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Restriction and Persistence of Polymorphisms of HLA and Other Blood Genetic Traits in the Parakanã Indians of Brazil

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ABSTRACT Results concerning HLA types and 22 other blood genetic systems are reported for the Parakanã Indians of northern Brazil, a tribe that is notable for the light color and pilosity of some of its members. No clear evidence of Caucasoid admixture was found, but the Parakanã show unusual frequencies in the EsD^1, PGM_1^1, Gc^2, Cp^B, Fy^a, Di^a, and L^M genetic markers. In addition, the very rare Rh allele r'' is present, as well as what seems to be a new PGM_2 variant. There is very limited heterogeneity in the HLA system. All these distinctive features may have arisen through a combination of founder effects and genetic drift. However, low F_{IS} values, as well as higher mean ages in heterozygous as compared to homozygous persons, suggest that an heterotic effect is counteracting these dispersive forces.

The Parakanã are a group of Indians with notable cultural similarities to the extinct Tupi population of the Brazilian coast. They now live in at least three villages in the general area of 49°30′ to 50°30′ W, 4° to 5°S. This is hilly terrain and completely forested except for garden clearings. Nimuendaju ('48) quotes Arara Indians as saying that the Parakanã displaced them from this area around 1910. One village, designated "Velho" in this paper, lived separately from others, and its inhabitants knew no individuals in the other villages. Velho first established regular contact with neo-Brazilians in 1971. Its culture and history until 1975 are the subject of a report by Magalhães Santos ('76). The other two known villages are interrelated, but have been at war with one another. The "Novo" village established contact with neo-Brazilians in 1976 after having been severely depopulated by the war and by disease. The third village, locally referred to as "Pacajá," remains unvisited by outsiders, but three persons from it migrated to the Novo group in 1978. In 1977 there were 98 Velho and 27 Novo Indians. From genealogies we estimated that all Velho tested could be traced to 48 independent gene sources and the Novo to 12 sources.

Like other Tupi-speaking tribes of Central Brazil (Wagley, '77), the Parakanã use a distinctive manioc processing method and bury their dead in the floor of their houses. They are polygamous and favor marriages of males to their sister's daughters, a custom that had been observed in extinct Tupi tribes. Seven of 21 marriages on which we have adequate information follow this pattern in the biological sense, and others seem to fit it in the classificatory sense. These Indians have a less aggressive history than the neighboring Cayapo. They included no acknowledged captive but there was one Novo whose mother was an Asurini and probably a captive.

Sightings of the Parakanã are probably the source of local stories concerning a tribe of "White" Indians, for indeed they include individuals whose skin color is as light as that of typical European Caucasoids. Many of their men also have unusually heavy beards. Other individuals, however, have skin colors which grade into those typical of the neighboring

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tribes, and other physical attributes are not distinctive. Since establishment of regular contacts, Brazilian Indian Service (FUNAI) officers have been stationed with the two "pacified" villages. Clothing has been adopted by all adults, and firearms have been introduced to the Velho village.

We hereby report data obtained among these Indians on HLA and 22 other blood genetic systems. As described here, they show a series of distinctive features that pose interesting problems in population genetics.

METHODS

Blood specimens were collected from the Velho population in November 1974, April 1977, and October 1978, and from the Novo at the later two times. The specimens were unrefrigerated for about 24 hours during transit to the city of Belém, Pará, or to the field laboratory at Pucurui. In Belém sera were separated from clotted specimens and refrigerated. ACD treated specimens were also refrigerated in Belém and shipped to Porto Alegre for the studies on serum proteins, cellular antigens, and enzymes. Fifty-four heparinized specimens were transported unrefrigerated to Caracas; they reached that laboratory and were entered into HLA test procedures about 40 hours after collection. The numbers of specimens included in each test are small, but they represent substantial proportions of the whole populations. Inasmuch as nearly everyone in each village is probably related to one another, it was not practical to distinguish unrelated sub-populations from the total.

Red cell antigens, enzymes, and serum proteins were characterized in the Porto Alegre laboratory using the following methods:

1) Tests for blood groups ABO, MNSs, Rh, Kell, Duffy, and Kidd were made on 2% washed red cell suspensions using commercial reagents according to the manufacturer's specifications (Ortho, Raritan; Johnson and Johnson, São Paulo). The Diego determinations were made with sera kindly donated by M. Layrisse.

2) Hemoglobins were typed by horizontal starch gel electrophoresis according to the method of Salzano and Tondo ('68).

3) Glucose-6-phosphate dehydrogenase (G-6-PD) and 6-phosphogluconate dehydrogenase (6-PGD) were characterized by the starch gel method of Fildes and Parr ('63) but with EDTA in the gel as described by Beutler et al. ('68). Phosphoglucomutase was characterized as described by Spencer et al. ('64), using the tris-maleic acid-EDTA-$MgCl_2$ buffer system, with the change suggested by Blake and Omoto ('75) for the gel buffer; adenylate kinase by the method of Fildes and Harris ('66); adenosine deaminase by the buffer systems of Fildes and Harris ('66) and the staining technique of Spencer et al. ('68).

4) Haptoglobin (Hp), transferrin (Tf), ceruloplasmin (Cp), and albumin (Al) were also typed by horizontal starch gel electrophoresis using the buffer systems of Poulik ('57) for Hp and Tf and that of Bowman and Bearn ('65) for the other two. Amido black 10B was used to stain Al and Tf, benzidine to stain Hp, and orthodianisidine for Cp. The CD specificity in the Tf system was compared with a TfD_1 serum kindly supplied by H.E. Sutton in the system described by Geserick et al. ('68) as well as that above. Acrylamide gels with trisglycine buffer pH 8.4 were used for comparison of CpAB variants in these sera with Cayapo and Porto Alegre Black specimens.

