Am J Hum Genet 32:246–257, 1980

Genetic Variability of HLA in the Dariusleut Hutterites. A Comparative Genetic Analysis of the Hutterities, the Amish, and Other Selected Caucasian Populations

K. MORGAN,[1] T. M. HOLMES,[1] J. SCHLAUT,[2] L. MARCHUK,[2] T. KOVITHAVONGS,[2] F. PAZDERKA,[2] AND J. B. DOSSETOR[2]

SUMMARY

There are three endogamous subdivisions of the Hutterite population, a North American religious isolate. These individuals live on communal farms, and residence is strictly patrilocal. We report on the distributions of *HLA-A* and *B* alleles and haplotypes in 203 married women from one subdivision – the Dariusleut – in Alberta, Canada. We demonstrate that there is significant linkage disequilibrium among a large fraction of the distinct haplotypes in the Dariusleut Hutterite data; there is a restriction in the number of distinct haplotypes present in the Dariusleut; the Hutterites and the Old Order Amish (Lancaster County, Pennsylvania) are the most genetically distant pair of populations in an ensemble of 11 Caucasian populations; and, finally, the Old Order Amish and the Hutterites are approximately as distant from the Indiana Amish as they are from the eight other Caucasian populations, which are tightly clustered in the space of gene frequencies. These results are consistent with the fact that the Amish and the Hutterites are genetic isolates with small numbers of founders. Certain haplotypes show significant linkage disequilibrium in these as well as in other Caucasian samples. Thus, some of the linkage disequilibrium antedates the formation of these Anabaptist sects.

Received May 7, 1979; revised July 6, 1979.

This work was supported by grants from the Medical Research Council of Canada, University of Alberta Hospital Special Services Research Committee, and the University of Alberta Computer Facilities and Policy Committee.

[1] Department of Genetics, University of Alberta, Edmonton, Alberta T6G 2E9, Canada.

[2] Clinical and Transplant Immunology Group, University of Alberta Hospital, Edmonton T6G 2B7.

INTRODUCTION

The evolution of multilocus systems is a major area of research in population genetics. Considerable interest has been focused on the statistical analysis [1] and evolutionary interpretation of linkage disequilibrium [2, 3]. Especially in the study of human populations, it is important to delineate the roles which history and population structure play in determining associations among alleles at different loci. Among Caucasian populations which permit an extensive demographic, social-structural, and genetic analysis are a few religious isolates; for example, the Amish and the Hutterites of North America. We studied the HLA system in the Hutterites and present an analysis of the genetic relationships among the Hutterites, the Amish, and other selected Caucasian populations. The HLA system is of general interest because of the tremendous variability at the *HLA-A* and *B* loci, the extensive diversity among human populations for allele and haplotype frequencies, and the significant linkage disequilibrium found in samples from geographically and racially diverse populations [1, 4].

The Hutterites, who live in farming colonies, comprise a religious and genetic isolate with a clearly defined hierarchical population structure. Eaton and Mayer [5], Hostetler [6], and Steinberg et al. [7] have provided a foundation for the study of the population genetics and demography of this group. Our study is concerned with a subdivision of the Hutterites—the Dariusleut—which has not previously been described in terms of its population genetics and demography. We studied a sample of individuals who reside in colonies in a particular geographical area of western Canada in order to characterize the genetic variability at the *HLA-A* and *B* loci. We chose for comparison: two other North American Caucasian isolates—two Amish "demes"; a sample of individuals of German descent living in Milwaukee, Wisconsin; a sample from the Ruhr area of Germany; and six samples from those areas of Europe which were historically important in the establishment of the Hutterites and the Amish.

THE HUTTERITE POPULATION

The Hutterites are members of an Anabaptist Christian sect who believe in communal living, pacifism, and adult baptism. Their history, culture, and social organization are well documented by Hostetler [6]. The major establishment of the Hutterites in Canada began in 1918 when they emigrated from South Dakota. Migration in the 1870s from Russia to the Dakota Territory in the United States and then to Canada was the culmination of a series of migrations to escape religious persecution. The origin of the Hutterites in the early sixteenth century was from an area which encompasses southern Germany, Austria, Switzerland, and northern Italy (formerly South Tyrol). They migrated eastward to central Czechoslovakia and Romania and then to the Ukraine. The Hutterite German dialect resembles that spoken in the province of Carinthia, Austria, and has been influenced by Slavic languages [6].

Since their arrival in North America, the Hutterites have maintained four major subdivisions (leuts)—the Dariusleut, Lehrerleut, Schmiedeleut, and Prairieleut. Only the first three groups practice communal living and constitute genetic isolates, and in this paper reference to the Hutterites is to these groups only. The Hutterites presently live on large farms, called colonies, in the western Canadian provinces and the United States border states—Minnesota, North and South Dakota, Montana, and Washington.

