Diabetes in Central America

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SUMMARY

The prevalence of diabetes in Central America was somewhat greater than in East Pakistan and Malaya, less than in Uruguay and Venezuela, and substantially less than in affluent societies such as the United States. Differences in prevalence among Central American countries were modest but probably significant in some instances. In all Central American countries diabetes was more common in females but this difference was probably attributable to the greater adiposity of the women. Age-matched populations from eleven different countries of three continents have now been tested using standardized methods. Prevalence of diabetes varied greatly, and differences were more related to environment than to race. These results support the hypothesis that environmental factors can increase or reduce prevalence by several-fold. DIABETES *19*:656-63, September, 1970.

Between 1965 and 1967 a large-scale nutrition survey was conducted in Central America as a cooperative undertaking of the Institute of Nutrition of Central America and Panama, the governments of the six republics of Central America, and the Office of International Research of the National Institutes of Health of the United States.[1-6] This survey provided an unusual opportunity to test a representative sample of the populations of each of the countries, and to compare the glucose tolerance of these subjects with many other variables. These circumstances also permitted us to compare our data with results in other populations tested previously by the same methods. Prevalence rates for diabetes had not been determined before in any of these countries.

The six contiguous republics (Guatemala, El Salvador, Honduras, Costa Rica, Nicaragua, and Panama) form a land mass of approximately 181,000 square miles, slightly larger than the state of California and about twice the size of the United Kingdom. The combined population of the six countries is approximately fifteen million. Most of the people live in small rural villages; there is, however, at least one large urban center in each of the countries. Levels of social and economic development in this region are higher than in Southeast Asia and substantially lower than in Europe or the United States; income levels per capita average about $300 (U.S.) per year. The economy is based mainly on agriculture. Most of the people are of mixed blood ("mestizos"). The predominate mixture is native Indian and European (usually Spanish). Smaller fractions of the total population are of pure Indian blood or of "pure" Caucasian (European) descent. Negroes make up a still smaller portion of the population. There are some racial differences among the countries. For example, there are more Indians of pure blood in certain parts of Guatemala, and there are fewer Indians and fewer of mixed blood in Costa Rica where most of the population is of Spanish descent.

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METHODS

Selection of subjects

In each country a highly systematic program was developed to identify and select a representative sample of the general population. Details of the methods employed have been described elsewhere.[1-8] Representative locations were selected by means of a systematic random procedure. In each country the number of locations selected in each of the several administrative divisions or regions was proportional to the population of that region. At each location twenty dwelling sites were selected at random from recent census data. In each country the ratio of rural dwellings to urban dwellings in the sample reflected the rural-urban distribution of the population (predominantly rural). In spite of efforts to obtain representative samples, several sources of potential bias developed. At most of the 209 locations the rate of participation was high, often exceeding 80 per cent of the families and of family members selected. On the other hand, at some sites the rate of recruitment for the diabetes-related studies was lower, so that only about two thirds of those in the total sample were tested. Specific data are given in table 1 by country

TABLE 1

Diabetes-related studies in Central America

Country	Sites of testing	Subjects tested			Mean per cent of standard weight	
			Males	Females	Males	Females
Costa Rica	39	446	180	266	97	109
% of sample*			60%	71%		
El Salvador	29	265	97	168	91	96
% of sample*			67%	68%		
Guatemala	48	498	204	294	92	99
% of sample*			67%	67%		
Honduras	26	342	134	208	95	100
% of sample*			66%	74%		
Nicaragua	35	389	130	259	98	107
% of sample*			54%	69%		
Panama	32	345	145	200	93	103
% of sample*			56%	69%		

*This represents the percentage of the subjects in the representative sample who were tested.

and sex with regard to the portion of the sample who were tested. Thus, the populations tested were only crudely representative of the universe from which they were drawn. Even so, the country-wide samples are much better than are usually available for estimating prevalence rates. As shown in table 1 the number of testing locations ranged from twenty-six to forty-eight per country. The nutrition survey included all age groups. Although some younger subjects were tested for diabetes, the results reported here include only persons more than thirty-four years of age. Glucose loading tests were performed and certain related data collected on 2,285 subjects. The frequency distribution of ages was the same for males and females. Frequency distribution of age by country and for all Central Americans is given in table 5.

