Prevalence of Diabetes in Mexican Americans

Relationship to Percent of Gene Pool Derived from Native American Sources

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SUMMARY

We have estimated the prevalence of non-insulin-dependent diabetes mellitus (NIDDM) in Mexican Americans and Anglos in three San Antonio neighborhoods. The age-adjusted NIDDM rates (both sexes pooled) for Mexican Americans were 14.5%, 10%, and 5% for residents of a low-income barrio, a middle-income transitional neighborhood, and a high-income suburb, respectively. In Mexican American women, though not in men, obesity also declined from barrio to suburbs. We have previously shown, however, that, although obesity is an important cause of NIDDM in Mexican Americans, there is a two- to fourfold excess in the rate of NIDDM in this ethnic group over and above that which can be attributed to obesity. We therefore speculated that genetic factors might also contribute to excess NIDDM in this ethnic group. The percent native American admixture of Mexican Americans as estimated from skin color measurements was 46% in the barrio, 27% in the transitional neighborhood, and 18% in the suburbs. The NIDDM rates in Mexican Americans thus paralleled the proportion of native American genes. Furthermore, the San Antonio Mexican American rates were intermediate between the NIDDM rates of "full-blooded" Pima Indians (49.9%), who presumably have close to 100% native American genes, and the San Antonio Anglo population (3.0%) and the predominantly Anglo HANES II population (3.1%), both of which presumably have few if any native American genes. The association of genetic admixture with NIDDM rates suggests that much of the epidemic of NIDDM in Mexican Americans is confined to that part of the population with a substantial native American heritage.

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Evidence from numerous epidemiological studies has shown that, despite widely varying diagnostic criteria and methods of ascertainment, prevalence rates of non-insulin-dependent diabetes mellitus (NIDDM) vary from country to country, between ethnic groups within the same country, and within the same ethnic group living under different conditions.[1–5] In particular, populations undergoing rapid westernization or which have migrated to more westernized countries have tended to develop high prevalences of NIDDM. For example, Nauru Islanders[1] and Pima Indians[6] have recently undergone dramatic changes in diet and exercise patterns leading to an increased prevalence of obesity. Prior to 1940, diabetes was virtually unknown in these populations,[7] whereas it is now epidemic, with prevalence rates in excess of 30%.

A possible explanation for the NIDDM epidemic in rapidly westernizing populations is that obesity may predispose to diabetes in certain genetically susceptible populations, i.e., obesity may unmask diabetogenic genes. It has been proposed that such populations may possess a "thrifty genotype," whereby individuals with the ability to store food efficiently gain a survival advantage in times of famine, but incur the disadvantage of developing obesity and diabetes in time of plenty.[8] The mechanism which expresses this hypothetical genotype is at present unknown.

The best way to prove the existence of excess diabetogenic genes in a population would be to have a true genetic marker for NIDDM. Unfortunately, such a marker is not currently available. A less powerful method would be to examine populations having different proportions of ancestry from parental populations thought to have differing genetic susceptibilities to NIDDM. Ideally, this method should specify the ancestry of each individual, which could then be related to whether or not the individual was diabetic. To form an adequately precise estimate of the proportional ancestry (admixture) of each individual in a population, multiple genetic markers, each with differing gene frequencies in the two parental populations, would be required. Alternatively,

if only a single trait were available (such as skin color, which is predominantly under genetic control), one could quantify the ancestry of various subgroups within the population and then relate these admixture estimates to the NIDDM prevalence of each subgroup. It is this latter approach which we have used in this study. The hypothesis we addressed is: if the excess rates of NIDDM in full-blooded native American populations (such as the Pima Indians) have a genetic component, then Mexican Americans should share this excess in proportion to their degree of native American genetic admixture. (It should be noted that the term "native American" is not restricted to Amerindian tribes indigenous to the United States only, but refers to Amerindian tribes in general, and, in this paper, particularly to those indigenous to Mexico.)

