# 1.1 What is cardiovascular disease?

## Deaths from cardiovascular disease

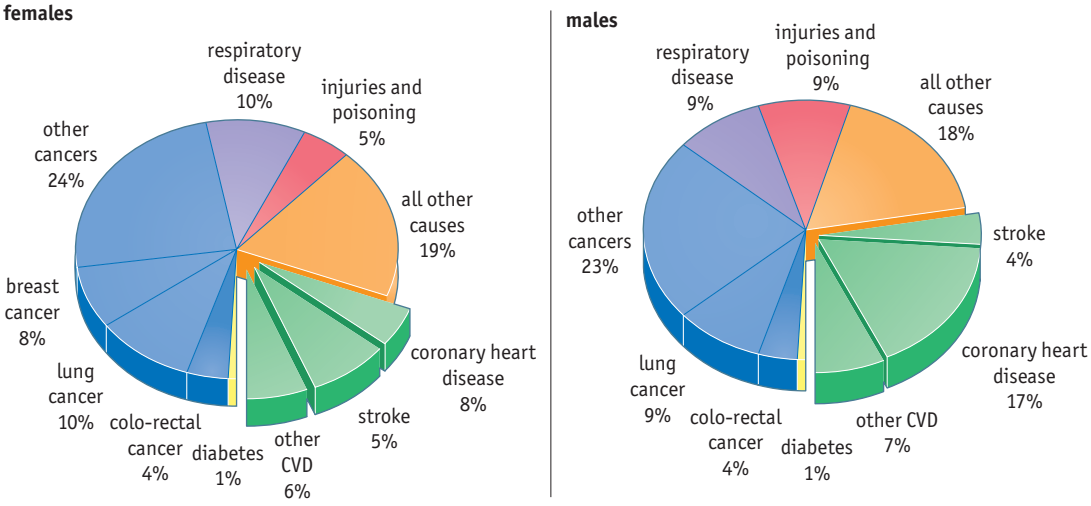



**Figure 1.7** Premature deaths by cause in the UK in 2010 for females (left) and males (right). (Premature death is death under the age of 75 years.) One person dies of a heart attack in the UK every 7 minutes. *Reproduced with the kind permission of the British Heart Foundation.*

**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.

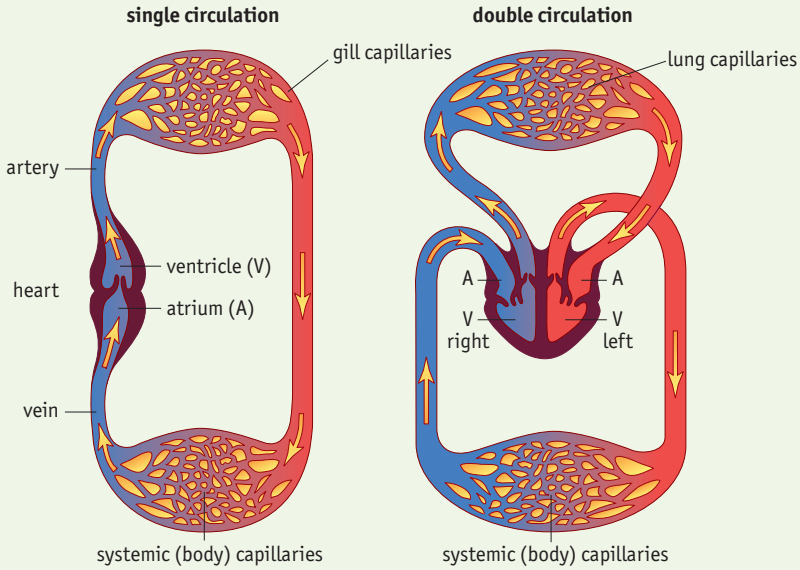



**Figure 1.8** Fish have a single circulation. Birds and mammals have a double circulation.

## 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.

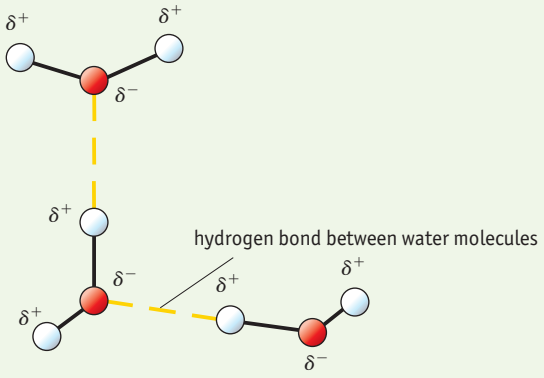



**Figure 1.9** The polarity of the water molecules results in hydrogen bonds between them. (Oxygen atoms in red, hydrogen atoms in white.)