The Hutterite population has increased by births at a rate of approximately 4% per annum. It has been closed to immigration since the late 1800s, and there has been minimal interleut migration since the initial settlement period in the United States.

The focus of our study is the Dariusleut Hutterites living in Alberta, Canada. In 1976, there was a total of 14,240 Hutterites living in 179 colonies in Canada. In Alberta, 7,005 Hutterites were living in 89 colonies, and of these, 4,159 were Dariusleut Hutterites living in 57 colonies (Statistics Canada, personal communication, 1979).

MATERIALS AND METHODS

The Dariusleut Hutterites are comprised of nine lineages, and since 1918, colony formation has been a binary fission process (fig. 1). When a colony divides, one moiety of related families stays at the original location and the other moiety moves to a new location. An attempt is made to attain a balanced age-sex structure in the two moieties. Colony sizes vary depending on local subsistence patterns and the stage of the "branching-out" process; for example, on June 1, 1971, there were 977 individuals living in the colonies of the Stahlville and Springvale lineages (fig. 1). Colony size ranged from 45 to 110, and the mean and standard deviation (SD) were 81.4 and 18.9, respectively. Residence is strictly patrilocal; therefore, we designate the colony lineages as patrilineages.

From December, 1974, to April, 1978, blood samples were obtained from Dariusleut Hutterites by visiting 24 colonies in Alberta (indicated by asterisks in fig. 1). *HLA-A* and *B* haplotypes were assigned to 991 individuals by family analysis. Considering the hierarchical, patrilineal structure of this population, we chose 203 women married prior to June 1, 1976, as our sample for analysis. A woman can move, upon marriage, to a different patrilineage, and thus the subsample comprised of Hutterite wives should be more representative of the genetic variability in the Dariusleut Hutterites.

HLA antigens were typed by the microlymphocytotoxicity test [11]. During the study period, a series of different sera were used to type for antigens; therefore, not all individuals were subtyped for the newer specificities: Aw23, Aw24, A25, A26, Bw38, and Bw39, or typed separately for Aw30 and Aw31. Nomenclature from the Seventh International Histocompatibility Testing Workshop is used [12].

STATISTICAL METHODS

We chose for analysis a set of HLA-A and B antigens which were typed in all of the 11 samples selected for comparative analysis. This included for HLA-A: A1, A2, A3, A9, A10, A11, A28, A29, Aw30 and Aw31 combined, and Aw32; and for HLA-B: B5, B7, B8, B12, B13, B14, B15, B17, B18, B27, Bw35, and B40. For some samples, the frequency of A9 was taken as the sum of the frequencies of Aw23 and Aw24; the frequency of A10, as the sum of A25 and A26; and the frequency of Aw30/Aw31, as the sum of Aw30 and Aw31. The frequencies of other alleles at each locus were pooled into one class. The frequency of this "allele" was calculated as one minus the sum of the alleles specified above. For the Old Order Amish sample, the frequencies of A29, Aw30/Aw31, and Aw32 were assigned to be zero since the frequency of the broad specificity antigen Aw19 was zero.

The genetic distance measure we used is Edwards' [13] measure, E, which is a modification of the method of Bhattacharyya developed and used by Cavalli-Sforza and Edwards [14]. Edwards' method is a stereographic projection of the spherical surface of the angular transformation of gene frequencies onto the tangent plane. This projection provides a representation of the populations in a Euclidean space. The matrix of squared genetic distances was transformed to a centroid-adjusted similarity matrix, and the principal coordinates were obtained according to Gower's [15, 16] procedure. *Principal coordinates analysis* is a form of *principal components analysis* concerned with the representation of a multivariate sample of size n as points P_1, P_2, . . . , P_n in a Euclidean space. When all the distances between n points are known, this

method finds their coordinates referred to principal axes. A primary goal of the principal coordinates analysis is to achieve a low-dimensional representation of the original gene frequency variability.

A least-squares solution for fitting a matrix of principal coordinates of the *HLA-A* locus to that of the *HLA-B* locus is obtained by applying the procedure of Schönemann and Carroll [17]. This procedure involves only rigid motions, that is, an orthogonal rotation, a translation, and a central