METHODS

Subjects from 25 to 64 yr of age were randomly selected from three San Antonio neighborhoods: a low-income census tract in an almost exclusively Mexican American section of town ("barrio") where a highly traditional Mexican American cultural orientation has been maintained; a middle-income ("transitional") census tract which is about 60% Mexican American and 40% Anglo American;* and a cluster of high-income census tracts ("suburbs") which is about 90% Anglo American and 10% Mexican American. Only Mexican Americans were sampled in the barrio and approximately equal numbers of each ethnic group were sampled in the transitional and suburban neighborhoods. Stratified random sampling, with oversampling of Mexican Americans, was used in the suburbs. A detailed description of our sampling procedures has been published previously.[9,10]

The study design included an initial home interview followed by a medical examination in a mobile clinic. In the barrio 849 study-eligible individuals were identified of whom 756, or 89.0%, participated in the home interview. Of these, 720 were considered eligible for a medical examination and 496, or 68.9%, of these individuals underwent the examination. (Reasons for loss of eligibility between the home interview and the medical examination included moving out of the area and discovery of pregnancy after completion of the home interview.) In the transitional neighborhood, 496 study-eligible individuals were identified of whom 383, or 77.2%, were interviewed; of these, 379 were considered eligible for the medical examination and 285, 75.2%, underwent the examination. In the suburbs, 884 study-eligible individuals were identified of whom 786, or 88.9%, were interviewed; of these, 768 were considered eligible for the medical examination and 642, or 83.6%, underwent the examination. The overall response rates may be obtained by multiplying the home interview response rate by the medical examination response rate. The overall response rates were thus 61.3% in the barrio, 58.1% in the transitional neighborhood, and 74.3% in the suburbs. Field work was carried out from October 1979 to August 1981.

Ethnic classification was accomplished using a multifactorial approach. The initial consideration was concordance between the surname (Spanish versus non-Spanish) of the subject's father and the maiden name of the subject's mother. Subjects with concordant *non*-Spanish parental surnames were classified as Anglos (excluding blacks and orientals). In the case of subjects with concordant Spanish parental surnames, further screening was carried out to identify persons not of Mexican origin (e.g., Cubans, Central and South Americans, Italians, etc.) and these individuals were excluded from the Mexican American ethnic category. For subjects with discordant parental surnames (one Spanish and one non-Spanish), stated ethnicity of all four grandparents was used to determine the subject's predominant ethnic background (3 or more Mexican grandparents vs. 3 or more Caucasian, non-Hispanic grandparents). Using this multifactorial approach, 91 individuals (largely non-Mexican Hispanics and the offspring of interethnic marriages) were identified as being neither clearly Mexican American nor Anglo and have been excluded from the present analyses.

Anthropometric measurements (stature, weight, and triceps and subscapular skinfolds thickness) were made with the participant wearing an examination gown, after having removed his or her shoes and upper garments. Details of the skinfold methods, including assessment of interobserver variation, have been published previously.[10] Two indices of obesity are used in this report: the sum of the triceps and subscapular skinfolds and the body mass index (wt/ht^2).

Plasma glucose samples were drawn after the participant had fasted at least 12 h. A 75-g glucose-equivalent load (Glucola, Ames Co., Elkhart, Indiana) was then given. Subsequent samples were drawn 1 and 2 h after the load. Glucose concentrations were measured using an Abbott Bichromatic Analyzer (Abbott Laboratories, South Pasadena, California). In this report, the sum of the three plasma glucose values is used as an overall index of glucose tolerance and is referred to as "glucose sum." Diabetes was diagnosed according to the criteria established by the National Diabetes Data Group (NDDG).[11] Although these criteria are of considerable heuristic value, especially in epidemiological studies, there are still unresolved questions about their ultimate predictive capability. Lack of reproducibility of the glucose tolerance test is a well-known problem.[12] Early follow-up studies suggested that only about 15–50% of individuals with abnormalities of glucose tolerance progress on to "overt" diabetes.[13,14] Many of those who do not progress actually revert to normal on follow-up. Most of these early follow-up studies, however, were performed on patients who would now be classified as having "impaired glucose tolerance," i.e., whose degree of hyperglycemia fell short of that required for a diagnosis of diabetes according to the new, more rigorous NDDG criteria. A more recent study has indicated that among subjects who meet the NDDG criteria, 85–95% remain in the diabetic range after an average duration of follow-up of 8.5 yr.[15] In any case, since we used the same definitions in all of our population sub-groups, these considerations probably have relatively little effect on the internal comparisons made in this report.

