NUMBER 13

CYTOPLAN

THE HEALTH INFORMATION SERIES

CHOLESTEROL

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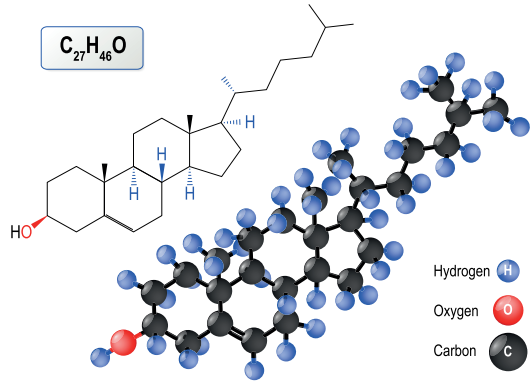
What is cholesterol?

Cholesterol is not technically a fat; rather, it is classified as a "sterol," which is a combination of a steroid and alcohol. Cholesterol is essential to all animal life. It plays a crucial structural role in the cell membrane, which controls how a cell moves, interacts with other cells, and what can enter and exit the cell.



The lipid hypothesis (also known as 'the cholesterol hypothesis)

The work of Ancel Keys, an American physiologist, led to 'the lipid hypothesis' which links raised blood cholesterol levels to the occurrence of heart disease. An accumulation of evidence resulted in the acceptance of the lipid hypothesis by most of the medical community; however, a growing minority argues that the evidence does not support it, and that mechanisms independent of blood cholesterol levels are responsible. This debate is referred to as the "cholesterol controversy". It is closely related to the saturated fat and cardiovascular disease controversy.

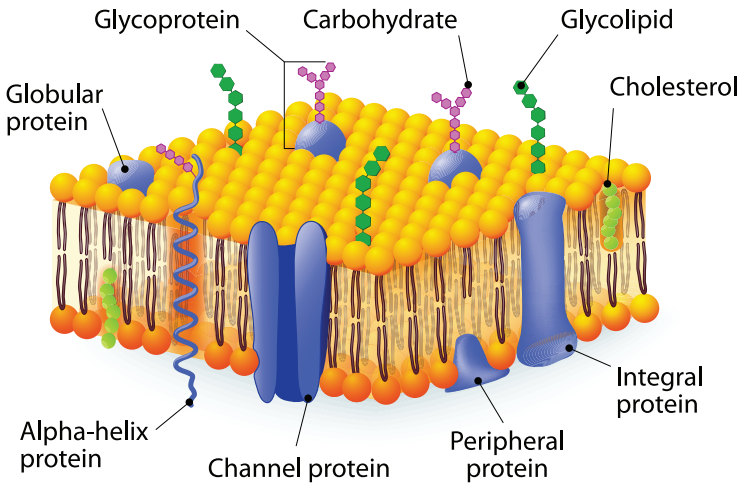
> *"Most researchers today consider that a high intake of saturated fat and elevated LDL cholesterol are the most important causes of atherosclerosis and coronary heart disease. The lipid hypothesis has dominated cardiovascular research and prevention for almost half a century although the number of contradictory studies may exceed those that are supportive. The harmful influence of a campaign that ignores much of the science extends to medical research, health care, food production and human life. There is an urgent need to draw attention to the most striking contradictions, many of which may be unknown to most doctors and researchers."* [1]
>
> *Ravnskov, 2008*

Functions of cholesterol

Cholesterol is a sterol molecule synthesised by all animal cells. It is an essential structural component comprising about thirty percent of animal cell membranes, where its function is to maintain membrane structural integrity and fluidity. In addition, cholesterol is a precursor for the synthesis of steroid hormones, bile acids and myelin.

Cell membranes: All animal cells are surrounded by a lipid bi-layer that comprises phospholipids (a phosphate group attached to a saturated or unsaturated fatty acid), membrane proteins and cholesterol. Through its interaction with the phospholipid fatty-acid chains, cholesterol alters membrane fluidity and maintains membrane integrity. Within the cell membrane, cholesterol also functions in intracellular transport and cell signalling.