## 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.

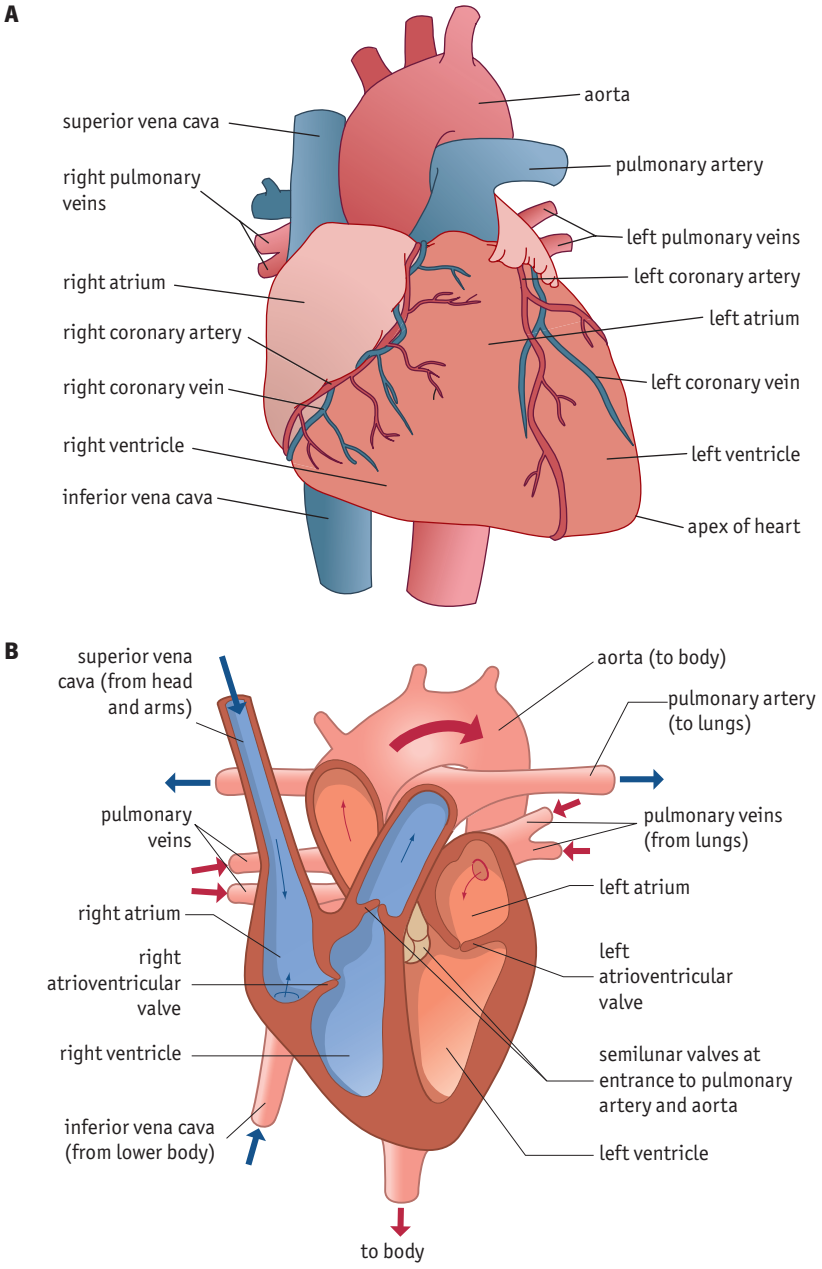



**Figure 1.10** **A** Diagrammatic external view of a human heart. **B** Diagrammatic cross-section of the human heart (ventral or front view).

