Effects of Plant-Based Diets on Plasma Lipids

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Dyslipidemia is a primary risk factor for cardiovascular disease, peripheral vascular disease, and stroke. Current guidelines recommend diet as first-line therapy for patients with elevated plasma cholesterol concentrations. However, what constitutes an optimal dietary regimen remains a matter of controversy. Large prospective trials have demonstrated that populations following plant-based diets, particularly vegetarian and vegan diets, are at lower risk for ischemic heart disease mortality. The investigators therefore reviewed the published scientific research to determine the effectiveness of plant-based diets in modifying plasma lipid concentrations. Twenty-seven randomized controlled and observational trials were included. Of the 4 types of plant-based diets considered, interventions testing a combination diet (a vegetarian or vegan diet combined with nuts, soy, and/or fiber) demonstrated the greatest effects (up to 35% plasma low-density lipoprotein cholesterol reduction), followed by vegan and ovolactovegetarian diets. Interventions allowing small amounts of lean meat demonstrated less dramatic reductions in total cholesterol and low-density lipoprotein levels. In conclusion, plant-based dietary interventions are effective in lowering plasma cholesterol concentrations. **(Am J Cardiol 2009;104:947–956)**

Dyslipidemia is a primary risk factor for heart disease, peripheral vascular disease, and stroke.[1–3] In the United States, these diseases account for >885,000 deaths and $634.2 billion in direct and indirect costs annually.[4] Cardiovascular disease and related mortality are strongly associated with elevated plasma concentrations of total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol.[3] About 1 in 500 individuals (0.2% of the general population) has familial hypercholesterolemia.[5] However, >48% of the adult population of the United States has TC levels >200 mg/dl, the desirable upper limit established by the National Cholesterol Education Program (NCEP),[6] suggesting that factors other than genetics are involved in hyperlipidemia. A summary analysis of 5 observational studies demonstrated that populations consuming plant-based (especially vegetarian and vegan) diets typically have significantly lower blood concentrations of TC and LDL cholesterol and correspondingly lower rates of coronary artery disease compared to the general population.[7] In 2004, the NCEP and the third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults recommended the Therapeutic Lifestyle Changes plan, which calls for limiting total and saturated fats and dietary cholesterol and including plant sterols, viscous fibers, soy protein, and nuts, as the initial intervention for cholesterol reduction.[3] We reviewed the published scientific research to ascertain the extent to which a plant-based diet alters plasma and serum lipids, as well as potential mechanisms for these actions.

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Methods

We conducted a search of the Medline and Cochrane Collaboration databases with the terms "cholesterol," "total cholesterol," "low density lipoprotein," and "lipids" cross-referenced with "vegetarian," "low-fat vegetarian," "vegetarianism," "plant-based diet," and "plant diet" for reports published from 1966 to February 2009. We also used bibliographies and studies suggested by search engines to further increase the range of data collected. Reports published in languages other than English were reviewed if English translations were available. Studies were included if (1) the reported studies included human volunteers of any age, gender, or health status; (2) the number of participants as well as their ages and clinical status were delineated; (3) the duration and type of trial were reported; (4) the trials involved plant-based diets (diets with no, or almost no, meat products); (5) for longitudinal studies or clinical trials, lipid values, including at least TC and LDL cholesterol concentrations, were drawn before and after the study intervals; (6) the trials included adequate control groups; and (7) studies included information about the statistical significance of such findings. Observational and intervention studies were included.

Results

We found 7,261 studies, of which 7,096 were excluded on the basis of screening using general criteria. The remaining 165 abstracts were reviewed, and full reports were evaluated. Of these, 27 met all inclusion criteria. Reports were excluded because they did not report the effects of diet on cholesterol, did not include LDL values, did not use plant-based diets, were not in English, or did not report human studies (Figure 1).

Four primary dietary interventions were identified: vegan (allowing no animal products), ovolactovegetarian (allow-

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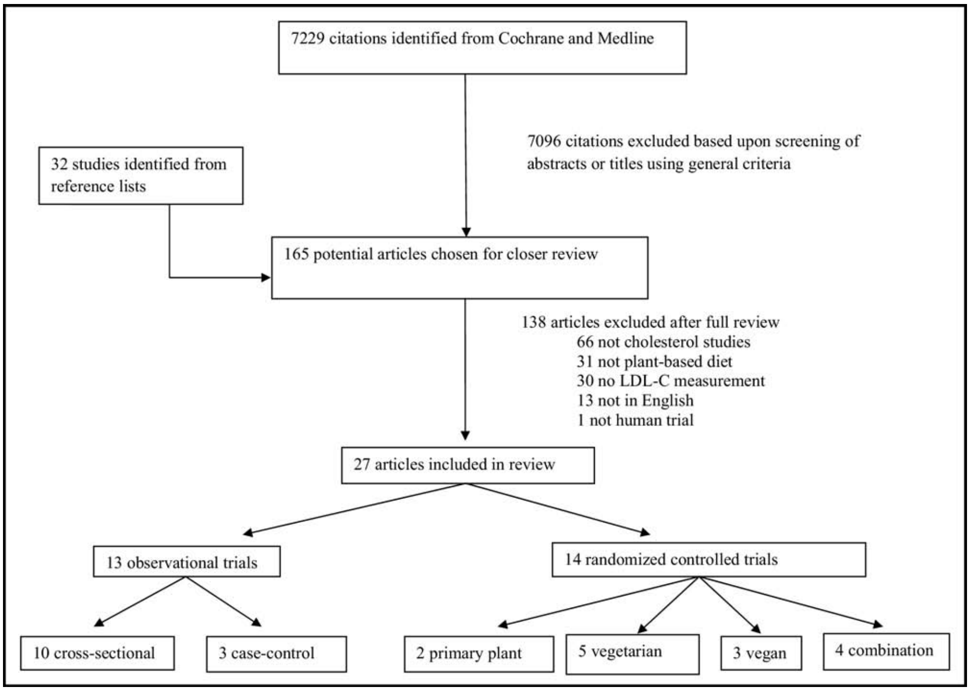

Figure 1. Flowchart of study selection for trials evaluating the effects of diet on cholesterol. LDL-C = LDL cholesterol.