Diagramatic cross-section through a cell membrane



Steroid hormones: Within cells, cholesterol is a precursor molecule for the synthesis of vitamin D and all steroid hormones, including the adrenal gland hormones cortisol and aldosterone, and the sex hormones progesterone, oestrogen and testosterone.

Bile acids: Bile acids are derivatives of cholesterol synthesised by hepatocytes (liver cells).

Myelin: Babies and children especially need cholesterol to ensure proper growth and development of their brains. Twenty percent of myelin (the material that forms a sheath around neurons) is cholesterol, and synapse formation in the brain is almost entirely dependent upon its availability (neurons communicate with each other across synapses).

Intestinal permeability: Cholesterol helps maintain the integrity of the intestinal lining, which keeps foreign substances out of our body and protects against autoimmunity and allergy.

Antioxidant: HDL cholesterol is an antioxidant that helps prevent oxidative damage which is associated with everything from heart disease to Alzheimer's to ageing. Coenzyme Q10, a critical antioxidant nutrient, is synthesised by the same pathway as cholesterol.

Sources of cholesterol

Since all animal cells manufacture cholesterol, all animal-based foods contain cholesterol in varying amounts. The body contains between 1,100 and 1,700mg of cholesterol at any one time. Twenty-five percent of that comes from diet and the rest is made in the body, mostly in the liver. The body cannot absorb much of the cholesterol found in food, and most of the cholesterol in the gut is of endogenous origin (i.e. synthesised by the liver). The body tightly regulates the amount of cholesterol in the blood by controlling internal production; when cholesterol intake in the diet goes down, the body makes more. When cholesterol intake in the diet goes up, the body makes less. Therefore, dietary cholesterol intake does not correlate well with blood plasma cholesterol levels. On the other hand, there is a correlation between saturated fat intake and cholesterol levels.

Major dietary sources of cholesterol include cheese, egg yolks, beef, pork, poultry, fish and shrimp. Human breast milk also contains significant quantities of cholesterol.

Synthesis and transport of cholesterol

Synthesis of cholesterol within the body starts with the 'mevalonate pathway' where two molecules of acetyl CoA condense to form acetoacetyl-CoA. This is followed by a second condensation reaction that is catalysed by the enzyme HMG CoA reductase – this is the rate-limiting step in the synthesis of cholesterol and the primary mechanism of statins is to inhibit this enzyme and thus reduce cholesterol synthesis (coenzyme Q10 synthesis is also inhibited, an unwanted side effect of statins). The HMG CoA reductase enzyme is not the final step in the pathway; over thirty enzyme steps are involved in the synthesis of cholesterol.

A decrease in cholesterol synthesis results in intracellular cholesterol becoming depleted. To compensate for this the number of LDL receptors on the cell surface increases – to allow more cholesterol to enter the cell.

Cholesterol is transported in the plasma within lipoproteins, particles with water-soluble proteins on the outer surface and lipid soluble triglycerides and cholesterol on the inner surface. There are several types of lipoproteins in the blood. In order of increasing density, they are: chylomicrons, very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL) and high-density lipoprotein (HDL).

Chylomicrons, which are the least dense cholesterol transport molecules, are assembled in the intestinal cells and carry fats from the intestine to muscle and other tissues in need of fatty acids for energy or fat production. The entire process of chylomicron metabolism is relatively rapid and the presence of chylomicrons in the serum after an overnight fast is considered an indicator of defective lipoprotein metabolism.

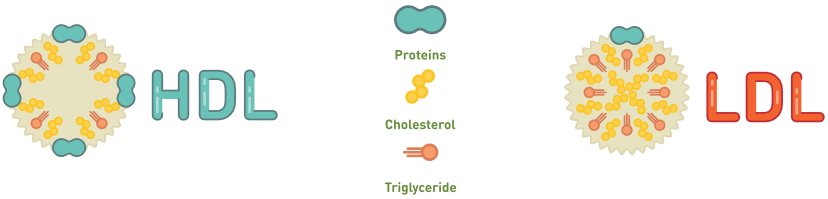
Very Low Density Lipoproteins (VLDL) are produced by the liver from triglycerides and cholesterol. VLDL vary in triglyceride content which they exchange with both LDL and HDL for a cholesterol molecule. Triglyceride enriched LDL molecules are then processed through another reaction that removes the triglycerides provided by VLDL. The result is small LDL particles, which contribute the most to atherosclerotic disease (i.e. LDL particles exist as 'large' or 'small' LDL particles).

