METABOLIC SYNDROME AND RELATED DISORDERS
Volume 1, Number 4, 2003

The Effects of a Low-Carbohydrate Regimen on Glycemic Control and Serum Lipids in Diabetes Mellitus

DANIEL F. O'NEILL,[1] ERIC C. WESTMAN, M.D., M.H.S.,[1]
and RICHARD K. BERNSTEIN, M.D.[2]

ABSTRACT

The Diabetes Complications and Control Trial (DCCT) established that diabetic complications could be reduced by improvement in glycemic control. The ideal diabetes treatment protocol would maintain blood glucose levels in normal ranges without resulting in frequent hypoglycemia. Because several studies suggest an inverse relationship between carbohydrate consumption and the level of glycemic control, the effects of an intensive treatment program, which included dietary carbohydrate restriction, are examined in this paper. A chart review was performed of 30 patients who self-reported the consumption of 30 g of carbohydrate daily, followed a strict insulin regimen, monitored blood glucose levels at least four times daily, and had follow-up clinical visits or phone calls with their physician. For both type I and type II diabetics, there were significant improvements in glycemic control and mean fasting lipid profiles at follow-up. The mean hemoglobin A1c decreased by 27.8% from 7.9 to 5.7 ($p < 0.001$). The LDL cholesterol decreased by 16.5%, from 155.4 to 129.7 mg/dL ($p = 0.004$). The triglycerides decreased by 31.1%, from 106.8 to 73.6 mg/dL ($p = 0.005$). The HDL cholesterol increased by 43.3%, from 50.4 to 72.2 mg/dL ($p < 0.001$). The cholesterol/HDL ratio decreased by 31.5%, from 4.99 to 3.42 ($p < 0.001$). A carbohydrate-restricted regimen improved glycemic control and lipid profiles in selected motivated patients. Therefore, further investigation of the effects of this protocol on treating diabetes mellitus should be considered. Additionally, the reduction of insulin afforded by this diet could theoretically lead to a reduction in hypoglycemic events.

INTRODUCTION

GOOD GLYCEMIC CONTROL is thought to be of paramount importance in preventing the many long-term complications of diabetes mellitus.[1,2] The Diabetes Control and Complications Trial (DCCT) revealed that subjects who followed an "intensive therapy" protocol compared with those who continued the "standard therapy" had a 76% reduction in retinopathy, a 50% reduction in nephropathy, a 60% reduction in neuropathy, and a notable

[1]Department of Medicine, Duke University Medical Center, Durham, North Carolina.
[2]Peripheral Vascular Disease Clinic, Albert Einstein College of Medicine, Jacobi Medical Center, Bronx, New York.

reduction in heart disease risk factors.[1] Additionally, in the UK Prospective Diabetes Study (UKPDS), intensive glycemic control in type II diabetics was shown to decrease the progression of microvascular disease as well as reduce the risk of heart attacks. In the UKPDS, subjects followed a conventional protocol regulated by diet alone, or an intensive protocol using either oral hypoglycemic agents or insulin. The results showed that subjects following the intensive protocol had a 32% reduction in risk for any diabetes-related endpoint and a 42% reduction in diabetes-related death when compared with the conventional group.[2] Clearly, the results of the DCCT and UKPDS support that tighter glycemic control leads to a reduction in diabetes-related complications.