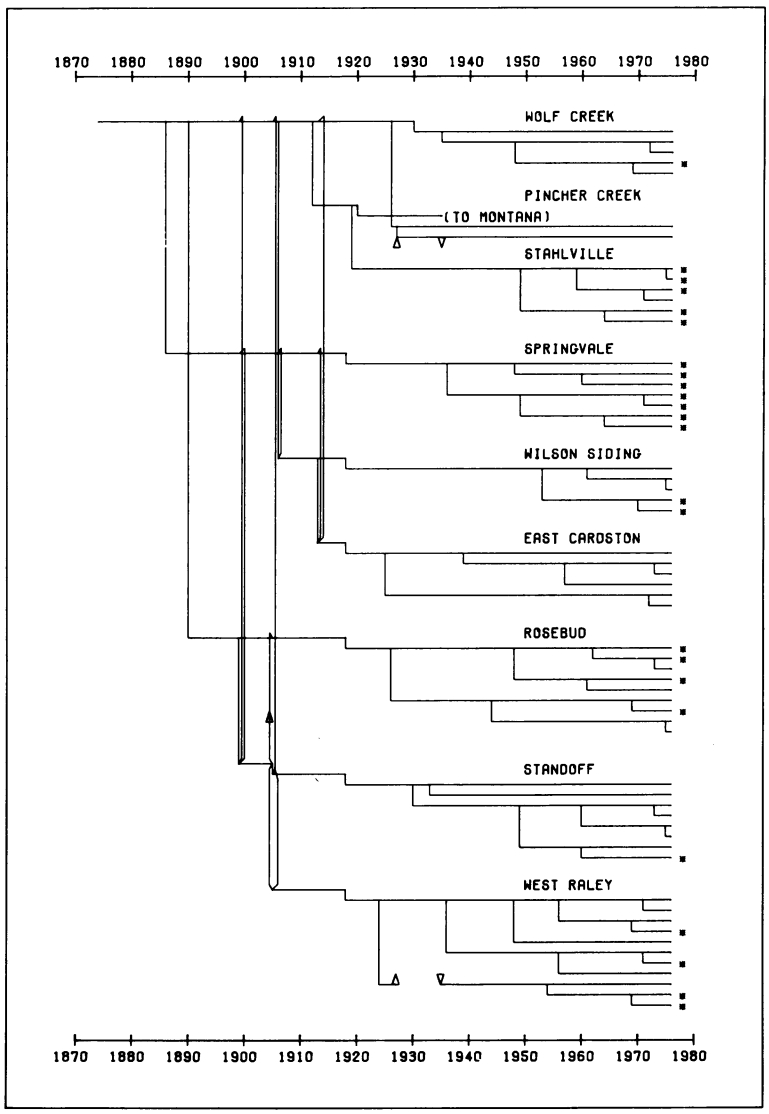

FIG. 1.—History of patrilineages of Dariusleut Hutterite colonies, 1874–1976. After 1930, only those colonies located in Alberta, Canada, are shown. Vertical displacement of a colony path represents relocation of colony. A colony of the West Raley lineage fused with a colony of the Pincher Creek lineage in 1927; some of the families re-established the former colony in 1935 (denoted by *arrowheads*). Blood samples for HLA analysis were obtained during 1974–1978 from those colonies (denoted by *asterisks*). [6, 8, 9, 10.]

dilation. The application of this procedure in population genetic analysis has been discussed by Lalouel [18]. In the present context of genetic distance analysis, such displacements leave invariant the relative magnitudes of the interpoint distances. To assess the fit of a low-dimensional representation of the *HLA-A* locus to that of the *HLA-B* locus, we computed the symmetric and norm-invariant measure, S, which is (0,1)-bounded [19].

The linkage disequilibrium parameter, Δ, for each combination of eight *HLA-A* and 13 *B* alleles was calculated by subtracting the product of the appropriate pair of allele frequencies from the observed haplotype frequency. The statistical significance of linkage disequilibrium was tested for each pair of alleles in turn, using the information from all $2N = 406$ observations, as a one degree of freedom (df) X^2 statistic. The critical value of chi-square at the nominal significance level, $\alpha = .001$, was adjusted for the number of comparisons of interest. Haplotypes in which one of the alleles was unidentified were not included in the number of comparisons.

RESULTS

The *HLA-A* and *B* allele frequencies obtained by gene counting are given in table 1. The fit of the observed genotypic distribution to the assumption of Hardy-Weinberg equilibrium is satisfactory for each of the loci (*HLA-A* locus: $X^2 = 25.70$, 28 df; *HLA-B* locus: $X^2 = 78.27$, 78 df). The numbers and proportions of homozygous and heterozygous women in the sample are given in table 2. It is clear that homozygosity at one locus is not independent of homozygosity at the other locus within individuals. Thus, for example, among individuals who are homozygous at the *A* locus, 25.6% are also homozygous at the *B* locus; while among individuals who are heterozygous at the *A* locus, only 4.9% are homozygous at the *B* locus. Furthermore, the higher heterozygosity observed at the *B* locus compared to that at the *A* locus, 91.1% vs. 80.8%, is partly a consequence of the more even distribution and the greater number of *B* alleles (table 1). The maximum heterozygosity at a k-allele locus, $1 - (1/k)$, occurs when each allele is equally frequent. The ratio of the observed heterozygosities at the *HLA-A* and *B* loci to their maximum possible values are .923 and .987, respectively.

