Genetic Structure of Populations in Western Tyrol

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Abstract ABO, MNSs, and RH blood groups of 920 indigenous inhabitants of two western Austrian mountain valleys were identified, and frequencies of 17 genes and haplotypes were estimated. F_{ST} coefficients between the six larger villages were computed and served as the basis for dendrograms by average linkage, a principal components analysis, and a nonlinear map that includes European groups in addition to the Tyrolean population. The genetic distances between the Tyrolean villages are somewhat larger than those among Appenine villages. The two most accessible villages are closest to the neighboring European groups, whereas the more remote villages appear more distant to these. Nevertheless, the gene frequencies are typical of central European populations.

Comparatively little is known about genetic variation in people of the western Alpine provinces of Austria. Frequencies of ABO types are known for the population of Innsbruck (Mourant et al. 1976), presumably from blood donors and army recruits. Holzer (1936) reported frequencies of ABO blood groups from the Tyrol, and Bernhart (1942) reported frequencies from Tyrol and the neighboring province of Vorarlberg. Böhme et al. (1983) published PI gene frequencies of the Tyrolean population. Frequencies of blood groups and other genetic markers from northern Italy and Switzerland (Morton et al. 1968; Zanardi et al. 1977) and Germany and eastern Austria are available from the literature (Mourant et al. 1976). Detailed studies of microgeographic genetic variation in Italy are available (Cavalli-Sforza and Feldman 1990).

Important traffic routes traverse western Tyrol, and three populations settled there in historic times: the original Raeto-Roman-speaking inhabitants; early Middle Ages Bavarian groups, who migrated westward up through the Inn valley; and Alemanian people who infiltrated from the north into western Tyrol across the northern Alps (Fernpass).

Sauser (1938) investigated the anthropometry of the Ötz valley in the western Tyrol using measures of the then-living population and of skeletal

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Human Biology, December 1996, v. 68, no. 6, pp. 915–927.

Table 1. Sample sizes

Locality	*Region*	*n*
Ötz	1	218
Umhausen	2	145
Längenfeld	3	121
Sölden	4	100
Lower Pitz valley	5	226
Upper Pitz valley	6	110
Total		920

remains, but Sauser refrained from genetic interpretation. To investigate possible changes in anthropometric measures, Mager (1980) performed a new anthropometric survey in 1973–1974 on the population of the Ötz valley. In Italy several studies deal with genetic variation between valleys and villages, but no such studies are available from the Austrian Alps. To increase our knowledge of microgeographic genetic variation in the western Austrian regions, we have supplemented the anthropometric investigation with a blood group survey. However, this survey was extended to the neighboring valley of Pitz, which runs parallel to the Ötz valley. A preliminary report on both the anthropometric and the blood group investigations was published by Mager and Janetschek (1986). Here, we present an analysis of blood group frequencies and integrate our results with data from other European populations.

Materials and Methods

Altogether 920 indigenous individuals participated in the survey. They represented 16% of the indigenous people of the Ötz and Pitz valleys and 11% of all inhabitants of these two valleys (Table 1). Blood samples were collected by K. Mager with the assistance of local medical doctors. The samples were analyzed in the blood typing laboratory at the University Clinic of Innsbruck.

The two valleys were divided into six regions coincidental with the larger villages (Figure 1): (1) Ötz (village), (2) Umhausen, (3) Längenfeld, (4) Sölden, (5) lower Pitz valley, and (6) upper Pitz valley. These villages, although composed of many hamlets, are separated from the neighboring villages by geographic features, such as river canyons and hills, and the two valleys are separated by a mountain range.

The people participating in the survey were born in the particular locality and had parents who were born in the respective valleys. As a rule,

