A Low-Fat Vegan Diet Improves Glycemic Control and Cardiovascular Risk Factors in a Randomized Clinical Trial in Individuals With Type 2 Diabetes

NEAL D. BARNARD, MD[1,2]
JOSHUA COHEN, MD[1]
DAVID J.A. JENKINS, MD, PHD[3]
GABRIELLE TURNER-MCGRIEVY, MS, RD[4]
LISE GLOEDE, RD, CDE[5]

BRENT JASTER, MD[2]
KIM SEIDL, MS, RD[2]
AMBER A. GREEN, RD[2]
STANLEY TALPERS, MD[1]

OBJECTIVE — We sought to investigate whether a low-fat vegan diet improves glycemic control and cardiovascular risk factors in individuals with type 2 diabetes.

RESEARCH DESIGN AND METHODS — Individuals with type 2 diabetes ($n = 99$) were randomly assigned to a low-fat vegan diet ($n = 49$) or a diet following the American Diabetes Association (ADA) guidelines ($n = 50$). Participants were evaluated at baseline and 22 weeks.

RESULTS — Forty-three percent (21 of 49) of the vegan group and 26% (13 of 50) of the ADA group participants reduced diabetes medications. Including all participants, HbA_{1c} (A1C) decreased 0.96 percentage points in the vegan group and 0.56 points in the ADA group ($P = 0.089$). Excluding those who changed medications, A1C fell 1.23 points in the vegan group compared with 0.38 points in the ADA group ($P = 0.01$). Body weight decreased 6.5 kg in the vegan group and 3.1 kg in the ADA group ($P < 0.001$). Body weight change correlated with A1C change ($r = 0.51$, $n = 57$, $P < 0.0001$). Among those who did not change lipid-lowering medications, LDL cholesterol fell 21.2% in the vegan group and 10.7% in the ADA group ($P = 0.02$). After adjustment for baseline values, urinary albumin reductions were greater in the vegan group (15.9 mg/24h) than in the ADA group (10.9 mg/24 h) ($P = 0.013$).

CONCLUSIONS — Both a low-fat vegan diet and a diet based on ADA guidelines improved glycemic and lipid control in type 2 diabetic patients. These improvements were greater with a low-fat vegan diet.

Diabetes Care **29**:1777–1783, 2006

D iabetes prevalence is relatively low among individuals following plant-based and vegetarian diets, and clinical trials using such diets have shown improvements in glycemic control and cardiovascular health (1,2). Most of these trials have also included exercise, thus making it impossible to isolate diet effects. In a 12-week pilot trial of a low-fat vegan diet in individuals with type 2 diabetes, conducted without increased exercise, fasting serum glucose concentration dropped 28% compared with 12% in the control group following a diet based on American Diabetes Association (ADA) guidelines ($P < 0.05$) (3). A similar diet, used in the absence of exercise, was associated with increased insulin sensitivity and reduced body weight in nondiabetic overweight women (4).

We therefore conducted a randomized controlled trial of a vegan diet with exercise held constant to test the hypothesis that, in individuals with type 2 diabetes, a low-fat plant-based diet improves glycemic, plasma lipid, and weight control compared with a diet based on current ADA guidelines.

RESEARCH DESIGN AND METHODS

— Individuals with type 2 diabetes, defined by a fasting plasma glucose concentration >6.9 mmol/l on two occasions or a prior diagnosis of type 2 diabetes with the use of hypoglycemic medications for ≥6 months, were recruited through newspaper advertisements in the Washington, DC, area on two occasions (October 2003 through December 2003 and October 2004 through December 2004) to complete the study from January 2004 through June 2004 and January 2005 through June 2005, respectively. Exclusion criteria were an HbA_{1c} (A1C) <6.5 or >10.5%, use of insulin for >5 years, current smoking, alcohol or drug abuse, pregnancy, unstable medical status, and current use of a low-fat vegetarian diet. The protocol was approved by the George Washington University Institutional Review Board. All participants gave written informed consent.

A1C was assayed using affinity chromatography on an Abbott IMx analyzer (5). Volunteers were ranked in order of A1C concentrations and randomly assigned in sequential pairs, using a random-number table, to a low-fat vegan diet or a diet following the 2003 ADA guidelines (6) for 22 weeks. Because assignment was done simultaneously, allocation concealment was unnecessary.

The vegan diet (~10% of energy from fat, 15% protein, and 75% carbohydrate) consisted of vegetables, fruits, grains, and legumes. Participants were asked to avoid animal products and added fats and to

---

favor low–glycemic index foods, such as beans and green vegetables. Portion sizes, energy intake, and carbohydrate intake were unrestricted.

The ADA diet (15–20% protein, <7% saturated fat, 60–70% carbohydrate and monounsaturated fats, and cholesterol ≤200 mg/day) was individualized, based on body weight and plasma lipid concentrations (6). ADA group participants with a BMI >25 kg/m^2 (all but three ADA group participants) were prescribed energy intake deficits of 500–1,000 kcal.

