# Bio Factsheet

Ischaemic (Coronary) Heart Disease

Ischaemia is the term used to describe the condition when there is a mismatch between the amount of oxygen which a cell needs and the amount which it receives. Insufficient oxygen supply results in anaerobic glycolysis and this produces lactic acid and a decrease in pH. When this occurs in cardiac (heart) muscle, it impairs the ability of the heart muscle to contract and the associated pain is known as angina. The most common cause of ischaemic heart disease (IHD) - also called coronary heart disease (CHD) - is atherosclerosis - the development of a lipid plaque known as an atheroma in a coronary artery i.e. in one of the arteries which supplies the heart itself with blood, nutrients and oxygen (Fig 1).

Fig 1. The coronary arteries
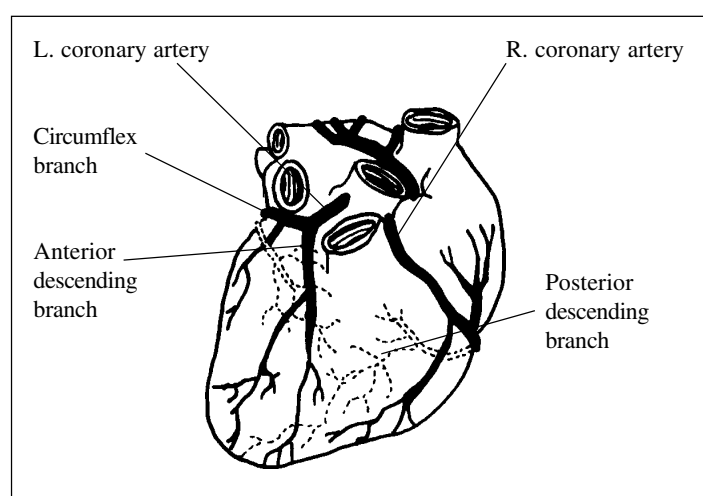
Atherosclerosis is just one of the causes of arteriosclerosis which is defined as the hardening and thickening of the arteries.

Table 1 contains definitions of words commonly used when describing heart disease.

IHD can be described as chronic or acute. Chronic IHD involves what is known as **stable angina** and is caused by decreased blood flow in the coronary arteries which become blocked by plaques. The build up of plaque decreases blood flow and hence decreases oxygen supply to the cardiac muscle. Acute IHD involves **unstable** (or crescendo) angina, which occurs when a plaque ruptures.

The pain of angina is usually experienced in the centre of the chest and often radiates to the neck and left arm. Angina can be brought on, or "precipitated", by a number of events (Table 2), all of which increase the amount of oxygen which the heart needs beyond that which can be supplied.
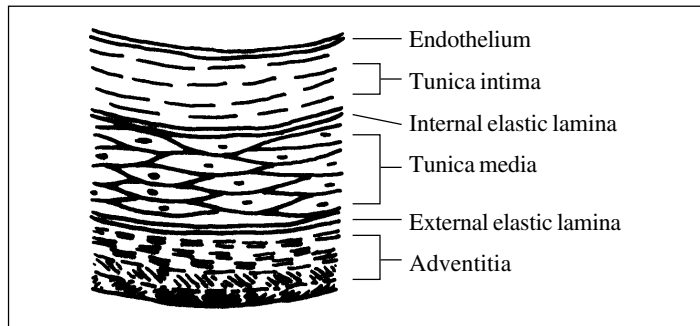
Table 2. Precipitants of angina

Event	Effect
Exercise	Causes tachycardia $\rightarrow$ $\uparrow$ the force and frequency of contraction, which $\uparrow$ oxygen consumption.
Emotional stress	$\uparrow$ stimulation of heart muscle by the sympathetic nervous system $\rightarrow$ $\uparrow$ heart rate $\uparrow$ force and frequency of contraction $\rightarrow$ $\uparrow$ oxygen consumption.
Cold weather	Vasoconstriction of the peripheral arterioles $\rightarrow$ $\uparrow$ volume of blood in the ventricles. This makes the heart muscle work harder and $\rightarrow$ $\uparrow$ its oxygen consumption.

