TOPIC 1: LIFESTYLE, HEALTH AND RISK

For the Edexcel Biology A Level (SNAB)

TOPICS COVERED

- The Circulatory System
- Water as a Transport Medium
- The Cardiac Cycle
- Atherosclerosis
- Blood Clotting
- Defining Risk
- Study Design
- Risk Factors for CVD - Blood Pressure, Energy Balance, Smoking, Weight, etc.
- Treating CVD including Drugs
- Biomolecules
- Cholesterol

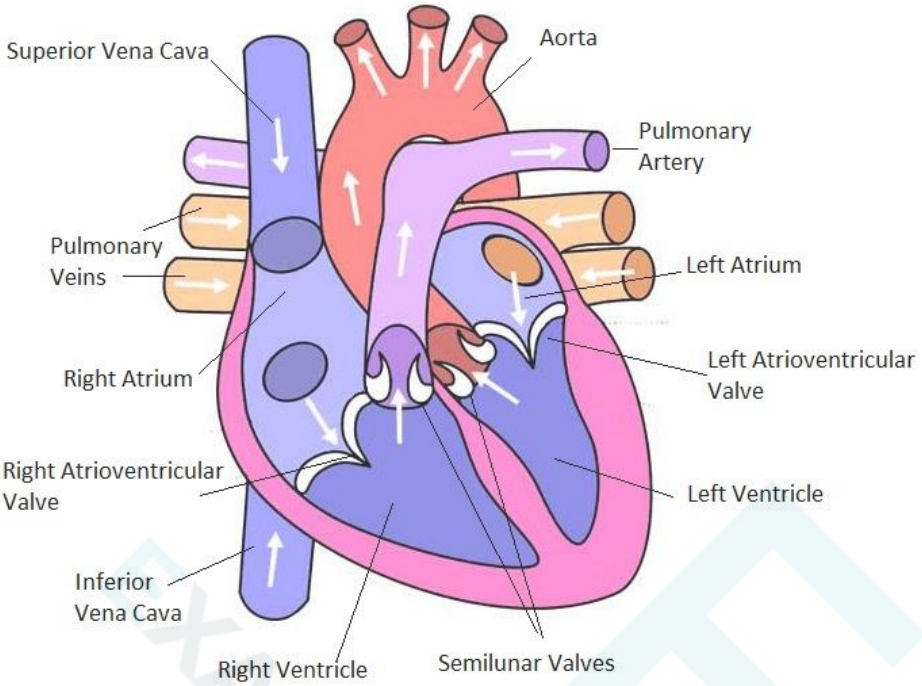
The Circulatory System

Key Terminology and Equations

Term	Definition
Mass Flow	All the particles in a liquid move in one direction through tubes due to pressure differences
Transport Medium	Fluid that transports substances around the body
Transport System	The vessels which carry a transport medium around the body
Open Circulatory System	Blood circulates in large open spaces. A simple heart pumps blood out into cavities surrounding organs, where exchange occurs. During diastole, blood is drawn back into the heart through small valved openings
Closed Circulatory System	Blood is enclosed within vessels; blood travels under high pressure and moves faster, thus increasing the efficiency of substance exchange Ventricle → Arteries → Arterioles → Capillaries → Venules → Veins → Atrium
Single Circulatory System	Contain two heart chambers; blood passes through the heart once, as these systems are located in smaller-sized organisms
Double Circulatory System	Blood flows into the heart twice after passing through the lungs, as a larger pressure difference is needed to cause vigorous blood flow to compensate for the greater size and metabolic rate of the endotherm, where pressure is lost in capillary beds and is restored by the second journey through the heart
Cardiac Cycle	Sequence of events during a heartbeat
Elastic Recoil	Ability of arteries to expand during systole and relax during diastole
Myocardium	Muscular tissue of the heart
Cardiac Output	Volume of blood pumped by the heart per minute
Stroke Volume	Volume of blood pumped from the left ventricle per beat
Coronary Arteries	Arteries which supply the heart with its own blood supply needed for respiration
Atheroma	Deposit containing cholesterol and other chemicals which is formed within the wall of an artery
Cholesterol	Important lipid constituents of cell membranes, but a high proportion in the blood is associated with an increased risk of coronary heart disease.
Thromboplastin	Enzyme involved in the conversion of prothrombin to thrombin
Prothrombin	A soluble protein plasma secreted in the liver using Vitamin K
Thrombin	An enzyme which catalyses the conversion of fibrinogen into fibrin
Fibrin	Protein which forms long, insoluble strands
Myocardial Infarction	Commonly known as a heart attack; when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle
Angina	Chest-pain, usually experienced during exertion, which causes oxygen-deprived myocardium to respire anaerobically
Arrhythmia	Irregular heart beat, which can itself lead to heart failure. This can be important in the diagnosis of coronary heart disease
Aneurysm	If part of an artery is narrowed and hardened, blood can build behind it. The artery bulges and an aneurysm forms, which will rupture, resulting in blood loss and shock, which could prove to be fatal
Risk	The probability of an occurrence for some event, usually in the context of hazards