5) Gc types were determined by immunoelectrophoresis in tris-HCl buffer, pH 8.6, using rabbit antiserum from Behring Diagnostics.

Lymphocyte isolation for HLA testing was carried out in Caracas following Boyum's method ('68) by layering the buffy coat suspended in medium 199 over an equal volume of Lymphoprep (sp. gr. 1077, Pharmacia) followed by differential centrifugation. Other tests, performed in Belém or in the field, used lymphocytes purified by Ficoll-Hypaque (Bionetics, Kensington, MD) floatation, passage over agarose-glass bead columns, and differential centrifugation. The micro-cytotoxicity test of Terasaki and McClelland ('64) was carried out in Caracas, using three or four monospecific antisera against each of 13 HLA-A antigens, 16 HLA-B antigens, and five HLA-C antigens. The antibodies were the best available for the sixth International Histocompatibility Workshop. In addition, the Novo and 10 Velho specimens were tested with the full seventh Workshop series of 176 antisera. The other tests used 65 to 82 antisera selected from the NIH catalogue to emphasize types previously encountered in South American Indians, plus two sera with BW46 specificity kindly donated by R. Payne and M.J. Simons and another with BW48 donated by F. Kissmeyer-Nielsen.

Genealogies were tabulated with the help of an interpreter from FUNAI. In the Velho village this was an Asurini Indian.

RESULTS

Red cell and serum data

Data on blood groups, serum proteins, and erythrocyte enzymes appear in Table 1. [The esterase D results have been published previ-

TABLE 1. Blood group, serum protein, and erythrocyte enzyme phenotypes and gene frequencies

System	Number tested	Phenotypes found	Number found	Gene frequency	
ABO	100	O	100	I^o	1.00
MNSs	100	MS	6	L^{MS}	0.19
		MSs	26	L^{Ms}	0.81
		Ms	68		
P	100	P_1	90	P^1	0.68
		P_2	10		
Rh	100	CDEe (R^1r^s or R^1R^z)	7	R^1	0.66–0.71
		CDe (R^1R^1)	51	R^2	0.02–0.08
		CcDE (R^2r^y or R^2R^z)	1	R^z	0–0.09
		CcDEe (R^1R^2 or R^2r)	10	r	0.16–0.22
		CcDe (R^1r)	23	r^y	0.01–0.05
		CcEe (r^yr)	2[1]		
		cDEe (R^2r)	4		
		ce (rr)	2[1]		
Kell	100	K−	100	k	1.00
Duffy	100	a+	100	Fy^a	1.00
Kidd	64	a+	51	Jk^a	0.55
		a−	13		
Diego	49	a+	31	Di^a	0.39
		a−	18		
Hemoglobin	97	A	97	Hb^A	1.00
G-6-PD	55 Male	Gd(+) B	55	Gd^B	1.00
	43 Female		43		
6PGD	98	PdA	98	PGD^A	1.00
Esterase D	37	1-1	4		
		2-1	19	EsD^1	0.36
		2-2	14		
Esterases A_1-A_4, B	37	Usual	37	EsA^1	1.00
Phosphoglucomutase$_1$	93	1-1	90	PGM_1^1	0.98
		2-1	3		
Phosphoglucomutase$_2$	93	1-1	92	PGM_2^1	0.99
		1-11	1	PGM_2^{11}	0.01
Adenylate kinase	93	1-1	93	AK^1	1.00
Adenosine deaminase	93	1-1	93	ADA^1	1.00
Haptoglobin					
Velho Village	98	1	4	Hp^1	0.25
		2-1	36		
		2-2	49		
		O	9		
Novo Village	31	1-1	19	Hp^1	0.78
		2-1	7		
		2-2	3		
		O	2		
Transferrin	129	C	128	Tf^C	0.99
		CD_1	1	Tf^{D1}	<0.01
Gc	113	1-1	9		
		2-1	66	Gc^2	0.63
		2-2	38		
Ceruloplasmin[2]	125	$A_{(CAY)}B$	18	$CP^{A(CAY)}$	0.07
		B	107	CP^B	0.93
Albumin	129	A	129	Al^A	1.00

[1] Tests for D^u yielded negative results.

[2] Three samples showed what seemed to be the A pattern. If they are considered true homozygotes Cp^ACp^A, however, a significant departure from Hardy-Weinberg expectations would occur. In addition, there is incompatibility between their phenotypes and those of either children or parents. Therefore, we decided to consider these results as artifacts, excluding them from the tabulation.

ously by Mestriner et al. ('76) but are reproduced here for completeness.] The genes I^o, k, Hb^A, Gd^B, PGD^A, EsA^1, PGM_2^1, AK^1, ADA^1, all have frequencies of 1.00 or nearly so, as is expected of a South American Indian tribe with little or no post-Columbian admixture from other races. The Jk^a frequency of 0.51 and P^1 of 0.68 are also usual for this race. The finding of a transferrin CD_1 individual among the Parakanã is not unexpected since this phenotype or an unclassified CD has been observed in at least 13 other tribes, sometimes in substantial frequencies. In this instance parallel tests with a known TfD_1 serum indicated that the pattern

was indeed TfD_1 and not $TfCD_{Chi}$ as found in six other South American Indian populations.