Information on the newer HLA specificities is available for individuals in the sample of 991 who were specifically subtyped or could be assigned subtypes by family analysis. For the antigen A9, only Aw24 was detected; for A10, 22% were A25 and

TABLE 1

HLA-A AND *B* ALLELE FREQUENCIES IN 203 DARIUSLEUT HUTTERITE MARRIED WOMEN

HLA-A	Frequency	*HLA-B*	Frequency
A1	.0911	*B5*	.1429
A2	.3325	*B7*	.0813
A3	.2488	*B8*	.1429
A9	.0517	*B12*	.0837
A10	.1355	*B13*	.0025
Aw30/w31	.0714	*B15*	.1232
Aw32	.0665	*Bw16*	.0764
Blank A	.0025	*B17*	.0493
		B18	.1256
		Bw22	.0074
		B27	.0320
		Bw35	.0961
		B40	.0369

TABLE 2

HLA HETEROZYGOSITY AND HOMOZYGOSITY IN DARIUSLEUT HUTTERITE MARRIED WOMEN

	HLA-B heterozygous	*HLA-B* homozygous	Total
HLA-A heterozygous	156 (76.8%)	8 (3.9%)	164 (80.8%)
HLA-A homozygous	29 (14.3%)	10 (4.9%)	39 (19.2%)
Total	185 (91.1%)	18 (8.9%)	203

78% were A26. Where the distinction could be made between Aw30 and Aw31, only Aw31 was detected; and for Bw16, only Bw38 was detected.

Samples from 11 populations comprise the ensemble for comparative analysis. In addition to the Hutterites, the three other North American populations are: two samples of the Amish, an Anabaptist sect which originated in Switzerland and southern Germany [20, 21], and a sample of Milwaukee residents [22] who are of German descent from families who lived in some of the areas which were important in the history of the Hutterites and the Amish. The seven European populations are: three German samples — from Munich, southwest Germany, and the Ruhr area [23, 24, 25]; two samples from Czechoslovakia — one from the District of Olomouc in central Moravia and the other mainly from the city of Bratislava in the province of Slovakia [26, 27]; one sample from Vienna, Austria [28]; and one from Geneva, Switzerland [29]. Except for the Ruhr area sample, the European samples are from areas which are of historical significance for the Hutterite and/or Amish founding populations. The Ruhr area sample, which includes individuals from Essen, was chosen because it has been shown to be centrally located in genetic distance analysis of 61 European populations [29].

The average genetic distance between each pair of samples is given in table 3. Principal coordinates analyses were carried out on the squared distances for the *HLA-A*

TABLE 3

PAIRWISE GENETIC DISTANCES, E, FOR 11 CAUCASIAN POPULATIONS BASED ON *HLA-A* AND *B* ALLELE FREQUENCIES

Samples	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
(1) Dariusleut Hutterites	.203	.163	.149	.148	.139	.137	.133	.130	.125	.122
(2) Old Order Amish [20]	...	.148	.130	.121	.132	.138	.123	.136	.132	.150
(3) Indiana Amish [21]	...	...	.123	.097	.078	.087	.085	.072	.079	.084
(4) Bratislava, Czechoslovakia [27]	...	...	...	.054	.065	.058	.065	.072	.072	.075
(5) Munich, Germany [23]	...	...	...	...	.044	.041	.031	.054	.047	.061
(6) Southwest Germany [24]	...	...	...	...	...	.035	.034	.041	.041	.046
(7) Olomouc, Czechoslovakia [26]	...	...	...	...	...	...	.037	.043	.040	.044
(8) Ruhr, Germany [25]	...	...	...	...	...	...	...	.046	.038	.052
(9) Geneva, Switzerland [29]	...	...	...	...	...	...	...	...	.040	.026
(10) Milwaukee Germans [22]	...	...	...	...	...	...	...	...	...	.045
(11) Vienna, Austria [28]	...	...	...	...	...	...	...	...	...	...

NOTE. — Data for samples are from references given.

and *B* loci, separately and together. The relative amounts of the genetic variation attributable to the first three principal axes are given in table 4. In figure 2, the 11 populations are plotted on the first three principal coordinate axes, which together account for 89% of the total genetic dispersion for both loci. Two of the three religious isolates, the Hutterites and the Old Order Amish, are relatively very distant from each other, and they appear to be about equally distant from the tightly clustered non-isolate populations. The Indiana Amish are closer to the Caucasian cluster than to the Hutterites or the Old Order Amish.

The distribution of haplotypes of the sample of Hutterite wives is given in table 5. With respect to the antigens in table 1, 28 distinct haplotypes are observed. The haplotype frequency, rank order, linkage disequilibrium parameter (Δ), and X^2 value are presented in table 6 for those haplotypes showing significant linkage disequilibrium ($P < .001$). Three haplotypes, *A2,B18*; *A3,B8*; and *A2,Bw35*, were not observed, and these deficiences appear to be significant.

DISCUSSION

The Hutterites comprise a genetic isolate: its three subdivisions were established by 443 individuals [5]. The number of independent genomes for the Schmiedeleut and Lehrerleut has been estimated to be not more than 158 [7].