Heart Beat (bpm) = 60 ÷ Period of One Cardiac Cycle (s)

The Structure of the Circulatory System

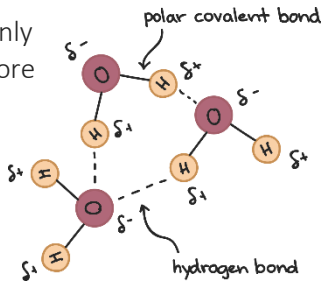


Blood is circulated through the body through arteries and veins. The walls of these vessels contain collagen, a fibrous protein, which makes them strong.

Each time the heart contracts, blood is forces into arteries and elastic fibres allow for stretching. During diastole, the elasticity causes recoil, forcing blood forward. The pulsing flow leads to the capillaries, where rapid exchange occurs. In the veins, low pressure draws blood back. Backflow is prevented by valves when skeletal muscles relax.

Vessels	Arteries	Arterioles	Capillaries	Veins and Venules
Function	Oxygenated blood to organs	Extend to connect capillaries to arteries	Site of exchange	Deoxygenated blood back to heart
Structure	Thick and smooth muscle and elastic layers, with endothelium further narrowing lumen.	One or two layers of smooth muscles with thin elastic layer	Single layer of cells form endothelium in an extensive network	Thin muscle and elastic tissue with outer coat of collagen fibres
Lumen	Very Narrow	Narrow	Narrow	Wide
Pressure	Very High	High	Low	Very Low
Valves	No	No	No	Yes – prevent backflow

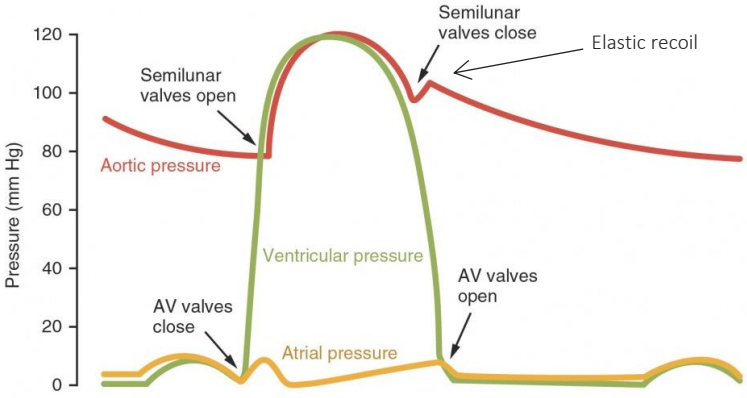
Water as a Transport Medium



- Water is a polar molecule, making it a useful transport medium, due to unevenly distributed charge - the oxygen ends has a slight negative charge as it is more electronegative, and the hydrogen end has a slight positive charge
- The negatively charged end of a water molecule attracts the positive ends of surrounding molecules; hydrogen bonding holds water molecules together and explains properties such as water's liquid state at rtp
- Ionic and polar molecules dissolve in water, allowing reactions to occur in the cytoplasm, but also allowing substances to be transported in the water. Hydrophobic substances, such as lipids, must combine with proteins to be transported
- Water also allows temperature regulation, as the specific heat capacity is very high, due to the hydrogen bonding requiring large amounts of energy to be overcome. Even extreme environmental variations will have little effect on the internal conditions due to this property of water

