Oxidized LDL, diet, and natural antibodies

Dear Sir:

Zock and Katan (1) gave a good analysis in their recent editorial of the diet–LDL oxidation–coronary artery disease hypothesis. We would like to expand on the theoretical pathways involved in the oxidation hypothesis. Our theories are an offshoot of our recent finding of autoantibodies to cholesterol oxides in healthy individuals (2). In an enzyme-linked immunosorbent assay, these natural antibodies to cholesterol oxides bound to target antigens that included 7-ketocholesterol, cholesterol epoxide, 7-hydroxycholesterol, and 19-hydroxycholesterol. These cholesterol oxides represent major components of LDL that are modified by oxidation (2, 3). Because natural antibodies have been postulated to have an “immunohousekeeping” function (4), these antibodies to cholesterol oxides may be involved in the immunophysiologic clearance of oxidized LDL and aged cell membranes that contain a substantial amount of cholesterol.

Previously, we showed the common occurrence of natural antibodies to phospholipids including cardiolipin and phosphatidylserine (5). Antibodies to phospholipids were recently shown to cross-react with oxidized LDL (6). Although the immunologic origin of natural antibodies to phospholipids is still unknown, it was interesting to note that the amounts of these antibodies could be affected by diet in an experimental mouse model of autoimmune disease (7). Presumably, the same dietary factors influence the natural antibody populations.

We thus propose that in addition to the current scheme of atherogenetic events as summarized by Zock and Katan, natural antibodies to phospholipids, cholesterol oxides, or both—and by extension, oxidized LDL—may also serve to modulate any pathobiologic effects of oxidized LDL on the endothelium, platelets, and macrophages. The amount and activity of circulating oxidized LDL could therefore be controlled by regulatory mechanisms involving endogenous and exogenous antioxidants as well as natural antibody activity (Figure 1). The postulated protective role of natural antibodies also extends the spectrum of effectors that have been described in the immunologic control of atherogenesis (8).

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REFERENCES

Reply to H-M Cheng and K Sundram

Dear Sir:

Chen and Sundram suggest that 7-ketocholesterol, cholesterol epoxide, and other cholesterol oxides represent major components of oxidized LDL, and that circulating autoantibodies to such cholesterol oxides may help to clear oxidized LDL in vivo. Treatment

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FIGURE 1. Potential influence of antioxidants and natural antibodies on the concentration and cellular effects of oxidized LDL (oxLDL). Besides containing antioxidants and other factors, the diet may also modulate the amount of natural antibodies to oxLDL.