LIFESTYLE, HEALTH AND RISK

Why a topic called Lifestyle, health and risk?

Congratulations on making it this far! Not everyone who started life's journey has been so lucky. In the UK only about 80% of conceptions lead to live births, and about 4 in every 1000 newborn babies do not survive their first year of life (Figure 1.1). After celebrating your first birthday there seem to be fewer dangers. Fewer than 1 in every 1000 children die between the ages of 1 and 14 years old. All in all, life *is* a risky business.

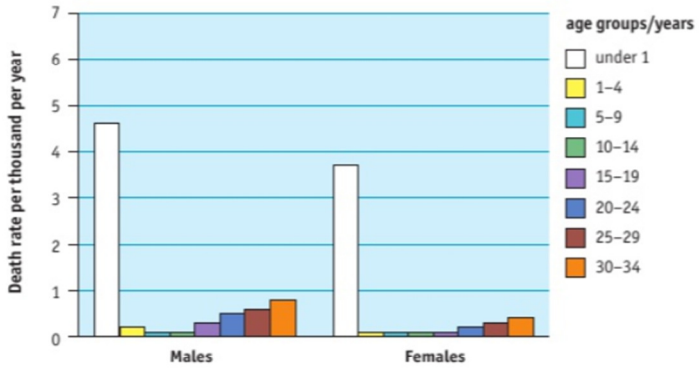


Figure 1.1 Death rates per 1000 population per year by age group and sex. Is life more risky for boys? *Source: England and Wales Office for National Statistics, 2012.*

Figure 1.2 Some activities are less obviously risky than others, but may still have hidden dangers.

In everything we do there is some risk. Normally we only think something is risky if there is the obvious potential for a harmful outcome. Snowboarding, parachute jumping and taking ecstasy are thought of as risky activities, but even crossing the road, jogging or sitting in the sun have risks, and many people take actions to reduce them (Figures 1.2 and 1.3).

Risks to health are often not as apparent as the risks facing someone making a parachute jump. People often do not realise that there are risks associated with lifestyle choices that they make. They underestimate the effect such choices might have on their health.

What we eat and drink, and the activities we take part in, all affect our health and well-being. Every day we make choices that may have short- and long-term consequences which we may be only vaguely aware of. What are the health risks that we are subjecting ourselves to? Will a cooked breakfast set us up for the day or will it put us on course for heart disease? Does the 10-minute walk to work really make a difference to our health?

Cardiovascular disease is the biggest killer in the UK, with around 1 in 3 people (32%) dying from diseases of the circulatory system. Does everyone have the same risk? Can we assess and reduce the risk to our health? Do we need to? Is our perception of risk at odds with reality?

In this topic you will read about Mark and Peter who have kindly agreed to share their experiences of cardiovascular disease. The topic will introduce the underlying biological concepts that will help you understand how cardiovascular diseases develop, and the ways of reducing the risk of developing these diseases.

OVERVIEW OF THE BIOLOGICAL PRINCIPLES COVERED IN THIS TOPIC

This topic will introduce the concept of risks to health. You will study the relative sizes of risks and how these are assessed. You will consider how we view different risks – our perception of risk. You will also look at how health risks may be affected by lifestyle choices and how risk factors for disease are determined.

Building on your GCSE knowledge of the circulatory system, you will study the heart and circulation and understand how these are affected by our choice of diet and activity.

You will look in some detail at the biochemistry of our food. This will give you a detailed understanding of some of the current thinking among doctors and other scientists about how our choice of foods can reduce the risks to our health.

REVIEW

Are you ready to tackle Topic 1 *Lifestyle, health and risk?*

Complete the GCSE review and GCSE review test before you start.

Figure 1.3 A UK male aged 15 to 19 is over three times more likely to have a fatal accident than a female of the same age. *Source: Department for Transport road accidents and safety annual report, 2012.*

Mark's story

On 28 July 1995 something momentous happened that changed my life …

Figure 1.4 Mark at 15.

I was sitting in my bedroom playing on my computer when I started to feel dizzy with a slight headache. Standing, I lost all balance and was feeling very poorly. I think I can remember trying to get downstairs and into the kitchen before fainting. People say that unconscious people can still hear. I don't know if it's true but I can remember my dad phoning for a doctor and that was it. It took 5 minutes from me being an average 15-year-old to being in a coma.

I was rushed to Redditch Alexandra Hospital where they did some reaction tests on me. They asked my parents questions about my lifestyle (did I smoke, take drugs, etc.?). Failing to respond to any stimulus, I was transferred in an ambulance to Coventry Walsgrave Neurological Ward. Following CT and MRI scans on my brain it was concluded that I had suffered a stroke. My parents signed the consent form for me to have an operation lasting many hours. I was given about a 30% chance of survival.

They stopped the bleed by clipping the blood vessels that had burst with metal clips and removing the excess blood with a vacuum. I was then transferred to the intensive care unit to see if I would recover. Within a couple of days I was conscious and day by day I regained my sight, hearing and movement (although walking and speech were still distorted).

This is a true story. Mark had a stroke, one of the forms of cardiovascular disease. It is rare for someone as young as Mark to suffer a stroke. Why did it happen? Was he in a high-risk group?

Figure 1.5 The experience is not stopping Mark living life to the full. He is now married and works in IT.

Peter's story

I got the first indication of cardiovascular problems aged 23 when I was told that I had high blood pressure. I didn't really take much notice. My father had died at the age of 53 from a heart attack but as he was about four stone overweight, had a passion for fatty foods and smoked 60 full strength cigarettes a day, I didn't compare his condition to mine. I had a keen interest in sport, playing hockey and joining the athletics team at work. I was never overweight but I must admit that I probably drank too much at times and didn't bother too much about calories and cholesterol in food.

In 1981, I ran my first marathon at the age of 42 and subsequently did another five. All was going well I thought, until a routine medical showed my blood pressure reading to be very high at 240 over 140. The doctor could not believe that I was still walking around, let alone running, and sent me straight to my GP. Since then I have always taken tablets for high blood pressure and have also reviewed my diet.

I did continue running and completed the Great North Run at the age of 63. Thinking about doing the Great North Run again, I was running 8 miles a week and playing hockey. Then my eight-day holiday in Ireland became three days touring and twelve days in hospital.

At 2 o'clock in the morning I woke up with a terrific pain in my chest. I was sweating profusely and looking very pale. I had had a heart attack and within an hour I was in intensive care. At 5 am I had a second attack and the specialist inserted a temporary pacemaker to keep my heart rate up as it was dropping below 40.

After five days in intensive care I was transferred to the general ward for recuperation. I was told that it was possible that, had I not looked after myself, I might have had a heart attack much earlier in life.

On returning home I had an angiogram and was told that I needed a triple bypass operation. I have to say it was not pleasant, but I had decided that it was necessary and I would cope with anything that happened if it would get me back to a decent lifestyle. Well, the operation, a quadruple bypass, was a success and after eight days I was back home.

This is a true story. Why did it happen to Peter, who seemed to be so active and healthy?

ACTIVITY

To find out what happened to Mark and Peter read their full stories in **Student Activity 1.1**.

Figure 1.6 Peter's active lifestyle did not prevent his heart attack but probably helped him to make a full recovery.

1.1 What is cardiovascular disease?

Deaths from cardiovascular disease

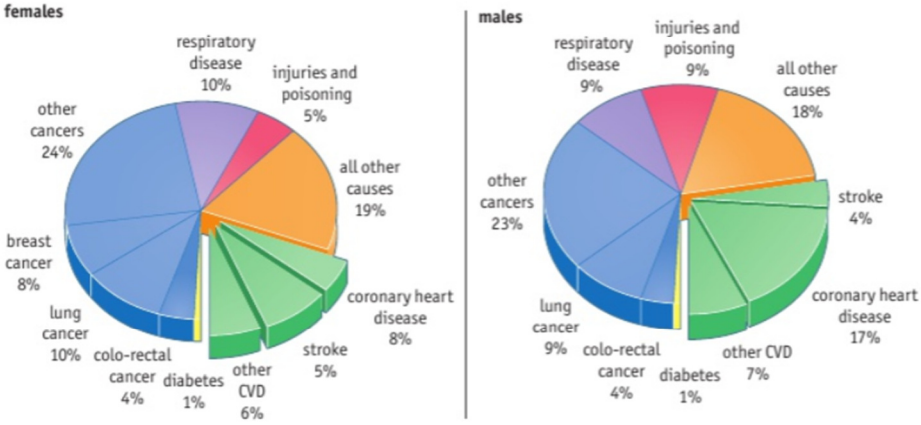


Figure 1.7 Premature deaths by cause in the UK in 2010 for females (left) and males (right). (Premature death is death under the age of 75 years.) One person dies of a heart attack in the UK every 7 minutes. *Reproduced with the kind permission of the British Heart Foundation.*

WEBLINK

To check out the most recent death rate figures for coronary heart disease see the National Statistics Office website and the British Heart Foundation website.

MATHS SUPPORT

Check why the data here in Figure 1.7 is presented as pie charts while the data in Figure 1.1 is in a histogram. See maths support 2 – presenting data graphs.

Cardiovascular diseases (**CVDs**) are diseases of the heart and circulation. They are the main cause of death in the UK, accounting for almost 180 000 deaths a year, and over 46 000 of these are premature deaths (Figure 1.7). Around one in three people in the UK die from cardiovascular diseases. The main forms of cardiovascular diseases are **coronary heart disease** (**CHD**), as experienced by Peter, and **stroke**, as experienced by Mark.

Almost half of all deaths from cardiovascular diseases are from coronary heart disease (45%) and over a quarter are from stroke (28%). Coronary heart disease is the most common cause of death in the UK. About one in five men and one in ten women die from the disease.

KEY BIOLOGICAL PRINCIPLE: WHY HAVE A HEART AND CIRCULATION?

The heart and circulation have one primary purpose – to move substances around the body. In very small organisms such as unicellular creatures where distances are short, substances such as oxygen, carbon dioxide and digestive products move around the organism by diffusion. **Diffusion** is the movement of molecules or ions from a region of their high concentration to a region of their low concentration by relatively slow random movement of molecules. In unicellular organisms diffusion is usually fast enough to meet the organism's requirements.

Most complex multicellular organisms, however, are too large for diffusion to move substances around their bodies quickly enough. These organisms rely on a **mass transport system** to move substances efficiently over long distance by **mass flow**. All the particles in a liquid move in one direction through tubes due to difference in pressure. Animals usually have blood to carry vital substances around their bodies and a heart to pump it instead of relying on diffusion. In other words, they have a circulatory system. Some animals have more than one heart – the humble earthworm, for instance, has five.

Open circulatory systems

In insects and some other animal groups, blood circulates in large open spaces. A simple heart pumps blood out into cavities surrounding the animal's organs. Substances can diffuse between the blood and cells. When the heart muscle relaxes, blood is drawn from the cavity back into the heart through small, valved, openings along its length.

Closed circulatory systems

Many animals, including all vertebrates, have a closed circulatory system in which the blood is enclosed within tubes – blood vessels. This generates higher blood pressures as the blood is forced along fairly narrow channels instead of flowing into large cavities. This means the blood travels faster and so the blood system is more efficient at delivering substances around the body:

- The blood leaves the heart under pressure and flows along **arteries** and then **arterioles** (small arteries) to **capillaries**.

- There are extremely large numbers of capillaries. These come into close contact with most of the cells in the body where substances are exchanged between blood and cells.
- After passing along the capillaries, the blood returns to the heart by means of **venules** (small veins) and then **veins**.
- Valves ensure that blood flows only in one direction.

Animals with closed circulatory systems are generally larger in size and often more active than those with open systems.

Single circulatory systems

Animals with a closed circulatory system have either single circulation or double circulation. Fish, for example, have single circulation (Figure 1.8):

- The heart pumps deoxygenated blood to the gills.
- Gaseous exchange takes place in the gills; there is diffusion of carbon dioxide from the blood into the water that surrounds the gills, and diffusion of oxygen from this water into the blood within the gills.
- The blood leaving the gills then flows round the rest of the body before eventually returning to the heart.

Note that the blood flows through the heart once for each complete circuit of the body.

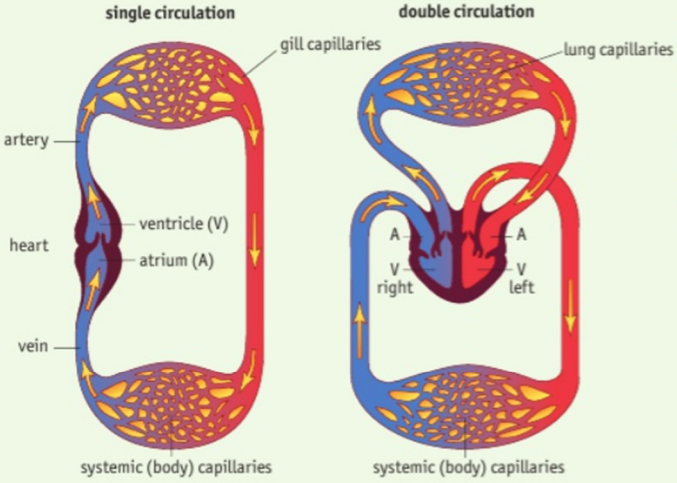


Figure 1.8 Fish have a single circulation. Birds and mammals have a double circulation.

Double circulatory systems

Birds and mammals have double circulation:

- The right ventricle of the heart pumps deoxygenated blood to the lungs where it receives oxygen.
- The oxygenated blood then returns to the heart to be pumped a second time (by the left ventricle) out to the rest of the body.

This means that the blood flows through the heart twice for each complete circuit of the body. The heart gives the blood returning from the lungs an extra 'boost' that reduces the time it takes for the blood to circulate round the whole body. This allows birds and mammals to have a high metabolic rate, as oxygen and food substances required for metabolic processes can be delivered more rapidly to cells and meet the needs of the organism.

Q 1.1 Why do only small animals have an open circulatory system?

Q 1.2 What are the advantages of having a double circulatory system?

Q 1.3 Fish have two-chamber hearts and mammals have four-chamber hearts.

(a) Sketch what the three-chamber heart of an amphibian, such as a frog, might look like.

(b) What might be the major disadvantage of this three-chamber system?

CHECKPOINT

1.1 Make a bullet point summary which explains why many animals have a heart and circulation.

ACTIVITY

Student Activity 1.2 demonstrates mass flow.

How does the circulation work?

The transport medium

In the circulatory system a liquid and all the particles it contains are transported in one direction due to a difference in pressure in a process known as **mass flow**. In animals the transport medium is usually called blood. The fluid, plasma, is mainly water and contains dissolved substances such as digested food molecules (e.g. glucose), oxygen and carbon dioxide. Proteins, amino acids, salts, enzymes, hormones, antibodies and urea, the waste product from the breakdown of proteins, are just some of the other substances transported in the plasma. Cells are also carried in the blood: red blood cells, white blood cells and platelets. Blood is not only important in the transport of dissolved substances and cells, but also plays a vital role in regulation of body temperature, transferring energy around the body.

ACTIVITY

Student Activity 1.3 lets you investigate some of the properties of water.

KEY BIOLOGICAL PRINCIPLE: PROPERTIES OF WATER THAT MAKE IT AN IDEAL TRANSPORT MEDIUM

Water, H_2O, is unusual among small molecules. It is a liquid at room temperature while most other small molecules, such as CO_2 and O_2, are gases. Water is a **polar molecule**; it has an unevenly distributed electrical charge. The two hydrogens are pushed towards each other forming a V-shaped molecule (Figure 1.9). The hydrogen end of the molecule is slightly positive and the oxygen end is slightly negative because the electrons are more concentrated at that end. Water is said to be a **dipole**. It is this polarity that accounts for many of its biologically important properties.

The slightly positively charged end of a water molecule is attracted to the slightly negative ends of surrounding water molecules. This **hydrogen bonding** holds the water molecules together and results in many of the properties of water including being liquid at room temperature.

Solvent properties

Many chemicals dissolve easily in water, due to their dipole nature, allowing vital biochemical reactions to occur in the cytoplasm of cells. Free to move around in an aqueous environment, the chemicals can react, often with water itself being involved in the reactions (for example in hydrolysis and condensation reactions, see page 31). The dissolved substances can also be transported around organisms, in animals via the blood and lymph systems, and in plants through the xylem and phloem.

Ionic substances, such as sodium chloride (NaCl), dissolve easily in water. In the case of sodium chloride, the negative Cl^- ions are attracted to the positive ends of the water molecules while the positive Na^+ ions are attracted to the negative ends of the water molecules. The chloride and sodium ions become hydrated in aqueous solution, they become surrounded by water molecules.

Polar molecules also dissolve easily in water. Their polar groups, for example the –OH group in sugars or the amine group, $–NH_2$, in amino acids, become surrounded by water and go into solution. Such polar substances are said to be **hydrophilic** – 'water-loving'.

Non-polar, **hydrophobic** substances, such as lipids, do not dissolve in water. To enable transport in blood, lipids combine with proteins to form lipoproteins.

Thermal properties

The specific heat capacity of water, the amount of energy in joules required to raise the temperature of 1 cm^3 (1 g) of water by 1 °C, is very high. This is because in water a large amount of energy is required to break the hydrogen bonds. A large input of energy causes only a small increase in temperature, so water warms up and cools down slowly. This is extremely useful for organisms, helping them to avoid rapid changes in their internal temperature and enabling them to maintain a steady temperature even when the temperature in their surroundings varies considerably. This also means that bodies of water in which aquatic organisms live do not change temperature rapidly.

Water also has a high boiling point because there are so many hydrogen bonds and a lot of energy is needed to break them all.

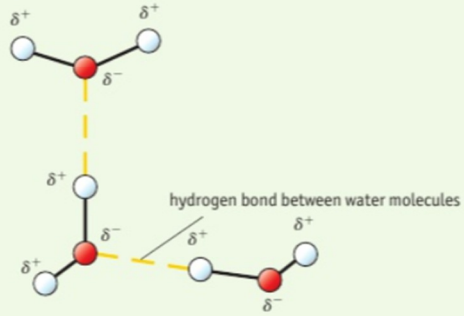


Figure 1.9 The polarity of the water molecules results in hydrogen bonds between them. (Oxygen atoms in red, hydrogen atoms in white.)

The structure of the heart

The heart is a double pump and is made of **cardiac muscle**. The right side of the heart receives deoxygenated blood from the body and pumps it to the lungs. The left side receives oxygenated blood from the lungs and pumps it to the body.

Study Figure 1.10 and locate the arteries carrying blood away from the heart and the veins returning blood to the heart.

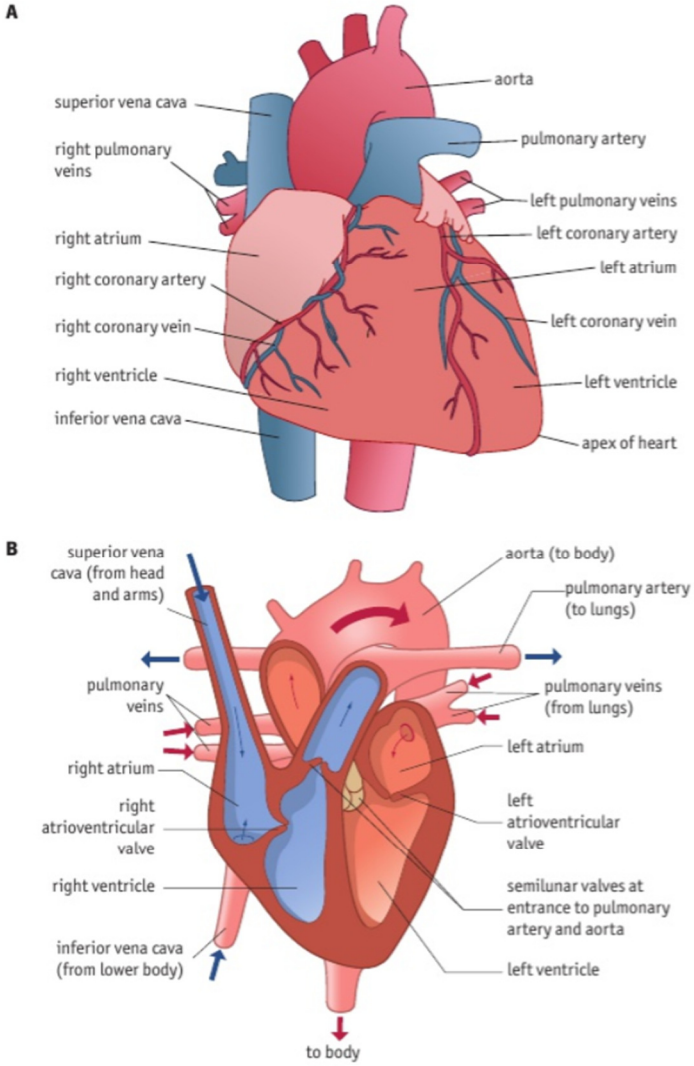


Figure 1.10 **A** Diagrammatic external view of a human heart. **B** Diagrammatic cross-section of the human heart (ventral or front view).

