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Glucose Tolerance in Two Unacculturated Indian Tribes of Brazil

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Summary. Plasma levels of glucose, insulin, growth hormone, and pancreatic polypeptide in response to a standard oral glucose load were studied in the Yanomama and the Marubo, two relatively unacculturated Amerindian tribes of the Brazilian Amazon. The findings in the two tribes differed significantly from each other and in the degree of deviation from control subjects. The average responses in both tribes differed significantly from those of age- and sex-matched Caucasoid control subjects studied in Ann Arbor, Michigan; however, of the two tribes, the Marubo, the more acculturated group, resembled the controls more closely. Plasma concentrations of glucose and the hormones at three time points (fasting, 1 h, 2 h) were compared by means of a multivariate analysis. When the Marubo were compared with the control subjects, the only highly significant difference was in the plasma glucose concentrations (all three points were higher in the Marubo); however, the Yanomama differed significantly from the control subjects with respect to all four plasma indicators ($p < 0.05$). Unlike the Marubo, the Yanomama showed no significant rise in plasma glucose at 1 h and no decrease at 2 h. Neither tribe exhibited the bimodality of the 2 h glucose value characteristic of acculturated Amerindians, such as the Pima, but the samples studied were small.

Key words: Oral glucose tolerance, plasma insulin, growth hormone, pancreatic polypeptide, Amerindian tribes, Marubo, Yanomama.

It has been suspected for some time that diabetes mellitus, particularly the non-insulin-dependent type, is a 'disease of civilization.' One particularly suggestive line of evidence comes from the extraordinarily high prevalence of glucose intolerance and overt diabetes in certain highly acculturated American Indian tribes [1–9] as well as among other recently primitive peoples [10–13]. It has been generally assumed that diabetes mellitus was relatively uncommon in these groups before their contacts with Western civilization, and has emerged in consequence of the recent change in their way of life which resulted from these contacts.

Baseline data on glucose metabolism and tolerance among reasonably undisturbed, pre-civilized peoples remain extremely rare. To our knowledge, the only studies of this kind were carried out by Rimoin, Merimee and associates on African Babinga pygmies and Bantu tribesmen [14, 15]. These studies suggest that the pygmies are distinctive in their response to a glucose load, particularly in their apparently normal handling of glucose with a minimal mobilization of insulin. While it is possible that this response is a general characteristic of primitive man, it is more likely that the pygmies do in fact exhibit lower insulin responses to glucose since they are deficient in growth hormone activity and have increased peripheral sensitivity to insulin.

In the course of fieldwork in 1976 among the Amerindian tribes of the Amazon basin we had the opportunity, under rather difficult field conditions, to augment the few existing observations on glucose tolerance in pre-civilized peoples with data on two tribes, the Marubo, who belong to the Central Pano, and the Yanomama. Although the numbers of subjects studied are modest, our studies provide the only data available for such peoples from the western hemisphere. The interpretation of the findings is complicated by an unexpected difference between the results in the two tribes.

Methods

Subjects

The study was restricted to healthy active young males with estimated ages between 18 and 35 years. The Marubo ($n = 11$), studied at the New Tribes Mission of Vida Nova at about 6° 47'S latitude, 72° 08'W longitude, are a subdivision of the Central Pano, whose present status

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was briefly summarized by Mohrenweiser et al. [16]. Although most of this group are now relatively acculturated, the Marubo have remained isolated until the last 30 years. However, with the effort to extend the Brazilian perimeter highway into this region, both government and mission groups have been more active in this area. In 1960 the New Tribes Mission initiated permanent contacts with the group. This usually consists of two couples living at a small outpost near a Marubo village. The Indian villages studied are near the Paraguaçu River. An occasional group of young Indians descends the river to the Amazon port town of Benjamin Constant, making contact with lumber workers as they go, and from time to time a neo-Brazilian trader ascends the river in search of skins. The Mission personnel have introduced salt as an item of barter for services, but have otherwise disturbed the dietary patterns of the Indians very little. Salt intake undoubtedly remains very low by the standards of civilization.

