Type 2 diabetes and the vegetarian diet[1–4]

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ABSTRACT Based on what is known of the components of plant-based diets and their effects from cohort studies, there is reason to believe that vegetarian diets would have advantages in the treatment of type 2 diabetes. At present there are few data on vegetarian diets in diabetes that do not in addition have weight loss or exercise components. Nevertheless, the use of whole-grain or traditionally processed cereals and legumes has been associated with improved glycemic control in both diabetic and insulin-resistant individuals. Long-term cohort studies have indicated that whole-grain consumption reduces the risk of both type 2 diabetes and cardiovascular disease. In addition, nuts (eg, almonds), viscous fibers (eg, fibers from oats and barley), soy proteins, and plant sterols, which may be part of the vegetarian diet, reduce serum lipids. In combination, these plant food components may have a very significant impact on cardiovascular disease, one of the major complications of diabetes. Furthermore, substituting soy or other vegetable proteins for animal protein may also decrease renal hyperfiltration, proteinuria, and renal acid load and in the long term reduce the risk of developing renal disease in type 2 diabetes. The vegetarian diet, therefore, contains a portfolio of natural products and food forms of benefit for both the carbohydrate and lipid abnormalities in diabetes. It is anticipated that their combined use in vegetarian diets will produce very significant metabolic advantages for the prevention and treatment of diabetes and its complications. *Am J Clin Nutr* 2003;78(suppl):610S–6S.

KEY WORDS Type 2 diabetes, plant foods, vegan and vegetarian diets, glycemic index, nuts, vegetable proteins, soy, plant sterols, fiber

DIABETES AND PLANT FOOD–BASED DIETS

There are few studies assessing the effects of a vegetarian diet in diabetes (1). Most of the studies involving plant foods, plant food components, or diets have been assessed for their ability to reduce blood lipids or other risk factors related to cardiovascular disease (CVD). Nevertheless, these attributes of diet are also very relevant to the treatment of diabetes because diabetes greatly increases the chance that an individual will suffer from CVD, possibly by 3–5-fold (2). Diabetes is a key factor in the predictive equations for CVD (3). It is therefore appropriate that dietary advice determined to be of use in the prevention and treatment of CVD should be considered as part of the advice for the prevention and treatment of diabetes. Thus, although an attempt will be made to discuss the effects of plant foods on glycemia, a large part of this discussion of the diabetic diet will deal with the role of plant foods in prevention of the major complications of diabetes, especially CVD.

Growth of interest in dietary fiber and its possible metabolic benefits in the prevention and treatment of chronic diseases, including diabetes, has been put forward as one of the reasons to include more plant foods in the diet (4). Notable are the early studies of Anderson using high-carbohydrate, high-fiber diets with initial carbohydrate contents of 70% and maintenance intakes of 60% (5). These diets resulted in improved glycemic control in type 2 diabetes, lower serum cholesterol levels, and no rise in serum triacylglycerol. Shortly after these studies, supportive data appeared from the Pritikin Institute (6, 7), where high-carbohydrate plant-based diets were emphasized together with exercise as part of the program for treatment of type 2 diabetic subjects. These studies demonstrated reductions in oral hypoglycemic agent use, together with improved blood glucose, cholesterol, and triacylglycerol levels, the latter 2 by 25% and 27%, respectively (6). These improvements tended to be maintained over the 2–3 y of follow-up (6). However, these studies were also confounded by exercise and weight loss, which has a major effect on all aspects of diabetes control (8). Confounding by weight loss has also existed in the majority of studies targeted more specifically at the use of vegetarian diets.

In assessing the overall impact of these very-low-fat (10% of energy) vegetarian diets, Barnard et al (9) reported their effects on 652 diabetic subjects. They showed that 39% of those treated with insulin (83 out of 212 subjects) could stop insulin and 71% of those on oral hypoglycemic agents (140 out of 197 subjects)

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could discontinue their use. At the same time, fasting blood glucose fell by 24% in those on diet alone at the start. In the whole group, serum cholesterol fell by over 20% and triacylglycerol by over 30%, while the fall in HDL was only half that seen in total cholesterol. Again, however, weight loss was significant: over 4 kg over the 26 d of the program. In the same year, Crane et al (10), using a vegan diet with daily exercise and weight loss (5 kg/25 d), showed similar metabolic advantages in type 2 diabetes together with complete relief of painful neuropathy in the legs within 2 wk in 81% (17 out of 21 subjects) of cases.

The only study to test the effect of a vegetarian (vegan) diet over a 12-wk period without a weight loss and exercise component showed a significantly greater weight loss on the vegan compared with the control diet of < 3 kg (1). Unexpectedly, despite weight loss, HDL cholesterol levels were reduced more on the vegan diet. On the positive side, fasting glucose levels were significantly lower on the vegan diet and, though not significant, 24-h microalbuminuria was reduced from baseline on the vegan diet but increased on the control diet. The lack of treatment difference in total cholesterol was surprising and contrasts markedly with the effect of plant-based diets on both normal and hypercholesterolemic subjects (11, 12).

