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# English Summary

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## CHOLESTEROL, HYPERCHOLESTEROLEMIA AND THE DRUGS AGAINST IT. A REVIEW.

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Lipoproteins (macromolecular complexes of lipid and proteins) transport lipids and cholesterol through the blood stream. Such a transport system is essential to life since these lipid materials are needed for cell growth, hormone production and transmembrane transport. However, an excess of one important class of lipoproteins known as low density lipoprotein (LDL) increases the risk of ischaemic heart disease.

Body cholesterol is derived from two sources, namely, (1) endogenous, obtained from synthesis, which occurs mainly in the liver with the help of an key enzyme HMG-CoA reductase, and (2) dietary cholesterol absorbed from the intestine. Cholesterol are degraded to bile acids, a process which is catalysed with 7 $\alpha$ -hydroxylase, or it will be secreted as cholesterol by biliary secretion and faecal loss.

National Education Program Coordinating Committee classifies serum cholesterol level  $\leq$  200 mg/dL as "desirable blood cholesterol", 200-239 mg/dL as "borderline high blood cholesterol", and above 240 mg/dL as

"high blood cholesterol". The diet therapy is still the first attempt that people should consider in reducing hypercholesterolemia. The dietary therapy should consist of at least 4 principles, namely (1) reduction of fat intake, maximum up to 30% of total intake of calory by reducing the intake of saturated fatty acids to  $\leq$  10% of total energy, (2) increasing dietary intake of mono and polyunsaturated fats. Ten to 15% percent of consumed energy should be supplied in form of mono- and 7 to 10% of polyunsaturated fats, (3) increasing dietary intake of complex carbohydrates and fiber, (4) reduction of cholesterol intake ( $\leq$  300 mg/day). Patients who do not respond appropriately to dietary therapy should be given lipid-lowering drugs. In making the decision to start drug therapy, it should be considered that the treatment will probably be a life-long therapy. A wide range of lipid-lowering drugs are available nowadays.

Cholestyramine and colestipol which belong to bile-acid sequestrant resins bind bile acids in the intestine and reduce their enterohepatic circulation thereby stimulating their faecal loss. Nicotinic acid inhibits, by unknown mechanism, the production of VLDL particles from the liver, leading to low VLDL-triglyceride concentrations and low levels of LDL-C in serum. This drug

increases also HDL-C. Estrogen is nowadays administered either as adjunction or as main therapy to the postmenopausal women, while the risk of CHD is increased due to sinking level of estrogen in the body.

Recently, a group of lipid-lowering drugs called statins had been proven to show a promising effect either through small group or population-based studies. These drugs competitively inhibit HMG-CoA reductase, the rate limiting enzyme in the biosynthesis of cholesterol leading to increased expression of LDL receptors. However, the mechanism of action of these drugs is more complex than the original concept. Pravastatin, simvastatin and fluvastatin are now available in the dispensaries. Pravastatin, which is more hydrophilic than simvastatin and fluvastatin, is implied more selective than the latter. It can be suggested, therefore, that pravastatin also reduces the synthesis of cholesterol in extra hepatic tissues.

With the availability of new pharmacological agents, an effective treatment of the common forms of hyperlipoproteinemia is now possible,

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