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7 KEYS to Reduce Cholesterol

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7 Keys to Reduce Cholesterol

As many Americans are now aware, abnormal levels of cholesterol carried in the blood—and in particular a high level of LDL, or so-called “bad,” cholesterol—significantly increase the risk for coronary heart disease and heart attack. It is also well established that managing blood cholesterol to achieve optimal levels can significantly reduce the risk of heart attacks and strokes.

Your cholesterol levels, of course, are not the only risk factor for coronary heart disease. Other major risk factors include older age, a family history of premature heart disease, obesity, smoking, high blood pressure, and diabetes; any decision about treating your cholesterol should be made with your doctor taking all risk factors into account.

But whatever your other risk factors are, it may be time for you to reevaluate whether you need to lower your cholesterol. The government’s National Cholesterol Education Program (NCEP) has estimated that at least 65 million Americans have blood cholesterol levels that merit treatment with dietary and other lifestyle changes—and that as many as 36 million people should be taking cholesterol-lowering medications. Yet only 12 to 15 million of them are currently taking such medication, and many (probably most) are taking too small a dose.

On the next page you will read the first of seven effective, proven, practical keys for managing cholesterol—with the latest, best information and advice from specialists at Johns Hopkins Medicine.



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KEY 1

**Know Your “Target”
Cholesterol Levels**



Know Your “Target” Cholesterol Levels

Cholesterol is a white, waxy lipid (fat) that is present in the tissues of humans and other animals and, thus, in all foods from animal sources. Cholesterol is essential for many bodily functions: It is a building block for hormones and for vitamin D; it is a component of the membranes of cells; and it is a part of the insulation sheath around nerve fibers that enables nerves to communicate.

How Cholesterol Contributes to Heart Attacks

Despite its importance to life, cholesterol isn't an essential nutrient, meaning that the diet does not need to contain cholesterol to meet the body's requirements. The liver can manufacture all the cholesterol the body needs. Particles called lipoproteins, formed in the liver, transport cholesterol and other fats through the bloodstream. The three lipoproteins are named according to their density: very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Most cholesterol is transported by LDL.

The liver secretes VLDL, which is converted to LDL in the bloodstream. The cholesterol on LDL is used to form membranes in cells throughout the body, and it also serves as the starting molecule for the formation of several hormones, such as estrogen, androgen, and cortisol. Deposits of LDL cholesterol in the arterial walls initiate the formation of plaques. As plaques build up, the arterial walls thicken and narrow.

Symptoms of coronary heart disease result when an advanced plaque narrows a coronary artery so much that it hinders blood flow to the heart. Plaque deposits also roughen arterial walls and make it easier for a blood clot to form along their surface. Complete blockage of a coronary artery by a clot can cause a heart attack. A portion of a clot can also break loose from its place of origin and cause a heart attack by lodging in a narrower section of the artery or in a smaller artery supplying blood to the heart.

HDL also carries cholesterol in the blood; however, HDL has the beneficial capacity to pick up cholesterol from cells and atherosclerotic plaques and bring it back to the liver for reprocessing or excretion. Therefore, HDL cholesterol is often referred to as “good” cholesterol, because it clears cholesterol from the arteries, while LDL cholesterol has been called “bad” because it deposits cholesterol in the arteries.

Because elevated cholesterol levels contribute to the development of atherosclerosis, reducing cholesterol levels can help prevent coronary heart disease and heart attacks.

Getting Your Cholesterol Levels Tested

According to current guidelines from the National Cholesterol Education Program (NCEP), everyone who is 20 years of age or older should have a blood test called a lipid profile (sometimes called a lipoprotein profile) at least once every five years. This test measures blood levels of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides.

Evaluating Blood Lipid Levels

Cholesterol and triglycerides are the two principal lipids, or fats, in the blood. Because they cannot dissolve in the blood, special proteins, called lipoproteins, carry them through the bloodstream. The cholesterol carried on low-density lipoproteins (LDL) is often called “bad” cholesterol because it contributes to risk for coronary heart disease (CHD). In contrast, high-density lipoprotein (HDL) cholesterol is often called “good” cholesterol because high HDL levels protect against CHD.

The chart here shows risk classifications for levels of blood lipids and lipoproteins (in milligrams per deciliter, or mg/dL) when measured according to guidelines from the National Cholesterol Education Program. These classifications apply to people without CHD. If you have CHD or diabetes or more than one risk factor for CHD, a desirable LDL level may be lower than 100 mg/dL. Because everyone’s situation is different, ask your doctor for help in interpreting the test results for cholesterol and triglycerides.

Total Cholesterol

| | |
|-----------------|---------------|
| Desirable | <200 mg/dL |
| Borderline-high | 200–239 mg/dL |
| Increased Risk | ≥240 mg/dL |

LDL Cholesterol

| | |
|----------------|---------------|
| Optimal* | <100 mg/dL |
| Desirable | 100–129 mg/dL |
| Borderline | 130–159 mg/dL |
| Increased Risk | ≥160 mg/dL |

HDL Cholesterol

| | |
|----------------|-------------|
| Desirable | ≥60 mg/dL |
| Borderline | 40–59 mg/dL |
| Increased Risk | <40 mg/dL |

Triglycerides

| | |
|----------------|---------------|
| Desirable | <150 mg/dL |
| Borderline | 150–199 mg/dL |
| Increased Risk | 200–499 mg/dL |

*For people with diabetes, peripheral arterial disease, history of stroke or aortic aneurysm, or known CHD, and for some people with two or more CHD risk factors, a target of LDL <70 mg/dL should be considered.

