

# Clinical Update

## When 'Good' Cholesterol Goes Bad

HDL analysis uncovers a dark side, but also a new way it fights heart disease

*(American Chemical Society Meeting, August 2007)*

It looks like HDL, the "good" cholesterol that supposedly protects against cardiovascular disease, might have a harmful side. New research suggests that some people's HDL is more protective for their hearts than others, and that certain proteins in HDL can exacerbate vessel damage, particularly in people with heart disease.

But there's good news, too, as scientists uncover a new means by which HDL boosts cardiovascular health. The findings are to be reported at the American Chemical Society's annual meeting in Boston.

So far, the cholesterol story has been a relatively simple one in which "bad" low-density lipoprotein (LDL) cholesterol formed plaques that eventually blocked arteries, while "good" high-density lipoprotein (HDL) cholesterol worked to carry away those deposits, explained Dr. Jay Heinecke, a professor of medicine at the University of Washington, Seattle.

"But in the last few years there has been growing evidence that HDL does other things," he said. "In particular, it may be inhibiting inflammation." Inflammation is the major villain in the new picture. Arteries are not only blocked because of the gradual growth of plaque. Instead, there comes a moment when plaque ruptures, causing a clot to form and block blood flow, Heinecke said. Proteins called proteases play a major role in these ruptures.

"What we found in HDL is a whole series of proteins that inhibit proteases," Heinecke said, describing what he called the most detailed analysis to date of HDL's protein composition. "So, part of [HDL's] protective effect is to prevent rupture." The Seattle analysis also found a lot of previously unrecognized HDL proteins, including 22 that play roles in cholesterol metabolism.

One finding of particular significance is that HDL protein composition can be different in people who have heart disease and those who do not -- meaning that some of the supposedly "good" HDL proteins are really bad. "With LDL cholesterol it's simple -- the lower the better," Heinecke said. "With HDL, it's much more complicated. The protein composition of people with and without heart disease is different."

So, measuring blood levels of LDL and HDL cholesterol is not as predictive of cardiac risk, as has been assumed, Heinecke stressed. "Protein composition [in HDL cholesterol] may be a better handle on whether someone is at risk," he added.

Animal studies have found "dysfunctional" HDL cholesterol, which works against coronary health, Heinecke said. "It is proposed that the same thing is going on in humans," he noted.

The finding of dysfunctional HDL proteins helps explain why a major pharmaceutical company ended work on an HDL-boosting drug when it was found to actually increase deaths and heart problems in a human trial.

A better understanding of the protein components of HDL could lead to more accurate tests for heart disease, Heinecke said. "Most people who have heart attacks have normal levels of HDL, so the composition of the HDL may tell who is vulnerable," he said.



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