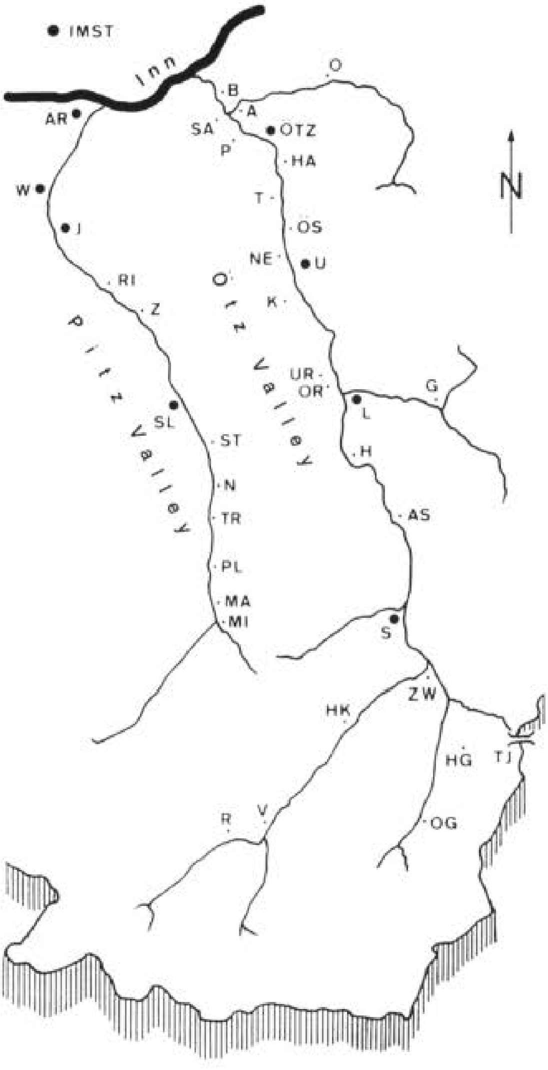

Figure 1. Study area. U, Umhausen; L, Längenfeld, S, Sölden; AR, W, J, lower Pitz valley; S, L, upper Pitz valley.

only one member of a family was sampled. The age of the participants varied between 18 and 73 years. Two-thirds of the sample was male.

The frequencies of the genes at the ABO locus were estimated by Bernstein's method (Bernstein 1930a,b). At the RH locus 10 alleles (haplotypes) were discerned, and their frequencies were estimated by allocation, as given by Ceppellini et al. (1955). At the MNSs locus four antisera were used, and haplotype frequencies were estimated by gene counting.

For investigation of the genetic structure of the population of the two valleys, genetic distances were computed using the method suggested by Cavalli-Sforza and Edwards (1967). For a wide range of gene frequencies angular transformation removes the dependence of the frequency variance on the frequency:

$$\cos \phi = \sum (p_a p_b)^{1/2} \tag{1}$$

where p_a and p_b refer to regions a and b and summation extends over all alleles at the locus. The genetic distance is estimated as

$$d = (1 - \cos \phi)^{1/2}, \tag{2}$$

which in the two-allele case corresponds to the chord between the two points on the surface of a sphere. The distance values can be converted to F_{ST} coefficients:

$$F_{ST} = \frac{4 \sum d^2}{\sum (k - 1)}, \tag{3}$$

where k denotes the number of alleles at a locus (in our data $k = 4$, 9, and 4 for the ABO, RH, and MNSs loci, respectively) and summation extends over the three loci.

Many methods can be used to group the observations. We constructed dendrograms using the average linkage method (Sneath and Sokal 1973) and computed principal components. In addition, nonlinear mapping for construction of linkage maps by a procedure introduced by Sammon (1969) was applied. Here, objects are positioned in a two-dimensional coordinate system in such a way that Euclidean distances d' correspond as closely as possible to observed distances d. The mean error of mapping is given by

$$\frac{|d - d'|}{d} N, \tag{4}$$

where N is the number of distances possible between observations. N should be smaller than 0.2. All grouping was based on F_{ST} values.

Results and Discussion

In Table 2 the gene (or haplotype) frequencies of the three blood group loci observed at each locality are given. The numbers from which the RH and MNSs groups were determined in each locality are similar but not identical.

We applied contingency chi-square tests to gene frequencies to examine heterogeneity among the localities. As is evident from Table 3, highly significant heterogeneity is apparent.