(Triglycerides are another type of lipid, which the body uses for energy. Like cholesterol, triglycerides are obtained from food and produced in the liver, and they are transported in the blood by lipoproteins, mostly VLDL. High triglyceride levels are a risk factor for coronary heart disease.)

The test should be performed at your doctor’s office. You will be asked to fast for at least 12 hours before the test, since what you eat can affect levels of blood triglycerides.

If fasting isn’t possible, then only the values for total cholesterol and HDL cholesterol are obtained. If you are considered at low risk for coronary heart disease and the test results confirm this assumption, no further testing may be required. Otherwise, your doctor may ask you to return for a fasting lipid profile.

- If you are healthy, your results are all in the desirable range (see the chart above), and you have no other major risk factors for coronary heart disease, then you should be retested in five years.

- The target for people with one coronary heart disease risk factor is an LDL cholesterol level of less than 160 mg/dL. In most individuals who do not have diabetes or known vascular disease, but have two or more risk factors, LDL cholesterol should be below 130 mg/dL.

- In patients with any form of known cardiovascular disease, the NCEP guidelines recommend that LDL cholesterol be lowered to less than 100 mg/dL—and possibly even less than 70 mg/dL. This target also applies to individuals with diabetes, which is now designated as a “coronary heart disease equivalent” rather



than, as in previous guidelines, simply another risk factor for coronary heart disease. Some individuals with two or more coronary heart disease risk factors are at particularly high risk and should also have their LDL cholesterol lowered to less than 100 mg/dL (with an optional goal of less than 70 mg/dL).

- A high level of HDL cholesterol (60 mg/dL or higher) is considered protective against coronary heart disease. A high HDL level cancels out the effects of one other coronary heart disease risk factor when determining the total number of risk factors.

- Your doctor will use the test results, along with the presence of other risk factors for coronary heart disease, to estimate your coronary heart disease risk. If your total cholesterol, LDL cholesterol, or triglyceride levels are elevated (or if your HDL level is too low), your doctor will determine the most effective risk reduction measures for you to take, usually beginning with lifestyle changes.

Now that you know what your cholesterol targets should be, you are ready for **Key #2** — **how to begin improving your cholesterol levels with changes in your diet.**

KEY 2 is titled:

Focus on the Right Fats

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KEY 2

**Focus on the
Right Fats**



Focus on the Right Fats

Lifestyle measures can have a greater impact on preventing coronary heart disease and heart attacks than on practically any other disorder. More specifically, lifestyle changes can reduce elevated cholesterol levels—and the simplest change to make is to limit your intake of saturated fat.

The average American diet contains about 35% to 40% of calories from fat. Not all of this fat is bad—in fact, some types of fat, such as mono- and polyunsaturated fat, have a beneficial effect on blood lipids and may lower the risk of developing coronary heart disease or dying of it. But the prevalent type of fat in the American diet is saturated fat, the major dietary factor that raises blood cholesterol levels. In fact, saturated fat has a bigger impact on blood cholesterol levels than dietary cholesterol itself. Saturated fat includes most animal and dairy fats and some oils, such as palm and coconut oils.

Modifying your fat intake. The National Cholesterol Education Program (NCEP) guidelines recommend reducing total fat to between 25% and 35% of total calories, with the majority of fat calories coming from mono- or polyunsaturated fat. Also advised is limiting the intake of saturated fat in order to reduce blood cholesterol levels—specifically LDL (“bad”) cholesterol.

The guidelines recommend these dietary measures even when blood cholesterol is normal, since a modified fat intake can help maintain optimal cholesterol levels. A reduction in total fat may also help to maintain an ideal weight, because a gram of fat contains more than twice as many calories (9 calories) as a

gram of carbohydrates or protein (4 calories). (Fat and protein are more filling than carbohydrates, however.)

Blood cholesterol levels are also raised by dietary cholesterol, but not as much as by saturated fat. A few foods—egg yolks, lobster, and shrimp—are especially high in dietary cholesterol. The NCEP guidelines also recommend limiting dietary cholesterol (see next page).

While modifying fat intake is desirable, it is important not to get too carried away with restricting fat in the diet. According to the American Heart Association, short-term studies reveal that lowering fat intake to 15% or less of total calories does not reduce LDL cholesterol levels much further than a standard low-fat diet.

In addition, very-low-fat diets decrease heart-protective HDL cholesterol and increase triglyceride levels, whereas the moderate-fat diet recommended by the NCEP guidelines can help reduce triglycerides and raise HDL cholesterol, particularly in people with metabolic syndrome, a condition that markedly increases the risk of coronary heart disease and diabetes. (Metabolic syndrome is characterized by abnormally high blood sugar levels due to insulin resistance, accompanied by other factors that include abdominal obesity, high blood pressure, low levels of HDL cholesterol, and high levels of triglycerides.)

Mono- and polyunsaturated fats. When fat is consumed, monounsaturated fats should be chosen whenever possible so that they contribute up to 20% of total calories. Olive and canola oils, almonds, and avocados contain large amounts of monounsaturated fat. When

they are substituted for saturated fat in the diet, monounsaturated fats can lower LDL cholesterol levels and stabilize or even raise HDL cholesterol levels. Polyunsaturated fats—found in safflower, sunflower, and corn oils—also lower LDL cholesterol levels.