Although the Parakanã data are typical of a racially unmixed South American Indian tribe in the above traits, the observed frequencies of EsD^1, PGM_1^1, Gc^2, Cp^B, Fy^a, Di^a, and L^M are unusual. The frequency of these traits in the Parakanã are, nevertheless, in no instance closer to Caucasian values (Race and Sanger, '75) than to the mean of South American Indian tribes (see below). The esterase D^1 frequency of 0.36 is the lowest thus far reported in any population (Ebeli-Struijk et al., '76). PGM_1^1, however, occurs with a very high prevalence (0.98; previous studies in South American Indians: 0.55–0.95). The Gc^2 value of 0.63 has only been exceeded by the Xavante frequencies of 0.67 to 0.70 (Neel et al., '64; Shreffler and Steinberg, '67). The only other instance in which the frequency of ceruloplasmin variants has exceeded 1% in Amerindians was in the Cayapo (Salzano et al., '72; Weitkamp et al., '72; Tanis et al., '73; Neel et al., '77). The variant present there is called Cayapo 1, and $A_{CAY1}B$ patterns were found in 9% of 184 members of that tribe. They also occur among the Macushi and Wapishana of the Brazilian Roraima Territory and southern Guiana, but in much lower prevalences: 0.002 and 0.006, respectively. The variant present among the Parakanã is indistinguishable electrophoretically from the Cayapo type, both being different from the CpAB pattern seen among blacks from Porto Alegre. The fact that the Cayapo and Parakanã live in adjacent territories strengthens the suggestion that we are dealing with the same variant, and that the corresponding gene, Cp^{ACAY1}, also occurs in polymorphic frequency (0.07) among the Parakanã.

As for the Duffy results, only six other South American Indian groups (Matson et al., '66c, '68b, '69; Van der Does et al., '74; Brown et al., '74), in studies where 30 or more specimens have been studied have shown exclusively Duffy (a+). The frequency of Di^a (0.39) is high, the only higher reported result on a sizable sample from an indigenous South American population being the frequency of 0.48, among the Chama of Bolivia (Matson et al., '66c). More striking is the complete absence of N positives in the MNSs system, as well as the large difference in the frequency of Hp^1 between the two Parakanã villages—the low value of 0.25 in the Velho and the more usual value of 0.78 in the Novo population.

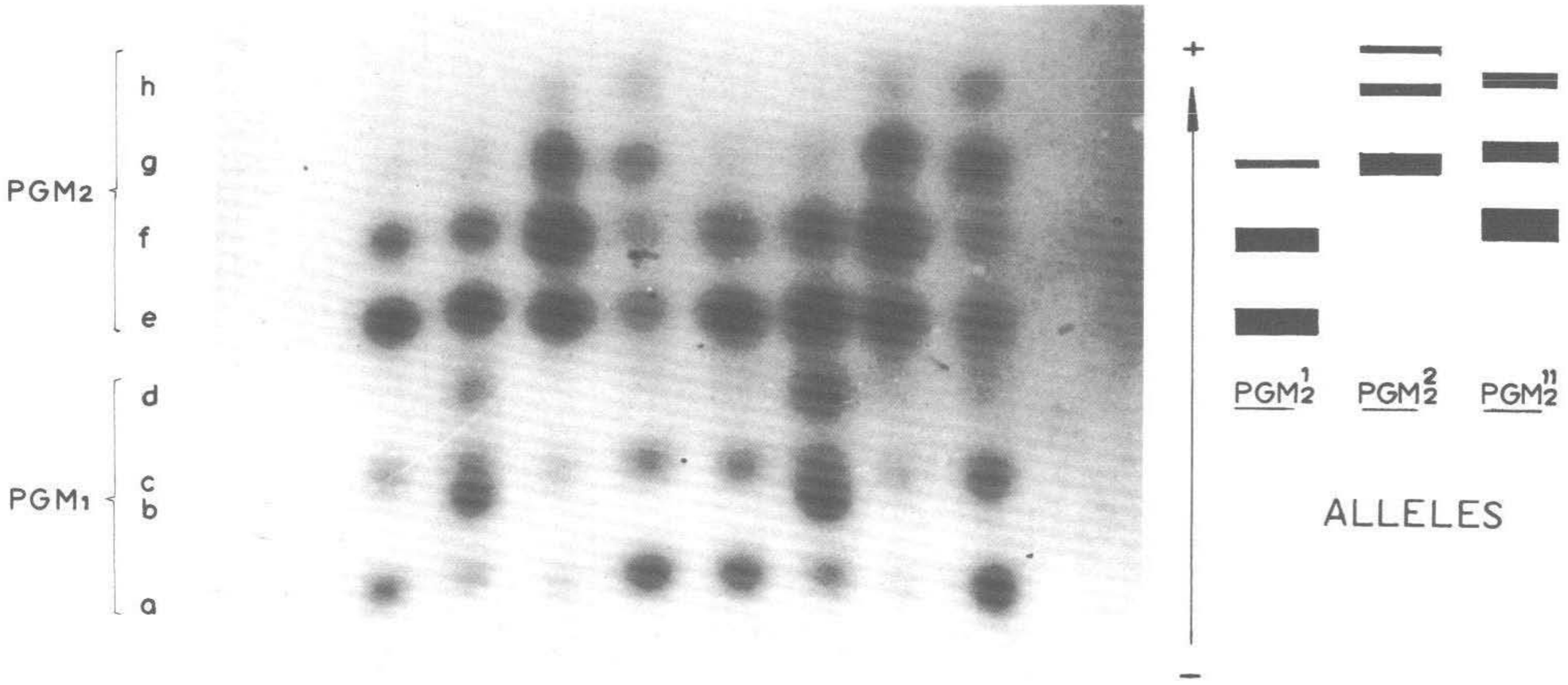
The Rh data are strange in another way. We found two Rh(D) negatives, a man and his daughter whose bloods gave positive reactions for C, c, E, and e. These tests were repeated several times, and a search for D^u yielded negative results. This is the second time that CcEe individuals have been reported among South American Indians; Geerdink et al. ('74) recorded one such instance among the Trio of Surinam, a group separated from the Parakanã by 1,000 km. These genotypes might be either *CdE/cde* ($r''r$) or *cdE/Cde* ($r''r'$). Since we have also found two *cde/cde* (*rr*) persons in this tribe and such individuals occur in at least 21 other populations of South American Indians, the genotype $r''r$ seems more probable. To explain the presence of r'', however, we must invoke one of four improbable sequences of events: that two rare intracistronic crossovers occurred between *cde* and *CDe* and *cDE;* that a suppressor of the D region product is present; that there was mutation from *CDE* to *CdE;* or that the r'' gene was introduced by admixture from Caucasians or Negroes among whom this gene is also very rare, without the persistence of other traits characteristic of these races. R^z is commonly found in other South American Indian tribes, but having postulated the presence of r'' in the Parakanã, we cannot be sure of the occurrence of R^z here. All of 37 samples tested for C^w were negative.

