Increased Serum Cholesterol Plus Inflammation Leads to Plaque Rupture and Death: How Can This Be Prevented?

NOTES

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Prevalence in the United States

The prevalence in the Unites States of coronary heart disease (CHD) is 12,900,000 cases, and of myocardial infarction is 7,600,000, with a mortality rate of 47%. About 80% of mortality owing to CHD in people under age 65 years occurs during first attack. Fifty percent of men and 63% of women who die suddenly of CHD had no previous symptoms.

Recent research has identified inflammation as a key player in the formation of the atherosclerotic plaque. Immune cells dominate the early atherosclerotic lesion, and their effector molecules accelerate plaque progression. Excess LDL infiltrates the intima; inflammatory lipids induce the endothelial cell to express leucocyte adhesion molecules. Macrophages scavenging modified LDL particles become foam cells, which release inflammatory cytokines, chemokines, and oxygen and nitrogen radicals, leading to tissue damage, especially at sites of hemodynamic strain. Activated T cells produce interferon-g and other cytokines that activate macrophages and other vascular cells, leading to inflammation. A cytokine cascade is initiated. Activation of the plaque rather than stenosis precipitates ischemia and infarction. Plaque rupture and endothelial erosion are the two major causes of coronary thrombosis. A balance between inflammatory and antiinflammatory activity controls the inhibition or progression of the process. Cysteine proteases and matrix metalloproteins are two principal players in plaque activation and may become therapeutic targets. A number of different inflammatory markers, such as C reactive protein, are present in smoldering and activated plaques, but it is more likely that they reflect local inflammatory processes in the artery rather than serve as actual causes of the atherosclerotic lesion.

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