A more detailed examination of the DCCT shows that the improvements in the intensive therapy group were found with only a modest reduction in hemoglobin A1c. The mean hemoglobin A1c for the intensive therapy group was 7.1%, corresponding to a mean serum glucose level of 155 mg/dL. The DCCT intensive therapy protocol included a daily carbohydrate intake of 230 g, self-monitoring of glucose levels at least four times daily, four daily insulin injections, monthly clinical visits, and a diet and exercise plan. Despite the extensive monitoring effort, the intensive therapy cohort had a threefold increase of severe hypoglycemic events compared with the standard therapy cohort. Accordingly, subjects following the intensive therapy had a reduction in long-term complications, but this benefit was tempered by an increased risk of severe hypoglycemic reactions.[1]

These DCCT findings suggest that normal glycemic control (hemoglobin A1c of 4.0–6.0%) is not possible even with intensive treatment, unless there is some other way to improve glycemic control without increasing the risk of hypoglycemia. Recent preliminary studies have suggested that reduction of daily carbohydrate intake leads to improved glycemic control. One study over a 19-month period found that diabetics who increased their daily carbohydrate consumption from 38.8% (206.3 g/day) carbohydrate to 45.4% (241.4 g/day) carbohydrate had an increase in mean hemoglobin A1c from 9.4% to 11.2%.[3] Another study with a cross-over design involving 28 type II diabetics found an increase in hemoglobin A1c from 7.8% to 9.2% after increasing dietary carbohydrate from 25% to 55% of the daily intake.[4] A third clinical series including type II diabetics who reduced their daily carbohydrate consumption to 100 g/day obtained a mean hemoglobin A1c of 6.9%.[5] Therefore, a growing number of studies suggest that carbohydrate restriction can lead to better glycemic control.

Along the lines of this research, we examined an approach using even greater carbohydrate restriction in the management of diabetes, involving a reduction of carbohydrate to less than 30 g/day, intensive glucose monitoring, and multiple, small insulin injections.[6] In this regimen, the 30 g of carbohydrate are obtained principally from vegetables with low glycemic indexes. Based on anecdotal reports of excellent glycemic control and no recounted instances of severe hypoglycemic reactions in diabetics following this protocol, one of the proponents of this approach (R.K.B.) was contacted, and he agreed to share clinical chart information of his patients for review.

MATERIALS AND METHODS

This study is a retrospective case series analysis of both type I and type II diabetics following a carbohydrate-restricted regimen and other supplementary protocols involving blood glucose measurements and methods of injecting insulin. The charts selected for the study were based on assessment of the patients' ability to comply with the regimen. Compliance was self-reported by the individual and indicated in the chart. Another criterion for selection was that the charts had available follow-up data. Thirty charts were selected, abstracted, and entered into a dedicated database without identifiers. The data were then transferred to a statistical program for analysis (SAS version 6.12, Cary, NC). A chi-square statistic, *t*-test, Wilcoxon signed rank test, or ANCOVA model was used for statistical comparisons, as appropriate. This de-identified analysis of existing clinical data was approved by the Duke Institutional Review Board.

The multi-component program began with an intensive 3-day clinical evaluation and explanation of the program at an outpatient diabetes specialty clinic. After this evaluation, patients followed the regimen on their own. This regimen included the following: a carbohydrate-restricted diet (30 g of carbohydrate daily); intensive glucose monitoring (>4 times daily); insulin regulation; and documentation of the time of glucose levels, meals, insulin dosages, and exercise.[5] Subsequent follow-up phone calls or office visits were used to tailor the individual regimen of each patient. The recommended daily carbohydrate intake of 30 g was distributed as follows: 6 g for breakfast, 12 g for lunch, and 12 g for dinner. No sugar or other rapid-acting carbohydrates were allowed, and eating was prohibited outside of regularly scheduled meals. Additionally, close scrutiny was kept of biological phenomena affecting glycemic levels, including gastroparesis and the dawn phenomenon. Depending on the effects of these phenomena, insulin requirements were adjusted accordingly under the physician's care.