The Cardiac Cycle

- Contractions of the myocardium generate pressure changes which result in the orderly movement of blood
- Blood flows from an area of high to low pressure unless flow is blocked by a valve
- Events on the right and left sides of the heart are the same, but pressures are lower on the left



Atrial Systole: Due to pressure increase, AV valves open and 70% of blood leak into the ventricles. Atrium contracts and remaining 30% of blood forced into ventricles

Ventricular Systole: When the atria are relaxed, ventricle walls contract, forcing blood out. Pressure of blood forces AV vales to slam shut and opens the semilunar valves. Blood passes into aorta and pulmonary veins

Diastole: The ventricles relax and the pressure of ventricles falls below that of arteries due to elastic recoil of relaxing heart. Blood under high pressure in the arteries causes semilunar vales to shut. Blood from the vena cava and pulmonary veins fill the atria due to low pressure and the cycle repeats

Atherosclerosis and Blood Clots

If arteries become very narrow or blocked then they cannot supply enough blood to carry oxygen to tissues, causing limited function. The fast-flowing blood under high pressure in the arteries makes them susceptible to risk of damage to the walls, so only arteries get atherosclerosis

1. Endothelial lining of the artery is damaged by high blood pressure or toxins caused by smoking
2. This triggers an immune response; white blood cells, which travel to the site of damage, cause the accumulation of LDL cholesterol, which forms the bases of an atheroma
3. Calcium salts and fibrous tissues cause the build up of a hard plaque underneath the endothelium
4. This causes a positive feedback loop, as the atheroma reduces the diameter of the lumen, increasing blood pressure further and further damage elsewhere to the endothelium is more likely
5. The hard plaque causes the artery wall to lose elasticity and harden, known as atherosclerosis
6. If the plaque ruptures, collagen in the endothelium is exposed, activating platelets in the blood, causing a change in shape to form a platelet plug at the site of damage
7. This triggers a cascade of chemical changes known as coagulation to form a blood clot
8. Prothrombin, a soluble plasma protein, synthesised in the liver using Vitamin K, is converted into the enzyme thrombin by the enzyme thromboplastin under the presence of calcium ions
9. Thrombin catalyses the change of soluble plasma protein fibrinogen into insoluble fibrin
10. Fibrin tangles red blood cells and sticky platelets together in a mesh, forming a blood clot

- Blood clots can leave areas ischaemic and unable to respire. They can also travel as an embolus
- If blood supply to the brain is interrupted, a stroke is caused, with numbness, confusion or paralysis
- Narrowing of the coronary arteries limits the volume of blood reaching the myocardium, resulting in chest pain called angina, experienced during exercise, when the heart has to respire anaerobically
- If blood supply to the heart is stopped, this can cause a heart attack

Risk Factors for CVD

Risk is defined as the probability of an occurrence for some event, usually in the context of hazards. Risk can be calculated as a percentage $(\frac{\text{Likelihood}}{\text{Population}} \times 100)$ or as 1 in $\frac{\text{Population}}{\text{Likelihood}}$.

Risk is overestimated if the occurrence is: involuntary, unnatural, unfamiliar, dreaded, unfair or small. Risk is underestimated if the occurrence is voluntary and familiar, or consequences are long term.

Correlation between two variables may suggest risk factors but does not guarantee causation

Risk factors can be deduces using different studies. A cohort study follows a group over time, and compares exposure to risk factors to people with and without a condition to draw a conclusion. A case control study compares the history of exposure to risk factors for individuals with an without a condition to find a conclusion. A good study should have:

- a clear aim and hypothesis to be tested
- representative sample without selection bias
- repeatable method which should produce valid and reliable results
- clearly defined disease diagnosis
- large sample size, to produce results that could not have occurred by chance
- consideration of other variables, such as age and gender

Blood Pressure

Hypertension is one of the most common factors in the development of CVD, as it increases the likelihood of the occurrence of atherosclerosis. Blood pressure is the measure of the hydrostatic force of the blood against the walls of a vessel, dependent on the diameter of the lumen and the pressure caused by the vessels. Pressure in the arteries is higher during ventricular systole (systolic pressure) and lower during diastole (diastolic pressure).

