Cholesterol and lipoproteins

Cholesterol

Without cholesterol your body wouldn't work as it forms part of the outer shell of every cell. It is abundant in the brain, nervous tissue, skin and adrenal glands. However, too much cholesterol in the blood increases the risk of cardiovascular disease (CVD).

Production and function

Cholesterol has three main functions within the body. It is a structural component of all cell membranes; is used to manufacture steroid hormones and Vitamin D; and is used to produce bile acids, which help us to the digest and absorb fats in the diet.

The body produces its own supply of cholesterol, mainly in the liver. It is also present in foods of animal origin, such as eggs, meat and dairy products. The amount of cholesterol made by the body varies to a small extent with intake of dietary cholesterol, but what is more important is the type of fat in the food you eat. Saturated fat is a more powerful influence as it reduces the ability of the liver to take cholesterol out of the circulation so increasing blood cholesterol.

Transport and removal

Cholesterol must be transported from the liver, where it is made, to the tissues where it is needed. It travels as a component of lipoproteins. Cholesterol is removed from the body in bile as either cholesterol or bile salts. About 98% of bile salts excreted from the gall bladder are reabsorbed by the large intestine, taken up by the liver, and re-excreted as bile. This process is known as the enterohepatic circulation.

Bile salts, which are not reabsorbed, are excreted in the faeces. Approximately one gram of cholesterol is eliminated from the body each day in this manner.

Triglycerides is another name for dietary fats. Triglycerides also circulate in the blood alongside cholesterol. Immediately after a meal the amount of triglyceride in the blood increases and then slowly decreases as triglycerides are either used up or stored for later use. In some cases the removal of triglycerides from the blood stream is less efficient and this results in raised triglycerides which has health implications. It can be caused by hereditary factors or by diet and lifestyle.

Lipoproteins

Structure and function

Lipoproteins are spherical particles and have an outer water soluble surface and an inner water-insoluble core. The outer portion is made up of phospholipid, protein and cholesterol, with triglyceride and cholesterol ester (a cholesterol molecule linked to a fatty acid) forming the core. Lipoproteins are divided into four main groups, each with a different proportion of cholesterol and triglyceride. They are classified by density, the lower the density of the lipoprotein, the greater the amount of fats contained within it.

Lipoproteins	Main Function
Chylomicrons	Transport triglycerides from intestine to tissues
VLDL (very low density lipoproteins)	Transport triglycerides from liver to adipose tissue and muscle
LDL (low density lipoproteins	Transport cholesterol from liver to tissues
HDL (high density lipoproteins)	Transport surplus cholesterol from tissues back to liver for removal/recycling

Chylomicrons

Chylomicrons, the largest and least dense of the lipoproteins are formed in the intestinal cell walls from dietary fat and cholesterol. Their main task is to carry triglycerides from the intestine to the tissues where they are needed as a source of energy. In the circulation triglycerides are removed from chylomicrons via the action of lipoprotein lipase (LPL), an enzyme present in the capillaries of many tissues. If present in large amounts, such as after a fatty meal, chylomicrons cause the plasma to appear milky.

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Very low density lipoproteins (VLDL)

VLDLs are synthesised in the liver. Like chylomicrons they function primarily to distribute triglycerides to target sites such as adipose tissue and skeletal muscle where they are used for storage and energy. The manner in which triglycerides are removed from the circulation is the same as that for chylomicrons. Gradually with removal of triglycerides and protein, VLDLs are converted to LDL. High plasma levels of VLDL are to be found in familial hypertriglyceridaemia, diabetes mellitus, underactive thyroid and in people with a high alcohol intake.

Low density lipoproteins (LDL)

LDLs are cholesterol-rich particles. About 70% of plasma cholesterol occurs in this form. LDLs are chiefly involved in the transport of the cholesterol manufactured in the liver to the tissues, where it is used. Uptake of cholesterol into cells occurs when lipoprotein binds to LDL receptors on the cell surface. LDL-cholesterol is then taken into the cell and broken down into free cholesterol and amino acids.

Conditions involving a defect in or lack of LDL receptors are usually characterised by high plasma cholesterol levels.

The cholesterol cannot be cleared efficiently from the blood and therefore accumulates. This is the case in the inherited condition familial hypercholesterolaemia. High levels of LDL-cholesterol in the blood are associated with an increased risk of CVD.

High density lipoproteins (HDL)

These particles are formed mainly in the liver. They are composed of 50% protein, with phospholipid and cholesterol as the remainder. HDL is commonly known as the 'good' cholesterol. The role of HDL is to transport excess cholesterol from the tissues (including the arterial wall) to the liver for disposal.

Epidemiological studies show that low levels of HDL-cholesterol are predictive of high risk of CVD. In men, levels of HDL-cholesterol below 1 mmol/L confer increased risk of CVD. HDL levels are higher in women than in men. In women, HDL-cholesterol levels below 1.2 mmol/L increase risk of CVD.

Apoproteins and Lipoprotein (a)

Apoproteins are the protein component on the outer surface of lipoproteins. They are involved in receptor recognition at cell surfaces and enzyme regulation. Lipoprotein (a) or Lp(a), is assembled in the liver from LDL-cholesterol and apoprotein (a). It is thought to increase CVD risk by interfering with clotting mechanisms and promoting thrombosis (blood clotting) at the endothelial surface (lining of blood vessel). It may also lead to an accumulation of cholesterol in the walls of the blood vessels. It is believed that the concentration of Lp(a) in the plasma is mostly genetically determined. As a risk factor for heart disease a high level of Lp(a) is of greater significance when LDL-cholesterol is also raised. Hence it is important to reduce elevated LDL-cholesterol levels.

Desirable limits for blood cholesterol levels

The main aim of treatment in most hyperlipidaemic patients is to reduce the risk of premature angina or heart attack, and to reduce the occurrence of further heart attacks in people who already suffer from CVD.

The average cholesterol in middle aged men and women in the UK is between 5.0mmol/L and 6.0mmol/L. Cholesterol experts agree that a total cholesterol of 5mmol/L or less, a non -HDL cholesterol of 4mmol/L or less and a LDL- cholesterol of 3mmol/L or less are considered healthy for most people. If you have existing CVD or are at a higher risk of developing CVD, it is likely that your GP will advise you to reduce your cholesterol further. Any target cholesterol levels that your doctor suggests will depend on the cause of the raised cholesterol, age and any other risk factors.

Risk factors must not be regarded in isolation, as their interaction multiplies the risk of CVD. In addition to tackling elevated lipids, modification of co-existing factors, such as smoking and hypertension, is necessary. The National Institute for Health and Care Excellence (NICE) Guideline CG181 gives recommendations for cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. They recommend a full formal risk assessment for those who have an estimated 10 year risk of cardiovascular disease of 10% or above. For guideline information please see references below.

References

- National Institute for Health and Care Excellence (NICE): Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (CG181)
  www.nice.org.uk/guidance/cg181/informationforpublic
- Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3)
  www.jbs3risk.com