

## **Anger hostility and depressive symptoms linked to high C-reactive protein levels**

22 Sep 2004

Researchers at Duke University Medical Center have discovered that otherwise healthy people who are prone to anger, hostility and mild to moderate depressive symptoms produce higher levels of a substance that promotes cardiovascular disease and stroke.

The substance, C-reactive protein (CRP), has garnered considerable attention for its role in both promoting and predicting cardiovascular disease and stroke in initially healthy people. It is produced by the liver in response to inflammation, and inflammation has recently been shown to underlie the plaque that forms inside arteries as they clog.

The Duke study is the first to link this combination of negative psychological attributes with higher levels of CRP in people without traditional risk factors for heart disease, said Edward Suarez, Ph.D., associate professor in the Duke Department of Psychiatry and Behavioral Sciences.

Results of his study are published in the September, 2004, issue of the journal *Psychosomatic Medicine*. The study was funded by a grant from the National Heart, Lung and Blood Institute.

People with traditional risk factors for heart disease ♦ obesity, smoking, diabetes, hypertension, high cholesterol and sedentary lifestyles ♦ have elevated CRP levels, said Suarez. But a large number of individuals without these traditional risk factors have elevated levels of CRP as well, without an identifiable cause.

The Duke study demonstrates that anger, hostile behavior and depressive symptoms could account for why apparently healthy individuals have higher CRP levels and are thus at increased risk for cardiovascular disease and stroke. Suarez said his findings could also explain why people with mild to moderate symptoms of depression are at increased risk for cardiac events and early death ♦ a link that has been clearly established but without an underlying mechanism to explain why.

"Fifty percent of all heart attacks occur among people without any traditional risk factors, so it is critical to identify other factors that may underlie heart disease and the inflammation that contributes to it," said Suarez.

In earlier studies, Suarez has shown that people who are prone to anger, hostility and depressive symptoms respond to stress with increased production of the stress hormone norepinephrine. Scientific evidence suggests that an increase in this stress hormone activates the inflammatory arm of the immune system and triggers the expression of genes that cause chronic, low-grade inflammation. This inflammation is characterized by high levels of CRP, he said.

"Individuals with these psychological attributes may evaluate their environment in a cynically hostile manner, and thus respond with greater anger, which is often accompanied by mild to moderate symptoms of depression," said Suarez. "These psychological attributes tend to cluster within the same individual, and the clustering of attributes may produce even greater risk than any single trait alone."

Suarez said the levels of depressive symptoms and angry/hostile moods necessary to raise CRP do not constitute psychiatric conditions. "That is, you don't have to be clinically depressed or have extreme and frequent bouts of anger to show higher levels of CRP," he said.

In the Duke study, 121 healthy men and women were asked to complete standard personality questionnaires in which they described their psychological attributes, including anger, hostility and depression. The volunteers did not have any pre-existing conditions -- such as smoking, high blood pressure, diabetes or heart disease -- that would predispose them to having high CRP levels. High-sensitivity blood tests were then conducted to measure CRP levels.

Respondents who were prone to anger, had high hostility levels, and showed mild to moderate symptoms of depression had two to three times higher CRP levels than their calmer counterparts. The more pronounced their negative moods, the higher CRP levels they had, the study showed.

The highest levels of CRP were in the range of 1.7 mg/L to 3.0 mg/L. While these levels are still considered relatively low ♦ fever, an active infection, or physical trauma is associated with CRP levels above 10.0/mg/L ♦ CRP levels in this range are associated with a moderate to high risk of heart attacks and strokes, said Suarez.

"CRP levels at this range are associated with inflammation that is likely to eventually increase the risk of a heart attack or stroke," he said. "If you add these psychological attributes together with the known impact of traditional risk factors, it could further elevate CRP levels."

Suarez has previously shown that hostile people who exhibit symptoms of depression have higher levels of stress hormones and circulating levels of an inflammatory substance called interleukin 6, another marker of inflammation that has been shown to predict heart disease in initially healthy people. The current data build upon his earlier research and demonstrate yet another mechanism through which the brain and the body interact to contribute to poor health, he said.

"Most individuals tend to think of heart disease as a condition that is associated with factors such as high cholesterol, high blood pressure, smoking and sedentary lifestyle," said Suarez. "Our findings, however, suggest the development of heart disease may also be due to psychological attributes that activate the inflammatory process shown to predict and contribute to the development of heart disease."

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