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Editorial Comment

Diet and Secondary Prevention of Coronary Disease: Is It Time to Stop Chewing the Fat?*

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Current recommendations endorsed by the American Heart Association and the American College of Cardiology for secondary prevention of coronary disease include dietary limitation of total fat to ≤30%, saturated fat to <7%, and cholesterol to <200 mg/day (1). Although the results of randomized studies of diet have been inconsistent, these guidelines are based on the known relations between dietary fat intake, serum lipids and coronary events. The objective with such a diet is to have favorable effects of decreasing total and low density lipoprotein cholesterol and of increasing high density lipoprotein cholesterol. The evidence has become more compelling that comprehensive risk factor modification, including a low fat, low cholesterol, high carbohydrate diet, has a favorable impact on serum lipids and that it reduces angiographic progression of coronary disease and hospital admissions for coronary events (2).

Aside from the well accepted goal of serum lipid modification, a number of dietary interventions have been proposed to be cardioprotective by other mechanisms. In recent trials of nutritional supplements, some reports, such as that of the antioxidant beta-carotene, have been disappointing (3), and others have been promising, such as the Cambridge Heart Antioxidant Study (CHAOS) evaluating vitamin E use (4). On the basis of epidemiologic data, many physicians recommend modest alcohol intake as an effective measure for prevention of coronary disease events (5).

Two general types of diet have drawn considerable attention recently: the "Mediterranean" diet, high in monounsaturated fat in olive oil, fruits, vegetables and wine; and diets high in omega-3 fatty acids, either in the form of oily fish (6) or the omega-3 fatty acid precursor alpha-linolenic acid, found in soya oil and canola (rapeseed) oil. The current study by de Lorgeril et al. (7), in this issue of the Journal, evaluated a combination of these two diets, with the intervention involving instructions to eat more vegetables and fruit to supply antioxidants and to substitute canola oil margarine for butter and cream to supply alpha-linolenic acid. Plasma samples from a subgroup of patients showed that the investigators were successful with the intervention at increasing antioxidants (vitamins E and C) and omega-3 fatty acid levels, although lipoprotein profiles were not affected. Proposed mechanisms of benefit of supplemental omega-3 fatty acids supported by experimental data include antithrombotic effects through changes in eicosanoids and platelet function, anti-inflammatory effects through changes in white blood cell function and antiarrhythmic effects through effects on membranes.

De Lorgeril et al. (7) found that dietary intervention reduced the 2-year rates of secondary events of unstable angina, stroke, heart failure and venous and arterial embolization, and when combined with the primary events, this represented a risk ratio (RR) of 0.24 (95% confidence interval [CI] 0.13 to 0.44, $p < 0.0001$). These results include twice the total number of events as were in the primary report (8), and de Lorgeril thereby extend the original findings of a reduction in major events (cardiac-related death and nonfatal myocardial infarction) (RR 0.27, 95% CI 0.12 to 0.59). The current report (7) demonstrates a consistency in the relative reduction of the primary and secondary events. There was a less striking reduction in minor events of stable angina, restenosis after angioplasty, thrombophlebitis and myocardial revascularization.

These remarkable results are almost certainly largely due to factors other than a true treatment effect. The 76% reduction in major clinical events reported in this study (7) is well beyond the range that would be expected, especially from a simple dietary intervention consisting of a single patient visit followed by an 8-week visit and then yearly visits. Several factors may have led to an overestimation of the true treatment effect. The effect was most likely overestimated in part because of chance. The analyses in the current report were not the primary end point of the trial, and no correction was made for multiple analyses or for the post hoc nature of the analysis. Although the analysis was reported as "intention to treat," the dropout and lost to follow-up rates were high at between 7% and 8% and included patients who were removed from the study because of intolerance of the diet. The study was conducted at a single center, with the attendant limitations of small sample size (605 patients) for a secondary prevention trial and lack of generalizability. Even with a blinded end point review committee, a single-center study, especially when not double blinded, provides greater potential for bias because of the lesser separation of clinical data recording, collection, management, analysis and interpretation.

Despite the probable overestimation of treatment effect, the results of this report, along with the original Lyon Diet Heart Study report (8), the Diet and Reinfarction Trial (6) study of fish oil, and the CHAOS study of vitamin E (4) provide support for the concept that different diets may have complex effects on modifying coronary risk. The currently accepted recommendations to limit total and saturated fat may be only part of the story,

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Abbreviations and Acronyms

CHAOS = Cambridge Heart Antioxidant Study
CI = confidence interval
RR = relative risk

and rather than chewing the fat, we should be studying in large, multicenter randomized trials the effect of swallowing it.

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