Correspondence

Letters to the Editor must not exceed 400 words in length and must be limited to three authors and five references. They should not have tables or figures and should relate solely to an article published in Circulation within the preceding 12 weeks. Authors of letters selected for publication will receive prepublication proofs, and authors of the article cited in the letter will be invited to reply. Replies must be signed by all authors listed in the original publication. Please submit three typewritten, double-spaced copies of the letter to Herbert L. Fred, MD, % the Circulation Editorial Office. Letters will not be returned.

Inflammatory Markers in Coronary Heart Disease: Coronary Vascular Versus Myocardial Origin?

To the Editor:

Two recent articles in Circulation highlight the pathophysiological importance of inflammatory processes in coronary and, more generally, cardiovascular atherosclerosis. They also emphasize the clinical use of inflammatory markers, such as C-reactive protein and tumor necrosis factor-α, to monitor disease progress and prognosis. The underlying assumption of these articles is that the inflammatory process is confined to the atherosclerotic vascular wall and that the inflammatory marker in peripheral blood is a spillover from the atherosclerotic vascular wall into the systemic circulation. However, this is possibly an incomplete view of the underlying pathophysiology. In fact, microembolization from a fissuring/rupturing atherosclerotic plaque in an epicardial coronary artery causes not only physical obstruction of the dependent microcirculation, but also a marked inflammatory response in the affected myocardium, as evidenced by experimental studies with coronary microembolization.

Clinically, statin therapy before percutaneous coronary interventions reduces the incidence of periprocedural infarctlets and improves event-free survival, both possibly due to atherosclerotic plaque stabilization and the attenuation of microembolization-induced myocardial inflammation. Therefore, in patients with coronary heart disease, inflammatory markers may also originate from and reflect myocardial inflammation in response to plaque rupture and microembolization and, in consequence, not only predict future events but also reflect subclinical events that have already occurred. Of course, this view highlights the prognostic use of inflammatory markers even more!

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Response

In their Letter to the Editor, Drs Heusch, Schulz, and Erbel correctly point out that the site of inflammation leading to increases in inflammatory markers is not proven to be the atherosclerotic lesion. In our statement for health professionals, we described the current belief about the site of the inflammation being the arterial wall both early in the atherosclerotic process as well as later during plaque destabilization. In fact, this is conjecture, and other origins such as sites of microemboli might contribute. In either case, the release of cytokines from an active disease process may be the key feature that induces the hepatic production of acute phase reactants. This may explain the poor correlation of high sensitivity C-reactive protein with the degree of atherosclerosis. It appears that high sensitivity C-reactive protein may be more predictive of an active disease process rather than atherosclerotic mass. More research is needed to specify the origins and implications of elevated inflammatory markers.

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