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Inflammation, C-reactive protein, and atherothrombosis.

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**Abstract**

Atherothrombosis of the coronary and cerebral vessels is understood to be a disorder of inflammation and innate immunity, as well as a disorder of lipid accumulation. From a vascular biology perspective, the processes of cellular adhesion, monocyte and macrophage attachment, and transmigration of immune cells across the endothelium are crucial steps in early atherogenesis and in the later stages of mature plaque rupture, particularly the transition of unstable plaque at the time of acute thrombosis. **There is abundant clinical evidence demonstrating that many biomarkers of inflammation are elevated years in advance of first ever myocardial infarction (MI) or thrombotic stroke and that these same biomarkers are highly predictive of recurrent MI, recurrent stroke, diabetes, and cardiovascular death.** In daily practice, the inflammatory biomarker in widest use is high-sensitivity C-reactive protein (hsCRP); when interpreted within the context of usual risk factors, levels of hsCRP <1, 1 to 3, and >3 mg/l denote lower, average, and higher relative risk for future vascular events. Risk-prediction models that incorporate hsCRP, such as the Reynolds Risk Score, have been developed that improve risk classification and the accuracy for global risk prediction, particularly for those deemed at "intermediate risk" by usual algorithms, such as the Framingham Risk Score. With regard to cerebral vessels, increased biomarkers of inflammation, including hsCRP, have been associated with increased stroke risk as well as an increased rate of atherosclerosis progression in the carotid vessels. Although the proportion of variation in hsCRP explained by genetic factors may be as large as 20% to 40%, diet, exercise, and smoking cessation remain critical tools for risk reduction and CRP reduction. Statin therapy reduces hsCRP in a largely low-density lipoprotein (LDL)-independent manner, and the "anti-inflammatory" properties of these agents have been suggested as a potential mechanism beyond LDL reduction for the efficacy of these agents. The ongoing multinational Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial of 17,802 initially healthy men and women with low levels of LDL cholesterol but increased levels of hsCRP will help to define whether vascular protection can be achieved with statin therapy, even in the absence of hyperlipidemia. Targeted anti-inflammatory therapies are being developed that may provide a direct method of translating the biology of inflammation into new clinical treatments across multiple vascular beds. This article summarizes data supporting a role for inflammation in cardiovascular disease and offers the possibility that other disorders characterized by inflammation, **such as periodontal disease**, may have an indirect role by influencing the risk, manifestation, and progression of vascular events.

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