Table 1 shows selected clinical characteristics of the 113 individuals in our study who met the NDDG criteria. Also shown in Table 1 are 56 individuals who gave a history of diabetes, but who did not, at the time of the survey, meet the NDDG criteria. Many of these latter individuals are no doubt genuine diabetics whose plasma glucose concentrations were well controlled at the time of the survey. Some, however, may have been misdiagnosed, particularly con-

*Anglo Americans are non-Hispanic Caucasians, commonly referred to as "Anglos" in the Southwestern United States.

TABLE 1
Diabetic patients according to plasma glucose level and therapy

	Patients who met the National Diabetes Data Group criteria	Patients who did not meet the National Diabetes Data Group criteria
Mexican Americans		
Newly discovered	50	—
Previously diagnosed:		
on dietary treatment only	12	36*
on oral agents	26	6
on insulin	13†	0
Anglo Americans		
Newly discovered	6	—
Previously diagnosed:		
on dietary treatment only	3	12*
on oral agents	1	2
on insulin	2‡	0
Total	113	56
Total classified as NIDDM in this report	107	8

*Not classified as diabetic.
†Four excluded as possible insulin-dependent diabetics.
‡Excluded as possible insulin-dependent diabetics.

sidering that the new NDDG criteria are stricter than previous criteria. For purposes of the present analyses, we elected to accept a self-report of diabetes only if the subject also reported taking antidiabetic medication.† Thus, the 48 "diabetics" in Table 1 who neither took medication nor met the NDDG criteria are excluded from the present analyses. Also excluded are 6 of the 15 insulin-taking diabetics on the basis of body mass index less than 27 kg/m^2 and age of onset less than 40 yr. These individuals were considered most likely to have insulin-dependent diabetes (IDDM) rather than NIDDM. A total of 115 individuals (107 + 8) were thus considered to have NIDDM.

Skin color was measured by light reflectance using a portable spectrophotometer (Photovolt, model 670). Although skin color is subject to environmental and developmental variation, previous research has established a strong degree of congruence between skin color and gene frequency measures of population differentiation,[16] particularly when measurements are made on a non-sun-exposed site to minimize environmental variation. Accordingly, we measured skin reflectance on the medial aspect of the upper arm. The skin surface was carefully cleaned with alcohol prior to the reflectance measurement. Mean skin reflectance was calculated as a weighted average of the skin reflectance values at three wave lengths (blue, green, and amber) as described by Korey.[17] The calculation of native American genetic admixture is based on Bernstein's equation,[18] using skin color rather than serological data. A detailed description of the skin reflectance methods, including discussion of the method of estimating the skin color of parental populations, has been published in an earlier report.[19] An important limitation of using skin color to estimate genetic admixture is that, since it relies on only a single trait, it is suitable for estimating the average admixture of groups of individuals, but not individual admixture.

Age adjustment of sum of skinfolds, glucose sum, and skin reflectance values was carried out separately for each sex by analysis of covariance using Biomedical Computer Program PIV, 1979 release.[20] The prevalence of NIDDM for the San Antonio subgroups, for Pima Indians, and for the HANES II population were directly age-standardized to the 1970 U.S. population using four age decades: 25–34, 35–44, 45–54, and 55–64 yr. The HANES II population is a probability sample of the entire, non-institutionalized civilian population of the United States.[21] As such, the NIDDM rates from this study reflect primarily the rates among Anglo Americans. Data from HANES II according to the appropriate age decades and using the NDDG criteria for diabetes‡ were kindly provided by Dr. Maureen Harris of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDKD). Data on full-blooded Pima Indians (as judged by four reported Pima grandparents) according to the same age decades were provided by Dr. William Knowler, also of NIADDKD. To stabilize the prevalence estimates from San Antonio, the sexes were pooled in Figure 1. Even after pooling, however, the numerators were still small for some of the subpopulations (particularly the San Antonio suburbs). Therefore, we have elected to present the age-adjusted rates without their variances and without any attempts at statistical inference. These rates are presented primarily to place the San Antonio NIDDM rates in perspective alongside of rates from other studies, comparably age-standardized and using comparable criteria for diabetes.