Omega-3 fatty acids, another type of polyunsaturated fat, seem to have cardioprotective benefits beyond lowering LDL cholesterol. There are three principal types of omega-3 fatty acids: eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (ALA). EPA and DHA, found only in fish (particularly fatty fish), can reduce the tendency for blood to clot, decrease the risk of arrhythmias (abnormal heart rhythms), and lower triglyceride levels; the benefits of ALA are unclear.

Trans fat. People should minimize their intake of trans fat—a type of fat found in foods made with hydrogenated or partially hydrogenated oils. Some examples are margarine and commercial baked goods. Trans fat (also known as trans fatty acids) is formed during the addition of hydrogen atoms to unsaturated oils to make them more saturated and therefore solid at room temperature and more shelf-stable.

Trans fat may be even more harmful to health than saturated fat because trans fat not only raises LDL cholesterol, but also lowers HDL cholesterol. The Institute of Medicine, a branch of the National Academy of Sciences, recommends that trans fat consumption be as low as possible.

Recommendations for Fat Intake

1. Above all, keep saturated fat intake to less than 7% of calories. This is the simplest dietary measure you can take to lower your risk of a heart attack. Reaching this goal will help reduce your blood cholesterol levels, specifi-

cally your LDL cholesterol. Meats, poultry skin, and whole-milk dairy products contain the most saturated fat and thus should be limited in the diet.

2. With few exceptions, limit total fat intake to between 25% and 35% of total calories. For those whose fat intakes have exceeded the recommended amount, fat calories should be replaced with ones from complex carbohydrates, with an emphasis on whole grains, vegetables, fruits, and legumes (beans and peas). As much as possible, avoid calories from products that contain a lot of refined carbohydrates, such as sugar and white flour.

3. Get half your total fat intake from monounsaturated fats. These fats are particularly plentiful in olive oil, canola oil, almonds, walnuts, and avocados. Because these sources are also concentrated sources of total fat calories, they must be eaten in moderation to maintain a diet containing no more than 35% of calories from fat and to avoid weight gain.

4. Get less than 300 mg of dietary cholesterol per day, and less than 200 mg if you have elevated levels of LDL cholesterol. Although saturated fat raises blood cholesterol levels more than dietary cholesterol, experts still recommend limiting dietary cholesterol.

5. Eat fatty fish at least twice a week. The omega-3 fatty acids in fatty fish appear to have some protective effects, and fish are a good source of protein and are low in saturated fat. Salmon, sardines, and albacore tuna are all good choices.

6. Limit trans fats to less than 1% of total calories. Check food labels. The Food and Drug Administration (FDA) now requires manufacturers to list the amount of trans fats on



food labels; the amount is listed below the amount of saturated fat.

7. Remember that these recommendations need not be followed at each meal. It is more important to even out fat intake over the course of a week. If you eat a high-fat lunch, for example, you can compensate by eating a low-fat dinner or a little less fat than usual over the next several meals.

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Assessing and modifying your intake of dietary fat is one of the most effective lifestyle measures that can impact blood cholesterol levels. **But as you will discover in Key #3, there are additional changes you can make to your diet to improve your cholesterol even further.**

KEY 3 is titled:

**Make the Most of
Cholesterol-Busting Foods**



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KEY 3

**Make the Most of
Cholesterol-Busting
Foods**



Make the Most of Cholesterol-Busting Foods

When people need to reduce their cholesterol, they often think about eliminating some foods from their diet. But research increasingly shows that adding certain foods can also lower cholesterol levels significantly. In fact, a study in *Metabolism* found that people with high cholesterol who ate a diet not only low in saturated fat but high in plant sterols, soluble fibers, soy protein, and almonds effectively lowered their LDL (“bad”) cholesterol levels by 35%. (Although this diet would be very difficult to follow for long periods, the study illustrated the feasibility of lowering LDL cholesterol through diet.)

To avoid consuming excess calories, it’s important to substitute the cholesterol-busting foods described below for other foods (preferably those high in saturated fat and cholesterol) rather than simply adding them to the diet.

Soluble Fiber

The American Heart Association recommends that people who are unsuccessful in lowering their cholesterol through other lifestyle changes boost their intake of dietary fiber to 25 to 30 grams each day. Fiber comes in two forms: soluble, the type in oatmeal that gets sticky when wet; and insoluble, the spongelike version in bran and fruit and vegetable skins that absorbs water. Both types of fiber are important, but soluble fiber is especially effective in lowering blood cholesterol levels. For this reason, you should include foods containing soluble fiber (such as oats, oat bran, barley, legumes, dried

plums [prunes], apples, carrots, and grapefruit) in your diet regularly.

A 2002 study from the *Journal of the American Dietetic Association* found that eating four servings of high fiber foods per day for seven weeks and receiving guidance about other lifestyle changes to lower cholesterol decreased total cholesterol levels by almost 6% and LDL cholesterol levels by over 7%. Fiber may help lower cholesterol by interfering with the reabsorption of bile acids from the intestine, so the liver converts more cholesterol to bile acids.

Nuts

Although nuts are high in fats, the fats are predominantly monounsaturated and polyunsaturated, which decrease LDL cholesterol levels. Although a number of types of nuts help lower LDL cholesterol levels—including walnuts, peanuts, pecans, macadamias, and pistachios—the best evidence exists for almonds. In one report, from a 2002 issue of *Circulation*, people with high cholesterol levels who added 37 grams of almonds (about a handful) to their diet each day lowered their LDL cholesterol levels by 4%; 74 grams of almonds daily lowered LDL cholesterol levels by 9%. People should be sure to choose dry roasted or natural nuts and not ones that contain added oil and salt.

