

## HARVARD GAZETTE ARCHIVES

## Better Way To Predict Heart Attacks Is Discovered

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For about \$20 you can determine your risk of a future heart attack, according to a new study from Harvard Medical School.

The test measures levels of a protein that increase with the amount of inflammation in coronary arteries. The study showed that healthy women with the highest levels of this substance, known as high-sensitivity C-reactive protein, have more than four times the risk of suffering a heart or blood-vessel problem than women with lower levels of the marker. Previous research revealed that men with the highest levels of this protein in their blood have three times the risk of heart attack and two times the risk of stroke compared to men with the lowest levels.



Paul Ridker uses a heart model to explain why high levels of a protein linked to inflammation can dramatically raise the risk of a heart attack.

“Cholesterol screening is currently the gold standard for predicting heart-attack risk, but nearly half of all heart attacks occur among men and women with normal cholesterol levels,” notes Paul Ridker, a cardiologist at Harvard-affiliated Brigham and Women’s Hospital in Boston.

“In fact, the amount of risk associated with high-sensitivity C-reactive protein is almost twice that associated with high levels of low density cholesterol.”

The Food and Drug Administration approved the first test for this protein last November. “It’s now available to all doctors and costs about \$15-\$20,” says Ridker, who is also an associate professor of medicine at Harvard Medical School.

An improved ability to predict risk of heart attack can reveal who will benefit most from preventive strategies, such as increased exercise, a healthier diet, and quitting smoking. Also, it pinpoints the best candidates for so-called statin drugs, such as pravastatin, which lower levels of both high-sensitivity C-reactive protein and low-density, or harmful, cholesterol.

“These drugs can prevent first heart attacks,” Ridker points out, “but they are too expensive to prescribe for everyone. The new test, along with cholesterol screening, should enable doctors to better determine who is most likely to benefit from their use.”

Not all tests for the protein are equal, however. “Doctors who use this new approach must use an accurate high-sensitivity test for C-reactive protein, not one of the older tests, which are far less reliable,” cautions Nader Rifai, a Harvard associate professor of pathology, who participated in this research.

### **Healing Begets Harm**

Exactly how the protein is linked to heart disease and stroke remains unclear. It’s known to help white blood cells destroy invading bacteria and viruses, a process accompanied by inflammation. But there’s a harmful side to such healing. Inflammation sometimes leads to vulnerable plaques, or raised clumps of cholesterol in the lining of blood vessels. The plaques are vulnerable because they are likely to rupture, and the fragments can block narrower arteries downstream, leading to a heart attack or stroke.

“Inflammation is now understood to play a critical role in the conversion of a stable cholesterol plaque into a worrisome, unstable lesion (injury),” Ridker points out.

To clarify the relationship between various markers involved in this process, including C-reactive protein, total cholesterol, low-density cholesterol, and other compounds, Ridker and his colleagues checked blood samples from 28,263 healthy, middle-aged women. The women were followed for three years, and levels of 12 different markers were compared with incidences of death from heart disease, heart attacks, stroke, and need for procedures to unblock their coronary arteries.

High-sensitivity C-reactive protein levels turned out to be the strongest and most significant predictor of who would suffer these cardiovascular problems. The relationship held true even among people with cholesterol levels considered safe by national guidelines.

“Heart disease is the number one killer of men and women in the United States,” Ridker says. “Any improvement we can make in a doctor’s ability to predict heart attacks will increase the number of lives we can save through targeted use of drugs like the statins and more aggressive changes in lifestyles.”

A report on this research was published today in the March 23 issue of the *New England Journal of Medicine*.