All changes in insulin dosage were made with small, incremental adjustments. Due to the restricted amount of carbohydrates in their diets, patients were instructed to inject very small insulin dosages (as small as one-fourth unit) for corrections. Timing and size of insulin injections were key elements of this regimen. Patients were instructed to wait 5 h between subsequent bolus insulin injections to assure that no crossover effect would occur in serum insulin levels from residual dosages. No more than 9 h could elapse between evening basal insulin dosages and morning basal dosages to prevent the effects of the dawn phenomenon. Additionally, as predetermined by their physician, patients learned how long to wait to eat after injecting each pre-meal bolus of insulin and were strongly encouraged to adhere to such constraints. All insulin injections had to be less than seven units in size. If a larger dosage was required, it would be divided into two or more separate injections. This technique is used to improve the predictability of the absorption of insulin injections.[7]

To treat hypoglycemia, patients were instructed to take glucose tablets that had a calibrated, predetermined effect on their glucose level. The physician would inform the patient of the effect a particular brand of glucose tablet would have on his or her blood glucose level, as determined by the patient's weight. This allowed for the individual, after having taken his or her glucose measurement, to calculate how many tablets would be needed to return to a target blood glucose level without overestimating how much glucose to consume.[6] This controlled approach in treating low blood glucoses made it less likely for patients to become hyperglycemic soon afterward from excessive glucose consumption, helping to improve the patients' overall glycemic control. Following this regimen, common "emergency food" would not suffice for treating hypoglycemia, as one could not be certain of exactly how much carbohydrate such foods would contain or their speed of action in raising glucose levels. It is important to note that patients were, of course, able to consume such "emergency foods" in the event that glucose tablets were not available.

Patients were required to keep careful records of their blood glucose levels, meals, exercise, medication, overeating, any other unusual life events or health problems, and the times of day at which these occurrences took place on a standardized flow sheet. Prior to planned telephone conferences with the physician, patients faxed their records for evaluation. The flow sheet was reviewed and any necessary adjustments in insulin dose, exercise, or meal plans were made.

After following this regimen for a variable length of time (2–79 months), patients returned to the clinic for a follow-up examination. At the follow-up appointments, the hemoglobin A1c, body weight, and fasting lipid profile were measured and recorded on a standardized flow sheet.

RESULTS

Thirty patients were identified with self-reported excellent program compliance. The mean age of patients was 51.4 years (SD = 14.9); 53.3% were male; 96.7% were Caucasian; 66.7% carried the diagnosis of type II diabetes

mellitus, and 33.3% were diagnosed with type I diabetes. The mean duration of diabetes was 13.8 years (SD = 11.3). Eighteen patients were taking insulin injections at baseline.

As shown in Table 1, there were significant improvements in glycemic control. Over a period of 21.4 months (SD = 22.3), the mean change in hemoglobin A1c from baseline was −2.2% (SD = 1.4, $p < 0.001$), while daily insulin dosage did not change significantly. Seven patients were started on insulin injections (mean dose of 22 units/day); 16 patients had insulin dosages reduced (36.8% reduction on average, range, 3–64% reduction); two patients had insulin dosages increased by 1 unit per day or less. Eight patients were taking oral insulin-sensitizing agents at baseline, and nine patients were taking oral agents at follow-up. In six patients, the oral agents were discontinued or decreased, and in 8 patients, they were initiated or increased.

There were also significant improvements in lipid profiles (Table 1). The LDL cholesterol decreased by 16.5%, from 155.4 to 129.7 mg/dL ($p = 0.004$). The triglycerides decreased by 31.1%, from 106.8 to 73.6 mg/dL ($p = 0.005$). The HDL cholesterol increased by 43.3%, from 50.4 to 72.2 mg/dL ($p < 0.001$). The distribution of follow-up HDL was as follows: 5 were 35–50 mg/dL; 10 were 50–65 mg/dL; 7 were 65–80 mg/dL; 8 were >80 mg/dL. The cholesterol/HDL ratio decreased by 31.5%, from 5.0 to 3.4 ($p < 0.001$). There was no significant change in total cholesterol from baseline to follow-up.