Table 2. Gene or Haplotype Frequencies

Gene or Haplotype	*Region* *Ötz Valley*	*Umhausen*	*Längenfeld*	*Sölden*	*Lower Pitz Valley*	*Upper Pitz Valley*
ABO						
p_1	0.237	0.258	0.199	0.129	0.186	0.171
p_2	0.024	0.042	0.048	0.045	0.041	0.086
q	0.086	0.041	0.111	0.148	0.085	0.056
r	0.653	0.659	0.643	0.678	0.688	0.688
MNSs						
MS	0.226	0.288	0.304	0.271	0.250	0.235
Ms	0.226	0.247	0.241	0.289	0.332	0.233
NS	0.170	0.173	0.155	0.163	0.090	0.251
Ns	0.379	0.292	0.300	0.276	0.328	0.281
RH						
r (*cde*)	0.461	0.466	0.591	0.521	0.557	0.406
R' (*Cde*)	0.002	0.002	0.001	0.015	0.035	0.001
R_0 (*cDe*)	0.002	0.026	0.005	0.010	0.001	0.028
R_1 (*CDe*)	0.373	0.390	0.271	0.345	0.287	0.423
R_2 (*cDE*)	0.115	0.092	0.054	0.097	0.044	0.140
R'' (*cdE*)	0.024	0.008	0.009	0.003	0.020	0.001
R_Z (*CdE*)	0.020	0.016	0.067	0.009	0.056	0.001
Ry (*CdE*)	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
U	0.003	0	0.002	0	0	0

The ABO gene frequencies are similar to the frequencies reported by Holzer (1936) and Bernhart (1942) for the whole province. As to regional patterns, region 4 differs from the others by low *ABO*A1* and high *ABO*B* frequencies, which along the Ötz valley (localities 1–4) show clinal variation. Also, the frequencies of the O blood group in regions 5 and 6 are nearly as high as the frequencies found in Basques, in the Irish, in Iceland, and from the Kleinwalsertal of Vorarlberg (western Austria). It is noteworthy that no records of black plague are known from the inner regions of the valleys (regions 3, 4, and 6) when the last epidemic ravaged the major part of Tyrol

Table 3. Heterogeneity Chi-Square Values for Gene Frequencies

Locus	χ^2	p
ABO (15 d.f.)	39.3	<0.001
MNSs (15 d.f.)	51.96	<0.001
RH (20 d.f.)[a]	92.2	<0.001

a. *cde*, *CDe*, *cDE*, *CDE*; all others pooled.

Table 4. F_{ST} Values

Region	*Ötz*	*Umhausen*	*Längenfeld*	*Sölden*	*Lower Pitz Valley*
Ötz					
Umhausen	0.0067				
Längenfeld	0.0099	0.0112			
Sölden	0.0107	0.0112	0.0103		
Lower Pitz valley	0.0139	0.0167	0.0083	0.0121	
Upper Pitz valley	0.0144	0.0075	0.0237	0.0120	0.0325

around 1630. Vogel et al. (1960) suggested that higher frequencies of blood group O are found only in areas that have no history of plague.

All four haplotypes of the MNSs locus are nearly equally frequent in region 6, whereas in the other regions the haplotype *NS* has a distinctly lower frequency. It is noteworthy that regions 1 and 5 border the Inn valley and thus are presumably least subject to isolation. They have *MS* frequencies similar to those quoted as typical for Europeans (Cavalli-Sforza and Bodmer 1971; Mourant et al. 1976).

At the RH locus the whole sample has a comparatively high *r* frequency, larger than commonly found in central Europe (15% Rh-negative; Prokop and Göhler 1976). The Rh-negative frequency culminates in regions 3 and 5, which also have comparatively high frequencies of the otherwise rare RH alleles R'' and R_Z, whereas in region 6 these rare RH alleles are rarer even than in other locations.

In Table 4 the matrix of F_{ST} coefficients is given. The average F_{ST} coefficients were 0.0150, 0.0073, and 0.0114 for the ABO, RH, and MNSs loci, respectively. The F_{ST} values are similar to values reported by Workman et al. (1978) for villages in Sardinia. As expected, the F_{ST} values are much smaller than values given by Cavalli-Sforza and Bodmer (1971) for global distributions but are considerably larger than values given by Roberts et al. (1981) for regions in Cumbria (United Kingdom). Cavalli-Sforza and Feldman (1990) compared F_{ST} values between neighborhoods of varying complexity and size in the Italian Parma region. The F_{ST} values decreased with increasing size of the neighborhoods. When computed for the smallest neighborhoods, the coefficients were larger than 1 but somewhat smaller than when they were estimated from neighborhoods comprising four villages or hamlets. One can conclude from this that the villages in the Parma region are or were somewhat less isolated than in the fairly narrow Tyrolean mountain valleys.

