Treating cardiovascular disease by treating inflammation: From magic bullets to smart bombs

In the treatment of cardiovascular disease, we have graduated from magic bullets to smart bombs. Bombs have a bigger impact than bullets, but their smartness still depends upon understanding the target.

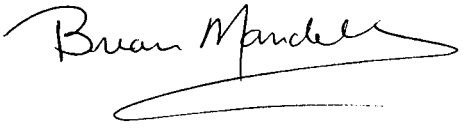
On page 760 in this issue, Drs. Shishebor, Patel, and Bhatt discuss the use of statins to reduce cardiovascular morbidity. They also discuss links between inflammation, markers of the acute-phase response (which some equate with inflammation), and statin therapy.

Statins seem to do it all. Originally thought to be therapeutic bullets that specifically target a pivotal enzyme in the synthesis of low-density lipoprotein cholesterol (LDL-C), they are now more akin to smart bombs capable of also decreasing the level of circulating C-reactive protein (CRP) and, by inference, diminishing the proatherosclerotic inflammatory response.

How much does measuring CRP independently contribute to the assessment of cardiovascular risk in an individual patient? This remains a point of debate, and I don't think evidence from directed clinical trials is available to support therapeutic decisions guided by CRP levels.

A more intriguing question is biological: whether CRP is a player in the pathogenesis of cardiovascular disease or merely a spectator. The answer could dramatically alter treatment strategies. We know that CRP is a component of the acute-phase response driven by mediators of inflammation such as interleukin 1 and interleukin 6, that CRP levels are slightly elevated in patients with coronary artery disease, and that statins can decrease LDL-C levels, CRP levels, and the risk of cardiac events. But these data in toto do not prove that CRP itself is a mediator of cardiovascular disease.

Until there is a selective agent that affects only CRP (perhaps a molecule targeting the CRP promoter), I don't believe that we really know how smart (or lucky) our bombs are.



BRIAN F. MANDELL, MD, PhD
Editor-in-Chief