RESULTS

Tables 2 and 3 present means and standard errors (age-adjusted by analysis of covariance) for selected characteristics of the study participants, according to neighborhood and ethnic group. Also included in these tables are the P-values for the *t* tests of neighborhood differences among Mexican Americans and of ethnic differences, pooled across neighborhoods. Table 2 shows that, for Mexican American women, both sum of skinfolds and body mass index declined from barrio to suburbs. Both of these obesity indices were significantly higher in barrio than in transitional or suburban women. The pooled ethnic contrasts indicate that Mexican American women were significantly more obese than Anglo women ($P < 0.0001$ for both obesity indices). For Mexican American men, neighborhood differences were of lesser magnitude, and did not follow a consistent pattern. None of these neighborhood differences were statistically significant. The pooled ethnic contrasts, however, show that Mexican American men were more obese than Anglo men, both by body mass index ($P = 0.0004$) and by sum of skinfolds ($P = 0.05$).

Table 3 shows that among Mexican Americans of both sexes, glucose sums declined sharply from barrio to suburbs. All three neighborhood contrasts were significant in Mexican American women. In Mexican American men the

†A history of antidiabetic medication was elicited at the time of the home interview. An effort was made to confirm this information at the time of the medical examination. Of the 50 individuals shown in Table 1 as taking either insulin or oral agents, 15 had their medication status confirmed by direct inspection of the bottle in which the medication had been dispensed by the pharmacist. An additional 25 provided the exact name of the medication prescribed. Of the remaining 10, 6 met the NDDG criteria and would therefore have been classified as diabetic regardless of their medication status.

‡Diagnosed cases from HANES II who did not meet the NDDG criteria, but who took antidiabetic medication, were also included to assure comparability between the HANES II NIDDM rates and those from San Antonio.

TABLE 2
Age-adjusted sum of skinfolds and body mass index (mean ± standard error) in Mexican Americans and Anglos

	Mexican Americans			
	Barrio	Transitional	Suburbs	Anglos
Women				
Sum of skinfolds (mm)	53.9 ± 0.9	46.3 ± 1.6	45.5 ± 1.3	40.2 ± 1.0
Body mass index (kg/m²)	29.1 ± 0.3	27.0 ± 0.5	24.8 ± 0.4	24.1 ± 0.3
N	301	105	146	229
Men				
Sum of skinfolds (mm)	37.0 ± 1.0	35.8 ± 1.6	37.5 ± 1.1	34.3 ± 1.0
Body mass index (kg/m²)	28.1 ± 0.3	28.3 ± 0.5	27.6 ± 0.4	26.5 ± 0.4
N	180	73	132	166

P values

	Mexican American			
	Barrio vs. Trans	Trans vs. Suburbs	Barrio vs. Suburbs	Anglo vs. pooled Mexican American
Women				
Sum of skinfolds (mm)	<0.0001	NS	<0.0001	<0.0001
Body mass index (kg/m²)	0.0006	0.0011	<0.0001	<0.0001
Men				
Sum of skinfolds (mm)	NS	NS	NS	0.05
Body mass index (kg/m²)	NS	NS	NS	0.0004

NS = nonsignificant.

transitional versus suburbs and barrio versus suburbs comparisons were significant (P = 0.02 and P = 0.0008, respectively). The pooled ethnic contrasts revealed that Mexican Americans of both sexes had significantly higher glucose sums than Anglos.

