

THE CARDIOLOGY PATIENT PAGE

Statins: Powerful Drugs for Lowering Cholesterol Advice for Patients

Antonio M. Gotto, Jr, MD, DPhil

The underlying cause of heart disease is a process called atherosclerosis. Atherosclerosis has been described simply as hardening of the arteries, but in truth, it involves a complex interaction of biological processes in the walls of arteries. In atherosclerosis, plaque may build up in the vessels that carry blood to the heart (coronary arteries). When one of these plaques tears or ruptures, a blood clot forms that may block the vessel completely and lead to a heart attack (also called a myocardial infarction, or MI, in medical terminology).

One of the key risk factors for the development of atherosclerosis is high cholesterol. Cholesterol is a fatty substance that is a normal component of the cells of the body. Cholesterol (measured in milligrams per deciliter of blood [mg/dL]) is carried through the blood by particles known as lipoproteins, which are classified by their densities. The cholesterol in low-density lipoprotein (LDL-C) is called the “bad” cholesterol, and high levels of LDL-C increase the risk for coronary heart disease. Cholesterol in high-density lipoprotein (HDL-C) is called the “good” cholesterol, and high levels of HDL-C decrease the risk for heart attack. High levels of triglycerides, fatty acids that your body uses to store energy that has been made by the body or obtained from food, also may be associated with increased heart attack risk. Table 1 may be used to help classify your lipid levels, using a scheme developed by the US National Cholesterol Education Program Adult Treatment Panel III.¹

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If I have an unfavorable cholesterol profile, what can I do to lower my risk for a heart attack?

High-fat diets are associated with increased cholesterol and increased risk for heart disease. One can reduce these risks with regular exercise and a prudent diet low in animal fat and cholesterol. Dietary modifications may lower the bad cholesterol by about 10%, on average. Aerobic exercise will help strengthen the heart muscle, and such exercise, to the equivalent of running 12 to 15 miles per week, will help raise HDL-C in most people. It is also important to control other risk factors that may be present (Table 2). Whether or not you already have had a heart attack, you should follow a heart-healthy lifestyle program. Many helpful tips can be found on the American Heart Association’s website, www.americanheart.org.

What if diet and exercise aren’t enough?

When diet and exercise alone are insufficient, drug therapy may help. The most effective and widely tested cholesterol drugs are called the statins, which block the formation of cholesterol in the liver and increase the production of the receptors on liver cells that clean the bad cholesterol from the blood (see the Figure). Five of these drugs are available in the United States: lovastatin, pravastatin, simvastatin, fluvastatin, and atorvastatin. Statins can reduce LDL-C by about 20% to 45%, depending on the dosage and drug. Judging from the results of large, well-conducted clinical trials of lovastatin, pravastatin, and simvastatin, these drugs decrease the risk for heart attack in men and women with both average and high levels of cholesterol, with low levels of the good cholesterol, and before and after a heart attack.²⁻⁵ In patients who have had a heart attack, the risk for dying and the risk for stroke are also decreased. Drug therapy, however, does not replace a heart-healthy diet, and lifestyle changes should be continued if a drug is started.

Statin therapy may be helpful in many kinds of patients (Table 3). However, if you do not fall into any of these categories, you may need to perform a calculation to determine if you are a candidate for statin therapy. This risk calculator and other information for patients from the US

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Circulation is available at <http://www.Circulationaha.org>
DOI: 10.1161/01.CIR.0000014245.25136.D2

TABLE 1. Classification of Lipids in Latest US Guidelines

Total cholesterol, mg/dL	
<200	Desirable
200–239	Borderline high
≥240	High
LDL-C, mg/dL	
<100	Optimal
100–129	Near optimal/above optimal
130–159	Borderline high
160–189	High
≥190	Very high
HDL-C, mg/dL	
<40	Low
≥60	High
Triglycerides, mg/dL	
<150	Normal
150–199	Borderline high
200–499	High
≥500	Very high

National Cholesterol Education Program Adult Treatment Panel III are available online at http://www.nhlbi.nih.gov/guidelines/cholesterol/pat_pub.htm. On the basis of this calculation, you and your physician can decide together whether prescribing a statin is right for you.

Are statins safe?

