Cholesterol and Human Health

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Abstract: Cholesterol plays a major role in human heart health and high cholesterol is a leading risk factor for human cardiovascular disease such as coronary heart disease and stroke. There are 102.3 million American adults who have total blood cholesterol values of 200 mg/dl and higher, and about 41.3 million. Cholesterol can be good (high-density lipoprotein) or bad (low-density lipoprotein) to the cardiovascular system. For the total cholesterol in blood: less than 200 mg/dl is desirable level, 200 to 239 mg/dl is the borderline high for heart disease, and 240 mg/dl and above is High blood cholesterol. A person with this level of 240 mg/dl or above has more than twice the risk of heart disease as someone whose cholesterol is below 200 mg/dl. Statin drugs are very effective for lowering LDL cholesterol levels and have few immediate short-term side effects. Some bacteria can change cholesterol in food to coprostanol that cannot be readily absorbed by the body and some oral bacteria such as *Lactobacillus acidophilus* have been commercial available for the cholesterol lowering. [Nature and Science. 2004;2(4) (Supplement): 17-21].

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1. Introduction

Cholesterol is a waxy substance made by animal liver and also supplied in diet through animal products such as meats, poultry, fish and dairy products. Cholesterol is needed in the body to insulate nerves, make cell membranes and produce certain hormones, and it is an important lipid in some membranes. However, the body makes enough cholesterol, so any dietary cholesterol isn't needed.

Cholesterol plays a major role in human heart health. Cholesterol can be both good and bad. High-density lipoprotein (HDL) is good cholesterol and low-density lipoprotein (LDL) is bad cholesterol. High cholesterol in serum is a leading risk factor for human cardiovascular disease such as coronary heart disease and stroke - America's number one killer (Tabas, 2002). Excess cholesterol in the bloodstream can form plaque (a thick, hard deposit) in artery walls. The cholesterol or plaque build-up causes arteries to become thicker, harder and less flexible, slowing down and sometimes blocking blood flow to the heart. When blood flow is restricted, angina (chest pain) can result. A heart attack will result when blood flow to the heart is severely impaired and a clot stops blood flow completely. When there is too much LDL cholesterol in the blood, it is deposited inside the blood vessels, where it can build up to hard deposits and cause atherosclerosis, the disease process that underlies heart attacks.

There are 102.3 million American adults who have total blood cholesterol values of 200 mg/dl and higher, and about 41.3 million American adults have levels of 240 mg/dl of cholesterol or above. Total blood cholesterol is the most common measurement of blood cholesterol. Cholesterol is measured in milligrams per deciliter of blood (mg/dl). A person's health cholesterol content is based on other risk factors such as age, gender, family history, race, smoking, high blood pressure, physical inactivity, obesity and diabetes.

2. Chemical Structure of Cholesterol

Cholesterol is present in eukaryotes but not in most prokaryotes. The oxygen atom in its 3-OH group comes from O_2 (Figure 1). Cholesterol evolved after the earth's atmosphere became aerobic. The animal plasma membranes of eukaryotic cells are usually rich in cholesterol, whereas the membranes of their organelles typically have lesser amounts of this neutral lipid (Stryer, 1988).
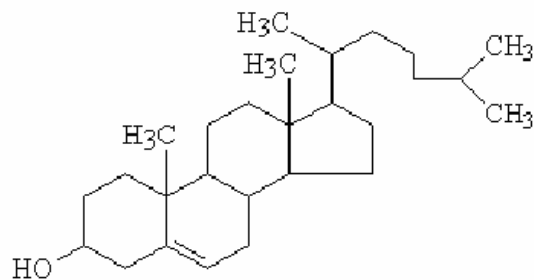
Figure 1. Chemical structure of cholesterol

3. Good Cholesterol and Bad Cholesterol

Cholesterol can be good or bad. HDL is called "good cholesterol" that is good for the cardiovascular system and LDL is called "bad cholesterol" that is bad for the cardiovascular system. These are the form in which cholesterol travels in the blood. LDLs have little protein

and high levels of cholesterol and HDL has a lot of protein and very little cholesterol. LDL is the main source of artery clogging plaque. HDL actually works to clear cholesterol from the blood.

The standard test of cholesterol is done after a 9-12 hours fast without food, liquids or pills. It gives information about total cholesterol, LDL, HDL and triglycerides (blood fats). The cholesterol content in blood is the key data for the health information of cholesterol related (Table 1). If a person's total cholesterol is 200 mg/dl or more, or his/her HDL cholesterol is less than 40 mg/dl, he/she needs to have a lipoprotein profile done to determine LDL cholesterol and triglyceride levels.