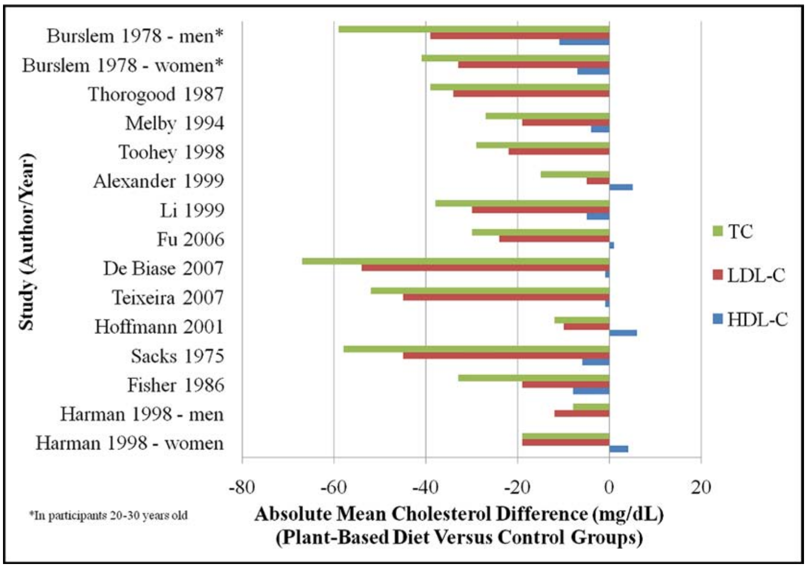

Figure 2. Effects of plant-based diets on cholesterol: observational studies. HDL-C = HDL cholesterol; LDL-C = LDL cholesterol.

ing eggs and dairy products), primary plant (similar to the ovolactovegetarian diet but allowing small amounts of lean meat), and combination (a vegetarian or vegan diet combined with nuts, soy, and/or fiber).

Observational studies: Of the 13 observational studies that met the inclusion criteria, 10 were cross-sectional studies and 3 were case-control studies. Reviewed in Figures 2 and 3 and listed Table 1, these trials evaluated 4,772 participants from 6 countries with populations of varied age ranges, gender representation, and racial and ethnic compositions.

Of the 10 cross-sectional studies, 9 demonstrated significant differences between the cholesterol levels of subjects eating plant-based diets and those of the general population.[8–16] In studies that evaluated the effects of different plant-based diets (i.e., ovolactovegetarian, lactovegetarian, and vegan), populations following vegan diets had the lowest cholesterol concentrations.[9–11,13,15] The only cross-sectional study that did not show an association between lower cholesterol and a plant-based diet used participants maximally treated with lipid-lowering medications before study onset.[17]

Of the 3 case-control studies, 2 demonstrated significantly lower TC and LDL cholesterol values in populations consuming plant-based diets.[18,19] The 1 study that examined

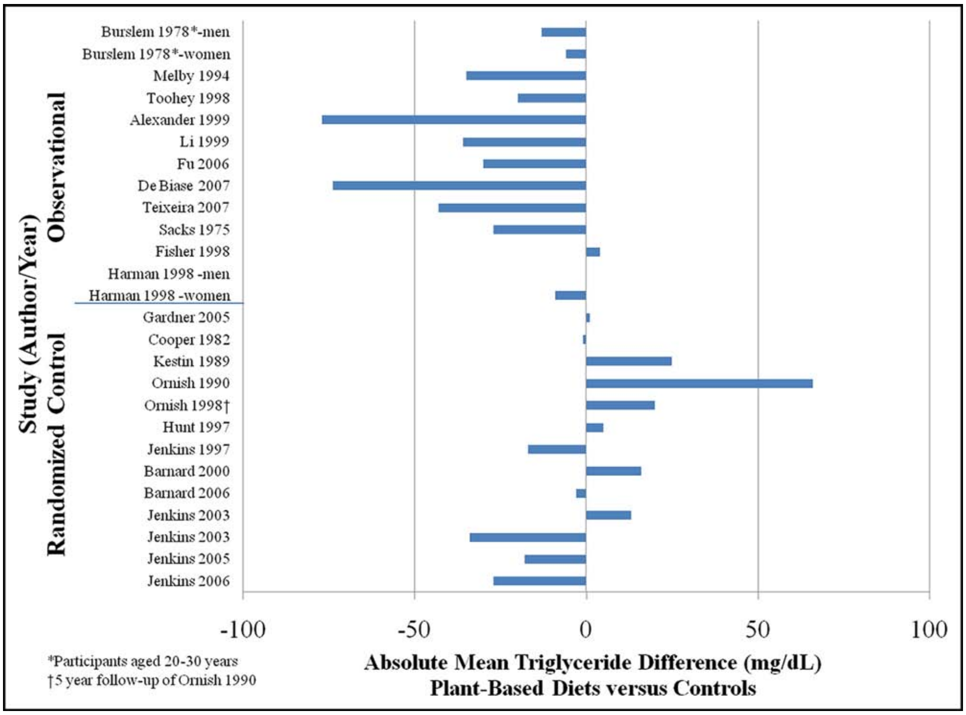

Figure 3. Effects of plant-based diets on triglycerides.

the effects of different plant-based diets showed the lowest lipid levels in vegans.[19] Harman et al[20] studied Seventh-Day Adventist vegetarians and nonvegetarians in New Zealand and reported significant differences in saturated fat (15.4% vs 10.4% of energy) and cholesterol intake (279 vs 133 mg/day) but found no significant differences in lipid parameters.

Randomized controlled trials: Fourteen randomized controlled trials met the inclusion criteria. These included 2 studies evaluating primary-plant diets, 5 studies evaluating vegetarian diets, 3 studies evaluating vegan diets, and 4 studies evaluating combination diets. Summarized in Figures 3 to 5 and listed in Table 2, these trials included 1,939 participants from 6 different countries.

PRIMARY-PLANT DIETS. In 2005, Gardner et al[21] compared a low-fat NCEP Step I diet and a "low-fat plus" diet in adults with hypercholesterolemia recruited from newspaper advertisements and brochures mailed to previous study participants and Stanford University employees. The diets were identical in total fat, saturated fat, protein, carbohydrate, and cholesterol contents, but the low-fat plus diet included "considerably more vegetables, legumes, and whole grains" and <1 serving of meat or eggs per week. All food was provided except for 1 "free-choice" meal per week. Lipid concentrations of participants assigned to the 2 groups decreased significantly, although the results were more dramatic in those in the low-fat plus arm.

The OmniHeart trial[22] tested the effects of macronutrient content in a racially diverse group of participants with hypertension and prehypertension who were not taking medications that affected lipids or blood pressure. Participants were primarily recruited through mass mailings and advertisements in Baltimore, Maryland, and Boston, Massachusetts. In an attempt to determine the best macronutrient combination, the investigators substituted either protein or monounsaturated fat for carbohydrate in a diet patterned after that used in the Dietary Approaches to Stop Hypertension (DASH) study. Protein (of which 2/3 came from plants) accounted for 25% of energy in the high-protein diet, and fat (55% monounsaturated) accounted for 37% of energy of the high-fat diet. Participants were provided with all food. Compared to participants assigned to the low-fat diet, participants assigned to the high-protein diet experienced significant decreases in TC, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and non-HDL cholesterol. Participants assigned to the monounsaturated fat diet experienced decreases in TC, triglycerides, and non-HDL cholesterol and increases in HDL cholesterol compared to participants assigned to the low-fat diet.

VEGETARIAN DIETS. Of 19 randomized controlled studies, 8 tested the effect of vegetarian diets on plasma lipids. Of these, 5 used ovolactovegetarian diets and 3 used low-fat vegan diets.

