Effects of Traditional and Western Environments on Prevalence of Type 2 Diabetes in Pima Indians in Mexico and the U.S.

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OBJECTIVE — Type 2 diabetes and obesity have genetic and environmental determinants. We studied the effects of different environments on these diseases in Pima Indians in Mexico and the U.S.

RESEARCH DESIGN AND METHODS — Adult Pima-Indian and non-Pima populations in the Sierra Madre mountains of Mexico were examined using oral glucose tolerance tests and assessments for obesity, physical activity, and other risk factors. Results were compared with those from Pima Indians in Arizona. Both Pima populations were typed for DNA polymorphisms to establish their genetic similarity.

RESULTS — The age- and sex-adjusted prevalence of type 2 diabetes in the Mexican Pima Indians (6.9%) was less than one-fifth that in the U.S. Pima Indians (38%) and similar to that of non-Pima Mexicans (2.6%). The prevalence of obesity was similar in the Mexican Pima Indians (7% in men and 20% in women) and non-Pima Mexicans (9% in men and 27% in women) but was much lower than in the U.S. Pima Indians. Levels of physical activity were much higher in both Mexican groups than in the U.S. Pima Indians. The two Pima groups share considerable genetic similarity relative to other Native Americans.

CONCLUSIONS — The much lower prevalence of type 2 diabetes and obesity in the Pima Indians in Mexico than in the U.S. indicates that even in populations genetically prone to these conditions, their development is determined mostly by environmental circumstances, thereby suggesting that type 2 diabetes is largely preventable. This study provides compelling evidence that changes in lifestyle associated with Westernization play a major role in the global epidemic of type 2 diabetes.

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The global prevalence of diabetes in the 20- to 79-year age range in 2003 was estimated to be 5.1%, but the prevalence varied dramatically by region and race (1). Rural areas of developing countries have a low prevalence of type 2 diabetes, but in many countries, prevalence is increasing rapidly due to increasing urbanization and aging of the population (2). Certain populations experience a disproportionately elevated prevalence of diabetes. For example, type 2 diabetes reaches epidemic proportions in Nauru (3), in the Aborigines of Australia (4), and many in American-Indian groups in the U.S. (5–7), and the prevalence is much higher in these ethnic groups than in others in the same countries. These observations, together with strong evidence of the importance of genetic susceptibility in type 2 diabetes (8), indicate that type 2 diabetes results from an interaction between genetic predisposition and lifestyles associated with unfavorable environments.

To elucidate the nature and contribution of environmental influences on type 2 diabetes, we studied two groups of Pima Indians in Mexico and in the U.S. The high prevalence of type 2 diabetes in the Pima Indians in the U.S. is well established (5,6), but the prevalence among their counterparts living in Mexico was previously unknown. The Pima Indians in the U.S. reside mainly in the desert regions of Arizona and have the world's highest recorded prevalence and incidence of type 2 diabetes (5,6). The Mexican Pima Indians live in a remote region in the Sierra Madre Mountains in an area only recently accessible by road. In contrast with the U.S. Pima Indians, they have experienced relatively little recent change in environmental conditions (9,10). The Pima Indians in the U.S. and Mexico are both members of the same Pima linguistic group. Living in the same area as the Mexican Pima Indians are Mexicans, not of Pima heritage, who are mainly farmers and ranchers. We compared these two Mexican groups to the U.S. Pima group with respect to diabetes and glucose tolerance and examined the differences in obesity and lifestyle to determine the extent to which environment and genetic background influence diabetes and obesity among these populations.

RESEARCH DESIGN AND METHODS

— The Pima Indians of Mexico and the non-Pima Mexicans examined live in a remote area on the eastern border of the state of Sonora in the region around the village of Maycoba. In 1994, we conducted a census of Maycoba and the surrounding inhabited region to

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Abbreviations: IGT, impaired glucose tolerance.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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enumerate all residents of the area and establish their ethnicity, dates of birth, and familial relationships. Based on this census, those with and without Pima heritage were identified. Subjects were considered full Pima if they reported that both their parents were full Pima and part Pima if one parent was Pima. The non-Pima Mexicans reported no parental Amerindian heritage. Pima heritage was established in a similar manner in the U.S. Pima group. Of 290 full and part Pima Mexicans enumerated in 1994, 224 (77%) participated in the study as did 193 of the 270 non-Pima Mexicans (71%).