Plant Sterols and Stanols

Plant sterols and stanols, plant compounds that are structurally similar to cholesterol, partially block the absorption of cholesterol from the

small intestine. They lower levels of LDL cholesterol without adversely affecting HDL (“good”) cholesterol levels.

The American Heart Association states that people whose elevated cholesterol levels are not controlled by increased physical activity, weight loss, and dietary changes (decreasing saturated fat and cholesterol intake) might consider adding about 2 grams of plant sterols or stanols daily to their diet. This dietary change can lower LDL cholesterol levels by about 10% and, over a lifetime, may decrease the risk of a heart attack by up to 20%. However, consuming more than 2 grams per day of plant sterols or stanols will not lower cholesterol any more effectively and may lead to excess caloric intake.

What foods contain sterols and stanols? The margarines Benecol, Take Control, and Smart-Balance OmegaPlus are fortified with either sterols or stanols. And an orange juice, Heart Wise by Minute Maid, has added sterols. In a March 2004 study from *Arteriosclerosis, Thrombosis, and Vascular Biology*, daily consumption of 16 ounces of orange juice fortified with plant sterols (for a total of 2 grams of sterols daily) decreased total cholesterol levels by 7% and LDL cholesterol levels by 12% over eight weeks.

Other types of food fortified with stanols or sterols, like salad dressings, cereals, breads, and yogurt, may become available. (Please note that these fortified products tend to be more expensive than the nonfortified versions.)

There are potential concerns about the efficacy and safety of plant sterols: With time, their LDL-lowering effect diminishes, and their level in the blood increases. And plant sterols have now been found in atherosclerotic plaques. However, according to Johns Hopkins cardiologist Christopher Sibley, M.D., while these findings are rather worrisome, “we don’t yet

know whether their presence in plaques actively predisposes to heart attack and stroke.”

The LDL-lowering effect of plant stanols, by contrast, does not decline with time, levels of stanols in the blood do not rise, and they have the added benefit of lowering plant sterol blood levels. Dr. Sibley comments, “Perhaps the most cautious response at present would be to choose supplements containing plant stanols to lower your cholesterol level until more definitive evidence is available regarding the long-term safety of sterol supplements. In short, plant stanols can provide the same benefits as the sterols with fewer question marks.”

To account for the increased calories of adding these margarines to your diet, you will have to cut down in other areas to avoid gaining weight. Finally, because increased dietary intake of either plant sterols or stanols may reduce absorption of beta-carotene (a vitamin A precursor), you should include more carotenoid-rich fruits and vegetables, such as carrots, sweet potatoes, pumpkins, tomatoes, and apricots, in your daily diet.

A Note on Soy Products

Soy products have received considerable attention for their potential ability to lower the risk of cardiovascular disease—a benefit supported by the Food and Drug Administration (FDA), which in 1999 began allowing food manufacturers to make health claims on soy products stating that consuming 25 grams of soy a day may reduce the risk of heart disease. The FDA concluded that foods containing soy protein, if included in a diet low in saturated fat and cholesterol, may reduce the risk of coronary heart disease by lowering blood cholesterol levels.

However, in 2006, members of the Nutrition Committee of the American Heart Association



(AHA) reviewed more recent research on soy products. In most of 22 studies examining the effect of isolated soy protein with isoflavones (various active compounds found in soy), LDL cholesterol decreased less than 3%—a “very small reduction” that required consuming large amounts of soy (study subjects consumed an average of 50 grams daily). The studies showed no significant effects on HDL cholesterol or triglycerides. In 19 studies of soy isoflavones, the average effect on LDL cholesterol was negligible.

For this reason, the AHA does not recommend using isoflavone supplements and takes the position that soy products should be beneficial to cardiovascular health not because of any special properties, but because they are low in saturated fat and high in fiber and polyunsaturated fat, so offer a healthy replacement for foods high in saturated fat.

Diet is typically considered the first steps and the cornerstone for managing high cholesterol levels—and they may be all that you need. However, many people can only reach recommended cholesterol levels by adding a medication. **In Key #4, you’ll learn whether you might benefit from a statin drug.**

KEY 4 is titled:

**Reduce Cholesterol
with Medication**

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KEY 4

**Reduce Cholesterol
with Medication**



Reduce Cholesterol with Medication

Not everyone responds to the same degree to the effects of a heart-healthy diet. Despite their benefits, these lifestyle measures don't always lower LDL ("bad") cholesterol sufficiently to significantly reduce the risk of a heart attack. When that is the case, medication is often recommended as well.

The benefits of reducing total blood cholesterol and LDL cholesterol with medication have been clearly demonstrated by a number of well-designed studies. About 90% of the cholesterol-lowering drugs taken by Americans are in a class of medications known as statins. These drugs lower cholesterol by at least 20% through the same basic action: They inhibit HMG-CoA reductase, a key enzyme that controls how much cholesterol is produced in the liver. The result is lower blood levels of LDL cholesterol. Statins also lower elevated triglycerides and raise HDL ("good") cholesterol.

Statins also reduce inflammation in arterial walls; relax blood vessels; improve blood flow to the heart; inhibit clotting; and stabilize and reduce the size of the fatty plaques that form in the walls of arteries. More research is needed to determine the clinical significance of these effects.

Is There a "Best" Statin?