The F_{ST} coefficients can be considered distance measures—indeed they are proportional to d^2. As evident from Table 4, region 6 is rather separate. This region, the upper (southern) Pitz valley, is isolated and can be approached only from the north through region 5; it has a smaller population than the other regions.

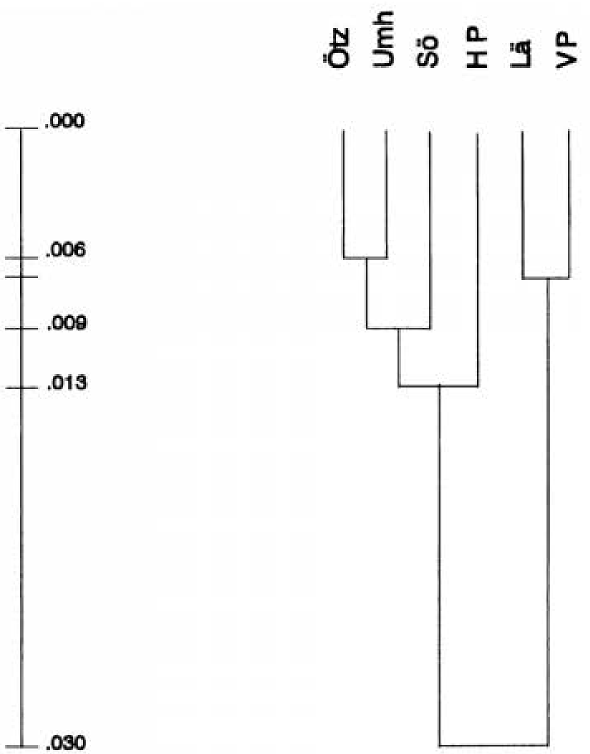

Figure 2. Genealogical tree of six local populations (average linkage, cophenetic correlation = 0.50). Ötz, Ötz valley; Umh, Umhausen; Sö, Sölden; H.P., upper Pitz valley; Lä, Längenfeld; V.P., lower Pitz valley.

In Figure 2 the tree constructed by average linkage (Sneath and Sokal 1973) is given. Two clusters appear: regions 1, 2, 4, and 6 on the one hand and regions 3 and 5 on the other. However, principal components I and II (Figure 3) place regions 4 and 6 far from the two clusters (regions 1 and 2 and regions 3 and 5).

Regions 1 and 2 are at the northern end of the Ötz valley, and they probably experienced the most intense immigration by people coming from the Inn valley. These people penetrated less into the more remote region 4 (Sölden) and more into the further westward and upward Pitz valley. The upper (southern) Pitz valley (region 6) remained largely isolated and received much fewer immigrants.

In contrast, region 3 (Längenfeld) is in the middle of the fairly wide Ötz valley bordering region 2 (Umhausen) to the north and region 4 (Sölden) to the south. There is a connection from region 5 to region 3 by means of a high mountain trail. Region 4, although at the upper (south) end of the valley,

