

Marked Improvement in Carbohydrate and Lipid Metabolism in Diabetic Australian Aborigines After Temporary Reversion to Traditional Lifestyle

KERIN ODEA

SUMMARY

The rationale for the present study was that temporarily reversing the urbanization process in diabetic Aborigines should improve all aspects of their carbohydrate and lipid metabolism that are linked to insulin resistance. Ten full-blood, diabetic Aborigines from the Mowanjumb Community (Derby, Western Australia) agreed to be tested before and after living for 7 wk as hunter-gatherers in their traditional country in north-western Australia. They were middle aged (53.9 ± 1.8 yr) and overweight (81.9 ± 3.4 kg), and all lost weight steadily over the 7-wk period (average, 8 kg). A detailed analysis of food intake over 2 wk revealed a low-energy intake (1200 kcal/person/day). Despite the high contribution of animal food to the total energy intake (64%), the diet was low in total fat (13%) due to the very low fat content of wild animals.

Oral glucose tolerance tests (75 g glucose) were conducted in the urban setting and repeated at the end of 7 wk of traditional lifestyle. The marked improvement in glucose was due to both a fall in fasting glucose (11.6 ± 1.2 mM before, 6.6 ± 0.8 mM after) and an improvement in postprandial glucose clearance (incremental area under the glucose curve: 15.0 ± 1.2 mmol/L/h before, 11.7 ± 1.2 mmol/L/h after). Fasting plasma insulin concentration fell (23 ± 2 mU/L before, 12 ± 1 mU/L after) and the insulin response to glucose improved (incremental area under the insulin curve: 61 ± 18 mU/L/h before, 104 ± 21 mU/L/h after). The marked fall in fasting plasma triglycerides (4.0 ± 0.5 mM before, 1.2 ± 0.1 mM after) was due largely to the fall in VLDL triglyceride concentration (2.31 ± 0.31 mM before, 0.20 ± 0.03 mM after).

In conclusion, the major metabolic abnormalities of type II diabetes were either greatly improved or completely normalized in this group of Aborigines by relatively short reversal of the urbanization process. At least three factors known to improve insulin sensitivity (weight loss, low-fat diet, and increased physical activity) were operating in this study and would have contributed to the metabolic changes observed. **DIABETES** 33:596-603, June 1984.

The high prevalence of diabetes in urbanized Australian Aboriginal communities¹⁻³ represents a serious and growing public health problem that has not responded to conventional therapies for a variety of cultural, historic, and economic reasons. In a previous study, we demonstrated that healthy, lean, young Aborigines from a community in which diabetes is highly prevalent among the people over 40 yr of age exhibited mild impairment of glucose tolerance, hyperinsulinemia, and elevated very-low-density lipoprotein (VLDL) lipids.⁴ It is possible that these metabolic characteristics in some way facilitated survival in the traditional hunter-gatherer lifestyle (the "thrifty gene"), but render these people highly susceptible to non-insulin-dependent (type II) diabetes mellitus when they change to a westernized lifestyle.⁵ In both short-term (2 wk) and longer-term (3 mo) studies, we have shown that temporary reversion to traditional diet and lifestyle in nondiabetic Aborigines was associated with improvement in glucose tolerance, reduction of hyperinsulinemia, and reduction in total plasma triglyceride concentrations.^{1,8} The change from an urban to a traditional lifestyle involves several factors that directly affect insulin sensitivity: increased physical activity, reduced energy intake and weight loss, and changes in the overall dietary composition. All of these factors improve insulin sensitivity and should, therefore, be of benefit to the insulin-resistant diabetic. In this way it is possible to link urbanization directly to the increasing prevalence of type II diabetes among Aborigines. The rationale of the present study was that temporarily reversing the urbanization process should improve all aspects of diabetic carbohydrate and lipid metabolism that are linked with insulin resistance.

