Will High-Carbohydrate/Low-Fat Diets Reduce the Risk of Coronary Heart Disease? (44564D)

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During the 1960s and '70s, general advice for reducing risk of coronary heart disease by dietary modification was heavily influenced by the results of controlled feeding studies, summarized by the well-known Keys and Hegsted equations (1, 2). In these equations, higher serum cholesterol levels were positively related to greater intake of saturated fat and dietary cholesterol and lower consumption of polyunsaturated fat. Thus, dietary advice focused on replacing saturated fat with polyunsaturated fat. Following this advice, polyunsaturated fat in the U.S. diet increased approximately two-fold (3), and coronary heart disease mortality declined dramatically (4). The degree to which these dietary changes contributed to the decline in coronary mortality has been controversial, but there is little doubt that these dietary changes contributed importantly. During the 1980s, a subtle shift developed in dietary recommendations that led to an emphasis on reducing fat intake in general, with less distinction about the type of fat. Thus the first recommendation of the American Heart Association became to reduce total fat intake, and similar emphasis on total fat reduction has been part of general U.S. dietary guidelines as well (5). This emphasis on total fat reduction is epitomized by the U.S. dietary pyramid, which indicates that all types of fat should be used sparingly, and complex carbohydrates should be consumed in large amounts. During recent years, the rate of decline in coronary heart disease appears to be flattening, and there is question whether the incidence is declining at all (6).

Although replacement of total and saturated fat with carbohydrate has been at the centerpiece of recommendations to reduce heart disease, the degree of risk reduction to be expected has received little attention. Recently, the Nutrition Committee of the American Heart Association provided an estimate of the reduction in risk that would be expected were the total U.S. population to decrease their intake of saturated fat to the Step 1 goal of 10% of energy (7). This calculation involved a two-step process using data from controlled feeding studies to estimate the effect of saturated fat reduction on serum cholesterol and, secondly, epidemiologic studies relating serum cholesterol to risk of coronary heart disease. The committee concluded that "equations developed from carefully conducted clinical studies indicate that reducing saturated fat from the current average intake of 12% to 14% of calories can lead to an average reduction of 3% to 5% in CHD risk in the population as a whole." One might reasonably ask whether such a modest reduction should be a sufficient reason for individuals to make major changes in their life, but there is good reason to suspect that even this estimate may be a serious overstatement because the same dietary change will have an adverse effect on lipid fractions other than total serum cholesterol.

The effect on blood lipids of replacing saturated fat with carbohydrate has been evaluated in numerous controlled feeding studies with consistent results (8). With this dietary change, serum total cholesterol and LDL decline, but HDL cholesterol also decreases, and triglyceride levels are elevated. Thus, the ratio of total cholesterol divided by HDL cholesterol is minimally affected by replacing saturated fat with carbohydrate, suggesting that there is little if any benefit to be expected. On the other hand, replacing saturated fat with olive oil or another fat high in monounsaturated fatty acids produces a similar decline in total and LDL cholesterol, but HDL cholesterol is not reduced, and triglycerides do not increase. Thus, these lipid changes would predict that the replacement of saturated fat with carbohydrate would have little effect on CHD risk, but that replacement with monounsaturated fat would be beneficial. The adverse effects of high-carbohydrate intake appear to be worse among individuals with underlying insulin resistance, as would be expected in a population that was overweight and sedentary (9).

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The effects of dietary fats on blood lipid fractions are further complicated because the isomeric position of double bonds can have a major impact on function of fatty acids, including their effects on blood lipids. In a controlled feeding study, Mensink and Katan (10) found that, compared with monounsaturated fat, *trans* fatty acids and saturated fat had similar effects on LDL cholesterol, but *trans* fat uniquely lowered HDL cholesterol. Thus the adverse effect of *trans* fat on the total cholesterol to HDL ratio was approximately twice as detrimental as that of saturated fat. This finding has been reproduced consistently in other metabolic studies, and further evidence indicates that *trans* fatty acids modestly elevate serum triglycerides and increase Lp(a) compared with saturated fat (11).