Table 1. Heart Disease Definitions

Term	Definition
Ischaemia	Mismatch between demand for and supply of O_2 to a cell, tissue or organ.
Ischaemic heart disease (IHD)	- Coronary heart disease (CHD) results when blood supply to heart muscle is insufficient for its needs.
Coronary arteries	The arteries which supply the heart itself with blood.
Plaque (Atheroma)	A lipid-rich deposit which blocks arteries.
Atherosclerosis	The development of a lipid plaque in the arteries. One cause of arteriosclerosis.
Arteriosclerosis	Thickening and hardening of the arteries.
Myocardial infarction	A heart attack, caused by death of part of the heart muscle. This may or may not be caused by CHD.
Heart failure	When the heart cannot maintain circulation to the tissues. This may be because the heart is damaged, e.g. via CHD or because the heart is having to overwork, for example as a result of hypertension.
Tachycardia	A rapid heartbeat or pulse rate
Electrocardiogram (ECG)	A recording of the electrical changes in the heart during the cardiac cycle. The ECG can be recorded from the surface of the body during the cardiac cycle.

The development of atherosclerosis

Atherosclerosis can develop anywhere in the arterial system but if it occurs within the coronary arteries it results in heart disease. Atherosclerosis results from the development of plaques (atheromas) in the walls of arteries. The plaque may involve the tunica intima and the tunica media, thus disrupting the distribution pattern of elastic tissue in the artery (so the artery is less elastic - hardening of the arteries). The plaque may also intrude into the lumen of the artery thus restricting the blood flow to the supplied organs and thus limiting oxygen supply. If this is heart muscle it may cause the pain of angina, or if the blood flow is seriously reduced, it may cause the death of some cardiac muscle fibres. This is called myocardial infarction. The basic structure of an artery is shown in Fig 2.

Fig 2. TS of an artery

- Endothelium
- Tunica intima
- Internal elastic lamina
- Tunica media
- External elastic lamina
- Adventitia

The main lipid content within plaques is cholesterol. This is made in the body by the liver using breakdown products from the metabolism of saturated fats. If the body ingests too much saturated fat (e.g. from butter, cheese, eggs, fatty meats) the liver, as a result, can produce too much cholesterol. The problem can also be increased by ingesting too much cholesterol, by over indulgence in dairy products. Cholesterol and saturated triglycerides cannot dissolve in water and thus cannot be transported in their unaltered forms in blood. They are thus combined with proteins produced by the liver and intestines, forming lipoproteins. These vary in size, molecular weight and density. **Low density lipoproteins (LDLs)** pick up cholesterol and deposit it into body cells which have LDL receptors, including smooth muscle cells in damaged arteries. LDLs thus increase the risk of heart disease. **High density lipoproteins (HDLs)** gather cholesterol from body cells and transport it to the liver for excretion. HDLs thus reduce the risk of heart disease.

Unsaturated fatty acids known as omega-3 fatty acids are known to decrease the risk of heart disease by reducing the blood content of LDLs and increasing the content of HDLs although the mechanisms involved are unknown. They also tend to reduce the risk of blood clot formation. They are found in high concentrations in red fish, such as salmon, trout, mackerel, herring and sardines. These should form a regular dietary component of potential heart disease sufferers. The probable sequence of events in plaque formation is as follows;

l. The endothelial cells lining the inside of the artery in some way become damaged. This could be mechanical damage caused by high blood pressure disrupting the endothelium, or biochemical damage to the cell membranes and receptors caused, for instance, by high blood carbon monoxide levels due to cigarette smoking, or to high blood glucose and ketone levels found in sugar diabetes, or even to high blood cholesterol levels in the form of LDLs.

2. Following endothelial cell damage, monocytes (white blood cells) stick to the endothelial cells and squeeze through into the underlying tissues. These monocytes are active macrophages and do two main things:

   (a) They take up large amounts of cholesterol from LDLs. (Remember that much of this can come from the capillary network that is within the arterial wall itself).

   (b) They secrete growth factors which stimulate adjacent smooth muscle cells in the tunica media to multiply by mitosis and also take up large amounts of cholesterol from LDLs. The more cholesterol there is in the blood, the faster the plaque develops.