No meals were provided. To meet the vitamin B_{12} needs of the vegan group while maintaining the same intervention in the ADA group, all participants were provided a vitamin B_{12} supplement (100 μg) to be taken every other day. For both groups, alcoholic beverages were limited to one per day for women and two per day for men. Participants were asked not to alter their exercise habits during the intervention period.

Each participant met for 1 h with a registered dietitian experienced in the use of the assigned diet to establish an appropriate diet plan. Thereafter, participants attended weekly 1-h meetings of their assigned groups for nutrition and cooking instruction conducted by a physician and a registered dietitian and/or a cooking instructor. Sessions for the two groups were similar in duration and content, except with regard to dietary details. Group leaders were instructed to make no comment favoring either diet over the other.

At weeks 4, 8, 13, and 20, a registered dietitian made unannounced telephone calls to each participant to administer a 24-h diet recall. These recalls were not statistically analyzed, but allowed the investigators to check for poor adherence and provide additional dietary counseling as needed.

In addition, a 3-day dietary record was completed by each participant at weeks 0, 11, and 22, on 2 weekdays and 1 weekend day, using a food scale, after participants had completed a 3-day practice record. Using the Nutrition Data System for Research software version 5.0 (Food and Nutrient Database 35 [released May 2004]; Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN) (7), a registered dietitian certified by the Nutrition Coordinating Center analyzed all 3-day dietary records and diet recalls. For purposes of statistical analysis, dietary adherence for the vegan group was defined as the absence of meat, poultry, fish, dairy, or egg intake reported on

24-h recalls or incidentally at any point, as saturated fat ≤5% and total fat ≤25% of energy, and as average daily cholesterol intake ≤50 mg on 3-day dietary records at 22 weeks. Adherence for the ADA group was defined as average daily energy intake on the 22-week 3-day dietary records being no more than 200 kcal in excess of the intake prescribed by the registered dietitian and saturated fat ≤10% of energy. Individuals who attended fewer than 10 of the 22 weekly sessions were also considered nonadherent on either diet.

Participants were asked to continue their preexisting medication regimens, except when fasting plasma glucose determinations fell below 4.4 mmol/l or hypoglycemic symptoms were accompanied by a capillary glucose reading <3.6 mmol/l. In such cases, medications were reduced for participant safety by a study endocrinologist, who remained blind to group assignment, following an established protocol.

Laboratory measurements were made after a 12-h fast by technicians blind to group assignment. A1C (the primary end point) was assayed at 0, 11, and 22 weeks, as described above. All other measures were assessed at baseline and 22 weeks, except as noted. Plasma glucose was measured by the glucose oxidase method using an Abbott Spectrum analyzer (Abbott Park, IL) (8). Plasma cholesterol and triglyceride concentrations were measured by enzymatic methods using an Abbott Spectrum analyzer (9,10). HDL cholesterol was measured after double precipitation with dextran and $MgCl_2$ (11). LDL cholesterol was estimated using the Friedewald equation (12). In individuals whose plasma triglyceride concentrations exceeded 400 mg/dl, LDL cholesterol was measured directly by precipitation and magnetic separation (LipiDirect; Polymedco, Cortlandt Manor, NY). Non-HDL cholesterol concentration was calculated as the difference between total and HDL cholesterol. Urinary albumin was measured on 24-h samples using an anionic dye–binding assay (13).

Physical activity was assessed over a 3-day period by pedometer (Omron HJ-112) and with the Bouchard 3-Day Physical Activity Record (14). Body weight was determined at 0, 11, and 22 weeks, before breakfast while participants wore hospital gowns, using a digital scale accurate to 0.1 kg. Waist circumference was measured with a tape measure placed 2.5 cm above the umbilicus. Hip circumfer-

ence was measured at the maximal protrusion of the buttocks.

Blood pressure was measured after participants had rested in a seated position for 5 min using a digital monitor (Omron HEM-711) and a standard cuff maintained at the level of the heart. Three measurements were taken at 2-min intervals; the first measurement was disregarded, and a mean was calculated for the remaining two values.

Statistical analyses
To have an 80% chance of detecting a 1.5–percentage point between-group A1C difference as significant (at the two-sided 5% level), with an assumed SD of 1.9% and a loss to follow-up of 26%, 34 participants were required per group. An interim analysis indicated group differences of 0.8% with an SD of 1.3%; therefore, a revised power analysis was conducted. To have an 80% chance of detecting a 0.8% difference as significant with an SD of 1.3% and loss to follow-up of 33%, an additional 15 participants were required per group.

Between-subject t tests were calculated for each measure to determine whether the changes associated with the intervention diet were greater than those associated with the control diet. Within each diet group, paired comparison t tests were calculated to test whether the change from baseline to 22 weeks was significantly different from zero. The primary analysis of the main end point was intention to treat and included all participants. Because medication changes influence the dependent measures, exploratory analyses were performed for the subgroup whose medications remained constant. An α of 0.05 was used for all statistical tests, with no adjustment for multiple comparisons.

Regression analyses assessed whether the diet group effects on A1C and body weight were significant, while controlling for baseline values, and whether the diet group effect on A1C was significant, while controlling for baseline A1C and changes in body weight. Pearson correlations were calculated for the relationship between A1C change and weight change.