The effects of dietary fat on blood lipids described above would suggest that reduction in fat intake *per se* is not likely to be beneficial. Further, were monounsaturated or polyunsaturated fats replaced with carbohydrate, risk of coronary heart disease might actually be increased. However, these expectations are based on the assumption that effects of dietary fat are totally predicted by their effects on blood lipid fractions. This assumption could be incorrect as risk of coronary heart disease is mediated by multiple mechanisms other than dietary lipids including platelet aggregability, thrombolysis, inflammation, susceptibility to serious arrhythmias, and endothelial function. Thus, data directly relating dietary fat to risk of coronary heart disease are also important.

Ideally, the various macronutrient substitutions would each be studied by large randomized trials with coronary heart disease as the outcome. However, this is extremely difficult because such studies need to be large and continue for many years to be informative. The next best evidence is likely to be large prospective studies with long follow-up periods. Thus our group has undertaken several large prospective studies to investigate the relationship between diet and coronary heart disease, including the Nurses' Health Study and Health Professionals' Follow-Up Study. The Nurses' Health Study began in 1976 under the leadership of Frank Speizer to investigate oral contraceptives in relation to risk of breast cancer. Diet was added as a major component in 1980 and has been reassessed using standardized questionnaires every 2–4 years since that time. Approximately 90,000 women were free from coronary heart disease and completed the dietary questionnaire in 1980. A parallel study among 52,000 men, the Health Professionals' Follow-Up Study, was started in 1986 and similarly used dietary questionnaires repeated at 4-year intervals. In both studies, incident cases of coronary heart disease are documented by hospital records and pathology reports. The validity of the dietary assessments used in these studies has been assessed by several means including comparisons with multiple weighed dietary records and comparisons with fatty acids in adipose tissue (12). We recently also documented that total fat intake as a percentage of calories was strongly inversely associated with fasting blood triglyceride levels as predicted by metabolic studies (unpublished data). This provides clear evidence that the dietary questionnaire is providing informative data on intake of total fat as well as specific fatty acids.

The most recent analysis of diet and coronary heart disease used follow-up from 1980 through 1994, during which time nearly 1000 women developed nonfatal or fatal coronary heart disease (13). The design of this prospective cohort study allowed the comparison of different sources of energy. As predicted by metabolic studies, substitution of carbohydrate for either monounsaturated or polyunsaturated fat intake was associated with an increased risk of coronary heart disease. On the other hand, replacement of saturated fat, and even more so *trans* fat, with either polyunsaturated or monounsaturated fat intake was associated with a large reduction in risk of coronary heart disease. When women were simultaneously classified by both polyunsaturated fat and *trans* fat intakes, the risk among women with high *trans* fat and low polyunsaturated intake was approximately three-fold greater than risk among women with low intake of *trans* fat and higher intake of polyunsaturated fat. Not surprisingly, because *trans* fat was positively associated with risk and *cis*-unsaturated fats were associated with reduced risks, total fat intake was not associated with risk of coronary heart disease. Similarly, substitution of saturated fat with carbohydrate was associated with only a small and not statistically significant lower risk.

Although randomized trials of saturated fat reduction and risk of coronary heart disease are seriously limited in both size and duration, they do provide some evidence that replacing saturated fat with polyunsaturated fat will reduce both serum cholesterol levels and risk of coronary heart disease (14). On the other hand, the limited data from randomized trials suggest little if any benefit on risk of coronary heart disease from replacing saturated fat with carbohydrate.

