

New findings on the role of inflammation in prevention of coronary heart disease

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This year, about 450,000 Americans will die of coronary heart disease – the leading cause of death for both men and women. Although we have made great strides in preventing and treating heart disease, we continue to explore the complex mechanisms involved in cardiovascular disease, and we are eager to refine risk assessment tools and preventive strategies to reduce the incidence of heart attack and stroke.

New results from three studies being presented at the American Heart Association (AHA) Scientific Sessions in New Orleans and published in scientific journals today provide the strongest evidence to date that a simple blood test for high-sensitivity C-reactive protein (hsCRP) is a useful marker for cardiovascular disease. Importantly, a much-anticipated study demonstrates for the first time that hsCRP levels in the blood can be used to guide treatment decisions to effectively lower the risk of heart attacks, stroke, and death. Together, these studies show great promise in helping clinicians better identify and treat individuals at risk for cardiovascular disease – potentially saving millions more lives.

For years, growing evidence has suggested that inflammation plays a strong role in developing cardiovascular disease, especially atherosclerosis, or hardening of the arteries. HsCRP is one of the most widely studied markers of inflammation in cardiovascular disease.

But, whether measuring hsCRP adds any measurable value for predicting risk for cardiovascular disease independent of traditional risk factors, such as age, blood cholesterol levels, blood pressure, diabetes, and

smoking has been a topic of great debate. Further, it has been uncertain whether hsCRP levels can be used to improve treatment decisions.

Two studies supported by the National Heart, Lung, and Blood Institute (NHLBI) show that adding hsCRP levels to assess risk of a first heart attack or stroke in middle-aged or older adults improves accuracy over the traditional assessment tools by between 5 percent and 14 percent. The information proved to be especially valuable in reclassifying the risk of heart disease and stroke among individuals considered to be at intermediate risk (10 percent to 20 percent risk of having a heart attack within 10 years) by traditional methods.

Using data from the 3006 participants in NHLBI's Framingham Heart Offspring Study, Peter W. F. Wilson, M.D., of Emory University in Atlanta and colleagues from NHLBI, Boston University, and Tufts USDA Nutrition Center in Boston found that using hsCRP levels to assess risk provided a more accurate risk assessment over traditional risk scores among people otherwise considered at intermediate risk. The researchers suggest a two-stepped approach to assessing risk – using traditional risk scores first, then adding hsCRP levels to those found to be at intermediate risk – to guide clinical decisions. These results are published online today in *Circulation Cardiovascular Quality and Outcomes*.

In the second study, researchers used data from 10,724 men in the Physicians Health Study-II to prospectively develop the Reynolds Risk Score for Men, which adds hsCRP levels and parental history of early heart disease to traditional risk factors to assess men's risk. The new assessment tool was significantly more accurate than traditional risk factors alone in the study population. The report, by Paul Ridker, MD, of Brigham and Women's Hospital and Harvard Medical School in Boston, and colleagues, is published online in the journal *Circulation* today and will be presented Tuesday at the AHA Scientific Sessions.

Previous work in the NHLBI-funded Women's Health Study led to the development of a comparable Reynolds Risk Score for women last year.

The third hsCRP study results released today are from JUPITER (the Justification for Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin), an international randomized clinical trial to test the effectiveness of treating individuals with high levels of hsCRP. Dr. Ridker and his colleagues demonstrate for the first time that a strategy of treatment decisions based upon hsCRP levels in otherwise healthy individuals significantly improves outcomes.

The study of 17,802 apparently healthy men and women was stopped early on March 30 after about 2 years because of the strong positive results. The researchers found that a daily dose of a commonly used statin, rosuvastatin (Crestor), reduced the risk of heart attack, stroke, and death by nearly half (44 percent) in individuals with high levels of hsCRP (2.0 mg/L or higher) but with normal or low levels of LDL (130mg/dL or lower). The treatment reduced LDL cholesterol by 50 percent and hsCRP by 37 percent. Supported by AstraZeneca, U.S., the study was presented today at the AHA Scientific Sessions and appears online in the *New England Journal of Medicine* (November 20, 2008, print issue).

These studies expand our understanding of the role of inflammation in detecting early signs of cardiovascular disease and identifying adults who are at risk for heart attack or stroke. These findings suggest that adding hsCRP levels to traditional risk factors could identify millions more adults for whom treatment with statins appears to lower the risk of heart attack.

Many clinicians now offer hsCRP testing to their patients, but until now the value of hsCRP levels to treatment decisions, especially in adults with desirable cholesterol levels, was unclear. As with any medical

discovery, however, broadly adopting a new approach to detect or treat a condition should first be critically tested, preferably through large-scale event-based randomized clinical trials like JUPITER, and proven to bear greater benefits than risks, including costs.

As part of the NHLBI strategic plan, we have engaged an expert panel to review and update the scientific evidence regarding the assessment and management of cardiovascular risk factors. Today's findings will be part of the rigorous scientific review to distill the scientific evidence and generate an evidence-based, comprehensive, set of clinical guidelines for primary care practitioners to help adult patients reduce their risk for cardiovascular disease.

In the meantime, however, we must not lose sight of the essential truth of what we already know to prevent heart disease: Cholesterol still counts, and we have proven ways to lower it and lessen its impact. The value of following a heart-healthy eating plan, being physically active, maintaining a healthy weight, and not smoking cannot be overestimated. And, statins can significantly reduce the risk of heart attack in those at high risk.

Let us continue to use our current knowledge as well as apply new discoveries based on solid evidence to take action for the betterment of individual and public health.

Links: What is Coronary Artery Disease?,
[www.nhlbi.nih.gov/health/dci/D ... /Cad/CAD_WhatIs.html](http://www.nhlbi.nih.gov/health/dci/D.../Cad/CAD_WhatIs.html)

Source: NIH/National Heart, Lung and Blood Institute

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