A person's LDL cholesterol goal depends on how many other risk factors he/she has: (1) If he/she does not have coronary heart disease or diabetes and have one or no risk factors, his/her LDL goal is less than 160 mg/dl. (2) If he/she does not have coronary heart disease or diabetes and have two or more risk factors, his/her LDL goal is less than 130 mg/dl. (3) If he/she has coronary heart disease or diabetes, his/her LDL goal is less than 100 mg/dl.

Table 1. Initial classification based on total cholesterol, HDL, LDL and Triglyceride

Cholesterol	Cholesterol Level	Category
Total Cholesterol	Less than 200 mg/dl	Desirable level.
	200 to 239 mg/dl	Borderline high for heart disease.
	240 mg/dl and above	High blood cholesterol. A person with this level has more than twice the risk of heart disease as someone whose cholesterol is below 200 mg/dl.
HDL Cholesterol	Less than 40 mg/dl	Low HDL cholesterol. A major risk factor for heart disease.
	40 to 59 mg/dl	The higher HDL level, the better.
	60 mg/dl and above	High HDL cholesterol. An HDL of 60 mg/dl and above is considered protective against heart disease.
LDL Cholesterol	Less than 100 mg/dl	Optimal
	100 to 129 mg/dl	Near or above optimal
	130 to 159 mg/dl	Borderline high
	160 to 189 mg/dl	High
	190 mg/dl and above	Very high
Triglyceride	Less than 150 mg/dl	Normal
	150-199 mg/dl	Borderline high
	200-499 mg/dl	High
	500 mg/dl and above	Very high

4. Triglyceride

Triglycerides are another fat in the bloodstream. High levels of triglycerides is also linked to heart disease.

Triglyceride is the most common type of fat in the body. Many people who have heart disease or diabetes have high triglyceride levels. Normal triglyceride levels vary by age and sex. A high triglyceride level combined with low HDL cholesterol or high LDL cholesterol seems to speed up atherosclerosis, which is the buildup of fatty deposits in artery walls that increase the risk for heart attack and stroke.

People should reduce the amount of saturated fat, *trans*-fat, cholesterol and total fat in their diet. Some studies have shown a higher mortality in people with low cholesterol levels - that is, lower than 160 mg/dl. These deaths are from non-coronary causes (some cancers, chronic respiratory disease, liver disease and trauma). On the other hand, some evidence suggests that total cholesterol levels below 160 mg/dl are not dangerous. In many countries a major portion of the population has cholesterol levels in this range throughout life without serious health problems. Also, less than 6 percent of the American population has a

cholesterol level below 160 mg/dl. It's rarely necessary to lower total cholesterol below that.

5. Hyperlipidemia

Hyperlipidemia is an elevation of lipids (fats) in the bloodstream. These lipids include cholesterol, cholesterol esters (compounds), phospholipids and triglycerides. They're transported in the blood as part of large molecules called lipoproteins. These are the five major families of blood (plasma) lipoproteins: (1) chylomicrons, (2) very low-density lipoproteins (VLDL), (3) intermediate-density lipoproteins (IDL), (4) low-density lipoproteins (LDL), (5) high-density lipoproteins (HDL). When hyperlipidemia is defined in terms of class or classes of elevated plasma lipoproteins, the term hyperlipoproteinemia is used. Hypercholesterolemia is the term for high cholesterol levels in the blood. Hypertriglyceridemia refers to high triglyceride levels in the blood. The average American man gets about 337 mg of cholesterol a day from food and the average woman gets about 217 mg. I suggest that a person should limit cholesterol from food to an average of no more than 300 mg per day.

6. Cholesterol from Foods

Cholesterol from food is hard to get away from, even though one may be watching his/her diet. All foods of animal origin contain cholesterol, including eggs, red meat, and shrimp. Generally, foods that are high in saturated fats or trans fats should also be limited. These include foods you may not even think of, such as grilled-cheese sandwich, margarine, potato with butter and chicken pot pie, etc. As we eat, cholesterol from food is absorbed by our digestive tract. It then makes its way into our liver and can circulate through our body in the bloodstream. That's one source. There's also a little-known second source of cholesterol — human body.

7. Cholesterol Produced by Body Based on Genetics

Like many people, one may not know that his/her body produces cholesterol naturally, based on family history genetically - despite the fact that it's where more of one's total cholesterol comes from. The liver makes cholesterol, as do other individual cells throughout the body. Once cholesterol is produced, it can make its way into the bloodstream.