ACTIVITY

Student Activities 1.4 and **1.5** let you look in detail at the structure of a mammalian heart using either a dissection or a simulation.

The structure of blood vessels

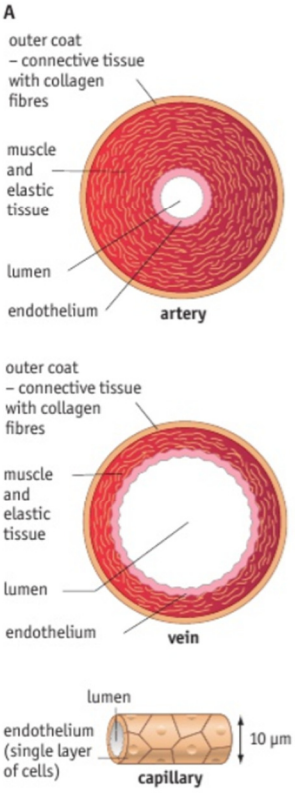
Arteries and veins can easily be distinguished, as shown in Figure 1.11. The walls of both vessels contain **collagen**, a tough fibrous protein, which makes them strong and durable. They also contain elastic fibres that allow them to stretch and recoil. Smooth muscle cells in the walls allow them to constrict and dilate. The key differences between the arteries and veins are listed below.

Arteries:

- narrow lumen
- thicker walls
- more collagen, smooth muscle and elastic fibres
- no valves

Veins:

- wide lumen
- thinner walls
- less collagen and smooth muscle, fewer elastic fibres
- valves



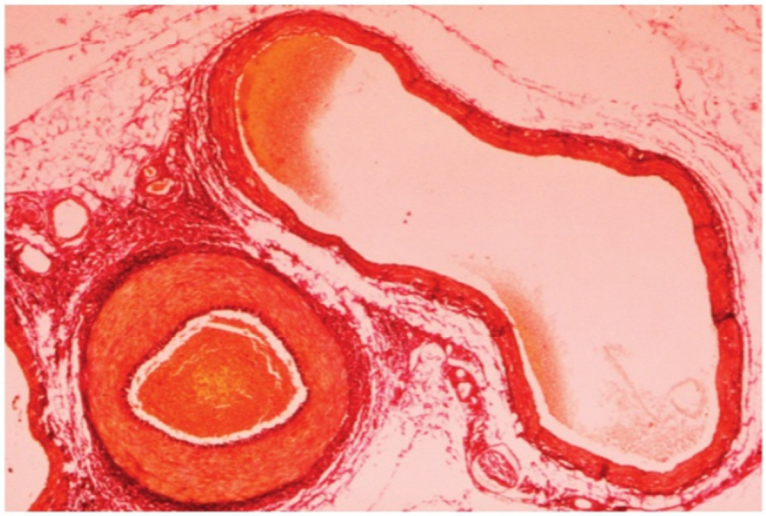


Figure 1.11 **A** Diagram of an artery, a vein and a capillary. The endothelium that lines the blood vessels is made up of epithelial cells (see page 59). **B** Photomicrograph of an artery (left) and vein (right) surrounded by connective tissue.

Q 1.4 **(a)** A student calibrating her eyepiece graticule found 5 units measured 3.5 units on the stage micrometer, which are each 1 mm in length. Work out the length of one eyepiece graticule unit in µm.

(b) Using the same eyepiece graticule (epg). The width of the artery wall in the photomicrograph in Figure 1.11B measured 0.2 epg units at its widest point. **(i)** what was the width in µm and **(ii)** what is the magnification of the photograph?

ACTIVITY

Student Activity 1.6 lets you investigate how the structure of blood vessels relates to their function. You will also learn how to measure using an eyepiece graticule.

The capillaries that join the small arteries (arterioles) and small veins (venules) are very narrow, about 10 µm in diameter, with walls that are only one cell thick.

These features can be directly related to the functions of the blood vessels, as described below.

How does blood move through the vessels?

Every time the heart contracts (**systole**), blood is forced into arteries and their elastic walls stretch to accommodate the blood. The thick artery walls can withstand the high pressure generated as the blood is forced against the walls. During **diastole** (relaxation of the heart), the elasticity of the artery walls causes them to recoil behind the blood, helping to push the blood forward and smoothing blood flow. The blood moves along the length of the artery as each section in series stretches and recoils in this way. The pulsing flow of blood through the arteries can be felt anywhere an artery passes over a bone close to the skin.

By the time the blood reaches the smaller arteries and capillaries there is a steady flow of blood. Blood flows more slowly in the capillaries due to their narrow lumens causing more of the blood to be slowed down by friction against the capillary wall. This slower steady flow allows exchange between the blood and the surrounding cells through the one-cell-thick capillary walls. The network of capillaries that lies close to every cell ensures that there is rapid diffusion between the blood and surrounding cells.

The heart has a less direct effect on the flow of blood through the veins. Blood flows steadily and without pulses in veins where it is under relatively low pressure. In the veins blood flow is assisted by the contraction of skeletal muscles during the movement of limbs and breathing. Low pressure developed in the thorax (chest cavity) when breathing in also helps draw blood back into the heart from the veins. Backflow is prevented by semilunar valves within the veins (Figure 1.12).

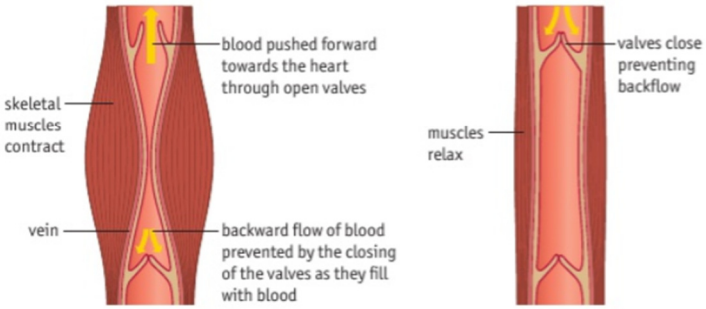


Figure 1.12 Valves in the veins prevent the backflow of blood.

Q 1.5 List the features shown in Figure 1.11A that enable the artery to withstand high pressure and then recoil to maintain a steady flow of blood.

Since the heart is a muscle it needs a constant supply of fresh blood carrying oxygen and glucose for aerobic respiration. You might think that receiving a blood supply would never be a problem for the heart. However, the heart muscle does not obtain oxygen and nutrients from the blood inside its pumping chambers due to the large diffusion distances involved. Instead, the heart muscle is supplied with blood through its own coronary circulation; two vessels called the **coronary arteries**, a network of capillaries, and two coronary veins. You can see the coronary arteries and coronary veins on the surface of the heart in Figure 1.10A.

ACTIVITY

Student Activity 1.7 lets you complete William Harvey's experiment that originally demonstrated one-way valves in veins.

CHECKPOINT

1.2 Identify the key structures of an artery, a vein and a capillary, and in each case explain how the structure is related to the function of the vessel.

How the heart works

Give a tennis ball a good, hard squeeze. You are using about the same amount of force that your heart uses in a single contraction to pump blood out to the body. Even when you are at rest, the muscles of your heart work hard – weight for weight, harder than the leg muscles of a person running.

The chambers of the heart alternately contract (systole) and relax (diastole) in a rhythmic cycle. One complete sequence of filling and pumping blood is called a **cardiac cycle**, or heartbeat. During systole, cardiac muscle contracts and the heart pumps blood out through the aorta and pulmonary arteries. During diastole, cardiac muscle relaxes and the heart fills with blood.

The cardiac cycle can be simplified into three phases: atrial systole, ventricular systole and diastole. The events that occur during each of the stages are shown in Figure 1.13.

Phase 1: Atrial systole

Blood returns to the heart due to the action of skeletal and muscles involved in breathing as you move and breathe. Blood under low pressure flows into the **left** and **right atria** from the pulmonary veins and vena cava. As the atria fill, the increasing pressure of blood against the **atrioventricular valves** pushes them open and blood begins to leak into the **ventricles**. The atria walls contract forcing more blood into the ventricles. This contraction of the atria is known as **atrial systole**.

Phase 2: Ventricular systole

After a *slight* delay, atrial systole is followed by **ventricular systole**. The ventricles contract from the base of the heart upwards, increasing the pressure in the ventricles. The pressure forces open the semilunar valves and pushes blood up and out through the pulmonary arteries and aorta. The pressure of blood against the atrioventricular valves closes them and prevents blood flowing backwards into the atria.

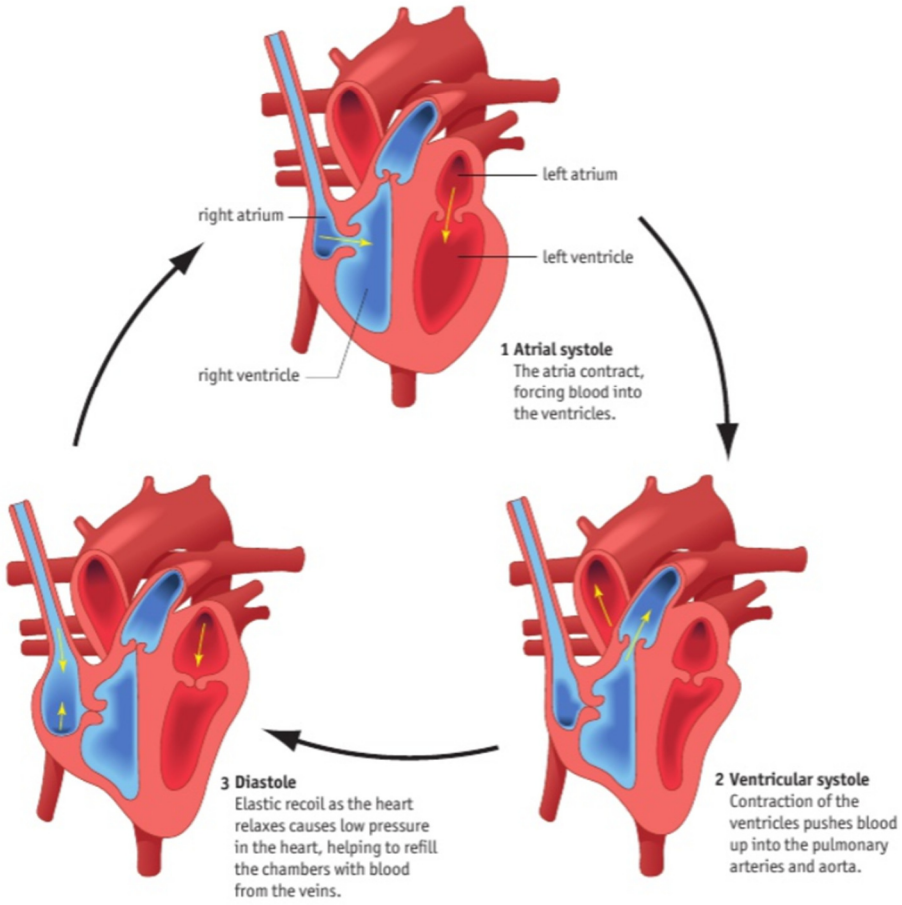


Figure 1.13 The three stages of the cardiac cycle. At each stage blood moves from higher to lower pressure.

Phase 3: Cardiac diastole

The atria and ventricles then relax during **cardiac diastole**. Elastic recoil of the relaxing heart walls lowers pressure in the atria and ventricles. Blood under higher pressure in the pulmonary arteries and aorta is drawn back towards the ventricles, closing the **semilunar valves** and preventing further backflow into the ventricles. The coronary arteries fill during diastole. Low pressure in the atria helps draw blood into the heart from the veins.

CHECKPOINT

1.3 Make a flowchart which summarises the events in the cardiac cycle.

Q 1.6 When the heart relaxes in cardiac diastole you might expect blood to move from the arteries back into the ventricles due to the elastic recoil of the heart and the action of gravity if you are standing or sitting upright. How is this prevented?

ACTIVITY
Student Activity 1.8 lets you test your knowledge of the cardiac cycle.

Pressure changes and valves determine the flow of blood in the cardiac cycle. At each stage in the cycle blood moves from high pressure to low pressure. Figure 1.14 shows changes in pressure in the left side of the heart during the cardiac cycle. The same sequence occurs in the right side of the heart but the maximum pressure in the right ventricle is only 30 mm Hg. The diagram also shows how the closing of the valves causes the sounds that we recognise as a heartbeat. The first sound ('lub') is caused by the closing of the atrioventricular valves and the second ('dub') by the closing of the semilunar valves.

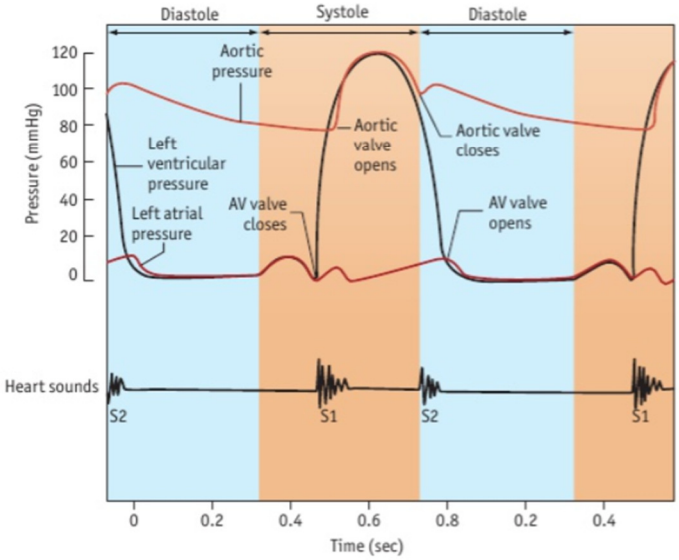


Figure 1.14 Pressure changes in the left side of the heart during the cardiac cycle. The differences in pressure determine the movement of blood and the opening and closing of the valves, and therefore maintain the flow of blood in one direction through the heart. The aortic valve is the semilunar valve in the aorta. Complete question 1.7 to make sure that you really understand what this diagram is showing you.

Q 1.7 **(a)** Using your knowledge of the cardiac cycle and information from the graph explain what causes:

(i) the rise in both atrial and ventricle pressure at about 0.3 s
(ii) the atrioventricular valve to close at about 0.45 seconds
(iii) the semilunar valve (aortic) to open at about 0.5 seconds
(iv) the rise in aorta pressure after the semilunar valve opens
(v) the closing of the semilunar valve (aortic) at about 0.75 seconds.

(b) Decide what state the valves will be in, open or closed, for each of the pressure gradients shown.

	Valves	Pressure gradient
(i)	Atrioventricular valves	Atrium pressure > ventricle pressure
(ii)	Semilunar valves	Ventricle pressure < aorta pressure

(c) Sketch a graph to show the pressure changes that would occur on the right side of the heart during a single cardiac cycle.

(d) Work out the heart rate for the cardiac cycle shown in Figure 1.14.

What is atherosclerosis?

Atherosclerosis is the disease process that leads to coronary heart disease and strokes. In atherosclerosis fatty deposits can either block an artery directly or increase its chance of being blocked by a blood clot (**thrombosis**). The blood supply can be blocked completely. If it is not restored very quickly, the affected cells are permanently damaged. In the coronary arteries this results in a heart attack (**myocardial infarction**). In the arteries supplying the brain it results in a **stroke**. The supply of blood to the brain is restricted or blocked, causing damage or death to cells in the brain. Narrowing of arteries to the legs can result in tissue death and gangrene (decay). An artery can burst where blood builds up behind an artery that has been narrowed as a result of atherosclerosis (see page 17 Did You Know?).

What happens in atherosclerosis?

Atherosclerosis can be triggered by a number of factors. Whatever the trigger, this is the course of events that follows:

1 The **endothelium**, a delicate layer of cells that lines the inside of an artery and separates the blood that flows along the artery from the muscular wall (Figure 1.15A), becomes damaged and dysfunctional for some reason. This endothelial damage can result from high blood pressure, which puts an extra strain on the layer of cells, or it might occur due to some of the toxins from cigarette smoke in the bloodstream.

2 Once the inner lining of the artery is breached there is an **inflammatory response**. White blood cells leave the blood vessel and move into the artery wall. These cells accumulate chemicals from the blood, particularly **cholesterol**. A fatty deposit builds up, called an **atheroma**.

3 Calcium salts and fibrous tissue also build up at the site, resulting in a hard swelling called a **plaque** on the inner wall of the artery. The build-up of fibrous tissue means that the artery wall loses some of its elasticity; in other words, it hardens. The ancient Greek word for 'hardening' is 'sclerosis', giving the word 'atherosclerosis'.

4 Plaques cause the lumen of the artery to become narrower (Figure 1.15B). This makes it more difficult for the heart to pump blood around the body and can lead to a rise in blood pressure. Now there is a dangerous **positive feedback** building up. Plaques lead to raised blood pressure and raised blood pressure makes it more likely that further plaques will form, as damage to endothelial tissue in other areas becomes more likely.

The person may be unaware of any problem at this stage, but if the arteries become very narrow or completely blocked they cannot supply enough blood to bring oxygen and nutrients to the tissues. The tissues can no longer function normally and symptoms will soon start to show.

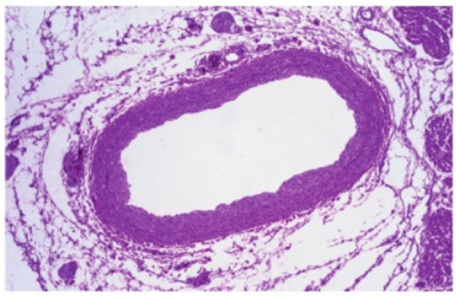


Figure 1.15 A Photomicrograph of a normal, healthy coronary artery showing no thickening of the arterial wall. The lumen is large. Magnification ×15.

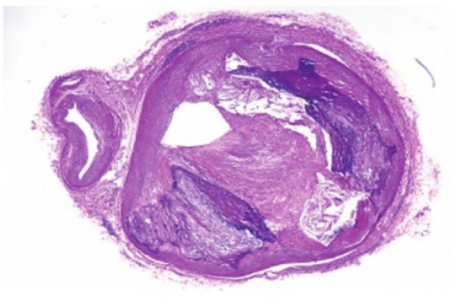


Figure 1.15 B Photomicrograph of a diseased coronary artery showing narrowing of the lumen due to atheroma deposits and build-up of atherosclerotic plaque. Magnification ×15.

Why do only arteries get atherosclerosis?

The fast-flowing blood in arteries is under high pressure so there is a significant chance of damage to the walls. The low pressure in the veins means that there is less risk of damage to the walls.

Why does the blood clot in arteries?

Blood clotting

Rapid blood clotting is vital when a blood vessel is damaged. The blood clot seals the break in the blood vessel and limits blood loss and prevents entry of pathogens through any open wounds. When **platelets**, a type of blood cell without a nucleus, come into contact with the damaged vessel wall they change from flattened discs to spheres with long thin projections (Figure 1.16). Their cell surfaces change, causing them to stick to the exposed collagen in the wall and to each other to form a temporary platelet plug. They also release substances that activate more platelets.

The direct contact of blood with collagen within the damaged blood vessel wall also triggers a complex series of chemical changes in the blood (Figure 1.17). A **cascade** of changes results in the formation of a blood clot (Figures 1.17 and 1.18).