3. The cells containing accumulated cholesterol are called **foam cells** and give the plaque the appearance of pearly gray or yellow mounds in the arterial walls. The plaque is made larger by the migration of newly formed smooth muscle cells into it.
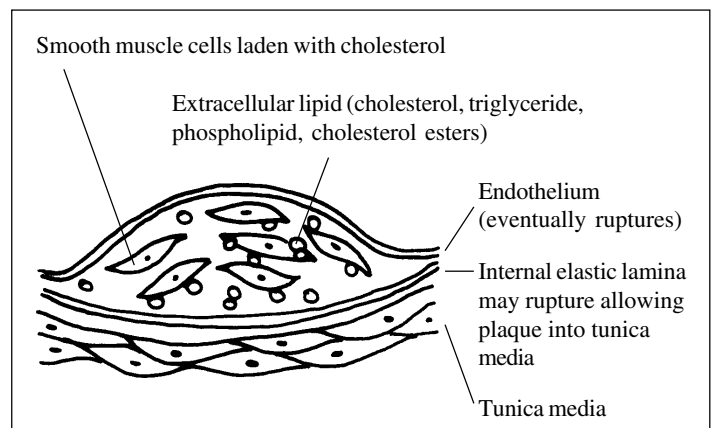
4. The protruding surface of the plaque has a roughened surface often containing collagen fibres. Platelets will stick to this and rupture causing two effects:

   (a) The platelets release a hormone called platelet derived growth factor (PDGF) which together with similar growth factors released from the macrophages and damaged endothelial cells cause the plaque to grow larger due to more proliferation of smooth muscle cells and cholesterol uptake. Eventually the arterial lumen may become completely blocked.

   (b) The ruptured platelets release clotting factors, which may, if in high enough concentration, initiate the clotting cascade forming a clot (thrombus) over the plaque surface. If this breaks off (an embolus) it may block a narrower artery further along the system, again contributing to myocardial infarction.

The structure of an atheromatous plaque is shown in Fig 3. The heart can continue working providing only small areas suffer myocardial infarction. Death of large amounts of cardiac muscle will result in the death of the individual due to heart failure.
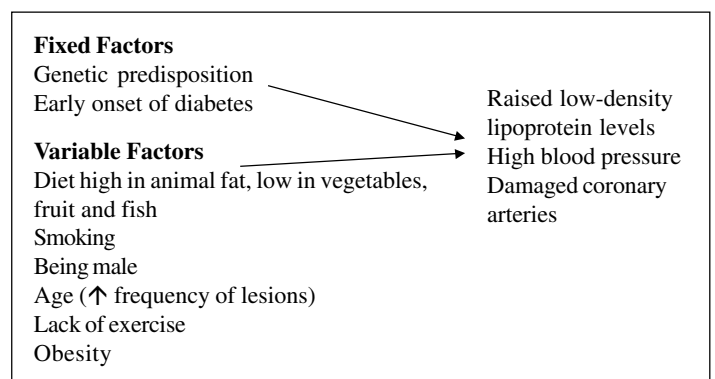
Fig 3. Structure of an atheromatous plaque

Smooth muscle cells laden with cholesterol

Extracellular lipid (cholesterol, triglyceride, phospholipid, cholesterol esters)

Endothelium (eventually ruptures)

Internal elastic lamina may rupture allowing plaque into tunica media

Tunica media

Causes of CHD

The precise causes of coronary heart disease are unknown. However, several predisposing factors have been identified (Fig 4).

Fig 4. Predisposing factors

Fixed Factors
Genetic predisposition
Early onset of diabetes

Variable Factors
Diet high in animal fat, low in vegetables, fruit and fish
Smoking
Being male
Age (↑ frequency of lesions)
Lack of exercise
Obesity

Raised low-density lipoprotein levels
High blood pressure
Damaged coronary arteries

1. **Smoking**. Cigarette smoking appears to accelerate the development of atherosclerosis and smokers have a lower ratio of HDL:LDL. Heavy smokers are more likely to suffer fatal myocardial infarctions (MI) and many cases of MI stem from atherosclerosis.

2. **Genetic predisposition**. Children who inherit high blood cholesterol levels (hypercholesterolemia) suffer increased incidence of coronary heart disease. Such children often lack the specific receptors that normally remove low-density lipoproteins from the blood.

3. **Diabetes mellitus**. Individuals who suffer from diabetes are more likely to develop CHD, and at an earlier age.

4. **Hypertension**. The higher the blood pressure, the greater the risk of coronary disease. However, hypertension only accelerates atherosclerosis when other risk factors - especially high blood lipid levels - are present.

5. **High blood lipid levels**, particularly low-density lipoproteins (LDLs). Excess LDL is deposited in the plaque. In contrast, high-density lipoprotein (HDL) appears to have a protective effect because this type of lipoprotein is responsible for carrying lipid out of the walls of the arteries. Physical activity may have a protective effect by increasing HDL levels and/or by reducing clotting.

6. **Obesity** is commonly associated with CHD but this may be because it is linked to other risk factors such as high plasma cholesterol levels.

