High cholesterol: an overview

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COMMENTARY

Cholesterol is a waxy, fat-like substance that's found in all the cells in your body. Your body needs some cholesterol to make hormones, vitamin D, and substances that help you digest foods. Your body makes all the cholesterol it needs. Cholesterol (from the Ancient Greek chole- bile and stereos, followed by the chemical suffix -ol for an alcohol) is an organic molecule. It is a sterol (or modified steroid), a type of lipid. Cholesterol is biosynthesized by all animal cells and is an essential structural component of animal cell membranes

Cholesterol also serves as a precursor for the biosynthesis of steroid hormones, bile acid and vitamin D. Cholesterol is the principal sterol synthesized by all animals. In vertebrates, hepatic cells typically produce the greatest amounts. It is absent among prokaryotes bacteria and archaea although there are some exceptions, such as Mycoplasma, which require cholesterol for growth.

Cholesterol is essential for all animal life, with each cell capable of synthesizing it by way of a complex 37-step process. This begins with the mevalonate or HMG-CoA reductase pathway, the target of statin drugs, which encompasses the first 18 steps. This is followed by 19 additional steps to convert the resulting lanosterol into cholesterol.

A human male weighing 68 kg normally synthesizes about 1 gram (1,000 mg) of cholesterol per day, and his body contains about 35 g, mostly contained within the cell membranes. Typical daily cholesterol dietary intake for a man in the United States is 307 mg.

Most ingested cholesterol is esterified, which causes it to be poorly absorbed by the gut. The body also compensates for absorption of ingested cholesterol by reducing its own cholesterol synthesis. For these reasons, cholesterol in food, seven to ten hours after ingestion, has little, if any effect on concentrations of cholesterol in the blood. However, during the first seven hours after ingestion of cholesterol, as absorbed fats are being distributed around the body within extracellular water by the various lipoproteins (which transport all fats in the water outside cells), the concentrations increase.

Plants do not make cholesterol but manufacture phytosterols, chemically similar substances which can compete with cholesterol for reabsorption in the intestinal tract, thus potentially reducing cholesterol reabsorption. When intestinal lining cells absorb phytosterols, in place of cholesterol, they usually excrete the phytosterol molecules back into the GI tract, an important protective mechanism. The intake of naturally occurring phytosterols, which encompass plant sterols and stanols, depending on eating habits. Specially designed vegetarian experimental diets have been produced yielding upwards of 700 mg/day.

Within cells, cholesterol is also a precursor molecule for several biochemical pathways. For example, it is the precursor molecule for the synthesis of vitamin D in the calcium metabolism and all steroid hormones, including the adrenal gland hormones cortisol and aldosterone, as well as the sex hormones progesterone, estrogens, and testosterone, and their derivatives.

Cholesterol is also implicated in cell signaling processes, assisting in the formation of lipid rafts in the plasma membrane, which brings receptor proteins in close proximity with high concentrations of second messenger molecules. In multiple layers, cholesterol and phospholipids, both electrical insulators, can facilitate speed of transmission of electrical impulses along nerve tissue. For many neuron fibers, a myelin sheath, rich in cholesterol since it is derived from compacted layers of Schwann cell membrane, provides insulation for more efficient conduction of impulses.Demyelination (loss of some of these Schwann cells) is believed to be part of the basis for multiple sclerosis.

Cholesterol binds to and affects the gating of a number of ion channels such as the nicotinic acetylcholine receptor, GABAA receptor, and the inward-rectifier potassium channel. Cholesterol also activates the estrogen-related receptor alpha, and may be the endogenous ligand for the receptor. The constitutively active nature of the receptor may be explained by the fact that cholesterol is ubiquitous in the body. Cholesterol production has been identified as a key mediator of the effects of statins and bisphosphonates on bone, muscle, and macrophages. On the basis of these findings, it has been suggested that the ERR should be de-orphanized and classified as a receptor for cholesterol.

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