Also shown in Table 3 are the mean skin reflectance measurements by neighborhood and ethnic group. As expected, Anglos of both sexes had lighter skin color than Mexican Americans (higher skin reflectance indicates lighter skin color). There were no neighborhood differences in skin color

TABLE 3
Age-adjusted sum of glucose and skin reflectance (mean ± standard error) in Mexican Americans and Anglos

	Mexican Americans			
	Barrio	Transitional	Suburbs	Anglos
Women				
Sum of glucose values* (mg/dl)	400.9 ± 7.2	363.3 ± 10.8	334.9 ± 8.1	315.2 ± 6.2
Skin reflectance (color) (%)	24.5 ± 0.2	28.3 ± 0.4	30.1 ± 0.3	33.8 ± 0.3
N	301	105	146	229
Men				
Sum of glucose values* (mg/dl)	402.6 ± 8.5	395.7 ± 12.5	361.0 ± 8.7	343.8 ± 7.3
Skin reflectance (color) (%)	22.4 ± 0.3	27.0 ± 0.5	29.1 ± 0.4	33.3 ± 0.3
N	180	73	132	166

P values

	Mexican American			
	Barrio vs. Trans	Trans vs. Suburbs	Barrio vs. Suburbs	Anglo vs. pooled Mexican American
Women				
Sum of glucose values (mg/dl)	0.0046	0.005	<0.0001	<0.0001
Skin reflectance (color) (%)	<0.0001	0.0005	<0.0001	<0.0001
Men				
Sum of glucose values (mg/dl)	NS	0.0211	0.0008	<0.0001
Skin reflectance (color) (%)	<0.0001	0.0011	<0.0001	<0.0001

*Since the distributions of glucose sum were skewed to the right, statistical analyses were performed on the log-transformation of this variable. The resulting adjusted group means were then back-transformed to natural units for presentation in this table.
NS = nonsignificant.

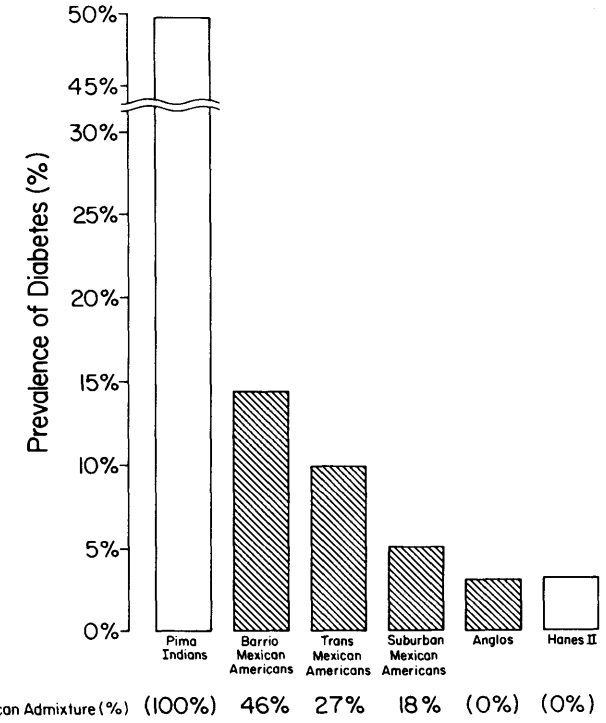

FIGURE 1. Age-adjusted NIDDM prevalence and native American admixture estimates of Pima Indians, San Antonio Mexican Americans and Anglos, and HANES II subjects. The hatched bars represent the San Antonio sub-populations.

among Anglos (data not shown). Among the Mexican Americans, however, skin color becomes progressively lighter from the barrio to the suburbs. These neighborhood contrasts in Mexican Americans were highly significant in both sexes.

Figure 1 presents age-adjusted NIDDM prevalence for Pima Indians, for San Antonio Mexican Americans (by neighborhood), for San Antonio Anglos, and for the nationwide HANES II population. The Pima Indian rates are more than three times as high as the rates for barrio Mexican Americans, the next highest group. The NIDDM rates then diminish progressively to the San Antonio Anglo population, which has a rate nearly identical to that of the predominantly Anglo HANES II population. Figure 1 also presents the percent of native American genetic admixture for Mexican Americans, pooled across both sexes, along with the presumptive admixture levels for the Pimas (100%) and Anglos (0%). For Mexican Americans these calculations assume a dihybrid model, i.e., two parental populations, native American and Spanish. The San Antonio data reveal progressively lower admixture as one moves from the barrio to the suburbs, reflecting the statistically significant neighborhood difference in skin color in this ethnic group.

