

## The Garbage Trucks in Your Blood

**The recent failure of a potential blockbuster drug designed to increase so-called 'good cholesterol' raises important issues about diet and heart health. What is HDL, anyway?**

**Dean Ornish M.D.**

Newsweek Web Exclusive

Cholesterol-lowering drugs are big business. Really big. Just one of these drugs, Lipitor, generated almost \$13 billion in sales this year for Pfizer, the drug company that makes it.

To its credit, Pfizer spent at least \$800 million developing and studying a new drug, torcetrapib, designed to prevent heart attacks and strokes by increasing levels of HDL cholesterol ("good cholesterol") by up to 50 percent. They had high hopes for it. Just last month, the CEO of Pfizer, Jeffrey B. Kindler, said, "This will be one of the most important compounds of our generation."

Unfortunately, it wasn't.

Earlier this month Pfizer made a stunning announcement. They stopped the study because they found that torcetrapib actually increased the number of heart attacks and strokes. There were 60 percent more deaths in those taking the new drug compared to a control group that was not taking it.

While the number of heart attacks did not decrease, Pfizer's stock price did, falling by 11 percent, which decreased the company's market capitalization by about \$21 billion in one day. (The stock has rebounded slightly since.) High stakes.

The most important lesson may be this: not everything that raises HDL is good for you, and not everything that lowers HDL is bad for you.

There are a lot of misconceptions about HDL and LDL. Most people, including many physicians, believe that HDL is "good cholesterol," and the higher it is, the better. LDL is often called "bad cholesterol." HDL gooooooooooooooood, LDL baaaaaaaaaaaaaaaaaad.

Like many things in life, the truth is not so simple.

Your body makes HDL to remove excessive cholesterol from your blood and tissues, a process known as "reverse cholesterol transport." Think of HDL like the garbage trucks of your body. HDL transports cholesterol back to your liver, where it is metabolized and removed from your body. Your body's ability to make more garbage trucks (raise your HDL) is, in part, genetically determined. Some people can make more garbage trucks than others.

Most Americans eat a diet that's relatively high in saturated fat and cholesterol—i.e., a lot of "garbage." Those people who have a lot of garbage trucks—in other words, who have high HDL levels—are more efficient at getting rid of extra fat and cholesterol in their diet. As a result, they have a lower risk of a heart attack or stroke than those who eat a high-fat, high-cholesterol diet who have lower HDL levels. However, the relationship of HDL to risk of heart disease and stroke assumes that people are not changing their diet.

Not everything that raises HDL is good for you. For example, if you increase the amount of fat and cholesterol in your diet (e.g., an Atkins diet), you may increase your HDL, because your body is trying to get rid of the extra "garbage" (fat and cholesterol) by increasing the number of available garbage trucks (HDL), if you are genetically able to do so. Eating a stick of butter will raise HDL in those who are able to do so, but that does not mean that butter is good for your heart. It isn't.

The way torcetrapib works is by interfering with reverse cholesterol transport, causing HDL to build up. It's like having a traffic jam of garbage trucks—more trucks, but they don't work as well.

Not everything that lowers HDL is bad for you. If you change from a high-fat, high-cholesterol diet to a healthy low-fat, low-cholesterol diet, your HDL levels may stay the same or even decrease because there is less need for it. When you have less garbage, you need fewer garbage trucks to remove it, so your body may make less HDL. Thus, a reduction in HDL on a low-fat diet is not harmful.

We know this is true because instead of just measuring risk factors like HDL, we measured what actually happens to the progression of coronary heart disease in people who went on diets that were very low in "garbage"—i.e., very low in cholesterol, saturated fat, total fat and refined carbohydrates, and high in fruits, vegetables, whole grains, legumes and soy products.

Their HDL levels came down by 9 percent after one year, but their LDL ("bad") cholesterol levels came down even more, by 40 percent. None of these patients was taking cholesterol-lowering drugs.

Even though their HDL levels decreased, these patients showed reversal of their heart disease using state-of-the-art measures such as quantitative coronary arteriography, cardiac PET scans, thallium scans and radionuclide ventriculography in randomized controlled trials published in the leading peer-reviewed journals. On average, they showed even more reversal of their heart disease after five years than after one year. Also, there were 2.5 times fewer cardiac events such as heart attacks, bypass surgery and angioplasty in these patients.

In summary, a low HDL in the context of a healthy low-fat diet has a very different prognostic significance than a low HDL in someone eating a high-fat, high-cholesterol diet. People living in many Asian countries, where they typically consume a low-fat diet, have low HDL levels yet among the lowest rates of heart disease in the world.

Drugs like torcetrapib raise HDL by slowing its metabolism. This may not be the optimal approach for raising HDL. Other strategies for raising HDL by different mechanisms are being actively explored. Also, torcetrapib increased blood pressure in some patients.

Dr. Steven Nissen at the Cleveland Clinic is conducting a study using a new, sophisticated measure of coronary-artery blockages called intravascular ultrasound to determine if torcetrapib affects plaque buildup in the coronary arteries. That study will be reported in March at the American College of Cardiology annual scientific sessions.