Low Density Lipoproteins (LDL) are the major blood cholesterol carriers; they carry cholesterol to cells that need it. Each one contains approximately 1,500 molecules of cholesterol. As explained above, LDL molecules are derived mostly from VLDL metabolism and can be described as 'small' or 'large'; it is the 'small' LDL that are the most damaging.

LDL molecules provide cholesterol for membrane biosynthesis or storage within the cell. LDL directly binds to and inactivates bacterial toxins (i.e. LPS - lipopolysaccharide).[2] The removal of LDL from the circulation is largely mediated through LDL receptors on the cell surface. The number of LDL receptors on the cell surface is controlled according to the cell's cholesterol needs. When this process becomes unregulated, LDL molecules without receptors begin to appear in the blood. These LDL molecules are oxidised and taken up by macrophages, which become engorged and form foam cells. These foam cells contribute to atherosclerotic plaque formation, which is the main cause of heart attacks, strokes and other serious medical problems.

In summary, LDL carries cholesterol to the cells that need it, but if there's too much cholesterol for the cells to use, it can build up in artery walls contributing to disease of the arteries. For this reason, LDL is known as "bad cholesterol". However, this is an over-simplification as it is a sub-type of LDL that is particularly dangerous – referred to as 'small' LDL.

High Density Lipoprotein (HDL) particles transport cholesterol back to the liver, either for excretion or for other tissues that synthesise hormones, in a process known as 'reverse cholesterol transport'. Large numbers of HDL particles correlate with better health outcomes. HDL can remove cholesterol from the macrophages of the arterial wall through a number of mechanisms including an active transport mechanism. Therefore increased concentrations of HDL correlate with lower rates of atheroma progression and thus HDL is sometimes referred to as "good cholesterol".



Lipoprotein (a), abbreviated to Lp(a), consists of an LDL like particle. Plasma levels vary widely between individuals and are thought to be mainly due to genetics. Individuals without Lp(a) or with very low Lp(a) levels seem to be healthy – so it is not considered necessary, at least under normal conditions.

Lp(a) is believed to have a role in wound healing and tissue repair; the mechanism may be through its oxidised phospholipids content (OxPL), which are generated by the oxidation of polyunsaturated fatty acid residues and can be formed on cell membranes under oxidative stress conditions, during apoptosis (cell death) or on LDL during its oxidative modification. During oxidative stress there may be uncontrolled generation of OxPL. Pathologically Lp(a) attracts inflammatory cells to vessel walls and leads to smooth muscle cell proliferation. It is thus highly atherogenic and prothrombotic. Lp(a) is considered a causal risk factor for cardiovascular disease (CVD).

Metabolism, recycling and excretion

Cholesterol is oxidised by the liver into a variety of bile acids. These, in turn, are conjugated with glycine, taurine, glucuronic acid or sulphate. A mixture of conjugated and non-conjugated bile acids, along with cholesterol itself, is excreted from the liver into the bile. Every day up to one gram of cholesterol enters the colon. Whilst approximately ninety-five percent of the bile acids are reabsorbed from the intestines, between fifteen and seventy-five percent of cholesterol excreted in the bile is eliminated in the faeces (i.e. predominantly non-conjugated cholesterol). Cholesterol from diet and shedding of intestinal cells is also eliminated in the faeces.

Causes of high cholesterol

Smoking	A chemical found in cigarettes called acrolein stops HDL transporting cholesterol from fatty deposits to the liver, leading to narrowing of the arteries (atherosclerosis). Quitting smoking has been shown to rapidly improve HDL levels[3]
Diabetes	High cholesterol (and hypertension) are established comorbidities of diabetes[4]
Chronic infections	Chronic infections such as *Helicobacter pylori*[5]
Thyroid	Poor thyroid function[6]
Environmental toxins	Environmental toxins[7], particularly mercury exposure[8]
Genetics	An inherited genetic condition, called familial hypercholesterolaemia, can cause high cholesterol[9]

Contrary to popular belief, a high fat diet may not be the cause of high cholesterol unless the genetic condition familial hypercholesterolaemia is present. Research has been put forward that links high carbohydrate intake and high insulin levels with elevated LDL levels, reduced HDL levels and elevated triglycerides.[10–13]

Current NHS cholesterol guidelines

Blood cholesterol is measured in units called millimoles per litre of blood, often shortened to mmol/L.

