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### Cardiovascular Heart Disease Risk Factors Part V: Cholesterol By James L. Holly, MD Your Life Your Health *The Examiner* July 28, 2005

According to the American Heart Association and the American College of Cardiology, there are nine major and independent risk factors for cardiovascular heart disease. Three of those nine are related to "Lipids," which are the fats in the blood. They are:

- elevated serum total cholesterol
- elevated low-density lipoprotein cholesterol (LDL-C)
- low serum high-density lipoprotein cholesterol (HDL-C)

#### **Definitions and Descriptions**

To completely understand the contribution of cholesterol to cardiovascular disease risk, it is important to understand the following terms:

**Apolipoprotein A-1 (ApoA1)** -- Apolipoprotein A-1 (ApoA1) is the major protein constituent of HDL (the "good" cholesterol). This molecule is responsible for the activation of two enzymes that are necessary for the formation of HDL, and this process may be a key factor in the relationship between HDL levels and the incidence of atherosclerosis. **Apolipoprotein B (ApoB)** -- Apolipoprotein B (ApoB) is the primary protein found in LDL (the "bad" cholesterol). Studies suggest that ApoB plays a major role in targeting the selective uptake of LDL by the liver, and has been identified as one component of the syndrome known as atherogenic lipoprotein phenotype which is a common disorder in persons at risk for atherosclerosis.

Lipoprotein(a) (spoken as "Lp little a") -- Lipoprotein(a) is a complex of ApoA and LDL, and an elevated status is associated with an increased risk for atherosclerosis and cardiovascular disease. The pathogenic role of lipoprotein(a) is similar to that of LDL in the development of atherosclerosis; it is localized in the blood vessel walls, then oxidized. Once oxidized, it forms the foam cells associated with atherosclerotic plaques. HDL cholesterol --HDL cholesterol (the "good" cholesterol) is a serum lipoprotein that contains ApoA1, cholesterol and triglycerides. A primary function of HDL is the removal of cholesterol from the body. Studies indicate that persons with high levels of HDL were less likely to develop atherosclerosis, thus significantly decreasing the risk of developing cardiovascular disease. LDL cholesterol -- LDL cholesterol (the "bad" cholesterol) is a serum lipoprotein that contains ApoB, cholesterol and triglycerides. LDL is the most atherogenic of the lipoproteins. Recent evidence suggests that the oxidized form of LDL may play a key

role in the initiation and progression of atherosclerosis, and like lipoprotein(a), oxidized LDL forms foam cells which are associated with the formation of atherosclerotic plaques. **Cholesterol** -- Cholesterol is a sterol that is essential for the proper functioning of the body. It

is a component of cell membranes and is necessary for the production of steroid hormones. Lipid disorders are significant risk factors for developing cardiovascular disease, and recent evidence suggests that the cholesterol/HDL ratio is a more significant predictor of cardiovascular risk.

**Triglycerides** -- Triglycerides are a family of complex lipids and make up 95% of all tissue-stored fat within the body. Recent studies have shown that persons with high triglycerides and low HDL are at significant risk for developing cardiovascular disease

### Lipids and Cardiovascular Risk

- There is a steep rise in cardiovascular artery disease (CAD) with increasing total cholesterol (TC) levels regardless of your HDL-C.
- Low HDL-C levels (<35 mg/dL) is associated with a more than 5-fold increase in CAD risk if your total cholesterol is over 300 mg/dL, but the increase is still 2.5- fold if your total cholesterol is less than 300 mg/dL.
- Hypertriglyceridemia (TG >200 mg/dL) is also associated with a substantially higher incidence of CAD if you have low HDL-C levels.

### The Six "Big" Cholesterol Studies

- **4S (Scandinavian Simvastatin Survival Study)** -- Shows without question that statin (a class of medications which lower cholesterol levels, particularly total cholesterol and LDL-C) therapy is beneficial in CHD patients with very high cholesterol levels.
- WOSCOPS (West of Scotland Coronary Prevention Study) -- Extended the evidence base for initiating cholesterol-lowering therapy and demonstrated that high-risk primary prevention populations with elevated cholesterol levels also benefit from this type of cholesterol reduction.
- CARE (Cholesterol and Recurrent Events) -- Established that CHD patients with average cholesterol levels benefit from statin therapy.
- AFCAPS (Air Force/Texas Coronary Atherosclerosis Prevention Study) --Confirms that even patients considered to be at average risk with average cholesterol levels achieve benefit from statin therapy.
- HPS (Heart Protection Study) -- Aimed at establishing whether statin therapy is of benefit to individuals who are at high risk for CVD but have average to low levels of total and LDL-C.
- MRFIT (Multiple Risk Factor Intervention Trial) -- Affirmed the relationship between serum cholesterol and 6-year risk of coronary artery disease death was strong, continuous and graded. Regardless how low a patient's level of cholesterol, cardiovascular risk can be reduced even further.

### Lessons learned from these studies:

- Statin Therapy is safe -- Muscle symptoms should be monitored, CPK levels measured when clinically indicated and liver enzymes measured periodically.
- Patients with diabetes benefit significantly from statin therapy -- the same

benefits were found in diabetes independent of the length of their disease, the control of blood sugar or the presence of hypertension.

