette introduces about 1 mg of nicotine into the bloodstream almost immediately. The first outcomes are the release of sugar from the liver and of adrenalin from the adrenal medulla – with stimulating effects on the body. Long before the nicotine circulating in the bloodstream can be expelled from the body, however, nicotine-rich blood reaches the brain, and nicotine crosses the blood–brain barrier. When present among the neurones of the brain, nicotine stimulates the release of chemical messengers in synapses there (page 320). For example, the release of the neurotransmitter dopamine is enhanced, so a sense of well-being is generated, and pain and anxiety are suppressed. Further, nicotine is similar in structure to the neurotransmitter acetylcholine and fits acetylcholine receptors on post-synaptic membranes. However, it is not broken down by enzymes that inactivate acetylcholine, so it remains attached, prolonging the effects. Initially, these are enhanced concentration and memory, so alertness appears to be enhanced. It is these combined psychoactive effects that generate the condition of dependence – leading to a state of addiction that is one of the hardest to break. Moreover, with increasing dependence on nicotine, the impact of the drug switches to a sedative effect.

### 2 As a vasoconstrictor.

The impacts of this effect on the vascular system are raised blood pressure and a reduced oxygen supply to the major organs and limbs. At the same time, the enhanced release of the hormone adrenalin causes an increased heart rate, which in these circumstances, contributes to raised blood pressure, too. A condition of permanently raised blood pressure is known as hypertension (see ‘Blood pressure and its measurement’ below). The epidemiological evidence is of an increased risk of coronary artery disease at an earlier age in smokers than in non-smokers. In fact the first evidence of the link between smoking and cardiovascular disease (CVD) established this relationship.

It was in 1950 that Dr Richard Doll and colleagues, working at St Thomas’s Hospital, London, published the results of their investigation of the causes of death due to cardiovascular disease in a large sample of working doctors (among whom the habit of smoking was widespread *at that time*). These implicated smoking as the culprit (Table 9.4). Today, few doctors smoke.

**Table 9.4** Mortality from cardiovascular disease among a sample of doctors

Cause of death in a sample of 40 000 doctors	Non-smokers	Cigarette smokers
Coronary heart disease	606	2067
Stroke	245	802
Aneurysm	14	136
Arteriosclerosis	23	111
Total	888	3116

## Extension

## Blood pressure and its measurement

By blood pressure we mean the pressure of the blood flowing through the arteries. We have noted that, initially, flow is a surge or **pulse** (page 168). So it is arterial blood pressure that is measured, in a part of our body relatively close to the heart. Blood pressure is quoted as two values (typically, one over the other). The higher pressure is produced by ventricular systole (systolic pressure) and is followed by a lower pressure at the end of ventricular diastole (diastolic pressure). Normally, systolic and diastolic pressures are about 15.8 and 10.5 kPa respectively. (The medical profession give these values as 120 and 70–80 mmHg. The unit 'mmHg' was recognised as a unit of pressure before the SI System was introduced.)

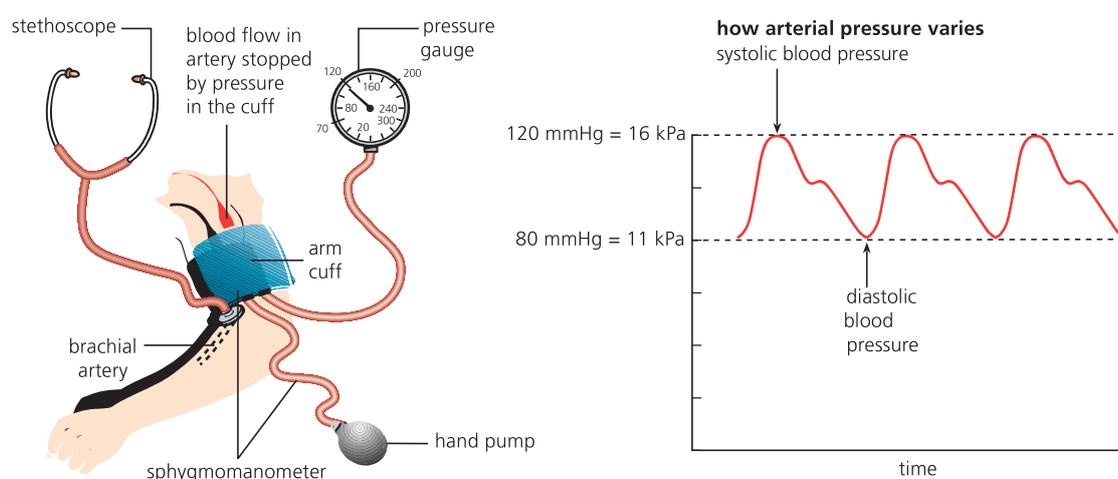
To measure these two values an inflatable cuff called a **sphygmomanometer** is used with a **stethoscope**, as shown in Figure 9.17. The three steps are as follows.