The Yanomama ($n = 17$) were studied at the New Tribes Mission of Mararí, just south of the Venezuelan border, at about 1° 17′N, 64° 50′W. The general lack of acculturation of the Yanomama has been described previously [17–19]. Access other than by small plane to this station (established in 1969) is extremely arduous; the Indians' only contact with non-Yanomama other than the few missionaries consists of infrequent visits by Brazilian public health groups and research groups. The missionaries do not distribute salt and the Indians maintain their native diet with the cooking banana (*Musa* spp.) as the staple; meat is eaten when available. The normal diet is therefore high in carbohydrate. This is probably true of the Marubo as well. Refined carbohydrates are not available to the Indians at either Mission.

The control subjects were 28 healthy male Caucasoid volunteers from Ann Arbor chosen to give an age distribution approximating that of the Indian subjects. All controls gave informed consent. Additional control glucose tolerance tests were performed at the same time as the Indian studies on three members of the field team. The small size of this latter sample precludes statistical analysis, but the results do provide a check on field processing and storage of specimens. One member of the field team had a glucose tolerance test at both Indian stations; the results of the two tests were very similar.

Glucose Tolerance

The Indian subjects were recruited the day before the glucose tolerance test was performed. The missionaries, who served as interpreters, obtained informed consent and stressed the importance of an overnight fast preceding the test. A fasting blood specimen was obtained before 07.00 h from every subject. Between 07.00 and 08.00 h a glucose load in the form of 'lemon sour' (VWR Scientific Co., Columbus, Ohio) was ingested. The dose for the Marubo was 1.75 g/kg actual body weight; for the control subjects 1.75 g/kg ideal body weight; a uniform dose of 100 g was given to the Yanomama. For the Yanomama, whose weight varied from 48.1 to 60.3 kg, this corresponded to a range in dose of 1.7 to 2.1 g/kg (mean ± SD: 1.8 ± 0.12). Obesity is rare in the Marubo and the Yanomama, and none of the Indians studied was overweight; all appeared in good nutritional balance. Actual weight was thus close to ideal body weight, at least as defined for predominantly Caucasoid North American populations and consequently the glucose challenge did not differ greatly between the three groups. Additional blood specimens were taken 1 and 2 h after the glucose meal; all samples were drawn in heparinized tubes and placed on ice immediately. Red cells were spun down with a hand centrifuge within 2 h, and the plasma was kept in an ice bath without preservative until it was transported by air to the base ship, where it was frozen 24–30 h later. The plasma specimens remained frozen at −20 °C until the assays were performed approximately 1 year later. The two sets of samples were handled identically in the field and were assayed together in the same batch in Ann Arbor.

Laboratory Procedures

For each subject, the three plasma samples were analyzed for glucose, immunoreactive insulin, pancreatic polypeptide, and growth hormone. Plasma glucose was determined by the hexokinase method of Bondar and Mead [20] and plasma insulin by the method of Morgan and Lazarow [21]. Plasma levels of human pancreatic polypeptide were assayed by a double-antibody radioimmunoassay method [22]; the assay procedure for human growth hormone was essentially that of Berger et al. [23]. The sensitivity and intra-assay coefficients of variation of these assays were: plasma glucose: 0.3 mmol/l, 1.2%; insulin: 0.15 μU/tube, 8.1%; pancreatic polypeptide: 2.4 pg/tube, 10.1%; growth hormone: 20 pg/tube, 7.8%.

Statistical Analysis

The results were analyzed by multivariate methods [24]. Since each type of plasma determination is treated as a separate variable, an individual is characterized by an array of observations or variables, a group by an array of means. The variances and correlations among variables are explicitly taken into account and the differences between two such arrays are condensed into a single number (Mahalanobis' D^2 or Hotelling's T^2) which serves as a composite measure of differences between group means. A particular advantage of combining information from many variables is that it obviates the evaluation of many separate but correlated comparisons, a procedure which artificially inflates the apparent significance of the differences.