As a general guide, the NHS recommends that total cholesterol levels should be:

- 5mmol/L or less for adults
- 4mmol/L or less for those at high risk

And that LDL levels should be:

- 3mmol/L or less for adults
- 2mmol/L or less for those at high risk

The NHS considers an ideal level of HDL to be above 1mmol/L. A lower level of HDL is considered to increase the risk of heart disease. The ratio of total cholesterol to HDL may be calculated. This is total cholesterol level divided by HDL. NHS guidelines recommend this ratio should be below four. NICE guidelines recommend considering other parameters such as IDL, VLDL and lipoprotein (a).[14]

Cholesterol is only one risk factor for cardiovascular disease and statin treatment will be recommended on the basis of cholesterol level and other risk factors, such as smoking and high blood pressure.

Recent developments for predictive markers in cardiovascular disease

Most recent research has shown that total cholesterol and LDL cholesterol are not strongly associated with heart disease, contrary to what current NHS guidelines say. High cholesterol itself does not usually cause any pathology, but high cholesterol alongside other health markers such as elevated triglycerides and elevated inflammatory markers such as highly sensitive C Reactive Protein (hs-CRP) may increase the risk of cardiovascular disease or stroke.

The ratio of total cholesterol to HDL cholesterol is a better predictor than total cholesterol or LDL cholesterol, however even more accurate are new markers like lipoprotein(a), LDL particle number and LDL particle size.[15]

Lipoprotein (a)

Lipoprotein(a), described above, consists of an LDL-like particle.

LDL Particle Number

LDL-P measures the actual number of LDL particles (particle concentration). LDL-P may be a stronger predictor of cardiovascular events than LDL cholesterol.

LDL Particle Size

Many recent studies have looked into the importance of LDL particle size. Studies show that people whose LDL particles are predominantly small and dense, have a threefold greater risk of coronary heart disease. Furthermore, the large and fluffy type of LDL may be protective.

Therefore LDL particle size may be more accurate than LDL particle number, as it determines whether the number is made up of small and dense or large and fluffy types.

LDL cholesterol levels and LDL particle number are often concordant (i.e. when one is high, the other is high, and vice versa), and this is probably why there is an association between LDL cholesterol and heart disease in observational studies. Elevated LDL cholesterol may be more of a proxy marker for elevated LDL particle number in previous research. But they can also be discordant. It is possible to have normal or even low cholesterol, but a high number of LDL particles.[15]

Cholesterol management

Nutritional and lifestyle approaches to support healthy cholesterol (and triglyceride) levels and metabolism include:

Dietary fibre

Dietary fibre can help maintain healthy cholesterol and triglyceride levels through a number of mechanisms:

1. it encourages the growth of friendly gut bacteria that can have beneficial effects on cholesterol levels

2. it provides bulk for elimination and so excess cholesterol can be eliminated via the bowel as explained above. Constipation will result in lower amounts being excreted and more being reabsorbed into circulation

3. it helps with glycaemic control (i.e. blood sugar regulation) – high blood sugar can increase VLDL/triglyceride production by the liver

Choose foods such as oats, legumes, apples, carrots and broccoli high in soluble fibre. Oats contain a soluble fibre called beta-glucan 1,3 1,4 which reduces cholesterol.

Carbohydrates

Carbohydrates stimulate the production of triglycerides, which are then transported in VLDL particles. So reducing carbohydrate consumption is an important part of cholesterol management. Choose low glycaemic carbohydrates e.g. sweet potatoes and oats and eat small portions only.