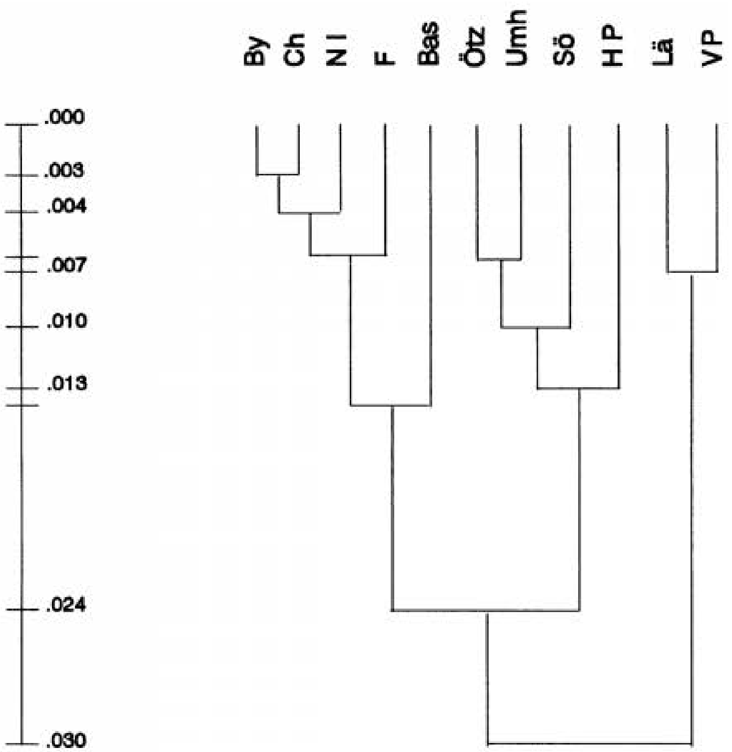

Figure 3. Genealogical tree of western European and Tyrolean populations (average linkage, cophenetic correlation = 0.63). By, Bavaria; Ch, Switzerland; NI, northern Italy; F, French; Bas, Basques; Ötz, Ötztal valley; Umh, Umhausen; Sö, Sölden; HP, upper Pitztal valley; Lä, Längenfeld; VP, lower Pitztal valley.

is connected by means of a high and snowfree (in the summer) pass to the Passeier valley of South Tyrol (Timmelsjoch).

Principal components I and II (Figure 4) separate regions 4 and 6 from the two clusters of regions 1 and 2 and regions 3 and 5. As already indicated, region 4 has been populated from or has close connections with South Tyrol (Passeier valley), whereas region 6 is the most isolated.

The two highest hamlets of region 4 (Sölden) were settled from South Tyrol and belonged to this district administratively until separated from Austria in 1918. South Tyrolean farmers still exercise their pasture claims in the southernmost regions of Sölden (region 4) even though they must drive their sheep flocks across glaciers.

In regions 3 and 5 Rh-negative and rare RH variants are fairly frequent, bringing the two locations close to each other. When MNSs frequencies are used to construct a tree, the closeness of the two regions disappears, but it

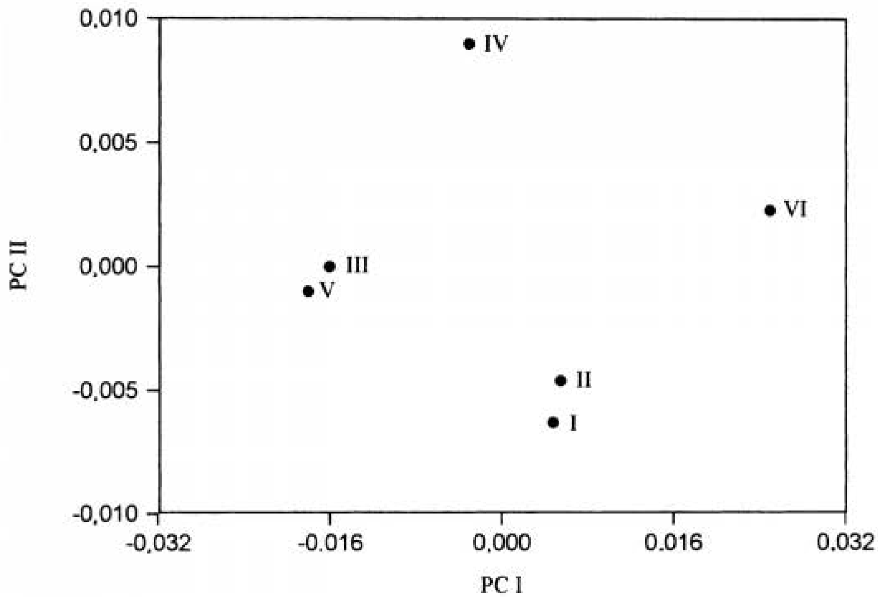

Figure 4. First two principal components from the three blood group systems. I to VI correspond to regions 1 to 6.

remains when ABO blood group frequencies are used. Constructing a tree with RH frequencies leaves region 3 isolated from the other regions.

To compare the people of the two valleys with other European populations, we used the blood group frequencies of Bavaria, eastern Switzerland, northern Italy, and as an outlier, Basques given by Mourant et al. (1976). Mourant's frequencies refer to larger undivided populations and therefore show comparatively less variation than the individual regions in our investigation.