The number of subjects tested in each country for each sex is given in table 1. The size of the sample in each country was not large, ranging from 265 in El Salvador to 498 in Guatemala, but these numbers were concentrated in one age group (over thirty-four). Even in El Salvador the number tested in this age group was four times greater in relation to its population than the portion tested in the National Health Survey of the United States.[9] An effort was made to avoid either a positive or negative bias for diabetes in the selection and recruitment of subjects. The subjects did not know that they were to be tested for diabetes.

The glucose loading test

All subjects received an oral glucose load of 1 gm./kg. of body weight, administered in an approximate concentration of 25 per cent. Venous blood was drawn at two hours. Glucose levels were determined on plasma, using the AutoAnalyzer method. The plasma values were later converted to whole blood values to facilitate comparison with results of other studies. This was done by assuming that plasma levels were 14 per cent higher than whole blood levels. The consistency of the relationship between plasma and whole blood levels has been well documented.[10]

With few exceptions the tests were performed in the latter part of the morning, as in other countries.[7] Usually the load was administered three to four hours after breakfast but the duration of the fasting ranged from one to fourteen hours. Except for a very few instances the subject had fasted for more than two hours prior to the administration of glucose. We are aware that in certain circumstances variations in time of day or duration of fasting may produce small but significant effects on glucose tolerance. However, systematic studies in other countries had indicated that these factors had little effect on our results under these

TABLE 2

Frequency distribution of two-hour glucose values in Central America

mg./100 ml.	>209	180-209	150-179	120-149	90-119	60-89	<60
Per cent	1.5	0.8	2.4	7.8	29.0	50.6	7.9
Cumulative %	1.5	2.3	4.6	12.4	41.4	92.1	100.0

TABLE 3

Frequency distribution of two-hour glucose values by country in Central America

	Per cent of values			
Glucose in mg. per 100 ml.	>149	120-149	100-119	<100
Costa Rica				
Males	3.3	5.6	12.2	79.9
Females	7.5	3.2	16.9	62.4
Both sexes*	5.4	9.4	14.6	70.7
Cumulative	5.4	14.8	29.4	100.1
El Salvador				
Males	2.1	6.2	16.5	75.3
Females	4.2	10.7	22.0	63.1
Both sexes*	3.2	8.5	19.3	69.2
Cumulative	3.2	11.7	31.0	100.2
Guatemala				
Males	2.9	2.9	8.8	85.3
Females	5.4	4.8	10.2	19.6
Both sexes*	4.2	3.9	9.5	83.5
Cumulative	4.2	8.1	17.6	100.1
Honduras				
Males	1.5	6.7	11.9	79.9
Females	6.7	12.5	20.7	60.1
Both sexes*	4.1	9.6	16.3	70.0
Cumulative	4.1	13.7	28.0	100.0
Nicaragua				
Males	2.3	4.6	11.5	81.5
Females	7.7	10.8	15.8	65.6
Both sexes*	5.0	7.7	13.7	73.5
Cumulative	5.0	12.7	26.4	99.9
Panama				
Males	0.0	2.8	9.0	88.3
Females	5.0	8.0	17.5	69.5
Both sexes*	2.5	5.4	13.3	78.9
Cumulative	2.5	7.9	21.2	100.1

*Rate based on projected results if an equal number of males and females had been tested.

particular conditions.[7] In order to confirm these previous observations we also analyzed the results of 1,013 tests in Central American subjects in which the duration of fasting was recorded. No significant effect of duration of fasting was found. There was no significant correlation between duration of fasting and age.