A group of established diabetic subjects from the Mowanjumb Community, Derby, in the northern Kimberley region

From the University of Melbourne, Department of Medicine, Repatriation General Hospital, Heidelberg, Victoria 3081, Australia.
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KERIN ODEA

TABLE 1
Design of the study and composition of the diet during the 7-wk lifestyle change period

Phase of study	Traveling		Coast		Inland				
	Week	Energy (kcal)	Week	Energy (kcal)	Week	Energy (kcal)			
Main foods (as % total calories)	Beef	75%	Fish	80%	Kangaroo	36%			
					Fresh-water fish (bream)	19%			
Composition of diet					Yams	28%			
					Honey, figs	17%			
			Birds	20%	birds, crocodiles				
			Kangaroo		turtle, yabbies				
			Turtle						
		Bream							
		Yams							
		Honey							
		Estimate only		Estimate only		Measured over a 2-wk period			
Carbohydrate		10%		5%		33%			
Protein		50%		80%		54%			
Fat		40%		20%		13%			
Energy (cal/person/day)		1100-1300		1100-1300		1200			
	Week	0	1	2	3	4	5	6	7
		↑							
	Baseline metabolic studies								Follow-up metabolic studies

of Western Australia agreed to be tested before and after living for 7 wk as hunter-gatherers in their traditional country in an isolated location in that region of Australia.

MATERIALS AND METHODS

Subjects. Ten diabetic (5 women, 5 men) and four nondiabetic (2 women, 2 men), full-blood Aborigines from the Mowanjumb Community (Derby, Western Australia) participated in this study. The mean age of the diabetic subjects was 53.9 ± 1.8 yr and of the nondiabetic subjects, 52.3 ± 4.3 yr. All subjects were weight stable before the study. The initial mean body weight of the diabetic subjects was 81.9 ± 3.4 kg, equivalent to a body mass index (BMI) of 27.2 ± 1.1 kg/m². The nondiabetic subjects had an initial mean body weight of 76.7 ± 3.4 kg, equivalent to a mean BMI of 25.3 ± 0.7 kg/m². Of the 10 diabetic subjects, only one was being treated with oral hypoglycemics (tolbutamide) before the study and none was on insulin. This subject's medication was withdrawn beginning on the morning of the baseline metabolic test. The same subject was also on antihypertensive medication (atenolol, amiloride, and hydrochlorothiazide) that was withdrawn under close supervision. This subject and another were also on thyroxine, which was continued. One previously undiagnosed case of severe hypertension was revealed during routine blood pressure measurements as part of the baseline studies in one of the nondiabetic subjects. She was treated with metoprolol for the duration of the 7-wk study. Five of the diabetic subjects (2 women, 3 men) were moderate-to-heavy drinkers in the urban setting, while the others were nondrinkers. Three of the four nondiabetic subjects were heavy drinkers in the urban setting.

Field study. The field study was carried out at Pantijan, the Mowanjumb Community's cattle station and traditional country of many of the Aborigines now resident at Mowanjumb. It is an extremely isolated location north of Derby, 1.5 days' travel by four-wheel drive vehicle or 1 h by light plane. The Abo-

rigines had no access to store foods or beverages from the time they left Derby until when they returned 7 wk later. This investigator was present throughout the study to ensure strict compliance with the experimental diet. The only food eaten after leaving Derby was that hunted or collected by the participants. They traveled from Derby to Pantijan by vehicle. The 7-wk period was spent as follows: en route to Pantijan, 1.5 wk; at the coastal location, 2 wk; and inland, 3.5 wk.

Experimental diet. During the 10-day trip from Derby to the coastal location, the diet was mixed and included locally killed beef, since supplies of bush food were inadequate, meat (beef, kangaroo), fresh-water fish and turtle, vegetables, and honey. It was estimated that beef comprised 75% of the energy intake during this 10-day period and the overall dietary composition was estimated to be: protein 50%, fat 40%, and carbohydrate 10%. No further beef was consumed once the group arrived at the coastal location.

During the 2-wk period spent on the coast, the diet was derived predominantly from seafood with supplements of birds and kangaroo. The lack of vegetable food in this area eventually precipitated the move inland to the now-abandoned site of the old homestead. The estimated dietary composition while on the coast was: protein 80%, fat 20%, and carbohydrate <5%.

At the inland location, which was on a river, the diet was much more varied: kangaroo, fresh-water fish and shellfish, turtle, crocodile, birds, yams, figs, and bush honey. A detailed analysis of the food intake was conducted over a 2-wk period during this phase of the study (Table 1). All food was weighed before it was eaten and samples were collected and stored in liquid nitrogen before being flown back to Melbourne for analysis. Energy intake over this period averaged 1200 kcal/person/day. In terms of total dietary energy consumed over the 2-wk period, kangaroo accounted for 36%, fresh-water bream 19%, and yams 28%. The remaining 17% was made up from wild honey, figs, birds, turtle, crocodile, and yabbies. The dietary composition in terms of total energy was 54% protein, 13% fat, and

