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The Diet–Heart Hypothesis: A Critique

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The low-fat "diet–heart hypothesis" has been controversial for nearly 100 years. The low-fat–high-carbohydrate diet, promulgated vigorously by the National Cholesterol Education Program, National Institutes of Health, and American Heart Association since the Lipid Research Clinics-Primary Prevention Program in 1984, and earlier by the U.S. Department of Agriculture food pyramid, may well have played an unintended role in the current epidemics of obesity, lipid abnormalities, type II diabetes, and metabolic syndromes. This diet can no longer be defended by appeal to the authority of prestigious medical organizations or by rejecting clinical experience and a growing medical literature suggesting that the much-maligned low-carbohydrate–high-protein diet may have a salutary effect on the epidemics in question. (J Am Coll Cardiol 2004;43:731–3) © 2004 by the American College of Cardiology Foundation

I am bound by my own definition of criticism: A disinterested endeavor to learn and propagate the best that is that is known and thought in the world.
—Mathew Arnold, 1861

The role of diet in the genesis of atherosclerosis has been studied extensively for nearly a century, since Anitschkow induced fatty deposits in rabbit aortas by feeding cholesterol and saturated fats to rabbits. Although today the relationship between elevated serum cholesterol (SC) and coronary artery disease (CAD) is well established, the role of diet in both the prevention and treatment of CAD remains unsettled and highly controversial. Mann wrote in 1977: "A generation of research on the diet–heart hypothesis has ended in disarray" (1). E. H. Ahrens, Jr., one of the originators of the diet–heart hypothesis, said in 1985 that it was not yet proven that dietary modification could prevent CAD (2). Studies, including comparative population-based dietary investigations, by Ancel Keys in the 1950s, focused on dietary saturated fats (3). In the 1960s, Senator George McGovern's bipartisan Senate committee and the U.S. Department of Agriculture (USDA) gave further impetus to the low-fat diet–heart hypothesis (4).

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Subsequent promotion of the low-fat diet, which came to dominate current nutritional thought, began in earnest with the National Institutes of Health (NIH)-sponsored Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT) (5). In this study, cholestyramine, given over some seven years, reduced SC by about 10% and mortality by a widely publicized relative 24%. Although statistically significant, the absolute reduction was far less impressive: 2% in the placebo and 1.6% in the treated cohort. In spite of much skepticism regarding the clinical significance of this result, the LRC-CPPT investigators concluded correctly that the lowering of SC was pivotal in the prevention and management of CAD. This decision was validated when statin trials reduced cholesterol by 30% to 35% and produced unassailable evidence of improved CAD end points, although it is increasingly recognized that some of the benefit from statins may reside in non-lipid mechanisms.

Another inference drawn from the LCR-CPPT proved to be less fortuitous. Even though the LCR-CPPT was a drug and not a diet trial, the LRC-CPPT investigators—the NIH, the National Cholesterol Education Program (NCEP), and the American Heart Association (AHA)—made a leap of faith: if lowering SC by medication was effective against CAD, reducing dietary fat intake would also lower SC and produce a similar result.

There followed what became perhaps one of America's most extensive public relations campaigns: convincing the profession as well as the public that avoiding dietary fat was a key element in the prevention and treatment of atherosclerotic CAD. The NIH, NCEP, AHA, USDA, and a host of medical organizations were joined by the food industry in publicizing and promoting this concept. One had only to walk through any supermarket to find a plethora of cookies, cakes, ice cream, and nearly every imaginable food product prominently marked "low-fat." The message, perhaps unintended, was unmistakable: eat all the low-fat foods you want; they are safe. Yet many of these low-fat foods were high in carbohydrates (Carb) and prepared with saturated and trans-fatty acids (6).

The medical literature contained warnings largely ignored by the profession and related organizations. Rosenman (7), in an extensive review, found that SC is not strongly related to or primarily regulated by diet. He also cited widespread discordant beliefs about a causal role of diet in CAD. Hu et al. (8) wrote that replacing saturated and trans-unsaturated fats with unhydrogenated mono-unsaturated and poly-unsaturated fats was more effective in preventing CAD in women than in reducing overall fat intake. They noted that low-fat–high-carbohydrate (LF-HCarb) diets were widely recommended to reduce the risk of CAD by reducing low-density lipoprotein (LDL) by limiting dietary fat. However, because of its high-

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Abbreviations and Acronyms

AHA	= American Heart Association
CAD	= coronary artery disease
Carb	= carbohydrate
HDL	= high-density lipoprotein
LCarb-HP	= low-carbohydrate–high-protein
LCR-CPPT	= Lipid Research Clinics–Primary Prevention Trial
LDL	= low-density lipoprotein
LF-HCarb	= low-fat–high-carbohydrate
NCEP	= National Cholesterol Education Program
NIH	= National Institutes of Health
SC	= serum cholesterol
USDA	= U.S. Department of Agriculture

Carb content, LF-HCarb diets also decrease high-density lipoprotein (HDL) and increase triglycerides, well-established independent risk factors for coronary disease (8).

