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Diet and Health: What Should We Eat?

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Many recent studies have implicated dietary factors in the cause and prevention of important diseases, including cancer, coronary heart disease, birth defects, and cataracts. There is strong evidence that vegetables and fruits protect against these diseases; however, the active constituents are incompletely identified. Whether fat per se is a major cause of disease is a question still under debate, although saturated and partially hydrogenated fats probably increase the risk of coronary heart disease. One clear conclusion from existing epidemiologic evidence is that many individuals in the United States have suboptimal diets and that the potential for disease prevention by improved nutrition is substantial.

For years, the Recommended Dietary Allowances (RDAs) served as nutritional guidelines for individuals and institutions (*1*). The original guidelines, aimed primarily at prevention of clinical deficiencies, were later supplemented with recommendations to reduce dietary fat and cholesterol. In recent years, attention has focused on the health effects of diet in the absence of overt clinical deficiency. Specific dietary factors have been associated with the cause or prevention of conditions as diverse as cancer, coronary heart disease, birth defects, and cataracts. The National Research Council (NRC) (*2*) examined broadly the relation between diet and health and in 1989 issued new recommendations (Table 1). Here I review subsequent findings and examine the current strength of support for the NRC recommendations.

Sources of Evidence

Historically, animal experiments and small studies of human metabolism have formed the basis of dietary recommendations. The need for epidemiologic studies became apparent with interest in the effects of diet on the incidence of chronic diseases that develop over decades. Initial analyses highlighted the large differences in diet and disease rates among various populations, but were limited because factors other than diet also vary across cultures. Case-control studies have been used to examine the relation between diet and disease in more detail; in such studies, the diets of diseased subjects, assessed retrospectively by questionnaire, are compared with those of nondiseased controls. Prospective studies that use validated questionnaires as well as biochemical indicators of diet are now also contributing data on diet and disease risk (*3*). Although prospective studies are more costly because they typically involve years of follow-up and thousands of subjects, such studies are less subject to biases that arise from the retrospective reporting of diet or the effects of disease on biochemical measurements. Randomized trials can be used to evaluate micronutrient supplements; however, trials of dietary interventions can sometimes be problematic because of the need for sustained compliance of the participants over long time periods. The best dietary recommendations will be based on a synthesis of epidemiologic, metabolic, animal, and mechanistic data.

Dietary Fat and Coronary Heart Disease (CHD)

The NRC recommendation (*2*) to decrease total fat, saturated fat, and dietary cholesterol (see Table 1) is expected to decrease the incidence of CHD. The longstanding view of the relation between diet and CHD has rested heavily on the observation that serum cholesterol levels predict CHD risk. Thus, serum cholesterol has functioned as a surrogate marker of CHD risk in hundreds of metabolic studies, summarized as equations by Keys and Hegsted (*4*). Serum cholesterol levels increase with higher intake of saturated fats and cholesterol, decrease with higher intake of polyunsaturated fat, and are not influenced by monounsaturated fat. More recently, it has been shown that high-density lipoprotein (HDL) cholesterol is strongly and inversely related to CHD risk; thus, a better predictor of risk is the ratio of total cholesterol to HDL (*5*). Substitution of carbohydrate for saturated fat in the diet [the basis of the American Heart Association (AHA) diets] tends to reduce the serum level of HDL as well as total and low-density lipoprotein (LDL) cholesterol (*6*, *7*). Thus, the reduction in CHD risk may be less than predicted by the effect of saturated fat on the level of total cholesterol in the serum. In contrast, substitution of monounsaturated or polyunsaturated fat for saturated fat reduces LDL levels without appreciably lowering HDL levels (*6*, *7*). In addition, monounsaturated fats reduce the levels of blood sugar and triglycerides in adult-onset diabetics (*8*). Some investigators have questioned whether the reductions in HDL levels that result from low-fat diets increase CHD risk (*9*). Although this question is difficult to address directly, it is clear that other factors that influence HDL levels, including alcohol, estrogens, obesity, smoking, exercise, and medications, do indeed alter CHD risk in the direction predicted by their effects on HDL levels (*10*).