Cooper et al[23] tested the lipid-lowering effects of a lactovegetarian diet in healthy, nonsmoking physicians and medical students recruited from the Chicago area. Participants were randomly assigned to a low–saturated fat vegetarian diet or a "typical American diet." While consuming the vegetarian diet, participants reported consuming 30% fewer calories, with 11% of energy from protein, 20% from fat, and 69% from carbohydrate. Participants consuming the vegetarian diet experienced significant decreases in TC and LDL cholesterol.

Kestin et al[24] studied the effects of an ovolactovegetarian diet, a lean-meat diet, and a typical Australian diet in participants with moderate cholesterol levels recruited from a "nonprofit fitness institute" in the Adelaide, Australia, area. Partic-

Table 1
Observational studies evaluating the effects of diet on lipids

Study	Country, Year	Population Studied	No. of Participants: Men/Women	Age (years)	TC* Diet (mg/dl)
Cross-sectional					
Burslem et al[8]	United States, 1978	Tennessee commune	60 (45%)/74 (55%)	17–40 (27)	125 ± 19†, 133 ± 26‡
Thorogood et al[9]	United Kingdom, 1987	British population	1,154 (35%)/2,123 (65%)	18–68 (39)	166 ± 5
Melby et al[10]	United States, 1994	African American Seventh-Day Adventists	44 (26%)/123 (74%)	(47.5)	182 ± 4
Toohey et al[11]	United States, 1998	African American Seventh-Day Adventists	65 (34%)/125 (66%)	(49.7)	145 ± 5
Alexander et al[12]	United States, 1999	Hispanic Seventh-Day Adventists	42 (45%)/52 (55%)	35–44 (43)	198 ± 5
Li et al[13]	Australia, 1999	Australian men	147 (100%)/0 (0%)	20–55 (36)	136 ± 32
Fu et al[14]	China, 2006	Postmenopausal Chinese women	0 (0%)/70 (100%)	(55 ± 1)	174 ± 4
De Biase et al[15]	Brazil, 2007	Brazilian population	28 (37%)/48 (63%)	(37 ± 12)	141 ± 31
Teixeira et al[16]	Brazil, 2007	Brazilian population	96 (48%)/105 (52%)	35–64 (47 ± 8)	173 ± 36
Hoffmann et al[17]	Germany, 2001	German women	0 (0%)/370 (0%)	25–65	209 (201–218)
Case-control					
Sacks et al[18]	United States, 1975	American population	73 (63%)/43 (47%)	16–62	126 ± 30
Fisher et al[19]	United States, 1986	American population	22 (44%)/28 (56%)	20–47	140 ± 28
Harman et al[20]	New Zealand, 1998	Seventh-Day Adventists	23 (49%)/24 (51%)	20–65 (43)	193 ± 31§, 186 ± 43‖

Data are expressed as mean ± SD, range (mean ± SD), mean (range), or number (percentage).
* To convert TC and LDL-C to millimoles per liter, divide by 38.67.
† Results for men aged 20 to 30 years.
‡ Results for women aged 20 to 30 years.
§ Results for men.
‖ Results for women.
LDL-C = LDL cholesterol.

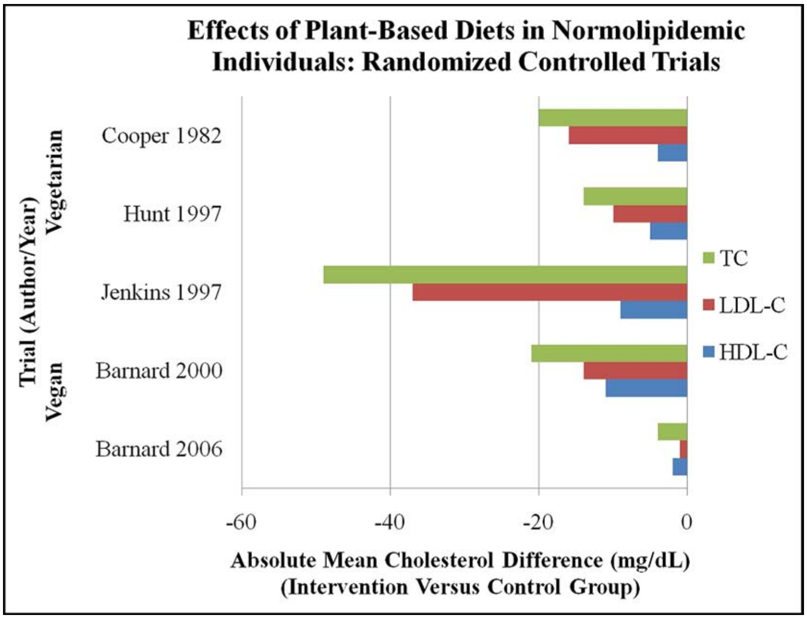

Figure 4. Effects of plant-based diets in subjects with normal lipid levels: randomized controlled trials. HDL-C = HDL cholesterol; LDL-C = LDL cholesterol.

ipants eating the lean-meat and ovolactovegetarian diets reduced TC and LDL cholesterol concentrations and increased triglycerides, with no change in HDL cholesterol. While consuming the ovolactovegetarian diet, participants' TC and LDL cholesterol concentrations decreased significantly more than while consuming the lean-meat or Australian diet.

In the Lifestyle Heart Trial, Ornish et al[25] evaluated whether a low-fat vegetarian diet, in addition to lifestyle modification (smoking cessation, exercise, and stress management), could improve plasma cholesterol concentrations and reverse atherosclerosis. Participants with diagnosed coronary artery disease and not taking lipid-lowering drugs were recruited from 2 San Francisco–area hospitals. After 1 year, the intervention group had lower TC and LDL cholesterol concentrations compared to controls. Triglycerides and HDL cholesterol concentrations remained unchanged in

Table 1
(*continued*)

TC* Control (mg/dl)	p Value (Between Groups)	LDL-C* Diet (mg/dl)	LDL-C* Control (mg/dl)	p Value (Between Groups)
184 ± 34†, 174 ± 35‡	<0.001	79 ± 14†, 81 ± 21‡	118 ± 31†, 114 ± 34‡	<0.001
205 ± 4	<0.001	88 ± 5	123 ± 3	<0.001
209 ± 7	<0.05	120 ± 4	139 ± 7	<0.05
174 ± 4	0.0002	80 ± 5	102 ± 3	0.009
214 ± 6	<0.05	125 ± 4	130 ± 6	NS
174 ± 28	<0.001	83 ± 27	113 ± 36	<0.001
204 ± 4	0.004	112 ± 6	136 ± 7	0.014
208 ± 49	<0.001	69 ± 30	123 ± 43	<0.001
225 ± 45	<0.0001	106 ± 35	151 ± 43	<0.0001
221 (212–229)	NS	128 (118–139)	138 (131–149)	NS
184 ± 37	<0.001	73 ± 24	118 ± 34	<0.001
173 ± 27	0.025	96 ± 22	115 ± 23	NS
201 ± 39§, 205 ± 39‖	NS	124 ± 27§, 116 ± 39‖	135 ± 39§, 135 ± 35‖	NS