If you are one of the millions currently taking a statin drug or are a candidate for starting on one, you are probably aware that there is more than one statin. The first statin, lovastatin (brand name: Mevacor), was introduced 17 years ago, and a total of six such drugs are now

on the market. The others include atorvastatin (Lipitor), fluvastatin (Lescol), pravastatin (Pravachol), simvastatin (Zocor), and rosuvastatin (Crestor), which is the most recent one (it was approved in August, 2003).

Three statins—lovastatin, pravastatin, and simvastatin—are available in generic form. Some of the statins are now available in combination with other lipid-lowering drugs, and one of them (atorvastatin) is sold in combination with a blood pressure lowering drug (in a pill called Caduet).

As the number of statins has increased, so have the efforts by drug companies to promote the advantages of their particular product. But is one statin "the best"—or are some statins better than others? Why should you be on atorvastatin when your friend is on pravastatin or simvastatin? What factors did your doctor consider in prescribing a specific statin for you? And should your preferences be taken into account?

Comparing Potency

Direct comparisons of the potency of the various statin formulations are limited. The Statin Therapies for Elevated Lipid Levels Compared Across Doses to Rosuvastatin (STELLAR) trial, reported in 2003 in the *American Journal of Cardiology*, is the largest comparison to date. A randomized, controlled trial that involved more than 2,400 people, STELLAR compared the three most widely prescribed statins—atorvastatin, simvastatin, and pravastatin—with the newest, rosuvastatin, across a range of doses.

After 6 weeks of treatment, rosuvastatin low-

ered LDL cholesterol by 46% to 55%, compared with 37% to 51% for atorvastatin, 28% to 46% for simvastatin, and 20% to 30% for pravastatin. Not surprisingly, more people taking rosuvastatin achieved their LDL cholesterol goals. Rosuvastatin and atorvastatin also lowered triglycerides by 20% to 28%, significantly more than pravastatin (8% to 13%) or simvastatin (12% to 18%). In addition, across dosage ranges, rosuvastatin produced a slightly greater rise in HDL cholesterol levels than the other statins—although the clinical benefit of such an increase is unknown.

Other Factors To Consider

In addition to potency, several other medical and nonmedical factors may influence you and your doctor's choice of a statin. They include:

- **Cost.** Statins vary widely in price. For example, the cost for 30 tablets of the 20-mg dose size ranges from about \$25 for generic lovastatin to about \$135 for brand-name simvastatin (Zocor).
- **When to take.** All of the statins, except atorvastatin and rosuvastatin, should be taken in the evening or at bedtime to achieve their maximal effect (because cholesterol production is highest at night). Atorvastatin and rosuvastatin have a relatively long duration of action and may be taken any time during the day. Lovastatin should be taken with meals to increase absorption.
- **Drug interactions.** Atorvastatin, simvastatin, and lovastatin may interact with certain drugs because they are metabolized by the same enzyme system in the liver (see chart). Pravastatin, rosuvastatin, and fluvastatin are metabolized differently and appear less prone to such interactions. However, safety data on rosuvastatin are more limited because the drug is so new.

- **Side effects.** Myopathy, or muscle pain and weakness, is the most common side effect of all the statins. More dangerous is myositis, a severe muscle inflammation that can progress to rhabdomyolysis, a potentially fatal condition that can damage the kidneys. Rhabdomyolysis is rare when currently available statins are taken alone, but it can occur when they are combined with the triglyceride-lowering fibrates gemfibrozil (Lopid) or fenofibrate (Tricor, Lofibra). Fibrates, particularly gemfibrozil, may raise the concentration of statins and increase their potential for causing muscle inflammation.

An uncommon adverse effect of all statins is an increase in liver enzymes. As a precaution, people taking these drugs should have periodic blood tests (e.g., every 4 to 6 months) to monitor liver function. Any elevation in liver enzymes rapidly reverses when the statin is discontinued. No instances of permanent liver damage have been reported.

Which One Is For You?

A statin's ability to lower LDL cholesterol is the most important factor to consider when choosing a statin. If your initial cholesterol level is only mildly elevated, your doctor may opt for any of the statins. On the other hand, if you are at elevated risk for heart disease, your initial cholesterol level is very high and your triglyceride levels are also high, or you've failed to respond adequately to one of the other statins, a more potent formulation—like atorvastatin, rosuvastatin, or simvastatin—may be more appropriate.

Once medical issues are addressed, other factors, such as cost and the time of day you prefer to take your medication, can be considered. No matter which drug is chosen, the standard approach is to start at a low dose and



increase the dosage if a greater drop in LDL cholesterol levels is needed. (If you take a statin drug, you should be monitored by your doctor to be sure the drug is lowering your LDL cholesterol sufficiently and also for any side effects, especially liver toxicity and muscle inflammation, which are rare).

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Some people don't respond adequately to a particular statin—and they may experience side effects from increasing the dose. Or they may have face special issues such as high levels of triglycerides. **As you'll learn in Key #5, combining a statin with another type of drug often provides a solution.**

KEY 5 is titled:

Consider Combo Therapy to Reduce Cholesterol



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KEY 5

**Consider Combo Therapy
to Reduce Cholesterol**



Consider Combo Therapy to Reduce Cholesterol

When it comes to cholesterol, LDL might as well stand for “Lower, Darn it, Lower”—at least for some of us. The results of several recent clinical trials have shown that patients who are at high risk for heart attack and death from cardiovascular disease can substantially lower their risk by reducing levels of LDL (“bad”) cholesterol well below previously recommended targets.