The use of the usual cholesterol prediction equations (*4*) has been further complicated by the recognition that different saturated fats and dietary sources of saturated fat vary in their influence on LDL levels: Butter and other dairy fats (high in 14:0, myristic acid) strongly increase LDL levels,

Table 1. Summary of National Research Council recommendations (*2*).

1. Reduce total fat intake to 30% or less of calories. Reduce saturated fatty acid intake to less than 10% of calories and the intake of cholesterol to less than 300 mg daily.
2. Every day eat five or more servings of a combination of vegetables and fruits, especially green and yellow vegetables and citrus fruits. Also, increase starches and other complex carbohydrates by eating six or more daily servings of a combination of breads, cereals, and legumes.
3. Maintain protein intake at moderate levels.
4. Balance food intake and physical activity to maintain appropriate body weight.
5. Alcohol consumption is not recommended. For those who drink alcoholic beverages, limit consumption to the equivalent of 1 ounce of pure alcohol in a single day.
6. Limit total daily intake of salt to 6 g or less.
7. Maintain adequate calcium intake.
8. Avoid taking dietary supplements in excess of the RDA in any one day.
9. Maintain an optimal intake of fluoride, particularly during the years of primary and secondary tooth formation and growth.

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beef fat (containing palmitic acid, 16:0, and stearic acid, 18:0) increases LDL levels to a lesser degree, and cocoa butter (containing largely stearic acid) increases LDL levels only slightly (*7, 11*).

The optimal amount of polyunsaturated fat intake in the diet remains uncertain. When the effects of polyunsaturated fat on blood lipids are the primary consideration (*4, 7*), it appears that intakes should be maximized; thus, the AHA has recommended intakes of 10% of energy (compared with U.S. averages of ~3% in the 1950s and ~6% at present). However, concerns have arisen because high intakes of N-6 polyunsaturated fat (usually as corn oil) promote tumors in some, but not all, animal models (*12, 13*) and might promote coronary thrombosis by competing with N-3 fatty acids (*14*). On the other hand, in monkeys the threshold for ventricular arrhythmias is increased by a diet high in N-6 polyunsaturated fat, suggesting that this diet may reduce the incidence of sudden deaths (*15*).

Evidence relating diet directly to heart disease (as opposed to blood lipid levels) is sparse. In a study of diet and CHD in seven countries (*16*), total fat intake showed little association with rates of CHD; indeed, the lowest rate was in Crete, which had the highest fat intake because of the large consumption of olive oil. In the same study, rates of CHD were highest in countries with the greatest intake of saturated fat. However, little association has been seen between saturated fat intake and CHD in prospective studies (*3, 17*), although these studies have not been sufficiently large or rigorous to exclude a modest relation. These studies do support a modest adverse effect of dietary cholesterol on CHD risk (*3, 17*). An inverse association with polyunsaturated fat was seen in one prospective study conducted in the 1950s when the average intake was low (*17*), but little association has been seen subsequently. Intervention trials of fat modification for prevention of CHD have yielded inconsistent results (*18–20*). In the one intervention trial that clearly reduced CHD mortality (Oslo), multiple components of the diet as well as weight and smoking habits were changed simultaneously. In the other trials that reduced CHD incidence (*19*), total fat intake was not substantially altered; instead, unsaturated fats were substituted for saturated fat.

High intake of N-3 fatty acids, found primarily in marine fish but also in some vegetable oils and plants, reduces platelet aggregability and prolongs bleeding time, slightly reduces blood pressure, decreases serum levels of triglycerides, and increases serum levels of LDL cholesterol (*14, 21*). Fish consumption was associated with a greatly reduced risk of CHD in one prospective study and in one randomized trial among patients with a previous infarction (*22*). However, other studies have not consistently supported an effect of fish consumption on risk of CHD (*23*).

