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## In The News

### C-REACTIVE PROTEIN IS A HEART DISEASE CULPRIT, NOT JUST A MARKER

High blood levels of C-reactive protein are a highly-sensitive marker of coronary artery disease, even in the absence of classical clinical signs such as high cholesterol, triglycerides and blood pressure.

Now researchers have found that C-reactive protein isn't merely a marker but an active participant in the inflammatory process that leads to atherosclerosis and, subsequently, heart attack and stroke. Researchers at the University of Texas Health Sciences Center in Houston have discovered that C-reactive protein triggers the expression of adhesion molecules in endothelial cells, which set off the inflammation process and cause plaque to stick to vessel walls. The findings, published in the journal of the American Heart Association, suggest that C-reactive protein may be a therapeutic target for designing drugs that block its biologic effect. The investigators conclude that "CRP may play a direct role in promoting the inflammatory component of atherosclerosis and present a potential target for the treatment of atherosclerosis." [Circulation 2000;102:2165-2168].

Earlier research only defined C-reactive protein as a predictor of heart disease risk, but a very accurate one. For example, one study followed 1086 apparently healthy men over an eight-year period using baseline levels of C-reactive protein as a measurement to predict their risk of having a first heart attack [New England Journal of Medicine 1997;336:973-979]. The results showed that men with the highest levels of the protein had a threefold increase in their risk of a future heart attack and a twofold increase in their risk of a future stroke, compared to men with lower C-reactive protein levels. The study's investigators had suggested that, since C-reactive levels are also a marker of systemic inflammation and underlying blood vessel damage, they may serve as a measurement tool in providing "new means for preventing cardiovascular disease." The findings also suggested that, if C-reactive protein is part of the cause of inflammation that lays the groundwork for atherosclerosis and cardiovascular events, it may also explain why aspirin lowers heart attack and stroke risk. And that raises "the possibility that anti-inflammatory agents may have clinical benefits in preventing cardiovascular disease." (Editors note: Aspirin helps to lower C-reactive protein levels.)

Another study, which looked more specifically at the risk-raising effect of C-reactive protein levels in healthy post-menopausal women, similarly found that the protein's presence was indicative of greater risk for heart disease and heart attack events [Circulation 1998;98(8):731-733]. The study, which included 366 women enrolled in the Women's Health Study, showed that women with the highest levels of C-reactive protein in their blood had a fivefold increase in the risk of any future cardiovascular disease, and a sevenfold jump in heart attack and stroke risk, compared to women with low levels.

Elucidating the role of C-reactive protein builds a better understanding of how inflammation may be an independent risk factor, separate and apart from other risk factors such as high cholesterol or blood pressure. Using C-reactive protein levels as a measurement of coronary heart disease risk and underlying damage may also help to identify people who are seemingly in a low-risk category, just because they don't have traditional risk factors such as high cholesterol, high blood pressure, smoking or a family history of heart disease. —Angela Pirisi



### High dose vitamin E lowers C-reactive protein

In a recent study published in the journal *Free Radical Biology and Medicine* [2000; 8: 790-792], high-dose vitamin E reduced C-reactive protein blood levels. Due to the pathological role inflammation plays in heart attacks, strokes and many other degenerative diseases, this finding could be of value in preventing and treating disease, improving health and extending life, according to experts.

People who took high doses of vitamin E for extended periods experienced significant drops in blood levels of C-reactive protein

(CRP), researchers at the University of Texas Southwestern Medical Center in Dallas found. CRP is a marker for inflammation and a strong predictor of cardiovascular disease, studies show.

Dr. Ishwarlal Jialal, professor of pathology and internal medicine and colleague Dr. Sridevi Deveraj, assistant professor of pathology, conducted a five-month study on a cohort of 72 people. The subjects were divided into three groups: 23 who suffered non-insulin dependent, or Type II diabetes and had evidence of heart disease; 24 who had Type II diabetes but no sign of heart disease; 25 people who had neither condition and whose health was normal.

Each person in each group received 1,200 International Units (IU) of natural vitamin E, or alpha-tocopherol, daily for three months. Investigators measured the CRP level of each subject before the study began, at the conclusion of the supplementation period and again two months after the study ended. In all three groups, vitamin E supplementation lowered CRP levels by 30%.

“This study shows that vitamin E lowers CRP significantly in both diabetics and non-diabetics. The research suggests that vitamin E could be an additional therapy in our quest to reduce cardiovascular disease,” said principal investigator Dr. Jialal.

At the same time, researchers observed reduced levels of interleukin-6, an inflammation-promoting cytokine compound. Interleukin-6 (Il-6) stimulates the secretion of CRP from the liver. Both markers have previously been shown to be predictors of heart attacks and strokes. Vitamin E supplementation cut Il-6 by an average of 50%.

In another study earlier this year, Drs. Jialal and Deveraj found that high-dose vitamin E reduced heart attack and stroke risk in diabetics by directly reducing inflammation caused by white blood cells, or monocytes. “Diabetics have increased inflammation and are more prone to cardiovascular disease,” said Dr. Deveraj. “This is another piece of evidence that shows that vitamin E decreases another prototypic marker of inflammation and may thereby contribute to reduction in cardiovascular disease in both diabetic and nondiabetic subjects.”

And now, explained Dr. Jialal, “we have shown that you can modulate these markers in diabetics, which has great implications, given that, in diabetes, you have at least a two-fold increased prevalence of strokes and heart attacks.” Cardiovascular disease is the leading cause of death and morbidity in type-II diabetics. —Jim O’Brien

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