In response to these findings, a National Cholesterol Education Program (NCEP) panel issued a statement in July, 2005 calling for more aggressive lowering of LDL cholesterol in people at high risk. According to the revised guidelines, a reasonable therapeutic option for people at “very high” risk (such as those who have experienced a heart attack) is to push LDL cholesterol levels below 70 mg/dL—30 points below the prior target level of 100 mg/dL for this group.

Lower Target = Higher Doses

The new recommendations also give doctors the option of prescribing drug therapy to people at “moderately” high risk who have LDL cholesterol levels higher than 100 mg/dL. Moderately high risk is defined as having multiple risk factors, including older age (45 or older for men, 55 or older for women), smoking, and high blood pressure, which confer a 10% to 20% chance of having a heart attack within 10 years. Previously, drug therapy was only advised for such patients if their LDL cholesterol levels were 130 mg/dL or higher. In addition, the guidelines now say that for people at high or moderately high risk for a heart attack, drug therapy

should aim to decrease LDL cholesterol levels by at least 30% to 40%.

Achieving these new, lower LDL cholesterol goals, however, can pose a challenge. Although statin drugs, which inhibit the synthesis of cholesterol, are effective at reducing LDL levels, researchers estimate that only about half of high-risk patients currently on statins have even reached the LDL cholesterol target of less than 100 mg/dL. For patients with very high initial LDL cholesterol levels, even maximal doses of statins aren’t able to bring levels below the new threshold. Other patients who require high statin doses to attain LDL cholesterol levels below 70 mg/dL are unable to tolerate the drugs because of side effects.

People in these circumstances should first focus on their lifestyle habits: The new guidelines stress that eating a healthy diet, low in saturated fat and cholesterol, and exercising regularly can be important in lowering blood cholesterol. In addition, another option can be very effective—combining a statin drug with a second cholesterol-lowering medication.

Advantages of Combos

First, combination therapy significantly enhances the likelihood of meeting LDL cholesterol goals, especially in high-risk patients with coronary heart disease. Second, cholesterol-lowering drugs that work by different mechanisms may have distinct, and potentially additive, beneficial effects on the fatty deposits in the coronary arteries (atherosclerosis).

Statins, for example, reduce inflammation associated with atherosclerosis and help stabi-

lize the lipid-rich plaques lining the arteries. Adding prescription-level doses of niacin to statin therapy can substantially increase HDL (“good”) cholesterol levels as well as lower LDL cholesterol and triglyceride levels. Niacin also appears to enhance reverse cholesterol transport, a process by which HDL particles ferry cholesterol from peripheral cells and arterial plaques to the liver for breakdown, and thus may help thwart the progression of atherosclerosis.

Another possible benefit of combination therapy is that it may help avert potentially serious side effects. When a statin is given at its maximal dose, there is a slight but significant increase in the risk of liver enzyme abnormalities and muscle toxicity. Giving a statin in lower doses together with another cholesterol-lowering drug could produce the same, or an even greater, degree of LDL lowering as the highest statin dose while minimizing the risk of serious side effects.

Combination Options

The drugs most often added to statin therapy are niacin; ezetimibe (Zetia), a drug that inhibits cholesterol absorption; or a bile-acid sequestrant such as colesevelam (WelChol). Drugs that join one of these cholesterol fighters with a statin in a single pill have recently become available: The drug Advicor combines lovastatin with extended-release niacin, while Vytorin puts together simvastatin (Zocor) and ezetimibe.

- **Niacin-statin.** Niacin has a beneficial effect on the overall lipid profile, lowering LDL and triglyceride levels while raising HDL cholesterol. “Niacin is primarily given in combination with a statin to patients who have low HDL levels,” says Roger S. Blumenthal, M.D., Director of the Johns Hopkins Ciccarone Preventive Cardiology Center. In a controlled study conducted in patients with known coronary heart disease and

published in *The New England Journal of Medicine* in 2001, the combination of simvastatin and niacin reduced LDL cholesterol levels by 42%, increased HDL cholesterol by 26%, and caused regression of fatty plaques in the coronary arteries. After 3 years, the incidence of major cardiovascular events was about 90% lower in patients treated with the simvastatin-niacin combination compared with the placebo group.

Muscle toxicity is a possible problem with the niacin-statin combination, but it is not as common as when a statin is combined with a fibrate, a drug that is mainly used to lower triglyceride levels,” notes Dr. Blumenthal. Some patients are unable to tolerate niacin because it produces flushing of the skin, but an extended-release form (Niaspan), which is available by prescription, causes less frequent and less severe flushing symptoms. Other side effects of niacin include liver toxicity, stomach ulcers, and gout.

- **Ezetimibe-statin.** Combining a statin, which inhibits cholesterol production, with ezetimibe, a drug that blocks the intestinal absorption of cholesterol, can lower LDL cholesterol more than a statin alone. “I think at this stage, most of us would prefer to reach the LDL cholesterol target with only a statin,” says Dr. Blumenthal, “but if someone can only tolerate a lower dose of a statin and cannot reach their LDL cholesterol goal with this dose, then we would certainly add ezetimibe.” Patients can take separate pills for each medication or choose the new drug Vytorin, which combines 10 mg of ezetimibe with different dosages of simvastatin.