Trans fatty acids are formed by the partial hydrogenation of liquid vegetable oils in the production of margarine and vegetable shortening and can account for as much as 40% of these fats. Intake of *trans* fatty acids from partially hydrogenated vegetable fats in the United States has increased from 0% in 1900 to ~5.5% of total fat in the 1960s and thus has closely paralleled the epidemic of CHD (*24*). In contrast, the intake of animal fat has steadily declined over this period. *Trans* fatty acids reduce serum levels of HDL and increase the levels of LDL and lipoprotein (a), another lipid fraction positively associated with CHD risk (*25*). Positive associations between intake of *trans* fatty acids and CHD have been seen in a prospective study of U.S. women, a case-control study of men and women, and among patients undergoing coronary arteriography (*26*).

Understanding the interrelations between dietary fats, blood lipids, and CHD risk has been further complicated by evidence that antioxidants may protect against atherosclerosis. Antioxidants such as vitamin E have been shown to block the oxidative modification of LDL, an important step in atherogenesis (*27*). Within Europe, countries with higher blood antioxidant levels have lower rates of CHD (*28*). Furthermore, in two recent prospective studies, men and women with the highest intake of vitamin E (mostly from supplements) had ~40% lower risk of myocardial infarction compared with those in the lowest intake group (*29*). The maximum reduction in risk was associated with vitamin E intakes of ≥100 international units per day—well above the levels achievable by diet alone. Liquid vegetable oils, particularly those that are minimally processed, are the primary source of vitamin E in our diets; thus, reduced intake of these oils could have adverse effects on CHD risk. Furthermore, LDL particles formed on a diet high in monounsaturated fat are relatively resistant to oxidation (*30*).

Dietary Fat and Cancer

A major justification for decreasing dietary fat has been the anticipated reductions in cancers of the breast, colon, and prostate (*2*). The primary support for the proposed link between dietary fat and cancer is that countries with low fat intake (also the less affluent nations) have had low rates of these cancers. These correlations with cancer have been seen primarily with animal fat and meat consumption rather than with vegetable fat consumption (*31, 32*).

The hypothesis that greater fat intake increases breast cancer risk is supported by many animal studies (*12*). However, much of the effect of dietary fat appears to be due to an increase in total energy intake, which profoundly increases mammary tumor incidence in animals (*12, 33*). Although an effect of dietary fat independent of energy intake has been seen in some animal models (*34*), no association was seen in a large study of animals that were not exposed to a tumor-inducing agent (*13*). In most human case-control studies, there has been little association observed between fat intake and breast cancer, although a weak positive association (relative risk ~1.07 for 40% as compared with 30% of energy from fat) was seen in the pooled data from 12 such studies (*35*). Data from six large prospective studies, collectively including ~3400 cases among ~280,000 women, have recently been published (*36*). In none of these studies was the risk of breast cancer significantly elevated among women with the highest fat intake, and the summary relative risk for the highest as compared with the lowest category of dietary fat consumption was 1.03 (*37*). In the largest prospective study, no reduction in risk was seen even with diets containing <25% of energy from fat. It should be noted that these studies focused on middle-aged women; the effect of fat intake early in life and the effect of much lower fat intake remain to be explored.

The large differences in breast cancer rates among various countries (approximately fivefold) are probably due to multiple factors that include reproductive patterns, physical activity, adiposity, alcohol intake, and use of exogenous estrogen (*38*). There is also indirect evidence that restricted growth rates that result from limited intake of energy (and possibly other essential nutrients) decrease breast cancer incidence in humans as well as animals. Adult height, in part a marker of early energy balance, is positively associated with breast cancer rates internationally and in many case-control and cohort studies (*39*). The effect of energy balance is mediated in part through delayed ovulation; greater childhood weight gain lowers the age at menstruation, which in turn increases risk of breast cancer (*40*). In rural China, where breast cancer rates remain low, age at menarche still is ~18 years (*41*).

Positive associations between animal (but not vegetable) fat consumption and colon cancer incidence have been seen in many, but not all, studies (*32, 42, 43*). A positive association has also been noted between animal fat consumption and the development of adenomatous polyps (precancerous lesions) in the colon (*44*). How-

ever, in some studies colon cancer has been linked more strongly with red meat consumption than with fat consumption (*43*), suggesting that other components of red meat such as heat-induced carcinogens or readily available iron may be responsible (*45*).