An interim analysis was performed after week 11 to assess whether benefits or adverse outcomes were statistically unusual.

RESULTS — Of 1,049 individuals screened by telephone, 99 met participation criteria and were randomly assigned

Table 1—*Baseline demographic and clinical variables*

	Vegan group	ADA group	P value
n	49	50	
Age (years)	56.7 (35–82)	54.6 (27–80)	0.29
Sex			0.26
Male	22 (45)	17 (34)	
Female	27 (55)	33 (66)	
Race, ethnicity			0.71*
Black, non-Hispanic	22 (45)	22 (44)	
White, non-Hispanic	21 (43)	22 (44)	
White, Hispanic	4 (8)	2 (4)	
Asian, non-Hispanic	2 (4)	4 (8)	
Marital status			0.08
Not married	20 (41)	26 (52)	
Married	29 (59)	24 (48)	
Education			0.69
High school, partial or graduate	6 (12)	3 (6)	
College, partial or graduate	26 (53)	25 (50)	
Graduate degree	17 (35)	22 (44)	
Occupation			0.04
Service occupation	3 (6)	7 (14)	
Technical, sales, administrative	16 (33)	18 (36)	
Professional or managerial	15 (31)	21 (42)	
Retired	15 (31)	4 (8)	
On insulin	11 (22)	5 (10)	0.09
On metformin	34 (69)	39 (78)	0.33
On sulfonylurea	25 (51)	29 (58)	0.49
On thiazolidinedione	16 (33)	15 (30)	0.78
On other diabetes medications	1 (2)	2 (4)	0.57
On blood pressure medications	31 (63)	38 (76)	0.17
On lipid-lowering medications	27 (55)	27 (54)	0.88
History of eye involvement	9 (18)	10 (20)	0.82
History of renal involvement	6 (12)	4 (8)	0.48
History of neuropathy	18 (37)	24 (48)	0.25
Mean BMI (kg/m^2)	33.9	35.9	0.18
<25 kg/m^2	5 (10)	2 (4)	
25–29.9 kg/m^2	14 (29)	5 (10)	
≥30 kg/m^2	30 (61)	43 (86)	

Data are mean (range) or n (%) unless otherwise indicated. P values refer to t test for continuous variables and χ^2 for categorical variables. *P value calculated for race distribution; for ethnicity (Hispanic vs. non-Hispanic), P = 0.39.

to the vegan (n = 49) or ADA (n = 50) groups. The reasons for exclusion were A1C values outside the required range (n = 201), failure to meet other participation criteria (n = 279), inability to attend scheduled meetings (n = 187), failure to keep interview appointment (n = 153), reluctance to change diet (n = 72), and other or unspecified (n = 58). The participants' demographic and clinical characteristics (Table 1) were similar to those of individuals with type 2 diabetes in the Washington, DC, area. All participants completed laboratory assessments at 22 weeks.

Three vegan participants and eight ADA participants failed to complete 22-week dietary records. Both groups reduced energy intake (vegan 1,759 ± 468 to 1,425 ± 427 kcal/day, P < 0.0001; ADA 1,846 ± 597 to 1,391 ± 382 kcal/day, P < 0.0001 [between-group P = 0.22]) and protein intake (vegan 77 ± 27 to 51 ± 16 g/day, P < 0.0001; ADA 85 ± 27 to 73 ± 23 g/day, P = 0.002 [between group P = 0.01]). Carbohydrate intake increased in the vegan group from 205 ± 69 to 251 ± 70 g/day (P < 0.0001) but fell in the ADA group from 213 ± 70 to 165 ± 51 g/day (P < 0.0001 [between-group P < 0.001]).

Fat intake fell in both groups (vegan 72 ± 28 to 30 ± 19 g/day, P < 0.0001; ADA 73 ± 35 to 52 ± 21 g/day, P < 0.0001 [between-group P = 0.002]), as did saturated fat (vegan 23 ± 10 to 6 ± 4

g/day, P < 0.0001; ADA 23 ± 12 to 14 ± 6 g/day, P < 0.0001 [between-group P < 0.001]) and cholesterol (vegan 291 ± 223 to 24 ± 57 mg/day, P < 0.0001; ADA 317 ± 200 to 189 ± 89 mg/day, P < 0.0001 [between-group P = 0.002]). Fiber increased only among vegans (18.8 ± 6.4 to 36.3 ± 13.3 g/day, P < 0.0001; ADA 19.5 ± 6.9 to 19.0 ± 7.9 g/day, P = 0.73 [between-group P < 0.001]).

Pedometer readings and self-reported energy expenditure revealed no significant between-group differences. Group-specific dietary adherence criteria were met by 67% (33 of 49) of vegan group participants and 44% (22 of 50) of ADA group participants. During the intervention period, 43% (21 of 49) of vegan group participants and 26% (13 of 50) of ADA group participants reduced their diabetes medications, mainly as necessitated by hypoglycemia, while 8% (4 of 49) of vegans and 8% (4 of 50) of ADA participants increased medications without investigators' authorization.