In addition to diet trials, cohort studies have tended to support vegetarian diets or increased consumption of plant foods in the prevention of diabetes. In the Seventh-day Adventist Study cohort of 25 698 adults identified in 1960 and followed for 21 y, self-reported diabetes was lower in vegetarians than in nonvegetarians. The association with meat consumption was not confounded by body weight, other dietary factors, or exercise (13). A 20-y follow-up of a US cohort of 9665 adults aged 25–74 in which 1018 developed diabetes indicated that participants consuming 5 or more servings of fruits and vegetables daily compared with none had a relative risk for diabetes of 0.73 (CI: 0.54, 0.98) largely because of the beneficial effect on women, for whom the relative risk was 0.54 (CI: 0.36, 0.81) (14). Supporting data came from the Health Professionals study of 42 504 men aged 40–75 y where consumption of a "prudent" diet (fish, poultry, vegetables) versus a "Western" diet (red and processed meats and French fries) resulted in a relative risk of 0.84 (CI: 0.70, 1.00) in the 12-y follow-up; during those 12 y, 1321 new cases of diabetes were diagnosed (15). Finally, from the same study there is a recent report that supports the contention that processed meats may increase the incidence of diabetes, possibly through their nitrite content, with bacon showing the most significant trend (16).

There is therefore an urgent need for further assessments of the effects of plant-based diets in diabetes, especially in view of the benefits of such diets in nondiabetic subjects and the increasing recognition of the potential benefits of components of plant-based diets in both hyperlipidemia and diabetes. These components include dietary fiber, vegetable proteins, plant sterols, unsaturated vegetable oils, and slow-release carbohydrates (especially of cereal and legume origin).

METABOLIC BENEFITS OF PLANT FOOD COMPONENTS

Increased intake of fruits and vegetables has been endorsed as public health policy for a number of reasons. Displacement of saturated fat and increased intake of fiber have been seen as general reasons for increasing fruit and vegetable consumption. Increased fiber intake may improve glycemic control in diabetes (17). Fruits and vegetables in the highly successful Dietary Approaches to Stop Hypertension Trial (DASH) diet, together with increased calcium intake and salt restriction in a diet low in total fat and very low in saturated fat, produced marked effects similar to those of the initial dose of single drug therapy in reducing blood pressure (18). Fruits and vegetables as sources of alkali also reduced urinary calcium loss (19). Recently, a lower proportion of animal protein in the diet was associated with reduced hip fracture risk (20). Substitution of vegetable for animal protein may preserve renal function (21, 22). Nevertheless, it is for the reduction of cardiovascular risk that plant-based diets have attracted the most interest. Large cohort studies of vegetarians have shown that they have a reduced risk of CVD (23). Vegan diets have been associated with very low LDL cholesterol levels (11). Short-term studies have confirmed large reductions in LDL cholesterol of 25–30% in healthy subjects on vegan diets based on fruits, leafy vegetables, and nuts (12). Cereal fiber consumption has consistently been associated with reduction in risk of both CVD and diabetes (24–26). Total fiber intake has been associated with reduced lipid risk factors for coronary artery disease (CAD) in young people (27), and increased whole-grain intake appears not only to reduce the incidence of CAD and diabetes but also to reduce blood glucose, fasting insulin, and evidence of insulin resistance in obese, insulin-resistant subjects (28).

Blood lipids

Related to the reduction in the high CAD mortality seen in diabetes is the need for tight control of established risk factors. Blood lipids are one of the best-established risk factors, and plant foods have clearly recognized effects in the control of blood lipids.

Vegetarian diets and body weight

Perhaps one of the major benefits that a vegetarian diet may have in the treatment of diabetes is its effect in increasing satiety, possibly related to amino acid composition or the sheer bulk of the diet (29). Evidence for this is the "confounding" effect of weight loss in interpreting the results of vegetarian diets on diabetic patients in the previous section. The weight loss, far from being "confounding," may be one of the advantages of vegetarian diets. The paramount importance of body weight has been illustrated in recent studies where diet and lifestyle changes have prevented the development of diabetes in susceptible individuals (30).

Lipid-lowering plant food components

The US Food and Drug Administration (FDA) has approved health claims for cholesterol lowering for specific components of plant foods, many of which tend to be at higher intake levels in the diets of vegetarians and more particularly in the diets of vegans compared with the general population. These include viscous fibers from oats (β-glucans) (31) and psyllium (32), soy protein (33), and most recently plant sterols (34). Although these so-called functional food components have for the most part been tested in healthy or hyperlipidemic subjects, their use is very relevant to diabetes patients, who have a CAD risk 3–5 times greater than the nondiabetic population and for whom lipid-lowering medications are recommended even with a relatively small elevation in serum lipids—that is, LDL cholesterol above 3.35 mmol/L (> 130 mg/dL) (35).