Like breast and colon cancer, prostate cancer occurs most frequently in affluent countries (*31, 32*). There are few detailed epidemiologic studies; in subsets of several case-control studies, men with prostate cancer reported higher fat intake than did controls (*46*). In a recent prospective study, a positive association was seen between intake of alpha-linolenic acid, primarily attributable to consumption of fat from red meat (*47*).

Dietary Fat and Body Fatness

Obesity is an important cause of morbidity and mortality, and short-term studies have suggested that reducing dietary fat can result in weight loss (*48*). However, population differences in weight are not explained primarily by fat intake. For example, Southern European countries have a lower fat intake than Northern European countries, but nevertheless have higher rates of obesity (*49*). Similarly, among 65 counties in China, where fat intake ranged to as low as ~5% of energy, there is no correlation with body weight (*41*). Inconsistent associations have been observed in cross-sectional and prospective studies within countries, but such observations are particularly prone to distortion because subjects may alter their diets on account of their weight. In randomized trials of fat reduction, the optimal way to study this relation, moderate weight reductions are typically seen early in the trial. However, in trials lasting 1 year or longer, reductions in fat to as low as 15% of energy had little effect on long-term body weight or composition (*50*). Very low fat intakes (<10% of energy) in conjunction with a high volume of bulky food may induce weight loss, but long-term studies are needed.

An Interpretation of Available Data on Dietary Fat

In light of the evidence discussed above, several conclusions can be drawn. Intake of partially hydrogenated vegetable fats and saturated fats, particularly those from dairy sources, should be minimized. Definitive data are not available on the optimal intake of polyunsaturated and monounsaturated fats, but the metabolic data as well as the experience of Southern European populations suggest that consumption of a substantial proportion of energy as monounsaturated fat would not be harmful and might even be beneficial. The available evidence suggests that reductions in dietary fat composition over the ranges currently recommended are not likely to have a substantial, sustained effect on body fatness. The recommended moderate reduction in dietary fat (*2*) is likely to have little effect on breast cancer risk, although decreases in red meat intake may well reduce the incidence of colon cancer. A decrease in saturated fat intake that reduces total fat from 37 to 30% of energy has been estimated to reduce mortality in the United States by only 2% (*51*). Indeed, this is likely to be overly optimistic, as the calculations did not account for reductions in HDL and assumed major causal associations between saturated fat intake and breast cancer.

Vegetables and Fruits

Recommendations to eat a generous amount of vegetables and fruits (*2*) are supported by a wealth of epidemiologic data, primarily relating to cancer incidence. In more than 200 case-control or cohort studies, persons consuming higher amounts of these foods or having higher levels of carotenoids in their blood were less prone to develop various cancers (*52, 53*). There is strong evidence for an inverse relation between vegetable and fruit intake and lung cancer (*52–54*), which has led to the suggestion that beta-carotene might be a protective factor (*55*). This hypothesis is supported by inverse associations between carrot intake and lung cancer risk in multiple studies (*56*), but most studies have not been sufficiently comprehensive to distinguish with confidence an effect of beta-carotene from that of other nutrients. Intake of vegetables and fruits has also been related to lower risk of stomach cancer in many case-control studies (*52, 53*); both the epidemiologic evidence and mechanistic studies (*57*) suggest a protective role for vitamin C. Vegetable and fruit consumption has also been inversely related to risk of colon cancer (*52, 53*). This relation has been attributed to intake of dietary fiber, but recent evidence suggests that folic acid might also account for the reduced risk (*58*). Although the studies are fewer, an inverse association with vegetable and fruit intake has also been noted for cancers of the oral cavity, larynx, pancreas, bladder, and cervix (*52, 53*). In a large prospective study, breast cancer incidence was about 25% higher among women with a low intake of vegetables (*59*).

