

A) Cholesterol and Lipoproteins

CHOLESTEROL

Cholesterol is essential for life and present throughout the body. It is abundant in the brain, nervous tissue, skin and adrenal glands.

Production and function

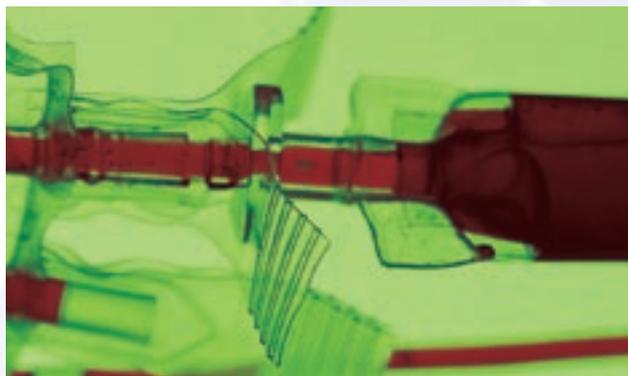
Cholesterol has three principal functions within the body. It is a structural component of all cell membranes; is used to manufacture steroid hormones and Vitamin D; and is used to produce bile acids, which facilitate the digestion and absorption of fats in the diet.

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 synthesised by the body varies to a small extent with intake of dietary cholesterol, but saturated fat is a more powerful influence. Excess saturated fat in the diet increases 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.



LIPOPROTEINS

Structure and function

Lipoproteins are composed of an outer water-soluble surface and an inner water-insoluble core. The outer portion comprises 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

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.

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.

Cholesterol and Lipoproteins continued...

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 is then taken into the cell and broken down into free cholesterol and amino acids.

Disorders 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 disorder familial hypercholesterolaemia. High levels of LDL in the blood are associated with an increased risk of coronary heart disease (CHD).

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 CHD. In men, levels of HDL cholesterol below 1 mmol/l confer increased risk of CHD; whereas levels exceeding 1.5 mmol/l lessen the risk attributed by other risk factors. HDL levels are higher in women than in men. In women, HDL levels below 1.2 mmol/l increase risk of CHD, while levels exceeding 1.7 mmol/l are favourable (1).

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 and apoprotein (a). It is thought to increase CHD risk by interfering with clotting mechanisms and promoting thrombosis at the endothelial surface. 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 genetically determined. As a risk factor for heart disease a high level of Lp(a) is of greater significance when LDL is also raised. Hence it is important to reduce elevated LDL 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 coronary heart disease. The New Joint British Society Guidelines recommend that for certain patient groups (listed below), along with lifestyle and blood pressure control the total cholesterol level should be no higher than **4 mmol/l** and the LDL cholesterol should be below **2 mmol/l**:

- **Patients with established coronary heart disease**
- **Patients with other major atherosclerotic disease**
- **Patients with hypertension, dyslipidaemias, diabetes, family history of premature CHD, or a combination of these risk factors, which puts them at high risk of developing CHD or other atherosclerotic disease.**

Risk factors must not be regarded in isolation, as their interaction multiplies the risk of CHD. In addition to tackling elevated lipids, modification of co-existing factors, such as smoking and hypertension, is necessary.

References

Joint British Recommendations on prevention of coronary heart disease in practice: summary. BMJ 2000 Vol 320: 705-708