The individual values for patients with type I and type II diabetes are shown in Tables 2 and 3, respectively. There was significantly greater improvement in the mean hemoglobin A1c for type II diabetics (from 8.4% to 5.8%) than type I diabetics (from 6.8% to 5.5%) ($p = 0.2$). There was significantly greater reduction in insulin use for type I diabetics (from 47.0 to 30.0 units) than for type II diabetics (from 22.3 to 22.1 units daily) ($p = 0.03$). Changes in lipid profiles were similar for both types of diabetics. Combining both groups, body weight decreased by 5.5 kg (from 82.0 to 76.5 kg, $n = 23$, $p < 0.01$). In assessing kidney function, we found that serum BUN and creatinine did not change significantly in 17 patients with complete baseline and follow-up measurements.

DISCUSSION

Several studies suggest a positive correlation between the amount of daily carbohydrate consumption and glycemic control in diabetes mellitus.[1,3–5] In this chart review, we found that a strict diabetic program—including a restriction of carbohydrate intake to about 30 g per

TABLE 1. EFFECT OF PROGRAM ON GLYCEMIC CONTROL AND LIPID PROFILES OF TYPE I AND II DIABETICS

Variable	*n*	*Baseline mean (SD)*	*Follow-up mean (SD)*	*Change (SD)*	*p value*
Hemoglobin A1C	26**	7.9 (1.7)	5.7 (0.9)	−2.2 (1.4)	0.0001*
Triglycerides	27	106.8 (69.3)	73.6 (41.3)	−33.2 (56.2)	0.005*
Total cholesterol	29	229.0 (47.9)	221.6 (33.8)	−7.4 (48.4)	0.41
HDL-C	29	50.4 (16.1)	72.2 (27.5)	+21.8 (19.2)	0.0001*
LDL-C	24	155.4 (47.2)	129.7 (28.0)	−25.7 (39.3)	0.004*
Cholesterol/HDL ratio	28	5.0 (1.9)	3.4 (1.0)	−1.6 (1.5)	0.0001*
Daily insulin dosage (units per day)	27	31.5 (29.5)	25.1 (12.7)	−6.4 (63.2)	0.15
Weight in kg	23	82.0 (22.2)	76.5 (18.1)	−5.5 (9.7)	0.01*

*$p < 0.05$, for baseline to follow-up change using Wilcoxon Signed Rank Test.
**Change in numbers reflects missing data.

TABLE 2. INITIAL AND FOLLOW-UP GLYCEMIC CONTROL AND LIPID PROFILES IN TYPE I DIABETICS

Case	*Age, years*	*Gender*	*Diabetes duration, months*	*Pre/ post*	*Hgb A1C, %*	*Trig, mg/dL*	*Chol, mg/dL*	*HDL-C, mg/dL*	*LDL-C, mg/dL*	*Chol/HDL*
1	43	Male	30	Initial	4.6	—	—	—	—	—
				13 mo.	4.7	43	250	73	152	3.4
2	14	Male	4.5	Initial	—	38	147	38	101	3.9
				61 mo.	—	59	198	55	131	3.6
3	60	Female	31	Initial	8.0	93	241	54	163	4.5
				8 mo.	5.4	72	198	54	114	3.7
4	55	Male	30	Initial	8.0	101	242	45	154	5.4
				12 mo.	7.3	89	184	56	108	3.3
5	37	Female	7	Initial	6.2	81	253	106	140	2.4
				12 mo.	5.1	98	277	142	114	2.0
6	41	Female	24	Initial	6.6	48	177	50	117	3.5
				27 mo.	5.8	31	168	67	94	2.5
7	45	Female	30	Initial	—	54	193	52	130	3.7
				17 mo.	8.0	76	177	83	79	2.1
8	56	Male	27	Initial	6.9	214	277	32	202	8.7
				10 mo.	5.3	—	206	38	141	5.4
9	41	Female	13	Initial	6.8	119	202	77	119	2.6
				12 mo.	5.4	45	207	90	108	2.3
10	31	Male	14	Initial	7.6	46	159	38	112	4.2
				15 mo.	4.8	41	179	55	116	3.3
Mean (SD)	42.3 (13.5)	50% male	21.1 (10.4)	Initial	6.8 (1.1)	72.5 (30.0)	210.1 (45.2)	54.7 (23.3)	137.6 (31.4)	4.3 (1.9)
				Post	5.5 (0.8)	63.9 (23.9)	199.3 (32.1)	71.1 (30.9)	111.7 (18.2)	3.1 (1.1)

—, missing data.