All drugs may be associated with potentially serious side effects. When a statin is given at a high dose, there is a risk of 1% to 2% per year for developing abnormalities in liver tests; these are almost always reversible when the drug is stopped or reduced. A much rarer side effect, occurring in somewhere between 1 in 1000 and 1 in 2000 patients, is inflammation of the muscles, called myopathy, in which an enzyme from the muscle leaks into the blood. Doctors and patients alike expressed a great deal of concern when the statin called cerivastatin was withdrawn from the US market in August 2001 because an extreme form of this rare side effect, called rhabdomyolysis, seemed to occur more often in patients receiving cerivastatin. Although this side effect may have been seen more frequently with cerivastatin than with

TABLE 2. Risk Factors for Coronary Disease Other Than Elevated LDL-C in Latest US Guidelines

Major, independent risk factors
Cigarette smoking
Hypertension
Low HDL-C
Family history of premature heart disease in father or brother younger than 55 years of age; in mother or sister younger than 65 years of age
Age (men, 45 years or older; women, 55 years or older)
Lifestyle risk factors
Obesity
Physical inactivity
Atherogenic diet

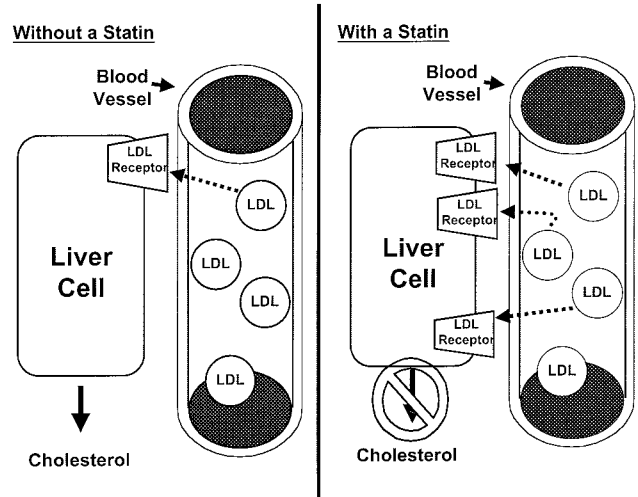


Diagram of the mechanism by which statins lower blood cholesterol levels. All cells in the human body require cholesterol to function properly. The formation of cholesterol in the body occurs mainly in the liver. In the absence of therapy with a statin (left side of diagram), liver cells not only make cholesterol for their own use but also secrete cholesterol into the blood, by which it is transported to other cells in the body. In the blood, cholesterol is transported in various forms, the most dangerous of which is LDL-C, which can build up in the walls of arteries, forming cholesterol deposits (known as plaques) that may narrow the blood vessel. Liver cells absorb some of the LDL-C from the blood and bring it inside liver cells by means of special outpouchings on their surface referred to as LDL receptors. The liver cell uses the LDL-C for its own purposes. The process of absorption of LDL particles by liver cells helps keep the concentration of LDL-C in check, but liver cells cannot keep up if the LDL levels in the blood are too high. When a patient takes a statin (right side of diagram) a key enzyme inside liver cells that is responsible for the formation of cholesterol is blocked. Because liver cells need a certain amount of cholesterol to function, they respond by putting out more LDL receptors on their surface and absorbing more LDL-C from the blood—leading to dramatic reductions in the concentration of bad cholesterol in the blood. It is important for patients to realize that the key enzyme in liver cells that is blocked by statins is more active at night. For this reason, physicians advise patients to take statin pills in the evening (between supper and bedtime) so that the amount of statin in the body is highest when the liver cell enzyme is most active.

TABLE 3. Types of Patients Who May Qualify for a Statin*

Patients who have:
Had a heart attack (myocardial infarction) or chest pain (angina pectoris)
Undergone bypass surgery or angioplasty
Heart disease and LDL-C greater than 100 mg/dL
Diabetes†
Multiple other risk factors for heart disease
Evidence of blockage in the arteries carrying blood to the brain (carotid artery disease) or to the legs (peripheral vascular disease)
LDL-C greater than 190 mg/dL after therapeutic lifestyle change

*Therapeutic lifestyle changes, such as healthful changes in your diet, regular exercise, weight loss, and quitting smoking, should be continued if a statin is started.

†Diabetic patients have a very high risk for developing heart disease. So great is their risk that many guidelines suggest treating this group as aggressively as those who have had a heart attack.

other statins, it should be emphasized that the actual number of cases was very low, considering the millions of prescriptions written for statins since their release.

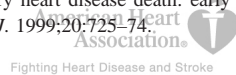
Although you should discuss these and other safety concerns with your physician, the statins have been shown to be extremely effective in a wide range of men and women and to be very safe when current dosages are used properly under a physician's supervision. The Heart Protection Study has shown that virtually all categories of individuals with high coronary risk benefit from statin therapy.⁶ Given how important aspirin can be for reducing the risk for heart disease, it is striking that the lead investigator of this study was confident enough to proclaim the statins as "the new aspirin" (Professor Rory Collins, public communication, 2001). It is clear that the statins are potentially life-saving drugs and that, like aspirin, they should be considered seriously by patients at risk for coronary disease.

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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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Circulation. 2002;105:1514-1516

doi: 10.1161/01.CIR.0000014245.25136.D2

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:

<http://circ.ahajournals.org/content/105/13/1514>

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