**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.

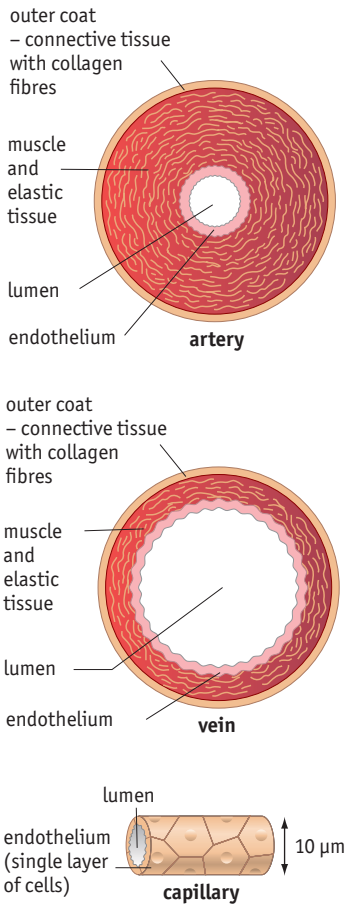
Arteries:

- 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

A




B

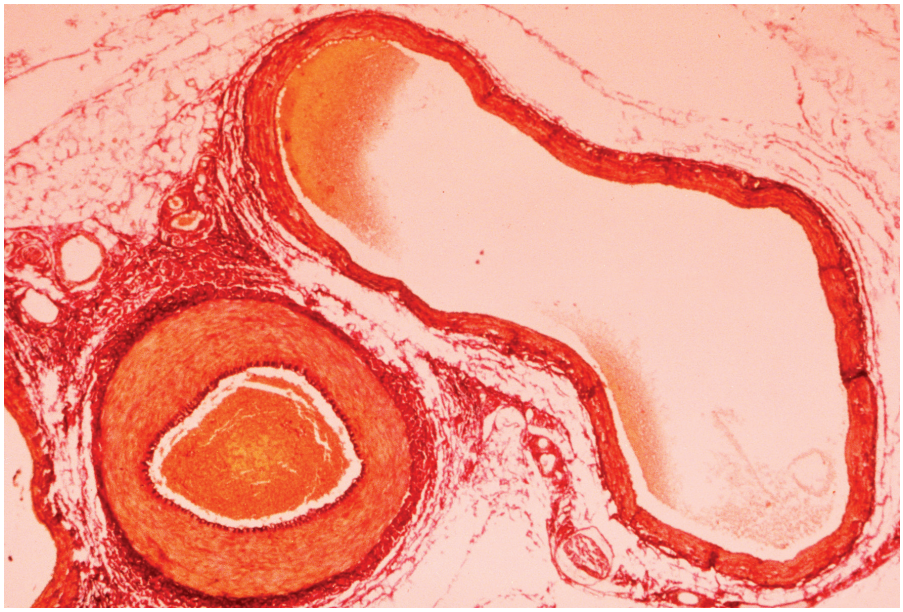


**Figure 1.11** **A** Diagram of an artery, a vein and a capillary. The endothelium that lines the blood vessels is made up of epithelial cells (see page 59). **B** Photomicrograph of an artery (left) and vein (right) surrounded by connective tissue.

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).

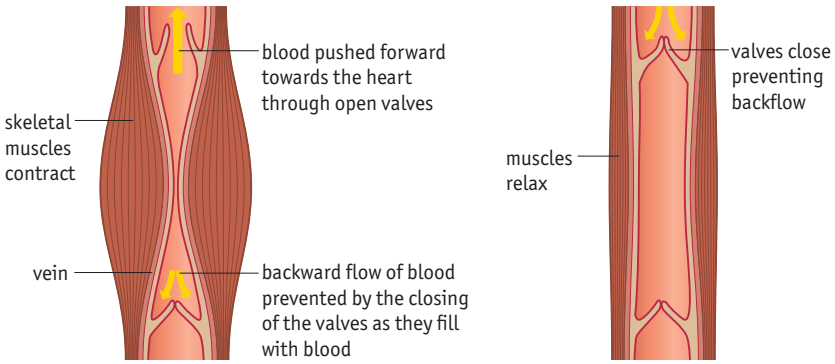



**Figure 1.12** Valves in the veins prevent the backflow of blood.

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.