The dietary components selected for FDA approval have all been well recognized for their cholesterol-lowering properties. Meta-analyses have suggested reductions in serum LDL cholesterol of 12.5% for 45 g soy protein/d (36); 6–7% for 9–10 g psyllium/d (37, 38), with smaller reductions for other viscous fibers (39); and 10% for 1–2 g plant sterol/d (40). These data come from studies often with background diets higher in saturated fat and cholesterol than current National Cholesterol Education Program (NCEP) recommendations (41–43). In studies of soy eaten in diets with lower intakes of saturated fat, in which subjects were in conformity with the NCEP dietary recommendations (44), smaller reductions in cholesterol of 4% for 52 g soy protein/d were seen (45). Similarly, plant sterols have also been shown to be less effective in diets lower in saturated fat and cholesterol (46).

On a theoretical basis, even if viscous fiber, soy protein, and plant sterols were additive only at the 5% level, in combination, a 15% or better reduction in cholesterol would be expected (47), which could be added to the 15–20% reduction reported with strict application of an NCEP Step 2 diet (48). Although again theoretical, this would result in a 30–35% reduction in serum cholesterol, equivalent to a therapeutic dose of the first-generation statins. Preliminary data in hyperlipidemic subjects have suggested that a 25–30% reduction in LDL cholesterol may be achieved by these means (49). Data are required in the treatment of diabetes, but there is reason to suppose that these plant food components may provide advantages for diabetic individuals that are similar to those seen in nondiabetic individuals (49).

Nuts

Nuts have traditionally been significant contributors to protein in the vegetarian diet. Nuts are also valuable sources of unsaturated fat, many (eg, almonds, hazelnuts) are excellent sources of monounsaturated fat, and walnuts contain n−3 fatty acids. Nuts' protein and associated phytochemicals may provide some of the same advantages as seen with soy, and inclusion of nuts in the diet has been shown to lower serum cholesterol in nondiabetic subjects (50–63).

A number of studies have been published on almonds with reductions of 15% in LDL cholesterol per 100 g/d (1% lowering for 7 g almonds/d) (50), 12% for 100 g/d (1% lowering for 8 g almonds/d) (52), and 10% for 84 g/d (1% lowering for 8 g almonds/d) (53). From data on other published nut studies, 1% reductions in LDL cholesterol for walnuts, pecans, peanuts (an oil seed legume), macadamias, and pistachios would be achieved with daily intakes of 4, 11, 4, 10, and 4 g, respectively (51, 54–61).

Dose-response studies have also been carried out with almonds confirming the 1% reduction in LDL cholesterol for every 7–10-g increase in almond intake (62, 63). It is also possible that nuts such as almonds may be of value as sources of monounsaturated fat, which some reports suggest improves glycemic control when substituted for carbohydrate in the diets of type 2 diabetic subjects (64).

Dietary fiber: glycemic and blood lipid effects

Dietary fiber is another potentially useful component of a vegetarian diet. Early studies with viscous fibers focused on cholesterol reduction (65–68). However, it soon became apparent that viscosity also related to a flattening of the postprandial glycemia (69) when viscous fibers were added to test meals of both nondiabetic (70) and diabetic subjects (68). Long-term addition of the viscous legume fiber guar gum to breads resulted in reduced urinary glucose losses (68). Further studies indicated similar effects for diets enriched with whole legumes (dried beans) (71). In none of these studies had Hb A_{1c} been measured. More recently, the viscous fiber psyllium has been used in the treatment of type 2 diabetes, with reductions in both blood lipids and day-long blood glucose but not Hb A_{1c} (72). The latest study to demonstrate benefits in type 2 diabetes involved a mixed high-fiber diet from cereals, fruits, and vegetables without a specific focus on viscosity. This study did not find a change in Hb A_{1c} over 6 wk but did find improvements in postprandial glycemia and blood lipids (17). However, when fiber-rich, low-glycemic-index foods were fed to type 1 diabetic patients for 24 wk, a fall in Hb A_{1c} was seen in compliant subjects (73).

The picture is much less clear with respect to wheat bran. Cohort studies—from the studies by Morris et al on Whitehall civil servants (24) to the assessments of the Nurses' Health Study, the Health Professionals Study, and the Iowa Women's Health study (74–79)—have repeatedly shown that wheat bran appears protective for the development of both diabetes and CVD.

Nevertheless, wheat bran at modest intake levels failed to make an impact on CVD in the Diet and Reinfarction Trial study (80). Furthermore, by and large wheat bran has little effect on serum lipids in healthy or hyperlipidemic volunteers (68), and although beneficial effects have been reported on carbohydrate tolerance in healthy volunteers (81) and diabetic subjects (82), no reductions in glycated proteins have been reported.

More recently, the picture has been clarified with demonstration that simple additions of wheat bran (equal to 20 g dietary fiber) to the diet of type 2 diabetic subjects made no difference over 3 mo to Hb A_{1c} concentrations (83). At the same time, studies of whole-grain cereals fed to insulin-resistant subjects appeared to improve insulin resistance parameters after a 6-wk feeding of whole-grain cereals as opposed to refined-cereal foods in the diet (84).