We have also observed a rare variant of phosphoglucomutase$_2$ in a 41-year-old man of the Velho village. Its electrophoretic pattern is compared with those found in 1-1 or 2-1 bloods in Figure 1. This uncommon type presents two bands with migration similar to those labeled *e* and *f*, but in this case *f* is stronger than *e*, unlike the patterns commonly found. In addition there are two other bands that are faster than *g* and *h* of phenotype 2-1. We interpret these findings as being the result of heterozygosis of the common PGM_2^1 with a rare, probably undescribed allele that we will call $PGM_2^{1'}$. The latter would produce three isozymes with migrations slightly faster than those of bands *f*, *g*, and *h*. The first of these could not be separated from the product f of PGM_2^1, thus giving rise to the stronger band seen in that region.

Lymphocyte data

The results of the HLA tests are presented in Table 2. The two villages are distinct with respect to HLA both in the frequencies and the representation of specific alleles. As in other genetically unmixed South American Indian tribes (Corley et al., '74; Cann et al., '74; Van der Does et al., '74; Tittor et al., '74; Layrisse et al., '76; Black et al., '76), the range of alleles represented in the Parakanã is small.

The BW16 splits could only be distinguished



PGM1	1-1	2-1	1-1	1-1	1-1	2-1	1-1	1-1
PGM2	1-1	1-1	11-1	2-1	1-1	1-1	11-1	2-1

Fig. 1. Electrophoretic pattern of phosphoglucomutase$_2$ in the unique Velho specimen. (V-1) in comparison with usual homozygous (1-1) and heterozygous (2-1) patterns. Original photograph and graphic representation.

in the specimens that were tested in the full Workshop trays. In these tests only BW39 was found. To simplify tabulation, it is presumed that the BW16's found in the other tests were also BW39. Types B5 and CW1, which have a high frequency in other tribes (Layrisse et al., '76), appear to be missing. Types B17 and CW2 were found only in one Velho child born in 1974. We believe that he represents an instance of racial mixing subsequent to initiation of regular contacts with non-Indians. All cells tested in the seventh Workshop trays showed BW6, confirming the unambiguous association with BW35, BW39, or B40 also present in the cells.

It has been possible to group the individual antigenic types into a relatively small number of recurring linkages (haplotypes). These are summarized in Table 3 and set out in genealogical array in Figures 2 and 3. Besides the unusual—,B17,CW2 haplotype, which we believe may derive from post-contact admixture, there were two other unique haplotypes, AW32,—,— and A28, B15, CW3. The mother of the carrier of AW32—,—was a member of another tribe, the Asurini. The parents of the AW28, B15, CW3 carrier are dead and unidentified. Three other linkage groups, A2,BW39,—; A2, BW35, CW4; and AW24, B15, CW3 could have arisen from other haplotypes in this set by a single crossover between the A and C loci. Such crossovers occur with a frequency of 1% per generation. One haplotype, A24, B40, CW3, was found

TABLE 2. HLA phenotypes and gene frequencies in 97 Parakanã Indians

Specificities	66 Velho donors		31 Novo donors[1]		Total
	Number positive	Gene frequency[2]	Number positive	Gene frequency[2]	Gene frequency
A2	38	0.31	6	0.10	0.246
A28	24	0.20	18	0.34	0.245
AW24	5	0.04	8	0.13	0.069
AW31	48	0.45	23	0.42	0.437
AW32	0	—	1	0.02	0.005
A Blank	0	0.01	0	—	0.005
B15	0	—	4	0.06	0.019
B17	1	0.01	0	—	0.005
BW35	51	0.51	25	0.56	0.523
BW39[3]	21	0.16	16	0.31	0.208
B40	38	0.33	3	0.05	0.244
B Blank	0	—	1	0.02	0.005
CW2	1	0.01	0	—	0.005
CW3	42	0.37	10	0.16	0.306
CW4	50	0.47	24	0.52	0.478
C Blank	1	0.16	3	0.32	0.211

[1] Includes three migrants from Pacajá, who account for the only B40 reactions.
[2] Determined by actual count of recognized haplotypes.
[3] B16 or BW39. See text.

TABLE 3. HLA haplotypes found among the Parakanã Indians

Designation	Composition	66 Velho		31 Novo		Homozygotes	
		% Phenotype	Haplotype frequency	% Phenotype	Haplotype frequency	Expected	Found
a	AW31,BW35,CW4	73	0.447	74	0.419	18.5	14
b	A28,B40,CW3	36	0.189	0	—	2.4	2
c	A28,BW39,—	—	—	51	0.307	2.8	3
d	A2,BW39,—	32	0.159	0	—	1.7	0
e	A2,BW35,CW4	3	0.015	19	0.097	0.3	0
f	AW24,BW35,CW3	9	0.045	10	0.048	0.2	0
g	A2,B40,CW3	24	0.136	0	—	1.2	2
j	AW32,—,—	0	—	3	0.016	0.0	0
k	AW24,B15,CW3	0	—	7	0.032	0.0	0
l	AW28,B15,CW3	0	—	7	0.032	0.0	0
m	AW24,B40,CW3	0	—	10	0.048	0.0	0
z	—,B17,CW2	2	0.008	0	—	0.0	0
					Total	27.1	21

only in the migrants from the Pacaja village. Two of the five remaining arrangements, A28, BW39,— and A2, B40, CW3, were found in only one village. Thus, apart from recent contributions from other groups, all the genetic information for HLA in each village could have originated with a single founder family.