A sphygmomanometer is a device used to measure blood pressure, consisting of a cuff and a manometer to measure pressure. Blood pressure is measured in mmHg, and is recorded as two numbers, systolic pressure over diastolic pressure.

Contact between blood and the walls of a vessel causes friction, impeding blood flow, called peripheral resistance. As the capillaries offer a greater surface area, blood is slowed and pressure falls. Fluctuations in pressure are caused by the cardiac cycle of the heart. Elastic recoil maintains pressure during diastole. Blood pressure increases as the lumen's diameter decreases, therefore any factor that causes constriction, such as adrenaline or high-salt diet, increases blood pressure.

At the arterial end of a capillary, blood is under pressure, forcing fluid and molecules from the plasma through the capillary walls into intercellular spaces, forming tissue fluid. This tissue fluid allows for exchange of substance; most returns to the capillary due to an increased water concentration gradient but some is drained by the lymph capillaries. If blood pressure is higher than normal, more fluid may be forced out, accumulating fluid within tissues, causing oedema, causing swelling, and is a symptom of high blood pressure.

Smoking

- Smoking damages the lining of the arteries, leading to a build-up of an atheroma, narrowing the lumen. This can cause angina, a myocardial infarction or a stroke
- CO in tobacco reduces O_2 concentration in the blood, meaning the heart must pump harder to supply oxygen to meet demand
- Nicotine in cigarettes stimulates the body to secrete adrenalin, making the heart beat faster and raising blood pressure
- Blood is therefore more likely to clot, increasing risk of CVD

Weight and Physical Activity

Research shows that being overweight or obese can raise blood cholesterol levels and increase blood pressure due to excess weight carried. Likelihood of developing Type II Diabetes, where the body does not secrete enough insulin or the body fails to respond to the insulin produced, increases, as continuously high blood glucose levels from frequent sugar-rich food reduces sensitivity of cells to insulin. Physical activity, however, can reduce blood pressure, control weight and raise HDL levels and is therefore recommended.

Energy Balance

The obesity epidemic is in part due to the sedentary modern lifestyle and the high proportions of fats and carbohydrates in diets.

The Health Department publishes dietary guidelines to get the energy balance right. Dietary Reference Values are not recommendations, but include an estimated average and a reference nutrient intake, providing a range for a healthy diet to fall into. Whilst carbohydrates and fats are required, overeating can lead to obesity.

The basal metabolic rate (BMR) is the constant supply of energy to maintain the essential body processes. This is higher in males, heavier people, younger people and more active people.

- A negative energy balance occurs due to excessive exercise, stress or high BMR. This can lead to weight loss as energy stored in the body is used to meet demand
- A positive energy balance occurs when a person routinely eats too much or does too little exercise. Additional energy is stored and the person gains weight

BMI is calculated using the formula $\frac{\text{mass (kg)}}{\text{height}^2(\text{m}^2)}$. A BMI of 25-29.9 is overweight, and 30 and above is normal. A BMI of 20-24.9 is normal, and anything below this is underweight. There is evidence to suggest that waist-to-hip ratio is a better measure, with a strong positive correlation with heart attack rate. It is measured by dividing waist circumference at the rib margin by the hip circumference around the buttock. Waist-to-hip ratio should be lower than 0.90 for men and 0.85 for women.

Genetic Risk Factors

Apolipoproteins are the protein component of lipoproteins, formed in the liver with important roles in stabilising lipoprotein structure and receptor recognition. The APO gene cluster has association with CHD, but the numerous mutations and their effects make it impossible to estimate the effect of a single gene, as CVD is multifactorial.