Yancey et al. (9) noted: "Information about the best diet (to prevent CAD) is incomplete, unscientific and often conflicting." These authors also contend that a low-fat diet promulgated without limitation of Carb intake would in reality become a high-Carb diet (9). The current epidemic of obesity, type II diabetes, and the metabolic syndrome in retrospect seems to be, in part, the inevitable result of the LF-HCarb diet, absent warnings against unlimited Carb intake. Yet these unfortunate nutritional approaches were promoted aggressively by the profession and by the most credible medical organizations and institutions, in concert with the USDA and the food industry.

In this milieu, obese Americans, frustrated by the failure of traditional medical dietary advice, sought weight loss through popular and highly publicized "Atkins" low-carbohydrate–high-protein (LCarb-HP) diets. These diets were rejected and criticized by mainstream medicine because of potential risks from increased protein and fat content. An AHA science advisory warned that LCarb-HP diets might cause metabolically induced kidney and liver damage and CAD (10). Thus far, however, there is little evidence to substantiate these warnings, and there is evidence that saturated fats, which represent the smallest proportion of calories by the USDA food pyramid, may carry little more risk than Carb, the class of food representing the bulk of USDA caloric recommendations (9).

In the current issue of the *Journal*, Kappagoda et al. (11) discuss the LCarb-HP diet and challenge its role in clinical cardiology. They report the wide media coverage that articles on the LCarb-HP diet received during the last AHA meeting and emphasize theoretical, but as yet unproven, dangers that LCarb-HP diets may pose. They tend to dismiss recent, somewhat promising LCarb-HP diet research. For example, they give short shrift to a study presented by Westman, Yancey, and Guyton at the 2002 AHA scientific sessions, which found that LCarb-HP diets reduced weight, SC, LDL, very-low-density lipoprotein, and percent of small LDL particles, suggesting possible usefulness in treating the metabolic syndrome (12). Kappagoda et al. (11) also minimize the findings of other recent studies of 6- to 12-month duration (13–15) that show no ill effects of LCarb-HP diets but rather a tendency toward greater weight loss, improved lipid patterns, and increased insulin sensitivity when compared with LF-HCarb diets. Kappagoda et al. (11) conclude that a LCarb-HP diet cannot be recommended, because of potential nutritional deficiencies and the absence of long-term data on efficacy and safety and because they "run counter to all current evidence-based dietary recommendations." They refer to the LF-HCarb diet as having an established record of "safety and efficacy," a position difficult to sustain without ignoring evidence supporting its culpability in the current epidemic of obesity, type II diabetes, and the metabolic syndrome.

In a systemic review of dietary fat in preventing CAD, Hooper et al. (16) point out: "Despite decades of effort, and many thousands of people randomized, there is still only limited and inconclusive evidence of the effects of modification of total, saturated, mono-unsaturated or poly-saturated fats on cardiovascular morbidity and mortality" (16). The Hooper et al. study (16) included 27 trials, with 30,902 patient-years of observation, and reported a reduction of 9% in cardiovascular mortality and 16% in cardiovascular events, with little effect on total mortality. Some criticized Hooper for underestimating the importance of these date from his own study. He responded: "Over 50 years of endeavor, dietary fat trials have managed only 30 thousand patient-years of observation in studies of at least 6 months duration and only 8,300 person-years in trials longer than 2 years in which usable data on mortality are available. Much more data is available already for statins—the 4S trials alone amassed over 19,000 person-years of observation, a mean of over 4 years for each . . . given the paucity of data available, we feel it is remarkable that an effect was seen at all." The Hooper review and the response to it illustrate the difficulty of arriving at consensus on the diet–heart hypothesis.