Thirteen of the Velho villagers have identical AW31, BW35, CW4/A2, BW39,— constitutions, and substantial proportions of the populations share other apparently identical genotypes. Out of a total of 44 mother–child pairs for whom data are available, there are 17 instances in which child and mother are mutually HLA compatible; eight instances in which the mother would be tolerant to the fetus, but the fetus responsive to the mother; two instances in which the fetus would exhibit tolerance, but not the mother; and 17 instances in which they would be mutually incompatible. This does not diverge significantly from the ratios expected, given the mothers' constitution as observed, and assuming the probability of the fathers' contributing a specific type equal to the frequency of that type in the village.

The small total number of haplotypes means that the probability of homozygosity in the histocompatibility region is high, and 21 individuals were found with only one recognizable haplotype.

Parentage exclusions

It was possible to check the correlation of our genealogies with biological characteristics by examining the correspondence of genetic traits between children and socially identified parents (Table 4). One-fourth of the socially identified fathers and one in 14 of the socially identified mothers did not correspond to the biological parent.

Genetic drift and departures from Hardy-Weinberg equilibria

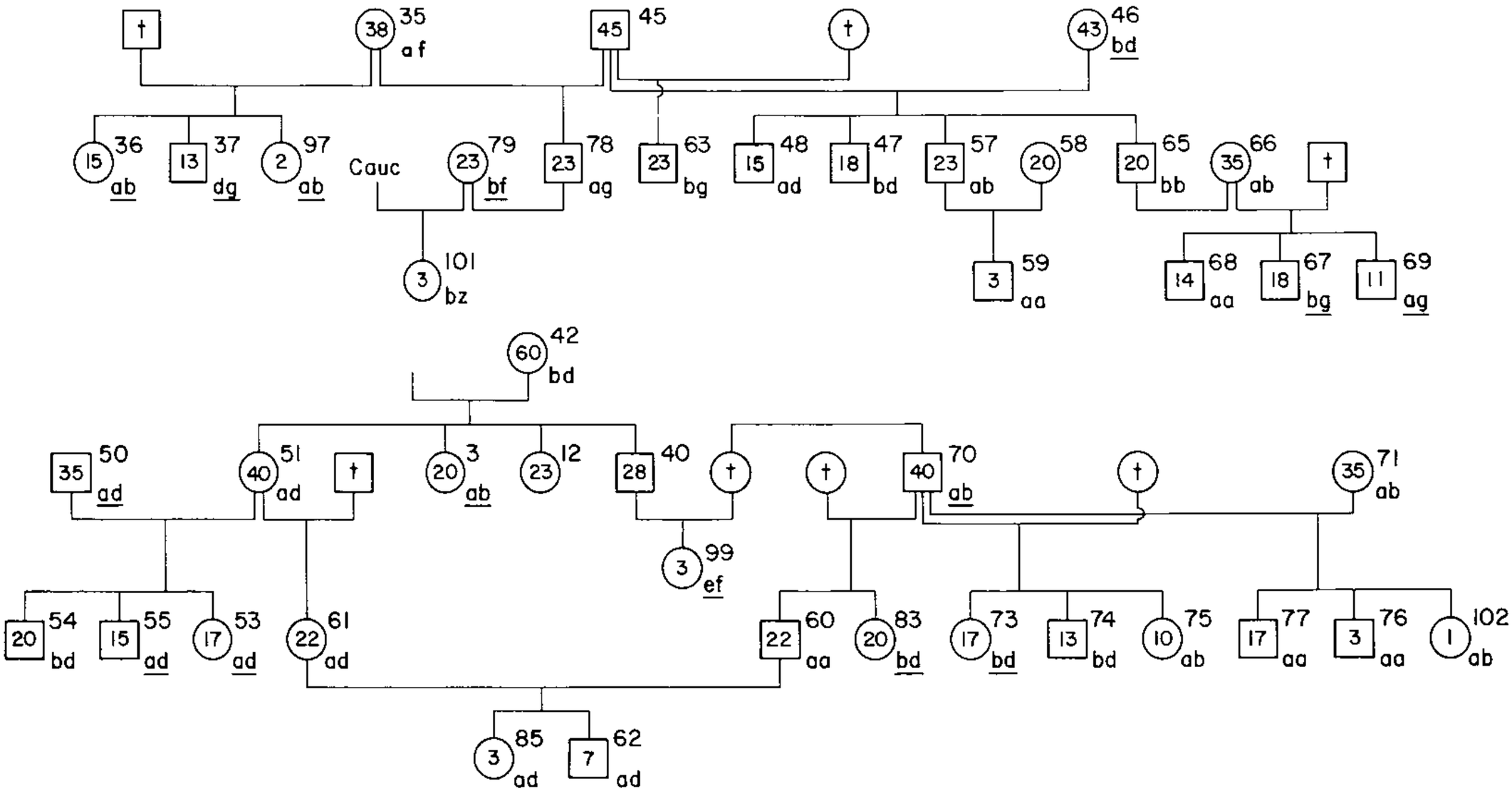
The restricted range of polymorphisms observed in the Parakanã may have been imposed on these people at several stages in their history. Only a limited variety of genes was brought to the continent by migrants over the Bering Bridge and isthmuses of Central America. Tribal formation presumably occurs by growth of groups initially segregated as villages. New villages form by fission of old along familial lines and segregate out relatively small numbers of alleles (Neel and Salzano, '67; Chagnon, '74). Finally, marriage practices, such as preferentially high reproductive rates of dominant men, and the uncle-niece pattern favored by the Parakanã enhance inbreeding within the tribe.