TABLE 2
The changes in body weight and fasting plasma triglyceride and cholesterol concentrations in 10 diabetic and 4 nondiabetic Aborigines after 7 wk of traditional lifestyle

Subjects	Diabetic subjects										Nondiabetic subjects				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Mean ± SEM
Sex	F	F	F	F	F	M	M	M	M	M	F	F	M	M	
Age (yr)	57	51	48	62	50	48	50	62	52	59	49	47	48	65	52.3 ± 4.3
Height (cm)	176	173	172	161	162	174	169	187	177	185	174	171	186	172	174 ± 4
Weight (kg)	pre 88.5	81.7	69.0	73.2	86.1	95.7	64.5	82.7	82.7	80.6	81.9	73.6	86.1	70.4	76.7 ± 3.4
	post 78.2	72.6	63.9	65.4	77.3	83.7	59.9	86.7	74.1	77.5	73.8	64.5	79.2	67.8	70.9 ± 3.2
Body Mass Index	pre 28.7	27.2	23.4	28.4	32.8	31.6	22.6	27.6	26.4	23.7	27.2	25.1	27.1	23.8	25.3 ± 0.7
	post 25.4	24.2	21.7	25.0	29.4	27.6	21.0	24.7	23.7	22.8	24.5	22.2	22.9	22.9	23.4 ± 0.8
Plasma triglyceride (mmol/L)	pre 3.95	3.50	4.41	5.54	2.64	6.87	2.21	2.60	5.20	3.50	4.02	1.69	1.76	1.27	1.57 ± 0.15
	post 0.90	1.10	1.31	1.62	1.51	1.08	1.40	0.76	1.02	0.75	1.15	1.08	0.59	0.59	0.83 ± 0.13
Plasma cholesterol (mmol/L)	pre 5.08	3.78	5.70	6.06	5.81	4.66	7.41	4.77	6.42	5.31	5.65	4.35	3.99	3.99	4.11 ± 0.12
	post 5.23	4.56	4.23	7.61	5.39	4.95	5.70	4.43	4.56	4.58	4.98	4.64	3.21	4.77	4.10 ± 0.37
Physical activity level* (prestudy)	3.2	2.5	2.9	3.2	3.3	2.1	1.3	2.3	2.5	1.0	2.1	2.9	2.8	3.4	2.8 ± 0.27

*Assessed on a scale of 1-5 (inactivity to hard work)

f, nondrinker; +, moderate alcohol intake; and ++, heavy alcohol intake

33% carbohydrate. Animal foods accounted for 64% of total energy with vegetable foods making up the remaining 36%. **Urban diet.** The main dietary components were flour, sugar, rice, carbonated drinks, alcoholic beverages (beer and port), powdered milk, cheap fatty meat, potatoes, onions, and variable contributions of other fresh fruit and vegetables. At the time of the study the composition of the diet was estimated to be: carbohydrate 50%, fat 40%, and protein 10%. There was considerable variation within the group depending on the contribution of alcohol to the diet. The nondrinkers were more concerned about their diet in the urban environment and tended to eat more fresh fruit and vegetables and wholemeal bread.

Metabolic tests. Immediately before the 7-wk experimental period, baseline metabolic studies were performed in the Derby Regional Hospital after a 12-h overnight fast. No alcohol had been consumed by the subjects for at least 24 h before the test. Two of the diabetic subjects (7 and 9) and 3 of the nondiabetic subjects (11, 13, and 14) had been drinking 2 days before the baseline OGTT, while 3 diabetic subjects (1, 4, and 10) had abstained for 2 days or more. The remaining subjects (2, 3, 5, 6, 8, and 12) were nondrinkers (Table 2). An indwelling i.v. cannula was inserted into a vein in the forearm and kept patent with heparinized saline. A 20-ml fasting blood sample was taken before the 75-g glucose load (Glucola) was consumed. Ten-milliliter blood samples were taken 0.5, 1, 2, and 3 h postprandially. At the conclusion of the 7-wk experimental period, the subjects were flown back to Derby at dawn and the metabolic studies repeated.

Measurements during the field study. Fasting blood glucose was measured weekly in the diabetic subjects using a battery-operated Ames Glucometer and Dextrostix. Blood pressure and body weights were monitored weekly in all subjects. Physical activity was assessed daily over a 2-wk period on a scale of 1 to 5, 1 being equivalent to sleeping for most of the day and 5 being equivalent to hunting or digging for yams at least 6 h.

