

**January 23, 2007**

THE CONSUMER

## An Old Cholesterol Remedy Is New Again

By MICHAEL MASON

Perhaps you heard it? The wail last month from the labs of heart researchers and the offices of Wall Street analysts?

Pfizer Inc., the pharmaceutical giant, halted late-stage trials of a [cholesterol](#) drug called torcetrapib after investigators discovered that it increased heart problems — and death rates — in the test population.

Torcetrapib wasn't just another scientific misfire; the drug was to have been a blockbuster heralding the transformation of cardiovascular care. Statin drugs like simvastatin (sold as Zocor) and atorvastatin (Lipitor) lower blood levels of LDL, the so-called bad cholesterol, thereby slowing the buildup of plaque in the arteries.

But torcetrapib worked primarily by increasing HDL, or good cholesterol. Among other functions, HDL carries dangerous forms of cholesterol from artery walls to the liver for excretion. The process, called reverse cholesterol transport, is thought to be crucial to preventing clogged arteries.

Many scientists still believe that a statin combined with a drug that raises HDL would mark a significant advance in the treatment of [heart disease](#). But for patients now at high risk of heart attack or stroke, the news is better than it sounds. An effective HDL booster already exists.

It is niacin, the ordinary B vitamin.

In its therapeutic form, nicotinic acid, niacin can increase HDL as much as 35 percent when taken in high doses, usually about 2,000 milligrams per day. It also lowers LDL, though not as sharply as statins do, and it has been shown to reduce serum levels of artery-clogging triglycerides as much as 50 percent. Its principal side effect is an irritating flush caused by the vitamin's dilation of blood vessels.

Despite its effectiveness, niacin has been the ugly duckling of heart medications, an old remedy that few scientists cared to examine. But that seems likely to change.

"There's a great unfilled need for something that raises HDL," said Dr. Steven E. Nissen, a cardiologist at the Cleveland Clinic and president of the American College of Cardiology. "Right now, in the wake of the failure of torcetrapib, niacin is really it. Nothing else available is that effective."

In 1975, long before statins, a landmark study of 8,341 men who had suffered heart attacks found that niacin was the only treatment among five tested that prevented second heart attacks. Compared with men on placebos, those on niacin had a 26 percent reduction in heart attacks and a 27 percent reduction in strokes. Fifteen years later, the mortality rate among the men on niacin was 11 percent lower than among those who had received placebos.

"Here you have a drug that was about as effective as the early statins, and it just never caught on," said Dr. B. Greg Brown, professor of medicine at the [University of Washington](#) in Seattle. "It's a mystery to me. But if

you're a drug company, I guess you can't make money on a vitamin."

By and large, research was focused on lowering LDL, and the statins proved to be remarkably effective. The drugs can slow the progress of cardiovascular disease, reducing the risk of heart attack or other adverse outcomes by 25 percent to 35 percent.

But recent studies suggest that the addition of an HDL booster like niacin may afford still greater protection.

After analyzing data from more than 83,000 heart patients who participated in 23 different clinical trials, researchers at the University of Washington calculated this month that a regimen that increased HDL by 30 percent and lowered LDL by 40 percent in the average patient would reduce the risk of heart attack or stroke by 70 percent. That is far more than can be achieved by reducing LDL alone.

Other small studies have produced similarly encouraging results, but some experts caution that the data on increased HDL and heart disease are preliminary.

Researchers at 72 sites in the United States and Canada are recruiting 3,300 heart patients for a study, led by Dr. Brown and financed by the [National Institutes of Health](#), comparing those who take niacin and a statin with those who take only a statin. This large head-on comparison should answer many questions about the benefits of combination therapy.

Many cardiologists see no reason to wait for the results. But niacin can be a bitter pill; in rare instances, the vitamin can cause liver damage and can impair the body's use of glucose. High doses should be taken only under a doctor's supervision.

A more frequent side effect is flushing. It becomes less pronounced with time, and often it can be avoided by taking the pills before bed with a bit of food. Doctors also recommend starting with small doses and working up to larger ones.

Extended-release formulations of the vitamin, taken once daily, are now available by prescription, and in many patients they produce fewer side effects. And a new Merck drug to counteract niacin-induced flushing is being tested in Britain. If it works, the company plans to bundle the drug with its own extended-release niacin and with Zocor, its popular statin.

Until then, consider this: If it means preventing a heart attack, maybe it is better to put up with flushing than to wait for the next blockbuster.

"If you can just get patients to take niacin, HDL goes up substantially," said Dr. Nissen of the Cleveland Clinic. "Most of the evidence suggests they'll get a benefit from that."

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