The issue of fiber and whole grains in the diet of the diabetic subject requires further study to determine whether these aspects of a vegetarian diet require emphasis in the treatment of diabetes.

Whole grains, legumes, and low-glycemic-index foods

Whole grains and legumes have also been staples in the diets of many vegetarians, both those living in traditional cultures and those who have adopted this lifestyle. These classes of foods processed in minimal or traditional ways may have a low glycemic index. Low-glycemic-index diets have attracted attention in terms of the prevention (85) and treatment of diabetes (86), with possibly beneficial effects on blood lipids and food intake regulation (87). Although the issue is being debated, the benefits of low-glycemic-index diets have also included higher HDL cholesterol levels (88), reduced CAD risk (89), and reduced risk of certain cancers associated with insulin resistance, namely, cancers of the colon (90) and breast (91). The low-glycemic-index components of a vegetarian diet may therefore be another potentially useful facet of foods in the prevention and treatment of type 2 diabetes.

The importance of slowing the rate of carbohydrate absorption has been illustrated recently by the results of the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) type 2 diabetes study, in which glucose-intolerant individuals had their risk of developing frank diabetes reduced by administration of acarbose, the α-glucosidase hydrolase inhibitor, which reduces the rate of carbohydrate digestion and absorption (92). There is a clear analogy here with the physiologic effect of viscous fibers and low-glycemic-index foods. These components of the vegetarian diet may therefore have the potential for similar effects of slowing carbohydrate absorption.

Nonlipid CAD risk factors: blood pressure and homocysteine

Plant food–based diets have the potential to reduce nonlipid risk factors for CVD. The success of the DASH diet—with its emphasis on increased fruit and vegetable consumption—in reducing blood pressure has already been mentioned (18). There is now a significant body of evidence to suggest that increased fruit and vegetable consumption in nondiabetic subjects protects from CVD (93–95). There has also been interest in the protein component of the diet and its effect on blood pressure. The DASH diet involves reduced meat consumption. Recent studies have focused on vegetable proteins; there is growing evidence that soy protein lowers blood pressure in both men and women (96–98). Other vegetable proteins remain to be tested. Indeed, studies involving the substitution of soy protein for animal protein in the diets of type 2 diabetic subjects have shown advantages in reducing not only lipids but serum homocysteine levels, possibly because of the lower sulfur amino acid content of the soy protein (99). Other plant proteins with lower sulfur amino acid content may have similar effects. At the same time, plant-based diets with high folate content will also contribute to the reduction in homocysteine levels as a possible risk factor for both CAD and stroke. This action, in addition to blood pressure control, provides another reason for their positive effect on cardiovascular health and therefore their potential importance in the diabetic diet.

Low-glycemic-index foods and glycemic control

The carbohydrate component of the diet is provided almost entirely by plant foods. When low-glycemic-index foods are selected, favorable effects may be seen on the blood lipid profile, as already discussed. The main interest in the glycemic index has been in relation to glycemic control, especially in type 2 diabetes. Selection of low-glycemic-index foods would be expected to allow increased consumption of carbohydrate to replace animal proteins and fat without compromising glycemic control in the postprandial period. Eleven studies where low-glycemic-index diets have been formally tested in type 2 as well as type 1 diabetes have now been reported in the literature. The conclusion of most (100, 101), though not all (102), analyses of these studies' data has been that there is an overall benefit in diabetes of consuming low-glycemic-index foods. Such foods include traditionally processed starchy foods such as pasta; parboiled rice; cracked wheat; and whole grain (pumpernickel) breads; legumes (peas, beans, and lentils); temperate climate fruits; and nuts. It is of interest that the foods that tend to reduce postprandial glycemia are also those that reduce blood lipids.

PLANT PROTEINS, SOY, AND RENAL DISEASE

Plant-based diets may be superior to traditional animal protein diets for prevention and treatment of diabetic kidney disease (22). Intake of meals rich in animal protein increases renal blood flow and glomerular filtration rates (GFR) in this order: beef, chicken, and fish. However, intake of equivalent amounts of soy protein does not appear to alter these renal parameters (103, 104). Two studies reported beneficial effects on renal function of diabetic individuals with proteinuria with changes from animal protein to vegetable protein diets. However, both studies had limitations in their clinical design and outcome measures and must be considered preliminary (105, 106).

Based on the available evidence, the soy protein hypothesis was developed: substitution of soy protein for animal protein in individuals with diabetic nephropathy would decrease hyperfiltration and glomerular hypertension with resultant protection from diabetic nephropathy (22). A recent study in individuals with type 1 diabetes provides support for this hypothesis. When 13 diabetic subjects with hyperfiltration (glomerular filtration rates $> 120\ \text{mL} \cdot \text{min}^{-1} \cdot 1.73\ \text{m}^{-2}$) incorporated 55 g soy protein daily into their diet and decreased animal protein intake, there was a significant reduction in GFR (107). Three of the subjects had microalbuminuria or albuminuria, and nonsignificant decreases in protein excretion were seen. Further studies are in progress to explore the effects of substitution of soy protein for animal protein in subjects with increased albuminuria.