Analytic methods. Glucose concentrations were measured in fluoride oxalate plasma by the glucose-oxidase method. Immunoreactive insulin concentrations in heparinized plasma were measured using dextran-coated charcoal for precipitation of free hormone after reaction of insulin with commercially available antiserum (Burroughs-Wellcome). Human insulin (Novo) was used as the standard. The range of the assay was 5-200 mU/L insulin and the interassay coefficient of variation was 5% at 50 mU/L. Fasting triglyceride concentrations were determined enzymatically after enzymatic hydrolysis using a Technicon autoanalyzer. The normal range for triglyceride concentrations in fasting plasma was 0.5-2 mmol/L. Total cholesterol concentration in fasting plasma was measured colorimetrically after reaction with acetic anhydride and concentrated sulphuric acid using a commercially available kit (Boehringer). The normal range for cholesterol concentration in fasting plasma from Caucasoids is 3.5-6.5 mmol/L.

Cholesterol and triglyceride concentrations were also measured by automated enzymic techniques in very-low-density lipoproteins (VLDL) and in high-density lipoproteins (HDL). VLDL were separated by 16-h ultracentrifugation of plasma at 40,000 rev/min in a Beckman L-50 centrifuge.

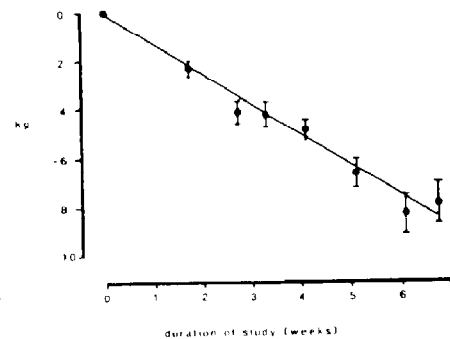


FIGURE 1. Fall in body weights of the 10 diabetic Aborigines over the 7-wk period of traditional lifestyle (mean ± SEM).

HDL were separated from other plasma lipoproteins that had been precipitated by heparin manganese chloride. Lipids in low density lipoproteins (LDL) were calculated from the differences between whole plasma and VLDL plus HDL.

Diagnostic criteria for diabetes. The criteria chosen for definition of diabetes were those of the National Diabetes Data Group¹¹ for venous plasma glucose. Diabetes: fasting > 7.8 mmol/L and 2-h oral glucose tolerance test > 11.1 mmol/L, impaired glucose tolerance: fasting < 7.8 mmol/L and 2-h oral glucose tolerance test between 7.8 and 11.1 mmol/L, and normal glucose tolerance: 2-h oral glucose tolerance test < 7.8 mmol/L.

Statistical methods. Statistical analysis of the results was carried out using Student's *t* test for unpaired data. The areas under the curves for insulin and glucose were calculated using the trapezoidal rule. Incremental areas under the curve were calculated by subtracting the total area from the baseline area.

RESULTS

The overall design of the study and composition of the diet over the 7-wk lifestyle change period is presented in Table 1. Animal foods comprised 90% of the energy intake during the first phase (traveling), essentially all of the energy intake on the coast, and 64% during the final (inland) phase of the study. When the Aborigines were eating wild animal foods exclusively (coast and inland, 5.5 wk) the diet was low in fat due to the low fat content of wild animals and fish.¹² This would have been an important factor in their weight loss. During the one period when their energy intake was accurately measured (2 wk in the third phase of the study), it was found to average 1200 kcal/person/day. Since weight loss was constant over the 3 phases of the study (Figure 1), it was assumed that the energy intake was also fairly constant (1100-1300 kcal/person/day) over the 7-wk period.

The mean change in body weight of the 10 diabetic subjects is shown in Figure 1. Initial and final body weights for all subjects are reported in Table 2. All subjects lost weight steadily over the 7-wk period; the mean total weight loss was 8.0 ± 0.9 kg (range 3.1-12.0 kg). The three leanest diabetic subjects (baseline BMI < 24 kg/m²) lost the least weight (3.1-5.1 kg), while the remaining seven diabetic subjects

(baseline BMI > 26 kg/m²) lost between 7.8 and 12.0 kg. Weight loss was highly correlated with baseline BMI ($r = 0.819$, $P < 0.01$). Despite this impressive weight loss, most of the diabetic subjects were still overweight at the end of the study (BMI > 24 kg/m²). Physical activity over the two periods of assessment (weeks 5 and 6) did not correlate with total weight loss.