Plant sterols

Plants do not contain cholesterol, but they contain similar substances called phytosterols, which can interfere with intestinal absorption of cholesterol. Some 'functional foods' have been developed containing these substances but they may have other undesirable features, so it is best to obtain plant sterols from natural sources such as vegetables, olive oil, nuts (almonds), seeds and legumes.

Healthy fats

Monounsaturated fats (found in nuts, seeds and avocado) and omega-3 fats (found in oily fish) have been shown to reduce levels of LDL cholesterol and increase HDL. In addition, omega-3 fatty acids decrease triglyceride concentration by reducing VLDL production. Avoid foods containing trans fats – these are found particularly in processed foods. Foods high in saturated fatty acids may be eaten in moderation (e.g. red meat, butter).

Antioxidants

It is oxidised cholesterol that is the most damaging, so a diet high in plant food antioxidants to protect against oxidative stress and cholesterol becoming oxidised is important.

Garlic

Garlic has been shown to have cholesterol-lowering effects and its antioxidant properties may protect cholesterol from oxidation. One study found this effect was enhanced when garlic was taken in conjunction with fresh lemon juice.[16]

Green tea

Green tea contains compounds, which have been found to lower cholesterol. It also has antioxidant properties.

Red rice yeast

Red rice yeast (found in supplements) contains naturally occurring statin-like metabolites. Red rice yeast has been used for centuries as a natural food preservative in China.

High dose niacin

High dose niacin has been shown to reduce cholesterol. However it can also raise homocysteine levels (a risk factor for cardiovascular disease) so caution is needed here.

Fermented foods

Fermented foods and/or consider a probiotic supplement - for example, *Lactobacillus plantarum* has been shown to have beneficial effects on cholesterol levels.

Stress

Chronic stress increases demand for steroid hormones and the synthesis of cholesterol by the liver increases to meet demand resulting in raised cholesterol levels in the blood. So it is important to address stress reduction and management as well.

Relevant Cytoplan Products

Red Rice Yeast Plus

This product contains red rice yeast, coenzyme Q10 and hawthorn berry extract. Red rice yeast and monacolin K have the following permitted health claim: Monacolin K from red rice yeast contributes to the maintenance of normal blood cholesterol levels (the beneficial effect is obtained with a daily intake of 10mg of monacolin K). Not suitable for those taking statins

CoQ10 Multi (also called 50+)

CoQ10 Multi is a wholefood multivitamin and mineral formula containing 80mg of coenzyme Q10 (as ubiquinol). Statins inhibit coenzyme Q10 synthesis and taking statins has been linked to depleted levels of coenzyme Q10

Krill Oil

Comprises krill oil which provides phospholipids, the omega-3 fatty acids EPA and DHA, and astaxanthin.

Alternative products: High Potency Fish Oil, Lem-0-3, Omega Balance, Omega 3 Vegan

Antioxidant plus CoQ10

Contains 50mg of CoQ10 along with beta carotene, vitamins C and E, zinc and selenium

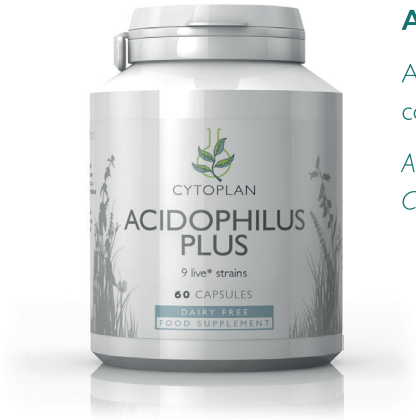
Organic Garlic

Provides 400mg of organic garlic powder per capsule. Certified organic by the Soil Association

Phytoshield

Phytonutrient and antioxidant supplement containing a variety of flavonoids and carotenoids

Alternative products: Cell-Active Curcumin Plus, Eye-Cyt, Cyto-Renew, Cell-Active Glutathione



Acidophilus Plus

A multi strain live bacteria supplement additionally containing 35mg of fructo-oligosaccharides

Alternative products: Fos-A-Dophilus, Cytobiotic Active

Blood Glucose Support

Cinnamon and multi mineral formula providing chromium, magnesium, zinc, copper, manganese, selenium and molybdenum

Cherry C

Provides 200mg of vitamin C from acerola cherry, therefore also provides naturally occurring bioflavonoids

Alternative products: Vitamin C (1000mg), Organic Vitamin C

References

1. Ravnskov, U. (2008) 'Hypercholesterolaemia. Should medical science ignore the past?', BMJ. 2008;337:a1681.

2. Netea, M.G. et al. (1996) 'Low-density lipoprotein receptor-deficient mice are protected against lethal endotoxemia and severe gram-negative infections', J Clin Invest.;97(6):1366-1372.

