Saturated fat prevents coronary artery disease? An American paradox

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It is an article of faith that saturated fat raises LDL cholesterol and accelerates coronary artery disease, whereas unsaturated fatty acids have the opposite effect (1, 2). One of the earliest and most convincing studies of the better efficacy of unsaturated than of saturated fat in reducing cholesterol and heart disease is the Finnish Mental Hospital Study conducted in the 12 y between 1959 and 1971. In this study, the usual high-saturated-fat institutional diet was compared with an equally high-fat diet in which the saturated fat in dairy products was replaced with soybean oil and soft margarine and polysaturated fats were used in cooking. Each diet was provided for 6 y and then the alternate diet was provided for the next 6 y (3). After a comparison of the effects of the 2 diets in both men and women, the incidence of coronary artery disease was lower by 50% and 65% after the consumption of polysaturated fat in the 2 hospitals.

In this issue of the Journal, Mozaffarian et al (4) report the opposite association. They found that a higher saturated fat intake is associated with less progression of coronary artery disease according to quantitative angiography. How can this paradox be explained? In food-frequency questionnaires, saturated fat intake is more precisely estimated than is total fat. If saturated fat is more precisely estimated, it will associate more strongly in statistical analyses with the outcome variable, even though other variables—such as total fat or carbohydrate—could be more relevant physiologically. We believe that these possibilities deserve a closer look.

Unlike the diet used in the Finnish Mental Hospital Study, the diet described by Mozaffarian et al was low in fat, averaging 25% of energy. The study subjects were women with coronary artery disease: most were hypertensive, many had diabetes (19–31%), their body mass index (kg/m²) ranged from 29 to 30, and their lipid profile indicated combined hyperlipidemia (triacylglycerol concentration: ≈200 mg/dL; HDL-cholesterol concentration: 40–50 mg/dL; above-average LDL concentration: 135–141 mg/dL); these characteristics are consistent with the metabolic syndrome. In addition, two-thirds of these women were taking sex hormones. The importance of each of these points is addressed below.

What are the effects of a low-fat, high-carbohydrate diet in comparison with those of a higher-fat, lower-carbohydrate diet? The response differs by the 2 main types of hyperlipidemia: simple hypercholesterolemia and combined hyperlipidemia. In our studies of simple hypercholesterolemia in men, a fat intake <25% of energy and a carbohydrate intake >60% of energy was associated with a sustained increase in triacylglycerol of 40%, a decrease in HDL cholesterol of 3.5%, and no further decrease in LDL in comparison with higher fat intakes (5). In contrast, a low-fat diet in persons with combined hyperlipidemia caused no worsening of triacylglycerol or HDL, but intakes of fat >40% of energy and of carbohydrate <45% of energy for 2 y were associated with a lower triacylglycerol concentration at a stable weight (6). In the subjects of Mozaffarian et al, a greater saturated fat intake paralleled a total fat intake, which ranged from 18% to 32% of energy in the first to fourth quartiles. Modest favorable trends in triacylglycerol and HDL-cholesterol concentrations were observed with higher fat intakes.

Triacylglycerol and HDL-cholesterol concentrations are stronger predictors of coronary artery disease in women, whereas the LDL-cholesterol concentration is a stronger predictor in men (7). Because VLDL triacylglycerol secretion and removal rates in healthy women are double those of men (8), conditions impairing lipoprotein removal would be expected to exaggerate the hyperlipidemic response in women as compared with that in men (9). This sex difference is seen with the development of diabetes. The increment in lipids is greater in women than in men and is associated with a greater increment in coronary artery disease risk in women than in men (9). Similarly, the development of insulin resistance and obesity is associated with a greater lipoprotein increment in women than in men (10). The exaggerated decreases in HDL- and LDL-cholesterol concentrations observed with the consumption of a low-fat Step II diet in women but not in men appear to be another facet of this effect (11).

The failure of female sex hormones to prevent coronary artery disease has been a great disappointment (9). This effect might also be due to an estrogen-induced increase in lipoprotein entry against a fixed or impaired rate of lipoprotein removal, as might be expected in women with the metabolic syndrome and coronary artery disease.

Would saturated fat still be bad for anyone? Not necessarily. The effect of saturated fat and cholesterol ingestion in the form of 4 eggs/d for 1 mo in obese, insulin-resistant subjects is ≈33% of that seen in lean, insulin-sensitive subjects, likely because of diminished cholesterol absorption (12). Thus, the classic effects of saturated fat as compared with those of unsaturated fat seen in...

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the Finnish Mental Hospital Study are likely blunted in the subjects of Mozaffarian et al, whereas the effects of low fat and high carbohydrate intakes on triacylglycerol and HDL-cholesterol concentrations appear to be exaggerated by the interactions of female sex, exogenous sex hormones, and the metabolic syndrome. A major effect on cardiovascular disease risk would be the result of hypertriglyceridemia and low HDL-cholesterol concentrations, which are attenuated by an increase in saturated fat intake itself or in total fat intake, for which saturated fat is a more statistically stable surrogate (4).

In conclusion, the hypothesis-generating report of Mozaffarian et al draws attention to the different effects of diet on lipoprotein physiology and cardiovascular disease risk. These effects include the paradox that a high-fat, high–saturated fat diet is associated with diminished coronary artery disease progression in women with the metabolic syndrome, a condition that is epidemic in the United States. This paradox presents a challenge to differentiate the effects of dietary fat on lipoproteins and cardiovascular disease risk in men and women, in the different lipid disorders, and in the metabolic syndrome.

REFERENCES