A1C fell 0.96 percentage points (P < 0.0001) in the vegan group and 0.56 percentage points (P = 0.0009) in the ADA group (between-group P = 0.089; baseline-adjusted P = 0.091; Table 2 and Fig. 1). Among participants whose diabetes medications remained unchanged throughout (n = 24 vegan and n = 33 ADA), A1C fell 1.23 points in the vegan group and 0.38 points in the ADA group (P = 0.01; baseline-adjusted P = 0.007). Subanalyses were conducted to assess the effects of dietary adherence. For those who met adherence criteria (n = 33 vegan and n = 22 ADA), the A1C changes were −1.20% for the vegan group and −0.88% for the ADA group (P = 0.31). For those who were both adherent and medication stable (n = 17 vegan and n = 12 ADA), A1C changes were −1.48% for the vegan group and −0.81% for the ADA group (P = 0.15).

To test whether the effect of diet on A1C was mediated by body weight changes, a regression model was constructed, including baseline A1C, weight change, and diet group as predictors of A1C change, among those whose hypoglycemic medications remained constant. In this model, the effect of diet group was no longer significant (P = 0.23). Controlling for diet group and for baseline A1C scores, weight change was significantly associated with A1C change; each kilogram of weight loss was associated with a 0.12% drop in A1C. For the subgroup that did not change diabetes medications,