APOA	Major protein in HDL	Helps remove cholesterol to the liver for excretion	Mutations in apoA gene associated with low HDL levels and reduced cholesterol removal, increasing CHD risk
APOB	Major protein in LDL	Transfers cholesterol from blood to cells	Mutations in apoB result in higher LDL levels and higher CVD risk
APOE	Major protein in HDL and VLDL	Remove cholesterol to the liver for excretion	Three alleles produce E2, E3 and E4. E4 slows removal of cholesterol and so increases risk of CHD

Antioxidants, Salt, Coffee, Alcohol and Stress

- During reactions in the body, unstable radicals result when an atom has an unpaired electron. Radicals damage many cell components, causing cancer and CVD. Vitamins like C, E and beta-carotene provide hydrogen atoms to stabilise these radicals. Fruits and vegetables are a good source of these antioxidants
- High salt diets cause the kidneys to retain water, and the higher fluid levels elevate blood pressure
- In the long term, caffeine, contained in coffee, may slightly increase risk of CVD as it is a stimulant, causing activity but also vessel constriction, increasing blood pressure slightly
- Stress triggers the secretion of adrenalin, causing the arteries to constrict, raising blood pressure. Stress can also lead to overeating, poor diet and higher alcohol consumption
- Heavy drinking raises blood pressure, contributes to obesity and causes irregular heartbeat, due to tissue damage, and the liver cells responsible for detoxification are damaged. Glucose and lipids are left in the blood and excess alcohol forms VLDLs. However, moderate alcohol levels lead to higher HDL levels

Reducing CVD Risk

Risk of CVD can be reduced by smoking cessation, maintaining low blood cholesterol, BMI and normal blood pressure, taking more physical exercise and moderate alcohol use.

Drugs to Treat High Blood Pressure

Drugs can be used to treat people with excessively high blood pressure and evidence of CVD. These may have side effects and vary in effectiveness in different people

- ACE Inhibitors: antihypertensive drugs which reduce the synthesis of angiotensin II. This hormone causes vasoconstriction of blood vessels to control pressure. The ACE inhibitors prevent the hormone from people produced from its inactive force I, lowering blood pressure
    - Side effects may include dizziness, abnormal heart rhythms and lower kidney function
- Calcium Channel Blockers: antihypertensive drugs which block the calcium channels in the muscle cells of the arterial lining. For the muscle to contract, calcium must pass through these channels into the muscle cells. Failure of calcium to enter the cell prevents muscular contraction of vessel walls, lowering blood pressure
    - Side effects may include headaches, swollen ankles and abnormal heart rhythms
- Diuretics: increase the volume of urine produced by the kidneys, reducing excel fluids and salts from the body. This reduces plasma volume and cardiac output, lowering blood pressure
    - Side effects may include dizziness, nausea or cramps

Reducing Blood Cholesterol Levels

- Statins are used to inhibit an enzyme involved in LDL cholesterol production, reducing risk of CVD
- Large studies show that risk of heart attack lowers by 33%
- There are very low increases in risks of death by non-vascular causes and gastronomical and respiratory cancers

Anticoagulant and Platelet Inhibitory Drug Treatment

- These drugs prevent the formation of an arterial blood clot for people at high risk of CHD or a stroke. The tendency for platelet aggregation and clotting is reduced by these drugs.
- Aspirin reduces the stickiness of platelets and the likelihood of a platelet plug forming. This drug may cause serious bleeding in combination with clopidogrel, another inhibitory drug, and this risk outweigh the benefits.
- Warfarin is an anticoagulant, affecting the synthesis of clotting factors. The benefits are higher than with aspirin but risk of bleeding is higher.

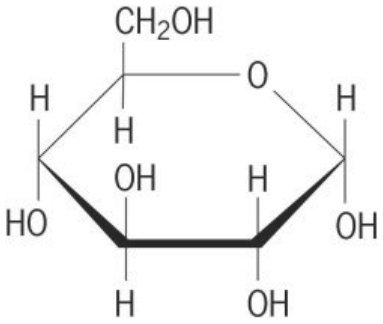
Dieting

An ideal diet to reduce CVD risk would have:

- an energy balance
- reduced saturated fat
- more polyunsaturated fats
- reduced cholesterol and salt.
- increased intake of fruit and vegetables. Non-starch polysaccharides, known as soluble fibre, are found in these. They are partially digested to form a gel to trap and prevent absorption of cholesterol. They also contain antioxidants
- consumption of oily fish, which contain omega-3 fatty acids. They have polyunsaturated fatty acids with the first double bond between the 3rd and 4th carbons. These are essential for cell function and reduce heart disease risk

Biomolecules

Carbohydrates are found as monosaccharides, disaccharides or polysaccharides. Monosaccharides are the simplest sugar units. Disaccharides are the sugars formed when two monosaccharides are joined by a glycosidic link formed by a condensation reaction. A polysaccharide is a carbohydrate molecule consisting of many sugar units linked by these glycosidic bonds. Oligosaccharides have 3-10 units.