The usual way to measure these processes is by means of Wright's ('21, '69) F statistics. These statistics break the total into two parts: F_{ST}, the difference between separate subgroups and the total, a value that may be equated with genetic drift; and F_{IS}, the deviation in distribution of individuals within a subgroup away from that which would be predicted by Hardy-Weinberg equilibria. In this paper, however, we are concerned with only one subgroup, the Parakanã, and only the second statistic is applicable. We have chosen to examine drift by estimating, by means of the binomial theorem (Snedecor and Cochran, '77), the extent to which the Parakanã differ from the composition of the founding stock. We have approximated the characteristics of the South American Indian founders by the unweighted mean of the gene frequencies in 40 tribes for which data are available for up to 16 loci (Table 5). These data were collected from summaries by Post et al. ('68) and Tanis et al. ('73), and original papers by Brown et al. ('74), Layrisse et al. ('73a, b), Matson et al. ('66a, b, c; '68a, b), Mestriner et al. ('76), Salzano et al. ('72, '74, '78), and Van der Does et al. ('74), and Tchen et al. ('78). Overall, in the 13 biallelic systems, these 40 tribes differed from their mean 65.4% of the time when 0.05% probability is used and 53.4% of the time when 0.001% probability is taken as the dividing line. Parakanã differed from this mean in 92.3% (12 of 13) or 73.9% (10/13) of their traits, respectively, with the two probability end points. The difference between the Parakanã and other South American Indians is not due to Caucasian admixture in the Parakanã, as their values are more remote, than the other Indians, from European figures cited by Race and Sanger (1975) in nine of the 12 marker frequencies.

F_{IS} was calculated from Wright's formula, $1 - (H_i/2p_iq_i)$, in which $2p_iq_i$ is the fraction of heterozygotes expected on the basis of Hardy-Weinberg equilibrium, and H_i is the fraction of heterozygotes observed. Seven of the 11 F_{IS} systems for which this statistic could be calculated have negative signs and their means differ significantly from zero.

This negative F_{IS} value stands in sharp contrast to high coefficients of inbreeding obtained by examination of the genealogies: 0.0383 and 0.223 for the Velho and Novo villages, respectively. Since the available genealogies were almost exclusively confined to living persons, the coefficients doubtless grossly underesti-