What does this process mean to people? Take the cholesterol the body makes and add it to the cholesterol one gets from food. Now one can see how easily cholesterol can build up in the bloodstream and how the overall cholesterol level can increase.

8. The Factors Affect Cholesterol Levels

A variety of factors can affect your cholesterol levels. They include:

8.1 Diet. Saturated fat, trans fat, and cholesterol in the food you eat increase cholesterol levels. Reducing the amount of saturated fat and trans fats and cholesterol in your diet helps lower your blood cholesterol level.

8.2 Weight. In addition to being a risk factor for heart disease, being overweight can also increase your cholesterol. Losing weight can help lower your LDL, total cholesterol levels, and triglyceride levels, as well as raise your HDL.

8.3 Exercise. Regular exercise can lower LDL cholesterol and raise HDL cholesterol. You should try to be physically active for 30 minutes on most days.

8.4 Age and Gender. As we get older, cholesterol levels rise. Before menopause, women tend to have lower total cholesterol levels than men of the same age. After menopause, however, women's LDL levels tend to rise.

8.5 Heredity. Your genes partly determine how much cholesterol your body makes. High blood cholesterol can run in families.

8.6 Medical conditions. Occasionally a medical condition may cause an elevation of cholesterol levels in the blood. These include hypothyroidism (an underactive thyroid gland), liver disease and kidney disease.

8.7 Medications. Some medicines, like steroids and progestins may increase the "bad" cholesterol and decrease the "good" cholesterol.

9. Medications

The main goal in lowering cholesterol is to lower your LDL and raise your HDL. To lower cholesterol, eat a heart-healthy diet, exercise regularly, and maintain a healthy weight. Some may also need to take cholesterol lowering medications. Cholesterol-lowering medicine is most effective when combined with a low-cholesterol diet and exercise program.

The drugs of first choice for elevated LDL cholesterol are the HMG CoA reductase inhibitors, e.g. lovastatin, pravastatin and simvastatin. Statin drugs are very effective for lowering LDL cholesterol levels and have few immediate short-term side effects (Jongh, 2002). They are easy to administer, have high patient acceptance and have few drug-drug interactions. Patients, who are pregnant, have active or chronic liver disease, or those allergic to statins shouldn't use statin drugs. The most common side effects of statins are gastrointestinal, including constipation and abdominal pain and cramps. These symptoms are usually mild to severe and generally subside as therapy continues.

Another class of drugs for lowering LDL is the bile acid sequestrants - cholestyramine and colestipol - and nicotinic acid. These have been shown to reduce the risk for coronary heart disease in controlled clinical trials. Both classes of drugs appear to be free of serious side effects. But both can have troublesome side effects and require considerable patient education to achieve adherence. Nicotinic acid is preferred in patients with triglyceride levels exceeding 250 mg/dl because bile acid sequestrants tend to raise triglyceride levels.

Other available drugs are gemfibrozil, probucol and clofibrate. Gemfibrozil and clofibrate are most effective for lowering elevated triglyceride levels. They moderately reduce LDL cholesterol levels in hypercholesterolemic patients, but the American FDA hasn't approved them for this purpose. Probucol also moderately lowers LDL levels and it has been received FDA approval for this purpose.

If a patient doesn't respond adequately to single drug therapy, combined drug therapy should be considered to further lower LDL cholesterol levels. For patients with severe hypercholesterolemia, combining a bile acid sequestrant with either nicotinic acid or lovastatin has the potential to markedly lower LDL cholesterol. For hypercholesterolemic patients with elevated triglycerides, nicotinic acid or gemfibrozil should be considered as one agent for combined therapy.

9.1 Drugs

There are a variety of medications available for lowering blood cholesterol levels. They may be prescribed individually or in combination with other drugs. Some of the common types of cholesterol-lowering drugs include (1) Clofibrate, (2) Gemfibrozil, (3) Nicotinic acid (niacin), (4) Resins, (5) Statins, (6) Fibric acid derivatives (7) Fibrates:

9.1.1 Clofibrate (Atromid-S). This drug raises the HDL cholesterol levels and lowers triglyceride levels.

9.1.2 Gemfibrozil (Lopid). This drug lowers blood fats and raises HDL cholesterol levels.

9.1.3 Nicotinic Acid (niacin). Niacin is a B-complex vitamin. It's found in food, but is also available at high doses by prescription. It lowers LDL cholesterol and raises HDL cholesterol. The main side effects are flushing, itching, tingling and headache. Niacin or nicotinic acid, includes the brand names Niacor, Niaspan, or Slo-niacin. Over-the-counter preparations include extended-release, timed-release, and controlled-release. Niacin found in dietary supplements should not be used to lower cholesterol. The doctor or lipid specialist will let patients know what type of niacin is best for them. This drug works in the liver by affecting the production of blood fats. It's used to lower

triglycerides, lower LDL cholesterol and raise HDL cholesterol.