In addition to the micronutrients noted above, plants contain numerous constituents that have potential anticancer activity (*53*); such chemicals could block the formation of carcinogens, induce detoxifying enzymes, and antagonize the effects of endogenous estrogens. Although the epidemiologic data on cancer provide solid support for recommendations to consume an abundance of vegetables and fruits, more study is needed for precise recommendations about the types and amounts of these foods.

In more limited studies, fiber intake has been associated with a decreased risk of CHD (*3, 60*), but the possibility that this association is due to other factors in plants has not been explored. Elevated serum levels of homocysteine constitute an independent risk factor for CHD; these levels can be reduced by higher intakes of folic acid and vitamin B-6 (*61*), which suggests another mechanism for the association. Vegetarians and nonvegetarians with a high intake of fruits and vegetables have reduced blood pressure (*62*), but the factor responsible remains unclear.

Suboptimal intake of folic acid, a nutrient obtained mainly from vegetables and fruits, clearly increases risk of neural tube defects, the most common severe birth defect (*63*), and may account for more than 50% of these cases. In both case-control and prospective studies (*64*), dietary antioxidants, including carotenoids and vitamin C, have been inversely associated with risk of cataracts, presumably because they reduce the accumulation of oxidized and denatured proteins in the lens.

Starches and Complex Carbohydrates

An increase in dietary carbohydrate, primarily in the form of starches and complex carbohydrate, has been recommended to replace dietary fat (*2*). Whole grain products, as opposed to highly refined carbohydrates, may help to reduce the risk of colon cancer, although this has been difficult to demonstrate epidemiologically (*47, 65*). Nevertheless, reduced constipation and risk of colonic diverticular disease (*66*) are clear benefits of higher fiber intake. The role of soluble fiber, found in oat bran and some other plants, in lowering blood cholesterol levels has been debated; recent evidence suggests that these levels are slightly reduced with large intakes of fiber (*67*).

The importance of micronutrients in the prevention of chronic diseases has reemphasized the problem of "empty calories" associated with diets high in sugar and highly refined grains. In the standard milling of white flour, as much as 60 to 90% of vitamins B-6 and E, folate, and other nutrients are lost (*68*); this loss may be nutritionally critical for persons with otherwise marginal intakes. Thiamin, riboflavin, and niacin are presently replaced by fortification, and folate may also be added soon for prevention of neural tube defects. Other nutrients lost during the

milling process are not being replaced, however. In addition to displacing nutrient-bearing foods, high intake of sugar promotes tooth decay.

Protein

The average protein consumption in the United States substantially exceeds requirements (2), and adequate intake can be maintained on most reasonable diets, including those without animal products. Animal protein increases urinary calcium loss, contributes to homocysteinemia, and has been hypothesized to increase the risk of various cancers (69, 70); however, evidence for the latter effect is limited.

Calcium and Dairy Products

Recommendations in the NRC report to "maintain adequate calcium intake" (2) (generally considered to be ~800 mg per day for most healthy adults) and to consume dairy products on a daily basis (71) reflect the importance of this mineral in maintaining bone strength. Although calcium supplements (in conjunction with vitamin D) have reduced fracture incidence in older adults (72), the optimal intake levels remain uncertain. Intakes as high as 1500 mg per day, which are difficult to achieve without supplements, have been suggested for older women at risk of fractures (73). However, adult populations with low fracture rates generally consume few dairy products and have low calcium intakes (74). Milk and other dairy products may not be directly equivalent to calcium from supplements, as these foods contain a substantial amount of protein, which can enhance renal calcium losses (69); few studies have directly addressed the relation between dairy product consumption and fracture incidence.

Inverse associations have been observed between calcium intake and blood pressure, but intervention trials of calcium supplementation suggest the benefit is small at most (75). Low calcium intake has been associated with risk of colon cancer, but the evidence has not been consistent (76).

Although recommended calcium intakes can be achieved by a high intake of greens and certain other vegetables, greatly increased intakes would be required for most women to achieve these levels without regular use of milk and other dairy products. Calcium supplements can effectively reduce bone loss and are inexpensive; thus, dairy products can be considered an optional rather than a necessary dietary component for adults.