Fasting plasma glucose concentrations in the 10 diabetic subjects fell from 11.6 ± 1.2 mmol/L before the study to 6.6 ± 0.5 mmol/L after it ($P < 0.001$, Table 3). Overall, glucose tolerance showed a striking improvement ($P < 0.001$, Figure 2). In addition to the lower glucose concentration in the basal state, there was also an improvement in glucose removal after glucose ingestion, as shown by the significant reduction in the postprandial rise in glucose concentration in the glucose tolerance test ($P < 0.005$, Figure 3). This is highlighted by the total and incremental areas under the curve (AUC) for glucose, which were reduced by 37% ($P < 0.001$) and 22% ($P < 0.005$), respectively (Table 3). However, in the final analysis, the marked reduction in basal glucose concentration contributed more to the improvement in glucose tolerance than did the improved glucose removal postprandially. Glucose tolerance also improved in the nondiabetic subjects ($P < 0.05$, analysis of variance, Table 3). However, there was no change in the fasting glucose concentration in the nondiabetic subjects.

Fasting plasma insulin also fell significantly in the diabetic subjects (23 ± 3 mU/L before, 12 ± 1 mU/L after the study, $P < 0.005$, Table 3). Although there was no significant difference in the peak postprandial insulin concentrations before and after the study (Figure 2), the actual insulin response (increase above fasting values) was significantly improved (Figure 3). This is brought out more clearly by comparing the total AUC for insulin, which was not changed by 7 wk of traditional lifestyle, with the incremental AUC for insulin, which was increased by 72% ($P < 0.05$, Table 3). The insulin response to a given blood glucose concentration was markedly improved in the diabetic subjects. There was no significant change in either the fasting insulin concentration or the insulin response to glucose in the nondiabetic subjects (Table 3).

The diabetic subjects were extremely hypertriglyceridemic before the study (Table 2), with the bulk of their excess triglycerides being carried in the very-low-density lipoprotein (VLDL) fraction (Table 4). There were striking falls in total plasma triglycerides by the end of the study ($P < 0.001$, Table 2), the most marked being in the VLDL fraction, which fell to one-tenth its baseline concentration ($P < 0.001$, Table 4). Similar, although less marked, changes were observed in the nondiabetic subjects.

Total plasma cholesterol concentrations, which were not high initially, did not fall significantly (Table 4). However, there was a change in the distribution of cholesterol between the different lipoprotein fractions that may have occurred, at least partly, to compensate for the greatly reduced contribution of VLDL to the total lipids at the end of the experimental period. Both VLDL and HDL cholesterol fell significantly, while LDL cholesterol tended to rise (Table 4). HDL cholesterol was highest initially in the heavy drinkers but fell in all subjects (including the nondrinkers) at the end of the study.

TABLE 3
The changes in plasma glucose and insulin concentrations in 10 diabetic and 4 nondiabetic Aborigines after 75 g oral glucose before and after 7 wk of traditional lifestyle