DISCUSSION

Obesity is the most well-established risk factor for NIDDM. It is thus appropriate to inquire if the neighborhood differences in glucose tolerance and NIDDM prevalence among Mexican Americans could be entirely explained by corresponding neighborhood differences in obesity. In addressing this question, it may first be noted that, whereas in Mexican American women declining glucose sums from barrio to suburbs were accompanied by parallel declines in the two obesity indices (Tables 2 and 3), this was not the case in men. For this sex, glucose sums declined from barrio to suburbs even though the obesity indices were quite similar in the three neighborhoods. More detailed analyses of the relationship between obesity and NIDDM in Mexican Americans have appeared in a previous publication by our group.[10] In these earlier analyses, we divided Mexican American men and women into lean, average, and obese categories and compared them with Anglo men and women who were closely matched on degree of adiposity. The results indicated both that Mexican Americans were more likely to be obese than Anglos and that, for both ethnic groups, the prevalence of NIDDM rose as expected with increasing degrees of obesity. Thus, a portion of the excess NIDDM prevalence in Mexican Americans is clearly related to their higher prevalence of obesity. Within obesity-matched strata, however, Mexican Americans still had from two to four times higher NIDDM prevalence rates than their Anglo counterparts. Thus, lean Mexican Americans still had more NIDDM than equally lean Anglos and obese Anglos were relatively protected compared with equally obese Mexican Americans. We concluded that, although obesity clearly explains a portion of the excess NIDDM prevalence in Mexican Americans, it does not explain the entire excess.

We believe that the results presented in this paper suggest that genetic factors—specifically, the degree of native American genetic admixture—contribute to that portion of the excess NIDDM prevalence in Mexican Americans which cannot be explained by their greater degree of obesity. Before accepting this conclusion, it is necessary to examine critically the adequacy of skin color measurements as an indicator of genetic background. A prerequisite of a satisfactory indicator of genetic background is that it be minimally or not at all influenced by environmental factors. In the case of skin color, sun exposure is clearly the major environmental influence to be considered. For that reason, we have chosen to

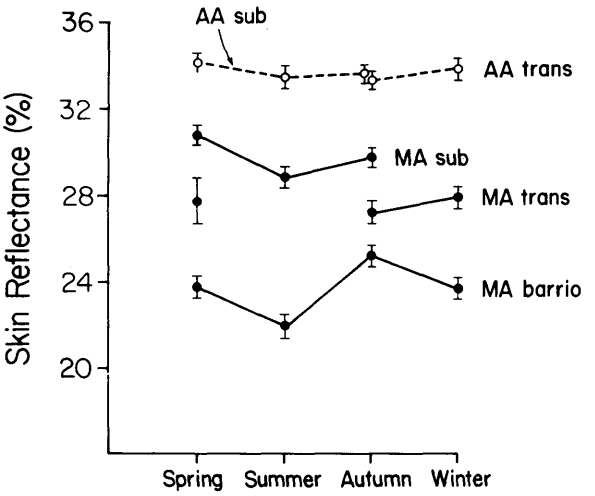

FIGURE 2. Mean and standard errors of percent skin reflectance measurements according to season of the year. Because of the scheduling of the survey, transitional neighborhood Mexican Americans and Anglos were not surveyed during the summer months, and suburbanite Mexican Americans and Anglos were not surveyed during the winter months.

measure skin color at a relatively sun-shielded site, the inner aspect of the upper arm. Previous work has suggested that this site is relatively unaffected by differential exposure to sunlight.[22] To examine this issue further, we analyzed skin color in our population according to season of the year. The results, presented in Figure 2, indicate that there is a slight tendency toward darkening of the skin during the summer months (lower reflectance indicates darker color). These seasonal variations, however, were relatively minor compared with the more marked differences between neighborhoods. Moreover, for Mexican Americans, the magnitude of the seasonal fluctuations appeared similar in the barrio and the suburbs suggesting that there were no major differences in exposure to sunlight—at least at the upper inner arm site—between neighborhoods. There was no suggestion, for example, of a greater degree of summer darkening in the barrio as might have been expected if lower income people had greater sun exposure than suburbanites. We believe, therefore, that the data presented in Table 3 and Figure 2 argue in favor of significant heterogeneity in native American genetic admixture in San Antonio Mexican Americans.