9.1.4 Resins. Resins are also called bile acid-binding drugs. They work in the intestines by promoting increased disposal of cholesterol. There are three kinds of medications in this class: (1) Cholestryamine (Questran, Prevalite, Lo-Cholest), (2) Colestipol (Colestid), (3) Coleseveiam (WelChol).

9.1.5 Statins. Statins block the production of cholesterol in the liver itself. They lower LDL, the "bad" cholesterol, and triglycerides and have a mild effect in raising HDL, the "good" cholesterol. Statin drugs are very effective for lowering LDL cholesterol levels and have few immediate short-term side effects. They work by interrupting the formation of cholesterol from the circulating blood. These drugs are the first line of treatment for most people with high cholesterol. Side effects can include intestinal problems, liver damage, and in a few people, muscle tenderness or weakness.

Examples of statins include: (1) Altocor, (2) Baycol (cerivastatin), (3) Crestor, (4) Lipitor (atorvastatin), (5) Lescol (Fluvastatin), (6) Mevacor (lovastatin), (7) Pravachol (pravastatin), (8) Zocor (simvastatin). Advicor is a combination of a statin and niacin. Caduet is a new drug that is a combination of a statin (Lipitor or atorvastatin) and a blood pressure-lowering drug called amlodipine (Norvasc). Commonly prescribed statins include: (1) Atorvastatin (Lipitor), (2) Cerivastatin (Baycol), (3) Fluvastatin (Lescol), (4) Lovastatin (Mevacor), (5) Pravastatin (Pravachol), (6) Simvastatin (Zocor).

9.1.6 Bile Acid Sequestrants. These drugs work inside the intestine, where they bind to bile and prevent it from being reabsorbed into the circulatory system. Bile is made largely from cholesterol, so these drugs work by reducing the body's supply of cholesterol,, thus lowering total and LDL cholesterol. The most common side effects are constipation, gas, and upset stomach. Examples of bile acid resins include: questran and questran light (cholestyramine), colestid (colestipol), WelChol (colesevelam).

9.1.7 Fibrates. Fibrates lower triglyceride levels and can increase HDL and lower LDL cholesterol. The mechanism of action is not clear but it is thought that fibrates enhance the breakdown of triglyceride-rich particles and decreases the secretion of certain lipoproteins. In addition, they induce the synthesis of HDL. Examples of fibrates include: tricor (fenofibrate), lopid (gemfibrozil), lofibra (fenofibrate).

9.1.8 Side Effects of Cholesterol-Lowering Drugs

The side effects of cholesterol-lowering drugs include: (1) Muscle aches, (2) Abnormal liver function, (3) Allergic reaction (skin rashes), (4) Heartburn, (5) Dizziness. (6) Abdominal pain, (7) Constipation, (8) Decreased sexual desire.

One newer drug is Zetia. This drug works by inhibiting the absorption of cholesterol from the blood. Side effects include back pain, joint pain, diarrhea and abdominal pain.

As of August 8, 2001, Bayer Pharmaceutical Division voluntarily withdrew the drug Baycol (cerivastatin) from the U.S. market because of reports of fatal muscle damage caused by the drug.

9.2 Bacteria on Cholesterol

Some bacteria can change cholesterol in food to coprostanol that cannot be readily absorbed by the body. These kinds of bacteria are called friendly bacteria. This helps recycle cholesterol to make hormones. Bifidobacterium and Lactobacillus acidophilus may play an important role in cholesterol metabolism of their host. Intestinal bacteria convert cholesterol into a less absorbable form coprostanol thus hampering its absorption from the intestinal tract (Lin, 2000). Lactic acid bacteria in intestine have the cholesterol lowering effect (Pereira, 2002). Some oral bacteria such as Lactobacillus acidophilus have been commercial available for the cholesterol lowering. Feeding friendly bacteria can do: (1) reduce the growth of unfriendly bacteria, (2) maintain regular bowel movements, (3) maintain cholesterol and triglyceride levels, (4) maintain healthy blood sugar levels (Ma, 2004).

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