Each individual was invited to participate in a health examination at our research clinic in the village of El Kipor 10 km east of Maycoba. These examinations, conducted in the mornings by Spanish-speaking interviewers and technicians, included a brief medical history, physical activity questionnaire, 24-h dietary recall, measurements of blood pressure and anthropometry, and a 75-g oral glucose tolerance test. Data from the Mexican groups were compared with those from the U.S. Pima-Indian population participating in the ongoing epidemiological study of type 2 diabetes in the Gila River Indian Community in Arizona, who had similar examinations during the same period (June 1995–June 1996) (6).

Oral glucose tolerance tests were performed using a 75-g glucose load after 10–12 h of fasting according to World Health Organization recommendations (11). Plasma glucose was measured in fasting and 2-h postload venous blood using a hexokinase method (Ciba Corning, Palo Alto, CA). Diabetes and impaired glucose tolerance were defined using 1999 World Health Organization criteria (11).

Obesity was assessed by BMI (weight in kilograms divided by the square of height in meters) with weight measured on a battery-operated electronic scale and height by a portable stadiometer. Subjects were classified as obese if BMI was ≥30 kg/m^2 and overweight if 25 kg/m^2 ≤ BMI < 30 kg/m^2. Percent body fat was estimated from bioelectrical impedance (BIA-103; RJL Systems) using an equation developed for the U.S. Pima Indians (12). Waist-to-hip ratio was assessed with waist circumference measured supine at the level of the umbilicus and hip circumference measured in standing position at the level of the greater trochanters.

All subjects were administered an activity questionnaire (13). A 24-h dietary recall was conducted in the Mexican populations. Dietary data were analyzed using the University of Minnesota food composition database (14) supplemented with composition analysis data from the local Mexican Pima and non-Pima foods (15).

Table 1—*Prevalence of type 2 diabetes in non-Pima Mexicans, Mexican Pima Indians, and U.S. Pima Indians*

Age (years)	Non-Pima Mexican	Mexican Pima	U.S. Pima
Men			
20–24	18 (0)	18 (0)	53 (7.5)
25–34	19 (0)	35 (2.9)	136 (18.4)
35–44	20 (0)	14 (14.3)	77 (37.7)
45–54	14 (0)	20 (5.0)	54 (68.5)
≥55	21 (0)	20 (10.0)	43 (67.4)
Total	92 (0)	107 (5.6)	363 (34.2)
Women			
20–24	13 (0)	29 (0)	79 (5.1)
25–34	37 (0)	35 (0)	169 (24.9)
35–44	19 (5.3)	19 (5.3)	134 (42.5)
45–54	10 (10.0)	22 (36.4)	53 (69.8)
≥55	22 (13.6)	12 (8.3)	90 (82.2)
Total	101 (5.0)	117 (8.5)	525 (40.8)

Data are *n* examined (% with diabetes).

Genetic analyses
DNA was extracted from immortalized lymphocyte cultures from 52 unrelated full Pima Indians from the population in Mexico and from 52 full Pima Indians in the U.S. DNA markers at 309 independent loci (including 175 multisite haplotypes and 134 single site loci) were typed to determine the genetic relationships between the two Pima groups in comparison with other populations. Allele frequencies for each single-site locus were estimated by gene counting with binomial SEs. Haplotype frequencies and jackknife SEs were estimated by an expectation-maximization algorithm (16) for loci with multiple markers. The allele and haplotype frequencies are being entered in ALFRED (http://alfred.med.yale.edu/) (17). F_{st}-based pairwise genetic distances were calculated (18), and a best least-squares tree was derived (19,20).

Statistical analysis
Statistical analyses were performed using programs of the SAS Institute (Cary, NC). Directly standardized age- and age- and sex-adjusted prevalence rates of diabetes were compared among the populations, using the combined Mexican Pima and non-Pima samples (within the age and sex groups shown in Table 1) as the reference population. 95% CIs were calculated (21). Unless stated otherwise, unadjusted data are presented.

RESULTS

Prevalence of diabetes
The age- and sex-specific prevalence rates of diabetes in the Mexican populations and U.S. Pima Indians are shown in Table 1. Complete glucose tolerance data were obtained for 77.2% of the eligible Mexican Pima Indians and for 71.5% of the non-Pima Mexicans. Among the Mexican Pima Indians, 5.6% of men and 8.5% of women had diabetes, prevalences significantly lower than those in the U.S. Pima Indians, of whom 34.2% of men and 40.8% of women had the disease ($P < 0.01$). Of the Mexican Pima Indians, 141 (58%) were of full Pima heritage, of whom 5.6% of the men and 7.1% of the women had diabetes. Among the U.S. Pima Indians, 622 (70%) had full Pima heritage, of whom 34.3% of the men and 46.8% of the women had diabetes. The prevalences were even lower in non-Pima Mexicans, of whom none of the men and 5.0% of women were affected, but differences between Mexican Pima and non-Pima Mexicans were not statistically significant.

