Journal of the American College of Cardiology Vol. 50, No. 1, 2007

Published by Elsevier Inc.
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2007.04.027

EDITORIAL COMMENT

Diet and Cardiovascular Disease Prevention

The Need for a Paradigm Shift*

Frank B. Hu, MD, PhD

Boston, Massachusetts

The traditional diet-heart hypothesis (that high intake of saturated fats and cholesterol leads to atheromatous plaque, narrowing of coronary arteries, and, eventually, myocardial infarction) dates back to evidence from the beginning of the 20th century (1). Early animal studies showed a relationship among dietary cholesterol, saturated fat, and arterial lesions, an effect mediated largely through elevations in plasma cholesterol. Subsequently, metabolic research found that dietary intake of specific fatty acids directly influenced blood cholesterol in humans, and epidemiologic studies identified elevated serum cholesterol as a strong independent risk factor for coronary heart disease (CHD). Together with ecologic correlations between diet and heart disease rates and findings from migration studies and special populations, these data heavily influenced the formation of the diet-heart hypothesis.

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This hypothesis has since played a major role in shaping national dietary guidelines. Prevailing recommendations to prevent cardiovascular disease (CVD) and promote weight loss have called for diets low in fat (particularly saturated fat) and high in complex carbohydrates. These recommendations unleashed a proliferation of low-fat or nonfat products, and, over the past 2 decades, led to a substantial reduction in the percentage of dietary energy from fat. At the same time, however, the prevalence of obesity and type 2 diabetes has increased dramatically. These trends cast doubt on the benefits of low-fat diets and contributed to a resurgence of interest in low-carbohydrate diets.

Although the initial intention of the low-fat campaign was to reduce saturated fat intake, the desire for a simple message designed for the general public resulted in the incrimination of all fats, despite clear evidence that this view was not supported scientifically. Human feeding studies from the 1950s showed that reduction of total fat intake had no effect on serum cholesterol and that polyunsaturated fat reduced cholesterol levels (2). In contrast, large prospective cohort studies and secondary prevention trials indicate that substitution of unsaturated fats for saturated fats, trans fats, or carbohydrates is beneficial for CHD prevention, whereas simply reducing total fat has no effect (1). In addition to fostering misunderstanding among the general public, the low-fat campaign has spurred a compensatory increase in consumption of refined carbohydrates and added sugars—an unintended consequence that likely fueled the twin epidemics of obesity and diabetes. In metabolic studies, low-fat, high-carbohydrate diets not only induce high glycemic and insulinemic responses, but also increase plasma triglycerides and decrease high-density lipoprotein (HDL) cholesterol.

Carbohydrates are traditionally classified as simple or complex depending on chemical structure. Simple sugars are typically digested and absorbed more quickly than complex ones, and thus are thought to induce more rapid postprandial glucose response. However, numerous metabolic studies have challenged this belief, and it is now recognized that many starchy foods (e.g., baked potatoes and white bread) produce even higher glycemic responses than simple sugars (3). Different glycemic responses to carbohydrate-containing foods underlie the development of the glycemic index (GI), a concept introduced by Jenkins et al. (4) in 1981.

The GI compares blood glucose levels after ingestion of a test food and a standard weight (50 g) of a reference carbohydrate (glucose or white bread). It ranks foods based on increase in blood glucose (area under the curve). The GI largely depends on rate of digestion and speed of carbohydrate absorption, but the physical form of foods is also an important determinant. Typically, foods with more compact granules (low starch gelatinization) and high levels of viscose soluble fiber (e.g., barley, oats, and rye) are digested at a slower rate and have lower GI values. Whole-grain products with intact bran and germ also meet these criteria. Refined carbohydrates (e.g., white bread), however, are digested more rapidly because grinding or milling of cereals reduces particle size, removes most of the bran and the germ, and allows for more rapid attack by digestive enzymes (5).

Blood glucose response is determined by the quality as well as the quantity of carbohydrates in food. Both factors are reflected in the concept of glycemic load (GL) (the product of the GI value of a food and its carbohydrate content). When white bread is used as the reference, each unit of dietary GL represents the equivalent glycemic effect of 1 g of carbohydrates from white bread. Data from several

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the Departments of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Massachusetts; and the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.

large population-based studies show that dietary GI or GL values have an inverse association with HDL levels and a positive association with triglycerides. Epidemiologic studies also show that higher dietary GL, especially when combined with low intake of cereal fiber, significantly elevates long-term risk of type 2 diabetes (6,7).