- **Colesevelam-statin.** Bile acid sequestrants partially prevent bile acid absorption from the intestine and cause the liver to convert more cholesterol into bile acids, thereby removing more LDL cholesterol from the circulation. Older drugs in this category were difficult to take and caused many gastrointestinal side effects. A newer bile acid sequestrant, coleseve-



lam, works more efficiently and thus can be administered in lower doses with fewer side effects. In a randomized controlled trial published in *Atherosclerosis* in 2001, patients given 10 mg/day of atorvastatin (Lipitor) alone experienced a 38% decrease in their LDL cholesterol, while the addition of colesvelam to atorvastatin produced a 48% drop in LDL cholesterol without any increase in adverse effects.

Are You Reaching Your Goal?

If your LDL cholesterol still exceeds the recommended target despite optimal statin therapy, or if you are unable to tolerate higher doses of statins because of side effects, ask your doctor if combination therapy would be an appropriate option. Similarly, if your HDL cholesterol level is too low or your triglycerides too high, ask about adding niacin or a fibrate to your regimen.

“Many doctors now try to push LDL cholesterol way down in high-risk asymptomatic patients,” says Dr. Blumenthal, “especially if tests have established they have a lot of plaque in their heart. At Hopkins, we are very aggressive about lowering LDL cholesterol levels and would

add ezetimibe if necessary. And if a patient’s HDL cholesterol or triglycerides are still suboptimal after treatment, we would probably add another drug to improve these levels.”

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Do you know your HDL level? Key #6 explains why it is worth focusing on HDL cholesterol—and gives you the drug and nondrug measures experts recommend for raising HDL.

KEY 6 is titled:

**Boost Your HDL—
for Multiple Benefits**



JOHNS HOPKINS
M E D I C I N E

KEY 6

**Boost Your HDL —
for Multiple Benefits**



Boost Your HDL— for Multiple Benefits

In discussions about managing cholesterol to prevent coronary heart disease, lowering LDL (“bad”) cholesterol is often cited as the first goal. But in recent years there has been growing emphasis on low levels of HDL (“good”) cholesterol as an independent risk factor for coronary heart disease. People with HDL cholesterol levels below 40 mg/dL have a significantly elevated rate of heart attacks. About 30% of people with coronary heart disease have low HDL cholesterol levels but normal levels of LDL cholesterol.

The American Heart Association (AHA) and the American Diabetes Association currently recommend that HDL levels be above 40 mg/dL for men, and above 50 mg/dL for women. However, the greatest benefits seem to come when a person’s HDL level is over 60 mg/dL.

High HDL: Key to a Longer Life?

HDL cholesterol exerts its good effects on the heart by removing cholesterol from the artery walls, thereby reducing the risk of atherosclerosis. In addition, there is intriguing evidence that having a high HDL level can even boost a person’s overall longevity.

As people grow older, a high HDL level seems to be a good marker for longevity. Once someone reaches age 85, low levels of HDL cholesterol—rather than high levels of LDL cholesterol—are associated with an increased risk of death from heart disease and stroke, according to a recent Dutch study in the *Archives of Internal Medicine*.

In this study, a group of 599 individuals aged

85 years were followed for 4 years, during which time 152 of them died. People with low levels of HDL cholesterol were twice as likely to die of a heart attack and 2.5 times more likely to have a fatal stroke, compared with those who had high HDL levels. Low HDL—as well as low LDL—levels more than doubled the risk of dying of infection.

Is it Genetic?

Research recently published in the *Journal of the American Medical Association* determined that many people who live exceptionally long, healthy lives—average age of study participants was 98 years—share a particular gene mutation that leads to higher HDL levels as well as larger HDL and LDL particles than those present in the general population.

It has been suggested that larger LDL particles may protect against cardiovascular disease because such large particles cannot readily penetrate the walls of arteries and contribute to atherosclerosis. The gene mutation responsible for high HDL levels and bigger HDL and LDL particles appears to protect against many chronic diseases associated with aging, such as heart disease, stroke, and diabetes.

Although we are not all lucky enough to inherit the “longevity gene,” there is much that we can do to raise our HDL level on our own—and perhaps increase our odds for a longer and healthier life.

Lifestyle Changes to Boost HDL

If your HDL is below recommended levels, cer-

tain lifestyle changes can help produce modest increases in HDL cholesterol. If lifestyle changes alone are insufficient, medications you can add to help improve your HDL level are discussed below.

- **Quit smoking.** HDL levels average 4 to 6 mg/dL lower in smokers compared with non-smokers. Quitting smoking can help raise your HDL as well as reduce your risk of heart disease and lung cancer.

- **Increase your physical activity.** Aerobic exercise is physical activity that uses large muscle groups rhythmically and continuously and elevates the heart rate and breathing for a sustained period. Regular aerobic exercise—any activity such as running, brisk walking, cycling, swimming, or dancing that raises the heart rate for 20 to 30 minutes at a time—can help boost HDL levels. Strength training, though it has many other benefits, does not affect HDL.

- **Lose weight.** If you are overweight, losing the excess pounds is an effective strategy for raising HDL. Experts estimate that for every 7 lbs. you drop, your HDL level will climb by 1 mg/dL.

- **Alter your diet.** Trans fatty acids, found in margarines and many baked goods, can lower HDL levels and should be avoided. Instead, you should try your best to incorporate healthier monounsaturated fats, such as olive oil and canola oil, into your diet because they can help improve HDL levels.