Box A. Diagnostic tests for coronary heart disease

24 hour ECG	Detects abnormal electrical activity of the heart over a 24 hour period
Exercise ECG	Monitors electrical activity whilst the patient is on a treadmill
Enzyme test	Damaged heart muscle releases characteristic enzymes
Echocardiography	The flow of blood through the heart is tracked using ultrasound imagery
Nuclear imaging	The flow of blood through the heart and its walls is tracked by the use of radioactive isotopes such as thallium
Arteriography by X-rays	Narrowing of the coronary arteries is detected by injecting a radio opaque dye
MRI scanning	Uses nuclear magnetic resonance imaging techniques

Treatment of angina

Remember that angina is the pain which results when the amount of oxygen being supplied to the heart is insufficient for its needs. The treatment of angina therefore involves either decreasing the activity, hence oxygen demand of the heart or increasing oxygen supplies to it, or both. Nitroglycerin based drugs may be taken to dilate the coronary arteries.
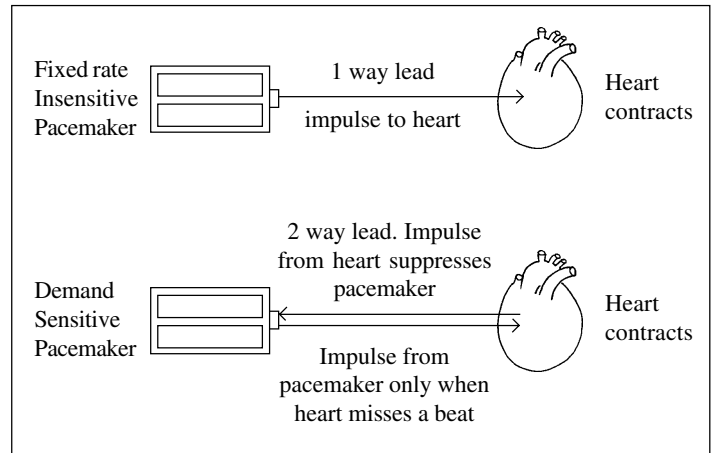
Treatment of myocardial infarction

If an area of heart muscle is deprived of oxygen for so long that it dies, the individual is said to have suffered a myocardial infarction. Myocardial infarction is usually precipitated by a blockage or by haemorrhage in an atherosclerotic coronary artery. The usual treatment for developing myocardial infarction is to try to break down the thrombus that has caused the blockage by use of thrombolytic substances such as streptokinase. If the damage involves the conducting system of the heart then the rhythm of the cardiac cycle may become abnormal. This may be controlled by the use of a Pacemaker.
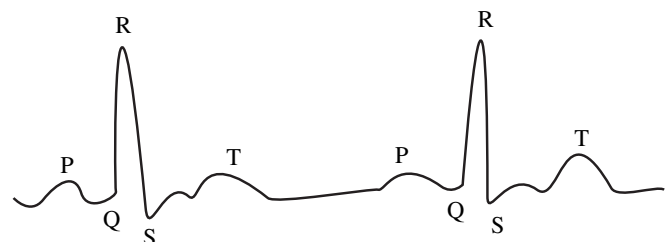
Pacemakers

Every year about 7000 patients in Great Britain have an electronic pacemaker (pulse generator) surgically implanted into the muscle of the chest wall. A pacemaker is about the size of a small matchbox and is used to correct slow heart rates caused by disease and ageing of the heart. They usually have lithium batteries as a power source which have a life of about 10 years before needing replacement. Some types (fixed rate insensitive pacemakers) deliver a regular impulse at about 60 times per minute, causing a regular but inflexible heart rate. Others are sensitive to the actual heartbeat (demand sensitive pacemakers) and only deliver an impulse when required. Pacemakers are shown in Fig 6.

Fig 6. Types of Pacemaker

ECG recording

The electrical activity of the heart throughout the cardiac cycle can be recorded at the body surface using a sensitive device known as an electrocardiograph machine (ECG). The recordings can give information about normal heart activity and can also show up any abnormalities in the cardiac rhythm. The ECG can be continually recorded over a 24 hour period whilst the patient is carrying out a normal daily routine. The 24 hour trace can then be electronically scanned to detect any abnormalities which occurred through the day. A normal ECG trace is shown in Fig 5. Such traces can either be displayed graphically or on an oscilloscope.