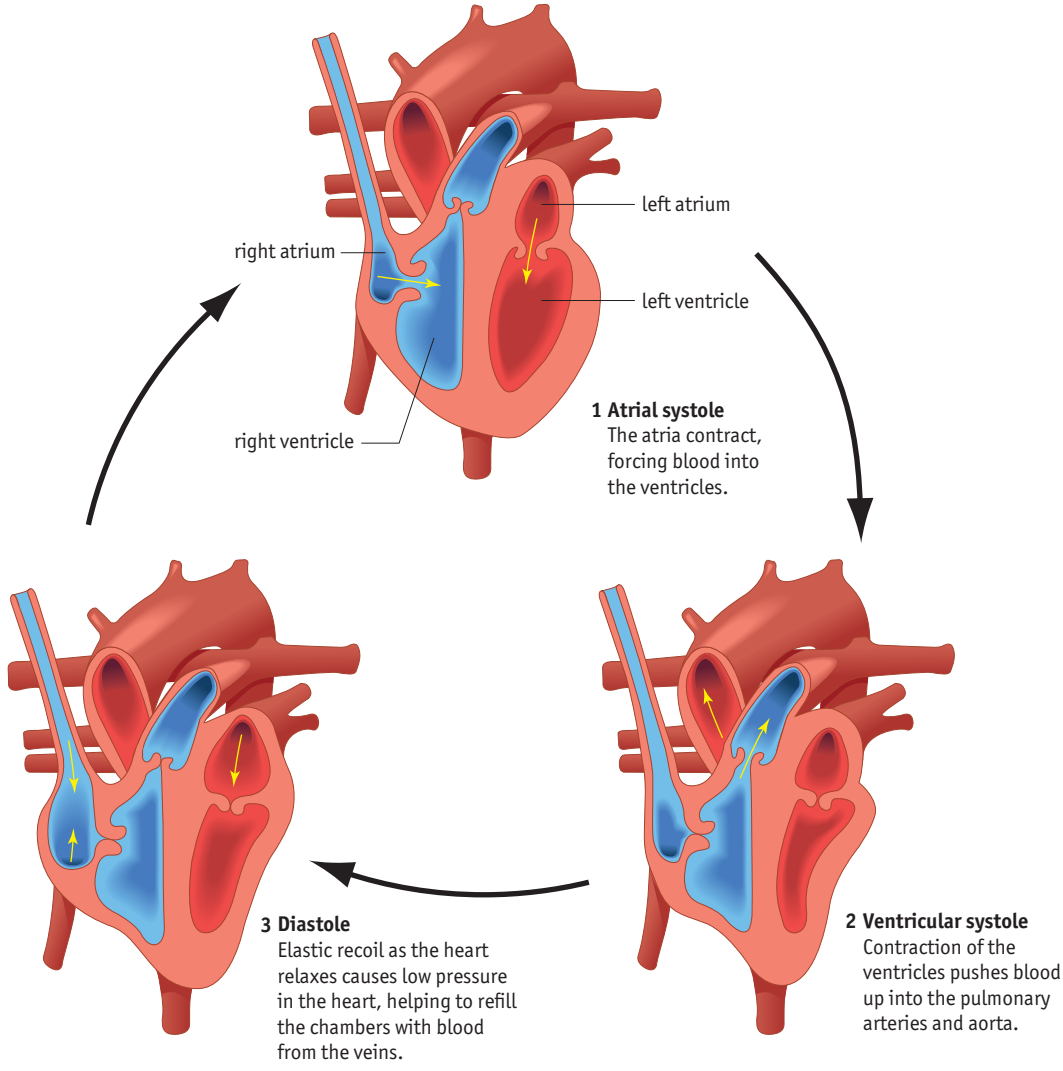



**Figure 1.13** The three stages of the cardiac cycle. At each stage blood moves from higher to lower pressure.

### 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.

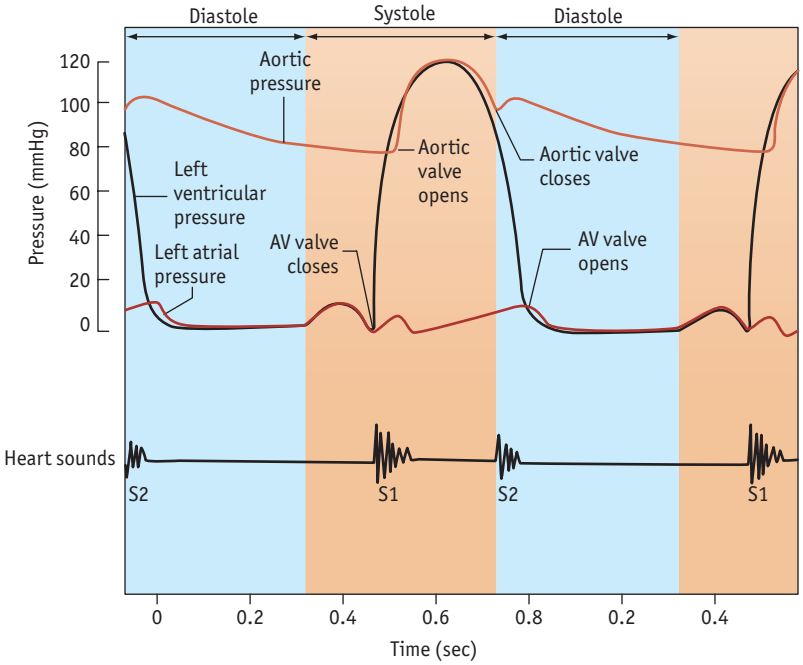



**Figure 1.14** Pressure changes in the left side of the heart during the cardiac cycle. The differences in pressure determine the movement of blood and the opening and closing of the valves, and therefore maintain the flow of blood in one direction through