- High-risk patients benefit from statin therapy regardless of baseline LDL-C levels -- the results of the HPS study extend cholesterol lowering benefits to patients who previously would not be considered candidates for therapy, notably those with LDL-C levels below current targets.
- Less emphasis should be placed on the actual lipid level and more consideration should be given to the cardiovascular risk profile of the patient.
- The decision to start lipid-lowering therapy should be based on cardiovascular risk and anticipated benefits, rather than on lipid levels alone.
- HPS raises the possibility that the ideal LDL-C level is <70 mg/dL in patients with atherosclerosis or diabetes.
- Lowering cholesterol in individuals with baseline low cholesterol is safe

# Conclusion

There is now ample evidence that cholesterol-lowering therapy with statins should be initiated in all high-risk groups, regardless of:

- 1. gender,
- 2. age,
- 3. presence of diabetes, or
- 4. baseline LDL-C levels.

# What Should You Do To Lower Your Cardiovascular Risk from Lipids?

# **Desirable Lipid values**

If you're healthy:

- Total cholesterol: Below 150 milligrams per deciliter (mg/dL)
- Total triglycerides: Below 150 mg/dL
- HDL cholesterol: Above 45 mg/dL
- LDL cholesterol: Below 100 mg/dL If

you have coronary artery disease:

- Total cholesterol: Below 120 mg/dL
- Total triglycerides: Below 90 mg/dL
- HDL cholesterol: Above 40 mg/dL
- LDL cholesterol: Below 70 mg/dL

Have a baseline cholesterol test in your 20s and then every 3 to 5 years. If your values are not within desirable ranges, your doctor may advise more frequent measurements.

### Treatment

Lifestyle changes are the first steps to take to improve your blood levels of cholesterol and triglycerides. These steps include changes in diet, exercising regularly and not smoking (see "Prevention"). But if you've made these important lifestyle changes and your total cholesterol

- especially your level of low-density lipoprotein (LDL) cholesterol
- remains high, your doctor may recommend prescription medication.

Your LDL cholesterol level is usually the deciding factor as to whether to start medication.

- If you have no risk factors for heart disease, an LDL level greater than 190 generally requires medication.
- With two or more risk factors, an LDL level greater than 160 may require medication.
- If plaques have narrowed the arteries around your heart and restricted the flow of oxygen-rich blood to your heart's muscles (coronary artery disease), your doctor may try medication and lifestyle changes to lower your LDL to less than 100.

### Eating a healthy diet

These changes in your diet can improve your blood cholesterol levels:

- **Control total fat.** Limit all types of fat saturated, polyunsaturated, trans fatty acids (trans fats) and monounsaturated to no more than 30 percent of your total daily calories. Because all foods with fats contain a combination of these fats, it's important to reduce total fat. Not every food you eat must have less than 30 percent of its calories from fat. Use the guideline as a daily average. By balancing occasional high-fat foods with low-fat choices, your fat intake should average no more than 30 percent of your daily calories. If your daily intake is 2,000 calories, 30 percent equals 65 grams of fat. Limit saturated fat to no more than 10 percent of total calories.
- **Limit dietary cholesterol.** Your daily limit for dietary cholesterol is 300 milligrams. To accomplish this goal, limit or avoid concentrated sources such as organ meats, egg yolks and whole milk products.
- Eat foods with soluble fiber. As part of a low-fat diet, soluble fiber can help lower your total blood cholesterol level. Foods high in soluble fiber include oat bran, oatmeal, beans, peas, rice bran, barley, citrus fruits, strawberries and apple pulp.
- Eat more fish. Some fish particularly fatty types prevalent in cold water such as salmon, mackerel and herring contain high amounts of a unique type of polyunsaturated fat called omega-3 fatty acids. Omega 3s may lower your level of triglycerides.
- **Consider soy products.** Soy compounds called isoflavones act like human hormones that regulate cholesterol levels. Eating soy proteins can reduce your levels of total cholesterol, low-density lipoprotein (LDL) cholesterol and triglycerides. Eating soy may also raise your level of high-density lipoprotein (HDL) cholesterol "good" cholesterol, which may protect you against heart

disease.

- Eat more foods with antioxidants. Antioxidant vitamins may help prevent cholesterol from damaging the lining of your arteries. They include vitamins C and E and the carotenoids, such as beta carotene. Oxidation is the process by which cells in your body called free radicals damage other cells as they seek to replace their missing electron. Antioxidants neutralize free radicals by donating the electrons the free radicals need. Oxidation causes changes in fatty acids and LDL cholesterol in your blood. These changes enable cells in your arteries to absorb fatty acids and LDL cholesterol more easily, leading to plaque buildup and narrowing of your arteries.
- **Drink alcohol in moderation, if at all.** Moderate consumption of alcohol may raise your level of HDL cholesterol. The best advice is to drink in moderation if you drink at all. Limit alcohol to one drink daily if you're a woman, to no more than two drinks daily if you're a man. If you're a nondrinker, don't start drinking alcohol. Don't drink alcohol if you have a high level of triglycerides.

### Getting more exercise

Being overweight promotes a high total cholesterol level. Losing weight improves your cholesterol levels. Set up an exercise program to lose weight using these guidelines and your doctor's advice:

- Choose an aerobic activity. Get involved in activities such as brisk walking, jogging, bicycling or cross-country skiing.
- **Build up the time and frequency of exercising.** Gradually work up to exercising for 30 minutes to 45 minutes at least three times a week. If you're significantly overweight or have been inactive for many years, take several months to gradually work up to this level. The higher the level of your activity, the greater your rate of weight loss.
- Stick with your exercise program. Schedule a regular time for exercise. Make exercise fun. If it's not enjoyable you may not feel like exercising regularly, year in and year out. Find a friend, or join an exercise group, to keep you motivated and committed to exercise. Or take up an activity that keeps you active.

# Not smoking

If you smoke, stop. If you don't smoke, don't start. Cigarette smoking damages the walls of your blood vessels, making them prone to accumulate fatty deposits. If you stop smoking, your HDL cholesterol may return to its former level.