RESULTS

Prevalence of diabetes

The frequency distribution of the two-hour blood glucose levels for all subjects tested in Central America is shown in table 2. The results for each country are given in table 3. We have arbitrarily classified as "diabetic" those subjects whose two-hour venous whole blood glucose values exceeded 149 mg./100 ml. However, examination of tables 2 and 3 permits determinations of prevalence rates using diagnostic criteria which are either more "conservative" or more "liberal" than ours. For example, 4.6 per cent of all subjects had "diabetes" by our criteria, but only 2.3 per cent had values above 179 mg./100 ml., while 12.4 per cent had values greater than 119 mg./100 ml. Although two-hour values as low as 120 mg./100 ml. have been considered abnormal by some workers, recent evidence suggests that in subjects in this age group values up to about 150 mg./100 ml. are probably normal.[11] O'Sullivan and Mahan have measured the degree to which prevalence rates are affected by changes in diagnostic criteria.[12] Because comparable frequency distribution data are available for each population, the prevalence of diabetes for these and other countries[7] can be compared with the use of any one of several diagnostic criteria. We recognize the limitations of a single two-hour value as a definitive diagnostic instrument in specific individuals. But it seems quite likely that the prevalence of elevated two-hour values in a group would be proportional to the prevalence of impairment of tolerance by more elaborate testing. Moreover, even if all subjects had "complete" tolerance tests with glucose determinations at five different intervals, the problems of classification and interpretation would remain with regard both to the group of tests and certain individual tests.[13]

In interpreting this rate of prevalence for Central

America (4.6 per cent) and those to be presented below for other groups, several considerations should be kept in mind. First, these rates apply only to the age group tested (over thirty-four years of age). Rates for the entire general population including all age groups would probably be less than half as great (see below). Second, prevalence rates based on testing *all* subjects with glucose loads can be expected to yield much higher rates than rates based on the methods that have been more commonly employed. Most prevalence rates have been based on screening with less sensitive methods such as urine glucose determinations. In testing subjects in Uruguay, Venezuela, Malaya, and Pakistan we had an opportunity to compare the sensitivity of several standard screening procedures in subjects who had glucose loading tests. It was found that in this age group prevalence rates based on loading all subjects were from two to five times higher than those based on certain traditional procedures in which only positive screenees received glucose loads. Finally, the prevalence rates given in this report include known diabetics as well as those in whom the presence of diabetes had not been identified previously. Of the 106 persons in whom "abnormal" tolerance (two-hour glucose over 149 mg./100 ml.) was found, twenty-four were known diabetics. Thus in this age group the observed prevalence of known (and confirmed) diabetes was 1.1 per cent, and the rate for occult "diabetes" was 3.5 per cent. Our results show that in every country of Central America most of the people with diabetes did not know they had it.

We have adjusted slightly the observed rate of prevalence for all of Central America by projecting a rate which takes into account the relative populations of the six countries; and another adjustment was applied to correct for the fact that the number of females tested was somewhat greater than the number of males. These two adjustments result in a small change from an observed prevalence rate of 4.6 per cent to a projected rate of 4.1 per cent.

Table 3 gives the prevalence rates for each of the countries. Differences among countries were modest, ranging from 2.5 per cent for Panama to 5.4 per cent in Costa Rica. Small differences among countries in observed prevalence rates, such as 4.2 per cent for Guatemala and 5.0 per cent for Nicaragua, may not be significant. We believe that larger differences, such as 5.4 per cent for Costa Rica and 3.2 per cent for El Salvador, are significant.

Figure 1 compares the prevalence of diabetes in

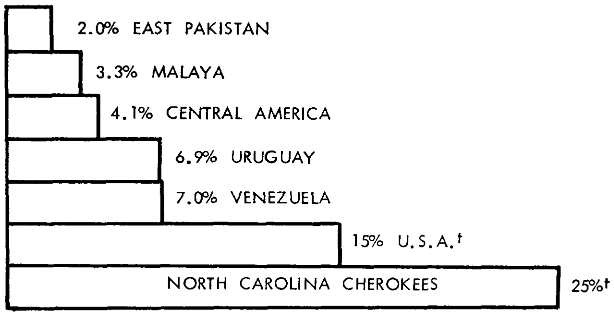

FIG. 1. Prevalence of diabetes in the older segments (over thirty-four years) of seven populations.
†Based on extrapolations and estimates (see text).