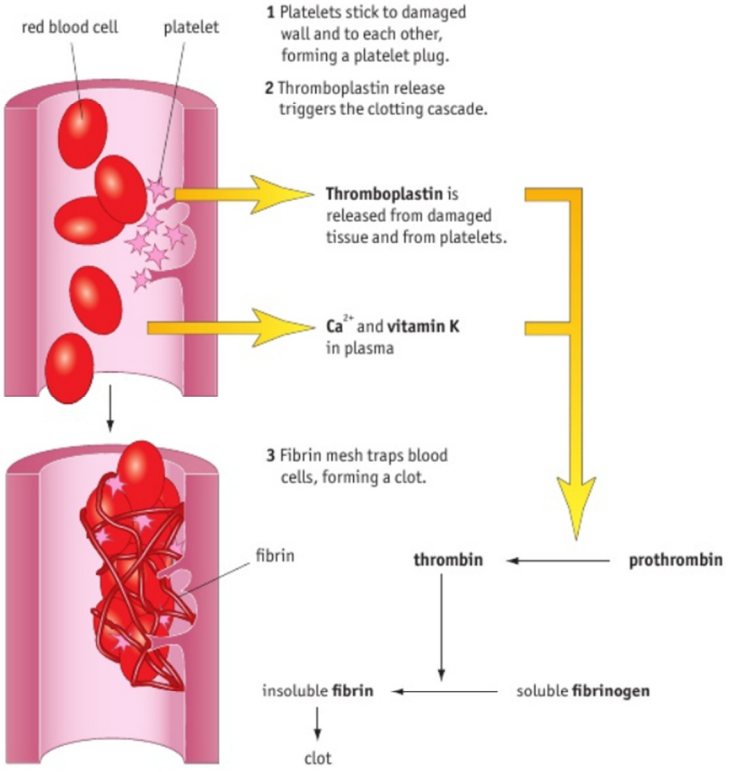


Figure 1.17 Damage to the vessel wall triggers a cascade of reactions that leads to clotting.

The clotting cascade

1 Platelets and damaged tissue release a protein called **thromboplastin**.

2 Thromboplastin activates an enzyme that catalyses the conversion of the protein **prothrombin** into an enzyme called **thrombin**. A number of other protein factors, vitamin K and calcium ions must be present in the blood plasma for this conversion to happen.

3 Thrombin then catalyses the conversion of the soluble plasma protein, **fibrinogen**, into the insoluble protein **fibrin**.

4 A mesh of fibrin forms that traps more platelets and red blood cells to form a clot.

ACTIVITY
Student Activity 1.9
lets you summarise the steps in development of atherosclerosis and clot formation.

ACTIVITY
Student Activity 1.10
lets you consider how narrowing arteries affect blood flow.

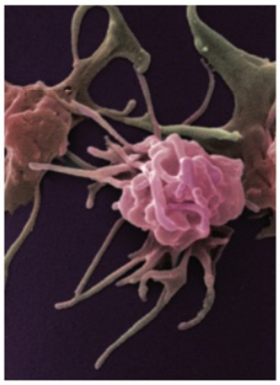


Figure 1.16 Electron micrograph showing activated platelets. Magnification ×6000.

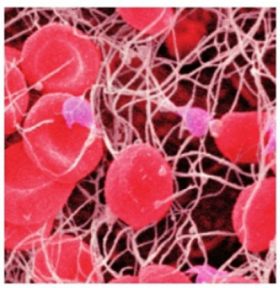


Figure 1.18 False-colour scanning electron micrograph showing red blood cells and platelets trapped in the yellow mesh of fibrin.

What happens inside arteries to cause blood clotting?

Usually blood does not clot inside blood vessels. Platelets do not stick to the endothelium (inner lining) of blood vessels. It is very smooth and has substances on its surface that repel the platelets. However, if there is atherosclerosis and the endothelium is damaged, the platelets come into contact with the damaged surface and any exposed collagen. The clotting cascade will be triggered within the vessel resulting in a clot as shown in Figure 1.19.

The consequences of atherosclerosis

Coronary heart disease

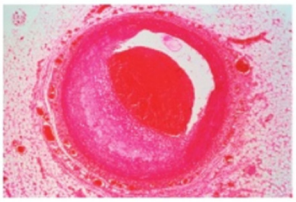


Figure 1.19 Photomicrograph of a diseased coronary artery showing narrowing and a blood clot.

Narrowing of the coronary arteries limits the amount of oxygen-rich blood reaching the heart muscle. The result may be a chest pain called **angina**. Angina is usually experienced during exertion when the cardiac muscle is working harder and needs to respire more. Because the heart muscle lacks oxygen, it is forced to respire **anaerobically**. It is thought that this results in chemical changes which trigger pain, but the detailed mechanism is still not known. Usually these symptoms will ease with rest.

If a fatty plaque in the coronary arteries ruptures, collagen is exposed which leads to rapid clot formation. The blood supply to the heart may be blocked completely. The heart muscle supplied by these arteries does not receive any blood, so it is said to be **ischaemic** (without blood). If the affected muscle cells are starved of oxygen for long they will be permanently damaged. This is what we call a **heart attack** or **myocardial infarction**. If the zone of dead cells occupies only a small area of tissue the heart attack is less likely to prove fatal (see Figure 1.20).

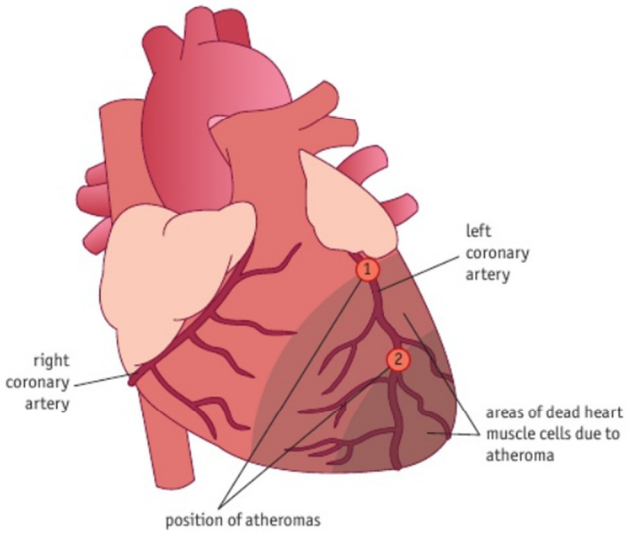


Figure 1.20 The seriousness of a heart attack is determined by the position of the blockage in the coronary artery. Blockage at position one is more likely to be fatal than a blockage at position two. Blockage at the position further along the coronary artery is less likely to be fatal.

Stroke

If the supply of blood to the brain is only briefly interrupted then a mini-stroke may occur. A mini-stroke has all the symptoms of a full stroke but the effects last for only a short period, and full recovery can happen quite quickly. However, a mini-stroke is a warning of problems with blood supply to the brain that could result in a full stroke in the future.

If a blood clot blocks one of the arteries leading to the brain, a full **stroke** will result. If brain cells are starved of oxygen for more than a few minutes they will be permanently damaged, and it can be fatal.

DID YOU KNOW?

The symptoms of cardiovascular disease

Coronary heart disease

Shortness of breath and angina are often the first signs of coronary heart disease. The main symptom of angina is intense pain, ache or a feeling of constriction and discomfort in the chest, or in the left arm and shoulder. Other symptoms are unfortunately very similar to those of severe indigestion and include a feeling of heaviness, tightness, pain, burning and pressure – usually behind the breastbone, but sometimes in the jaw, arm or neck. Women may not have chest pain but experience unusual fatigue, shortness of breath and indigestion-like symptoms.

Sometimes coronary heart disease causes the heart to beat irregularly. This is known as **arrhythmia** and can itself lead to heart failure. Arrhythmia can be important in the diagnosis of coronary heart disease.

Stroke

The effects of a stroke will vary depending on the type of stroke, where in the brain the problem has occurred, and the extent of the damage. The more extensive the damage, the more severe the stroke and the lower the chance of full recovery. The symptoms normally appear very suddenly and include:

numbness
dizziness
confusion
slurred speech
blurred or lost vision, often only in one eye.

Visible signs often include paralysis on one side of the body with a drooping arm, leg or eyelid, or a dribbling mouth. The *right* side of the brain controls the *left* side of the body, and vice versa, therefore the paralysis occurs on the opposite side of the body to where the stroke occurred.

DID YOU KNOW?

Aneurysms

If part of an artery has narrowed and become less flexible, blood can build up behind it. The artery bulges as it fills with blood and an **aneurysm** forms. An atherosclerotic aneurysm of the aorta is shown in Figure 1.21.

What will eventually happen as the bulge enlarges and the walls of the aorta are stretched thin? Aortic aneurysms are likely to rupture when they reach about 6–7 cm in diameter. The resulting blood loss and shock can be fatal. Fortunately, earlier signs of pain may prompt a visit to the doctor. The bulge can often be felt in a physical examination or seen with ultrasound examination and it may be possible to surgically replace the damaged artery with a section of artificial artery.

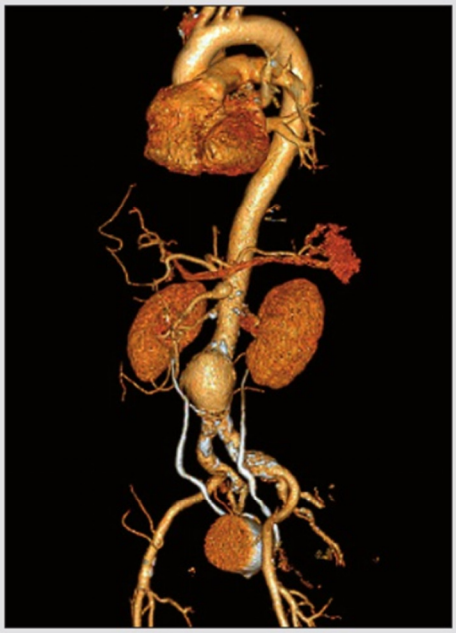


Figure 1.21 An aneurysm in the aorta below the kidneys. If an aneurysm ruptures it can be fatal.

EXTENSION

Read **Student Extension 1.1** to find out how you may be able to save someone's life by carrying out cardiopulmonary resuscitation.

EXTENSION

There are several tests used to diagnose cardiovascular disease that can be requested by doctors and you can read more details of these tests in **Student Extension 1.2**.

1.2 Who is at risk of cardiovascular disease?

Probability and risk

What do we mean by risk?

Risk is defined as 'the probability of occurrence of some unwanted event or outcome'. It is usually in the context of hazards, that is, anything that can potentially cause harm, such as the chance of contracting lung cancer if you smoke. Probability has a precise mathematical meaning and can be calculated to give a numerical value for the size of the risk. Do not panic – the maths is simple!

Taking a risk is a bit like throwing a die (singular of 'dice'). You can calculate the chance that you will have an accident or succumb to a disease (or throw a six). You will not *necessarily* suffer the accident or illness, but by looking at past circumstances of people who have taken the same risk, you can estimate the chance that you will suffer the same fate to a reasonable degree of accuracy.

Working out probabilities

There are six faces on a standard die. Only one face has six dots, so the chance of throwing a six is 1 in 6 (provided the die is not loaded). Scientists tend to express '1 in 6' as a decimal: 0.166 666 recurring (about 0.17). In other words, each time you throw a standard die, you have about a 0.17 or 17% chance of throwing a one, about a 17% chance of throwing a two, and so on.

When measuring risk you must always quote a time period for the risk. Here you have a 17% chance of throwing a one with each throw of the die.

In a Year 5 class of 30 pupils, six children caught head lice in one year. The risk of catching head lice in this class was therefore 6 in 30, or 1 in 5, giving a probability of 0.2 or 20% in a year.

Q 1.8 **(a)** In 2011 there were 727 724 recorded births in England and Wales. Of these, 3811 were stillbirths. Work out the chance of having a stillbirth in 2011.

(b) In 2012 there were 733 232 recorded births. There were 6.6% fewer still births than in 2011. Calculate how many stillbirths there were in 2012, and then calculate the probability of having a stillbirth in 2012.

Estimating risks to health

In 2010, 19 900 people in the UK died due to injuries or poisoning. The total UK population at the time was 62 262 000, so we can calculate the average risk in a year of someone in the UK dying from injuries or poisoning as:

19 900 in 62 262 00

or 1 in $\frac{62\,262\,00}{19\,900}$

= 1 in 3129

= $\frac{1}{3129}$

= 0.000 32 or 0.032%

Another way of working this out is as:

$\frac{19\,900}{62\,262\,00} = 0.000\,32$

However, when calculating a probability in relation to health, most people would find, for example, 1 in 3129 more meaningful than 0.000 32 or 0.032%.

SUPPORT
For help with working out probabilities look at the maths support sheet 8 – probability.

Assuming the proportion of people that die from injuries or poisoning remains much the same each year, this calculation gives an estimate of the risk for any year.

If we calculated the risk of any one of us developing lung cancer in our lifetime we would find a probability of 1 in about 1600. However, because lung cancer is much more likely if you smoke, the risk for smokers is far greater. When looking at calculated risk values you need to think about exposure to the hazard.

Q 1.9 Look at the causes of death listed below and put them in order, from the most likely to the least likely. You could also have a go at estimating the percentage probability of someone in the UK dying from each cause during a year.

- accidental poisoning
- heart disease
- injury purposely inflicted by another person
- lightning
- lung cancer
- railway accidents
- road accidents

Did you get it right?

People frequently get it wrong, underestimating or overestimating risk. We can say that there is about a 1 in 1700 risk of each of us dying from lung cancer in any one year, a 1 in 100 000 risk of our being murdered in the next 12 months, and a 1 in 1.7 million risk of our being involved in a fatal rail accident in a year. However, recent work on risk has concentrated not so much on numbers such as these but on the perception of risk.

ACTIVITY

Student Activity 1.11 asks you to estimate risks for a range of diseases using National Office for Statistics data.

Perception of risk

The significance of the perception of risk can be illustrated by decisions about eligibility for blood donation made by the American Red Cross, which provides about half of the USA's blood supplies. In 2001, they decided to ban all blood donations from anyone who has spent six months or more in any European country since 1980. They now ban blood donations from anyone who spent three or more months in the UK between 1980 and 1996, and from anyone spending five years or more in Europe since 1980. Their reason is the risk of transmitting variant Creutzfeldt–Jakob disease (vCJD) through blood transfusion. There is a chance of this happening. In the UK there have been a total of 174 cases of this fatal condition, which causes brain damage, with four cases associated with blood transfusions between 1996 and 1999. However, in the UK, only individuals who have received a blood transfusion since 1980 are ineligible to donate blood. As the USA is short of blood for blood transfusions, it is possible that more people may have died as a result of these 'safety precautions' than would have been the case without them.

WEBLINK

You can find out more about vCJD, the human form of bovine spongiform encephalopathy (BSE), by visiting the World Health Organisation website or the National CJD Research and Surveillance Unit website.

So why did America ban European blood donations? The likely reason was public perceptions of the risk of contracting vCJD. People will *overestimate* the risk of something happening if the risk is:

- involuntary (not under their control)
- not natural
- unfamiliar
- dreaded
- unfair
- very small.

If you look at this list you should be able to see why people may greatly overestimate some risks (such as the chances of contracting vCJD from blood transfusions) while underestimating others (such as the dangers of driving slightly faster than the speed limit or playing on a frozen lake).

Nowadays many risk experts argue that perceptions of risk are what really drive people's behaviour. Consider what happened when it became compulsory in the UK to use seat belts for children in the rear seats of cars (Figure 1.22). The number of children killed and injured *increased*. How could this be? John Adams, an academic at University College London, argues that this is because the parents driving felt safer once their children were wearing seat belts and so drove slightly less carefully. Unfortunately, this change in their driving behaviour was more than enough to compensate for any extra protection provided by the seat belts.

There is a tendency to overestimate the risks of sudden imposed dangers where the consequences are severe, and to *underestimate* a risk if it has an effect in the long-term future, even if that effect is severe, for example, the health risks associated with smoking or poor diet.

A useful distinction is sometimes made between risk and uncertainty. When we lack the data to estimate a risk precisely we are *uncertain* about the risk. For example, we are uncertain about the environmental consequences of many chemicals.

Figure 1.22 Some research suggests that young children who wear rear seat belts are more likely to die in an accident than those who don't, but this may be explained by parents' driving habits. Health risks are greatly affected by human behaviour.

Q 1.10 **(a)** In a school of 1300 students, in one term 10 students contracted verrucas from the school pool. In a letter to parents the head teacher said there was a less than 1% chance of any child catching a verruca in any term. Was the figure she quoted correct and what assumptions had she made in making this statement?

(b) In 2013, 208 755 cases of chlamydia were reported in England, with 43 386 of these cases being reported in London. One newspaper wanted to write a front page headline claiming that there was a higher risk of contracting this sexually transmitted infection in the capital compared with the rest of the country. Would they have been correct? Support your answer with calculated risk values. The population of England in 2013 was 53.5 million; the population of London was 8.3 million.

Different types of risk factor

In the UK the estimated risk of any one of us having fatal heart disease in any one year is about 1 in 600, compared with 1 in 1050 for a fatal stroke. However, these probabilities use figures for the whole population, giving averages which make the simplistic assumption that everyone has the same chance of having cardiovascular disease. This is obviously not the case.

The averages take no account of any risk factors – things that increase the chance of the harmful outcome. When assessing an individual's risk of bad health, all the contributing risk factors need to be established.

There are many different factors that contribute to health risks, for example:

- age
- heredity
- physical environment
- social environment
- lifestyle and behaviour choices.

CHECKPOINT

1.4 List the circumstances that make people more likely to **a** underestimate and **b** overestimate the risk of an event happening. Suggest an example for each situation.

Identifying risk factors – correlation and causation

To determine what the risk factors are for a particular disease, scientists look for **correlations** between potential risk factors and the occurrence of the disease. There is a correlation between two variables when a change in one variable is accompanied by a change in the other.

Two variables are *positively correlated* when an increase in one is accompanied by an increase in the other (Figure 1.23A). For example, the length of a TV programme and the percentage of the class asleep might be positively correlated. There is a positive correlation between the number of cigarettes smoked over a lifetime and the chance of developing cardiovascular disease. If the values of one variable decrease while the other increases, there is a *negative correlation* (Figure 1.23B).

SUPPORT

To find out more about correlations and how to statistically test whether there is a correlation between two variables see maths support sheet 12 – Spearman's rank correlation.

Large amounts of data are needed to ensure that the correlation is statistically significant; in other words, not just an apparent correlation due to chance.

It is important to realise that a correlation between two variables does not necessarily mean that the variables are causally linked. Two variables are *causally linked* when a change in one is responsible for a change in the other. It is easy to think of variables that are correlated where there is no **causation**. For example, worldwide, speaking English as your first language correlates quite well with having a greater-than-average life expectancy. This, though, is simply because countries like the USA, UK, Australia and Canada have a higher-than-average standard of living. It is this that causes increased life expectancy through better nutrition, medical care and so on, rather than the language spoken.

It is because of this logical gap between correlation and causation that scientists try, whenever they can, to carry out experiments in which they can control variables, to see if altering one variable really does have the predicted effect. To do this, scientists often set up a **null hypothesis**. They assume for the sake of argument that there will be no difference between an experimental group and a control group, and then test this hypothesis using statistical analysis.

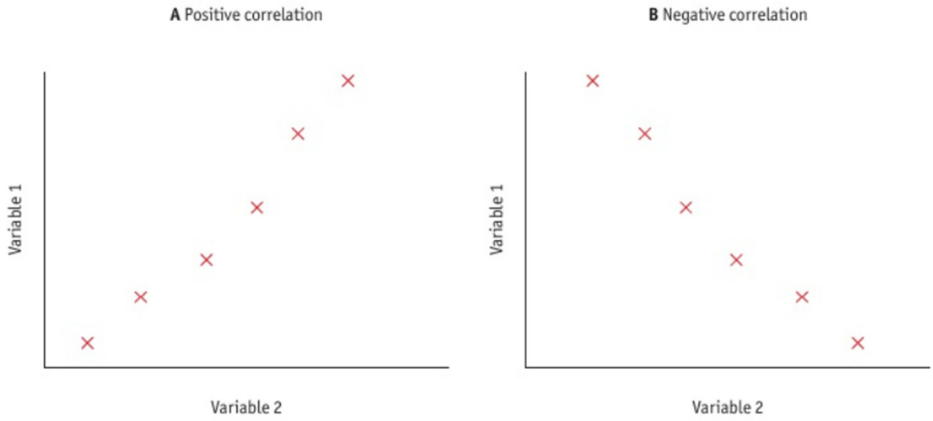


Figure 1.23 **A** When an increase in one variable is accompanied by an increase in the other, there is a positive correlation, giving a scattergram rising from left to right. **B** With a negative correlation, one set of data increases while the other falls, resulting in a graph going down from left to right.