the heart. The aortic valve is the semilunar 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.

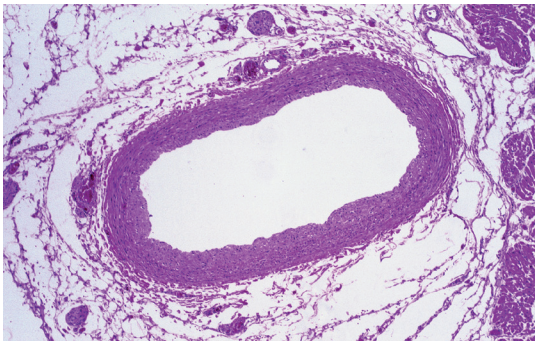


**Figure 1.15 A** Photomicrograph of a normal, healthy coronary artery showing no thickening of the arterial wall. The lumen is large. Magnification ×15.

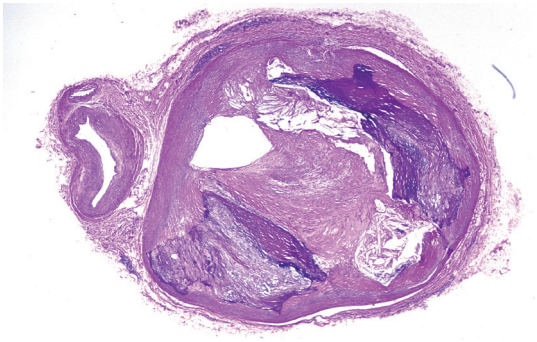


**Figure 1.15 B** Photomicrograph of a diseased coronary artery showing narrowing of the lumen due to atheroma deposits and build-up of atherosclerotic plaque. Magnification ×15.

