

Cynical People Pay Inflammatory Price

ANN ARBOR, Mich., Jan. 23 -- Pollyanna is more likely to be in good cardiovascular health than Doubting Thomas, researchers here suggested.

People who are cynically distrustful tend to have higher levels of inflammatory markers associated with atherosclerosis than those with everlastingly sunny dispositions, reported epidemiologist Nalini Ranjit, Ph.D., of the University of Michigan, and colleagues.

Other psychosocial factors associated with inflammation included chronic stress and depression, the investigators reported in the Jan. 22 *Archives of Internal Medicine*.

"We found that cynical distrust, depression, and chronic stress are associated with higher concentrations of inflammatory markers in a population-based healthy sample," they wrote. "Our cross-sectional results are compatible with a mediating role of behaviors, body mass index, and diabetes mellitus, although definite conclusions regarding mediation can only be drawn from longitudinal design."

Previous studies have exhaustively mined the connection between psychosocial factors such as temperament and outlook on cardiovascular disease and its consequences.

In the current study, the authors delved into the possible associations between psychosocial factors and inflammation, one of the primary factors associated with atherosclerosis and cardiovascular disease.

"Psychosocial factors may be associated with health behaviors predictive of inflammation, including smoking, physical activity, and alcohol intake," they wrote. "In addition, psychosocial factors are associated with obesity and insulin resistance, which are established correlates of systemic inflammation. Psychosocial factors may also be associated with proinflammatory changes in the autonomic nervous system and the hypothalamic-pituitary-adrenal axis."

To find a possible link between psychosocial factors and inflammation, Dr. Ranjit and colleagues conducted a cross-sectional study using data from the Multi-Ethnic Study of Atherosclerosis, a multisite study of 6,814 men and women ages 45 to 84.

The participants, all were free of cardiovascular disease at baseline, were evaluated at that time for chronic stress, mood, attitude and other psychosocial factors, and were evaluated for diabetes and other co-morbidities, BMI, tobacco and alcohol use, and medications.

The investigators also measured levels in serum of the inflammatory markers C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen. They used regression analysis to estimate associations of the psychosocial factors cynical distrust, chronic stress, and depression with the markers before and after adjustment for potential confounding factors.

They found that higher levels of cynical distrust were progressively and most consistently associated with higher levels of the inflammatory markers. Comparing people in the 80th percentile for cynical distrust with those in the 20th percentile, they found that the more distrustful souls had a 7% (95% confidence interval, 3%-10%, $P < 0.001$) higher level of IL-6, 9% (95% CI, 2%-16%, $P = 0.008$) higher level of C-reactive protein, and 1.3% (95% CI, 0.1%-2.4%, $P = 0.04$) higher level of fibrinogen.

Similarly, higher levels of chronic stress were associated with higher concentrations of IL-6 and C-reactive protein. Compared with stress-free folk, people with two ongoing stressful circumstances had 4% (95% CI, 1%-8%, $P = 0.004$) higher levels of IL-6, and 5% (95% CI 1%- 11%, $P = 0.03$) levels pf CRP.

Depression was positively associated only with levels of IL-6, with people having Center for Epidemiologic Studies Depression Scale scores ≥ 21 having 7% (95% CI, 1%- 14%, $P = 0.02$) higher levels than people with scores < 21 .

After adjusting for behavioral factors such as smoking and alcohol use, the associations of psychosocial factors with inflammatory markers were reduced by 20% to 55%, and after adjusting for BMI and diabetes the associations were reduced by 45% to 100%, primarily from the effects of BMI on inflammation, the investigators noted.

No associations between inflammatory marker levels and psychosocial factors remained after they controlled for the combination of socioeconomic position, behaviors, BMI, and diabetes.

"Although we also report analyses after adjustment for socioeconomic position, we do not view socioeconomic position as a mediator of psychosocial effects on health," the authors wrote. "Rather, socioeconomic position is likely to be an antecedent to psychosocial characteristics, as well as to other factors (e.g., behaviors, BMI, and diabetes) associated with inflammation. The reduction of associations after adjustment for socioeconomic position may simply reflect associations of socioeconomic position

with these factors."

They pointed out that the design of the study makes it impossible to determine causality but that there are several potential explanations of the relationships.

"Although it is impossible to determine the causal relationships between these factors from cross-sectional analyses, our results are compatible with the hypothesis that at least part of the association of psychosocial factors with inflammatory markers is due to the mediating role of behaviors; i.e., psychosocial factors are causally associated with uptake of behaviors such as smoking that result in increased concentrations of inflammatory markers," they wrote.

"Significant weakening of associations after adjustment for BMI and diabetes are compatible with one or both of two possible explanations," they continued. "Body mass index and diabetes may mediate the associations between psychosocial factors, or they may confound these associations."

They acknowledged that the study was limited by the difficulty in measuring psychosocial factors, and by the exclusion at baseline of people with clinical cardiovascular symptoms, which could have caused underestimation of possible association between psychosocial factors and inflammation.

Action Points

Explain to patients who ask that this study associated inflammation with a cynical, distrustful attitude and chronic stress from job, family, and finances, leading to enhanced risk for atherosclerosis and cardiovascular disease.

Point out that these purported effects would be mediated by health behaviors, body mass index, and diabetes.

Consider offering patients stress-management techniques and/or appropriate referrals to stress-management programs.

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Reviewed by [Zalman S. Agus, MD; Emeritus Professor at the University of Pennsylvania School of Medicine.](#)

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