- 1 The cuff is inflated and blood flow is monitored in the artery in the arm (the brachial artery) at the elbow. Inflation is continued until there is no sound (indicating there is no flow of blood).
- 2 Air is now allowed to escape from the cuff, slowly, until blood can just be heard spurting through the constriction point in the artery. This pressure at the cuff is recorded, as it is equal to the maximum pressure created by the heart (the **systolic pressure**).
- 3 Pressure in the cuff is allowed to drop until the blood can be heard flowing constantly. This is the lowest pressure the blood falls to between beats (the **diastolic pressure**).

**Table 9.5** Screening of blood pressure in adults

Systolic pressure/mmHg	Diastolic pressure/mmHg	Condition	Response
120	80	Optimum	
120–129	80–84	Normal	Biennial checks
130–139	85–89	High-normal	Annual checks
140–159	90–99	Stage 1 hypertension	Check in two months
160–179	100–109	Moderate (stage 2) hypertension	Treatment essential if these conditions persist.
180–209	110–119	Severe (stage 3) hypertension	
210+	120+	Very severe (stage 4) hypertension	

The pascal (Pa) and its multiple the kilopascal (kPa) are generally used by scientists to measure pressure, but in medicine the older unit of pressure, 'millimetre of mercury' (mmHg) is still used (1 mmHg = 0.13 kPa).



**Figure 9.17** Measuring blood pressure

## Short-term effects of carbon monoxide on the cardiovascular system

The iron of haemoglobin (Figure 8.10, page 160) is not oxidised to iron(III) during oxyhaemoglobin formation in the lungs. This oxidation can occur, however – with serious consequences. For example, carbon monoxide converts this iron(II) to iron(III) when it reacts with haemoglobin, in the formation of carboxyhaemoglobin. In this form, the haemoglobin molecule cannot carry oxygen. In the blood of smokers about 10 per cent of their haemoglobin occurs in the form of carboxyhaemoglobin, due to exposure to the carbon monoxide in cigarette smoke. Carboxyhaemoglobin does not dissociate, for the reaction between carbon monoxide and haemoglobin is irreversible. Oxygen transportation in the blood is hampered, and so too is the supply of oxygen to body organs and the brain.

### Extension

### Prevention – a challenging but more sustainable response?



Figure 9.18 Persuasive advertising, it seems!

Smoking is clearly a health risk with life-threatening consequences. Perhaps the best response is to prevent the problems arising by persuasion, backed up by legislation where this is thought effective. One developed country's current response to the issue is to restrict the advertising and display of tobacco products, enforce bold, unavoidable health warnings on cigarette packets and outlaw smoking in public buildings and workplaces. At the same time, the authority responsible for public health is assisting those addicted to nicotine through smoking to discard the habit if they can. This sustainable 'carrot and stick' approach is having some significant positive outcomes but there remain many who continue to smoke.

Meanwhile, throughout the world there continues to be huge investments by the tobacco industry in the growing of the crop, the manufacturing of 'attractive' packaging for tobacco products and the placing of advertisements in countries and places that are open to them.

### Question

**11** Cardiovascular disease was not an issue for people before the twentieth century. Today it is a major health issue. Make a concise, annotated list of all the factors that you think may lie behind this change to use in a group discussion with your peers.