Central America with rates in other age-matched populations tested by these methods.[7] The prevalence rate in Central America was lower than in Venezuela and Uruguay and somewhat higher than rates for East Pakistan and Malaya. The prevalence of diabetes is substantially lower in Central America than in age-matched groups of certain affluent nations. Studies have not been reported for representative samples of the general populations of affluent countries using these methods. It is possible, however to make crude comparisons by making certain extrapolations. Results of studies by Hayner et al.,[14] by Gordon et al.,[15] and by Unger[16] suggest that in the United States the rate of "abnormal" tolerance by criteria equivalent to ours is roughly 15 per cent *for this age group*. Our own studies in Bangor, Pennsylvania yielded a rate of 17 per cent in this age group using these methods and these criteria.[7] Extrapolations from glucose loading results for general populations in Norway[17] and Britain[18] suggest that a similar or slightly lower portion (about 10 to 15 per cent) of those in this age group have "impairment" of tolerance by standards equivalent to those employed here. We also tested the Cherokee Indians of North Carolina by these methods. They are very obese. The population sample tested was not adequate to establish a prevalence rate with precision, but the data suggested a prevalence rate of roughly 25 per cent in this age group.[19]

Association of prevalence with other factors

As indicated in table 3 the prevalence of diabetes was higher in females than in males in every country. For all subjects in Central America the observed rate in males was 2.1 per cent while the observed prevalence in females was 6.2 per cent. The higher rate in females cannot be attributed to parity because no association was demonstrable between parity and diabetes prevalence (see below). On the other hand, overweight was

TABLE 4

Relationship of age and glucose tolerance in Central America

	Two-hour glucose in mg./100 ml.				
	<100	100-129	130-149	150-199	>199
"Young" (35-44 yrs.)	77%	17%	4%	2%	0.4%
"Middle-aged" (45-64 yrs.)	72%	20%	4%	3%	2.0%
"Old" (more than 64 yrs.)	68%	20%	4%	4%	5.0%

much more common in females than in males, and this could account for the difference in prevalence between the sexes. Detailed information will be reported elsewhere concerning the association between adiposity and diabetes in these and other populations. Suffice it to say here that in Central America the mean per cent of standard weight[8] for women was 103 per cent and for men 95 per cent. These subjects were considerably thinner than age-matched subjects in the United States,[9] and decidedly fatter than the Asian populations studied.[7] The data in table 1 show the mean per cent of standard weight for each country by sex. Although the differences among countries were relatively small with respect to both diabetes prevalence and mean per cent of standard weight, there was a good correlation between the two. For example, weights were lowest and prevalence rates lowest in Panama and El Salvador, while both prevalence rates and weights were greatest in Costa Rica and Nicaragua.

There were small variations in the diet among the countries and in various parts of individual nations.[1-6] However, the diet for the entire region can be characterized in a general way. In comparison to the typical diet in the United States, the diet in Central America is lower in calories, protein, and animal fat. In Central America a greater portion of the total caloric intake is derived from carbohydrates. But in comparison to most Asian diets the Central American diet is low in carbohydrate and high in fat.

The number of full-term pregnancies (seven or more months) was recorded for each of the women tested. Mean parity was seven, and a substantial portion of these women had had from nine to twenty-two pregnancies. No significant relationship was found between parity and prevalence of diabetes. In Venezuela and Uruguay we had found an impressive association between parity and diabetes, but part or all of this association could have been attributable to a positive relationship between parity and adiposity.[7]

Table 4 shows the negative relationship between age and glucose tolerance in Central America. This same inverse relationship was observed in each of the six countries, as shown in table 5. These data demonstrate the crucial importance of matching for age before making comparisons of prevalence.