Q 1.11 Strong correlations have been reported between the following pairs of variables. In each case, decide if it is a positive or negative correlation and if there is likely to be a causal link between the variables or not. Suggest a possible reason for the correlation.

(a) shark attacks and ice cream sales

(b) children's foot sizes and their spelling abilities

(c) lung cancer and smoking

(d) number of alcoholic drinks consumed and manual dexterity.

ACTIVITY

In **Student Activity 1.12** you can investigate the correlation between Internet access and life expectancy.

1.3 Risk factors for cardiovascular disease

Identifying risk factors for CVD

Large-scale studies have been undertaken to find the risk factors for many common diseases, including cardiovascular disease. Epidemiologists, scientists who study patterns in the occurrence of disease, look for correlations between a disease and specific risk factors.

Two commonly used designs for this type of study are cohort studies and case-control studies.

Cohort studies

Cohort studies follow a large group of people over time to see who develops the disease and who does not (Figure 1.24). These types of studies are prospective; at the start of the study none of the participants have the disease. Researchers are interested in what happens to them in the future. During the study people's exposure to suspected risk factors and whether they develop the disease is recorded so any correlations between the risk factors and disease development can be identified. It may take a long time for the condition to develop so these studies can take years and be very expensive.

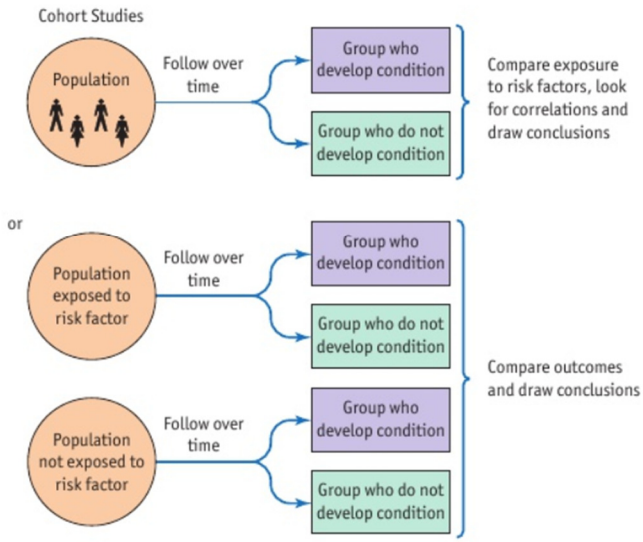


Figure 1.24 In cohort studies, risk factors experienced by those who develop the disease are compared with the risk factors of those who do not develop the disease to identify any correlations.

Cohort studies for CVD

The first major cohort study into CVD started in 1948. At the time, little was known about the causes of heart disease and stroke. The aim of the Framingham Heart Study was to identify the factors that contribute to the development of the disease. A random sample of 5209 men and women between the ages of 30 and 62 from the town of Framingham, Massachusetts, was recruited for the study. At the time of recruitment they had no symptoms of cardiovascular disease. In 1971, 5124 of the participants' adult children joined the study. A third generation was recruited to the study in 2002, adding a further 4095 individuals to the study, which continues to the present day.

Every two years the participants are asked to provide a detailed medical history, undergo a physical examination and tests, and answer questions about their lifestyle. The data are used to look for common features that contribute to the development of CVD. High blood pressure, high blood cholesterol, smoking, obesity, diabetes and physical inactivity were all identified as major CVD risk factors as a result of this study.

Other studies have confirmed these findings. The World Health Organization MONICA study (MONItoring trends and determinants in CArdiovascular disease), involving over 10 million people aged between 25–64 years old in 21 countries over 10 years, confirmed the link between several of these factors and increased occurrence of the disease. Although the study was completed in the late 1990's, the data is still being used for analysis in studies today.

Case-control studies

In a case-control study, a group of people with a disease (cases) are compared with a control group of individuals who do not have the disease (Figure 1.25). Information is collected about the risk factors that they have been exposed to in the past, allowing factors that may have contributed to development of the disease to be identified. These type of studies are retrospective.

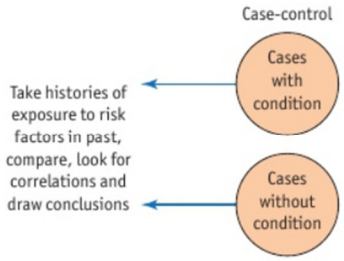


Figure 1.25 In case-control studies, risk factors experienced by those who have the disease are compared with the risk factors experienced by those who do not have the disease to identify any correlations.

The control group should be representative of the population from which the case group was drawn. Sometimes controls are individually matched to cases; known disease-risk factors, such as age and sex, are then similar in each case and control pair. This allows scientists to investigate the potential role of unknown risk factors. It should be noted that factors used to match the cases and controls cannot be investigated within the study, so it is important not to match any variables which could potentially turn out to be risk factors.

One of the first case-control studies was conducted in the 1950s by two British scientists, Richard Doll and Austin Bradford Hill, to determine whether there was a link between smoking and lung cancer. A group of hospital patients with lung cancer was compared with a second group who did not have cancer. The data indicated a correlation between smoking and lung cancer.

Q 1.12 Did the study by Doll and Hill prove that smoking caused lung cancer? Give a reason for your answer.

Case-control studies and CVD

Put the terms case-control and coronary heart disease into any search engine and you will find numerous case-control studies investigating the risk factors for CVD, including whether factors such as passive smoking or a siesta can increase your risk.

One global case control study, the INTERHEART study, screened all patients with a first heart attack admitted to 262 participating hospitals in 52 countries. A total of 15 152 cases and 14 820 controls, matched by age and gender, were included in the study. The researchers' original hypothesis was that risk factors for cardiovascular disease differ between people of varying ethnic and geographic origin. However, the study results, published in *The Lancet* in 2004, concluded that nine risk factors accounted for over 90% of the risk and they are the same for men and women in almost every geographic region, and for every racial/ethnic group.

Features of a good study

To identify correlations between risk factors and disease, studies need to be carefully designed. Recording a higher rate of heart disease in 50 people who drink more alcohol than the recommended amount compared with 50 people who drink less than the recommended amount, supports the suggestion that excess alcohol consumption increases the risk of developing heart disease. However, the group who drink more alcohol might also smoke more, do less exercise and eat a fatty diet. Any of these factors could be linked to developing the disease. A well-designed study tries to overcome these problems. When designing an epidemiological study there are some key points to consider.

ACTIVITY

In **Student Activity 1.13** you evaluate the design of studies used to determine health risk factors.

Clear aim

A well-designed study should include a clearly stated hypothesis or aim. The design of the study must be appropriate to the stated hypothesis or aim and produce results that are valid and reliable.

Representative sample

A representative sample must be selected from the wider population that the study's conclusions will be applied to. Selection bias occurs when those who participate in a study are not representative of the target population. For example, if a study aiming to look at the prevalence of disease in a community only sent out questionnaires to people on the electoral voting register, the findings may not be representative. This is because people under 18 years old, people who had recently moved in or out of the area, and people in temporary accommodation would be missed.

Differences between people asked to take part in a study and those who actually respond should also be considered before generalising findings to the target population. Non-participants can differ in important respects from participants. For example, if a study involves interviewing people at home during the day, those employed outside the home may be less likely to participate. The health and lifestyle of employed and non-employed people differs in many ways, so the findings could be misleading.

The proportion of individuals who drop out of a study after it has begun should be kept to a minimum. This is particularly important in cohort studies which follow people over long periods of time. People who drop out of studies often share common features. It is important to monitor the characteristics of the remaining participants to ensure that they are still representative of the target population.

Valid and reliable results

Any methods used must produce valid data. Measurements that provide information on what the study set out to measure, in other words data, are 'valid' if it measures what it is supposed to be measuring. If studying the effect of blood pressure on development of CVD, valid blood pressure measurements would be made using an appropriate blood pressure monitor. A survey to study the effect of alcohol consumption on the development of coronary heart disease could introduce problems with validity if it relied on the participants recalling the quantity of alcohol they consumed. Participants may not recall correctly because they were intoxicated, or they may underestimate because they are reluctant to admit their true consumption.

The method used to collect results must be reliable. A reliable method produces measurements that are repeatable and reproducible. The method will give similar results when repeated by one person using the same equipment and procedure under the same conditions over a short timescale. It will also give similar results when used at different times, or by different people. If measuring blood pressure, the same type of equipment and same procedure should be used each time the measurement is made. Any variables that could affect the measurement should be controlled or taken into account. A method using questionnaires, for example to conduct a survey on lifestyle factors, should use the same questions for each participant.

The disease diagnosis must be clearly defined, to ensure that different doctors record and measure symptoms in the same way. The development of coronary heart disease or onset of Alzheimer's, for example, must be measured and recorded using standard methods that are the same for all participants in the study.

Sample size

A sample must be large enough to produce results that could not have occurred by chance. In cohort studies of a rare disease, only a small proportion of the population will develop the disease. In case-control studies, only a few people may have been exposed to the factors under investigation, or, in the case of rare diseases, the number of cases may be low to start with. With larger samples more accurate estimates for the wider population can be calculated. For a condition that affects 5% of the population each year, a cohort of 1000 people would need to be followed for 10 years in order to collect information on 50 people with the disease. Similarly, in case-control studies, sufficient participants need to be recruited in order to detect any effects due to rare exposures.

Controlling variables

The potential effect of all variables that could be correlated with the disease should be considered when designing the study. For example, in a study of blood pressure and development of CVD, a group of people with low blood pressure is compared with a group with higher blood pressure. The data shows that the group with lower blood pressure has less CVD. However, if the average age of this group is less than the high pressure group, the difference in CVD development may be due to the age difference and not blood pressure. Age is a factor known to be associated with CVD. Matching case and control groups on variables known to correlate with the disease being studied will ensure that only the factor under investigation is influencing the outcome.

Q 1.13 The Framingham cohort is primarily white. Explain whether it would be valid to extrapolate these results to the general population of the USA.

CHECKPOINT

1.5 Produce a checklist of the features of a well-designed health risk study that ensure valid and reliable data are collected.

Risk factors for CVD

Your chances of having coronary heart disease or a stroke are increased by several inter-related risk factors, the majority of which are common to both conditions. These include:

- high blood pressure
- obesity
- blood cholesterol and other dietary factors
- smoking
- inactivity
- genetic inheritance.

Some of these you can control, while others you cannot.

Figure 1.26 Some of the potential risk factors for developing coronary heart disease are easy to identify, but may be difficult to control.

Age and gender make a difference

Q 1.14 Look at Table 1.1. What happens to your risk of developing cardiovascular disease as you get older?

Q 1.15 Does this mean that, at your age, you need not worry?

Age/years	Male		Female	
	Heart attack	Stroke	Heart attack	Stroke
16–44	1	1	1	1
45–64	19	8	8	3
65–74	47	17	31	12
75 and over	72	26	37	14

Table 1.1 Rates per 1000 population reporting longstanding diseases of the circulatory system by sex and age, 2011, Great Britain. *Source: Office for National Statistics General Household Survey.*

Q 1.16 Look at Table 1.2. Do these data suggest that males and females face the same risk of cardiovascular disease? Support your answer with calculated risk values.

	Male population (thousands)	Male deaths	Female population (thousands)	Females deaths
Under 35	13959	193	13620	98
35–44	4427	905	4513	297
45–54	4261	3054	4341	1011
55–64	3631	7025	3744	2308
65–74	2589	12835	2820	6410
75+	1938	41866	2916	53932
Totals	30805	65878	31954	64056

Table 1.2 Population and mortality data from cardiovascular disease (coronary heart disease and stroke combined) for the United Kingdom in 2010. *Sources: Office for National Statistics Population Estimates for UK, mid-2010; British Heart Foundation/Department of Public Health University of Oxford CHD Statistics 2012 edition.*

Q 1.17 Comment on the reliability of the data presented in Tables 1.1 and 1.2.

Q 1.18 Many people now think that a woman's reproductive hormones offer her protection from coronary heart disease until they decline during the menopause in middle age when her monthly periods cease. Do these data support this view? Explain whether it is valid to draw this conclusion from these data.

ACTIVITY

In **Student Activity 1.14** you compare data for coronary heart disease and stroke and look at trends over a ten-year period.

The risk of cardiovascular disease is higher for men than women in the UK. In England in 2010 the incidence of heart attacks among men was 154 per 100000, whereas the rate for women was only 34 per 100000 (*Source: BHF 2012*). These figures are about a half of those recorded in 2002. In both sexes, the prevalence of cardiovascular disease (the proportion of cases in the population) increases with age. This may be due to the effects of ageing on the arteries; they tend to become less elastic and may be more easily damaged. With increasing age the risks associated with other factors may increase, causing a rise in the number of cases of disease.

Q 1.19 Suggest what might have caused the fall in heart attacks described above.

High blood pressure

Elevated blood pressure, known as **hypertension**, is considered to be one of the most common factors in the development of cardiovascular disease. High blood pressure increases the likelihood of atherosclerosis occurring.

Blood pressure is a measure of the hydrostatic force of the blood against the walls of a blood vessel. You should remember that blood pressure is higher in arteries and capillaries than in veins (Figure 1.28). The pressure in an artery is highest during the phase of the cardiac cycle when the ventricles have contracted and forced blood into the arteries. This is the **systolic pressure**. Pressure is at its lowest in the artery when the ventricles are relaxed. This is the **diastolic pressure**.

Measuring blood pressure

A **sphygmomanometer** is the traditional device used to measure blood pressure. It consists of an inflatable cuff that is wrapped around the upper arm, and a manometer, or gauge, that measures pressure (Figure 1.27). When the cuff is inflated the blood flow through the artery in the upper arm is stopped. As the pressure in the cuff is released the blood starts to flow through the artery. This flow of blood can be heard using a stethoscope positioned on the artery below the cuff. A pressure reading is taken when the blood first starts to spurt through the artery that has been closed. This is the *systolic* pressure. A second reading is taken when the pressure falls to the point where no sound can be heard and it equals the lowest pressure in the artery. This is the *diastolic* pressure.

Figure 1.27 Nowadays blood pressure monitors can give digital readouts.

The SI units (International System of Units) for pressure are kilopascals, but in medical practice it is still traditional to use millimetres of mercury, mmHg. The numbers refer to the number of millimetres the pressure will raise a column of mercury.

Blood pressure is reported as two numbers, one 'over' the other, for example $\frac{140}{85}$. This means a systolic pressure of 140 mmHg and a diastolic pressure of 85 mmHg. For an average healthy person you would expect a systolic pressure of between 100 and 140 mmHg and a diastolic pressure of between 60 and 90 mmHg.

systolic pressure, the maximum blood pressure when the heart contracts → $\frac{140}{85}$ ← diastolic pressure, the blood pressure when the heart is relaxed

Peter's blood pressure was an incredible $\frac{240}{140}$

ACTIVITY

In **Student Activity 1.15** you use a sphygmomanometer, a blood pressure monitor, or the accompanying simulation to measure blood pressure.

What determines your blood pressure?

Contact between blood and the walls of the blood vessels causes friction and this impedes the flow of blood. This is called peripheral resistance. The arterioles and capillaries offer a greater total surface area than the arteries, resisting flow more, slowing the blood down and causing the blood pressure to fall. Notice in Figure 1.28 that the greatest drop in pressure occurs in the arterioles. The fluctuations in pressure in the arteries are caused by contraction and relaxation of the heart. As blood is expelled from the heart, pressure is higher. During diastole, elastic recoil of the blood vessels maintains the pressure and keeps the blood flowing.

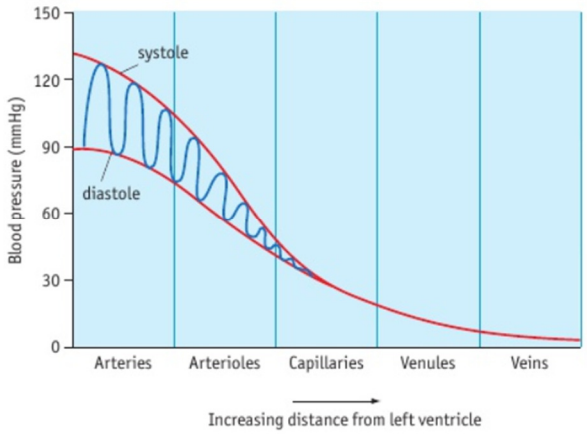


Figure 1.28 Blood pressure in the circulatory system. As peripheral resistance increases with greater total surface area, the flow of blood slows causing pressure to fall.

ACTIVITY

Draw a **concept map** for blood pressure to bring together all the ideas covered. A pro-forma is available in **Student Activity 1.16** if you do not want to start from scratch.

If the smooth muscles in the walls of an artery or an arteriole contract, the vessels constrict, making the lumen narrower and increasing resistance. In turn, your blood pressure is raised. If the smooth muscles relax, the lumen is dilated, so peripheral resistance is reduced and blood pressure falls. Any factor that causes arteries or arterioles to constrict can lead to elevated blood pressure. Such factors include natural loss of elasticity with age, release of hormones such as adrenaline, and a high-salt diet. High blood pressure can lead to atherosclerosis.

Tissue fluid and oedema

One sign of high blood pressure is **oedema** – fluid building up in tissues and causing swelling. Oedema may also be associated with kidney or liver disease, or with restricted body movement.

At the arterial end of a capillary, blood is under pressure. This forces fluid and small molecules normally found in plasma out through the tiny gaps between the cells of the capillary wall into the intercellular space, forming **tissue fluid**, which is also called interstitial fluid (Figure 1.29). Blood cells and larger plasma proteins stay inside the capillary; their larger size prevents them passing through the gaps in the capillary wall. The tissue fluid drains into a network of lymph capillaries which returns the fluid to the blood via a lymph vessel which empties into the vena cava.

If blood pressure rises above normal, more fluid may be forced out of the capillaries. In such circumstances, fluid accumulates within the tissues causing oedema.

Q 1.20 During left-side heart failure (the most frequent type) there is an increase in pressure in the pulmonary vein and left atrium. This is because blood continues to flow out of the right side of the heart to the lungs and return to the heart due to the action of breathing muscles whereas the left atrium and ventricle no longer pump blood out of the heart efficiently. Where in the body will blood pressure rise and oedema form?

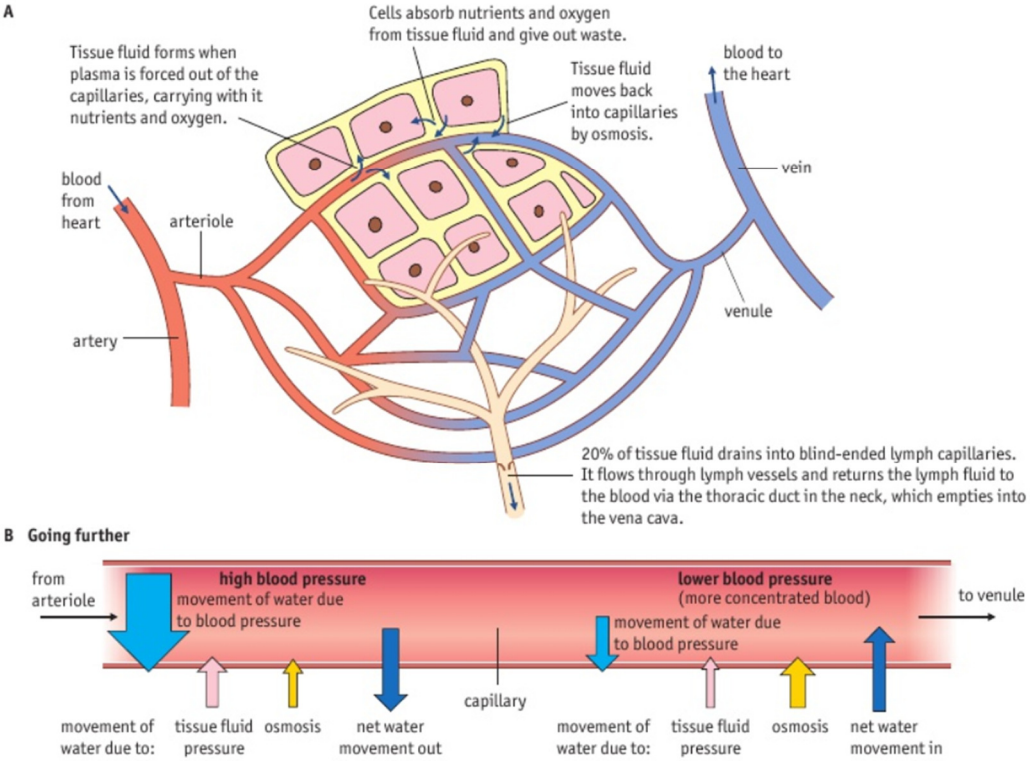


Figure 1.29 **A** Production of tissue fluid in a capillary bed. **B** Notice how the net movement in is less than the movement out. The excess fluid formed is drained away through the lymphatic system. For details on osmosis see page 70.