Age-adjusted diabetes prevalences in men and women are shown in Fig. 1. The age- and sex-adjusted prevalence in the U.S. Pima Indians was 5.5 times higher than that in the Mexican Pima Indians ($P < 0.01$) and 16 times higher than that in the non-Pima Mexicans ($P < 0.01$). In the Mexican Pima Indians, although the

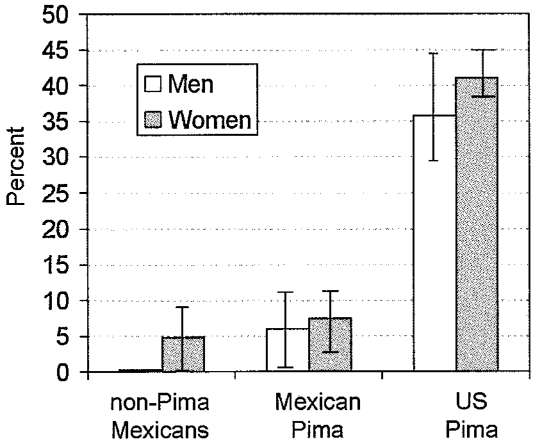

Figure 1—*Age-adjusted prevalence (±95% CIs) of diabetes in non-Pima Mexicans, Mexican Pima Indians, and U.S. Pima Indians.*

prevalences were 2.8-fold higher than those in non-Pima Mexicans, they were not statistically significantly different.

Impaired glucose tolerance (IGT) was present in 6.5% of Mexican Pima men and 6.0% of women, in 4.4% of non-Pima men and 12.9% of women, and in 9.9% of U.S. Pima men and 12.4% of women. There was no difference in IGT prevalence between the non-Pima and Pima Indians in Mexico ($P > 0.05$), but IGT was more prevalent in the U.S. Pima Indians than in the two Mexican groups ($P = 0.02$). The combined prevalence of IGT and diabetes did not differ significantly between the non-Pima (11.4%) and Pima Mexicans (13.4%) but was higher in the U.S. Pima Indians (49.4%; $P < 0.01$).

Obesity

The large differences in diabetes prevalence between the Pima Indians in the U.S. and the non-Pima and Pima Indians in Mexico were paralleled by differences in obesity (Table 2). BMI, waist and hip circumference, and percent body fat were similar in the Pima and non-Pima Mexican men and women, respectively, but markedly greater in the U.S. Pima group. In each group, BMI and percent body fat were greater in women than in men. No significant differences were found for BMI and percent fat among same-sex Pima and non-Pima Mexicans, but each was highly significantly different from values for the U.S. Pima Indians. Obesity was 10 times more frequent in U.S. Pima men and >3 times more frequent in the women than in their Mexican Pima counterparts.

Physical activity

Both non-Pima Mexicans and Mexican Pima men and women had similar levels of moderate or heavy occupational and leisure physical activity (Table 2). However, both Mexican groups had significantly higher physical activity levels than U.S. Pima Indians, independently of sex and age ($P < 0.0001$). The levels of moderate to heavy physical activity were ~2.5-fold higher in the Mexican men and 7-fold higher in the Mexican women than in their U.S. Pima-Indian counterparts.

Diet

Energy intake did not differ between the Mexican Pima and the non-Pima Mexi-

Table 2—*Physical characteristics, obesity, dietary intake, and physical activity*

	Non-Pima Mexican		Mexican Pima		U.S. Pima	
	Male	Female	Male	Female	Male	Female
Obesity						
n	92	101	107	117	362	515
Weight (kg)	72 ± 12	66 ± 13	66 ± 11	63 ± 13	98 ± 25	91 ± 23
Height (cm)	172 ± 6.0	156 ± 5.7	166 ± 6.0	154 ± 5.8	171 ± 5.8	160 ± 6.1
BMI (kg/m^2)	24.3 ± 3.7	27.1 ± 5.0	23.8 ± 3.4	26.3 ± 4.8	33.3 ± 7.6	35.5 ± 8.1
Waist (cm)	86 ± 10	84 ± 11	83 ± 9	86 ± 14	107 ± 18	113 ± 18
Hip (cm)	96 ± 8	101 ± 11	94 ± 7	98 ± 11	112 ± 14	122 ± 17
Waist-to-hip ratio	0.90 ± 0.10	0.83 ± 0.07	0.89 ± 0.07	0.87 ± 0.08	0.96 ± 0.09	0.93 ± 0.07
Percent fat	21 ± 7	37 ± 7	19 ± 8	36 ± 7	34 ± 8	47 ± 5
Overweight (%)	33.7	35.6	25.2	38.8	24.8	17.2
Obese (%)	8.7	26.7	6.5	19.8	63.8	74.8
Dietary intake						
n	107	117	93	101		
Energy (kcal/day)	2,747 ± 688	2,453 ± 507	2,610 ± 581	2,370 ± 546		
Protein (% of energy)	12.3 ± 2.5	12.2 ± 2.0	11.2 ± 2.0	11.5 ± 1.9		
Carbohydrate (% of energy)	62.3 ± 7.4	61.9 ± 5.4	61.9 ± 6.6	62.3 ± 5.7		
Fat (% of energy)	24.6 ± 6.6	26.1 ± 4.9	26.6 ± 6.9	26.1 ± 5.6		
Dietary fiber (g/day)	56.3 ± 20.1	50.9 ± 14.3	55.4 ± 17.0	50.7 ± 15.2		
Physical activity						
n	89	99	105	116	316	412
Activity (h/week)	30.4 (26.9–32.0)	23.8 (22.0–27.3)	32.9 (27.7–36.5)	22.0 (19.5–24.0)	12.1 (9.7–15.6)	3.1 (2.4–3.8)