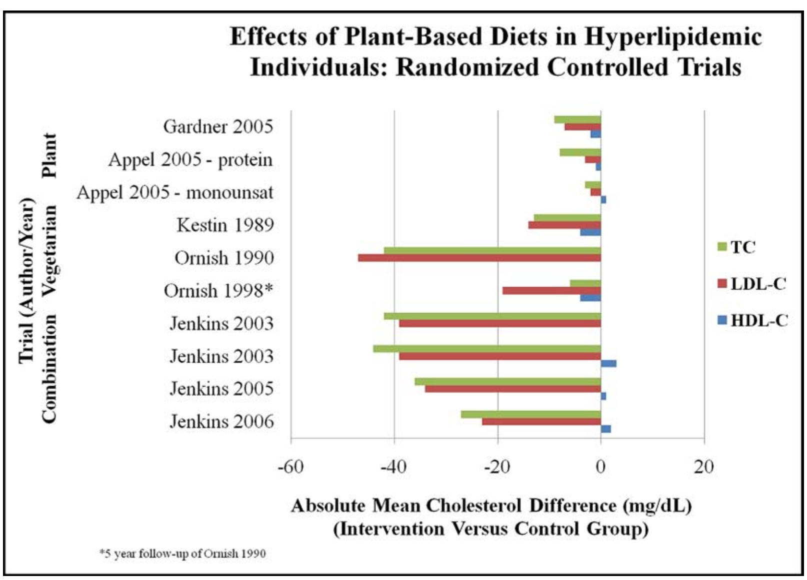

Figure 5. Effects of plant-based diets on cholesterol in subjects with hyperlipidemia: randomized controlled trials. HDL-C = HDL cholesterol; LDL-C = LDL cholesterol.

the 2 groups. Lipid values did not change significantly in the control group. Atherosclerotic stenosis decreased by 2.2% in mean diameter in the intervention group, while lesions worsened by 3.4% in the control group.

After an additional 4 years, with 35 of the original participants,[26] the intervention group continued to maintain decreased TC and LDL cholesterol values without medication. The investigators noted the addition of statins in 9 of the control subjects (60%), compared to none in the intervention group. Atherosclerotic stenosis decreased by 3.1% in mean diameter in the intervention group, whereas lesions worsened by 11.8% in the control group (p = 0.001). Control-group participants experienced twice as many cardiac events compared to intervention-group participants.

Assessing mineral absorption and lipids, Hunt et al[27] recruited premenopausal women with no apparent underlying diseases through public advertisements in North Dakota. Participants were assigned, in random order, to a nonveg-

Table 2
Randomized controlled trials evaluating the effects of diet on lipids

Study	Country, Year	Type of Study	No. of Participants: Men/Women	Age (years)	TC* Intervention, Baseline (mg/dl)	TC* Intervention (% Change)
Primary plant						
Gardner et al[21]	United States, 2005	Prospective randomized	60 (50%)/60 (50%)	30–65 (48)	222 ± 22	−18 (7.9%)
OmniHeart[22]	United States, 2005	Prospective crossover	91 (55%)/73 (45%)	(54 ± 11)	204 ± 36	−20 (9.8%)[‡], −15 (7.6%)[§]
Vegetarian						
Cooper et al[23]	United States, 1982	Prospective crossover	10 (67%)/5 (33%)	21–34 (28)	160 ± 22	−20 (11.9%)
Kestin et al[24]	Australia, 1989	Prospective crossover	26 (100%)/0 (0%)	28–64 (44)	234 (228–237)	−24 (10.1%)
Lifestyle Heart Trial[25]	United States, 1990	Prospective randomized	36 (88%)/5 (12%)	35–75 (58)	227 ± 50	−55 (24.3%)
Lifestyle Heart Trial[26]	United States, 1998	Prospective randomized	32 (91%)/3 (9%)	39–79	225 ± 12	−37 (16.5%)
Hunt et al[27,†]	United States, 1997	Prospective crossover	0 (0%)/21 (100%)	20–42 (33 ± 7)	172	−14 (8.3%)
Vegan						
Jenkins et al[28]	Canada, 1997	Prospective crossover	7 (70%)/3 (30%)	(33 ± 4)	182 ± 9	−39 (21.3%)
Barnard et al[29]	United States, 2000	Prospective crossover	0 (0%)/35 (100%)	22–48 (36)	163 ± 30	−22 (13.2%)
Barnard et al[30]	United States, 2006	Prospective randomized	39 (39%)/60 (61%)	27–82 (56)	187 ± 37	−28 (14.8%)
		Subanalysis[‖]	80	—	191 ± 37	−34 (17.8%)
Combination						
Jenkins et al[32]	Canada, 2003	Prospective randomized	16 (64%)/9 (36%)	36–85 (60 ± 10)	251 ± 10	−68 (26.6%)
Jenkins et al[33,†]	Canada, 2003	Prospective randomized	25 (54%)/21 (46%)	36–85 (59 ± 1)	268	−59 (22.0%)
Jenkins et al[34,†]	Canada, 2005	Prospective crossover	20 (59%)/14 (41%)	36–71 (58 ± 9)	261	−58 (22.3%)
Jenkins et al[35]	Canada, 2006	Prospective	55[¶]	32–86 (59 ± 1)	261 ± 4	−27 (10.4%)

Data are expressed as mean ± SD, range (mean ± SD), mean (range), or number (percentage).
* To convert TC and LDL-C to millimoles per liter, divide by 38.67.
† No SD or confidence intervals given.
‡ Protein diet.
§ Monounsaturated fat diet.
‖ Subset of participants without changes in lipid or diabetes medications.
¶ The initial numbers of men and women were 31 and 35, but no final numbers were given.

etarian or an ovolactovegetarian diet. All foods were provided. The ovolactovegetarian diet included more whole grains, legumes, fruits, vegetables, nuts, and seeds, with 25% less protein, 12% less fat, and 16% more carbohydrate, as well as 96 mg/day less cholesterol and 24 g/day more fiber. While consuming the intervention diet, the women experienced decreased TC, LDL cholesterol, and HDL cholesterol. Apolipoprotein (apo) A-1, apo B, and lipoprotein(a) were also significantly decreased.

VEGAN DIETS. Jenkins et al[28] evaluated the effects a very high fiber vegan diet compared to a control diet (usual diet) on plasma lipid concentrations in healthy volunteers recruited from the University of Toronto graduate student population and the university and hospital staff population. While following the vegan diet, participants had decreases in TC, LDL cholesterol, and triglyceride concentrations. Significant reductions were also noted in the TC/HDL cholesterol ratio, the LDL cholesterol/HDL cholesterol ratio, and the apo B/apo A-1 ratio. Reductions in TC were 34% to 49% greater than expected by differences in dietary fat and cholesterol alone.