Our sample of Dariusleut Hutterites was obtained by visiting 24 colonies located in Alberta, and, in general, we sampled families. Since the total sample of 991 Dariusleut individuals was not obtained randomly among all colonies, we have chosen to use the subsample of married women as a representative sample of the genetic diversity in the Dariusleut Hutterites. This should be a valid approach because all of the nine patrilineages shown in figure 1 are represented among the 203 married women; 57% of these marriages were exogamous for patrilineage. This is a relatively large migration rate among lineages, almost 30% in each generation. Regarding the lineage endogamous marriages, in 80% either the wife was born in the same colony as her husband or they resided in the same colony prior to marriage. Thus, when a Dariusleut woman moves to her husband's colony upon marriage, the migration is, in most instances, to another patrilineage.

As shown in table 4, the genetic variation among the 11 Caucasian samples can be satisfactorily represented by a Euclidean space of three dimensions. Furthermore, the representations for the two *HLA* loci, *A* and *B*, are very similar. The fit of these two

TABLE 4

PROPORTION OF VARIATION ASCRIBABLE TO THE FIRST THREE PRINCIPAL AXES IN PRINCIPAL COORDINATES ANALYSES OF THE HLA SYSTEM

	PROPORTION OF TOTAL DISPERSION			
LOCUS	Axis 1	Axis 2	Axis 3	Total of axes 1, 2, and 3
HLA-A	.525	.243	.172	.941
HLA-B	.440	.252	.180	.873
HLA-A and *B*	.467	.250	.171	.889

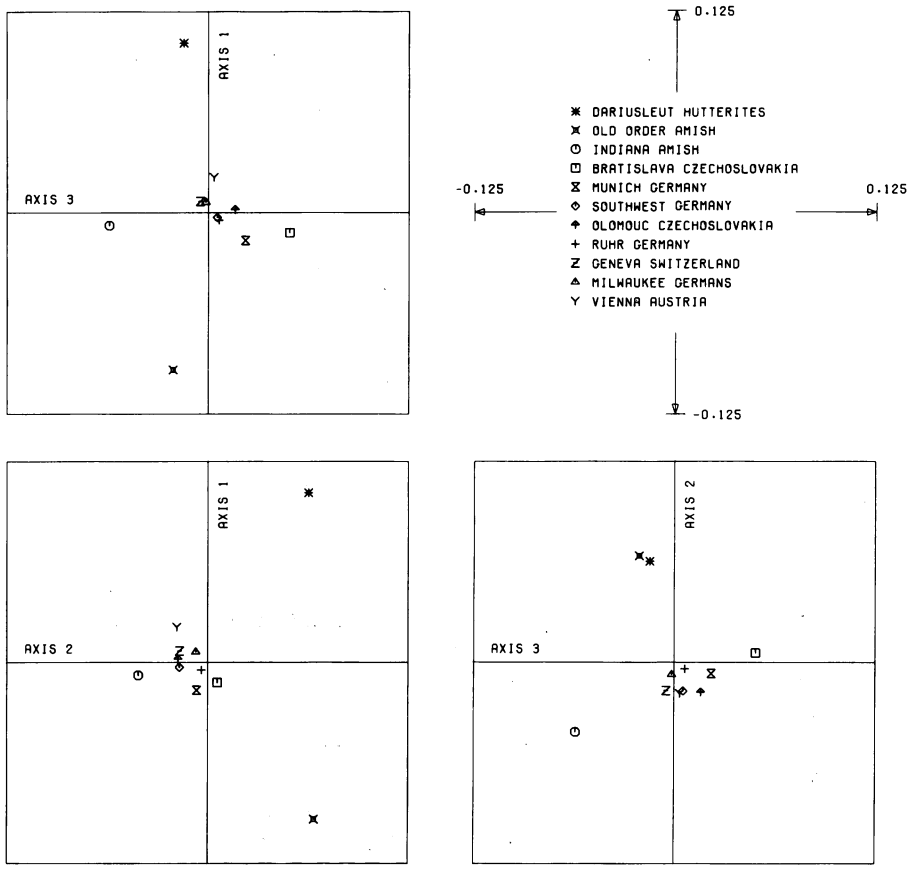

FIG. 2.—Location of 11 Caucasian samples with respect to the first three axes of principal coordinates analysis of allele frequencies of *HLA-A* and *B* loci combined. Proportion of total genetic dispersion accounted for by each axis is: *Axis 1*, .47; *Axis 2*, .25; *Axis 3*, .17.

representations to each other can be expressed as the squared correlation between the population coordinates referred to their respective first three principal axes. The value of the squared correlation is .87 using $1-S$ as the goodness of fit measure.