IMPLICATIONS FOR FUTURE RESEARCH

Much work has been carried out on the effect of plant food components on blood lipids, and much still remains to be done, especially in studies where effective plant components are combined in the same diet to maximize the lipid-lowering outcome and provide an alternative to drug therapy (the "portfolio diet") (47). This concept provides an opportunity for useful new plant components to be incorporated into the diet as they are identified (108). Apart from glycemic index testing, very few studies, by comparison, have been carried out in diabetes to assess the effects of plant foods on glycemic control in the long term. These are needed before the most useful combination of components can be assembled in the same diet to maximize the effect on glycemic control. Furthermore, there is a need for studies to be carried out in diabetes using vegetarian diets where weight loss is not a study objective. In the case of all but one study so far (1), weight loss has been an objective. However, this has not permitted an accurate assessment of the effect of the diet because of the potent effect of weight loss on glycemic control. Although weight loss in type 2 diabetes may be achieved in studies, it is not part of the natural history of this disease. It is therefore important to test diets in the same situation in which most type 2 diabetes subjects find themselves—at best, weight maintenance.

CONCLUSION

There have been no major studies in the absence of weight loss that have attempted to determine the potential advantages of a vegetarian or vegan diet in the treatment of diabetes. However, there are many facets or components of a plant-based diet that might confer benefits on glycemia and, more specifically, on blood lipids. Traditionally processed cereals and legumes have a low glycemic index, and whole-grain cereals appear to reduce the risk of developing diabetes. Serum lipid abnormalities are an increasing concern and reason for medication use in diabetes and may be improved by viscous fibers, soy, and other vegetable proteins and plant sterols. Nuts are also increasingly seen as useful in improving the blood lipid profile. There is therefore good reason to expect that all these factors combined as a dietary portfolio in the treatment of diabetes will have significant metabolic benefits when formally tested in the future.

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REFERENCES

1. Nicholson AS, Sklar M, Barnard ND, Gore S, Sullivan R, Browning S. Toward improved management of NIDDM: a randomized, controlled,