Translation of Evidence to Eating Patterns

The dietary pyramid recently released by the U.S. Department of Agriculture attempts to translate current nutritional knowledge to a recommended eating pattern in terms of food groups (Fig. 1). Inevitably, such a document represents a mix of well-supported findings, educated guesses, and political compromises with powerful economic interests such as the dairy and meat industries. The Mediterranean and Asian diets have attracted considerable attention as alternatives because of the extremely low rates of CHD and long life expectancies in Greece, Southern Italy, and Japan (Table 2). Although nondietary factors are likely to contribute to longevity in these countries, the findings reviewed above support an important role of diet.

In the 1960s, before recent changes in food habits, the total fat content of the average diets in Greece and Japan was strikingly different; total fat accounted for ~40% of energy in the Greek diet and ~10% of energy in the Japanese diet (Table 3). However, both countries had low intakes of saturated and partially hydrogenated fat; olive oil, high in monounsaturates, was the primary fat in Greece and throughout the Mediterranean region. Apart from this great difference in dietary fat, the two traditional eating patterns had many similarities: Grains, legumes, and other vegetables formed the basic diet; red meat and eggs were consumed infrequently; and poultry and fish were eaten more often but not in large amounts (Table 3). Fruits were abundant in the Greek but not the Japanese diet. In both countries, alcohol was regularly consumed by men, less so by women. Regular physical activity, regular alcohol consumption by men, and low

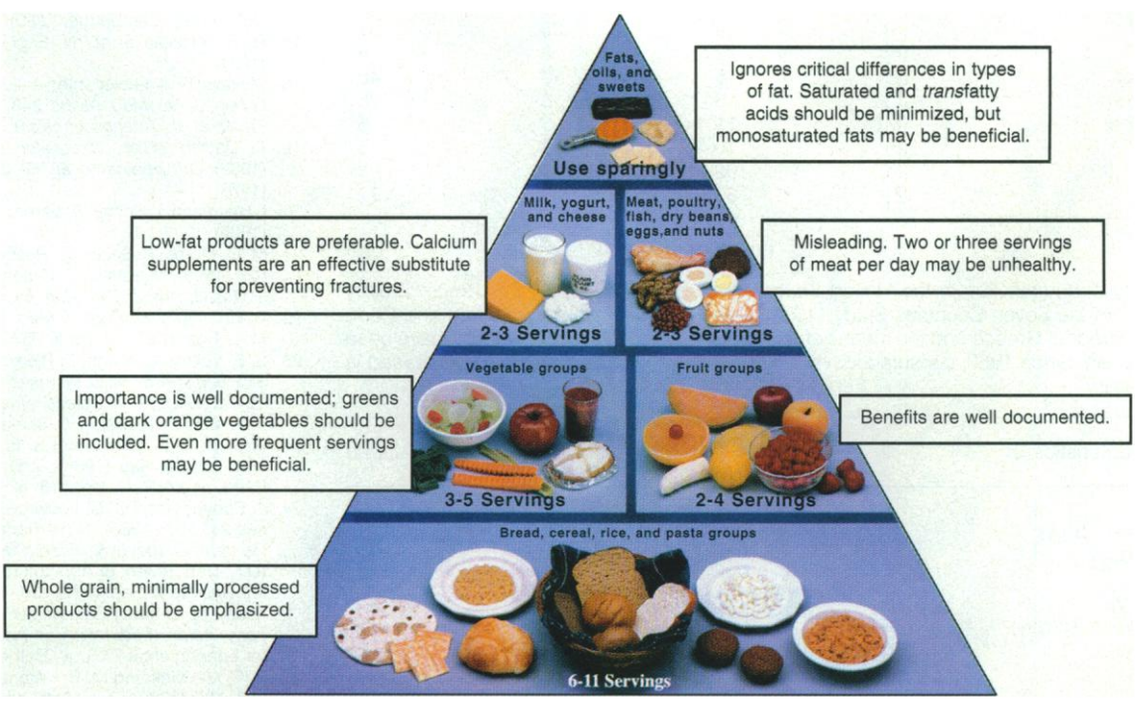

Fig. 1. Annotated version of the U.S. Department of Agriculture food pyramid, indicating the recommended daily servings of various food groups. Annotations (boxes) were added to summarize issues addressed in this review. Optimal food intakes for children and pregnant or lactating women may need further consideration. [Modified figure reproduced with permission of Nasco Nutrition Teaching Aids, Fort Atkinson, Wisconsin]