TABLE 3. INITIAL AND FOLLOW-UP GLYCEMIC CONTROL AND FASTING LIPID PROFILES IN TYPE II DIABETICS

Case	*Age, years*	*Gender*	*Diabetes duration months*	*Pre/ post*	*Hgb A1C, %*	*Trig, mg/dL*	*Chol, mg/dL*	*HDL-C, mg/dL*	*LDL-C, mg/dL*	*Chol/HDL*
11	66	Female	6	Initial	8.9	47	293	56	220	5.2
				71 mo.	6.4	32	215	69	140	3.1
12	36	Male	0.1	Initial	8.9	41	199	34	166	6.5
				13 mo.	5.3	50	187	57	151	3.3
13	32	Male	0.5	Initial	11.2	79	199	51	132	3.9
				4 mo.	5.1	64	212	61	138	3.5
14	64	Female	8	Initial	7.0	191	244	39	196	6.3
				16 mo.	4.8	113	257	52	182	5
15	58	Female	13	Initial	—	124	250	52	173	4.8
				4 mo.	—	—	220	69	—	3.2
16	59	Male	5	Initial	—	347	207	57	102	3.6
				2 mo.	5.6	99	206	83	103	2.5
17	47	Female	9	Initial	7.8	47	187	71	107	2.6
				75 mo.	6.8	32	200	105	83	1.9
18	45	Female	15	Initial	8.6	107	238	41	176	5.8
				29 mo.	7.2	99	276	61	195	4.5
19	71	Male	15	Initial	11.2	202	331	30	271	11
				8 mo.	6.7	59	172	49	111	3.5
20	49	Male	1	Initial	6.2	88	317	67	232	4.7
				9 mo.	5.0	63	263	68	172	3.9
21	50	Female	5	Initial	8.4	118	302	56	222	5.4
				79 mo.	6.7	40	271	146	117	1.9
22	49	Female	11	Initial	10.7	151	275	58	187	4.7
				20 mo.	6.9	159	257	70	155	3.7
23	55	Male	—	Initial	10.7	79	252	43	193	5.9
				13 mo.	7.0	75	256	61	180	4.2
24	52	Female	1	Initial	7.5	229	221	39	131	5.7
				6 mo.	5.7	218	240	46	97	5.2
25	68	Male	41	Initial	9.5	69	143	47	82	3
				49 mo.	5.6	43	223	121	94	1.9
26	82	Female	27	Initial	7.0	89	200	67	111	3
				31 mo.	5.8	57	280	104	145	2.7
27	75	Male	7	Initial	5.6	144	224	39	127	5.7
				7 mo.	4.4	103	233	62	135	3.7
28	35	Male	4	Initial	8.0	66	221	37	146	6
				7 mo.	4.8	61	218	49	147	4.5
29	69	Male	13	Initial	6.7	103	200	50	129	4
				4 mo.	4.9	58	222	73	131	3
30	58	Male	9	Initial	6.7	106	248	37	190	6.7
				9 mo.	5.5	50	224	49	153	4.6
Mean (SD)	56.0 (13.6)	55% male	10.0 (10.0)	Initial:	8.4 (1.7)	121.2 (76.4)	237.6 (47.7)	48.6 (11.8)	164.2 (51.3)	5.2 (1.8)
				Post:	5.8 (0.9)	77.6 (46.7)	231.6 (30.1)	72.8 (26.6)	138.4 (31.6)	3.5 (1.0)

—, missing data.

day—can lead to excellent glycemic control. In addition to restricting carbohydrates, this regimen incorporated a medication therapy more rigorous than the intensive therapy cohort of the DCCT. The mean follow-up hemoglobin A1c was 1.4% lower than the DCCT's intensive therapy cohort. Though data regarding hypoglycemic episodes is not available for the carbohydrate-restricted studies, no cases of severe hypoglycemia with loss of consciousness were reported to the clinic in our case series.