This is an α-glucose monosaccharide, which you should be able to draw out. During a condensation reaction, the two identical glucose monosaccharides react to form the disaccharide maltose, eliminating water. These two monomers are joined by a glycosidic bond. To split this disaccharide, water is added in a hydrolysis reaction.

There are three common disaccharides: maltose, sucrose and lactose.

Maltose = Glucose + Glucose

Sucrose = Glucose + Fructose

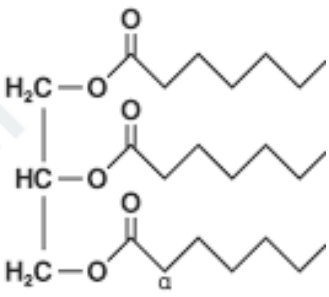
Lactose = Glucose + Galactose

Starch is a polymer made of glucose monomers. There are two possible structures within starch

Amylose	Has 1,4 glycosidic links. Coils into a compact helix due to hydrogen bonding, making it a good storage molecule
Amylopectin	Has 1,4 glycosidic links to form helices. However, it has 1,6 glycosidic bonds to form side branches within the molecule

Name	Structure and Chemical Properties	Biological Role and Use
Glucose	Sweet, soluble, crystalline Monosaccharide	Substrate for cellular respiration to release energy
Maltose	Sweet, soluble, crystalline Disaccharide	Found in Germinating Seed Substrate for cellular respiration to release energy
Sucrose	Sweet, soluble, crystalline Disaccharide	Transport molecule in translocation through the phloem Substrate for cellular respiration to release energy
Starch	Insoluble polysaccharide with amylose and amylopectin	Storage molecule of glucose found in plants Broken down to produce glucose for respiration
Glycogen	Insoluble polysaccharide with many 1,6 glycosidic links and higher proportions of amylopectin	Compact storage molecule in the liver, broken down to raise blood glucose levels. Structure with many short branches allows for rapid hydrolysis. Insoluble, meaning it does not affect the osmotic gradient.

Lipids contain carbon, hydrogen and oxygen, though with lower carbon proportions. They form fats for energy and electrical and thermal insulation, phospholipids and cholesterol for membranes and form the basis of steroids.



A triglyceride is formed when three fatty acids are linked to a glycerol molecule by ester bonds formed in condensation reactions.

Saturated fats contain the maximum number of hydrogen atoms, with long straight chains which pack closely together. Monounsaturated fatty acids have one double bond between carbon atoms in each chain, while polyunsaturated acids have many. C=C bonds introduce kinks in the chain, preventing chains from packing closely together, with weaker intermolecular forces.

Cholesterol is a short lipid molecule, and is a vital component of cell membranes with roles in structure and function. Steroid sex hormones such as progesterone and testosterone are produced from cholesterol. Cholesterol is made in the liver from saturated fats and is obtained in our diet.

Cholesterol is combined with proteins to form soluble lipoproteins to be transported around the body

- High Density Lipoproteins (HDLs) have a higher percentage of protein compared with LDLs and are made when triglycerides from unsaturated fats combine with cholesterol and protein. HDLs transport cholesterol from body tissues to the liver to be broken down, lowering blood cholesterol levels and helping to remove fatty plaques of atherosclerosis.
- Low Density Lipoproteins (LDLs) have a lower percentage of protein and are made when triglycerides from saturated fats combine with cholesterol and protein. LDLs are the main cholesterol carrier in the blood. They circulate and bind to receptor sites of cell membranes to be taken in. Excess LDLs overload these receptors, resulting in higher blood cholesterol levels. Statured fats may also reduce the activity of LDL receptors, so the LDLs are not removed, further increasing blood cholesterol. This LDL can be deposited in artery walls to form atheromas

It is desirable to maintain a higher level of HDL and a lower level of LDL. Eating a low-fat diet which particularly avoids saturated fats will reduce total blood cholesterol, and especially LDL cholesterol.