PARAKANÃ VELHO



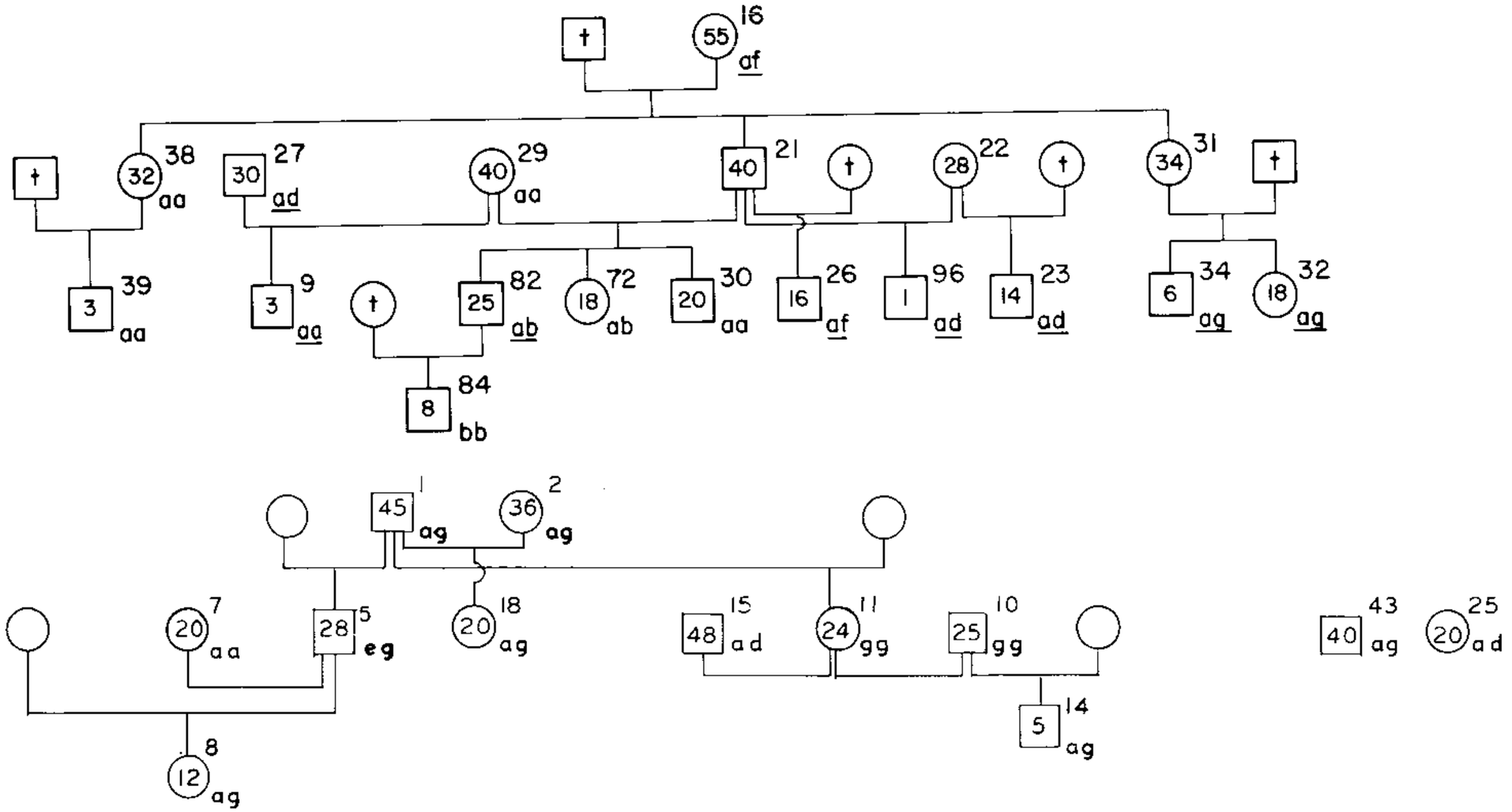


Fig. 2. Parakanã Velho HLA data in genealogical array. Letters symbolizing haplotypes correspond to designation in Table 3. Field test results are underlined. Numbers inside the symbols represent age in years; numbers outside are serial designations.

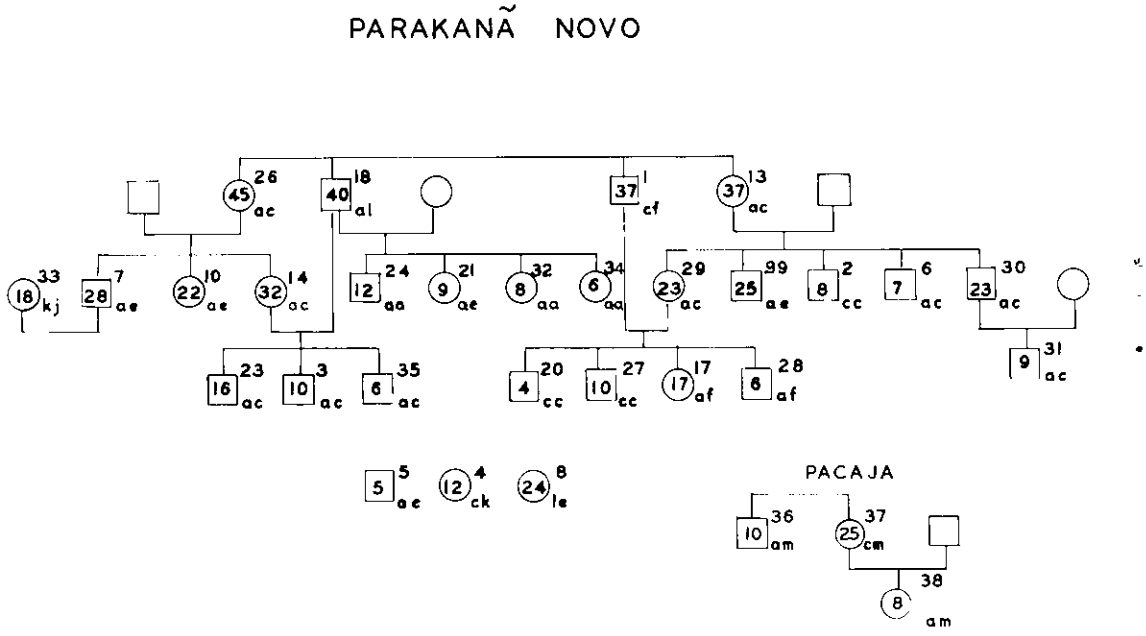


Fig. 3. Parkanã Novo HLA data in genealogical array.

TABLE 4. Parentage exclusions among the Parakanã Indians

Systems	Both parents tested		One parent tested		Number of exclusions			
	Number	Efficiency[1]	Number	Efficiency[1]	Both	Mother	Father	Undefined
HLA	18	71.7	44	26.5	0	1	1	1
Hp, Tf, Gc, Cp	38	61.7	44	9.4	1	0	9	0
Ss, P, Rh, Jk	15	91.6	28	28.7	0	2	5	0
Estimated total	Number excluded / Σ Number tested × effic			Fathers 27.3% Mothers 7.1%				

[1] Efficiency of tests in detecting traits deriving randomly within the tribe from individuals other than socially designated parent.

mate the total inbreeding. Combining data for the two tribes, there is an 8% chance that two alleles carried by an individual came, within three generations, from the same progenitor. By itself, this factor would lead to an F_{IS} of +0.116. The statistic might be reduced if the parental exclusions that we identify were selectively concentrated in the most closely consanguineous marriages; but in fact field observations lead us to believe that most maternal exclusions resulted from adoption of a child, whose mother had died, by a close surviving relative or co-wife. A like proportion of the paternal exclusions can be explained in the same way. These adoptions by close relatives would have a minimal effect on the inbreeding coefficient and on F_{IS}. The difference between the observed mean F_{IS} and zero is of marginal significance ($P = 0.05$), but the difference between this value and that expected when inbreeding is taken into account is highly significant ($p = <0.001$).

A possible explanation of the difference between the F_{IS} value expected on the basis of the genealogy and that actually found, −0.060, derives from an examination of the ages of heterozygous and homozygous individuals (Table 6). Homozygous HLA haplotypes occur less frequently in adults (>15 years) than children, and homozygous persons have a lower mean age than heterozygous individuals. The same pattern is repeated in the Ss, Rh, Gc, and Cp systems, but the probability of significance in these other systems is lower.

