Do dietary fatty acids cause endothelial activation? How might endothelial activation contribute to thrombogenesis?[1,2]

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There is considerable evidence that oxidized lipoproteins are present in vessel walls in fatty streaks and fibrous plaques (1). Our group has found that interaction of minimally oxidized low-density lipoprotein (MM-LDL) can alter endothelial cells in several ways that might contribute to thrombogenesis. Incubation of monolayers of endothelial cells with MM-LDL for 4 h results in an increased binding of monocytes to the endothelium; the production of MCP-1, a chemotactic factor for monocytes (2, 3); and increased synthesis of colony-stimulating factors (4). In a coculture system with endothelial cells and smooth muscle cells, MM-LDL caused a migration of monocytes across the endothelium into the matrix separating the two cell types. If similar processes occur in vivo, then minimally oxidized LDL may be at least partly responsible for entry of monocytes into vessel walls, where they form foam cells. These expanding foam cells may cause breaks in the endothelium to which platelets adhere (5) or may interact with platelets as they migrate back across the endothelium (6). Either process could initiate thrombus formation. In addition we recently found that treatment of monolayers of human aortic-valve endothelium with MM-LDL increases the amount of tissue factor on the cell surface as much as 50-fold (7). Tissue factor can act as an initiator of thrombus formation on intact endothelium.

The molecule in MM-LDL responsible for these effects has not been determined, but we showed that it is a lipid and that the activity is found in the polar lipid fraction from a diol column. MM-LDL contains both oxidized fatty acids and cholesterol oxidation products. Whether an oxidized fatty acid or oxidized cholesterol is responsible for the action of MM-LDL, it is clear that fatty acids play an important role in oxidation of lipoproteins because of the ease of oxidation of polyunsaturates.

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