Results

The results for the four plasma components for Indian and control subjects are shown in Table 1. The control values are typical of those encountered in other studies from this laboratory, except for the failure to observe a decline in growth hormone after the administration of glucose. Close examination of Table 1 suggests that, except perhaps for plasma glucose, the data from the Yanomama all deviated further from the control subjects than did those from the Marubo. For plasma glucose, the Yanomama response was 'flat' compared with the control subjects, while the Marubo response, though similar in shape, was shifted upward. Both Indian glucose tolerance tests, therefore, appear 'deviant' but in different ways.

Even single sets of three points are difficult to compare objectively by univariate methods. When there are four such sets, as in the present data, it is essential to use a multivariate method. When this was done, the analysis confirmed the impression that the Yanomama response differed from that of the Marubo. If the Yanomama were compared directly with the Marubo, the aggregate D^2 for 12 variables was 13.9 ($p < 0.005$). The largest contribution to this difference was made by pancreatic polypeptide, and D^2 was not quite significant ($p \approx 0.06$) if this component was ignored. The analysis also confirmed that the Yanomama deviated more from the control subjects than did the Marubo. The D^2 for the Yanomama-control comparison was 17.0 ($p < 0.001$); that for the Marubo-control only 4.6 ($p = 0.05$). Although the levels of pancreatic polypeptide accounted for a large part of this difference, there was also evidence from the other variables that the Yanomama were more different from the control subjects than were the Marubo. When D^2 was calculated separately for

Table 1. Concentration of glucose and relevant hormones in the plasma of two tribes of South American Indians and Caucasoid control subjects during a 2 h oral glucose tolerance test

	Time (min)	Yanomama (n = 17)	Marubo (n = 11)	US Caucasoid control subjects (n = 28)	In-jungle Caucasoid control subjects (n = 3[a])
Age (years)		26.5 ± 7.0	27.2 ± 4.0	25.3 ± 5.1	30.7 ± 3.1
Height (cm)		154.8 ± 4.9	159.9 ± 5.7	180.4 ± 7.0	
Weight (kg)		54.7 ± 3.7	61.2 ± 3.9	71.7 ± 9.8	73.6 ± 9.9
Ponderal index (for mean weight, height)		2.45	2.47	2.30	
Plasma glucose (mmol/l)	0	4.9 ± 0.8	5.2 ± 0.6	4.7 ± 0.5	5.2 ± 0.7
	60	5.0 ± 1.0	6.6 ± 2.1	5.8 ± 1.2	5.4 ± 0.1
	120	5.2 ± 1.5	5.9 ± 1.4	4.5 ± 1.0	4.7 ± 1.1
Plasma insulin (mU/l)	0	10.5 ± 5.1	9.7 ± 3.6	10.4 ± 4.5	5.5 ± 3.9
	60	52.5 ± 34.9	87.2 ± 65.2	95.0 ± 47.2	40.0 ± 24.6
	120	42.9 ± 32.0	56.3 ± 32.5	57.2 ± 21.9	35.5 ± 32.5
Plasma human pancreatic polypeptide (ng/l)	0	116.9 ± 57.3	63.0 ± 32.7	82.4 ± 61.7	113.5 ± 86.1
	60	207.2 ± 124.2	106.2 ± 36.9	101.4 ± 76.3	190.3 ± 119.3
	120	163.8 ± 104.4	93.5 ± 49.6	114.1 ± 83.6	231.2 ± 147.6
Plasma human growth hormone (μg/l)	0	1.11 ± 0.71	2.26 ± 2.41	3.13 ± 1.53	1.03 ± 0.06
	60	0.96 ± 0.18	1.48 ± 1.11	3.47 ± 1.82	1.60 ± 0.96
	120	0.98 ± 0.24	1.80 ± 1.50	3.20 ± 1.57	1.22 ± 0.23

Results are expressed as mean ± SD. Time '0' sample was obtained after an overnight fast. [a] Three members of the fieldwork team served as control subjects, but one individual was given a glucose tolerance test on both occasions that Indians were studied. The two resulting values for each plasma determination were averaged

each set of three determinations, all four sets were significant for the Yanomama ($p < 0.05$), and the glucose and pancreatic polypeptide arrays were highly significant ($p < 0.01$). For the Marubo, the deviation of the glucose array was highly significant ($p < 0.01$), that of growth hormone barely significant ($p = 0.05$) and neither of the other components deviated significantly from the control subjects.

