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Cholesterol Confusion: Researchers Closer to Understanding Which Forms of Cholesterol Can Really Hurt Us

A protein may turn good cholesterol bad and bad cholesterol lethal

By Thea Singer

We have been hearing for years that high-density lipoprotein (HDL)—the "good cholesterol"—may not be all it's cracked up to be. Now a new study shows that a certain subclass of HDL may actually be "bad," increasing the risk of coronary heart disease.

A small protein may be to blame. HDL with a small proinflammatory protein called **apolipoprotein C-III** (apoC-III) on its surface may nearly double the risk of heart disease in healthy men and women, according to Frank Sacks, professor of cardiovascular disease prevention at the Harvard School of Public Health and senior author on a paper in the April *Journal of the American Heart Association*. Conversely, Sacks's **study found, HDL without apoC-III may be especially heart-protective.** A number of studies have shown that LDL (low-density lipoprotein)—the "bad cholesterol"—with apoC-III on its surface is particularly harmful, leading to higher incidence of plaque buildup in artery walls. Yet, Sacks says, this is the first large-scale prospective study with healthy subjects to show that apoC-III on HDL may have similar effects.

The scientists examined blood samples taken from 572 women in the Nurses' Health Study and from 699 men in the Health Professionals Follow-Up Study, two of the largest long-term investigations of factors that affect women's and men's health. Over 10 to 14 years of follow-up, they documented 634 cases of coronary heart disease, which they matched with control subjects for age, smoking status and the date blood was drawn. After adjusting for those and other lifestyle-based cardiovascular risk factors, they found a nearly twofold increase in risk for HDL with apoC-III. The men and women whose levels of HDL with apoC-III were in the top 20 percent had a 60 percent higher risk of developing heart disease than those in the bottom 20 percent.

Sacks says the techniques his team used to measure the levels of the two HDL subclasses, which Harvard is patenting, could lead to more precise tests to evaluate heart disease risk and treatment response. Moreover, the findings, if replicated in his and others' ongoing studies, could spur development of drugs that target HDL subclasses, working to raise HDL without apoC-III and lower HDL with it. "The bottom line is, there's a lot more to be learned about HDL and how it acts," says Nilesh Samani of the University of Leicester in England and co-author of a paper that found raising HDL levels might not change heart disease risk.