3. Forey, B.A. et al. (2013) 'The effect of quitting smoking on HDL-cholesterol - a review based on within-subject changes', Biomark Res.;1(1):26.

4. Lin, P.-J. et al. (2015) 'Multiple chronic conditions in type 2 diabetes mellitus: prevalence and consequences', Am J Manag Care.;21(1):e23-34.

5. Kim T.J. et al. (2016) 'Helicobacter pylori is associated with dyslipidemia but not with other risk factors of cardiovascular disease', Sci Rep.;6(1):38015.

6. Rizos, C.V. et al. (2011) 'Elisaf MS, Liberopoulos EN. Effects of thyroid dysfunction on lipid profile', Open Cardiovasc Med J.;5:76-84.

7. Nelson, J.W. et al. (2010) 'Exposure to polyfluoroalkyl chemicals and cholesterol, body weight, and insulin resistance in the general U.S. population', Environ Health Perspect.;118(2):197-202.

8. Cho, Y.M. (2017) 'Fish consumption, mercury exposure, and the risk of cholesterol profiles: findings from the Korea National Health and Nutrition Examination Survey 2010-2011', Environ Health Toxicol. 2017;32:e2017014.

9. Varghese, M.J. (2014) 'Familial hypercholesterolemia: A review', Ann Pediatr Cardiol. 2014;7(2):107-117.

10. Wang, L. et al. (2008) 'High-carbohydrate diets affect the size and composition of plasma lipoproteins in hamsters (Mesocricetus auratus)', Comp Med. 2008;58(2):151-160.

11. Ma, Y. et al. (2006) 'Association between carbohydrate intake and serum lipids,' J Am Coll Nutr.;25(2):155-163.

12. Reaven, G. (2012) 'Insulin Resistance and Coronary Heart Disease in Nondiabetic Individuals', Arterioscler Thromb Vasc Biol.;32(8):1754-1759.

13. Garg, A. et al. (1994) 'Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus', JAMA.;271(18):1421-1428.

14. NICE Clinical Guideline CG181 (2016) 'Cardiovascular disease: risk assessment and reduction, including lipid modification' | Guidance and guidelines | NICE. https://www.nice.org.uk/guidance/cg181/chapter/1-Recommendations.

15. Davidson, M.H. et al. (2011) 'Clinical utility of inflammatory markers and advanced lipoprotein testing: Advice from an expert panel of lipid specialists', J Clin Lipidol.;5(5):338-367.

16. Aslani, N. et al. (2016) 'Effect of Garlic and Lemon Juice Mixture on Lipid Profile and Some Cardiovascular Risk Factors in People 30-60 Years Old with Moderate Hyperlipidaemia: A Randomized Clinical Trial', Int J Prev Med.;7:95.

Cytoplan Ltd provides an innovative range of science-based nutritional supplements supplying the needs of healthcare professionals and consumers. The company was founded in 1990 by health practitioners, including doctors and nutritionists, with many years' experience in nutrition therapy.

Cytoplan is a leader in the highly specialised food-based supplementation sector with a product range continually developed based on the latest nutrition research for optimally 'bio-effective' products. Not all vitamins and minerals are the same and a bio-effective nutrient is one that will easily be taken up into human metabolic pathways and have a biological outcome that is beneficial to health.

Cytoplan is wholly owned by the AIM foundation, a charitable organisation that addresses the issue of community wellbeing plus health and nutrition projects in the UK and overseas. Cytoplan has supplied supplements to over 6,000 health professionals in the UK and overseas such as doctors, dentists and nutrition therapists. The company offers an incentivised, nurturing and supportive programme for health professionals and students.

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