Basic calculus may explain how carbohydrate restriction can reduce the risk of hypoglycemia. In general, reducing the size of the inputs of any system will cause a reduction in the degree of variation in the outputs. Because insulin is secreted in response to dietary carbohydrate, it follows that insulin requirements will decrease as carbohydrate consumption declines. Reductions in carbohydrate and corresponding insulin dosages decreases the size of the inputs introduced into the body's system, helping the individual more accurately predict and control his or her glucose levels with a minimal margin of error. Decreasing the amount of insulin one uses ensures a greater and more predictable rate of absorption, allowing for the insulin to be used more efficiently.[6,7] Less insulin also makes correction easier should one make a mistake in timing or the type of insulin used. This follows from the rationale that small inputs make for small mistakes, just as large inputs make for large mistakes. In the context of diabetes mellitus, mistakes in the calculation of insulin and carbohydrate intake are manifested as hypoglycemic or hyperglycemic episodes. In this way, a carbohydrate-restricted regimen may be a way to improve glycemic control without increasing the risk of hypoglycemia.

In addition to achieving normal glycemic control, a carbohydrate-restricted regimen may help to sustain or perhaps improve the minimal amounts of insulin some diabetics produce. This effect may show to be significantly helpful for both type II and recently diagnosed type I diabetics while in their transient remission or "honeymoon phase," as both still produce some of their own insulin. Symptoms of diabetes appear when approximately 80% of one's islets cells have been destroyed.[6] However, the presence of measured C-peptide indicates insulin production in the remaining islet cells. One hypothesis may suggest that today's recommended, high-carbohydrate diet may hasten the death of the diabetic's remaining islet cells, a process termed "beta cell exhaustion."[6] It has been shown that elevated glucose levels also diminish the islet cells' ability to produce insulin by inhibiting the gene expression and binding of two critical insulin transcription factors.[8] This effect combined with beta cell exhaustion accelerates the destruction of the islet cells, increases insulin requirements, and leads to worse glycemic control. These reports corroborate the possibility that a carbohydrate-restricted diet may also play a role in prolonging the existence of the remaining islet cells. Such evidence suggests that a carbohydrate-restricted diet may protect the islet cells from overexertion, helping to reduce the need for insulin in type II diabetics and to perpetuate the "honeymoon phase" of recently diagnosed type I diabetics.[6]

It is interesting to note that, prior to the discovery of insulin, Elliot P. Joslin recommended a low-carbohydrate diet as a treatment for diabetes mellitus.[9] The strict diet allowed for consumption of only foods without sugar—including meats, poultry, game, fish, clear soups, gelatin, eggs, butter, olive oil, coffee, tea, and cracked cocoa. The recommended daily caloric distribution of the diet was approximately 2% carbohydrate, 17% protein, 75% fat, and 6% alcohol, for a total of 1,795 calories. The 2% carbohydrate equates to 10 g of carbohydrate per day. Perhaps diabetics today may refer back to these initial treatment protocols, to help improve their glycemic control in conjunction with the aid of modern advancements.