There are other drugs in development like torcetrapib that raise HDL, but until the reason for these excessive deaths is well understood, they are not likely to reach the market, and this may take many years.

In the meantime, if you have a low HDL level, what else can you do to raise HDL that is good for you rather than harmful?

1. Lower your LDL cholesterol. It's easier to lower LDL than raise HDL. I think there should be less emphasis on raising HDL and more on lowering LDL via diet and lifestyle or, as a second choice, with lipid-lowering drugs. If you reduce your LDL below 100 mg/dl, or even lower if you have coronary heart disease, then your HDL level will be much less important.

If you don't have heart disease, you can begin by making moderate changes in your diet, such as recommended by the American Heart Association and the National Cholesterol Education Program: eat less red meat, more fish and chicken, less than 30 percent of calories from fat. Replace saturated fat with monosaturated fat. If that's enough to lower your LDL sufficiently, great; if not, then you can make progressively bigger reductions in saturated fat, trans fatty acids, total fat, dietary cholesterol and refined carbohydrates, and eat more fruits, vegetables and other whole foods in their natural forms. These dietary changes will not only lower your LDL, they will help prevent other chronic diseases and also help you to look better, feel better, lose weight and gain health.

If you are not interested in changing your diet to this degree, then consider taking lipid-lowering drugs that your doctor may prescribe, including statin drugs such as Lipitor or Zocor. Some studies suggest that taking coenzyme Q10 with statin drugs may help prevent some of the adverse side effects in muscles.

2. Niacin. In small doses, niacin is a vitamin. In large doses, it becomes a cholesterol-lowering drug. It raises HDL somewhat (not as much as torcetrapib) and lowers LDL.

Niacin is available in nonprescription forms. Most doctors recommend starting with relatively small doses of 100 mg three times per day and working up to 500 mg three times per day or even higher doses. Niacin is also available as a prolonged-release prescription drug, Niaspan, which has two advantages: you only have to take it once a day, and the potency of the drug is more well-standardized than those available over-the-counter.

Niacin may cause liver damage, so it's important for your doctor to do blood tests to make sure that your liver is OK, especially at higher doses. Also, niacin may cause flushing and itching. Fortunately, these side effects tend to get better over time, especially if the dose of niacin is increased slowly over time. Taking it with food and with aspirin may also reduce some of these side effects.

Two years ago, Dr. Allen Taylor of the Walter Reed Army Medical Center reported niacin plus statin drugs kept blockages in heart arteries from getting worse. There were fewer heart attacks, strokes and deaths in those taking niacin plus statins than in those taking statins alone. Dr. Greg Brown of the University of Washington is conducting a large multicenter study comparing the effects of niacin plus a statin drug (Zocor) with Zocor alone.

3. Exercise. Regular aerobic exercise will raise HDL levels. In some people, this may be significant, but in most people it only raises HDL about 5 percent.

4. Alcohol. Moderate intake of alcohol (no more than one to two drinks per day) may raise your HDL level. One drink is usually considered to be 12 ounces of beer, 4 ounces of wine, or 1½ ounces of spirits (hard liquor). However, some studies suggest that alcohol may raise a subfraction of HDL that is not related to the risk of coronary heart disease, but others show that it does.

In general, I neither prescribe nor proscribe alcohol, since a significant number of people are prone to alcohol abuse. If you're going to drink, do it moderately.

5. Fish oil. Taking 3 grams per day of fish-oil capsules provides substantial health benefits, including a 50 percent reduction in sudden cardiac death, reduction in the risk of prostate cancer and breast cancer, and significant reductions in blood triglyceride levels. The effect on HDL is modest and appears to affect one of the HDL subfractions that are protective against heart disease.

6. Eat fewer refined carbohydrates and more whole, unrefined foods that are high in fiber. Refined carbohydrates tend to lower HDL. A low HDL in the context of high LDL, obesity, high blood sugar, high blood pressure and high triglycerides is called metabolic syndrome. This is generally caused by high insulin levels and creates an especially high risk for developing coronary heart disease. People with metabolic syndrome should be especially mindful of their intake of refined carbohydrates such as white flour and concentrated sweeteners.

7. Soy. Soy protein, plus the isoflavones found in soy, may raise HDL levels. Some studies suggest that it may take at least three months to see this benefit. Soy may also reduce LDL and triglycerides to some degree.

8. Quit smoking, which may raise your HDL a little, as well as help your health in numerous other ways.

9. Lose weight. Being overweight is a factor in low HDL levels.

10. Orange juice. Studies have shown that drinking orange juice may lower LDL and raise HDL.

While it would be nice to find a pill that allows us to prevent heart disease while eating and doing anything, changes in diet and lifestyle may be the most powerful way of preventing and even reversing the progression of coronary heart disease.

URL: <http://www.newsweek.com/id/37693>

---

© 2006