Barnard et al[29] studied the effects of a vegan diet consisting of grains, vegetables, legumes, and fruits in a population of premenopausal women with normal plasma lipid concentrations. Participants were recruited by newspaper advertisements and brochures mailed to physicians in the Washington, District of Columbia, area. Participants were asked either to continue their customary diets and to take a placebo pill or to begin a low-fat (10% of energy from fat) vegan diet, each for 2 menstrual cycles, in random order. Food was not provided, but participants received weekly group nutrition instruction. While consuming the vegan diet, participants' TC, LDL cholesterol, and HDL cholesterol concentrations decreased and their triglycerides increased significantly more than while consuming the control diet.

Barnard et al[30] evaluated the effects of diet in 99 volunteers with type 2 diabetes recruited by advertisements in Washington-area newspapers. Participants were randomized to a low-fat, low–glycemic index vegan diet, or control diet based on 2003 American Diabetes Association guidelines.[31] At the end of the trial, more participants following the vegan diet decreased their cholesterol and diabetes medications, compared to participants following American Diabetes Association guidelines. After controlling for changes in lipid-lowering medications, participants assigned to the vegan diet experienced greater decreases in TC and LDL cholesterol values compared to participants assigned to the American Diabetes Association diet.

COMBINATION DIETS. Certain foods appear to have specific lipid-lowering properties: plant sterols, viscous fibers, soy proteins, and almonds may all contribute to lowering

Table 2
(*continued*)

TC* Control, Baseline (mg/dl)	TC* Control (% Change)	p Value (Between Groups)	LDL-C* Intervention, Baseline (mg/dl)	LDL-C* Intervention (% Change)	LDL-C* Control, Baseline (mg/dl)	LDL-C* Control (% Change)	p Value (Between Groups)	Study Duration
223 ± 30	−9 (4.1%)	0.014	148 ± 50	−14 (9.5%)	150 ± 23	−7 (4.6%)	0.016	4 wk
204 ± 36	−12 (6.1%)	<0.05‡, NS§	129 ± 32	−14 (11.0%)‡, −13 (10.1%)§	129 ± 32	−12 (9.0%)	0.01‡, NS§	3 6-wk periods
160 ± 22	0 (0%)	<0.01	109 ± 23	−16 (14.7%)	109 ± 23	0 (0%)	<0.025	2 3-wk periods
234 (228–237)	−11 (4.6%)	<0.01	155 (149–161)	−24 (15.2%)	155 (149–161)	−10 (6.7%)	<0.01	2 6-wk periods
245 ± 39	−13 (5.3%)	0.019	152 ± 48	−57 (37.4%)	167 ± 30	−10 (6.0%)	0.007	12 mo
248 ± 9	−31 (12.5%)	0.60	144 ± 11	−29 (20.1%)	144 ± 11	−10 (6.9%)	0.76	5 yrs
172	0 (0%)	0.001	106	−10 (9.2%)	106	0 (0%)	0.001	2 8-wk periods
179 ± 10	+10 (5.8%)	<0.001	107 ± 10	−32 (29.3%)	106 ± 9	+5 (4.4)	<0.001	2 2-wk periods
163 ± 30	−1 (1.0%)	<0.001	97 ± 24	−17 (16.9%)	97 ± 24	−3 (3.1%)	<0.001	8–10 wk
199 ± 44	−24 (12.2%)	NS	104 ± 33	−16 (15.7%)	119 ± 42	−15 (13.0%)	NS	22 wk
195 ± 41	−19 (9.7%)	0.01	107 ± 34	−23 (21.4%)	115 ± 40	−11 (10.5%)	0.02	22 wk
258 ± 6	−26 (9.9%)	<0.001	170 ± 10	−61 (35.0%)	179 ± 6	−22 (12.1%)	<0.001	4 wk
246	−15 (6.2%)	<0.001	179	−53 (28.6%)	166	−14 (8.4%)	<0.001	1 mo
263	−22 (8.2%)	0.001	174	−51 (29.6%)	177	−17 (8.5%)	0.001	3 1-mo periods
—	—	<0.001	173 ± 3	−23 (14.6%)	—	—	<0.001	12 mo

cholesterol. Accordingly, Jenkins et al[32] evaluated the effects of a vegan dietary "portfolio" including plant sterols 1.2 g/1,000 kcal, soy protein 16.2 g/1,000 kcal, viscous fiber 8.3 g/1,000 kcal, and almonds 16.6 g/1,000 kcal. Participants were recruited from patients attending the Risk Factor Modification Center at St. Michael's Hospital in Toronto, Ontario, Canada, and from newspaper advertisements and asked to follow a low-fat diet for 1 month. Participants were then randomized to either the portfolio diet or an NCEP Step II ovolactovegetarian diet. Participants assigned to the portfolio diet experienced greater decreases in TC, LDL cholesterol, apo B, TC/HDL cholesterol ratio, LDL cholesterol/HDL cholesterol ratio, and apo B/apo A-1 ratio compared to participants assigned to the control diet.

In a population similar to the previous study, Jenkins et al[33] directly compared a vegetarian portfolio diet (plant sterols 1.0 g/1,000 kcal, soy protein 21.4 g/1,000 kcal, viscous fiber 9.8 g/1,000 kcal, and almonds 14 g/1,000 kcal) to a low-fat diet plus placebo (control group) and a low-fat diet plus lovastatin. Compared to controls, participants assigned to the lovastatin and portfolio groups significantly reduced TC and LDL cholesterol concentrations. The lovastatin and portfolio diet groups significantly reduced C-reactive protein levels, TC/HDL cholesterol ratios, HDL cholesterol/LDL cholesterol ratios, apo B values, and apo B/apo A-1 ratios. There were no differences between the lovastatin and portfolio diet groups in any changes in plasma lipid concentrations.

Jenkins et al[34] compared 3 dietary interventions: a low-fat NCEP Step II diet, lovastatin 20 mg plus a low-fat NCEP Step II diet, and the portfolio diet (plant sterols 1.0 g/1,000 kcal, soy protein 21.4 g/1,000 kcal, viscous fiber 10.0 g/1,000 kcal, and almonds 14 g/1,000 kcal) in a crossover trial. Participants, recruited as in previous studies, were assigned in random order to all 3 groups. TC and LDL cholesterol concentrations decreased significantly in participants in the lovastatin and portfolio groups. However, subjects taking lovastatin lowered TC and LDL cholesterol to a significantly greater extent than those following the portfolio diet ($p = 0.013$).

Jenkins et al[35] tested the portfolio diet in a less restrictive, "real-world" environment. Participants, recruited from 2 sets of newspaper advertisements in the Toronto area and from an earlier study, were instructed to consume a low–saturated fat (<7% of calories) and low-cholesterol (<200 mg/day) diet for 2 months before study onset. All participants were then instructed to follow a portfolio diet. Food was not provided. After 1 year, participants experienced significant reductions in plasma lipid concentrations. This study did not include a control group, relying on baseline values and previous control measures in about 1/2 of the studied subjects. The investigators reported that a significant correlation was found between dietary adherence and change in LDL cholesterol (r = −0.42, p <0.001).