Table 2—Diet effects on clinical measures

	Vegan group (n = 49, except as noted)			ADA group (n = 50, except as noted)			Effect size	P value
	Baseline	22 weeks	Change	Baseline	22 weeks	Change		
Anthropometric and glycemic variables								
All participants								
A1C (%)	8.0 ± 1.1	7.1 ± 1.0	−1.0 ± 1.2*	7.9 ± 1.0	7.4 ± 1.0	−0.6 ± 1.1†	−0.4 (−0.9 to 0.1)	0.09
Fasting plasma glucose (mmol/l)	9.08 ± 2.95	7.11 ± 1.97	−1.97 ± 2.68*	8.90 ± 1.91	6.98 ± 1.91	1.92 ± 2.48†	−0.05 (−1.08 to 0.98)	0.92
Fasting plasma glucose (mg/dl)	163.5 ± 53.2	128.0 ± 35.5	−35.5 ± 48.3*	160.4 ± 40.7	125.8 ± 34.4	−34.6 ± 44.7*	−0.9 (−19.5 to 17.6)	0.92
Weight (kg)	97.0 ± 22.9	91.1 ± 22.4	−5.8 ± 4.4*	99.3 ± 21.0	95.0 ± 20.9	−4.3 ± 4.4*	−1.6 (−3.3 to 0.2)	0.08
BMI (kg/m²)	33.9 ± 7.8	31.8 ± 7.5	−2.1 ± 1.5*	35.9 ± 7.0	34.3 ± 7.3	−1.5 ± 1.5*	−0.6 (−1.2 to 0.1)	0.08
Waist (cm)	110.8 ± 18.4	105.5 ± 18.1	−5.3 ± 4.4*	112.3 ± 14.9	109.5 ± 14.7	−2.8 ± 4.7*	−2.5 (−4.3 to −0.7)	0.008
Hip (cm)	118.4 ± 17.8	114.5 ± 17.8	−3.9 ± 3.4*	121.3 ± 12.7	117.5 ± 12.2	−3.8 ± 3.9*	−0.1 (−1.5 to 1.4)	0.94
Waist-to-hip ratio (cm)	0.94 ± 0.08	0.92 ± 0.07	−0.02 ± 0.03‡	0.93 ± 0.07	0.93 ± 0.07	0.01 ± 0.04	−0.02 (−0.03 to 0.01)	0.003
Participants whose diabetes medications remained unchanged (n = 24 vegan, n = 33 ADA)								
A1C (%)	8.07 ± 1.24	6.84 ± 0.84	−1.23 ± 1.38†	7.88 ± 0.93	7.50 ± 1.03	−0.38 ± 1.11	−0.85 (−1.51 to −0.19)	0.01
Fasting plasma glucose (mmol/l)	9.85 ± 2.95	7.12 ± 1.80	2.73 ± 3.05†	8.90 ± 2.05	7.34 ± 2.05	1.57 ± 2.50‡	−1.17 (−2.64 to 0.31)	0.12
Fasting plasma glucose (mg/dl)	177.4 ± 53.2	128.2 ± 32.4	−49.2 ± 55.0†	160.3 ± 37.0	132.2 ± 36.9	−28.2 ± 45.0‡	−21.1 (−47.6 to 5.5)	0.12
Weight (kg)	102.4 ± 23.6	95.9 ± 22.4	−6.5 ± 4.3*	100.0 ± 19.4	96.9 ± 19.1	−3.1 ± 3.4*	−3.4 (−5.5 to −1.4)	0.001
BMI (kg/m²)	36.1 ± 7.5	33.8 ± 7.2	−2.3 ± 1.5*	36.0 ± 5.8	34.9 ± 5.9	−1.1 ± 1.2*	−1.2 (−1.9 to −0.5)	0.001
Waist (cm)	115.3 ± 17.9	110.3 ± 17.8	−5.0 ± 3.7*	113.3 ± 13.1	111.0 ± 13.5	−2.3 ± 4.2‡	−2.7 (−4.8 to −0.5)	0.017
Hip (cm)	123.3 ± 17.4	119.1 ± 17.3	−4.1 ± 2.8*	121.7 ± 12.1	118.6 ± 11.6	−3.1 ± 3.3*	−1.0 (−2.7 to 0.7)	0.23
Waist-to-hip ratio (cm)	0.94 ± 0.08	0.93 ± 0.07	−0.01 ± 0.03	0.93 ± 0.07	0.94 ± 0.08	0.00 ± 0.04	−0.02 (−0.03 to 0.00)	0.10
Renal variable								
Urinary albumin/24 h	33.0 ± 51.8	14.6 ± 17.8	−18.4 ± 39.0‡	55.0 ± 263.1	43.7 ± 212.0	−11.3 ± 53.9	−7.1 (−25.9 to 11.7)	0.45
With albumin >30 mg/24 h (n)	12	5	−7	8	6	−2	NA	NA
Blood pressure (n = 48 vegan, n = 50 ADA) (mmHg)§								
Systolic	123.8 ± 17.1	120.0 ± 18.3	−3.8 ± 12.6‖	122.9 ± 15.1	119.4 ± 16.5	−3.6 ± 13.7	−0.2 (−5.5 to 5.1)	0.93
Diastolic	77.9 ± 11.1	72.8 ± 10.2	−5.1 ± 8.3*	80.0 ± 10.5	76.7 ± 11.1	−3.3 ± 8.8‖	−1.8 (−5.2 to 1.6)	0.30
All participants								
Total cholesterol (mg/dl)	187.0 ± 37.4	159.3 ± 31.9	−27.7 ± 28.5*	198.9 ± 44.0	174.6 ± 36.2	−24.2 ± 30.5*	−3.5 (−15.3 to 8.3)	0.56
HDL cholesterol (mg/dl)	52.3 ± 19.7	47.3 ± 16.9	−5.0 ± 7.1*	49.8 ± 14.5	46.6 ± 11.8	−3.2 ± 11.0‖	−1.8 (−5.5 to 1.9)	0.34
Non-HDL cholesterol (mg/dl)	134.7 ± 39.2	112.0 ± 31.9	−22.7 ± 28.2*	149.0 ± 44.1	128.0 ± 35.0	−21.0 ± 31.5*	−1.7 (−13.6 to 10.2)	0.78
Total cholesterol/HDL (mg/dl)	4.0 ± 1.6	3.7 ± 1.2	−0.3 ± 0.9‖	4.3 ± 1.7	3.9 ± 1.2	−0.4 ± 1.2‖	−0.0 (−0.4 to 0.4)	0.92
LDL cholesterol (n = 49 vegan, n = 48 ADA) (mg/dl)¶	104.4 ± 32.9	88.0 ± 27.8	−16.4 ± 30.6†	118.5 ± 41.5	103.1 ± 33.3	−15.4 ± 25.1*	−1.0 (−12.3 to 10.3)	0.86
VLDL cholesterol (n = 47 vegan, n = 47 ADA) (mg/dl)	26.2 ± 14.4	23.0 ± 10.2	−3.2 ± 10.0‖	26.8 ± 13.8	22.3 ± 10.0	−4.4 ± 12.4‖	1.2 (−3.4 to 5.8)	0.60
Triglycerides (mg/dl)	148.1 ± 112.5	119.7 ± 56.0	−28.5 ± 80.0‖	158.1 ± 133.1	132.9 ± 114.4	−25.1 ± 124.7	−3.3 (−45.2 to 38.6)	0.87
Log triglycerides	2.08 ± 0.28	2.03 ± 0.21	−0.05 ± 0.17‖	2.11 ± 0.25	2.05 ± 0.23	−0.07 ± 0.20‖	0.02 (−0.05 to 0.09)	0.61

Participants with no changes to lipid-controlling medications (n = 39 vegan, n = 41 ADA, except as noted)							
Total cholesterol (mg/dl)	190.5 ± 36.8	156.9 ± 25.1	−33.5 ± 21.5*	194.9 ± 40.9	175.9 ± 36.2	−19.0 ± 28.5*	−14.5 (−25.8 to −3.2)	0.01
HDL cholesterol (mg/dl)	54.6 ± 21.0	48.6 ± 18.4	−6.0 ± 6.8*	49.2 ± 15.5	46.4 ± 12.2	−2.8 ± 11.6	−3.2 (−7.5 to 1.1)	0.14
Non-HDL cholesterol (mg/dl)	135.9 ± 38.4	108.3 ± 25.6	−27.6 ± 21.1*	145.7 ± 42.9	129.4 ± 35.9	−16.3 ± 30.1‖	−11.3 (−22.9 to 0.3)	0.05
Total cholesterol/HDL (mg/dl)	3.9 ± 1.5	3.6 ± 1.2	−0.3 ± 0.6‡	4.4 ± 1.8	4.0 ± 1.3	−0.3 ± 1.2	−0.0 (−0.4 to 0.4)	0.98
LDL cholesterol (n = 39 vegan, n = 39 ADA) (mg/dl)¶	107.3 ± 34.3	84.6 ± 22.5	−22.6 ± 22.0*	115.3 ± 40.4	104.6 ± 33.7	−10.7 ± 23.3‖	−11.9 (−22.2 to −1.7)	0.02
VLDL cholesterol (n = 38 vegan, n = 38 ADA) (mg/dl)	26.6 ± 15.4	23.1 ± 10.9	−3.5 ± 10.5‖	25.5 ± 13.2	21.7 ± 9.0	−3.8 ± 12.1	0.4 (−4.8 to 5.6)	0.89
Triglycerides (mg/dl)	140.3 ± 89.1	118.2 ± 57.3	−22.2 ± 58.5‖	157.4 ± 143.0	134.6 ± 122.9	−22.8 ± 134.3	0.6 (−45.9 to 47.2)	0.98
Log triglycerides	2.06 ± 0.28	2.02 ± 0.22	−0.04 ± 0.16	2.11 ± 0.25	2.05 ± 0.24	−0.06 ± 0.21	0.02 (−0.1 to 0.1)	0.68