Dietary factors

Our choices of food, in particular the type and quantity of high-energy food that we eat, can either increase or decrease our risk of developing certain diseases, including cardiovascular diseases.

Energy units – avoiding confusion

Most packet foods these days detail the energy content per 100 g or other appropriate quantity. Figure 1.30 shows the energy content for a bar of chocolate. Why are two different units of energy quoted? Which should we use?

Traditionally, energy was measured in **calories**; one calorie is the quantity of heat energy required to raise the temperature of 1 cm^3 of water by 1 °C. Food labels normally display units of 1000 calories, called **kilocalories** (also called **Calories** with a capital C).

Figure 1.30 Nutritional information on a chocolate wrapper. How much energy does this chocolate contain? Notice that the label displays energy values in kilojoules and kilocalories.

The SI unit for energy is the joule (J), and 4.18 joules = 1 calorie. The **kilojoule** (1 kJ = 1000 joules) is used extensively in stating the energy contents of foods. In the popular press the Calorie is still used as the basic unit of energy, particularly with reference to weight control. Hence most food labels in the UK continue to quote both Calories and kilojoules (Figure 1.30).

Q 1.21 A newborn baby requires around 2000 kJ per day. Express this **a** in calories **b** in Calories.

SUPPORT
For information about SI units see maths support sheet 5 – SI units and standard form.

Where do we get energy from in our diet?

Carbohydrates, **lipids** (often called fats and oils) and **proteins** are constituents of our food that contain energy. Alcohol can also provide energy. The relative energy content of these nutrients is shown in Table 1.3.

Nutrient	Energy available per gram/kJ
Carbohydrates	16
Lipids	37
Proteins	17
Alcohol	29

Table 1.3 Energy content of nutrients.

Carbohydrates

The term carbohydrate was first used in the nineteenth century and means 'hydrated carbon'. If you look at each carbon in a carbohydrate molecule (see Figure 1.33) you should be able to work out why, bearing in mind that hydration means adding water.

ACTIVITY
Complete the interactive tutorial in **Student Activity 1.17** to help you understand carbohydrate structure.

Most people are familiar with sugar and starch being classified as carbohydrates, but the term covers a large group of compounds with the general formula $C_x(H_2O)_n$.

Sugars are either **monosaccharides**, single sugar units, or **disaccharides**, in which two single sugar units have combined in a condensation reaction. See Figures 1.31 and 1.32. Long straight or branched chains of sugar units form **polysaccharides**. The names tell the story – mono means one, di – two, and poly – many.

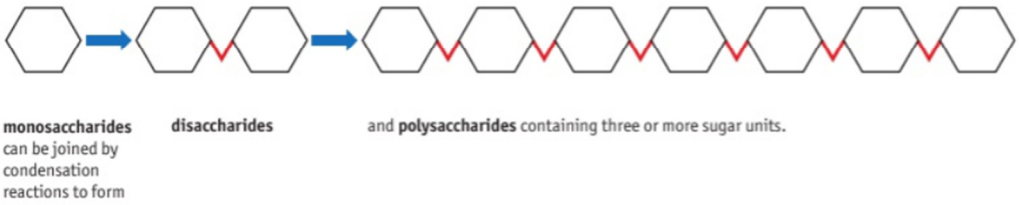


Figure 1.31 A simplified diagram to show how simple sugar units (monomers) can be joined to form more complex carbohydrates (polymers).

KEY BIOLOGICAL PRINCIPLE: LARGE BIOLOGICAL MOLECULES ARE OFTEN BUILT FROM SIMPLE SUBUNITS LINKED IN CONDENSATION REACTIONS

All organisms rely on the same basic building blocks as a result of our shared evolutionary origins. Hydrogen, carbon, oxygen and nitrogen account for more than 99% of the atoms found in living organisms. Relatively simple molecules join together in different ways to produce many of the large important biological molecules.

Polymers, such as polysaccharides (Figure 1.31), proteins and nucleic acids, are made by linking identical or similar subunits, called monomers, to form straight or branched chains. Lipids are another group of biological molecules also constructed by joining smaller molecules together, though they are not polymers since they are not chains of monomers. Large biological molecules have structures that are well suited to their functions.

In each case, the small molecules join together in a condensation reaction, so called because a water molecule is released as the two molecules combine in the reaction (see Figure 1.32). **Condensation** reactions are common in the formation of complex molecules. Addition of water in a **hydrolysis** reaction splits the molecule (Figure 1.32 and 1.36).

In Topic 1 we are looking at the structure and function of some carbohydrates and lipids, returning in later topics to see how these molecules have many other roles. In Topic 2 the structure and function of nucleic acids and proteins will be examined in detail.

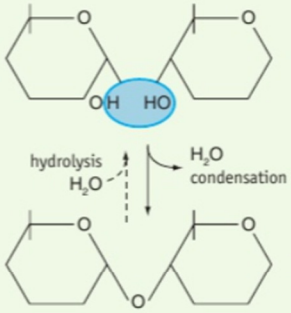


Figure 1.32 A simplified diagram to show the condensation and hydrolysis reactions involved in the formation or splitting of a disaccharide. In this example it is the reaction between two glucose molecules. Full details can be found in Figure 1.34.

Monosaccharides

Monosaccharides are single sugar units with the general formula $(CH_2O)n$, where n is the number of carbon atoms in the molecule. Monosaccharides have between three and seven carbon atoms, but the most common number is six. For example, the monosaccharides **glucose**, **galactose** and **fructose** all contain six carbon atoms and are known as **hexose** sugars (Figure 1.33).

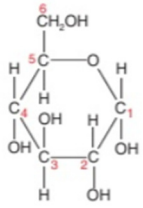
Q 1.22 What are the ratios of carbon, hydrogen and oxygen in monosaccharides?

A hexose sugar molecule has a ring structure formed by five carbons and an oxygen atom; the sixth carbon projects above or below the ring. The carbon atoms in the molecule are numbered, starting with 1 on the extreme right of the molecule. The side branches project above or below the ring, and their position determines the type of sugar molecule and its properties.

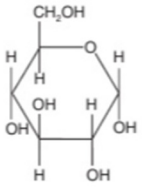
Monosaccharides provide a rapid source of energy. They are readily absorbed and require little or, in the case of glucose, no change before being used in cellular respiration. Glucose and fructose are found naturally in fruit, vegetables and honey; they are both used extensively in cakes, biscuits and other prepared foods.

Q 1.23 At first glance galactose and glucose look similar. Compare their molecular structures shown in Figure 1.33 and describe how they differ.

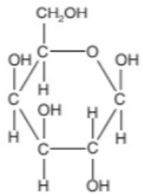
Glucose is important as the main sugar used by all cells in respiration. Starch and glycogen are polymers made up of glucose subunits joined together. When starch or glycogen is digested, glucose is produced. This can be absorbed and transported in the bloodstream to cells. This is known as α glucose, there is another form you will study in Topic 4.



This can also be shown more simply by omitting the Cs in the ring:



Galactose occurs in our diet mainly as part of the disaccharide sugar lactose, which is found in milk. Notice that the –OH groups on carbon 1 and carbon 4 lie on the opposite side of the ring compared with their position in glucose.



Fructose is a sugar which occurs naturally in fruit, honey and some vegetables. Its sweetness attracts animals to eat the fruits and so help with seed dispersal.

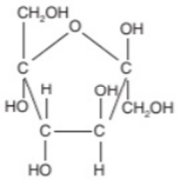


Figure 1.33 Glucose, galactose and fructose are examples of monosaccharides. They are all hexose sugars.

SUPPORT

For information about chemical reactions, bonds and carbohydrates see the biochemistry support on the website.

Disaccharides

Two single sugar units can join together and form a disaccharide (double sugar) in a **condensation** reaction releasing a water molecule as the two sugar molecules combine in the reaction. The bond that forms between the two sugar units is known as a **glycosidic bond** or link. Figure 1.34 shows the formation of the disaccharide maltose by a condensation reaction between two glucose molecules.

The bond in maltose is known as a 1,4 glycosidic bond because it forms between carbon 1 on one molecule and carbon 4 on the other. Remember that the carbons are numbered anticlockwise from the oxygen.

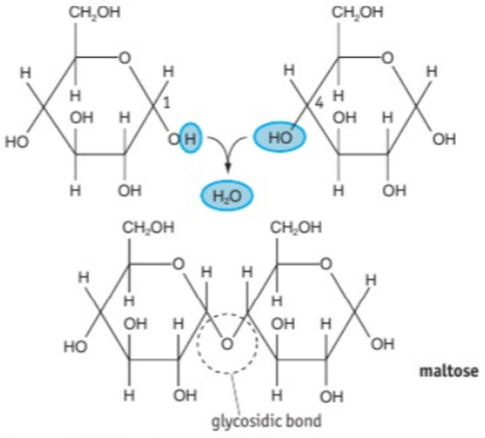
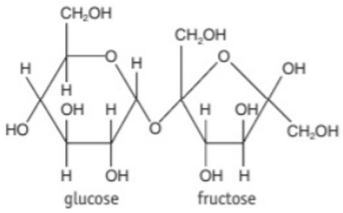


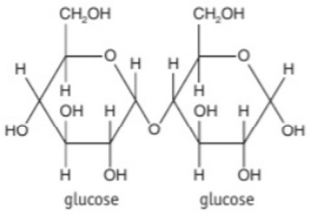
Figure 1.34 Two glucose molecules may join in a condensation reaction to form the disaccharide maltose. A water molecule is released during the reaction.

Common disaccharides found in food are **sucrose**, **maltose** and **lactose**. Their structures are shown in Figure 1.35.

Sucrose
Sucrose, formed from glucose and fructose, is the usual form in which sugar is transported around the plant.



Maltose
Maltose, formed from two glucose molecules, is the disaccharide produced when amylase breaks down starch. It is found in germinating seeds such as barley as they break down their starch stores to use for food.



Lactose
Galactose and glucose make up lactose, the sugar found in milk.

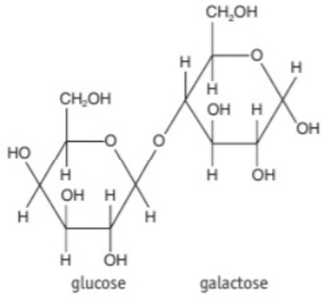


Figure 1.35 Disaccharides formed by joining two monosaccharide units.

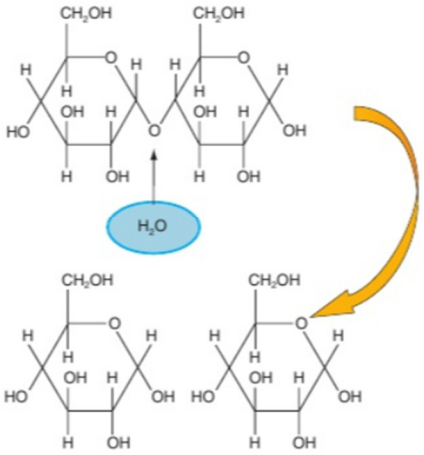


Figure 1.36 The glycosidic bond between the two glucose molecules in maltose can be split by hydrolysis. In this reaction water is added.

Q 1.24 Identify the glycosidic bond in each molecule shown in Figure 1.35.

(a) sucrose

(b) maltose

(c) lactose

The white or brown crystalline sugar we use in cooking, and the sugar in golden syrup or molasses, is sucrose. It is extracted from sugar cane or sugar beet.

The glycosidic link between two sugar units in a disaccharide can be split by **hydrolysis**. This is the reverse of condensation: water is added to the bond and the molecule splits into two (Figure 1.36). Hydrolysis of carbohydrates takes place when carbohydrates are digested in the gut and when carbohydrate stores in a cell are broken down to release sugars.

Q 1.25 Using the molecule in Figure 1.35, sketch what the monomers that make up lactose would look like after hydrolysis.

If monosaccharides are eaten they are rapidly absorbed into the blood causing a sharp rise in blood sugar. Polysaccharides and disaccharides (complex carbohydrates) have to be digested into monosaccharides before being absorbed, which takes some time, so the monosaccharides are released more slowly. Eating complex carbohydrates does not cause the swings in blood sugar levels we see after eating monosaccharides.

Lactose is the sugar present in milk. Many adults are intolerant of lactose and drinking milk will produce unpleasant digestive problems for these people. Asian and Afro-Caribbean people have a particularly high rate of lactose intolerance. One solution is to hydrolyse the lactose in milk, which converts the *disaccharide* lactose into the *monosaccharides* glucose and galactose. Industrially this is carried out using the enzyme lactase. Lactase can be immobilised in a gel, and milk is poured in a continuous stream through a column containing beads of the immobilised enzyme (Figure 1.37).

Figure 1.37 Lactose free milk is produced industrially by pouring milk through a column containing the enzyme lactase immobilised in gel beads. The lactase catalyses the hydrolysis of the lactose. Syrup which is used in the food industry is produced in the same way from whey waste from cheese-making.

ACTIVITY

In **Student Activity 1.18** you immobilise lactase and use it to hydrolyse lactose.

DID YOU KNOW?

Why do we have such a sweet tooth?

We have taste receptors on the tongue for five main tastes – sweet, sour, bitter, salty and umami (the taste associated with monosodium glutamate or MSG). It is likely that the sweet-taste receptors enable animals to identify food that is easily digestible, whereas bitter-taste receptors provide a warning to avoid potential toxins. Humans, along with many other primates (apes and monkeys), have many more sweet-taste receptors than most other animals. Our sweet-taste receptors help us to identify when fruit is ready to eat.

Polysaccharides

Polysaccharides are polymers made up from simple sugar monomers joined by glycosidic bonds into long chains, as shown in Figure 1.38. Each sugar monomer is joined to the chain in a condensation reaction with a water molecule released during the reaction.

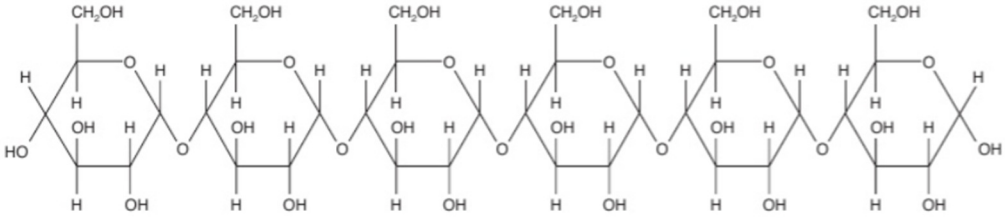


Figure 1.38 Glycosidic bonds join the glucose molecules that make up this polysaccharide.

Q 1.26 How many water molecules will have been released in the formation of the molecule in Figure 1.38?

There are three main types of polysaccharide found in food: **starch** and **cellulose** in plants, and **glycogen** in animals. Although all three are polymers of glucose molecules, they are sparingly soluble (they do not dissolve easily) and do not taste sweet.

Starch and glycogen act as energy storage molecules within cells. These polysaccharides are suitable for storage because they are compact molecules with low solubility in water. This means that they do not affect the concentration of water in the cytoplasm and so do not affect movement of water into or out of the cell by osmosis. See Topic 2 for details of osmosis.

Starch, the storage carbohydrate found in plants, is made up of a mixture of two molecules, **amylose** and **amylopectin**.

- Amylose is composed of a straight chain of between 200 and 5000 glucose molecules with 1,4 glycosidic bonds between adjacent glucose molecules. The position of the bonds causes the chain to coil into a spiral shape.
- Amylopectin is also a polymer of glucose but it has side branches. A 1,6 glycosidic link holds each side branch onto the main chain.

Figure 1.39 attempts to show these complex 3D structures. Starch grains in most plant species are composed of about 70–80% amylopectin and 20–30% amylose. The compact spiral structure of starch and its insoluble nature make it an excellent storage molecule. It does not diffuse across cell membranes and has very little osmotic effect within the cell.

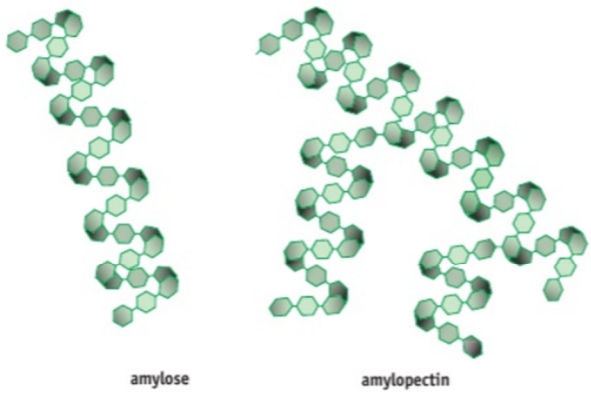


Figure 1.39 The two forms of starch – amylose and the branched chain amylopectin. The chains of glucose molecules coil to form a spiral. This is held in place by hydrogen bonds that form between the hydroxyl (OH) groups which project into the centre of the spiral.

Starch is a major source of energy in our diet and is common in many foods (Figure 1.40). It occurs naturally in fruit, vegetables and cereals, often in large amounts. The sticky gel formed when starch is mixed with water makes it a good thickening agent and it is also added to many food products as a replacement for fat.

Figure 1.40 Foods high in starch.

Glycogen is used by bacteria, fungi and animals instead of starch as an energy store. It is another polymer composed of glucose molecules. Its numerous side branches (Figure 1.41) mean that it can be rapidly hydrolysed, giving easy access to stored energy. In humans glycogen is stored in the liver and muscles.

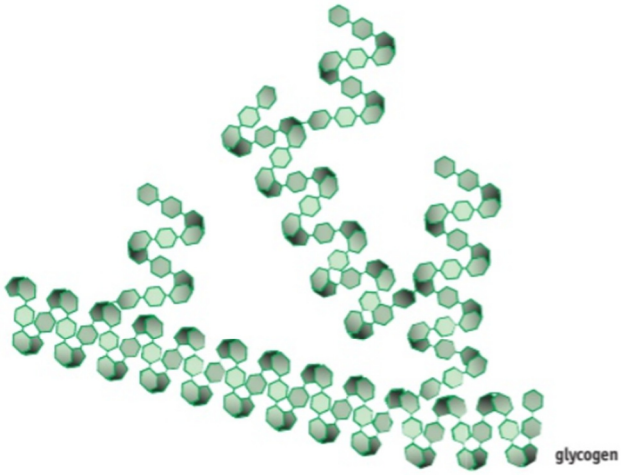


Figure 1.41 Glycogen, the storage carbohydrate found in animal cells, has a branched structure similar to amylopectin.

CHECKPOINT

1.6 Produce a table of comparison, differences and similarities, between monosaccharides, disaccharides and polysaccharides.

Cellulose in the diet is known as **dietary fibre**, and it is also referred to as a non-starch polysaccharide. Up to 10 000 glucose molecules are joined to form a straight chain with no branches (the glucose molecules have a slightly different structure to those found in starch). The structure and function of cellulose are considered in Topic 4; it is not required at this stage.