Subjects	Diabetic subjects										Nondiabetic subjects					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Mean ± SEM	
Plasma glucose (mmol/L)																
Baseline	14.4	17.5	15.7	7.1	7.7	13.3	9.8	9.0	13.8	7.8	5.2	5.2	4.6	5.1 ± 0.2		
1 h	16.5	19.7	18.0	9.2	11.3	15.5	12.9	11.6	17.9	11.1	8.8	8.8	7.7	7.9 ± 0.4		
2 h	9.1	21.1	21.1	12.7	13.8	18.9	17.1	13.7	21.5	13.9	8.5	8.5	6.5	8.7 ± 0.9		
3 h	19.7	23.9	21.9	12.6	13.6	20.4	21.9	16.9	19.8	13.3	9.2	4.7	6.9	7.3 ± 1.0		
7 wk	5.6	9.0	8.3	5.6	6.3	5.7	8.3	5.7	5.5	8.7	5.8	4.1	5.1	4.6 ± 0.6		
1 h	8.5	11.9	10.1	7.0	8.9	8.1	10.1	8.4	9.2	5.5	5.6	4.8	5.5	5.2 ± 0.2		
1 h	9.8	12.5	13.1	10.4	10.4	10.0	13.1	11.0	10.6	8.9	9.2	7.2	6.6	6.9 ± 0.2		
2 h	12.5	12.1	15.3	8.2	11.4	9.8	15.3	11.4	11.5	9.6	11.1	7.3	7.2	6.9 ± 0.2		
3 h	10.7	11.6	16.3	4.9	9.0	5.3	16.3	7.3	9.0	7.1	6.4	5.2	4.4	5.3 ± 0.6		
Area under glucose curve (mmol/L/h)																
Total	57.1	66.2	61.5	33.1	37.0	55.3	54.7	43.2	56.4	35.6	26.6	26.6	21.7	21.3 ± 1.5		
7 wk	30.9	35.5	40.4	23.4	29.7	25.4	45.0	28.9	29.9	25.9	25.4	18.9	19.0	17.6 ± 1.3		
Incremental	13.9	12.2	14.4	11.8	13.9	15.4	25.3	16.2	15.0	12.2	18.9	19.1	18.5	17.6 ± 1.3		
7 wk	14.1	8.5	15.4	6.6	10.8	8.3	18.9	11.8	13.4	9.4	1.8	4.7	3.7	6.0 ± 1.7		
Plasma insulin (mU/L)																
Baseline	29	20	18	21	18	30	5	18	42	31	22	26	9	16 ± 5		
1 h	27	26	18	49	40	49	11	42	46	70	38	38	53	94 ± 27		
1 h	32	30	18	101	48	50	11	60	53	86	49	51	107	129 ± 48		
2 h	35	27	13	109	48	37	19	50	80	69	143	81	72	83 ± 18		
3 h	42	24	25	91	36	46	18	37	47	44	41	40	31	38 ± 15		
7 wk	17	16	8	13	15	10	9	11	16	12	12	12	8	17 ± 8		
1 h	19	48	13	22	51	33	25	33	49	111	20	38	3	79 ± 16		
1 h	29	38	19	47	42	49	30	67	57	85	47	58	58	91 ± 25		
2 h	29	33	16	9	75	73	50	44	46	129	59	77	63	85 ± 31		
3 h	26	25	19	46	67	23	52	28	54	99	44	52	40	59 ± 27		
Area under insulin curve (mU/L/h)																
Total	101	80	53	260	127	130	43	139	177	198	131	286	164	256 ± 51		
7 wk	75	102	48	168	173	141	113	128	144	301	139	222	141	227 ± 71		
Incremental	14	20	-2	197	73	40	28	85	51	105	61	220	166	211 ± 36		
7 wk	54	54	24	129	128	110	86	95	964	265	104	375	117	174 ± 68		

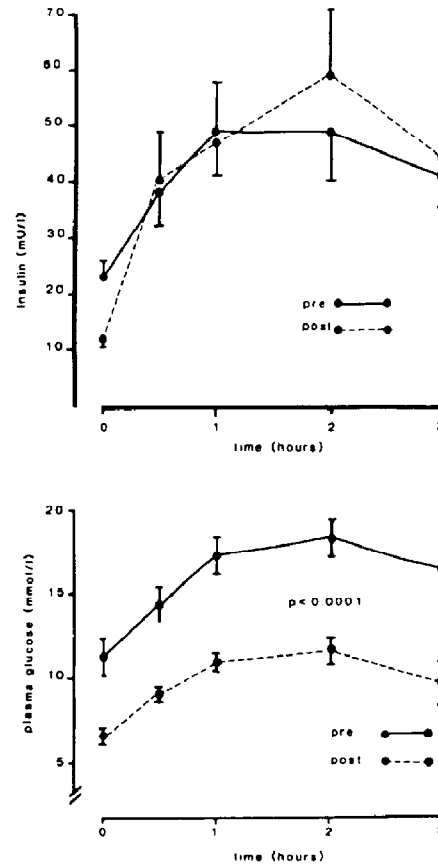


FIGURE 2. Change in plasma glucose (lower) and insulin (upper) concentrations in 10 diabetic Aborigines after 75 g oral glucose before and after 7 wk of traditional lifestyle (mean ± SEM).

DISCUSSION

The major finding in this study was the marked improvement in glucose tolerance in 10 diabetic Aborigines after a 7-wk reversion to traditional hunter-gatherer lifestyle. There were two components to this improvement: a striking fall in the basal (fasting) glucose concentration and a less marked, but nevertheless significant, improvement in glucose removal after oral glucose. Associated with the improvement in basal glucose metabolism was a significant fall in the fasting insulin concentration in the diabetic subjects. Although peak post-prandial insulin concentrations were no different before and after the temporary lifestyle change, the fall in fasting insulin concentrations indicated that the actual insulin response to oral glucose had increased in these diabetic subjects. This increased response occurred despite the markedly reduced glycaemic stimulus.