Discussion

The present studies were motivated by two previous sets of findings: the unusually high prevalence of overt diabetes and glucose intolerance in various tribes of North American Indians and studies on the Bantu and the much less acculturated pygmies [14, 15]. All but the latter group had undergone considerable acculturation before being studied. Thus it seemed possible that the very unusual insulin response of the pygmies to a glucose load was characteristic of undisturbed primitive man. This possibility receives no support from the present study. Both the Yanomama and Marubo are much less acculturated than any US Indian tribe, but neither exhibits the flat insulin response of the pygmies. In this connection, we note that the Yanomama are quite small in stature, in some portions of their distribution almost pygmoid [25] and that growth hormone levels in both tribes appear to be lower after an oral glucose load than those of the control subjects.

The finding that the two tribes differ significantly from each other is unexpected. With respect to plasma glucose alone, the slightly more acculturated Marubo are clearly the more deviant (Table 1). The limited data available suggest that the Marubo deviate in the same direction as do the more highly acculturated Amerindians, for example, the Pima Indians, for whom data on glucose tolerance are available [26]. Comparison with our results is complicated by the bimodality of the Pima data, and by the facts that their glucose tolerance tests were not preceded by a fast and that the glucose dose was only 75 g. However, we have calculated from the data [26] that at the mean age of our two South American samples (26.5 years), the Pima Indians would have a 2 h glucose level of approximately 7.8 ± 5.6 mmol/l. We conclude that the Marubo 2 h level (5.9 mmol/l), though significantly higher than for control subjects, is much less elevated than the corresponding value for the Pima. Thus, neither South American tribe shows the dramatic glucose intolerance of the highly acculturated (and quite obese) North American Pima.

With respect to the differences among the three groups studied, one possible explanation is different distributions of weight. Direct measurements of adiposity (by skin-fold thickness) are not available, but a roughly comparable measure is provided by the ponderal index: 100 x weight$^{1/3}$/height. Calculated for the mean height (cm) and weight (kg) of our subjects, the ponderal index is 2.45, 2.47, and 2.30 for the Yanomama, Marubo, and Caucasoid control subjects, respectively. The standard deviation within a group is 0.6–0.8, so the very similar values of the index for the two Indian tribes imply that the weight difference between them is almost exactly accounted for by differences in height (the Marubo average 5.0 cm taller). The smaller ponderal index for the Caucasoid control subjects (on average 20.6 cm taller still) indicates that they are less heavy for their height than the Indians. We recognize that the ponderal index is only a crude measure of adiposity, especially when applied across ethnic groups in this manner. Nevertheless, there is certainly no evidence that the Yanomama's total response to the glucose challenge is due to a lesser degree of adiposity.

Can the statistically significant differences between our three groups be due to artefacts, rather than reflecting genuine metabolic differences? The in-jungle control glucose tolerance tests suggest that no significant deterioration occurred during storage or transport of the samples. Thus technical artefacts seem unlikely. In contrast to the Ann Arbor control subjects, the Indians were all highly heat adapted and on low salt diets [27], but no reason for relating the difference between the two tribes to the probably small difference in salt intake is known.

Finally, there are of course genetic differences between these groups, the Indians from each other and both tribes from the Caucasoids. Whether these are relevant to the different responses observed cannot be determined from the data at hand. Given, however, the pressure for acculturation now overtaking even the most remote Amerindian tribes, the future medical history of these two Indian groups should provide important information for distinguishing genetic from 'life style' factors in the aetiology of non-insulin dependent diabetes mellitus.

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