Data are means ± SD or median (95% CI) unless otherwise indicated.

cans but was higher in men compared with women (by 266 kcal/day; $P < 0.001$). In both groups, the diet was remarkable for the low percentage of calories derived from fat with an average of ~25% and no difference between groups. The amount of dietary fiber was >50 g/day and similar in both groups ($P > 0.05$). Dietary intake was not evaluated in this sample of U.S. Pima Indians. An earlier dietary study among U.S. Pima Indians (32), however, reported a lower energy intake, but a considerably higher percentage of calories derived from fat and a lower fiber intake than we found in the Mexicans.

Relationship between Mexican Pima and U.S. Pima Indians

Tree analysis of the genetic data on 309 independent markers typed across 42 populations (including eight Native-American groups) continues to show the pattern shown in previously published figures (18,20) based on subsets of the current data. The two Pima groups are not identical but cluster together and share common ancestry distinct from other Native Americans with a supporting bootstrap value of 95% (947 of 1,000). Based on these data, the U.S. Pima and the Mexican Pima Indians are closely related to each other and share a very similar gene pool.

CONCLUSIONS — Type 2 diabetes has both genetic and environmental determinants. During the same time period, we compared the prevalence of type 2 diabetes in two populations, the Mexican Pima and the U.S. Pima Indians, who share a common genetic background but have contrasting lifestyles. Both are members of a formerly much larger group of Pima Indians who at the time of the Spanish conquest inhabited northwest Mexico and what is now southern Arizona (6). Despite geographic separation, linguistic studies and the current genetic distance estimates indicate that they share a very similar genetic background and therefore, in all likelihood, carry similar diabetes and obesity susceptibility genes.

Many U.S. American-Indian groups have high prevalences of type 2 diabetes, but the U.S. Pima Indians have the highest prevalence ever recorded (6,7). The data in the U.S. Pima-Indian sample used for comparison are typical of those seen in the larger Pima population examined in the ongoing longitudinal study. In contrast, the Mexican Pima Indians had only one-fifth the prevalence of diabetes and a prevalence no different from that of the non-Pima Mexicans living in the same location. Given the similar genetic background of the Mexican and U.S. Pima-Indian populations, it is most likely that the fivefold difference in diabetes prevalence can be attributed only to differences in lifestyles and environments. Nonetheless, a difference between these Pima populations in frequencies of as yet unidentified diabetes susceptibility genes resulting from genetic drift or founder effects cannot be excluded. No diabetes was found in the non-Pima Mexican men all meals at home. Up to the time of the present study, there was no piped water or central electricity supply and a paved road into the area had been present for <2 years. In contrast, the U.S. Pima Indians, although traditionally farmers, now have a more typical rural U.S. lifestyle with very low levels of occupational physical activity (23). The majority have access to vehicular transportation, and those who still farm do so using a high degree of mechanization. Almost all purchase their food supplies at local supermarkets or receive supplies from a commodity food program.

In summary, this study presents a striking example of the variation in the prevalence of type 2 diabetes found in populations of similar genetic background but in differing environmental circumstances. The low prevalence of type 2 diabetes and obesity in the Pima Indians in Mexico in a more traditional rural environment contrasts sharply with that in the U.S. Pima population living in a Westernized environment. The difference in diabetes prevalence in these populations is mirrored by the differences in physical activity and obesity. The findings indicate that, even in a genetically highly susceptible population, type 2 diabetes is not inevitable and is preventable in environments that promote low levels of obesity and high levels of physical activity.

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