The associations between prevalence and certain other factors such as socioeconomic status, electrocardiographic findings, and nutritional status will be reported in detail in other presentations. Suffice it to say here that there was a strong association between the preva-

TABLE 5

Frequency distribution of ages and prevalence of diabetes by age group for each country

Country	All subjects	Age in years 35-44	45-54	55-64	>64
Costa Rica %	100	37.4	29.6	14.1	18.8
Prevalence %	5.8	4.2	5.3	3.2	11.9
El Salvador %	100	36.2	28.3	18.9	16.6
Prevalence %	3.4	1.0	2.7	6.0	6.8
Guatemala %	100	36.5	32.3	14.7	16.5
Prevalence %	4.4	1.6	3.7	11.0	6.1
Honduras %	100	38.0	26.3	19.3	16.4
Prevalence %	4.7	4.6	2.2	3.0	10.7
Nicaragua %	100	32.1	27.2	20.6	20.1
Prevalence %	5.9	1.6	6.6	7.5	10.3
Panama %	100	27.8	32.7	22.0	17.4
Prevalence %	2.9	0.0	3.5	3.9	5.0
All countries %	100	34.6	29.6	17.8	18.1
Prevalence %	4.6	2.4	4.1	5.9	8.7

lence of diabetes and socioeconomic status. In an independent survey these families were classified as having "high," "medium," or "low" socioeconomic status. Diabetes was more than twice as common in those with "high" status as in those with "low" status.

We have now studied by a common method populations made up of many races and genetic groups including Chinese (in Malaya), Malays, Indians (in Malaya and Pakistan), American Indians, Negroes (in Central America), and Caucasians in Central, South, and North America. Differences in prevalence were quite small when races or populations were matched for fatness. For example, diabetes was twice as common in Venezuela as in Guatemala, but the rate of diabetes was the same in weight-matched groups from the two countries. In Central America diabetes was more than three times as frequent in subjects whose weights exceeded 109 per cent of standard than in leaner persons in the same population.

Our methods were not designed to evaluate directly and thoroughly the effects of race and heredity on the prevalence and character of diabetes. No evident differences were noted in the character of diabetes in those of different races. The prevalence of diabetes was somewhat higher in Costa Rica (mainly persons of Spanish descent) than in Guatemala (Indians and persons of mixed blood), but these small differences may be attributable to other factors such as the greater adiposity of subjects from Costa Rica where income levels are a little higher.

Character of diabetes

These studies were not designed to evaluate certain of the clinical characteristics of diabetes, and the group of 106 persons who had impairment of glucose tolerance was not studied systematically with respect to several important manifestations of diabetes. It was possible, however, to determine the frequency distribution of hyperglycemia. Table 2 shows that most of those with abnormal tolerance were only mildly diabetic; only about one third (thirty-four of 106) of those with abnormal tolerance had two-hour glucose levels greater than 209 mg./100 ml. but severe hyperglycemia was occasionally found. Ten persons had blood glucose levels between 300 and 400 mg./100 ml., and three persons had values of 500, 506, and 563 mg./100 ml., respectively. The results of blood pressure and urine glucose determinations will be reported elsewhere.

DISCUSSION

In view of the other pressing health problems in Central America, diabetes-related programs would not seem to warrant highest priority. Nevertheless, diabetes is a very significant health problem in the region. No systematic studies were made in children or younger adults, but on the basis of glucose tolerance tests in a small number of military and civilian personnel, clinical experiences of local conditions, and more than 1,000 family histories, we concluded that diabetes was much less common in the younger segment of the population than in those over thirty-four years of age. Assuming that the prevalence of diabetes is very small in young adults and that approximately two thirds of the population are less than thirty-five years of age, about 225,000 people in Central America have "diabetes" (1.5 per cent of fifteen million). Our data show that a majority of these "diabetics" have very mild abnormalities of glucose tolerance. Therefore, the total number of people in the six countries with "clinical" diabetes is roughly fifty to one hundred thousand.