TABLE 5. Deviations from mean allele frequency of South American Indians and Wright's Fixation Index for the Parakanã

Alleles or loci	Frequency of 1st Allele in South American Indians*		Frequency of 1st Allele in Parakanã specimens	Probability that Parakanã do not differ from mean	F_{IS}†	χ^2†
L^M, L^N	0.73		1.00	<0.001	—	—
L^S, L^s	0.36		0.19	<0.001	+0.155	2.41
P^1, P^2	0.55		0.68	0.008	—	—
C, c	0.62		0.76	0.004	+0.011	0.01
E, e	0.39		0.12	<0.001	−0.051	0.26
Fy^a, Fy^b	0.70		1.00	<0.001	—	—
Jk^a, Jk^b	0.43		0.55	0.07	—	—
Di^a, Di^b	0.14		0.39	<0.001	—	—
EsD^1, EsD^2	0.78		0.36	<0.001	−0.108	0.43
PGM_1^1, PGM_1^2	0.87		0.98	0.001	0.0	0.0
Hp^1, Hp^2‡	0.57	Velho	0.25	<0.001		
					+0.014	.02
		Novo	0.78	0.03		
Gc^1, Gc^2	0.66		0.37	<0.001	−0.251	7.12
Cp^A, Cp^B	0.02		0.07	<0.001	−0.075	0.70
HLA^A‡					−0.140	1.90
HLA^B‡					−0.096	0.89
HLA^C‡					−0.135	1.77
Weighted average					−0.060	3.87

*Unweighted mean of data from 40 tribes.
†Wright's Fixation Index = $1 - (H_i/2p_iq_i)$, where H_i is the observed proportion of heterozygotes at locus i and p_i and q_i are the corresponding gene frequencies. χ^2 for this statistic is equal to F^2N.
‡F_{IS} is calculated separately for the two villages and combined as a weighted mean.

TABLE 6. Ages of heterozygous and homozygous Parakanã Indians

Type of heterozygote	Children <15 yrs: Number tested	Children <15 yrs: % heterozygous	Adults >15 yrs: Number tested	Adults >15 yrs: % heterozygous	Mean age in years (± SE): Heterozygotes	Mean age in years (± SE): Homozygotes
L^S, L^s	40	17	56	32	19.6 ± 2.3	17.7 ± 1.6
Rh	40	47	56	48	18.2 ± 2.1	18.2 ± 1.7
EsD^1, EsD^2	8	62	24	54	21.8 ± 2.3	20.1 ± 2.6
Hp^1, Hp^2	38	40	79	37	20.1 ± 2.1	17.8 ± 1.5
Gc^1, Gc^2	35	57	50	68	19.8 ± 1.9	15.1 ± 1.8
Cp^A, Cp^B	35	11	50	18	19.8 ± 4.1	17.7 ± 1.5
HLA	37	68	60	85*	26.8 ± 2.0	14.3 ± 2.6**
Mean		43.1		48.9	20.9 ± 2.2	17.2 ± 1.73

*$p < 0.05$.
**$p < 0.01$.

DISCUSSION

The Parakanã represent a population very little affected by the larger society with which they have only recently established regular contacts. In this sense they are an ideal subject for the study of man's primitive heritage. They live in an area where nutritional resources are ample and intergroup warfare has been the chief external source of stress (Black et al., '77; Chagnon and Hames, '79). In spite of what first appeared to be Caucasoid features, we found no clear evidence of European or African blood groups in persons born before 1974. No one cultural group can, however, represent all the variants of primitive society. The Parakanã are different for many others in favoring marriage between closely related partners. Polygamy restricts the effective size of the breeding population. Lack of bellicosity restricts broadening their gene pool by addition of captives from other populations, and genetic drift is not coun-

tered by exogamous marriage practices, as among the tribes of the Xingu Park. The differences observed between the gene frequencies of the Parakanã and the South American Indian mean may reflect these dispersive factors. Their effect has been to increase the frequency of certain usually rare genes such as Di^a and Cp^A but more generally to reduce polymorphism, so that in the other 11 systems analyzed the average fraction expected to be heterozygous has been reduced from 0.44 (or taking inbreeding into account, from 0.48) to 0.29.

Our data are unique in the small amount of heterogeneity demonstrated in the HLA system. Where thousands of different haplotypes may be postulated, only 11 were found, and four chromosomes might account for all gene sources present in one village for more than one generation. Zinkernagle and Dougherty ('77) have suggested that "alloantigen differences may be crucial in the feto-maternal relationship preventing invasion of the maternal tissue by fetal cells." Mother–child incompatibility, however, does not seem to be an important selective factor among the Parakanã, the antigenic combinations observed being those expected under the assumption of proportional probability of occurrence. Thus a hypothetical force that would favor HLA polymorphism is not operative in measurable degree in this population.

Three interrelated measurements, the negative F_{IS} values, the ratio of adults to children who are homozygous, and the difference in average age of homozygous and heterozygous persons, all indicate that Hardy-Weinberg equilibria are disturbed in the Parakanã. There are fewer homozygous individuals in any age group than would be predicted by random mating and progressively fewer homozygous individuals as age advances. This trend is individually significant for the HLA system and broadly reproduced in the averages of all systems examined. Such a pattern might result from selective migration, but migration rates to and from these villages are very low and no basis for selective migration is apparent. The pattern would also arise if persons with homozygous constitutions had lower survival potential over an extended age span. The Parakanã have been subject to an important new set of selective pressures in the increased exposure to infectious disease during recent years (Black et al., '78). To postulate a specific heterotic advantage on the basis of such a small population may seem inappropriate. However, as evidenced by the consistency with which a few HLA haplotypes recur, linkage sequences in this small population are less diverse than would be true in a larger group; the traits we have measured may simply be serving as markers for other functional loci.

In summary, the Parakanã seem to be under the influence of strong, but sometimes conflicting evolutionary forces. Their isolation and marriage practices may have favored the action of genetic drift, leading to the observed lack of heterogeneity in the HLA and other systems, and a set of unusual gene frequencies manifested both in their blood and in their physical appearance. This tendency toward homogenization is being counteracted by selection in favor of heterozygous persons, possibly manifested through resistance to infectious diseases.

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