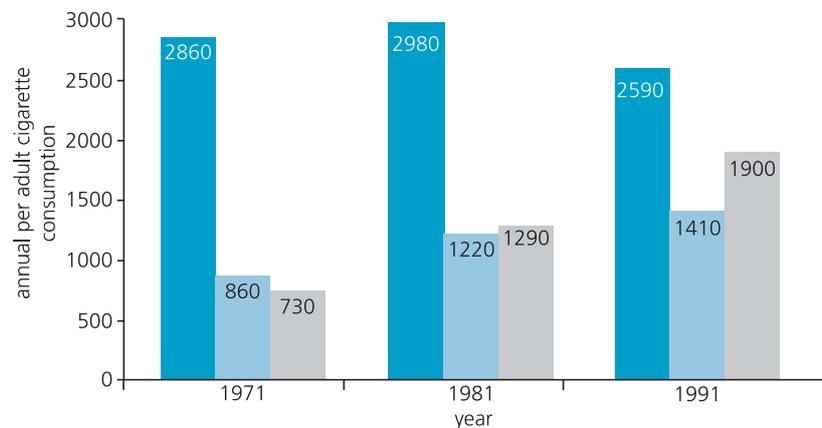


Figure 9.19 World trends in per capita cigarette consumption

(Continues)

Whilst the number of people smoking cigarettes is actually falling in developed countries, smoking is on the rise in the developing world (Figure 9.19). The global health issues generated by cigarette smoking are of epidemic proportions – about one-third of the global adult male population smokes. Among the World Health Organisation areas, the East Asia and the Pacific Region has the highest smoking rate, with nearly two-thirds of men smoking. Today, apparently, one in every three cigarettes is smoked in China.

Globally, the consumption of manufactured cigarettes continues to rise steadily. Consequently, the death toll from the use of tobacco, currently estimated to be 6 million per year worldwide, is predicted to rise to steeply (Figure 9.20b). This is inevitable because of the continuing popularity of cigarettes and of the time lag between the taking up of smoking and the appearance of the symptoms of lung cancer (Figure 9.20a).

How has such a detrimental personal habit gained such a foothold worldwide? Why does it continue to attract people? The answer must lie partly in the impact of the drug nicotine on the central nervous system. Another is that people, particularly the young, have been (and are still being) persuaded that the use of tobacco is linked with highly desirable, personal qualities, such as adult sophistication, self-fulfilment, athletic prowess and sexual attractiveness.

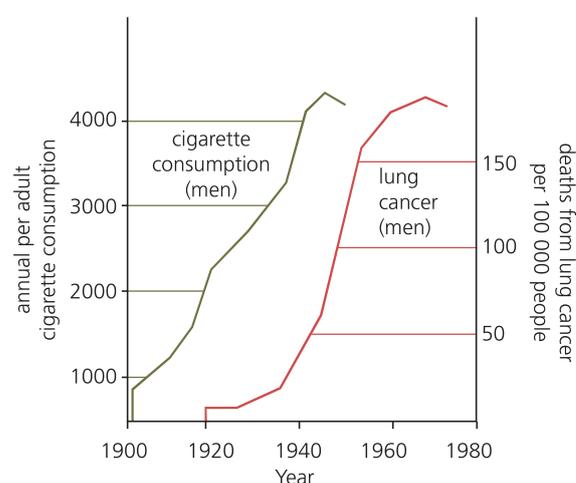
- Studies show that teenagers are strongly influenced by tobacco advertising.
- Today, the multinational conglomerates that form the bulk of the tobacco industry have huge budgets – in Asia, they are among the top ten advertisers.

In attempting to deal with this health issue, the scale of industrial investment focused on this product is a huge problem. There is a sound economic and moral case for continuous, powerful advertising campaigns that more effectively discourage the use of tobacco – despite the cost of such initiatives. This is an ethical issue for all nations.

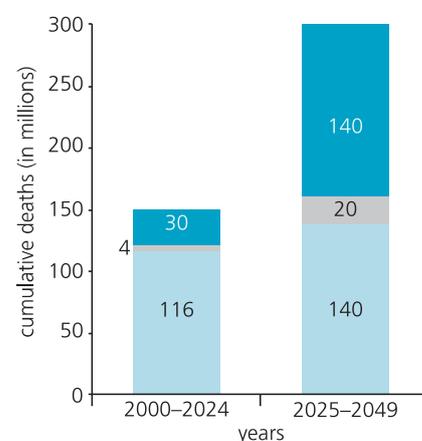
### Question

- 12** List the effects of tobacco smoke on the cardiovascular system.