### 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).

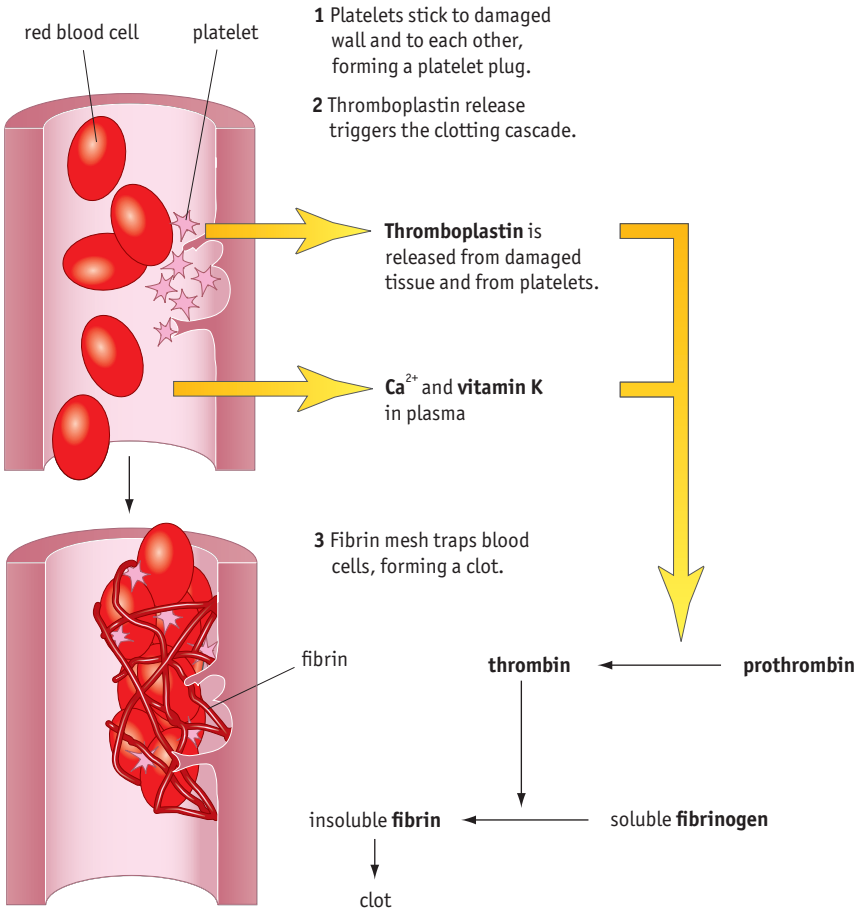



**Figure 1.17** Damage to the vessel wall triggers a cascade of reactions that leads to clotting.

### 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.

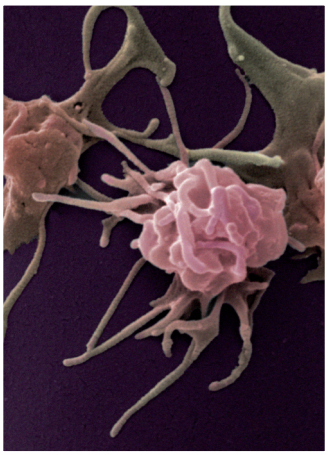


**Figure 1.16** Electron micrograph showing activated platelets. Magnification ×6000.

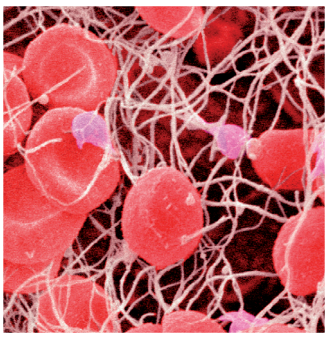


**Figure 1.18** False-colour scanning electron micrograph showing red blood cells and platelets trapped in the yellow mesh of fibrin.

### 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

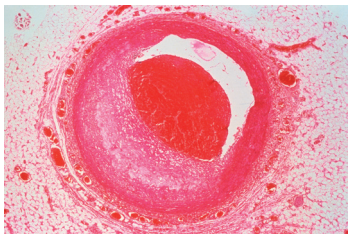


**Figure 1.19** Photomicrograph of a diseased coronary artery showing narrowing and a blood clot.

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).