Indigestible in the human gut, cellulose has an important function in the movement of material through the digestive tract. Dietary fibre is thought to be important in the prevention of 'Western diseases' such as coronary heart disease, diabetes and bowel cancer.

Lipids

Lipid is the general term for fats and oils. In food, lipids enhance flavour and palatability, making it feel smoother and creamier (Figure 1.42). They supply over twice the energy of carbohydrates with 37 kJ of energy per gram of food. This can be an advantage if large amounts of energy need to be consumed in a small mass of food. It also means a large amount of energy can be stored in a small mass, for example in seeds.

Figure 1.42 Which is more popular – with or without fat?

Lipids are organic molecules found in every type of cell. They are insoluble in water but soluble in organic solvents such as ethanol. Most of the lipids that we eat are **triglycerides** which are used as energy stores in plants and animals. Triglycerides are made up of three fatty acids and one glycerol molecule linked by condensation reactions (Figure 1.43). The bond that forms between each fatty acid and the glycerol is known as an **ester bond**. Three ester bonds are formed in a triglyceride. Each is formed in a condensation reaction with the release of a water molecule.

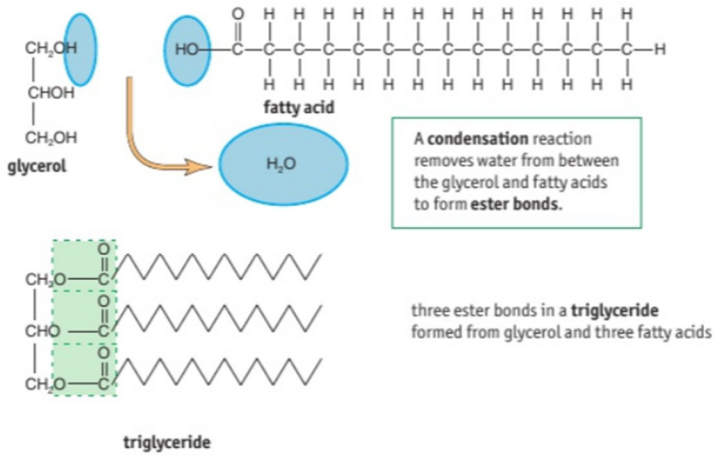


Figure 1.43 The formation of a triglyceride, a common type of lipid. The fatty acid chains in the triglyceride are simplified, each point in the zig-zag shows the position of a carbon atom.

Saturated fats

If the fatty acid chains in a lipid contain the maximum number of hydrogen atoms they are said to be **saturated**. In a saturated fatty acid the hydrocarbon chain is long and straight (Figure 1.44).

There are no carbon to carbon double bonds in the saturated fatty acid chain and no more hydrogens can be added to it. Animal fats from meat and dairy products are major sources of saturated fats.

Straight, saturated hydrocarbon chains can pack together closely. The strong intermolecular bonds between triglycerides made up of saturated fatty acids result in fats that are solid at room temperature.

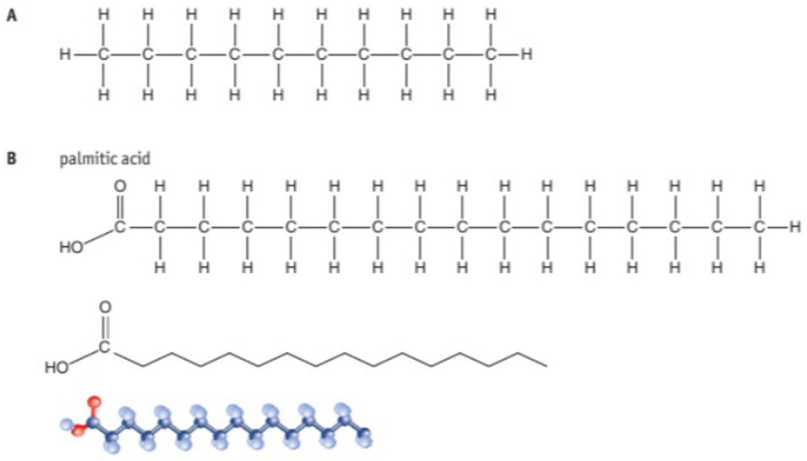


Figure 1.44 **A** A saturated hydrocarbon chain. **B** Palmitic acid, a saturated fatty acid with a straight hydrocarbon chain containing 16 carbons in total. It can be drawn in several ways with or without the carbons and hydrogens in the chain, or as a 3D model.

Unsaturated fats

Monounsaturated fats have one double bond between two of the carbon atoms in each fatty acid chain (Figure 1.45). **Polyunsaturated** fats have a larger number of double bonds. A double bond causes a kink in the hydrocarbon chain. These kinks prevent the unsaturated hydrocarbon chains packing closely together. Increasing the distance between the molecules weakens the intermolecular forces between the unsaturated triglycerides resulting in oils that are liquid at room temperature. Olive oil is particularly high in monounsaturated fats. Most other vegetable oils, nuts and fish are good sources of polyunsaturated fats.

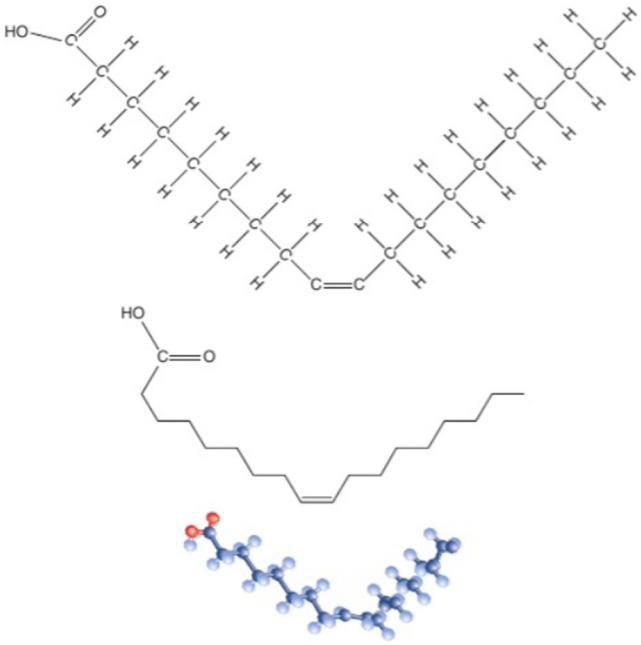


Figure 1.45 Oleic acid, an unsaturated fatty acid, has a double bond which causes a kink in the hydrocarbon chain. It can be drawn in several ways.

Unsaturated fats can be made more solid at room temperature by adding hydrogen to the double bonds making them saturated. These hydrogenated-, or trans-, fats are sometimes produced by the food industry and used in processed foods. Trans-fats do occur naturally at very low levels in meat and dairy products.

Other types of lipid

Cholesterol (Figure 1.46) is a short lipid molecule which is essential for good health. It is a vital component of cell membranes with roles in their organisation and functioning. The steroid sex hormones (such as progesterone and testosterone) and some growth hormones are made

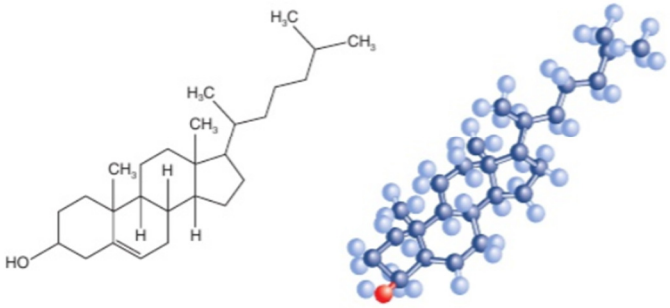


Figure 1.46 Alternative ways of showing the structure of cholesterol.

ACTIVITY

Student Activity 1.19
Complete this ICT-based tutorial to understand lipid structure.

from cholesterol. Bile salts, involved in lipid digestion and assimilation, are also formed from cholesterol. Cholesterol is made in the liver from saturated fats and also obtained in our diet. It is found associated with saturated fats in foods such as eggs, meat and dairy products. However, there are concerns that a high blood cholesterol level can be bad for us.

Phospholipids are similar to triglycerides but one of the fatty acids is replaced by a negatively charged phosphate group. In Topic 2 you will study the detailed structure of phospholipids and their role in forming cell membranes.

Fats provide more than just energy

As well as supplying energy in the diet fats also provide a source of **essential fatty acids**, that is, fatty acids that the body needs but cannot synthesise. Fats must therefore be present in a balanced diet to avoid deficiency symptoms. For example, a deficiency of linoleic acid (an essential fatty acid) can result in scaly skin, hair loss and slow wound healing. In addition, the fat-soluble vitamins (A, D, E and K) can only be absorbed if our diet includes food containing fat.

The energy balance

Look on food labels and you will often see recommended daily amounts for nutrients along with daily energy requirements for men and women. But how much energy is right for each of us, and what happens if we do not get it right?

Getting it right

The UK Department of Health publishes dietary guidelines for most nutrients. They used to give recommended daily amounts but in 1991 these were largely replaced with dietary reference values (DRVs). DRVs are estimates of requirements and are not recommendations or goals for individuals. DRVs include:

- an estimated average requirement (EAR)
- a lower reference nutrient intake (LRNI)
- a higher reference nutrient intake (HRNI).

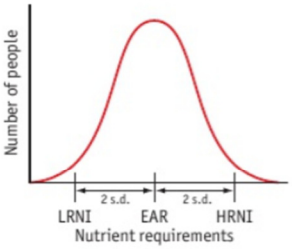


Figure 1.47 For a group of people who receive adequate nutrients, the range of intakes will vary around the EAR.

These effectively provide a range of values within which a healthy balanced diet should fall (Figure 1.47). Upper and lower limits have not been set for carbohydrates and fats. Instead, estimated average requirements for energy are suggested plus the average percentage that should come from the different energy components of a diet. Tables 1.4 and 1.5 give the recommendations.

SUPPORT
The LRNI and HRNI lie two standard deviations from the EAR. For more information on standard deviation see maths support 10 – standard deviation.

Q 1.27 Look at Table 1.4. Compare the energy requirements of males and females, commenting on changes with age.

Estimated average requirements (EARs) for energy per day				
Age	Males		Females	
	(kJ/day)	(kcalories/day)	(kJ/day)	(kcalories/day)
15 years	11800	2820	10000	2390
16 years	12400	2964	10100	2414
17 years	12900	3083	10300	2462
18 years	13200	3155	10300	2462
19–24 years	11600	2772	9100	2175
25–34 years	11500	2749	9100	2175
35–44 years	11000	2629	8800	2103
45–54 years	10800	2581	8800	2103
55–64 years	10800	2581	8700	2079
65–74 years	9800	2342	8000	1912
75+ years	9600	2294	7700	1840

Table 1.4 Estimated average requirements for energy in kJ per day. The recommendation for the general adult population is 2000 kcal for women and 2500 kcal for men. *Source: Scientific Advisory Committee on Nutrition (SCAN), 2011.*

WEBLINK
The British Nutrition Foundation website provides detailed information on nutrient requirements and recommendations.

% of daily total food energy intake excluding alcohol			
Fat		Carbohydrates	
Saturated	Unsaturated	Starch	Sugars
11	24	39	11

Table 1.5 Dietary guidelines for percentage of daily energy that should come from carbohydrate and fat. Alcohol should provide no more than 5% of energy in the diet.

Getting it wrong

We have to be aware that we need both carbohydrates and fats in our diet for good health, but that there are consequences if we get it wrong by consuming too much energy or if the percentage supplied by the various components differs greatly from the guidelines.

You need a constant supply of energy to maintain your essential body processes, such as the pumping of the heart, breathing and maintaining a constant body temperature. These processes go on all the time, even when you are completely at rest. The energy needed for these essential processes is called the **basal metabolic rate** (BMR) and varies between individuals. BMR is higher in:

- males
- heavier people
- younger people
- more active people.

ACTIVITY

Student Activity 1.20 uses dietary analysis software to help you to work out your own energy budget and determine whether you are getting the right amount of energy from the best sources.

The estimated average requirements for energy shown in Table 1.4 were calculated by multiplying basal metabolic rate by a physical activity level factor of 1.4, which reflects current average levels of physical activity. This gives estimates suitable for people who do little physical activity at work or in leisure time.

Q 1.28 The requirements in Table 1.4 can be altered to give estimates for very active people by using a physical level factor of 1.9. Use this value to work out what the EAR of a very active 17 year old male and female.

Adult females usually require about 8400 kJ a day and adult males usually need about 10 500 kJ a day, but an athlete may require double this quantity or even more (Figure 1.49).

If you eat fewer kilojoules per day than you use you have a negative energy balance and energy stored in the body will be used to meet the demand. A regular shortfall in energy intake will result in weight loss. If you routinely eat more energy than you use, you have a positive energy balance. The additional energy will be stored and you will put on weight (Figure 1.48).

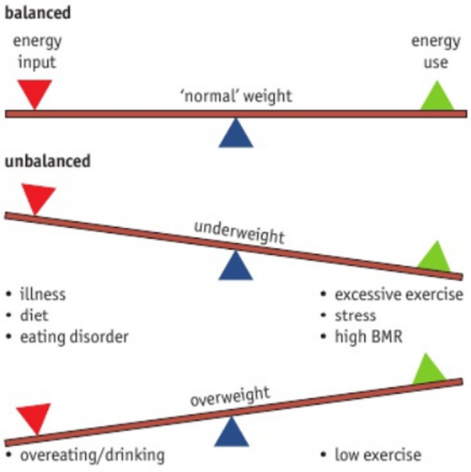


Figure 1.48 The balance between energy input and energy output determines whether the body maintains, gains or loses weight.

Figure 1.49 The winner of the Tour de France 2014, Vincenzo Nibali. During the tour the cyclists use about 33 000 kJ a day.

In England it is estimated that over 65% of men (16 years and over) and over 55% of women (16 years and over) are either overweight or obese. Approximately 25% of the adult population are obese (2010 – 26%) and **obesity** in men has tripled since the mid-1980s 6–8%. The 2010 Health Survey of England reported that about 30% of 2–15-year-olds were overweight, including 13.7% who were obese. The increasing prevalence of obesity among both children and adults has been called an epidemic in Western Europe and the USA.

Defining 'overweight' and 'obese'

Body mass index (BMI) is a conventionally used method of classifying body weight relative to a person's height. To calculate BMI, body mass (in kg) is divided by height (in metres) squared:

$$\text{BMI} = \frac{\text{body mass/kg}}{\text{height}^2/\text{m}^2}$$

For example, the BMI of a person with a body mass of 65 kg and height of 1.72 m is 22.0. This figure can then be used to identify the category of body weight to which that person belongs, as shown in Table 1.6. BMI does not have an exact correlation with fat levels in the body. BMI may not be accurate for athletes, children, people over 60, or those with long-term health conditions.

ACTIVITY
Work out BMI and waist-to-hip ratio using **Student Activity 1.21**.

BMI	Classification of body weight
<18.5	Underweight
18.5–24.9	Normal
25.0–29.9	Overweight
30.0–40.0	Obese
>40.0	Severely obese

Table 1.6 The use of BMI to classify body weight.

Q 1.29 **(a)** Calculate the body mass index of a person with a body mass of 85 kg and height of 1.68 m. How would you describe the body weight of this person?

(b) Rajesh is 191 cm tall. His BMI is 30. How much does he weigh in kg?

There is evidence that **waist-to-hip ratio** is a better measure of obesity than BMI and shows a highly significant association with risk of heart attack. A large-scale case-control study, the INTERHEART Study, looked at 27 098 people in 52 countries; 12 461 of these people had already had a heart attack and they were matched with control individuals of the same sex and similar age who had no history of cardiovascular disease. The participants were asked about their health, economic status, lifestyle and family history of coronary heart disease. Their weight, height, waist and hip circumference were measured to allow BMI and waist-to-hip ratios to be calculated.

The results found that BMIs in men and women who had previously had a heart attack were only slightly higher than the BMIs of the control group. However, their waist-to-hip ratios were much higher than those of the control group. There is a continuous positive correlation between waist-to-hip ratio and heart attack (Figure 1.50). Waist-to-hip ratio gives a better indication of who is at risk of a heart attack, even in people with BMIs of less than 20.

Waist-to-hip ratio is calculated by dividing waist circumference by hip circumference. The waist is measured unclothed at the narrowest point between the rib margin and the top of the hip bone. The hip circumference is measured in light clothing at the widest point around the buttocks. A non-stretchable tape measure is used attached to a spring scale with a tension of 750 g. Ideally men should not have a waist-to-hip ratio over 0.90 and women's should not be greater than 0.85.

Q 1.30 A 45-year-old man has a waist measurement of 91 cm and a hip measurement of 115 cm. Calculate his waist-to-hip ratio and comment on his risk of heart disease.

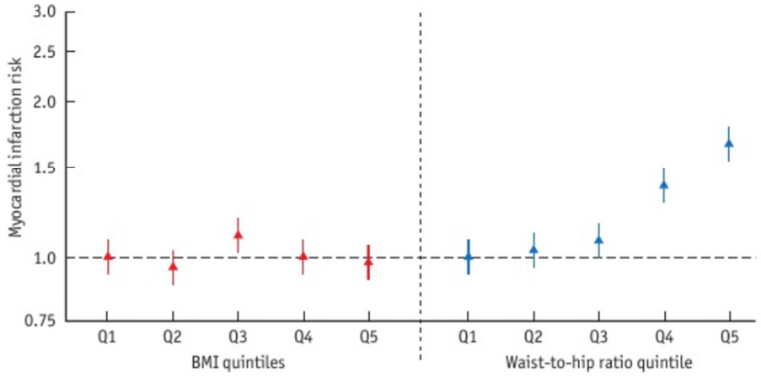


Figure 1.50 The relationship between waist-to-hip ratio and heart attack.

A poor diet, particularly one high in sugar and fat, and a sedentary lifestyle are the major contributing factors to the development of obesity. There is evidence in the UK that fat consumption has actually declined since 1990, but greater inactivity means that obesity and associated conditions are on the increase.

A high-fat diet will not necessarily result in weight gain if combined with a high level of physical activity. This was clearly illustrated by Ranulph Fiennes and Mike Stroud during their 1993 expedition to cross the Antarctic on foot – they found 23 000 kJ a day inadequate to meet their energy needs (Figure 1.51).

Figure 1.51 Over 23 000 kJ a day and Ranulph Fiennes still lost weight! Even with a padded jacket he looks thin.

Consequences of obesity

Obesity increases your risk of coronary heart disease and stroke, even without other risk factors being present. The more excess fat you carry, especially around your middle, the greater the risk to your heart. Obesity can also greatly increase your risk of type II diabetes. Type II diabetes is also referred to as non-insulin-dependent diabetes or late-onset diabetes. It, in turn, increases your risk of coronary heart disease and stroke.

DID YOU KNOW?

What is type II diabetes?

There are about 3 million people with diabetes in the UK and probably at least another 850 000 people with diabetes who do not know they have the condition. Type I occurs when the body is unable to make insulin.

In type II diabetes the body either does not produce sufficient insulin or the body fails to respond to the insulin that is produced. You probably know that **insulin** is the hormone that helps regulate **blood glucose levels**. After a meal the level of blood glucose rises. In response to this change, the **pancreas** produces insulin and secretes it into the bloodstream. The insulin causes cells to absorb glucose, and therefore the blood glucose level returns to normal. Continually high blood glucose levels due to frequent consumption of sugar-rich foods can reduce the sensitivity of cells to insulin, resulting in type II diabetes. It may take years to develop and may not even be diagnosed. It is thought that up to a million people in the UK could be unaware that they have type II diabetes. Type II is the more common of the two main types of diabetes and accounts for between 85 and 95% of all people with diabetes.

Obesity can also raise your blood pressure and elevate your blood lipid levels, two classic risk factors for cardiovascular disease. Much media attention, particularly in advertising, is focused on saturated fats and cholesterol.

Why is cholesterol such a problem?

There is a considerable amount of evidence to show that the higher your blood cholesterol level, the greater your risk of coronary heart disease (Figure 1.52A). The British Regional Heart Study reported similar results, with blood cholesterol having a log-linear relationship with CHD risk (Figure 1.52B).