Discussion

Our review demonstrates that individuals following plant-based diets experience significantly lower blood lipid concentrations compared to those following diets that include animal products. In observational studies, vegetarians also appear to have fewer and smaller age-related increases in lipids compared to nonvegetarians.

Although it is difficult to directly compare the effects of dietary interventions from various studies, the reviewed studies suggest that a greater reduction in dietary animal products yields greater reductions in lipid levels. In randomized controlled trials, compared to baseline values, primary plant-based and ovolactovegetarian dietary interventions were associated with decreases of TC and LDL cholesterol of about 10% to 15%, vegan dietary interventions were associated with decreases of approximately 15% to 25%, and combination dietary interventions (vegetarian diets with additional fiber, soy, and nuts) were associated with decreases of approximately 20% to 35%. The studies were not subjected to a meta-analysis. Although the combination dietary interventions prescribed by Jenkins et al[32–35] contained varying amounts of plant sterols, soy protein and isoflavins, viscous fibers, and nuts, other plant-based diets in the reviewed trials contained some or all of these components in unknown amounts, making direct comparisons difficult.

Like all cholesterol subfractions, HDL cholesterol is typically lower in vegetarians compared to nonvegetarians. Trials of low-fat vegetarian diets, in which carbohydrates replace fats, have demonstrated decreases in HDL cholesterol. The mechanism for the effect of diet on HDL cholesterol is unclear, but lower apo A-1 production rates have been suggested as a contributing factor.[36] Observational mortality studies in subjects who consume low-fat vegetarian diets, such as American Seventh-Day Adventists[37] and individuals living in Asia,[38] suggest that decreased HDL cholesterol associated with low-fat vegetarian diets is not associated with poor cardiovascular health. In a randomized controlled trial, Ornish et al[25,26] showed decreases in atherosclerotic lesions and cardiac events in subjects following an intervention including a low-fat vegetarian diet and moderate exercise, even in those with decreased HDL cholesterol. Also, although long-term adherence to a vegetarian diet is consistently associated with lower plasma triglyceride concentrations, randomized trials have demonstrated varied effects on triglycerides. Although diets high in refined carbohydrates may increase triglyceride concentrations, high-fiber and low–glycemic index foods appear to have the opposite result.[39]

Plant-based diets reduce plasma cholesterol concentrations through several mechanisms. Reduced dietary intake of total fat, saturated fat, and cholesterol leads to less absorption and conversion to blood cholesterol.[40–43] Most plant-based diets are low in saturated fat and cholesterol. However, the reductions in these macronutrients account for only a portion of the decrease in TC.[8,22,32,33] Plant-based diets include compounds such as dietary fiber, phytosterols, phenolics, carotenoids, flavonoids, and saponins, derived primarily from whole grains, fruits and vegetables, and legumes.[44] These compounds appear to affect cholesterol through multiple mechanisms. Viscous fiber intake can increase cholesterol removal through binding of bile acids and cholesterol.[45,46] Plant sterol intake reduces cholesterol absorption through binding of cholesterol and bile acids.[47,48] Increases in dietary soy may slightly decrease cholesterol synthesis with soy protein intake.[49,50] Soy intake may also improve cardiovascular health by increasing LDL cholesterol oxidation resistance[51] and inhibiting thrombus formation[52] due to isoflavin (genistein and daidzein) effects. Markers of cardiovascular health, such as decreased C-reactive protein, LDL cholesterol particle size, and increased resistance to oxidation of LDL cholesterol, have been associated with the intake of monounsaturated fats, nuts, and fruit and vegetables.[53–58]

Observational studies have demonstrated that populations following plant-based diets have lower overall and ischemic heart disease mortality.[14,59,60] Vegetarian diets have been associated with lower blood pressure,[14,61] lower body weight and body mass index,[26,30,61,62] lower C-reactive protein levels,[32,63] lower blood concentrations of inflammatory markers,[64] improved insulin sensitivity,[58] and better glycemic control in patients with diabetes.[30,57,62]

Multiple studies investigating the acceptability of plant-based diets have found the acceptability of these diets to be similar to that of other therapeutic diets across racially diverse populations.[28,29,65–67] Compared with other therapeutic diets, plant-based diets have the advantage of not requiring macronutrient content calculations or portion-size control. Plant-based diets are also high in fiber, improving satiety, which sets them apart from calorie-restricted weight-loss diets. With adequate planning, vegetarian diets meet all nutritional needs.[68]

Dietary trials have certain limitations. Dietary intervention studies typically cannot be double blinded. Study interventions (type of dietary intervention, degree of fat restriction, and duration) and end points vary, making direct comparisons and meta-analyses difficult. Most of the studies reviewed were observational studies or randomized controlled trials with relatively small sample sizes and brief intervention periods. Confounding factors such as different baseline cholesterol levels, baseline diets, glucose homeostasis, insulin sensitivity, and body fat composition and distribution can affect the effectiveness of dietary interventions. Few studies have examined the effect of diet on morbidity or mortality. Long-term, large prospective studies, with consistent diets and outcomes, may clarify questions surrounding the effects of plant-based diets on cardiac and total mortality, effects in patients already treated with lipid-lowering medications and associated direct and indirect costs.

Hypercholesterolemia and associated coronary artery disease, peripheral vascular disease, and stroke are major contributors to morbidity, mortality, and health care costs. The treatment of dyslipidemia accounts for significant costs and potentially adverse effects. Dietary changes are recommended as first-line therapy for dyslipidemia because they are safe and cost effective. However, to date, studies have shown NCEP diets and similar regimens to be only modestly effective, reducing TC and LDL cholesterol concentrations by 5% to 10%. However, plant-based diets, which follow the current recommendations of the Third Adult Treatment Panel and the American Heart Association, have demonstrated greater cholesterol reductions and are a preferable option for cholesterol reduction.