Data are means ± SD unless otherwise indicated. Listed *P* values are for comparisons of between-group (vegan vs. ADA) changes (baseline to 22 weeks). *$P < 0.0001$, †$P < 0.001$, ‡$P < 0.01$, and ‖$P < 0.05$ for within-group changes. §Blood pressure was not determined on one vegan group participant due to equipment failure. ¶When triglycerides exceeded 400 mg/dl, LDL was calculated via direct-LDL; two ADA-group individuals were excluded due to lack of sufficient plasma samples. SI conversion: to convert HDL, LDL, and total cholesterol to mmol/l, multiply by 0.0259; for triglycerides, multiply by 0.0113.

the Pearson's correlation of weight change with A1C change was $r = 0.51$, $P < 0.0001$ (within the vegan group [n = 24], $r = 0.39$, $P = 0.05$; within the ADA group [n = 33], $r = 0.49$, $P = 0.004$).

Body weight fell 5.8 kg in the vegan group ($P < 0.0001$) and 4.3 kg in the ADA group ($P < 0.0001$) (between-group $P = 0.082$; baseline-adjusted $P = 0.066$). Among medication-stable participants, vegan participants lost 6.5 kg compared with 3.1 kg for ADA participants ($P < 0.001$; baseline-adjusted $P = 0.001$).

The reduction in urinary albumin was significant in the vegan group ($P = 0.002$) but not in the ADA group ($P = 0.14$). The unadjusted between-group difference was not significant. However, after adjustment for baseline values, the effect of diet was significant ($P = 0.013$).

For the entire sample, there were no between-group differences in lipid values. Among those whose lipid-controlling medications remained constant (80% [39 of 49] of vegan group, 82% [41 of 50] of ADA group), reductions in total cholesterol were −0.866 mmol/l (−33.5 mg/dl, −17.6%) for the vegan group and −0.491 mmol/l (−19.0 mg/dl, −9.7%) for the ADA group ($P = 0.0125$). Changes in LDL cholesterol were −0.58 mmol/l (−22.6 mg/dl, −21.2%) for the vegan group and −0.277 mmol/l (−10.7 mg/dl, −9.3%) for the ADA group ($P = 0.023$). Changes in HDL cholesterol were −0.16 mmol/l (−6.0 mg/dl, −11.0%) for the vegan group and −0.07 mmol/l (−2.8 mg/dl, −5.7%) for the ADA group ($P = 0.14$). The total-to-HDL cholesterol ratio fell for both groups, as did triglyceride concentrations.

There were no treatment-related serious adverse events.

CONCLUSIONS — Both diets were associated with significant clinical improvements, as indicated by reductions in A1C, body weight, plasma lipid concentrations, and urinary albumin excretion. Among medication-stable participants, changes in A1C, weight, BMI, waist circumference, total cholesterol, and LDL cholesterol were significantly greater in the vegan group. The magnitude of A1C reduction in medication-stable vegan group participants, 1.23 percentage points, compares favorably with that observed in single-agent therapy with oral diabetes drugs (15).

A low-fat plant-based diet influences nutrient intake and body composition in several ways that may, in turn, affect in-
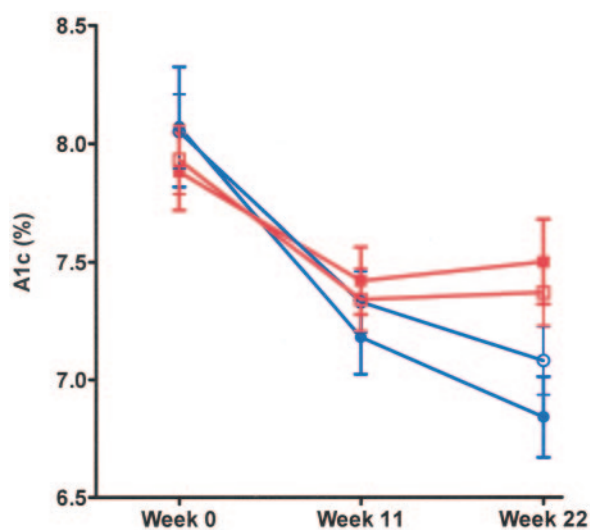
Figure 1—*A1C at baseline and at 11 and 22 weeks. Open circles: all vegan group participants* (n = 49); *closed circles: medication-stable vegan group participants* (n = 24); *open squares: all ADA group participants* (n = 50); *closed squares: medication-stable ADA group participants* (n = 33). *Error bars represent SE of the mean.* P = 0.09 *for between-group comparison from baseline to 22 weeks for full sample;* P = 0.01 *for medication-stable participants (vegan vs. ADA).*