Fig 5. A normal ECG trace

P wave = atrial depolarisation
QRS complex = ventricular depolarisation
T wave = ventricular repolarisation
P-Q distance = delay in impulse passage through atrioventricular node and bundle of His

Practice questions

1. Read through the following account of ischaemic heart disease and then fill in the spaces with the most appropriate word or words.
During ischaemic heart disease the .... arteries become narrowed by the formation of .... These accumulate the lipid .... derived from .... lipoproteins in the blood plasma. The narrowing of the arteries impedes the blood flow thus reducing the supply of .... to parts of the heart muscle. This may cause the pain of .... but does not actually result in the death of cardiac muscle. Clots may form in the narrowed arteries and break off forming .... These could be carried on in the circulation and eventually block smaller arteries. Thus the cardiac muscle supplied would die. This is known as .... It is possible to treat the clots with the enzyme .... which will dissolve them before they cause death of the heart muscle.
(9 marks)

2. Distinguish between each of the following pairs.

   (a) Atheroma and thrombus   (4 marks)

   (b) LDLs and HDLs   (4 marks)

   (c) Angina pectoris and myocardial infarction   (4 marks)

3. Suggest why diet influences the development of ischaemic heart disease.
(6 marks)

4. Which of the following statements can be correctly applied to cholesterol and which cannot? Indicate your answer by writing true or false.

   (a) It is a major constituent of plants, fungi, yeasts and bacteria.

   (b) It is synthesised in the liver from acetyl coenzyme A, much of which comes from surplus saturated fatty acids.

   (c) It is a constituent of many lipoproteins.

   (d) It is a normal component of fluid mosaic cell membranes in mammals.

   (e) Sex hormones are synthesised from cholesterol.   (5 marks)

5. Suggest an explanation for each of the following:

   (a) Why eating red fish regularly is supposed to be good for you.
(3 marks)

   (b) Why the reduction of blood supply to the cardiac muscle can result in the pain of angina.   (3 marks)

   (c) Why cigarette smoking may lead to the development of angina.
(3 marks)

Answers
Semicolons indicate marking points

1. coronary;
   plaques/atheromas;
   cholesterol;
   low-density;
   oxygen;
   angina;
   emboli/embolisms;
   myocardial infarction;
   streptokinase;

2. (a) Atheroma is a plaque;
       thrombus is a blood clot;
       atheroma contains smooth muscle cells/macrophages rich in cholesterol;
       clot contains fibrin meshwork with trapped blood cells;

   (b) LDLs are low density lipoproteins HDLs are high density lipoproteins;
       both carry cholesterol through the blood;
       LDLs unload cholesterol into cells/artery walls resulting in plaque formation;
       HDLs lift cholesterol out of cells/plaques and take it to the liver for excretion;

   (c) Angina pectoris is when cardiac muscle receives insufficient oxygen to meet its needs;
       thus builds up an oxygen debt and accumulates lactic acid which causes the pain;
       in myocardial infarction the cardiac muscle receives insufficient oxygen to survive/to respire;
       thus the muscle dies in that section of the heart wall;

3. Raised blood cholesterol levels/LDL levels can cause plaque formation;
   impedence of blood flow by plaques in coronary arteries can cause ischaemic heart disease;
   the liver synthesises cholesterol from products/acetylCoA derived from the respiration of saturated fat;
   thus too much saturated fat in the diet can cause increased cholesterol synthesis;
   ref dairy products/some animal products rich in saturated fats versus plant products/fruit/vegetables low in saturated fats;
   high fibre levels in the diet help to reduce gut absorption of lipids into the blood/lymph;
   some foods are also cholesterol rich such as cheese, eggs, pork etc.;

4. (a) False;
   (b) True;
   (c) True;
   (d) True;
   (e) True;

5. (a) Red fish contain high concentrations of omega-3 fatty acids in their oily bodies;
       omega-3 fatty acids are known to reduce blood levels of LDLs which cause plaque development;
       omega-3 fatty acids are also though to raise blood levels of HDLs which remove cholesterol from artery walls thus reducing plaque size;
       omega-3 fatty acids also reduce the risk of unwanted blood clotting;

   (b) Reduction of blood supply means a reduction of oxygen supply to the muscle;
       the effect is greater if the heart muscle is having to work harder during exercise;
       aerobic respiration/respiratory chain/Krebs cycle will be impeded resulting in an oxygen debt;
       thus lactic acid accumulates causing the pain of angina;

   (c) Smoking cigarettes results in carbon monoxide carriage in the blood/ ref carboxyhaemoglobin;
       This can damage the endothelial lining/can alter the biochemical groupings on the endothelial cell membranes of arteries;
       This causes the onset of plaque formation by stimulating cholesterol uptake from LDLs;