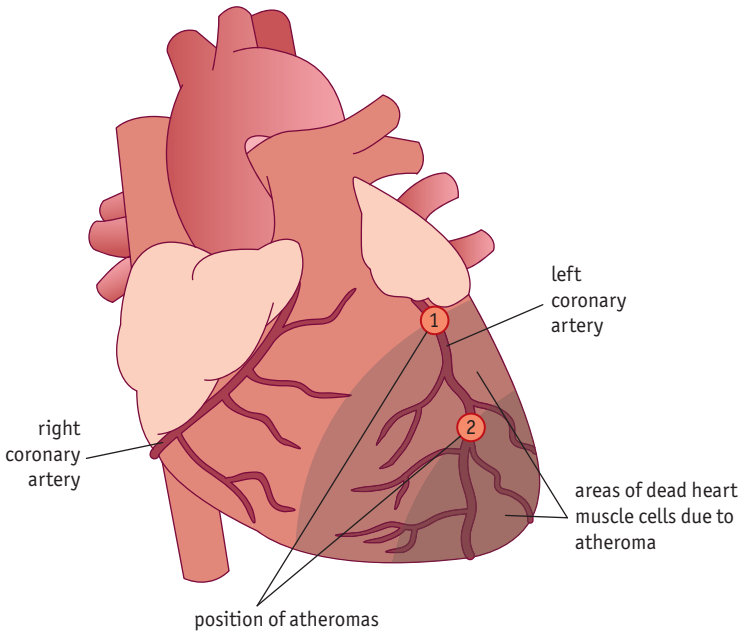



**Figure 1.20** The seriousness of a heart attack is determined by the position of the blockage in the coronary artery. Blockage at position one is more likely to be fatal than a blockage at position two. Blockage at the position further along the coronary artery is less likely to be fatal.

### 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.

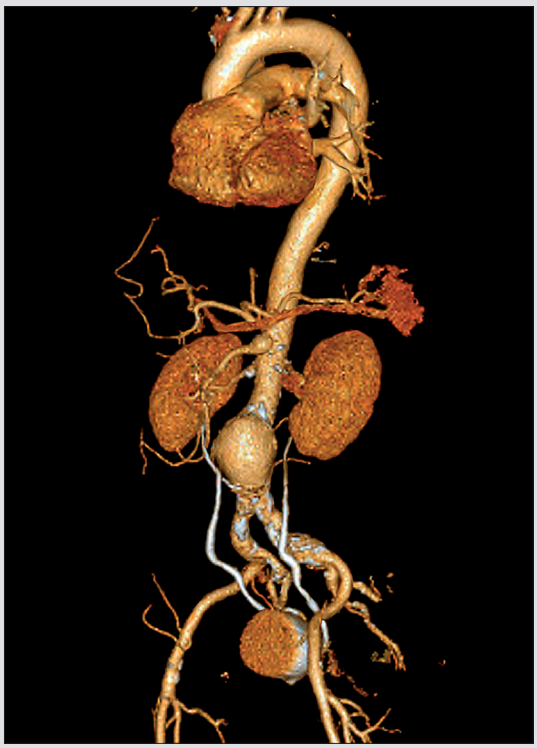


**Figure 1.21** An aneurysm in the aorta below the kidneys. If an aneurysm ruptures it can be fatal.

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**.

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.

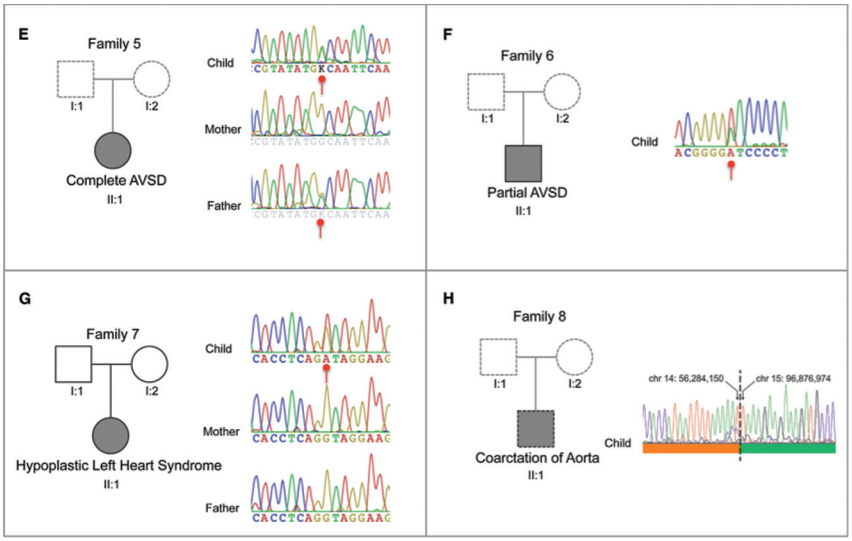
The team found that these genetic variants were typically only present in the child and not the parents, revealing that congenital heart disease producing variants occur in the womb.

*"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*



Links across the course

1.1 1.2 1.3 1.4 YOU ARE HERE 2.1 2.2 2.3 2.4 2.5 2.6