Liu et al. (8) first reported a positive association between a higher dietary GL and risk of CHD in the Nurses' Health Study (NHS). In this issue of the *Journal*, Beulens et al. (9) report a similar association between GL and risk of CVD in the Dutch EPIC (European Prospective Investigation into Cancer and Nutrition) cohort. The analysis included 15,714 women ages 49 to 70 years without diabetes or CVD at baseline. During 9 years of follow-up, 556 incident cases of major CVD events were documented. After adjusting for CVD risk factors and dietary fat and fiber, the investigators found a significant association between dietary GL and increased risk of CVD (risk ratio comparing extreme quartiles = 1.47, 95% confidence interval 1.04 to 2.09, p for trend = 0.03). There was also an association between higher dietary GI and increased risk of CHD. Similar to the results from the NHS, the increased risk was more pronounced among overweight and obese women compared with normal-weight women.

Accurate quantification of dietary intakes in free-living populations is a major challenge in large nutritional epidemiologic studies. In the past 2 decades, the semiquantitative food frequency questionnaire (FFQ) has become the method of choice because of its low cost and ability to assess usual diet, the main interest in most epidemiologic studies of diet and chronic diseases. Beulens et al. (9) validated the FFQ against twelve 24-h recalls; the Spearman correlations between the FFQ and 24-h recalls ranged from 0.56 to 0.78 for major carbohydrate-containing foods that contribute most to overall GL (including potatoes, bread, soft drinks, and sweets). Consistent with metabolic and other epidemiologic studies, the authors also found an inverse association between dietary GL/GI and HDL levels.

Measuring dietary GL in mixed meals presents another methodologic challenge. A major concern has been the relevance of the GI values of individual foods to glucose and insulin responses to mixed meals. However, strong correlations have been found between observed GI values of mixed meals and calculated values based on individual component foods (10). In epidemiologic studies, GL measures a dietary pattern characterized by higher intakes of refined carbohydrates and added sugar rather than absolute glycemic effects of a diet.

In both Beulens et al. (9) and the NHS (8), the greater impact of GL on CVD in overweight and obese people suggests that adverse effects of dietary GL may be further aggravated by underlying insulin resistance. Because two-thirds of Americans are overweight or obese, these findings have important public health and clinical implications. In the past several decades, the increase in dietary GL has been proportional to the decrease of dietary fat as a percentage of energy intake. This trend, together with the obesity epidemic, creates ideal conditions for the development of cardiometabolic disorders. For this reason, reducing dietary GL should be made a top public health priority.

Several dietary strategies can be used to reduce GL. These include replacing carbohydrates (especially refined grains and sugar) with unsaturated fats and/or protein or exchanging whole grains for refined ones. A combination of these approaches may increase benefits and adherence. The types or sources of fat and protein used to replace carbohydrates are as important as the amounts consumed. A recent comparison of a low-carbohydrate diet high in vegetable fat and vegetable protein and a low-fat, high-carbohydrate diet showed that the former was associated with a significantly lower risk of CHD during 20 years of follow-up in the NHS (11). In the NHS, most of the vegetable fat came from vegetable oil (e.g., soybean, corn, and canola oils), olive oil, mayonnaise, peanut butter, and nuts. Most of the vegetable protein came from whole-grain foods (e.g., dark bread and cold cereals), legumes (e.g., beans and peas), peanut butter, and nuts. Benefits of the plant-based low-carbohydrate diet on CHD are likely to stem from the vegetable fat and protein as well as the reduced GL in the dietary pattern.

Another important way to reduce GL is to restrict consumption of sugar-sweetened beverages, which account for nearly 50% of added sugar and 8% of total energy intake in the U.S. diet (12). Between 1977 and 2001, consumption of sugar-sweetened soft drinks increased by 135%. These beverages, particularly soda, provide little nutritional benefit. They do, however, cause weight gain and likely increase the risk of diabetes, fractures, and dental caries. Thus, regular consumption of sugar-sweetened beverages should be strongly discouraged.

It is clear that the initial diet-heart hypothesis relating total and saturated fat to CHD is overly simplistic and that sound nutritional guidelines must take into account different types of fats and carbohydrates as well as several other aspects of diet, some more easily modified than intake of dietary fat. Because multiple lines of evidence implicate high GL in adverse metabolic effects that increase risk of diabetes and CVD, it is time to shift the diet-heart paradigm away from restricted fat intake and toward reduced GL. This change can help prevent CVD and improve overall health, and, as such, should be considered a public health priority.

Reprint requests and correspondence: Dr. Frank B. Hu, Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, Massachusetts 02115. E-mail: frank.hu@channing.harvard.edu.

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