Q 1.31 Using the data in Figure 1.52A, comment on the relationship between serum cholesterol levels and the risk of death from coronary heart disease.

SUPPORT
To find out more about using logs look at maths support sheet 2 Presenting data – graphs on the website.

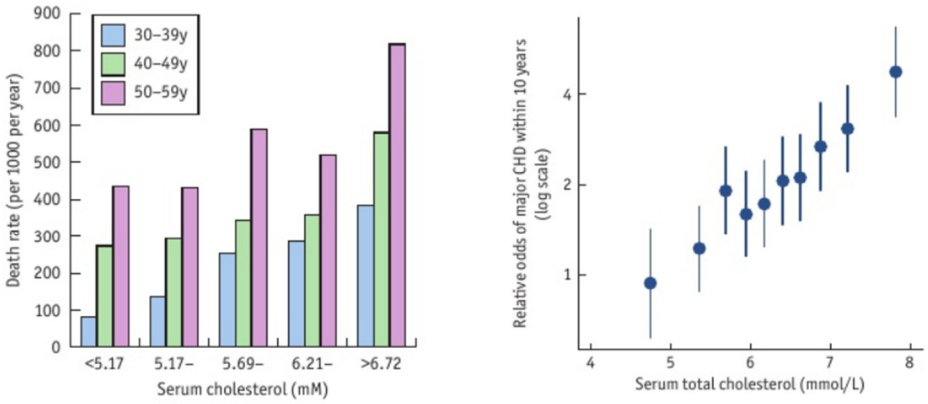


Figure 1.52 **A** The effect of blood cholesterol levels on the incidence of coronary heart disease. Data from the Framingham Study. **B** Relative odds of major CHD within 10 years by usual serum total cholesterol. Estimates are presented for each of ten equal groups and are adjusted for age, smoking status, diastolic blood pressure and serum total cholesterol.

The World Health Organisation has estimated that in high-income countries, 50% of CVD events can be attributed to blood cholesterol levels over 3.8 mmol/l.

The INTERHEART case control study estimated that in Western Europe, 45% of heart attacks are due to an abnormal blood cholesterol level.

However, as you may realise, it is not quite as simple as that! Like all lipids, cholesterol is not soluble in water. In order to be transported in the bloodstream, insoluble cholesterol is combined with proteins to form soluble **lipoproteins**.

There are two major transport lipoproteins.

- **Low-density lipoproteins (LDLs)** – triglycerides from fats in our diet combine with cholesterol and protein to form LDLs which transport the cholesterol to body cells. LDLs circulate in the bloodstream and bind to receptor sites on cell membranes before being taken up by the cells where the cholesterol is involved in the synthesis and maintenance of cell membranes. Excess LDLs overload these membrane receptors, resulting in high blood cholesterol levels. This LDL cholesterol may be deposited in the artery walls forming atheromas.
- **High-density lipoproteins (HDLs)** – HDLs have a higher percentage of protein and less cholesterol compared with LDLs, hence their higher density. High-density lipoproteins are made when triglycerides from fats combine with cholesterol and protein. HDLs transport cholesterol from the body tissues to the liver where it is broken down. This lowers blood cholesterol levels and helps remove the fatty plaques of atherosclerosis.

LDLs are associated with the formation of atherosclerotic plaques whereas HDLs reduce blood cholesterol deposition. Therefore, it is desirable to maintain a higher level of HDL (the so-called 'good cholesterol' or 'protective cholesterol') and a lower level of LDL (the so-called 'bad cholesterol'); a higher HDL:LDL ratio in the blood.

Saturated fats versus unsaturated fats

Studies have shown that saturated fat in the diet increases LDL and HDL cholesterol, however, the increase in LDL cholesterol is greater. Studies have also reported that although replacing saturated fat with polyunsaturated fat decreases both LDL and HDL levels, a greater reduction in LDLs means that the HDL:LDL ratio is increased with a protective effect. It is recommended that eating a low-fat diet that particularly avoids saturated fats will help reduce total blood cholesterol, and especially LDL cholesterol, which constitutes the major component of the cholesterol risk for CVD. Saturated fats may also reduce the activity of LDL receptors so the LDLs are not removed from the blood, thus further increasing the blood cholesterol levels and CVD risk

Q 1.32 Up until the menopause, women generally have higher HDL: LDL ratios than men. What consequences would you expect this to have for the incidence of coronary heart disease in women compared with men?

Q 1.33 A person stops eating butter on their toast and starts using a 'lighter' butter instead that contains 25% vegetable oil. What effect will this have on their blood LDL levels? Explain your answer.

Q 1.34 It been suggested that HDLs may reduce platelet aggregation. Explain why this might reduce the risk of a heart attack occurring.

Measuring blood LDL level is difficult and expensive, but it is relatively easy to measure the total cholesterol level. You can even test your own cholesterol at home now, using a home test kit (Figure 1.53). Testing for total cholesterol may be part of a cardiovascular assessment for someone suspected of being at risk of CVD.

Conflicting evidence

Many studies provide evidence for a positive correlation between fat consumption and CHD mortality rates (Figure 1.52). However, conflicting evidence has also been reported. For example, in France CHD is low despite high intake of cholesterol and saturated fat. The mean total blood cholesterol levels in France and the UK are similar but the mortality rate due to CHD is much lower in France.

An analysis of 72 cohort and randomised control studies into fatty acid intake and CHD published in 2014 concluded that there was no significant association between saturated fat and coronary disease, or evidence that polyunsaturated fats have a protective effect. However, the authors noted limitations in the studies and the need for further study. It did conclude that there was a significant risk associated with trans-fats, which are polyunsaturated oils hydrogenated to make them more solid for use in processed food industry. The Scientific Advisory Committee in Nutrition recommend that trans-fats should not exceed 2% of food energy. Since 2008, UK supermarkets and fast food chains have stopped using trans-fats. Food manufactured outside of the UK could still contain trans-fats.

Q 1.35 Several hypotheses have been put forward to explain the difference in CHD in France and the UK. Suggest what might cause the difference.

Smoking

Smoking cigarettes is one of the major risk factors for the development of cardiovascular disease. A 50-year cohort study of British doctors found that CHD mortality was 60% higher in smokers compared with non-smokers. The constituents in smoke affect the circulatory system in the following ways.

- Carbon monoxide in the smoke binds to the haemoglobin (the oxygen-carrying protein in red blood cells) instead of oxygen. This reduces the supply of oxygen to cells. This will result in an increased heart rate as the body reacts to provide enough oxygen for the cells.
- Nicotine in smoke stimulates the production of the hormone adrenaline. This hormone causes an increase in heart rate and also causes arteries and arterioles to constrict, both of which raise blood pressure.

ACTIVITY

In **Student Activity 1.22** you look at some evidence for a causal relationship between blood cholesterol levels and cardiovascular disease and some conflicting evidence.

Figure 1.53 A home cholesterol kit.

- The numerous chemicals that are found in smoke can cause damage to the lining of the arteries, triggering atherosclerosis.
- Smoking has also been linked with a reduction in HDL cholesterol level.

Q 1.36 Suggest why doctors might prescribe nicotine patches if nicotine causes an increase in blood pressure?

Inactivity

The British Heart Foundation considers physical inactivity to be one of the most common risk factors for heart disease. They estimate that only three or four in every 10 men and two or three in every 10 women do sufficient exercise to give some protection against heart disease. It has been shown that being active can halve the risk of developing coronary heart disease.

Moderate exercise such as walking, cycling or swimming, helps prevent high blood pressure and can help to lower it. Exercise not only helps maintain a healthy weight, it also seems to raise HDL cholesterol without affecting LDL cholesterol levels. It also reduces the chance of developing type II diabetes and helps in controlling the condition.

A person who is physically active is much more likely to survive a heart attack or stroke compared with someone who has been inactive. The Department of Health recommends adults undertake two and a half hours of moderate to vigorous physical activity each week and aim to do some exercise each day.

My dad had a heart attack – will I?

If one or other of your parents suffers or suffered from cardiovascular disease, you are more likely to develop it yourself. There may be inherited predisposition for the disease.

Heredity and risk

Some diseases, such as some simple genetic disorders, have a single risk factor. These diseases are determined by the inheritance of a defective allele, and the risk of suffering from the conditions follows the Mendelian rules of inheritance that you have already met at GCSE.

For example, consider two people who are carriers of sickle cell anaemia. This is a recessive genetic condition in which an abnormal form of haemoglobin is produced. This abnormal haemoglobin is less soluble and at low oxygen concentrations it crystallises, causing the red blood cells to become distorted. The sickle- or crescent-shaped cells are less efficient at carrying oxygen and can block small blood vessels.

In Figure 1.54, two carriers decide to try to have a child. The chances of this child, or any others they have, inheriting the defective form of the gene from both parents is 1 in 4.

	Mother		Father	
Parent genotype	Aa		Aa	
Parent phenotype	normal red blood cells		normal red blood cells	
Gametes	A	a	A	a

	A	a
A	AA	Aa
a	Aa	aa

Any child with this genotype will have sickle cell anaemia.

Figure 1.54 If both parents carry one defective allele there is a 1 in 4 chance of any child inheriting two copies of the defective allele and suffering from sickle cell anaemia.

With some genetically inherited conditions the risks are very clear cut. However, inheritance is often much more complex. Even in some conditions that are controlled by a single gene, it is now known that different mutations of that gene determine how severe the person's condition is. This is true for cystic fibrosis, which you will study in detail in Topic 2.

Some diseases result from several genes interacting. In other diseases, genes have been identified that do not *cause* the condition directly but that still increase the individual's chance of developing it. There is no clear-cut relationship between having these genes and having the condition; rather the genes *increase* the individual's susceptibility to the disease.

Genes and CHD

There are some single gene disorders that increase the likelihood of early development of coronary heart disease. For example, in familial hypercholesterolaemia (FH), mutations in the LDLR gene cause the LDL receptors, involved in removal of LDL from the blood, not to form or to have a shape that makes them less efficient. This results in high blood LDL levels with early onset of CHD. It is thought that about 1 in 500 people carry a mutation in this gene and it may account for 5–10% of the coronary artery disease in people below 55 years of age. However, even with this gene mutation the development of CHD will still be dependent on other environmental factors, such as lifestyle and diet.

ACTIVITY

You can read about the role of genes in the sudden death of athletes in **Student Activity 1.23**.

Apolipoprotein gene cluster

The inheritance of cardiovascular disease is rarely a simple case of a single faulty gene for the condition being passed from one generation to the next. There are several genes that can affect your likelihood of developing cardiovascular disease. The apolipoprotein gene cluster has been identified as associated with coronary heart disease and other conditions such as Alzheimer's disease. This group of genes has been extensively researched, and it appears that some alleles are linked to higher risk whereas others may reduce the risk.

Apolipoproteins are the protein component of lipoproteins. They are mostly formed in the liver and intestines and have important roles in stabilising the structure of the lipoproteins and recognising receptors involved in lipoprotein uptake on the plasma membrane of most cells in the body. There are several types of apolipoproteins, including the three described below.

- Apolipoprotein A (APOA) – the major protein in HDL, which helps in the removal of cholesterol to the liver for excretion. Mutations in the apoA gene are associated with low HDL levels and reduced removal of cholesterol from the blood, leading to increased risk of coronary heart disease.
- Apolipoprotein B (APOB) – the main protein in LDL, the molecule that transfers cholesterol from the blood to cells. Mutations of the apoB gene result in higher levels of LDL in the blood and a higher susceptibility to CVD.
- Apolipoprotein E (APOE) – a major component of HDLs and very low-density lipoproteins (VLDLs), which are also involved in removal of excess cholesterol from the blood to the liver. The apoE gene has three common alleles, producing three forms of the protein, E2, E3 and E4. APOE4 slows removal of cholesterol from the blood and therefore having the E4 allele may increase the risk of coronary heart disease.

Q 1.37 How many phenotypes of APOE are possible?

Q 1.38 One mutation of APOA, known as Milano (because it is common in people from Milan in Italy), results in very low levels of HDL, but each HDL is very efficient at removing cholesterol from the blood. How will this affect the risk of developing CVD for those who are carriers of the mutation?

APO gene mutations and CHD risk

There are numerous mutations in the APO genes and the effects of these mutations are modified in different environments and when in different combinations, making it impossible to estimate the effect of a single gene or single environmental risk factor. In the future, testing for levels of apolipoproteins in a person's blood may be a better indicator of a person's risk of CHD than cholesterol levels themselves.

CHD is multifactorial

The chance that a person will suffer from cancer or cardiovascular disease, for example, is rarely the consequence of genetic inheritance alone. Many such diseases are **multifactorial**, with heredity, the physical environment, the social environment and lifestyle behaviour choices *all* contributing to the risk. The combination of risk factors experienced by the individual determines their risk of developing the disease.

Families do not pass on just their genes. You may also acquire your parents' lifestyle and its associated risk factors, such as smoking, lack of exercise and poor diet. Genetic tests are available for alleles associated with single gene disorders that increase the likelihood of early development of coronary heart disease (Figure 1.55). For the majority of people genetic testing for alleles associated with increased risk of CHD is of little value due to the interaction of risk factors.

Figure 1.55 Genetic testing is becoming more common. Some companies now provide such testing so that individuals can see if they are at high or low risk of developing certain diseases.

ACTIVITY
Student Activity 1.24 lets you determine if your diet contains enough antioxidant vitamins.

Other risk factors

The most important factors that increase the risk of cardiovascular disease are smoking, having high blood pressure, having a high level of blood cholesterol and lack of physical activity. As we have seen, obesity is also a major risk factor. In addition, there are other things you should think about when deciding what to do if you want to lower your CVD risk.

The role of antioxidants

During reactions in the body, unstable radicals result when an atom has an unpaired electron. For example, the superoxide radical, which is oxygen with an unpaired electron; this is often represented as $O_2^{\cdot}$. Radicals (sometimes known as free radicals) are highly reactive and can damage many cell components including enzymes and genetic material. This type of cellular damage has been implicated in the development of some types of cancer, heart disease and premature ageing. Some vitamins, including vitamin C, beta-carotene and vitamin E, can protect against radical damage. They provide hydrogen atoms that stabilise the radical by pairing up with its unpaired electron. The MONICA study (mentioned on page 23) found that high levels of antioxidants seemed to protect against heart disease. Partly because of their function as a good source of antioxidants, the current Department of Health recommendation is to include at least five portions of fruit or vegetables per day in our diet. Analysis of 2008 Health Survey of England data showed that people eating seven or more a day had a 33% reduced risk of death due to CVD or cancer compared with people who ate less than one.

Wine and some fruit juices contain chemicals that have antioxidant properties and also help stop platelets sticking together.

Q 1.39 How might the antioxidants in wine help reduce the incidence of cardiovascular disease?

ACTIVITY
Student Activity 1.25 lets you investigate the quantity of the antioxidant vitamin C in fruit juice.

Salt

You need some salt in your diet for the healthy functioning of your body but too much can have adverse effects. The Food Standards Agency recommends a salt intake of no more than 6 g per day for an adult, but the UK average intake is double that figure. Approximately 75% of the salt eaten comes from processed food. An average-sized bowl of breakfast cereal can contain as much as 1 g of salt; a standard-sized bag of crisps about 0.5 g. Often the value for sodium rather than salt is given; the value for salt is about 2½ times greater. A high-salt diet causes the kidneys to retain water. Higher fluid levels in the blood result in elevated blood pressure with the associated cardiovascular disease risks.

ACTIVITY
Student Activity 1.26 is a teacher-led demonstration that lets you take part in an investigation of some factors that affect blood pressure and heart rate.

Stress

How you respond to stress in your life is very important. There is evidence that coronary heart disease is sometimes linked to poor stress management. In stressful situations the release of adrenaline causes arteries and arterioles to constrict, resulting in raised blood pressure. Stress can also lead to overeating, a poor diet and higher alcohol consumption, which are all potential contributors to CVD.

Alcohol

Heavy drinkers are at far greater risk of heart disease and a number of other diseases. Heavy drinking raises blood pressure, contributes to obesity and can cause irregular heartbeat. However, there has also been much research and debate concerning *potential* protective effects of *moderate* drinking.

If you have a glass of wine, the alcohol it contains (1 unit or 8 g) is very quickly absorbed, 20% through the wall of the stomach and the remainder through the walls of the small intestine. Excess alcohol consumption can result in direct tissue damage, including damage to the liver, brain and heart. Such damage contributes to an increased risk of cardiovascular disease. The liver has many functions but two of its main ones are processing carbohydrates, fats and proteins, and detoxification, including the removal and destruction of alcohol. High levels of alcohol can damage liver cells. This impairs the ability of the liver to remove glucose and lipids from the blood. In the liver alcohol is converted into ethanal, a three-carbon carbohydrate. Most of the ethanal is used in respiration but some may end up in very low-density lipoproteins (VLDLs), increasing the risk of plaque deposition.

Given these harmful consequences of drinking alcohol, it seems remarkable to claim that moderate drinking may actually offer some degree of protection against cardiovascular disease. However, studies have shown a small protective effect of alcohol, in particular wine, compared with abstinence. This is thought to be because moderate alcohol consumption is correlated with higher HDL cholesterol levels (the 'good' cholesterol).

If you do drink, moderation is the key! The UK recommended limits to avoid health problems are 2–3 units per day for women, and 3–4 units per day for men, with no binge drinking. There is one unit of alcohol in half a pint of average strength beer, a small glass of table wine or a measure of spirits (Figure 1.56). One unit of alcohol is approximately the amount that an adult eliminates from the body in one hour.

Coffee

Epidemological studies have positively and negatively correlated drinking coffee and health risk. Some studies suggest increased CVD risk whereas others suggest moderate consumption may have health benefits.

Figure 1.56 Many larger glasses of wine available in pubs, restaurants and wine bars contain 2–3 units of alcohol, the recommended daily limit for women to avoid health problems.

ACTIVITY

In **Student Activity 1.27** you can find out whether caffeine increases heart rate and blood pressure.

ACTIVITY

In **Student Activity 1.28** you can 'Test your healthy heart IQ'.

CHECKPOINT

1.7 Produce a concept map or table which shows the risk factors for CVD and their effects.

1.4 Reducing the risks of cardiovascular disease

The risk of cardiovascular disease can be reduced in a range of different ways, including:

- stopping smoking
- maintaining resting blood pressure below 140/85 mmHg
- maintaining low blood cholesterol level
- maintaining a normal BMI/low waist-to-hip ratio
- taking regular physical exercise
- moderate or no use of alcohol.

If people in the UK did not smoke, the British Heart Foundation estimates that 10 000 fewer men and women of working age would die from heart attacks each year. After stopping smoking, your risk of coronary heart disease is almost halved after only one year.

Controlling blood pressure

If a person is diagnosed with high blood pressure, changes in diet and lifestyle would be recommended. Medications are also available to reduce high blood pressure. These would normally be prescribed for people with sustained systolic pressure of ≥160 mmHg or sustained diastolic pressure of ≥100 mmHg. People with sustained blood pressure over 140/90 mmHg and who show evidence of CVD may also be treated.

Three main types of drugs are used to treat high blood pressure.

ACE inhibitors

ACE inhibitors (angiotensin converting enzyme inhibitors) are effective antihypertensive drugs which reduce the synthesis of angiotensin II. This hormone causes vasoconstriction of blood vessels to help control blood pressure. The ACE inhibitors prevent the hormone being produced from the inactive angiotensin I, therefore reducing vasoconstriction and lowering blood pressure.

Some people experience side effects when taking ACE inhibitors. These include a dry cough, dizziness due to rapid lowering of blood pressure, abnormal heart rhythms and a reduction in the function of the kidney. However, for anyone with kidney disease the drug may reduce the risk of kidney failure. Patients intolerant to ACE inhibitors will be prescribed an alternative drug that blocks the angiotensin II receptors.

Calcium channel blockers

Calcium channel blockers are antihypertensive drugs that block the calcium channels in the muscle cells in the lining of arteries. For the muscle to contract, calcium must pass through these channels into the muscle cells. Failure of calcium to enter the cell prevents contraction of the muscle, the blood vessels do not constrict, and this lowers blood pressure. In Topic 7 you will look at muscle contraction and the role of calcium in more detail.