sulin sensitivity. First, because such diets are low in fat and high in fiber, they typically cause associated reductions in dietary energy density and energy intake, which are not fully compensated for by increased food intake (16,17). Our data suggest that the weight-reducing effect of the vegan diet (4) is responsible for a substantial portion of its effect on A1C.

Independent of their effect on body weight, reductions in total fat intake and in the proportion of dietary saturated to unsaturated fat increase insulin sensitivity (18), as do increased intake of low–glycemic index and high-fiber foods (1).

Finally, limited evidence suggests that reductions in iron stores increase insulin sensitivity (19). A vegan diet provides iron in its nonheme form, which is somewhat less absorbable than heme iron. A study comparing 30 ovolactovegetarians and 30 meat eaters, all of whom were healthy and had BMIs <23 kg/m^2, showed that vegetarians had adequate, but lower, body iron stores, compared with meat eaters (serum ferritin concentration 35 μg/l [95% CI 21–49] vs. 72 μg/l [45–100]). The vegetarians also demonstrated less insulin resistance (steady-state plasma glucose concentration 4.1 mmol/l [3.5–5.0] vs. 6.9 mmol/l [5.2–7.5], respectively) (19).

Insulin resistance is related to lipid accumulation within muscle cells (intramyocellular lipid), apparently due to a genetically based reduction in mitochondrial activity identifiable many years be-

fore diabetes manifests (20). This lipid accumulation may be responsive to diet. High-fat diets appear to downregulate the genes required for mitochondrial oxidative phosphorylation in skeletal muscle (21). In contrast, a case-control study found that soleus muscle intramyocellular lipid concentrations were significantly lower in a group of 21 vegans compared with 25 omnivores (−9.7 [95% CI −16.2 to −3.3], $P = 0.01$) (22).

The lipid-lowering effect of vegan diets, attributable to their absence of dietary cholesterol, low saturated fat content, and a specific cholesterol-reducing effect of soluble fiber and other plant constituents (23), is particularly important given that cardiovascular complications are the primary cause of morbidity and mortality in diabetes. While diets high in refined carbohydrate may increase triglyceride concentrations, high-fiber and low–glycemic index foods appear to have the opposite result (24).

The limited compliance of the ADA group merits comment. Researchers have long lamented the difficulties in adhering to diets for diabetes (25). The A1C reduction observed in the ADA group was similar to that found in previous studies (26). A potential weakness of the ADA guidelines is that they require portion size limits for overweight individuals, and limitations on saturated-fat intake are based on these limited energy intakes. Individuals who exceed their prescribed energy intake limits with overly large

portions can, as a result, easily exceed recommended limits on saturated fat. In contrast, the vegan diet includes no animal fat, so variations in food quantity are less likely to result in substantial increases in saturated fat intake. Because the vegan diet is based on the elimination of certain foods, it may be easier to understand than regimens that limit quantities of certain foods without proscribing any. The acceptability of low-fat vegan diets in clinical studies is similar to that of seemingly more moderate diets (27).

This study's strengths include its analysis of dependent measures without regard to variations in dietary adherence and applicability outside the research setting. A study limitation was that both diets made participants vulnerable to the hypoglycemic effect of their diabetes medications, resulting in medication reductions that confound the interpretation of A1C changes and necessitating a subgroup analysis of medication-stable participants. Because these episodes occurred early in the trial, there was no opportunity to bring interim laboratory values forward. Also, most study participants were taking antihypertensive medications, which may have blunted the effect of diet on blood pressure.

In conclusion, in individuals with type 2 diabetes participating in a 22-week clinical trial, both a low-fat vegan diet and a diet following ADA guidelines improved glycemic control; however, the changes were greater in the vegan group. Further research is necessary to establish longer-term diet effects and sustainability.