Comparison of gene frequencies among the ensemble of samples from selected Caucasian populations demonstrates the consequences of founder effects and random genetic drift. The samples from the three genetic isolates—the Indiana Amish, the Old Order Amish, and the Hutterites—can be distinguished from the samples of the eight other Caucasian populations by genetic distance analysis. The sample from the Ruhr area is at the center of the ensemble; as shown by Ryder et al. [29], it is also the closest among 61 European samples. Furthermore, the three isolates are widely separated from each other (fig. 2). However, the Indiana Amish are closer to the tight cluster of the eight other Caucasian samples. The two Amish samples are considered to be separate genetic isolates [30]. Assuming that these results for the *HLA-A* and *B* loci are representative of the genetic divergence of these three isolates, we conclude that the

TABLE 5

DISTRIBUTION OF HLA HAPLOTYPES IN 203 DARIUSLEUT HUTTERITE MARRIED WOMEN

	HLA-A								
HLA-B	*A1*	*A2*	*A3*	*A9*	*A10*	*Aw30/31*	*Aw32*	*Blank*	Total
B5	0	21	2	11	0	23	0	1	58
B7	0	5	22	2	0	4	0	0	33
B8	18	32	0	8	0	0	0	0	58
B12	0	34	0	0	0	0	0	0	34
B13	0	0	1	0	0	0	0	0	1
B15	0	28	0	0	1	0	21	0	50
Bw16	0	0	0	0	29	2	0	0	31
B17	19	0	1	0	0	0	0	0	20
B18	0	0	51	0	0	0	0	0	51
Bw22	0	0	0	0	3	0	0	0	3
B27	0	0	0	0	13	0	0	0	13
Bw35	0	0	24	0	9	0	6	0	39
B40	0	15	0	0	0	0	0	0	15
Total	37	135	101	21	55	29	27	1	406

numbers of founders were smaller and subsequent genetic isolation more complete for both the Dariusleut Hutterites and the Old Order Amish than for the Indiana Amish.

A number of antigens which are present in Caucasian populations were not observed even in our larger sample of 991 individuals; these are: A11, A28, A29, B14, and Bw21. However, in the one Lehrerleut colony that we visited, Bw21 was present, suggesting that within the Hutterite population, the three major subdivisions have diverged genetically as well.

Among the 203 married women, there are 28 distinct haplotypes with respect to the alleles listed in table 1. In the entire sample of 991, this number is increased to 41. In a sample of 102 "unrelated" individuals from the Indiana Amish, 59 distinct haplotypes

TABLE 6

HAPLOTYPES SHOWING LINKAGE DISEQUILIBRIUM IN THE DARIUSLEUT HUTTERITES, SIGNIFICANT AT $P < .001$

Haplotype	Δ	X^2	Frequency	Rank order
A1, B17	.0423	187.35	.0468	11
A10, Bw16	.0611	183.42	.0714	4
A3, B18	.0944	176.14	.1256	1
Aw32, B15	.0435	114.78	.0517	9.5
Aw30/w31, B5	.0464	107.84	.0567	7
A10, B27	.0277	85.71	.0320	14
A2, B12	.0559	74.49	.0837	2
A1, B8	.0313	39.26	.0443	12
A3, B7	.0340	33.57	.0542	8
A2, B40	.0247	31.27	.0369	13
A3, Bw35	.0352	31.03	.0591	6
A2, B18	−.0418	29.06	.0	···
A9, B5	.0197	26.25	.0271	15
A3, B8	−.0355	22.41	.0	···
A2, Bw35	−.0319	21.49	.0	···

were observed [21]. (Comparison is not made with the Old Order Amish because 35% of the observed haplotypes involved an unidentified allele; however, there is a minimum of 28 distinct haplotypes [20].) To examine the amount of restriction in the number of distinct haplotypes due to finite sampling, we utilized a simulation of a sample drawn from a multinomial distribution. The expected frequency of each haplotype was set equal to the product of the frequencies of the appropriate pair of alleles. For the Hutterite data of table 1, the mean and SD of the number of distinct haplotypes in 1,000 random samples of $2N = 406$ are 74.5 and 2.7, respectively, with a range of 65 to 83 distinct haplotypes. A comparable simulation for the Indiana Amish data ($2N = 204$) gave a mean and SD of 72.0 and 4.1, respectively, and a range of 56 to 87 distinct haplotypes. Thus in both these isolates, there is restriction of the number of distinct haplotypes. There is a qualitative correspondence between the number of distinct haplotypes and the relative "effective size" of the populations, as indicated by the number of unique surnames. We have found nine surnames among contemporary Dariusleut males, whereas there are 65 names among contemporary Indiana Amish heads of families [21]. Although the observed number of distinct haplotypes in the Amish fell within the range of the 1,000 sample simulation, only two out of 1,000 samples had as few or fewer distinct haplotypes. The small number of distinct haplotypes in the Hutterites is unlikely to have occurred by chance in random samples from a large population in equilibrium under multinomial sampling of haplotypes.