McDonald has recently reviewed the literature on the prevalence of diabetes in the Americas.[20] It has been evident for a long time that environmental factors influence the prevalence of diabetes. But, as Knowles[21] has pointed out, it has been difficult to collect data which would clearly demonstrate the extent and character of these effects. Our results show that prevalence rates sometimes differ markedly even when standardized methods and criteria are used, and the data suggest that the differences observed were related more to environment than to race. Diabetes is very common in the Indians of East Africa,[22] certain Yemenites of Israel,[23] urban Uruguayans,[7] and rich Central Americans, while it is rare in their racial and genetic counterparts who have lived in different circumstances. Apparently diabetes is also many times more common in those Polynesians[24] and Haitians[25] who have lived in relative affluence than in their poor relatives. All of these comparisons, including our studies, leave something to be desired with respect to the experimental conditions.

On the other hand, in making comparisons, we did have the advantages of standardized methods, age-matched groups, and population samples which were at least crudely representative. Considered in the aggregate the epidemiologic evidence suggests that genetic susceptibility to diabetes is common in most or all of the major races, and that under certain environmental conditions a large portion of genetically susceptible persons do not develop diabetes. The data do not argue against the hypothesis that diabetes is an hereditary disorder, but they suggest that the penetrance may be very low in some circumstances. Our data do not exclude the possibility that there are significant differences among the races in the frequency of diabetes-related genetic traits. But differences in prevalence among the populations and subpopulations we tested were modest when subjects were matched for adiposity. Jackson and his associates[26] have reported an exception to the general correlation between adiposity and prevalence of diabetes. A group of fat African women had less diabetes than other leaner groups tested under similar conditions. Other small and relatively isolated populations have rates of diabetes that suggest rates of genetic susceptibility which are higher (Maltese,[27] and Pima[28] and Cherokee[19] Indians) or lower (certain Eskimos[29]) than those prevailing in the major races, but environmental factors may be at least partly responsible for these unusual prevalence rates. For example, the Cherokees and Pimas are quite fat. The preponderance of recent evidence suggests that hyperinsulinism is the effect and not the cause of obesity.[30] Rimoin[31] has recently shown some interesting differences between the Amish and the Navajo Indians with respect to the pathologic physiology and characteristics of diabetes.

If glomerulosclerosis and retinopathy are genetic manifestations unrelated to hyperglycemia or relative insulin insufficiency, they would occur commonly in populations protected from hyperglycemia by their environments. We know of no reports of typical glomerulosclerosis or retinopathy in normoglycemics of Pakistan, Malaya, Israel, India, Central America or rural Uruguay. While not conclusive, these circumstances suggest that those who are protected from hyperglycemia by environmental conditions such as relative undernutrition are also protected from certain (or perhaps all) clinical manifestations of diabetes. Therefore, these epidemiologic observations fit best the hypotheses that the vascular lesions of diabetes are not independent and inevitable manifestations in genetically susceptible persons, and that these lesions can be prevented by avoiding insulin insufficiency (absolute or relative).

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The major responsibility for the testing activities in the field was borne by third and fourth year medical students from the United States and the survey team members in the different countries. These medical students included Rod Tripplet from Vanderbilt who worked in El Salvador, and Philipp Bornstein from Washington University at St. Louis who worked in Honduras. The following students from the University of Texas Medical Center at Galveston participated: Michael Cabazos (Honduras), E. G. Vega (Nicaragua), Ron Smotherman (capitol cities), Rudolfo Villarreal (Panama), and Orlando Garza (Costa Rica). The following students from the University of Oklahoma participated: R. Lee Jeffrey and Muriel McGlamery (Guatemala), Tom Carter (El Salvador), James Waren (Panama), Martin Glasser (Costa Rica), and Patrick Freeny (capitol cities).

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