

Do You Know Your HDL?

The 'good cholesterol' proves a strong predictor of coronary risk — and a potent provoker of controversy

First of two articles

By JANET RALOFF

The death of a seemingly healthy 39-year-old man in his sleep baffled the Framingham, Mass., coroner evaluating the case. Knowing the man had participated in the Framingham Heart Study, the coroner phoned the study's research office to ask whether the victim's medical history might suggest a heart attack risk. When he learned that the man's cholesterol last came to just 198 milligrams per deciliter (mg/dl) of blood — within a range generally deemed desirable — the coroner began to suspect foul play. Imagine his surprise when the autopsy revealed an arterial network clogged with massive fatty deposits.

William P. Castelli, medical director of the 40-year-old, ongoing Framingham project, says he might have prepared the coroner for this atherosclerotic revelation had he not been out of town when the call came. Castelli has seen all too many similar cases. Young as he was, the deceased "was a heart attack waiting to happen," Castelli says.

Undeniably, the man's blood levels of total cholesterol and low-density lipoprotein (LDL) cholesterol — two classic markers of coronary artery disease risk — looked good, Castelli says. But his high-density lipoprotein (HDL) cholesterol was just 29 mg/dl — far below the average of 45 to 55.

LDLs, the so-called "bad" lipoproteins, transport cholesterol to sites of fatty deposits, called plaques, in blood vessel walls. HDLs, often called the "good" lipoproteins, help clear LDL cholesterol from the bloodstream by transporting it to the liver, where it gets broken down and excreted.

Castelli suggests the man did not have enough HDLs to handle even the normal levels of cholesterol coursing through his bloodstream. In fact, his ratio of total cholesterol to HDL cholesterol — last measured at 6.8 — exceeded by more than 50 percent the "red flag" value of 4.5 that signals seriously elevated heart disease risk, according to Framingham data. To calculate this ratio, physicians divide the total cholesterol level by the HDL value.

A growing number of studies point to HDL levels — and especially the ratio of total cholesterol to HDL cholesterol — as a superior gauge for spotting people at risk of artery-clogging heart disease. However, a spirited controversy exists over

whether to initiate widespread HDL screening. One faction argues that physicians must screen everyone for HDL levels if they ever hope to identify those likely to develop coronary artery disease in time to prevent impending heart attacks. Others counter that population-wide screening seems premature when scientists still do not know exactly how HDLs function or how to increase them.

The debate raged last June at a panel discussion convened in Washington, D.C., by the International Lipid Information Bureau, a drug-company-supported information center based in New York City. Castelli and several other coronary disease specialists took the National Heart, Lung, and Blood Institute (NHLBI) to task for the federal guidelines identifying people at high risk of coronary artery disease. Those guidelines largely ignore HDLs, they complained.

Basil Rifkind, who heads NHLBI's lipid metabolism and atherogenesis branch, acknowledged wide criticism of the guidelines for failing to include HDL cholesterol levels in the primary screening for early coronary disease. But he also defended the guidelines, saying "not all the evidence is in" to establish why HDL serves as such a good marker or even to suggest how patients and physicians should respond to worrisome HDL levels.

Humans, perhaps from infancy onward, spend a lifetime collecting deposits of lipids — cholesterol and fats — within their vascular networks. "About half of us eventually go on to die from the coronary heart disease this causes," Castelli says. But not everyone deposits lipids at the same rate.

To anticipate whose arteries will clog fastest, heart researchers have assembled a host of diagnostic risk factors. In October 1987, the NHLBI-administered National Cholesterol Education Program (NCEP) issued the now-controversial guidelines for gauging coronary disease risk through blood lipid assays (SN: 10/17/87, p.254). Summarized, those guidelines state:

- Total cholesterol levels below 200 mg/dl are desirable and require no immediate follow-up.
- People with total cholesterol levels

between 200 and 240 but no other obvious risk factors (such as smoking, hypertension, diabetes or a family history of heart disease) should receive dietary counseling now and new tests in a year. If physicians happen to know that a patient has low HDL, they should consider this a risk factor as well.

- Physicians should assay LDL cholesterol levels in the patients with additional risk factors.

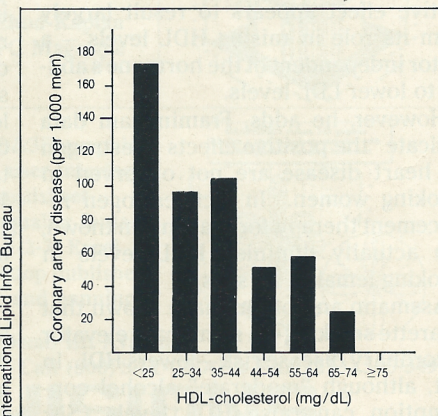
- Total cholesterol levels above 240 warrant immediate lifestyle changes and possibly drug therapy.

Castelli points out that these guidelines would never identify the roughly 15 percent of U.S. heart attack victims who, like the 39-year-old Framingham man, develop coronary disease while maintaining total cholesterol levels under 200 mg/dl. Using the total-to-HDL cholesterol ratio, physicians could flag at least 75 percent of these individuals for treatment, he argues.

Moreover, he notes, a significant number of people whose total cholesterol levels exceed 240 mg/dl will never suffer heart attacks.

NCEP recommends trying to identify likely victims by requesting follow-up LDL measurements in people with total cholesterol over 240 mg/dl. Depending on whether the patient has additional risk factors, treatment to lower blood cholesterol is usually recommended when LDL cholesterol levels move into the range of 130 to 160 mg/dl.

Yet a number of studies indicate that low HDL cholesterol levels predict coro-



Even a decade ago, data linked coronary artery disease with low HDL levels.