References
1. Jenkins DJA, Kendall CWC, Marchie A, Jenkins AL, Augustin LSA, Ludwig DS, Barnard ND, Anderson JW: Type 2 diabetes and the vegetarian diet. *Am J Clin Nutr* 78:610S–616S, 2003
2. Fraser GE: Vegetarianism and obesity, hypertension, diabetes, and arthritis. In *Diet, Life Expectancy, and Chronic Disease*. Oxford, U.K., Oxford University Press, 2003, p. 129–148
3. Nicholson AS, Sklar M, Barnard ND, Gore S, Sullivan R, Browning S: Toward improved management of NIDDM: a ran-

domized, controlled, pilot intervention using a low-fat, vegetarian diet. *Prev Med* 29:87–91, 1999

4. Barnard ND, Scialli AR, Turner-McGrievy G, Lanou AJ, Glass J: The effects of a low-fat, plant-based dietary intervention on body weight, metabolism, and insulin sensitivity. *Am J Med* 118:991–997, 2005

5. Wilson DH, Bogacz JP, Forsythe CM, Turk PJ, Lane TL, Gates RC, Brandt DR: Fully automated assay of glycohemoglobin with the Abbott IMx analyzer: novel approaches for separation and detection. *Clin Chem* 39:2090–2097, 1993

6. American Diabetes Association: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (Position Statement). *Diabetes Care* 26 (Suppl. 1):S51–S61, 2003

7. Schakel SF, Sievert YA, Buzzard IM: Sources of data for developing and maintaining a nutrient database. *J Am Diet Assoc* 88:1268–1271, 1988

8. Barthelmai W, Czok R: Enzymatic determinations of glucose in the blood, cerebrospinal fluid and urine. *Klin Wochenschr* 40:585–589, 1962 [in German]

9. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC: Enzymatic determination of total serum cholesterol. *Clin Chem* 20:470–475, 1974

10. Wieland H, Seidel D: A simple specific method for precipitation of low density lipoproteins. *J Lipid Res* 24:904–909, 1983

11. Finley PR, Schifman RB, Williams RJ, Licht DA: Cholesterol in high-density lipoprotein: use of Mg2+/dextran sulfate in its enzymatic measurement. *Clin Chem* 24:931–933, 1978

12. Friedewald WT, Levy RI, Fredrickson DS: Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 18:499–502, 1972

13. Corcoran RM, Durnan SM: Albumin determination by a modified bromocresol green method (Letter). *Clin Chem* 23:765–766, 1977

14. Bouchard C, Tremblay A, LeBlanc C, Lortie G, Savard R, Theriault G: A method to assess energy expenditure in children and adults. *Am J Clin Nutr* 37:461–467, 1983

15. Krentz AJ, Bailey CJ: Oral antidiabetic agents: current role in type 2 diabetes mellitus (Review). *Drugs* 65:385–411, 2005

16. Kendall A, Levitsky DA, Strupp BJ, Lissner L: Weight loss on a low-fat diet: consequence of the imprecision of the control of food intake in humans. *Am J Clin Nutr* 53:1124–1129, 1991

17. Howarth NC, Saltzman E, Roberts SB: Dietary fiber and weight regulation (Review). *Nutr Rev* 59:129–139, 2001

18. Lovejoy JC, Windhauser MM, Rood JC, de la Bretonne JA: Effect of a controlled high-fat versus low-fat diet on insulin sensitivity and leptin levels in African-American and Caucasian women. *Metabolism* 47:1520–1524, 1998

19. Hua NW, Stoohs RA, Facchini FS: Low iron status and enhanced insulin sensitivity in lacto-ovo vegetarians. *Br J Nutr* 86:515–519, 2001

20. Petersen KF, Dufour S, Befroy D, Garcia R, Shulman GI: Impaired mitochondrial activity in the insulin-resistant offspring of patients with type 2 diabetes. *N Engl J Med* 350:664–671, 2004

21. Sparks LM, Xie H, Koza RA, Mynatt R, Hulver MW, Bray GA, Smith SR: A high-fat diet coordinately downregulates genes required for mitochondrial oxidative phosphorylation in skeletal muscle. *Diabetes* 54:1926–1933, 2005

22. Goff LM, Bell JD, So PW, Dornhorst A, Frost GS: Veganism and its relationship with insulin resistance and intramyocellular lipid. *Eur J Clin Nutr* 59:291–298, 2005

23. Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, Emam A, Parker TL, Vidgen E, Lapsley KG, Trautwein EA, Josse RG, Leiter LA, Connelly PW: Effects of a dietary portfolio on cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. *JAMA* 290:502–510, 2003

24. Jenkins DJ, Wolever TM, Kalmusky J, Guidici S, Giordano C, Patten R, Wong GS, Bird JN, Hall M, Buckley G, et al.: Low-glycemic index diet in hyperlipidemia: use of traditional starchy foods. *Am J Clin Nutr* 46:66–71, 1987

25. Laitinen JH, Ahola IE, Sarkkinen ES, Winberg RL, Harmaakorpi-Iivonen PA, Uusitupa MI: Impact of intensified dietary therapy on energy and nutrient intakes and fatty acid composition of serum lipids in patients with recently diagnosed non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 93:276–283, 1993

26. Franz MJ, Splett PL, Monk A, Barry B, McClain K, Weaver T, Upham P, Bergenstal R, Mazze RS: Cost-effectiveness of medical nutrition therapy provided by dietitians for persons with non-insulin-dependent diabetes mellitus. *J Am Diet Assoc* 95:1018–1024, 1995

27. Barnard ND, Scialli AR, Turner-McGrievy GM, Lanou AJ: Acceptability of a low-fat vegan diet compares favorably to a step II diet in a randomized, controlled trial. *J Cardiopulm Rehabil* 24:229–235, 2004

©