The data in the present study indicate that there have been

improvements in two of the major metabolic defects in type II diabetes (insulin secretion and insulin action) as a result of the lifestyle change. The improvement in insulin response to oral glucose was not as striking as the reduction in basal insulin concentrations. Nevertheless, it is consistent with numerous other reports that reducing hyperglycemia in type II diabetic subjects restores, at least in part, the pancreatic β-cell secretory function.¹³⁻¹⁶ Despite the improved insulin response to glucose, which was evident in the diabetic subjects at the end of the study, this response remained clearly defective relative to that of the nondiabetic subjects.

The lifestyle changes operating in the present study encompassed three main factors that are known to improve insulin sensitivity: weight loss, low-fat diet, and increased physical activity.^{17,20} Theoretically at least, they could all have contributed to the improved metabolic control evident in these diabetic subjects at the end of the study. The marked

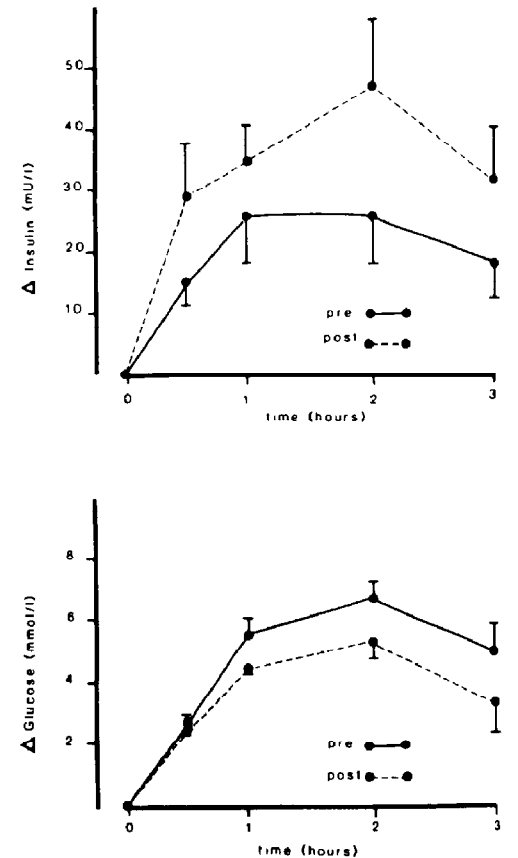


FIGURE 3. Incremental glucose (lower) and insulin (upper) responses to 75 g oral glucose in 10 diabetic Aborigines before and after 7 wk of traditional lifestyle (mean ± SEM).

TABLE 4
Changes in the triglyceride and cholesterol concentrations in total plasma and lipoprotein fractions in 10 diabetic subjects after the 7-wk lifestyle change

	Pre	Post
Total cholesterol	5.65 ± 0.23	4.98 ± 0.34
triglyceride	4.02 ± 0.46	1.15 ± 0.03*
VLDL cholesterol	1.01 ± 0.15	0.18 ± 0.03*
triglyceride	2.31 ± 0.31	0.20 ± 0.03*
LDL cholesterol	3.34 ± 0.27	4.10 ± 0.32
triglyceride	0.95 ± 0.23	0.64 ± 0.07
HDL cholesterol	1.29 ± 0.16	0.69 ± 0.06*
triglyceride	0.76 ± 0.08	0.29 ± 0.03*

*P < 0.005. †P < 0.001

weight loss that occurred in all subjects was probably a major factor in the improvement. However, it should be emphasized that the type II diabetic subjects in the present study were neither grossly overweight initially (BMI 27.2) nor slim by the end of the study (BMI 24.5). In this respect the present study differs from other reports of reversal of type II diabetes, in which the subjects have tended to be considerably more obese initially.¹⁴⁻¹⁷ The results of this study support the concept of a multifactorial basis for the improvements in carbohydrate and lipid metabolism. Under the conditions of this study it is difficult to separate out effects of dietary composition, low energy intake, and weight loss. Reduced stress in the traditional lifestyle may also have contributed to the improvements; however, it was not possible to accurately assess this variable in the present study.

