Plasma lipoproteins and atherosclerosis in man: an immunohistochemical study

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Abstract

The localization pattern of apoLDL, the major protein constituent of the plasma low density lipoproteins, was determined in normal and atheroelastic areas of human arteries from various vascular beds. Goat antisera were prepared against apoLDL, conjugated with a fluorescein isothiocyanate label, and purified by affinity chromatography on a solid immunoabosorbent of LDL Sepharose. By fluorescence microscopy, the following distribution patterns of apoLDL were found: in fibrous plaques spread diffusely throughout the lipid core usually together with acid mucopolysaccharides, along bands of collagen in fibrotic areas of intimal plaques and aneurysms, and often, but not always, accompanied by lipid deposition, along fragmented fibers of elastica and collagen bundles, and in smooth muscle cells and macrophages of fatty streaks and fibrous plaques of subjects with type II hyperlipoproteinemia. No LDL protein was detected in arterial segments without atherosclerotic involvement. This information may help to elucidate those tissue components which are responsible for the retention of LDL, thereby leading to its accumulation and potential contribution to the pathogenesis of atherosclerosis.
In animal studies, C pneumoniae inoculation increases atherosclerosis, and azithromycin attenuates this effect. [43] It is unclear whether the organism is causally related to atherosclerosis in humans, however. Large-scale clinical trials have not demonstrated a benefit of antichlamydial therapy in reducing the risk of vascular events in patients with established coronary artery disease. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a macrophage-derived enzyme involved in metabolism of LDL in arterial walls that is responsible for release of inflammatory mediators. [99, 100] Recent epidemiologic studies have provided evidence that relative elevations in serum levels of Lp-PLA2 are associated with increased risk of incident ischemic stroke. 

A study documenting the localization in human arteries of apoproteins from human plasma high density (HDL), low density (LDL), and very low density (VLDL) lipoproteins was undertaken in light of their possible roles in the pathogenesis and regression of the atherosclerotic process in man. Apo A-I from HDL, apo B from LDL, apo C-III from VLDL were all localized by immunohistochemical techniques to generally the same areas of atherosclerotic lesions. These consisted of certain bands of collagen and elastic fibers in fatty streaks and fibrous plaques, and extracellular pools of neutral lipid in fibrous plaques. Lipoprotein particles vary in the primary lipoprotein present and the relative contents of the different lipid components. There is strong evidence that lipoproteins play a fundamental role in atherosclerosis and their interaction with the arterial wall appears to initiate the cascade of events that leads to atherosclerosis. Lipoproteins that promote atherosclerosis are termed atherogenic. Apolipoprotein B (apoB) is an important component of atherogenic lipoproteins. One study found that plasma oxLDL was the strongest predictor of CAD events compared with a conventional lipoprotein profile and other traditional risk factors for CAD. OxLDL particles may promote atherosclerosis through several mechanisms. Atherosclerosis, the underlying cause of cardiovascular disease, is characterized by chronic inflammation and altered immune response. Cholesterol is a well-known risk factor associated with the development of cardiovascular diseases. This review provides an overview of immune response to lipoproteins and the fascinating possibility of developing an immunomodulatory therapy for atherosclerosis.