pilot intervention using a low fat, vegetarian diet. Prev Med 1999;29: 87–91.
2. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993;16: 434–44.
3. Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile: a statement for health professionals. Circulation 1991;83:356–62.
4. Trowell H. Diabetes mellitus and dietary fiber of starchy foods. Am J Clin Nutr 1978;31(suppl):S53–7.
5. Anderson JW. High carbohydrate, high fiber diets for patients with diabetes. Adv Exp Med Biol 1979;119:263–73.
6. Barnard RJ, Massey MR, Cherny S, O'Brien LT, Pritikin N. Long-term use of a high-complex-carbohydrate, high-fiber, low-fat diet and exercise in the treatment of NIDDM patients. Diabetes Care 1983;6: 268–73.
7. Barnard RJ, Lattimore L, Holly RG, Cherny S, Pritikin N. Response of non-insulin-dependent diabetic patients to an intensive program of diet and exercise. Diabetes Care 1982;5:370–4.
8. Anderson JW, Konz EC, Jenkins DJ. Health advantages and disadvantages of weight-reducing diets: a computer analysis and critical review. J Am Coll Nutr 2000;19:578–90.
9. Barnard RJ, Jung T, Inkeles SB. Diet and exercise in the treatment of NIDDM: the need for early emphasis. Diabetes Care 1994;17: 1469–72.
10. Crane MG, Sample C. Regression of diabetic neuropathy with total vegetarian (vegan) diet. J Nutr Med 1994;4:431–9.
11. Sacks FM, Ornish D, Rosner B, McLanahan S, Castelli WP, Kass EH. Plasma lipoprotein levels in vegetarians: the effect of ingestion of fats from dairy products. JAMA 1985;254:1337–41.
12. Jenkins DJ, Kendall CW, Popovich DG, et al. Effect of a very-high-fiber vegetable, fruit, and nut diet on serum lipids and colonic function. Metabolism 2001;50:494–503.
13. Snowdon DA, Phillips RL. Does a vegetarian diet reduce the occurrence of diabetes? Am J Public Health 1985;75:507–12.
14. Ford ES, Mokdad AH. Fruit and vegetable consumption and diabetes mellitus incidence among U.S. adults. Prev Med 2001;32:33–9.
15. van Dam RM, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. Ann Intern Med 2002;136:201–9.
16. van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. Diabetes Care 2002;25:417–24.
17. Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med 2000;342:1392–8.
18. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3–10.
19. Sebastian A, Harris ST, Ottaway JH, Todd KM, Morris RC Jr. Improved mineral balance and skeletal metabolism in postmenopausal women treated with potassium bicarbonate. N Engl J Med 1994;330:1776–81.
20. Sellmeyer DE, Stone KL, Sebastian A, Cummings SR. A high ratio of dietary animal to vegetable protein increases the rate of bone loss and the risk of fracture in postmenopausal women. Study of Osteoporotic Fractures Research Group. Am J Clin Nutr 2001;73:118–22.
21. Anderson JW, Smith BM, Washnock CS. Cardiovascular and renal benefits of dry bean and soybean intake. Am J Clin Nutr 1999; 70(suppl):464S–74S.
22. Anderson JW, Blake JE, Turner J, Smith BM. Effects of soy protein on renal function and proteinuria in patients with type 2 diabetes. Am J Clin Nutr 1998;68(suppl):1347S–53S.
23. Key TJ, Fraser GE, Thorogood M, et al. Mortality in vegetarians and non-vegetarians: a collaborative analysis of 8300 deaths among 76,000 men and women in five prospective studies. Public Health Nutr 1998;1:33–41.
24. Morris JN, Marr JW, Clayton DG. Diet and heart: a postscript. Br Med J 1977;2:1307–14.
25. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545–50.
26. Liu S, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr 2000;71:1455–61.
27. Ludwig DS, Pereira MA, Kroenke CH, et al. Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. JAMA 1999;282:1539–46.
28. Pereira MA, Jacobs DR Jr, Pins JJ, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. Am J Clin Nutr 2002;75:848–55.
29. Rolls BJ, Fedoroff IC, Guthrie JF, Laster LJ. Foods with different satiating effects in humans. Appetite 1990;15:115–26.
30. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403.
31. US Food and Drug Administration. Food labeling: health claims; soluble fiber from whole oats and risk of coronary heart disease. Washington, DC: US Food and Drug Administration, 2001:15343–4. (Docket no. 95P-0197.)
32. US Food and Drug Administration. Food labeling: health claims; soluble fiber from certain foods and coronary heart disease. Washington, DC: US Food and Drug Administration, 1998. (Docket no. 96P-0338.)
33. US Food and Drug Administration. Food labeling: health claims; soy protein and coronary heart disease. Final rule. Fed Regist 1999:64; 57700–33.
34. US Food and Drug Administration. FDA authorizes new coronary heart disease health claim for plant sterol and plant stanol esters. Washington, DC: US Food and Drug Administration, 2000. (Docket nos. 00P-1275 and 00P-1276.)
35. American Diabetes Association. Management of dyslipidemia in adults with diabetes. Diabetes Care 2000;23(suppl):S57–60.
36. Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. N Engl J Med 1995;333: 276–82.
37. Olson BH, Anderson SM, Becker MP, et al. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: results of a meta-analysis. J Nutr 1997;127:1973–80.
38. Anderson JW, Allgood LD, Lawrence A, et al. Cholesterol-lowering effects of psyllium intake adjunctive to diet therapy in men and women with hypercholesterolemia: meta-analysis of 8 controlled trials. Am J Clin Nutr 2000;71:472–9.
39. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am J Clin Nutr 1999;69:30–42.
40. Law M. Plant sterol and stanol margarines and health. BMJ 2000; 320:861–4.
41. Miettinen TA, Puska P, Gylling H, Vanhanen H, Vartiainen E. Reduction of serum cholesterol with sitostanol-ester margarine in a mildly hypercholesterolemic population. N Engl J Med 1995;333:1308–12.
42. Jones PJ, Ntanios FY, Raeini-Sarjaz M, Vanstone CA. Cholesterol-lowering efficacy of a sitostanol-containing phytosterol mixture with a prudent diet in hyperlipidemic men. Am J Clin Nutr 1999;69: 1144–50.
43. Sirtori CR, Agradi E, Conti F, Mantero O, Gatti E. Soybean-protein diet in the treatment of type-II hyperlipoproteinaemia. Lancet 1977; 1:275–7.
44. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on

Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–97.
45. Jenkins DJ, Kendall CW, Jackson CJ, et al. Effects of high- and low-isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. Am J Clin Nutr 2002;76:365–72.
46. Raeini-Sarjaz M, Ntanios FY, Vanstone CA, Jones PJ. No changes in serum fat-soluble vitamin and carotenoid concentrations with the intake of plant sterol/stanol esters in the context of a controlled diet. Metabolism 2002;51:652–6.
47. Jenkins DJ, Kendall CW, Vuksan V. Viscous fibers, health claims, and strategies to reduce cardiovascular disease risk. Am J Clin Nutr 2000; 71:401–2.
48. Schaefer EJ, Lamon-Fava S, Ausman LM, et al. Individual variability in lipoprotein cholesterol response to National Cholesterol Education Program Step 2 diets. Am J Clin Nutr 1997;65:823–30.
49. Jenkins DJ, Kendall CW, Faulkner D, et al. A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins, and viscous fibers in hypercholesterolemia. Metabolism 2002;51:1596–604.
50. Spiller GA, Jenkins DA, Bosello O, Gates JE, Cragen LN, Bruce B. Nuts and plasma lipids: an almond-based diet lowers LDL-C while preserving HDL-C. J Am Coll Nutr 1998;17:285–90.
51. Zambon D, Sabate J, Munoz S, et al. Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women: a randomized crossover trial. Ann Intern Med 2000;132:538–46.
52. Spiller GA, Jenkins DJ, Cragen LN, et al. Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins. J Am Coll Nutr 1992;11:126–30.
53. Abbey M, Noakes M, Belling GB, Nestel PJ. Partial replacement of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol. Am J Clin Nutr 1994;59:995–9.
54. Almario RU, Vonghavaravat V, Wong R, Kasim-Karakas SE. Effects of walnut consumption on plasma fatty acids and lipoproteins in combined hyperlipidemia. Am J Clin Nutr 2001;74:72–9.
55. Curb JD, Wergowske G, Dobbs JC, et al. Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts. Arch Intern Med 2000;160:1154–8.
56. Kris-Etherton PM, Pearson TA, Wan Y, et al. High-monounsaturated fatty acid diets lower both plasma cholesterol and triaglycerol concentrations. Am J Clin Nutr 1999;70:1009–15.
57. Sabate J, Fraser GE, Burke K, et al. Effects of walnuts on serum lipid levels and blood pressure in normal men. N Engl J Med 1993; 328:603–7.
58. Edwards K, Kwaw I, Matud J, Kurtz I. Effect of pistachio nuts on serum lipid levels in patients with moderate hypercholesterolemia. J Am Coll Nutr 1999;18:229–32.
59. Morgan WA, Clayshulte BJ. Pecans lower low-density lipoprotein cholesterol in people with normal lipid levels. J Am Diet Assoc 2000; 100:312–8.
60. O'Byrne DJ, Knauft DA, Shireman RB. Low fat-monounsaturated rich diets containing high-oleic peanuts improve serum lipoprotein profiles. Lipids 1997;32:687–95.
61. Rajaram S, Burke K, Connell B, et al. A monounsaturated fatty acid-rich pecan-enriched diet favorably alters the serum lipid profile of healthy men and women. J Nutr 2001;131:2275–9.
62. Sabate J, Haddad E, Tanzman JS, Jambazian P, Rajaram S. Serum lipid response to the graduated enrichment of a Step I diet with almonds: a randomized feeding trial. Am J Clin Nutr 2003;77:1379–84.
63. Jenkins DJ, Kendall CW, Marchie A, et al. Dose response of almonds on coronary heart disease risk factors: blood lipids, oxidized low-density lipoproteins, lipoprotein(a), homocysteine, and pulmonary nitric oxide: a randomized, controlled, crossover trial. Circulation 2002; 106:1327–32.
64. Garg A, Bantle JP, Henry RR, et al. Effects of varying carbohydrate content of diet in patients with non-insulin-dependent diabetes mellitus. JAMA 1994;271:1421–8.
65. Fahrenbach MJ, Riccardi BA, Grant WC. Hypocholesterolemic activity of mucilaginous polysaccharides in White Leghorn cockerels. Proc Soc Exp Biol Med 1966;123:321–6.
66. Palmer GH, Dixon DG. Effect of pectin dose on serum cholesterol levels. Am J Clin Nutr 1966;18:437–42.
67. Jenkins DJ, Newton C, Leeds AR, Cummings JH. Effect of pectin, guar gum, and wheat fibre on serum-cholesterol. Lancet 1975;1:1116–7.
68. Jenkins DJ, Goff DV, Leeds AR, et al. Unabsorbable carbohydrates and diabetes: decreased post-prandial hyperglycaemia. Lancet 1976; 2:172–4.
69. Jenkins DJ, Wolever TM, Leeds AR, et al. Dietary fibres, fibre analogues, and glucose tolerance: importance of viscosity. Br Med J 1978;1:1392–4.
70. Jenkins DJ, Leeds AR, Gassull MA, et al. Decrease in postprandial insulin and glucose concentrations by guar and pectin. Ann Intern Med 1977;86:20–3.
71. Simpson HC, Simpson RW, Lousley S, et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. Lancet 1981;1:1–5.
72. Anderson JW, Allgood LD, Turner J, Oeltgen PR, Daggy BP. Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia. Am J Clin Nutr 1999;70:466–73.
73. Giacco R, Parillo M, Rivellese AA, et al. Long-term dietary treatment with increased amounts of fiber-rich low-glycemic index natural foods improves blood glucose control and reduces the number of hypoglycemic events in type 1 diabetic patients. Diabetes Care 2000; 23:1461–6.
74. Liu S, Stampfer MJ, Hu FB, et al. Whole-grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. Am J Clin Nutr 1999;70:412–9.
75. Liu S, Manson JE, Stampfer MJ, et al. A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women. Am J Public Health 2000;90:1409–15.
76. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545–50.
77. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921–30.
78. Wolk A, Manson JE, Stampfer MJ, et al. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. JAMA 1999;281:1998–2004.
79. Jacobs DR, Pereira MA, Meyer KA, Kushi LH. Fiber from whole grains, but not refined grains, is inversely associated with all-cause mortality in older women: the Iowa Women's Health Study. J Am Coll Nutr 2000;19:326S–30S.
80. Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). Lancet 1989;2:757–61.
81. Brodribb AJ, Humphreys DM. Diverticular disease: three studies, III: metabolic effect of bran in patients with diverticular disease. Br Med J 1976;1:428–30.
82. Bosello O, Ostuzzi R, Armellini F, Micciolo R, Scuro LA. Glucose tolerance and blood lipids in bran-fed patients with impaired glucose tolerance. Diabetes Care 1980;3:46–9.
83. Jenkins DJ, Kendall CW, Augustin LS, et al. Effect of wheat bran on glycemic control and risk factors for cardiovascular disease in type 2 diabetes. Diabetes Care 2002;25:1522–8.
84. Pereira MA, Jacobs DR Jr, Pins JJ, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. Am J Clin Nutr 2002;75:848–55.
85. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472–7.