1. Pekkanen J, Linn S, Heiss G, Suchindran CM, Leon A, Rifkind BM, Tyroler HA. Ten-year mortality from cardiovascular disease in relation to cholesterol level among men with and without preexisting cardiovascular disease. *N Engl J Med* 1990;322:1700–1707.
2. Rosengren A, Hagman M, Wedel H, Wilhelmsen L. Serum cholesterol and long-term prognosis in middle-aged men with myocardial infarction and angina pectoris. A 16-year follow-up of the Primary Prevention Study in Goteborg, Sweden. *Eur Heart J* 1997;18:754–761.
3. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Third report of the National Cholesterol Education Program (NCEP) (Adult Treatment Panel III). *Circulation* 2002;106:3143–3421.
4. Heart disease and stroke statistics 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Committee. *Circulation* 2008;117:e25–e146.
5. Austin MA, Hutter CM, Zimmern RL, Humphries SE. Genetic causes of monogenic heterozygous familial hypercholesterolemia: a HuGE prevalence review. *Am J Epidemiol* 2004;160:408–420.
6. Carroll MD, Lacher DA, Sorlie PD, Cleeman JI, Gordon DJ, Wolz M, Grundy SM, Johnson CL. Trends in serum lipids and lipoproteins of adults, 1960–2002. *JAMA* 2005;294:1773–1781.
7. Key TJ, Fraser GE, Thorogood M, Appleby PN, Beral V, Reeves G, Burr ML, Chang-Claude J, Frentzel-Beyme R, Kuzma JW, Mann J, McPherson K. Mortality in vegetarians and nonvegetarians: detailed findings from a collaborative analysis of 5 prospective studies. *Am J Clin Nutr* 1999;70(suppl):516S–524S.
8. Burslem J, Schonfeld G, Howald M, Weidman S, Miller JP. Plasma apoprotein and lipoprotein lipid levels in vegetarians. *Metabolism* 1978;27:711–719.
9. Thorogood M, Carter R, Benfield L, McPherson K, Mann JI. Plasma lipids and lipoprotein cholesterol concentrations in people with different diets in Britain. *Br Med J* 1987;295:351–353.
10. Melby C, Toohey ML, Cebrick J. Blood pressure and blood lipids among vegetarian, semivegetarian, and nonvegetarian African Americans. *Am J Clin Nutr* 1994;59:103–109.
11. Toohey ML, Harris MA, DeWitt W, Foster G, Schmidt WD, Melby CL. Cardiovascular disease risk factors are lower in African-American vegans compared to lacto-ovo-vegetarians. *J Am Coll Nutr* 1998;17:425–434.
12. Alexander H, Lockwood LP, Harris MA, Melby CL. Risk factors for cardiovascular disease in two groups of Hispanic Americans with differing dietary habits. *J Am Coll Nutr* 1999;18:127–136.
13. Li D, Sinclair A, Mann N, Turner A, Ball M, Kelly F, Abedin L, Wilson A. The association of diet and thrombotic risk factors is healthy male vegetarians and meat-eaters. *Eur J Clin Nutr* 1999;53:612–619.
14. Fu CH, Yang CCH, Lin CL, Kuo TBJ. Effects of long-term vegetarian diets on cardiovascular autonomic functions in healthy postmenopausal women. *Am J Cardiol* 2006;97:380–383.
15. De Biase SG, Fernandes SF, Gianini RJ, Duarte JL. Vegetarian diet and cholesterol and triglyceride levels. *Arq Bras Cardiol* 2007;88:35–39.
16. Teixeira Rde C, Molina Mdel C, Zandonade E, Mill JG. Cardiovascular risk in vegetarians and omnivores: a comparative study. *Arq Bras Cardiol* 2007;89:237–244.
17. Hoffmann I, Groeneveld MJ, Boeing H, Koebnick C, Golf S, Katz N, Leitzmann C. Giessen Wholesome Nutrition Study: relation between a health-conscious diet and blood lipids. *Eur J Clin Nutr* 2001;55:887–895.
18. Sacks FM, Castelli WP, Donner A, Kaas EH. Plasma lipids and lipoproteins in vegetarians and controls. *N Engl J Med* 1975;292:1148–1151.
19. Fisher M, Levine P, Weiner B, Ockene I, Johnson B, Johnson MH, Natale AM, Vaudreuil CH, Hoogasian J. The effect of vegetarian diets on plasma lipids and platelet levels. *Arch Int Med* 1986;146:1193–1197.
20. Harman S, Parnell W. The nutritional health of New Zealand vegetarian and non-vegetarian Seventh-Day Adventists: selected vitamin mineral and lipid levels. *N Z Med J* 1998;111:91–94.
21. Gardner CD, Coulston A, Chatterjee L, Rigby A, Spiller G, Farquhar JW. The effect of a plant-based diet on plasma lipids in hypercholesterolemic men. *Ann Intern Med* 2005;142:725–733.
22. Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller ER 3rd, Conlin PR, Erlinger TP, Rosner BA, Laranjo NM, Charleston J, McCarron P, Bishop LM; OmniHeart Collaborative Research Group. Effect of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA* 2005;294:2455–2464.
23. Cooper R, Goldber R, Trevisan M, Tsong Y, Liu K, Stamler J, Rubenstein A, Scanu AM. The selective lipids-lowering effect of vegetarianism on low density lipoproteins in a cross-over experiment. *Atherosclerosis* 1982;44:293–305.
24. Kestin M, Rouse IL, Correll RA, Nestel PJ. Cardiovascular disease risk factors in free living men: comparison of two prudent diets, one based on lactoovovegetarianism and the other allowing lean meat. *Am J Clin Nutr* 1989;50:280–287.
25. Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, Gould KL. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet* 1990;336:129–133.
26. Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, Sparler S, Armstrong WT, Ports TA, Kirkeeide RL, Hogeboom C, Brand RJ. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998;280:2001–2007.
27. Hunt J, Matthys L, Johnson LK. Zinc absorption, mineral balance, and blood lipids in women consuming controlled lactoovovegetarian and omnivorous diets for 8 wk. *Am J Clin Nutr* 1998;67:421–430.
28. Jenkins DJ, Popovich DG, Kendall CW, Vidgen E, Tariq N, Ransom TP, Wolever TM, Vuksan V, Mehling CC, Boctor DL, Bolognesi C, Huang J, Patten R. Effect of a diet high in vegetables, fruit, and nuts on serum lipids. *Metabolism* 1997;46:530–537.
29. Barnard ND, Scialli AR, Bertron P, Hurlock D, Edmonds K, Talev L. Effectiveness of a low-fat vegetarian diet in altering serum lipids in healthy premenopausal women. *Am J Cardiol* 2000;85:969–972.
30. Barnard ND, Cohen J, Jenkins DJ, Turner-McGrievy G, Gloede L, Jaster B, Seidl K, Green AA, Talpers S. A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a random clinical trial in individuals with type 2 diabetes. *Diabetes Care* 2006;29:1777–1183.
31. American Diabetes Association. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (position statement). *Diabetes Care* 2003;26:S51–S61.
32. Jenkins DJ, Kendall CW, Marchie A, Faulkner D, Vidgen E, Lapsley KG, Trautwein EA, Parker TL, Josse RG, Leiter LA, Connelly PW. The effect of combining plant sterols, soy protein, viscous fibers, and almonds in treating hypercholesterolemia. *Metabolism* 2003;52:1478–1483.
33. Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vigden E, Lapsley KG, Trautwein EA, Lapsley KG, Josse RG, Leiter LA, Singer W, Connelly PW. Effects of a dietary portfolio of cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. *JAMA* 2003;290:502–510.
34. Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Trautwein EA, Lapsley KG, Josse RG, Leiter LA, Singer W, Connelly PW. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. *Am J Clin Nutr* 2005;81:380–387.
35. Jenkins DJ, Kendall CW, Faulkner DA, Nguyen T, Kemp T, Marchie A, Wong JM, de Souza R, Emam A, Vidgen E, Trautwein EA, Lapsley KG, Holmes C, Josse RG, Leiter LA, Connelly PW, Singer W. Assessment of the longer-term effects of a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia. *Am J Clin Nutr* 2006;83:582–591.
36. Desroches S, Paradis ME, Pérusse M, Archer WR, Bergeron J, Couture P, Bergeron N, Lamarche B. Apolipoprotein A-I, A-II, and VLDL-B-100 metabolism in men: comparison of a low-fat diet and a high-monounsaturated fatty acid diet. *J Lipid Res* 2004;45:2331–2338.
37. Fraser GE, Shavlik DJ. Ten years of life: is it a matter of choice? *Arch Intern Med* 2001;161:1645–1652.