The skin color measurements were transformed into quantitative estimates of native American admixture using Bernstein's method.[18] This approach has been previously validated in several studies.[16–18] Relethford and Lees applied this method in several *mestizo* populations in Mexico and found that admixture estimates from skin color measurements were in close agreement with estimates based on serological markers.[16] In another study, these workers estimated admixture from skin color in five hybrid populations whose exact ancestry was known from pedigree information.[18] Again, excellent agreement was found between the estimates based on skin color and the known ancestry of these hybrid populations. These results were subsequently confirmed by Korey.[17] A comprehensive review of this topic has recently been published.[23]

Further evidence in support of the validity of our admixture estimates is their general agreement with admixture estimates for Mexican Americans reported in the literature. These previous estimates were based on red cell and serologic markers. An admixture level of 40% was observed for Colorado Mexican Americans,[24] which is similar to the level we found in our barrio population. (The socioeconomic status was not reported in the Colorado study but is likely to have been low.) An admixture level of 32% was reported for Mexican American subscribers to a large prepaid health plan in Oakland, California.[25] This level is similar to that which we observed in the San Antonio transitional neighborhood.

The stepwise decline from barrio to suburbs in both NIDDM prevalence and native American genetic admixture in Mexican Americans suggests that the proportion of native American genes may contribute to NIDDM prevalence in this ethnic group. Similar findings have been reported for the Three Affiliated Indian tribes (Mandan, Arickara, and Hidatsa) in North Dakota among whom NIDDM prevalence decreased progressively in full inheritance, between half and full, and less than half inheritance Indians.[26] In this study, degree of Indian inheritance was assessed from Indian Health Service medical records.

It should also be recognized that other, as yet unidentified factors associated with low socioeconomic status could also contribute to excess NIDDM in barrio Mexican Americans. For example, qualitative aspects of the diet (not directly linked to obesity) could play a role, although the evidence for this is weak. Also, NIDDM could itself lead to low socioeconomic status (rather than the reverse) by impairing employment prospects. Further work is needed to assess these possibilities.

Any epidemiologic investigation demonstrating on ecological association between NIDDM prevalence and the percent of genetic admixture in a population can only be viewed as suggestive rather than conclusive. An important limitation of the current study is that the estimates of admixture are attributes of groups, i.e., neighborhoods, rather than of individuals, precluding analyses based on individuals. More conclusive studies would need either a characterization of admixture for each individual,[27] or a useful genetic marker for NIDDM. We are currently carrying out a genetic marker study which will eventually generate, for each subgroup in our study, gene frequencies for 25 erythrocyte surface antigens, erythrocyte enzymes, and plasma proteins. We are exploring methods which would allow us, in addition to forming admixture estimates for populations, to estimate individual admixture.

The expression of the NIDDM susceptibility in populations with significant native American admixture appears to be linked to an environmental stimulus, presumably obesity secondary to overeating. The nature of the genetic susceptibility, whether a gene related to premature failure of insulin production, abnormally refractory beta-cells,[28] or an exaggerated degree of insulin resistance, is unknown. Further investigations in populations with high NIDDM prevalence should be undertaken, as they may uncover genes regulating these functions, producing genetic markers for NIDDM which may be usable in other populations.

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REFERENCES

[1] Zimmet, P.: Epidemiology of diabetes and its macrovascular complications in Pacific populations: the medical effects of social progress. Diabetes Care 1979; 2:144–53.

[2] Jackson, W. P. U.: Epidemiology of diabetes in South Africa. Adv. Metab. Disord. 1978; 9:111–46.

[3] Medalie, J. H., Papier, C. M., Goldbourt, U., and Herman, J. B.: Major factors in the development of diabetes mellitus in 10,000 men. Arch. Intern. Med. 1975; 135:811–17.

[4] Ahuja, M. M. S., Siraji, L., Garg, V. K., and Mitroo, P.: Prevalence of diabetes in northern India (Delhi Area). Horm. Metab. Res. 1974; 4:321.

[5] West, K. M.: Epidemiology of Diabetes and Its Vascular Lesions. New York, Elsevier, 1978:207.