Estimation and hypothesis testing, appropriate for small samples, of the several components of linkage disequilibrium is not undertaken here. However, the analysis presented of linkage disequilibrium in the Hutterite sample (table 6) is an approximation to the test of the null hypothesis that non-allelic genes are associated at random within gametes or that the sum of the two components of linkage disequilibrium, between and within individuals, is equal to zero [31]. If there are factors that lead to non-random union of gametes in the Hutterite population, for example, non-random mating between genetically divergent patrilineages, they will contribute to both the within and between individual components of linkage disequilibrium. For many of the haplotypes, there appears to be significant linkage disequilibrium in the Hutterites. In the Hutterite sample, alleles at *HLA-A* and *B* appear to be in significant linkage disequilibrium for 12 of the 28 distinct haplotypes observed (table 6). For comparison, we identically computed the statistical significance ($P < .001$) of the value of the linkage disequilibrium parameter in four of the other samples: the Indiana Amish, the Old Order Amish, southwest Germans, and Viennese. Of the 12 haplotypes which show significant linkage disequilibrium in the Dariusleut Hutterites and were observed in the sample, three also show significant linkage disequilibrium in at least three of the other four samples: *A1,B8*; *A3,B7*; and *A10,Bw16*. The haplotypes *A1,B8* and *A3,B7* are common in North American and European Caucasians and show significant positive linkage disequilibria [1]. Therefore, not only is the association between certain *HLA-A* and *B* alleles in the same direction in Hutterites as in other Caucasian populations, but it can be large even in outbred Caucasian populations. For example, correlation coefficients between *A1* and *B8* are .549, .547, 1.0, .609, and .311 in southwest Germans, Viennese, Old Order Amish, Indiana Amish, and Dariusleut wives, respectively. For *A3* and *B7*, the corresponding correlation coefficients are:

.266, .301, .634, .222 (not significant), and .288; and for *A10* and *Bw16*: .192, .201, (not tested in the Old Order Amish), .496, and .672. These observations suggest that some of the associations between alleles at the *HLA-A* and *B* loci antedate the founding of the Hutterites, and perhaps the other Anabaptist sects as well, and there has not been sufficient time for recombination to reduce the linkage disequilibrium to negligible values.

ACKNOWLEDGMENTS

We are indebted to the Hutterites for their participation and thank them for their generous hospitality. Rev. J. K. Wipf clarified particular historical events of colony formation in the Dariusleut Hutterites, which we have incorporated in the diagram of patrilineages. We acknowledge the assistance in the laboratory or field of H. Acton, C. Falcon, S. B. Fowlow, V. Lao, G. M. Lathrop, G. Nicks, D. Ostertag, V. Pazderka, S. Saidman, and S. Shivji; and discussions with C. Strobeck.

REFERENCES

1. PICKBOURNE P, PIAZZA A, BODMER WF: Population analysis, in *Histocompatibility Testing 1977*, edited by BODMER WF, BATCHELOR JR, BODMER JG, FESTENSTEIN H, MORRIS PJ, Copenhagen, Munksgaard, 1978, pp 259–278
2. THOMSON G, BODMER WF, BODMER J: The HL-A system as a model for studying the interaction between selection, migration, and linkage, in *Population Genetics and Ecology*, edited by KARLIN S, NEVO E, New York, Academic Press, 1976, pp 465–498
3. DEGOS L, DAUSSET J: Human migrations and linkage disequilibrium of HL-A system. *Immunogenetics* 3:195–210, 1974
4. BODMER J, BODMER WF: Population genetics of the HL-A system. A summary of the data from the Fifth International Histocompatibility Testing Workshop. *Isr J Med Sci* 9:1257–1268, 1973
5. EATON JW, MAYER AJ: The social biology of very high fertility among the Hutterites. The demography of a unique population. *Hum Biol* 25:206–264, 1953
6. HOSTETLER JA: *Hutterite Society*. Baltimore, Johns Hopkins University Press, 1974
7. STEINBERG AG, BLEIBTREU K, KURCZYNSKI TW, MARTIN AO, KURCZYNSKI EM: Genetic studies on an inbred human isolate, in *Proceedings of the Third International Congress of Human Genetics*, edited by CROW JF, NEEL JV, Baltimore, Johns Hopkins University Press, 1967, pp 267–289
8. HOSTETLER JA: *Education and Marginality in the Communal Society of the Hutterites*. Research report, University Park, Pennsylvania State University, 1965
9. ALBERTA SPECIAL ADVISORY COMMITTEE ON COMMUNAL PROPERTY AND LAND USE: *A Report to the Minister of Municipal Affairs, October 1975*. Province of Alberta, Queen's Printer, 1975
10. ALBERTA SELECT COMMITTEE OF THE ASSEMBLY (COMMUNAL PROPERTY): *Report on Communal Property, 1972*. Province of Alberta, Queen's Printer, 1972
11. MITTAL KK, MICKEY MR, SINGAL DP, TERASAKI PI: Serotyping for homotransplantation. XVIII. Refinement of microdroplet lymphocyte cytotoxicity test. *Transplantation* 6:913–927, 1968
12. BODMER WF, BATCHELOR JR, BODMER JG, FESTENSTEIN H, MORRIS PJ, EDS.: *Histocompatibility Testing 1977*. Copenhagen, Munksgaard, 1978, pp 14–20
13. EDWARDS AWF: Distances between populations on the basis of gene frequencies. *Biometrics* 27:873–881, 1971
14. EDWARDS AWF, CAVALLI-SFORZA LL: Affinity as revealed by differences in gene frequencies, in *The Assessment of Population Affinities in Man*, edited by WEINER JS, HUIZINGA J, Oxford, Clarendon Press, 1972, pp 37–47