a) The 20-year time lag between smoking and the diagnosis of lung cancer



b) Premature death from tobacco use, projections for 2000–2004 and 2025–2049



- preventable if adults quit (halving global cigarette consumption by 2020)
- preventable if young adults do not start (halving global uptake of smoking by 2020)
- other premature deaths from tobacco-related causes

Figure 9.20 World smoking habits and the consequent premature deaths

## Summary

- **Gaseous exchange**, the exchange of gases between an organism and its environment, makes possible aerobic respiration in the cells of the body. Gaseous exchange between individual cells and their immediate environment occurs by **diffusion**.
- **Mammals**, with their compact bodies and protected external surface, require specialised respiratory organs, the **lungs**. These efficient organs are housed in the air-tight thorax which moves rhythmically to ventilate the lungs. The **blood circulation system** serves the lungs and transports oxygen all over the body, facilitated by the respiratory pigment **haemoglobin**, present in the red blood cells. Carbon dioxide is returned to the lungs.
- The **alveoli** (the air sacs where gaseous exchange occurs) are reached via the trachea, bronchi and bronchioles, a branching system referred to as the '**bronchial tree**'. The walls of these tubes are variously supported by **cartilage and smooth muscle** and their surface is lined by a **ciliated epithelium** with **goblet cells** that secrete mucus.
- Air is warmed and made moist as it is drawn into the thorax. Dust and foreign bodies are trapped in the **mucus** that is continually swept up and out of the bronchial tree by the beating movements of the **cilia**.
- The millions of individual alveoli are served by terminal bronchioles and both are thin walled and surrounded by fine capillaries. Here, a huge, thin surface area is provided for **efficient exchange of gases** between the air and the blood circulation. Detritus and bacteria are removed by **macrophages** and the walls are kept flexible by the secretions of **surfactant cells**.
- **Smoking** generates major health problems because of carcinogenic aromatic hydrocarbons in the 'tar', the addictive nature of the nicotine and the presence of carbon monoxide – all ingredients released by the burning of tobacco. Many of them reach delicate body cells when cigarette smoke is inhaled.
- Chronic obstructive pulmonary disease (mainly **bronchitis and emphysema**) and **lung cancer** are caused by frequent and regular exposure to cigarette smoke. Cardiovascular disease (CVD) is also caused by smoking, leading to likely hypertension, coronary heart disease, strokes and aneurisms.
- Cardiovascular disease (and cancers) may be treated by various drugs and surgical procedures but **prevention** of these conditions arising by stopping smoking and wiser lifestyle choices would give superior results. However, **nicotine** is so strongly addictive and advertising campaigns by cigarette manufacturers are so influential, there is currently a growing and **global menace to human health** from the smoking of cigarettes.

## Examination style questions

- 1 Fig. 1.1 shows the heart and associated blood vessels.

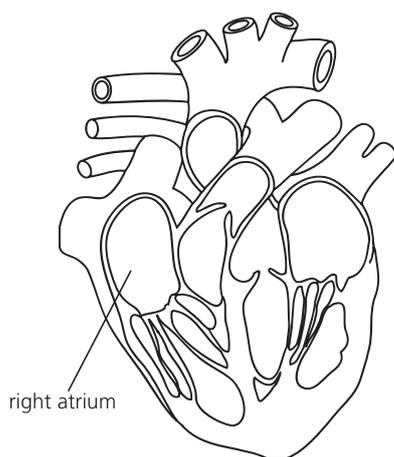


Fig. 1.1

- a) On a copy of Fig. 1.1, draw label lines and use the letters **P**, **Q** and **R** to indicate the following structures:  
**P** a blood vessel that carries deoxygenated blood  
**Q** a structure that prevents backflow into a ventricle  
**R** a blood vessel that carries blood at high pressure [3]
- b) The changes in blood pressure in the right atrium are the same as those in the left atrium. The changes in blood pressure in the right ventricle are different from those in the left ventricle.  
 Explain why this is so. [4]
- c) Some components of tobacco smoke are absorbed into the blood stream and affect the cardiovascular system.  
 Describe the effects of nicotine and carbon monoxide on the cardiovascular system. [4]

[Total: 11]

(Cambridge International AS and A Level Biology 9700, Paper 02 Q1 June 2008)

- 2 The global consumption of manufactured cigarettes continues to rise steadily and the health issues generated by cigarette smoking are of epidemic proportions worldwide.
- a) Suggest why young people today may still choose to smoke cigarettes.
- b) Explain the chief ways that cigarette smoke is directly harmful to the body.
- c) Identify why cigarette smoking, once begun, is addictive.