With the discovery of insulin, diabetics were ostensibly able to include carbohydrates in the diet while controlling hyperglycemia. Because diabetics have been shown to have an increased risk of developing coronary heart disease (CHD), a "heart-healthy" diet restricting fat and cholesterol became the prescribed regimen of the American Diabetes Association (ADA). The ADA bases its dietary recommendations on the food pyramid, appropriating over half of a diabetic's daily caloric intake to

carbohydrates. It focuses primarily on the restriction of fat from the diabetic's diet, replacing these calories with complex carbohydrates. Currently, with the introduction of *lispro* or Humalog insulin and different "carbohydrate-counting" protocols, some diabetics are told that "sweets" (i.e., simple sugars) are acceptable to eat if factored into one's diet in moderation. Nonetheless, much discrepancy exists today as to what is the optimal diet for diabetics.[10]

Low-carbohydrate diets have been avoided because of the high-fat nature of the diets and the predicted associated hypercholesterolemia.[11] While there is variability in the fasting serum lipid response, serum lipids generally improve with this low-carbohydrate regimen, especially the triglyceride and HDL measurements. Research into understanding the variable lipid response and its health consequences is needed.

The limitations of this retrospective case series analysis are its relatively small sample size and sampling bias. The patients chosen for review were those who had self-reported excellent compliance with the regimen. Because not all patients were compliant, the regimen's feasibility is unknown. The program included carbohydrate restriction, medication management, and monitoring, and from this review it is not possible to determine the extent to which each component contributed to the response. Nevertheless, this case series shows that the regimen can lead to excellent glycemic control and improved lipid profiles in at least a subset of those who follow it.

Based on clinical experience, physicians and diabetics must use caution in transitioning from a diet that is high in carbohydrate content to one that has only 30 g of carbohydrate per day. Due to the potentially powerful effect of carbohydrate restriction, the risk of hypoglycemia is high without immediate medication adjustment. Therefore, such change should only be made under the close supervision of medical personnel experienced with this approach.

In conclusion, a multi-component diabetes program, including a low-carbohydrate diet and intensive medication therapy, appears efficacious for normalizing hemoglobin A1c and improving lipid profiles in motivated patients. By limiting the inputs of carbohydrate and insulin, this program may provide a model for achieving excellent glycemic control without hypoglycemia. Due to these favorable findings, further controlled investigation into the effects of this approach appear in order.

REFERENCES

1. Diabetes Control and Complications Trial (DCCT). *N Engl J Med* 1993;329:977–986.
2. U.K. Prospective Diabetes Study (UKPDS). Effect of intensive blood-glucose control with metformin on complications in overweight patients with type II diabetes. *Lancet* 1998;352:854–865.
3. McCulloch DK, Mitchell RD, Ambler J, et al. A prospective comparison of "conventional" and high-carbohydrate/high-fibre/low-fat diets in adults with type I diabetes. *Diabetologia* 1985;28:208–212.
4. Gutierrez M, Akhavan M, et al. Utility of a short-term 25% carbohydrate diet on improving glycemic control in type II diabetes mellitus. *J Am Coll Nutr* 1998;17:595–600.
5. Hays JH, et al. Abstract presented at the 81st Annual Meeting of the Endocrine Society, 1999.
6. Bernstein RK. *Diabetes Solution*. New York: Little, Brown, 1997.
7. Lauritzen T, Pramming S, et al. Absorption of isophane (NPH) insulin its clinical implications. *Br Med J* 1982;285:159–162.
8. Moran A, Zhang HJ, et al. Differentiation of glucose toxicity from beta cell exhaustion during the evolution of defective gene expression in the pancreatic islet cell line, HIT-T15. *J Clin Invest* 1997;99:534–539.
9. Osler W, McCrae T. *The Principles and Practice of Medicine*. New York: D. Appleton and Company, 1923.
10. Waldron S. Current controversies in the dietary management of diabetes in childhood and adolescence. *Br J Hosp Med* 1996;56:450–455.
11. 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;19:578–590.

Address reprint requests to:
Eric C. Westman, M.D., M.H.S.
Duke University Medical Center
Suite 200—B Wing
Box 50
Durham, NC 27705

E-mail: ewestman@duke.edu