38. Campbell TC, Parpia B, Chen J. Diet, lifestyle, and the etiology of coronary artery disease: The Cornell China Study. *Am J Cardiol* 1998;82(suppl):18T–21T.
39. Jenkins DJ, Wolever TM, Kalmusky J, Guidici S, Giordano C, Patten R, Wong GS, Bird JN, Hall M, Buckley G, Csima A, Little JA. Low-glycemic index diet in hyperlipidemia: use of traditional starchy foods. *Am J Clin Nutr* 1987;46:66–71.
40. Hu FB, Stampfer MJ, Manson JE, Rimm E, Colditz GA, Rosner BA, Hennekens CH, Willett WC. Dietary fat intake and the risk of coronary heart disease in women. *N Engl J Med* 1997;337:1491–1499.
41. Dreon DM, Fernstrom HA, Miller B, Krauss RM. Low-density lipoprotein subclass patterns and lipoprotein response to a reduced-fat diet in men. *FASEB J* 1994;8:121–126.
42. Mensink RP, Katan MB. Effect of dietary fatty acids on serum lipids and lipoproteins: a meta-analysis of 27 trials. *Arterioscler Thromb* 1992;12:911–919.
43. Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. IV. Particularly saturated fatty acids in the diet. *Metabolism* 1996;14:776–787.
44. De Lorgeril M, Salen P, Martin JL, Mamelle N, Monjaud I, Touboul P, Delaye J. Effect of a Mediterranean type of diet on the rate of cardiovascular complications in patients with coronary artery disease. Insights into the cardioprotective effect of certain nutriments. *J Am Coll Cardiol* 1996;28:1103–1108.
45. 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.
46. Cara L, Dubois C, Borel P, Armand M, Senft M, Portugal H, Pauli AM, Bernard PM, Lairon D. Effects of oat bran, rice bran, wheat fiber, and wheat germ on postprandial lipemia in healthy adults. *Am J Clin Nutr* 1992;55:81–88.
47. Tilvis RS, Miettinen TA. Serum plant sterols and their relation to cholesterol absorption. *Am J Clin Nutr* 1986;43:92–97.
48. Lichtenstein AH, Deckelbaum RJ. AHA Science Advisory. Stanol/sterol ester-containing foods and blood cholesterol levels. A statement for healthcare professionals from the Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. *Circulation* 2001;103:1177–1179.
49. Anderson JW, Johnstone BM, Cook-Newel ME. Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995;333: 376–382.
50. Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M; American Heart Association Committee. Soy protein, isoflavones, and cardiovascular health: an American Heart Association advisory for professionals from the Nutrition Committee. *Circulation* 2006;113:1034–1044.
51. Damasceno NRT, Apolinário E, Flauzino FD, Fernandes I, Abdalla DSP. Soy isoflavones reduce electronegative low-density lipoprotein (LDL) and anti-LDL autoantibodies in experimental atherosclerosis. *Eur J Nutr* 2007;46:125–132.
52. Rimbach G, Boesch-Saadatmandi C, Frank J, Fuchs D, Wenzel U, Daniel H, Hall WL, Weinberg PD. Dietary isoflavones in the prevention of cardiovascular disease—a molecular perspective. *Food Chem Toxicol* 2008;46:1308–1319.
53. Reaven P, Parthasarathy S, Grasse BJ, Miller E, Steinberg D, Witztum JL. Effects of oleate-rich and linoleate-rich diets on the susceptibility of low density lipoprotein to oxidative modification in mildly hypercholesterolemic subjects. *J Clin Invest* 1993;91:668–676.
54. Lu SC, Wu WH, Lee CA, Chou HF, Lee HR, Huang PC. LDL of Taiwanese vegetarians are less oxidizable than those of omnivores. *J Nutr* 2000;130:1591–1596.
55. Zambon D, Sabate J, Munoz S, Campero B, Casals E, Merlos M, Laguna JC, Ros E. Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women. A randomized crossover trial. *Ann Intern Med* 2000;132:538–546.
56. Nagyova A, Krajcovicova-Kudlackova M, Kivanova J. LDL and HDL oxidation and fatty acid composition in vegetarians. *Ann Nutr Metab* 2001;45:148–151.
57. Lahteenmaki TA, Seppo L, Laakso J, Korpela R, Vanhanen H, Tikkanen MJ, Vapaatalo. Oxidized LDL from subjects with different dietary habits modifies atherogenic processes in endothelial and smooth muscle cells. *Life Sci* 2000;66:455–465.
58. Mori TA, Burke V, Puddey IB, Watts GF, O'Neal DN, Best JD, Beilin LJ. Purified eicosapentaenoic and docosahexaenoic acids have differential effects on serum lipids and lipoproteins, LDL particle size, glucose, and insulin in mildly hyperlipidemic men. *Am J Clin Nutr* 2000;71:1085–1094.
59. Chang-Claude J, Frentzel-Beyme R. Dietary and lifestyle determinants of mortality among German vegetarians. *Int J Epidemiol* 1993;22: 228–236.
60. Thorogood M, Mann J, Appleby F, McPherson K. Risk of death from cancer and ischaemic heart disease in meat and non-meat eaters. *Br Med J* 1994;308:1667–1671.
61. McDougall J, Litzau K, Haver I, Saunders V, Spiller GA. Rapid reduction of serum cholesterol and blood pressure by a twelve-day, very low fat, strictly vegetarian diet. *J Am Coll Nutr* 1995;14:461–466.
62. 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.
63. Krajcovicova-Kudlackova M, Blazicek P. C-reactive protein and nutrition. *Bratisl Lek Listy* 2005;106:345–347.
64. Hostmark AT, Lystad E, Vellar OD, Hovi K, Berg JE. Reduced plasma fibrinogen, serum peroxidases, lipids, and apolipoproteins after 3-week vegetarian diet. *Plant Foods Hum Nutr* 1993;43:55–61.
65. Barnard ND, Scialli AR, Turner-McGrievy G, Lanou AJ. Acceptability of a low-fat vegan diet compares favorably to a Step II diet in a randomized controlled trial. *J Cardiopulm Rehabil* 2004;24:229–235.
66. Smith CF, Burke LE, Wing RR. Young adults remain on vegetarian diet longer than weight loss diets. *Ann Behav Med* 1999;21:S090.
67. White RF, Seymour J, Frank E. Vegetarianism among U.S. women physicians. *J Am Diet Assoc* 1999;99:595–598.
68. American Dietetic Association. Position of the American Dietetic Association: vegetarian diets. *J Am Diet Assoc* 1997;97:1317–1321.