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EDITORIAL
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Dietary fat and atherosclerosis

The idea that atherosclerosis originates as an inflammatory disease [1] is now fairly well accepted. The initial events occur in the vascular endothelium [2] and an array of cytokines and adhesion molecules that are known to play a role in the early vascular events. Lusis [3] has described the process in detail. The diagnosis of heart disease still rests, largely, on analysis of the circulating lipids—total cholesterol, lipoproteins and triglycerides. Newer diagnostic tests—homocysteine, C-reactive protein and the like—are coming into greater use but are relegated to minor roles. Insofar as treatment is concerned the focus is still largely on blood lipids. Initial enthusiasm for dietary treatment with polyunsaturated fat (PUFA) was moderated by the observation that PUFA lower levels of all lipoproteins whereas monounsaturated fat (MUFA) exerted its major effect only on the LDL fraction [4]. However a meta analysis by Gardner and Kraemer [5] suggests that MUFA and PUFA have similar effects on plasma lipoproteins.

The observation that oxidized LDL triggered early steps in atherogenesis [6,7] focused attention on the role(s) of antioxidants and also created concerns relating to the oxidizable components of LDL—most likely the PUFA content. Thus while dietary PUFA decreases plasma levels of the atherogenic LDL [8,9] they may provide a substrate for the oxidized lipid that plays a role in initiation of the atherogenic process.

Earlier this year Toborek et al. [10] demonstrated that PUFA induce inflammatory processes in human endothelial cells *in vitro.* In this issue of the *Journal of Nutritional Biochemistry* a paper by Nicolosi et al. [11] shows that LDL oxidation is enhanced and aortic fatty streak formation is increased in hamsters fed PUFA compared to those fed MUFA. Hamsters fed PUFA-rich diets also exhibited impaired endothelium-dependent relaxation. These relative actions of MUFA and PUFA have been recognized in current dietary suggestions that the level of dietary PUFA be considered as well as the level of total fat.

Rudel et al. [12] have shown that a diet rich in PUFA protects African green monkeys from coronary artery atherosclerosis when compared with diets rich in MUFA or saturated fat. Cholesteryl oleate accumulated in the coronary arteries of the monkeys fed MUFA or saturated fat compared with those fed PUFA. Is there a dichotomy? Animals fed the diet that minimized LDL oxidation (and, by extension, atherosclerosis) actually exhibited more severe coronary lesions and increased levels of coronary cholesteryl oleate. Are we looking at the two ends of the atherosclerotic process and is it possible that the dietary factors exert opposite effects at various stages of atherogenesis?

The Nicolosi paper [11] is concerned with the initiating events of atherogenesis, one of which is stimulation by oxidized lipids. The Rudel paper [12] is examining the end result. We are learning ever more about the early stages of atherogenesis and we know that the final lesion, among its many components, is rich in cholesteryl ester. We really don't know too much about what goes on in between. Aging tissue accumulates cholesteryl ester, the storage form of cholesterol ([13] and oleic acid appears to be the favored substrate for cholesteryl ester. Perhaps we are seeing a process that requires a bimodal approach, namely, MUFA to reduce early oxidation and endothelial injury and PUFA to reduce later possibilities of *in situ* esterification. It should not be difficult to design experiments to test this question. It may well be that the findings of Nicolosi et al. [11] and Rudel et al. [12] are not contradictory but part of the atherogenic continuum.

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References

[1] R. Ross, The pathogenesis of atheroclerosis, a perspective for the 1990s, Nature 362 (1993) 801–809.
[2] S. Kinlay, P. Libby, P. Ganz, Endothelial function and coronary artery disease, Curr Opinion Lipidology 12 (2001) 383–389.
[3] A.J. Lusis, Atherosclerosis, Nature 407 (2000) 233–241.
[4] F.H. Mattson, S.M. Grundy, Comparison of effects of dietary saturated, monounsaturated and polyunsaturated fatty acids on plasma lipids and lipoproteins in man, J Lipid Res 26 (1985) 194–202.
[5] C.D. Gardner, H.C. Kraemer, Monounsaturated versus polyunsaturated dietary fat and serum lipids. A meta analysis, Arterioscler Thromb Vasc Biol 15 (1995) 1917–1927.
[6] D. Steinberg, C. Parthasarathy, T.W. Carew, J.C. Khoo, J.L. Witztum, Beyond cholesterol: modifications of low density lipoprotein that increase its atherogenicity, N Engl J Med 320 (1989) 915–924.
[7] J.L. Witztum, D. Steinberg, Role of oxidized low-density lipoprotein in atherosclerosis, J Clin Invest 88 (1991) 1785–1792.
[8] M.S. Wolfe, J.K. Sawyer, T.M. Morgan, B.C. Bullock, L.L. Rudel, Dietary polyunsaturated fat decreases coronary artery atherosclerosis in a pediatric-aged population of African green monkeys, Arterioscler Thromb 14 (1994) 587–597.
[9] R.J. Nicolosi, J.L. Hojnacki, N. Llansa, K.C. Hayes, Diet and lipoprotein influence on primate atherosclerosis, Proc Soc Exp Biol Med 156 (1977) 1–7.
[10] M. Toborek, Y.W. Lee, R. Garrido, S. Kaiser, B. Hennig, Unsaturated fatty acids selectively induce an inflammatory environment in human endothelial cells, Am J Clin Nutr 75 (2002) 119–125.
[11] R.J. Nicolosi, T.A. Wilson, T.L. Foxall, F.J. Keaney Jr., J.A. Vita, Decreased aortic fatty streak formation in hamsters fed diets high in monounsaturated fat versus polyunsaturated fat, J Nutr Biochem
[12] L.L. Rudel, J.S. Parks, J.K. Sawyer, Compared with dietary monounsaturated and saturated fat, polyunsaturated fat protects African green monkeys from coronary artery atherosclerosis, Arterioscler Thromb Vasc Biol 15 (1995) 2101–2110.
[13] D. Kritchevsky, Lipid metabolism in aging, Mech Aging Dev 1 (1972) 275–284.

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