86. Wolever TM, Miller JB. Sugars and blood glucose control. Am J Clin Nutr 1995;62(suppl):212S–21S.
87. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA 2002;287: 2414–23.
88. Ford ES, Liu S. Glycemic index and serum high-density lipoprotein cholesterol concentration among US adults. Arch Intern Med 2001; 161:572–6.
89. Liu S, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. Am J Clin Nutr 2000;71:1455–61.
90. Franceschi S, Dal Maso L, Augustin L, et al. Dietary glycemic load and colorectal cancer risk. Ann Oncol 2001;12:173–8.
91. Augustin LS, Dal Maso L, La Vecchia C, et al. Dietary glycemic index and glycemic load, and breast cancer risk: a case-control study. Ann Oncol 2001;12:1533–8.
92. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 2002;359:2072–7.
93. Joshipura KJ, Hu FB, Manson JE, et al. The effect of fruit and vegetable intake on risk for coronary heart disease. Ann Intern Med 2001; 134:1106–14.
94. Liu S, Manson JE, Lee IM, et al. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. Am J Clin Nutr 2000;72:922–8.
95. Bazzano LA, He J, Ogden LG, et al. Fruit and vegetable intake and risk of cardiovascular disease in US adults: the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Am J Clin Nutr 2002;76:93–9.
96. Jenkins DJ, Kendall CW, Jackson CJ, et al. Effects of high- and low-isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. Am J Clin Nutr 2002;76:365–72.
97. Washburn S, Burke GL, Morgan T, Anthony M. Effect of soy protein supplementation on serum lipoproteins, blood pressure, and menopausal symptoms in perimenopausal women. Menopause 1999; 6:7–13.
98. Rivas M, Garay RP, Escanero JF, Cia P Jr, Cia P, Alda JO. Soy milk lowers blood pressure in men and women with mild to moderate essential hypertension. J Nutr 2002;132:1900–2.
99. Hermansen K, Sondergaard M, Hoie L, Carstensen M, Brock B. Beneficial effects of a soy-based dietary supplement on lipid levels and cardiovascular risk markers in type 2 diabetic subjects. Diabetes Care 2001;24:228–33.
100. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA 2002;287: 2414–23.
101. Jenkins DJ, Kendall CW, Augustin LS, et al. Glycemic index: overview of implications in health and disease. Am J Clin Nutr 2002; 76:266S–73S.
102. Mezitis NH, Maggio CA, Koch P, Quddoos A, Allison DB, Pi-Sunyer FX. Glycemic effect of a single high oral dose of the novel sweetener sucralose in patients with diabetes. Diabetes Care 1996;19: 1004–5.
103. Nakamura H, Yamazaki M, Chiba Y, et al. Acute loading with proteins from different sources in healthy volunteers and diabetic patients. J Diabet Complications 1991;5:140–2.
104. Kontessis P, Jones S, Dodds R, et al. Renal, metabolic and hormonal responses to ingestion of animal and vegetable proteins. Kidney Int 1990;38:136–44.
105. Barsotti G, Morelli E, Cupisti A, Bertoncini P, Giovannetti S. A special, supplemented 'vegan' diet for nephrotic patients. Am J Nephrol 1991;11:380–5.
106. Jibani MM, Bloodworth LL, Foden E, Griffiths KD, Galpin OP. Predominantly vegetarian diet in patients with incipient and early clinical diabetic nephropathy: effects on albumin excretion rate and nutritional status. Diabet Med 1991;8:949–53.
107. Stephenson TJ. Therapeutic benefits of a soy protein rich diet in the prevention and treatment of nephropathy in young persons with type 1, insulin-dependent, diabetes mellitus. PhD dissertation. University of Kentucky, Lexington, 2001.
108. Vuksan V, Jenkins DJ, Spadafora P, et al. Konjac-mannan (glucomannan) improves glycemia and other associated risk factors for coronary heart disease in type 2 diabetes. A randomized controlled metabolic trial. Diabetes Care 1999;22:913–9.