The role of increased physical activity in mediating these benefits is difficult to assess. Physical fitness per se was not assessed in this study. However, the mean daily activity estimated on a scale of 1 to 5 over a 2-wk period indicated that the level of physical activity during the study period was not particularly high, despite being greater than in the urban setting. There was no correlation between level of physical activity and improvement in any of the metabolic parameters. This may, of course, have been due to lack of appropriate data on true level of physical activity or improved physical fitness.

The striking fall in VLDL triglyceride concentrations that was also observed in the diabetic subjects at the end of this study is consistent with improved insulin sensitivity in these people.¹⁸ Elevation of VLDL triglyceride concentrations to the levels evident in this group before the study are generally considered to arise from a combination of increased hepatic production and reduced peripheral clearance.^{19,20} A recent study on VLDL triglyceride metabolism in diabetic Pima Indians revealed normal VLDL production rates but defective clearance.²¹ In this latter group of diabetic subjects, the triglyceride concentrations were not elevated to anywhere near the same extent as the baseline values of the diabetic Aborigines in the present study, although the two groups did exhibit very similar degrees of fasting hyperglycemia. Although alcohol intake may have contributed to the high pre-study triglyceride concentrations, the lower concentrations in the heavy drinking, nondiabetic subjects and the high concentrations in several of the nondrinking, diabetic subjects indicate that diabetes was the major contributing factor to the hypertriglyceridemia. The complete normalization of

both total plasma and VLDL triglyceride levels by the end of the study was consistent with lower basal insulin levels, since hyperinsulinemia has been shown to stimulate triglyceride production in man.²² However, an alternative explanation would be that the glucose intolerance and insulin resistance were secondary to the hypertriglyceridemia, and that the very-low-fat diet, together with the weight loss achieved, were responsible for the dramatic reductions in VLDL levels that, in turn, mediated the improvement in glucose tolerance.²³

Although HDL cholesterol levels were highest initially in the heavy drinkers, they had fallen in all subjects, including the nondrinkers, by the end of the study. Low HDL cholesterol levels, associated with low total cholesterol levels, have been reported in numerous nonurbanized populations including Australian Aborigines.²⁴⁻²⁷ The general fall in HDL cholesterol (even in the nondrinkers) may have been partly in response to the greatly reduced VLDL concentrations in all subjects at the end of the study. Similarly, the rise in LDL cholesterol (although not statistically significant) may have occurred to compensate for the greatly reduced VLDL. Thus, although total cholesterol did not fall significantly (despite a trend in that direction) there was a change in the distribution of cholesterol between the different lipoprotein fractions.

The three most striking metabolic changes that occurred in this study, namely the reductions in fasting glucose, insulin, and triglyceride concentrations to normal or near-normal levels, were almost certainly interrelated. Hyperinsulinemia and insulin resistance are associated, ipso facto, with a reduced ability of a given concentration of insulin to stimulate glucose uptake or inhibit lipolysis.²⁸ However, hepatic triglyceride synthesis does not appear to be subject to insulin resistance.^{29,30} As a consequence, the co-existent elevations in insulin, glucose, and free fatty acids in insulin-resistant states provide the setting for increased hepatic triglyceride synthesis and increased VLDL triglyceride secretion. Ameliorating the insulin resistance (by any combination of weight loss, low-fat diet, and increased physical activity) should reverse these processes by improving glucose uptake, inhibiting lipolysis, and lowering basal insulin concentrations, thereby removing the conditions previously promoting excessive VLDL triglyceride production and secretion.

However, the interpretation of the results of the present study is complicated by the observation that despite the marked improvement in basal glucose homeostasis, postprandial glucose clearance was only moderately improved. This is perhaps even more unexpected in view of the improvement in postprandial insulin secretory response. It is interesting to note that this pattern of response has been reported in other studies of the dietary treatment of diabetes. The improvement in glucose tolerance in diabetic subjects after a high-carbohydrate, high-fiber diet was largely accounted for by falls in basal glucose concentrations and not by improved postprandial glucose clearance per se.^{31,32}

In summary, all of the metabolic abnormalities of type II diabetes were either greatly improved (glucose tolerance, insulin response to glucose) or completely normalized (plasma lipids) in a group of diabetic Aborigines by a relatively short (7 wk) reversion to traditional hunter-gatherer lifestyle. The public health implications of these results are striking: diabetes is potentially preventable in these

people. It should be emphasized that although it is not necessary to revert totally to traditional lifestyle in order to prevent or attempt to reverse diabetes, certain characteristics of that lifestyle must be incorporated into any future public health programs: high physical activity, low-fat diets, and control of body weight.

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