A clinical debate published in the *New England Journal of Medicine* further demonstrated the intensity of the diet–heart hypothesis controversy (17). Connor and Connor defended the LF-HCarb diet, pointing out USDA data that showed that energy intake from dietary fat decreased from 40% to 33%, whereas Carb intake increased from 45% to 52% from the 1960s to 1995. Between 1970 and 1995, annual refined sugar consumption rose from 120 pounds to 150 pounds per capita. Although the Connors did lament the plethora of fat-free foods that led to increased sugar intake in cookies, sweet rolls, frozen yogurt, and the like, they wrote that there was little doubt that Americans had improved their health by lowering their intake of dietary fat. In that debate, Katan, Grundy, and Willet questioned whether reduction in dietary fat intake would provide the health benefits claimed by the Connors. Katan et al. (17) were concerned by the growing public perception that Carb was innocuous and warned that LF-HCarb diets, while

reducing LDL, also lowered HDL and elevated triglycerides, which were independent CAD risk factors. They noted that, although dietary fat consumption had decreased since 1976, obesity in the U.S. had increased by one-third.

Subsequently, Hu et al. (18) reported that obesity was the single most important element in the occurrence of type II diabetes and that the public was generally not aware of the relationship between obesity and diabetes. They advocated diets emphasizing unsaturated fats and high-fiber cereals and a low content of saturated fat, trans-fatty acids, and foods with a high glycemic index. The latter include refined starches and sugars, which tend to cause a hyper-insulin state and promote type II diabetes. Trans-fatty acids are believed to be particularly unfavorable and are found in hydrogenated oils, margarines, and commercially baked low-fat products and fast foods.

There is growing literature exploring the nature and efficacy of the LCarb-HP diet. Westman et al. (12) found that the LCarb-HP diet led to sustained weight loss during a six-month trial. Serum cholesterol was decreased by 11 mg/dl, LDL by 10 mg/dl, and triglycerides by 56 mg/dl, while HDL increased by 8 mg/dl. There were no adverse effects (13). Bravada et al. (19) systematically reviewed 107 studies with 3,168 participants in order to determine the efficacy and safety of the LCarb-HP diet. There was wide disparity in the duration and design of these studies, which complicated the analyses. These authors concluded that there was inadequate evidence to make recommendations for or against the LCarb-HP diet, particularly among participants older than age 50 (19). Samaha et al. (14) assigned 132 severely obese patients with a mean body mass index of 43 and a 30% prevalence of diabetes or the metabolic syndrome to either LF-HCarb or LCarb-HP diets. Seventy-nine subjects completed the six-month study. Those receiving the LCarb-HP diet lost more weight than did the LF-HCarb group, with relative improvement in insulin sensitivity and triglyceride levels, even after adjustment for weight loss. Insulin sensitivity was measured only in subjects without diabetes and improved more among the LCarb-HP group. Weight loss and assignment to the LCarb-HP diet were independent predictors of improvement in triglyceride levels and insulin sensitivity (14). Foster et al. (15) reported a one-year multi-center randomized trial comparing LCarb-HP and LF-HCarb diets in obese subjects. The LCarb-HP group had a greater decrease in serum triglycerides and increase in HDL than those receiving the LF-HCarb diet. Although this may have been due partly to the greater weight loss with the LCarb-HP diet, the changes were larger than expected from weight loss alone. There were no significant differences between the two groups in blood pressure, LDL, and insulin sensitivity (15). The authors of both these studies were conservative in presenting their results. They did not dwell on modest improvement in some risk factors, such as increased insulin sensitivity, reduction in weight, reduction in triglycerides, and in one study, elevation of HDL. Rather, in objective and scientific fashion, they called for larger studies of longer duration comparing LCarb-HP and LF-HCarb diets with regard to cardiovascular outcomes and safety.

A balanced appraisal of the diet–heart hypothesis must recognize the unintended and unanticipated role that the LF-HCarb diet may well have played in the current epidemic of obesity, abnormal lipid patterns, type II diabetes, and the metabolic syndrome. Defense of the LF-HCarb diet, because it conforms to current traditional dietary recommendations, by appealing to the authority of its prestigious medical and institutional sponsors or by ignoring an increasingly critical medical literature, is no longer tenable. The categoric rejection of experience and an increasingly favorable medical literature, though still not conclusive, which suggests that the much-maligned LCarb-HP diet may have a favorable impact on obesity, lipid patterns, type II diabetes, and the metabolic syndrome, is also no longer tenable.

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