Recent economic changes in Poland have provided the opportunity to evaluate abrupt changes in the type of dietary fat on rates of coronary heart disease. In the early 1990s, price supports were eliminated for animal fats such as lard and butter. Largely for economic reasons, consumption of polyunsaturated fats, primarily as margarines low in *trans* fatty acids, increased greatly so that the P:S ratio increased from $\approx$ 0.30 to 0.5 (15). Based on the relationship between P:S ratio and risk of coronary heart disease within the Nurses Health Study population (16) the magnitude of risk reduction predicted by such a change would be $\approx$ 20%, which is close to the 20%–25% reduction in coronary heart disease observed in Poland during the mid-1990s. This finding suggests that dramatic and rapid reductions in coronary heart disease risks are potentially achievable by changes in the type of dietary fat. Notably, in Poland there was little change in the total percentage of energy from fats.

The notion that total fat intake is not an important risk factor for coronary heart disease may appear heretical as this is inconsistent with the general advice conveyed to the

U.S. public. However, it is hardly a revolutionary conclusion. The Executive Summary of the major 1989 review on diet and health by the National Academy of Sciences concludes that "intake of total fat *per se*, independent of the relative content of different types of fatty acids, is not associated with high blood cholesterol levels and coronary heart disease" (17). In particular, this message is inconsistent with the emphasis on total fat reduction in the U.S. dietary pyramid. The likelihood that coronary heart disease risk will actually be increased by replacing mono- and polyunsaturated fats with carbohydrate is important because unsaturated fats actually comprise the majority of dietary fat in the United States. Further, individuals who are particularly concerned about their health frequently avoid foods such as nuts and salad dressings that are high in unsaturated fats, including the N-3 fatty acid, α-linolenic acid. In the Nurses Health Study, we observed a lower risk of coronary heart disease among individuals with higher nut consumption (18), a finding that has also been observed in other studies (19). Also as expected on the basis of its high content of unsaturated fats, oil and vinegar salad dressing in the Nurses' Health Study was inversely associated with risk of coronary heart disease (16).

On the basis of metabolic and epidemiologic evidence, replacing unsaturated fats with carbohydrates would be expected to increase risk of coronary heart disease. However, some have argued that decreasing the percentage of energy from fat in the diet will reduce weight importantly, so that the overall effect would be beneficial. Despite this argument, an important benefit of dietary fat reduction on body weight has not been supported in longer-term, randomized trials (20). In short-term feeding studies, a modest, often 1–2-kg weight loss is observed. Although such a small change in weight is not clinically important, if this rate of weight loss were to continue for several years, it would be meaningful. However, in studies lasting one or more years, the weight loss described above appears to be transient, and the effect on weight over the longer time is minimal, typically about 1–3kg. However, even this small loss is likely to be exaggerated because in most studies there was intensive diet monitoring and counseling in the intervention group and no intervention in the control group. In a few longer-term studies in which the control group also received an intervention with a similar level of intensity, there is little effect on body weight. A recent report by Knopp *et al.* (21) was particularly informative as it lasted for 1 year and included several hundred adults. Individuals were assigned to four levels of fat intake, and weight loss in each group was about 3 kg. Although weight loss did not differ by fat consumption as a percentage of energy, the low-fat intake group experienced a 39% increase in plasma triglyceride levels, as predicted by earlier controlled metabolic studies. This substantial increase in triglyceride levels does indicate that a low-fat group was complying with their dietary assignment of high-carbohydrate intake. Although more research is needed on the effects of long-term fat intake on body weight control, the available evidence is quite clear that there will be little if any effect on body weight with reductions in dietary fat, at least over the range of about 18%–40% of energy from fat.

Although further studies are warranted relating specific types of fat to risk of coronary heart disease, the available evidence suggests several conclusions. First, coronary heart disease rates can be dramatically reduced by nutritional means, but this will not be achieved by replacing saturated fat with carbohydrates. Second, we should abandon recommendations regarding the percentage of energy from fat and pejorative references to fat or fatty foods. Finally, advice about dietary fat should focus on replacement of saturated and *trans* fatty acids with unsaturated fats, including sources of α-linolenic acid.

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