There are some side effects with these drugs, such as headaches, dizziness, swollen ankles due to a build-up of fluid in the legs, abnormal heart rhythms, flushing red in the face and constipation. In people with heart failure, taking some types of calcium channel blockers can make symptoms worse or be fatal, so they may not be prescribed to people who have had a heart attack.

Diuretics

Diuretics increase the volume of urine produced by the kidneys and therefore rid the body of excess fluids and salt. This leads to a decrease in blood plasma volume and cardiac output (volume of blood expelled from the heart in a minute), which lowers blood pressure.

A few people taking diuretics may have some side effects, such as dizziness, nausea or muscle cramps. If you are taking a diuretic it is important not to have too much salt in food as this counteracts the diuretic effect.

Most people take two of these drugs to control blood pressure, usually an ACE inhibitor in combination with one of the others. In 2006 the British Hypertension Society and the National Institute for Clinical Excellence (NICE) published guidelines on the appropriate selection of these drugs to use, with the drugs selected according to what is effective and carries the lowest risk of side effects.

Reducing blood cholesterol levels

There is evidence from both the UK and the USA that untargeted cholesterol screening of the general population combined with dietary advice has little effect on lowering blood cholesterol levels. A further problem is associated with 'labelling' people; when told that they have high blood pressure, many people react by signing off sick!

Q 1.40 Why do you think untargeted screening and dietary advice are not very effective at lowering blood cholesterol?

Some people need to reduce blood cholesterol. One way to achieve this is through a low-fat diet. The media constantly remind us of the need to do this.

Table 1.7 shows the extent of cholesterol-lowering that is obtained from following a low-fat diet in high-risk patients, namely people who have already experienced a heart attack, compared with the general population.

	Blood cholesterol reduction	
	mmol/l	%
general population	0.22	3
high-risk patients	0.65	9

Table 1.7 The effect of lipid-lowering diets in reducing blood cholesterol levels.

Q 1.41 Can you suggest why the effect of dietary change appears to have been more successful in reducing blood cholesterol in patients who had experienced a heart attack than in the general population?

Cholesterol-lowering drugs

Individuals diagnosed with high cholesterol who have CVD or have a 20% chance of developing CVD in the next 10 years may also be prescribed cholesterol-lowering drugs. The most commonly prescribed are statins. Statins work by inhibiting an enzyme involved in the production of LDL cholesterol by the liver. Side effects of statins are tiredness, disturbed sleep, feeling sick, vomiting, diarrhoea, headache and muscle weakness.

Several large studies have investigated the effects of these drugs and researchers have collaborated to analyse the results of 14 randomised trials. The results, drawing on 90 000 participants, were published in 2005, and showed that statins quickly reduce the risk of heart disease and stroke. Studies have shown that there is a linear relationship between absolute reductions in LDL cholesterol and reductions in the incidence of major vascular events such as heart attack and stroke. In patients who have CVD, treatment with statins can reduce the risk of heart attack by up to 33%. In people who do not have CVD but have elevated cholesterol levels, statins lower total and LDL cholesterol by more than 20% and the risk of CVD by a similar amount.

Some studies have raised concerns that the use of statins may increase the risk of death by other non-vascular causes, and also increase the risk of developing particular cancers, such as gastrointestinal and respiratory cancers. To determine if this was the case, researchers in the UK and Australia analysed the results of 14 large randomised trials for statins. They found no evidence that lowering LDL cholesterol by 1 mmol/l with five years of statin treatment increased the risk of death by other non-vascular causes or of developing particular cancers. However, they did highlight the need for extended study of patients using statins over long periods to identify any adverse effects that might occur with long-term use.

There is an ongoing debate (2014) about whether the use of statins should be extended to those at low risk of CHD, as advocated by the University of Oxford Clinical Trials Service and Health Economics Research Centre study that looked at the results of randomised trials involving 175 000 participants for an average of five years.

A diet to reduce the risk of cardiovascular disease

A diet to offer protection against cardiovascular disease would include the following key features (Figure 1.57).

- Energy balanced.
- Reduced saturated fat.
- More polyunsaturated fats.
- Reduced cholesterol.
- Reduced salt.
- More non-starch polysaccharides, such as pectins and guar gum.

These polysaccharides, known as soluble fibre, have been found to lower blood cholesterol. They are found in fruit, vegetables, beans, pulses and some grains (e.g. oats). They are only partially digested, forming a gel that traps the cholesterol and prevents its absorption.

Figure 1.57 A diet to reduce the risk of developing cardiovascular disease.

- Includes oily fish.

Fish such as mackerel, sardines, anchovies, salmon and trout contain omega-3 fatty acids, a group of polyunsaturated fatty acids with their first double bond between the third and fourth carbon atoms. These fatty acids are essential for cell functioning and have been linked to a reduction in heart disease and joint inflammation. The evidence for the importance of omega-3 fatty acids is seen in the Inuit in Greenland and the inhabitants of certain Japanese islands. They regularly eat oily fish and have very low rates of coronary heart disease.

- More fruit and vegetables.

Fruits and vegetables contain antioxidants and often non-starch polysaccharides.

Studies suggest that including foods containing about 2 g/day of plant sterols can reduce LDL cholesterol levels by about 9%. These are naturally produced substances in plants, similar to cholesterol. They compete with cholesterol during its absorption in the intestine. Unfortunately, we would have to eat vast quantities of foods such as vegetable oils and grains in order to reduce our cholesterol levels through this competition. Products have therefore been developed that can incorporate sterols into everyday foodstuffs such as yogurts. However, NICE consider there is currently (2014) insufficient evidence for them to recommend them as they are unlikely to give additional benefit for the majority of people over a low-fat diet. There are no studies to show an impact on the occurrence of CHD.

REVIEW
In **Student Extension 1.3** you can find out more about functional food trials.

Figure 1.58 Some yoghurts and margarines include sterols to help lower cholesterol. These products are known as functional foods.

Anticoagulant and platelet inhibitory drug treatment

If someone has had a heart attack or stroke, or is identified as being at high risk of one, in addition to the lifestyle changes and drug treatments to reduce blood pressure and blood cholesterol, they may be given drugs to prevent formation of a blood clot in an artery.

The tendency for platelet aggregation and clotting is reduced by platelet inhibitory drugs and anticoagulant drugs. Aspirin reduces the stickiness of platelets and the likelihood of clot formation. But some people are allergic to aspirin, and for others it is not effective or is only partially effective. In these cases an alternative platelet inhibitory drug, clopidogrel, may be used. A combined treatment involving a daily dose of aspirin and clopidogrel can have a dramatic effect. However, it has been shown that there is a risk of bleeding in the gastrointestinal tract with aspirin, and in trials there have been high rates of serious bleeding when aspirin is used in combination with clopidogrel. This risk of bleeding may outweigh the benefits. If a person has only a low risk of a vascular event (less than 1% per year risk of a heart attack or stroke), the risk of bleeding outweighs the benefits. The risks and benefits need to be considered for each individual patient, though guidelines suggest use when the 10-year risk of a heart attack or stroke is greater than 20%.

Warfarin is an anticoagulant drug. It interferes with the production of vitamin K and therefore it affects the synthesis of clotting factors. It can be taken orally for extended periods of time to prevent clotting. The benefits may be greater than with aspirin for some patients but the risk of bleeding is higher than with aspirin.

ACTIVITY

In **Student Activity 1.29** you can discuss how people use scientific information to reduce their risk of coronary heart disease.

EXTENSION

You can read about new treatments for coronary heart disease in **Student Extension 1.4**. 'New treatments for cardiovascular disease' provides a fine start. It even gives you the opportunity to observe surgery!

Q 1.42 **(a)** Reeta has a high risk of heart attack and is discussing drug treatments with her doctor. What information would they have to consider before making a decision about the best drug to use?

(b) Regular low doses of aspirin reduce the risk of bowel cancer. Would it be sensible for everyone to take low doses of aspirin to reduce their risk of cancer? Give a reason for your answer.

Q 1.43 Look back at the section on blood clotting then explain how warfarin prevents blood clotting.

Think back to Mark and Peter. What is most surprising is that Mark was only 15 when he had his stroke. Mark had no obvious risk factors that would have alerted him to the possibility of having a stroke. He reports having taken exercise, eaten a reasonably healthy diet and having not smoked. If you read Mark's full story in Activity 1.1 at the start of the topic, you will find that he had a type of stroke in which a blood vessel supplying blood to the brain bursts.

An artery can burst due to an aneurysm, where blood builds up behind a section of artery that has narrowed as a result of atherosclerosis. However, with no risk factors and in one so young, the likelihood of atheroma deposits having built up to this extent in Mark's arteries seems unlikely. Although there was no history of stroke in Mark's family, he thinks that he inherited an allele causing him to have thin artery walls more prone to bursting.

Q 1.44 What additional information would you need from Mark to determine if his stroke was due to this type of inherited condition or due to atherosclerosis?

Mark remains healthy today (Summer 2014) and has not had a recurrence of the problem. Peter was lucky to be alive having had a blood pressure of 240/140 mmHg, two heart attacks and heart surgery (Figure 1.55). If you look back at his story you will recall that his father died aged 53 from a heart attack. This suggests that there may have been an inherited predisposition for the condition. Thankfully, Peter's active lifestyle will have helped him survive for many years after his surgery.

DID YOU KNOW?

Haemorrhagic stroke

Blood vessels on the surface of the brain and those within the brain are susceptible to bursting resulting in a stroke. A haemorrhagic stroke occurs when a blood vessel supplying blood to the brain bursts. If the burst occurs within the brain it is known as an *intracerebral haemorrhage*, whereas bursting of a vessel on the surface causes what is known as a *subarachnoid haemorrhage*. Look at Figure 1.59 and work out why the different types of stroke were given these names. There is no need for you to remember the names, but it is worth being aware of them as doctors and medical scientists use this sort of language.

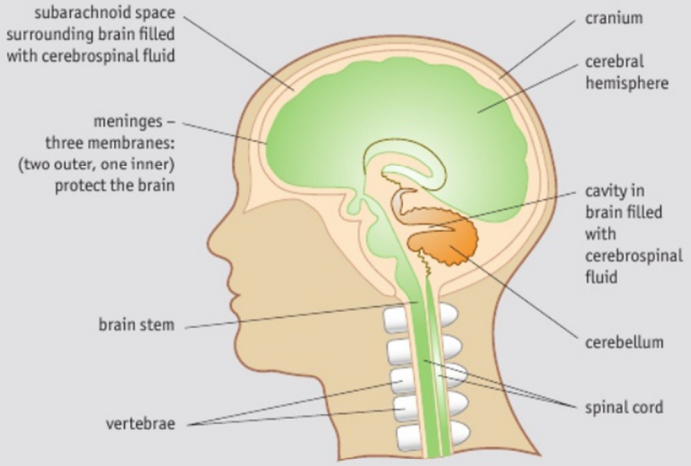


Figure 1.59 Cross-section through a human brain.

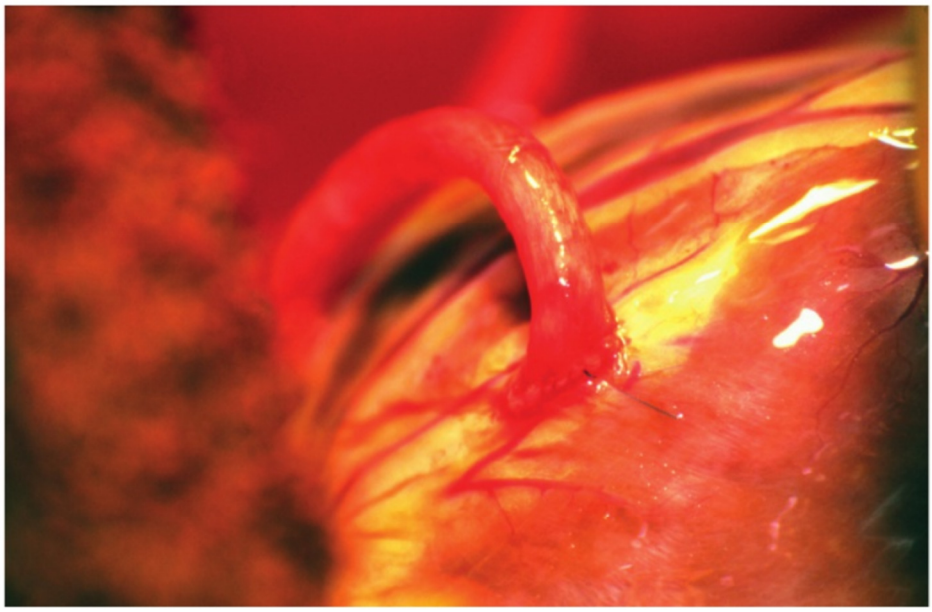


Figure 1.60 A vein taken from the patient's leg is used to bypass the sections of coronary artery that are narrowed. The photograph above shows the section of vein that has been grafted onto a patient's heart.

ACTIVITY

Use **Student Activity 1.30** to check your notes using the topic summary provided.

TOPIC TEST

Now that you have finished Topic 1, complete the end-of-topic test before starting Topic 2.

Q 1.45 What advice would you recommend Peter gives to his two daughters and son?

THINKING BIGGER

GENETIC DEFECTS OF THE HEART

We tend to think of heart disease as being a problem of older age due to atherosclerosis, largely unaware that some babies are born with heart disease. This is known as congenital heart disease; it refers to a heart defect or condition that is present at birth. There are many different types of congenital heart disease with some being minor and easily treated. whereas others are more serious. Some conditions are inherited and researchers are working hard to understand the causes.

8 April 2014

CONGENITAL HEART DISEASE GENE FOUND

Severe forms of congenital heart disease caused by variants of the *NR2F2* gene

Researchers have explored the role of a master gene that controls the functioning of other genes involved in heart development. Variations in this gene – *NR2F2* – are responsible for the development of severe forms of congenital heart disease.

Approximately one per cent of all babies are born with congenital heart disease, where the normal workings of the heart are affected. Because the damage to the heart is structural, most babies will need surgery to correct the problem. Although genetic causes are known to underlie the disease, these causes are not very well understood.

Scientists have previously shown that mice with a less active *NR2F2* gene had abnormal heart development. To see if the gene was involved in severe forms of human congenital heart disease, the team looked at DNA sequences of parents and affected children and found that variation on the *NR2F2* caused the structural damage that underlies these conditions.

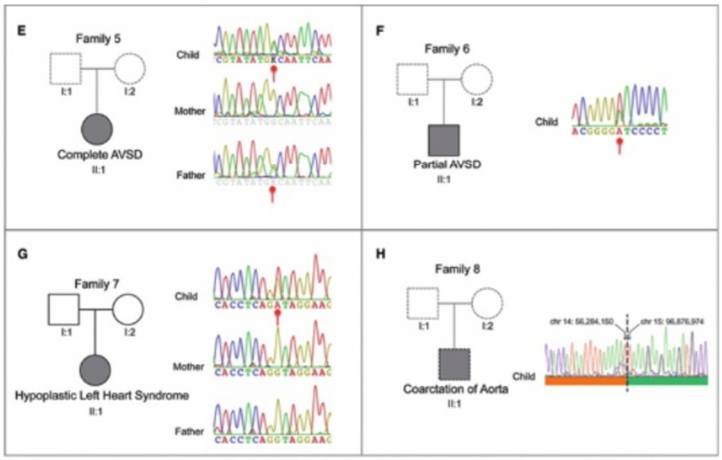
The team found that these genetic variants were typically only present in the child and not the parents, revealing that congenital heart disease producing variants occur in the womb.

"What we see is that these rare variants in the NR2F2 gene interfere with the normal heart development and cause severe forms of congenital heart disease during human development," says Saeed Al Turki, first author from the Wellcome Trust Sanger Institute.

NR2F2 is a master regulator for other genes involved in the development of a healthy functioning heart – once the activity of *NR2F2* is affected it has a knock-on effect on these other genes affecting the healthy development of the heart.

The team found that different types of damage in the *NR2F2* gene cause different types of heart defects. Genetic variants that completely deactivate the *NR2F2* gene tended to cause damage to the left side of the heart. In contrast, genetic variants that alter activity of the gene but do not deactivate it more commonly caused a specific sub-type of holes in the hearts of patients.

"With this knowledge, we are getting closer to understanding the full genetic causes behind congenital heart disease, which will provide better diagnoses and in turn provide better patient management," says Dr Matthew Hurles, senior author from the Wellcome Trust Sanger Institute.



Family charts and sequencing results of NR2F2 variants in eight families affected by congenital heart disease (part of the diagram is shown above). Solid lines in pedigree charts indicate both whole-exome sequencing data and capillary sequencing are available; dashed lines indicate samples with NR2F2 capillary sequencing data only.

Publication details

Rare variants in NR2F2 cause congenital heart defects in humans. Al Turki S, Manickaraj AK, Mercer CL, Gerety SS, Hitz MP, Lindsay S, D'Alessandro LC, Swaminathan GJ, Bentham J, Arndt AK, Low J, Breckpot J, Gewillig M, Thienpont B, Abdul-Khaliq H, Harnack C, Hoff K, Kramer HH, Schubert S, Siebert R, Toka O, Cosgrove C, Watkins H, Lucassen AM, O'Kelly IM, Salmon AP, Bu'lock FA, Granados-Riveron J, Setchfield K, Thornborough C, Brook JD, Mulder B, Klaassen S, Bhattacharya S, Devriendt K, Fitzpatrick DF, UK10K Consortium, Wilson DI, Mital S and Hurles ME
American journal of human genetics 2014; **94**; 4; 574–85
Press release published on the Wellcome Trust Sanger Institute website at http://www.sanger.ac.uk/about/press/2014/140408.html

Command words
Note that when the word critically is used in this context it does not mean that one should necessarily critise, it means that you should express your reasoned judgement.

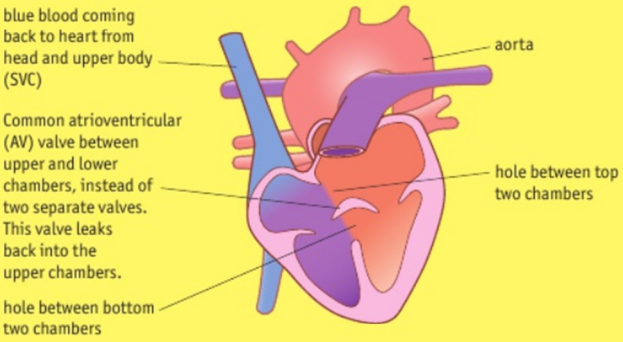
START BY REVIEWING THE SOURCE
This article about the finding of a gene for congenital heart disease comes from the Wellcome Trust Sanger Institute website.

1. Read the article and comment on who you think the article might be aimed at.
2. Comment critically on the reliability of the article as a source of scientific information.

Biological vocabulary
As you read the article identify any unfamiliar words. Look these up to check you understand their meaning, you could look in the SNAB online glossary however if they are more specialised terms use the Internet to find a definition, making sure that the website you access is reliable, it is worth looking at a range of sources to check.

REVIEWING THE BIOLOGY
Having read the article, draw on your knowledge gained so far in the course and answer the following questions.

1. Explain in detail what the presence of the genetic variant in the child and not the parent tells you about how and where the variant may have arisen.
2. The article figure shows that most of the babies in these families had a congenital defect known as AVSD (Atrioventricular Septal Defect). These babies have a defect in their septum – the wall between the left and right sides of the heart. They have a hole through their septum between the atria and between the ventricles, with only a common atrioventricular valve between the atria and ventricles as shown in the diagram below. Using your knowledge of the function of the heart describe how these defects in the heart are likely to affect the circulation of blood. Think carefully about the pressure within the heart.



3. A baby born with coarctation of aorta has narrowing of the aorta just beyond the branches that supply the head and arms. as occurred in family H. Suggest how the baby might be affected by this narrowing.

Once you have completed the remainder of the course come back and have a go at answering the following questions.

1. The figure caption refers to family charts, what would the left hand part of each diagram normally be called and describe what the circles and squares on this part of the diagram represent.
2. Suggest what might be meant by variant in the article?
3. Look at the figure and decide if you can work out what has happened to the DNA of each child in families one to four.
4. Explain the role of a master gene in control of development.

To find out more detail about congenital heart defects and how they can be treated visit the British Heart Foundation website.