[6] Bennett, P. H., Rushforth, N. B., Miller, M., and LeCompte, P. M.: Epidemiologic studies of diabetes in the Pima Indians. Recent Prog. Horm. Res. 1976; 32:333–76.

[7] West, K. M.: Diabetes in American Indians and other native populations of the new world. Diabetes 1974; 23:841–47.

[8] Neel, J. V.: Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? Am. J. Hum. Genet. 1962; 14:353–62.

[9] Stern, M. P., Pugh, J. A., Gaskill, S. P., and Hazuda, H. P.: Knowledge, attitudes and behavior related to obesity and dieting in Mexican Americans and Anglos: the San Antonio Heart Study. Am. J. Epidemiol. 1982; 115:917–28.

[10] Stern, M. P., Gaskill, S. P., Hazuda, H. P., Gardner, L. I., and Haffner, S. M.: Does obesity explain excess prevalence of diabetes among Mexican

Americans? Results of the San Antonio Heart Study. Diabetologia 1983; 24:272–77.

[11] National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979; 28:1039–57.

[12] McDonald, G. W., Fisher, G. F., and Burnham, C.: Reproducibility of the oral glucose tolerance test. Diabetes 1965; 14:473–80.

[13] Keen, H., Jarrett, R. J., and McCartney, P.: The ten-year follow-up of the Bedford Survey (1962–1972): glucose tolerance and diabetes. Diabetologia 1982; 22:73–78.

[14] O'Sullivan, J. B., and Mahan, C. M.: Prospective study of 352 young patients with chemical diabetes. N. Engl. J. Med. 1968; 278:1038–41.

[15] Ito, C., Mito, K., and Hara, H.: Review of criteria for diagnosis of diabetes mellitus based on results of follow-up study. Diabetes 1983; 32:343–51.

[16] Relethford, J. H., and Lees, F. C.: Admixture and skin color in the transplanted Tlaxcaltecan population of Saltillo, Mexico. Am. J. Phys. Anthropol. 1981; 56:259–67.

[17] Korey, K. A.: Skin colorimetry and admixture measurements: some further considerations. Am. J. Phys. Anthropol. 1980; 53:123–28.

[18] Lees, F. C., and Relethford, J. H.: Admixture estimation using skin reflectance data. Am. J. Phys. Anthropol. 1978; 49:505–10.

[19] Relethford, J. H., Stern, M. P., Gaskill, S. P., and Hazuda, H. P.: Social class, admixture and skin color variation in Mexican Americans and Anglo Americans living in San Antonio, Texas. Am. J. Phys. Anthropol. 1983; 61:97–102.

[20] Biomedical Computer Programs P-Series. Dixon, W. J. and Brown, M. B., Eds. Berkeley, California University of California Press, 1979.

[21] National Center for Health Statistics. Overweight adults in the United States. Advance data. Vital Health Stat. 1979; 51:1–9.

[22] Hulse, F. S.: Selection for skin color among the Japanese. Am. J. Phys. Anthropol. 1967; 27:143–56.

[23] Relethford, J. H., and Lees, F. C.: The use of quantitative traits in the study of human population structure. Yearbook Phys. Anthropol. 1982; 25:113–32.

[24] Gottlieb, K., and Kimberling, W. J.: Admixture estimates for the gene pool of Mexican Americans in Colorado. Am. J. Phys. Anthropol. 1979; 50:444.

[25] Reed, T.: Ethnic classification of Mexican Americans. Science 1975; 185:283.

[26] Brosseau, J. D., Eelkema, R. C., Crawford, A. C., and Abe, T. A.: Diabetes among the Three Affiliated Tribes: correlation with degree of Indian inheritance. Am. J. Public Health 1979;; 69:1277–78.

[27] Maclean, C. J., and Workman, P. L.: Genetic studies of hybrid populations. I. Individual estimates of ancestry and their relation to quantitative traits. Ann. Hum. Genet. 1973; 36:341–51.

[28] Savage, P. J., Bennion, L. J., Flock, E. V., and Bennett, P. H.: Recovery of beta cell function in diabetes following weight reduction. Diabetes 1976; 26 (Suppl.):414.