- 3 Scientists at the Tibet Institute of Medical Sciences in Lhasa investigated differences between adult Tibetans who had lived in Lhasa (altitude 3658 m) all their lives and adult Han Chinese residents who had lived there for about 8 years. The Tibetans and the Han Chinese exercised at maximum effort and various aspects of their breathing were measured. Some of the results are shown in Table 3.1.

Table 3.1

Feature	Tibetans	Han Chinese
minute volume / $\text{dm}^3 \text{ min}^{-1}$	149	126
oxygen uptake / $\text{cm}^3 \text{ kg}^{-1} \text{ min}^{-1}$	51.0	46.0

- Minute volume. This is the volume of air breathed in during one minute.
- Oxygen uptake. This is the volume of oxygen absorbed into the blood during one minute. It is expressed per kg of body mass.

The researchers observed that

- the greater minute volume of the native Tibetans resulted from a greater tidal volume
- the tidal volumes of the Tibetans showed a positive correlation with their vital capacity measurements
- the Han Chinese had lower values for both tidal volume and vital capacity.

- a) State what is meant by the term *tidal volume*. [1]
- b) Suggest why the researchers also measured the *vital capacity* of the people in the study. [2]
- c) Explain how the minute volume **at rest** would be determined. [2]
- d) Suggest two differences in the **structure** of the lungs that may account for the greater oxygen uptake by the Tibetans shown in Table 3.1. [2]
- e) When people who have lived all their lives at low altitude go to a place at high altitude, such as Lhasa, they are often breathless, lack energy and suffer from altitude sickness. However, with time, they often acclimatise to the high altitude.

In another study, researchers found that the red blood cell count increases in such people by about 30% over several weeks.

Explain why the red blood cell count increases so much when people visit places at high altitude. [2]

**[Total: 9]**

(Cambridge International AS and A Level Biology 9700, Paper 02 Q4 June 2008)

- 4 Fig 5.1 shows a drawing made from an electron micrograph of a cell from the ciliated epithelium of the bronchus.

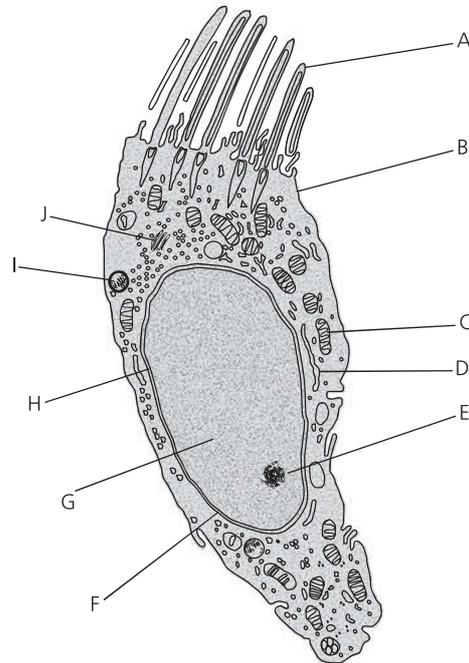


Fig. 5.1

- a) Copy and complete the table below by writing the appropriate letter from the diagram to indicate the structure that carries out each of the functions listed. The first one has been completed for you. [5]

Function	Structure
facilitated diffusion of glucose	B
creates a current to move mucus	
aerobic respiration	
makes ribosomes	
a site of transcription	
packages proteins into lysosomes	

- b) The alveoli in the lungs are lined by a squamous epithelium. Explain why gas exchange occurs in alveoli and not in the bronchus. [3]
- c) Describe the likely appearance of the lining of the bronchus in a person who has been a heavy smoker for many years. [3]

**[Total: 11]**

(Cambridge International AS and A Level Biology 9700, Paper 02 Q1 June 2007)