15. GOWER JC: Some distance properties of latent root and vector methods used in multivariate analysis. *Biometrika* 53:325–338, 1966
16. GOWER JC: Measures of taxonomic distance and their analysis, in *The Assessment of Population Affinities in Man*, edited by WEINER JS, HUIZINGA J, Oxford, Clarendon Press, 1972, pp 1–24
17. SCHÖNEMANN PH, CARROLL RM: Fitting one matrix to another under choice of a central dilation and a rigid motion. *Psychometrika* 35:245–255, 1970
18. LALOUEL JM: Topology of population structure, in *Genetic Structure of Populations*, edited by MORTON NE, Honolulu, University Press of Hawaii, 1973, pp 139–152
19. LINGOES JC, SCHÖNEMANN PH: Alternative measures of fit for the Schönemann-Carroll matrix fitting algorithm. *Psychometrika* 39:423–427, 1974
20. WARD FE, BIAS WB, REISNER EG, AMOS DB: HL-A specificities among Old Order Amish—a genetic isolate, in *Histocompatibility Testing 1972*, edited by DAUSSET J, COLOMBANI J, Copenhagen, Munksgaard. 1973, pp 93–98
21. KOSTYU D, AMOS DB, HARRIS S, ET AL.: HL-A antigens of the Indiana Amish. I. General description of frequent haplotypes and report of the mixed lymphocyte reactions of an HL-A recombinant. *Tissue Antigens* 4:415–418, 1974
22. STEVENSON JC, DUQUESNOY RJ: Distribution of HLA antigens in Polish and German populations in Milwaukee, Wisconsin. *Am J Phys Anthropol* 50:19–22, 1979
23. ALBERT ED, SCHOLZ S, ROSENTHAL I, BALTIN H, BERTRAMS J: Study of the HL-A system in the Turkish and German populations, in *Histocompatibility Testing 1972*, edited by DAUSSET J, COLOMBANI J, Copenhagen, Munksgaard, 1973. pp 147–152
24. BENDER K, MAYEROVÁ A, FRANK R, HILLER C, WIENKER T: Haplotype analysis of the linkage group HLA-A:HLA-B:Bf and its bearing on the interpretation of linkage disequilibrium. *Hum Genet* 36:191–196, 1977
25. BERTRAMS J, THRAENHART O, LUBOLDT W, KUWERT E: Histokompatibilitäts-(HL-A-) Antigene bei 1000 Blutspendern Ein Beitrag zum Aufbau einer Thrombozyten-, Leukozyten- und Knochenmark-Spenderbank. *Z Immunitaetsforsch Immunobiol* [*Suppl*] 148:73–91, 1974
26. LENHART K, BÁRTOVÁ A, LENHARTOVÁ E: HLA genetic structure of population in the District of Olomouc (Czechoslovakia). *Tissue Antigens* 9:220–222, 1977
27. NYULASSY S, HIRSCHOVÁ V, BUC M, SILVÁNOVÁ E, ŠTEFANOVIČ J: Sledovanie HLA systému v slovenskej populácii. Frekvencia antigénov A, B a C lokusu. *Bratisl Lek Listy* 68:436–444, 1977
28. MAYR WR: HLA-A,B,C gene and haplotype frequencies in Vienna. An analysis of family data. *Hum Genet* 37:41–48, 1977
29. RYDER LP, ANDERSEN E, SVEJGAARD A: An HLA map of Europe. *Hum Hered* 28:171–200, 1978
30. MCKUSICK VA, HOSTETLER JA, EGELAND JA: Genetic studies of the Amish. Background and potentialities. *Bull Johns Hopkins Hospital* 115:203–222, 1964 (Reprinted in *Medical Genetic Studies of the Amish*, edited by MCKUSICK VA, Baltimore, The Johns Hopkins University Press, 1978, pp 3–22)
31. COCKERHAM CC, WEIR BS: Digenic descent measures for finite populations. *Genet Res* 30:121–147, 1977