- **Drink alcohol in moderation.** People who drink in moderation—for example, consuming about 2 to 6 ounces of wine with their evening meals—can raise their HDL levels significantly. However, because of the potential risks of alcohol consumption, experts do not recommend that lifelong non-drinkers start drinking just to boost their HDL.

Extra Help with Medication

Many people are unable to raise their HDL level sufficiently with lifestyle changes alone and may need to combine these healthy habits with one or more medications.

- **Fibrates.** The fibrates gemfibrozil (Lopid) and fenofibrate (Tricor) are an effective therapy for people with high triglycerides and low HDL levels, raising HDL by an average of 5% to 15%.

- **Niacin.** Niacin is the most potent drug currently available for raising HDL levels—it boosts HDL from 15% to 35% depending on the daily dose. In a study reported in *Annals of Internal Medicine* in January, 2005, niacin combined with gemfibrozil and cholestyramine raised HDL levels by 36% and caused regression of fatty plaques in coronary arteries.

Niacin is available in over-the-counter preparations, but because it can cause serious side effects, you should take it only under your doctor's supervision. Niacin may cause facial flushing, but this effect can be minimized by taking an extended-release preparation (Niaspan), which is available only by prescription. Taking the drug at bedtime with aspirin and a low-fat snack can help further reduce flushing. Niacin can also cause headache, indigestion, itching, and nausea, as well as gout and liver damage.

- **Thiazolidinediones.** Rosiglitazone (Avandia) and pioglitazone (Actos) are antidiabetic drugs, which may be an option for boosting HDL levels if you have diabetes.

- **Torcetrapib.** Torcetrapib is an experimental drug that was shown to more than double HDL levels in a recent study published in *The New England Journal of Medicine*. Torcetrapib and similar HDL-raising drugs are currently undergoing further testing in clinical trials.

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Reducing blood cholesterol is one of the most important measures for lowering your risk of a heart attack. **But as you will discover in Key #7, there are additional steps you can take to further reduce your risk.**

KEY 7 is titled:

**The ABC's of
Heart Attack Prevention**



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M E D I C I N E

KEY 7

The ABCs of Heart Attack Prevention



The ABCs of Heart Attack Prevention

Managing undesirable cholesterol levels is one of the most important steps you can take to prevent a heart attack. Fortunately, most of the other risk factors for a heart attack can also be modified to reduce risk. Here is an easy-to-remember checklist of recommended strategies

you can take to prevent a first heart attack. (For some measures, more stringent recommendations apply to people with known cardiovascular disease or who are at very high risk.) Taking these steps will also help lower the risk of subsequent heart attacks.

□ Aspirin

A daily low-dose aspirin (75–162 mg a day) is often advised for people with an elevated risk of a heart attack; in some individuals, an aspirin dose of 325 mg is recommended. Aspirin is not advisable for all people, so be sure to consult with a physician before starting aspirin therapy.

□ Blood Pressure

Keep your blood pressure below 140/90 mm Hg (and ideally less than 120/80 mm Hg). If you have diabetes or kidney disease, make sure your blood pressure is kept below 130/80 mm Hg. If you're unable to reach these goals after 3–9 months of lifestyle changes, your doctor may prescribe a blood pressure drug.

□ Cholesterol

Your *total cholesterol* should be below 200 mg/dL. Keep your *LDL ("bad") cholesterol* under 160 mg/dL if you are at low risk for a heart attack, below 130 mg/dL if you are at moderate risk, or less than 100 mg/dL if you are at high or very high risk (and preferably lower than 70 mg/dL if you've had a recent heart attack). Your *HDL ("good") cholesterol* should be 40 mg/dL or greater if you are a man and 50 mg/dL or more if you are a woman (and preferably 60 mg/dL or higher regardless of your gender). Your *triglyceride* level should be under 150 mg/dL. If you're unable to reach your LDL goal after 3–9 months of lifestyle changes, your doctor may prescribe medication. Exercise, dietary changes, and possibly medication can help you meet your HDL goal. Losing excess weight, exercising regularly, and medication can help reduce your triglyceride level.

□ Diet and Weight Control

Consume a variety of fruits, vegetables, grains, low saturated fat or nonfat dairy products, fish, beans, poultry, and lean meats. Saturated fats should make up less than 7% of total calories. If you're overweight, reduce your calorie intake and increase your physical activity to achieve and maintain a desirable body weight (a body mass index below 25). If you drink, limit your alcohol intake (no more than 2 drinks a day for men, 1 drink a day for women).

□ Exercise

Perform at least 30 minutes of moderate-intensity physical activity, such as brisk walking, on most (and preferably all) days of the week. Exercising for longer periods (60–90 minutes a day) or more vigorously can provide additional benefits, including weight loss if that's 1 of your goals.

Additional Goals

- If you smoke, you should stop completely.
- If you have diabetes, strive for the best possible control of your blood glucose level (HbA1c level less than 7%). If diet and exercise do not adequately lower blood glucose, your doctor will recommend medication. Other risk factors for CHD, such as elevated LDL cholesterol levels and high blood pressure, must be treated aggressively if you have diabetes.
- If you have prediabetes, keep your fasting blood glucose level below 100 mg/dL. You can do this by reaching a healthy weight and engaging in regular physical activity.

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- **Coronary Heart Disease** – looks at the best ways to manage conditions that result from coronary heart disease, including angina, heart attacks, congestive heart failure, and arrhythmias.
- **Hypertension and Stroke** – explains what you can do to manage high blood pressure (a major risk factor for both heart attack and stroke), including the newest recommendations on medications, diet, and exercise.

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