rates of smoking (now very high) likely contributed to the low rates of CHD in both Greece and Japan. However, the form of dietary fat, low intakes of meat, and generous intake of vegetables were almost certainly important as well. In Greece, the rates of virtually all cardiovascular diseases and cancers were remarkably low (except liver cancer, which is largely viral in origin), providing compelling evidence for, at a minimum, the long-term safety of this diet. In Japan, however, rates of hemorrhagic stroke were elevated, and cancers of the stomach as well as liver were so high that total cancer incidence was similar to that in the United States, suggesting that some aspects of that traditional diet may have been hazardous. The high rates of hemorrhagic stroke are of particular concern because the low serum cholesterol levels characteristic of Japan have been associated with this devastating condition within both Japan and the United States (*77*). This observation raises the question of whether very low fat intake over a lifetime may in fact have adverse effects. The high frequency of stomach cancer is likely to be explained in part by high intake of salt, low intake of fresh fruits, and perhaps by *Helicobacter pylori* infection (*78*), but other dietary factors may have also contributed.

The U.S. food industry is responding rapidly to widespread concerns about diet and health, primarily with an array of new low-fat products. However, many of these products have substituted the fat with sugar, diglycerides (which do not count as fat on food labels), artificial sweeteners, and sucrose polyesters. In addition, there has been an increase in consumption of lean meat. The long-term health effects of these changes are unclear and in some cases could be adverse. Although much remains to be learned, most epidemiological data suggest that optimal health can be achieved from a diet that emphasizes a generous intake of vegetables and fruit. Such plant-enriched diets, as embodied by other cultures, can be not only healthy, but interesting and enjoyable as well.

Table 2. Life expectancy and disease rates in the United States, Greece, and Japan in the 1960s. Standardized mortality rates are per 100,000 people, ages 0 to 64. Since the 1960s, the rates of stroke and stomach cancer have greatly decreased in Japan, so that life expectancy is now greatest in that country, followed by Greece. For males (M) and females (F), life expectancies at age 45 in 1989 to 1991 were 33.3 and 39.1 years for Japan, 32.4 and 36.5 years for Greece, and 30.8 and 36.1 years for the United States (*79*).

Life expectancy and disease rates		United States	Greece	Japan
Life expectancy at age 45 (years)	(M)	27	31	27
	(F)	33	34	32
Coronary heart disease	(M)	189	33	34
	(F)	54	14	21
Cerebrovascular diseases	(M)	30	26	102
	(F)	24	23	57
Breast cancer	(F)	22	8	4
Stomach cancer	(M)	6	10	48
	(F)	3	6	26
Colorectal cancer	(M)	11	3	5
	(F)	10	3	5
Total cancers	(M)	102	83	98
	(F)	87	61	77

Table 3. Dietary characteristics in the United States, Greece, and Japan in the 1960s. Dietary information is from the Seven Countries Study (*16, 80*). The means of data from Crete and Corfu have been averaged for Greece and the means of data from Tanushimaru and Ushibuka have been averaged for Japan. Since 1960, consumption of red meat and animal fat has greatly increased in Greece and Japan.

Dietary characteristics	United States	Greece	Japan
Fat (% energy)	39	37	11
Saturated fat (% energy)	18	8	3
Vegetables (g/day)	171	191	198
Fruits (g/day)	233	463	34
Legumes (g/day)	1	30	91
Breads and cereals (g/day)	123	453	481
Potatoes (g/day)	124	170	65
Meat* (g/day)	273	35	8
Fish (g/day)	3	39	150
Eggs (g/day)	40	15	29
Alcohol (g/day)	6	23	22

*Includes poultry.

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