As is evident from the dendrogram of Figure 3, the cluster of regions 3 and 5 is separate from the rest. However, the other regions cluster together, as do the European populations, among which the Basques, as expected, are most distant.

The nonlinear map given in Figure 5 shows the central European populations closely connected and some distance from the French population, which in turn is about as far removed from the Basques as from the central European group. The cluster of regions 1 and 2 is equally distant from the central European group but closer to them than to the other regions, among which, again, regions 3 and 5 are closer to each other than to the others. The Tyrolean groups are distant from the western European populations.

We also compared the gene frequencies of the Ötz and Pitz valleys with those of Hutterites (Steinberg et al. 1967), who originated in the Tyrol, which

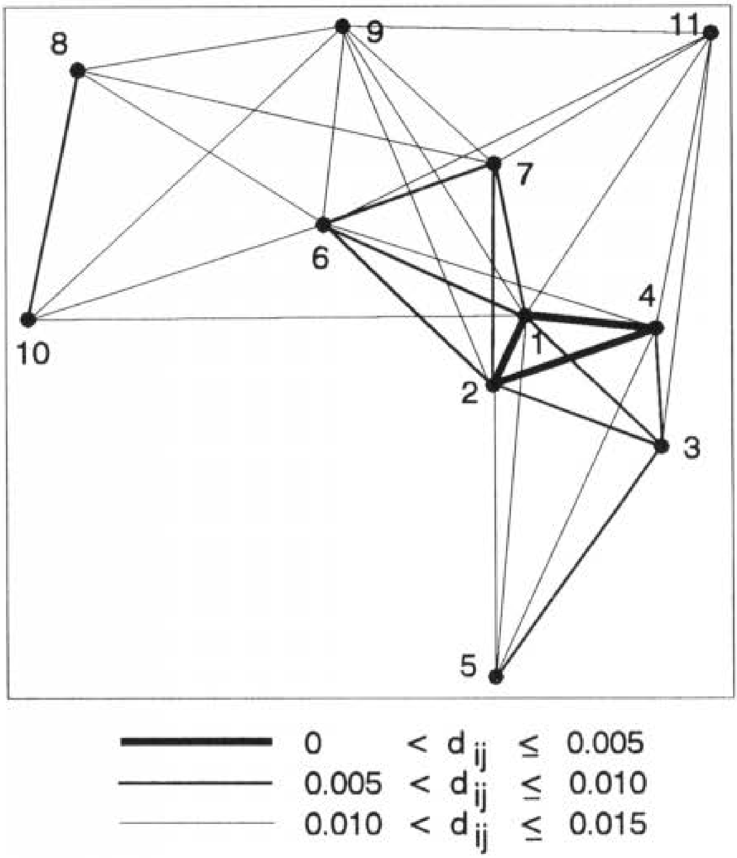

Figure 5. Nonlinear linkage map of western European and Tyrolean populations. (1) Bavaria, (2) Switzerland, (3) French, (4) northern Italy, (5) Basques, (6) Ötz valley (region 1), (7) Umhausen (region 2), (8) Längenfeld (region 3), (9) Sölden (region 4), (10) lower Pitz valley (region 5), (11) upper Pitz valley (region 6).

they left in the sixteenth century, and of Slovenes, even though Mourant et al. (1976) do not list frequencies of rarer alleles from these populations. Therefore we pooled our frequencies of rare alleles. The Hutterites appear to be well separated both from the populations of the two valleys and from populations of central Europe. This may reflect the infusion of genes from other populations on their long migration through eastern Europe and finally to North America and also genetic drift in these small groups. The Slovenes grouped together with our region 6 (data not shown).

An interpretation might be as follows: Regions 1 and 2 are next to the fairly wide Inn valley and may have experienced the most intense immigration, probably of mostly Bavarian people. Regions 3 and 5, from the point of view of westward migration up through the Inn valley, are more distant, and their gene frequencies may reflect people who settled earlier and were less influenced by this last wave of settlers. Region 4 was probably influenced by South Tyrolean neighbors, whereas frequencies in region 6, the most isolated, may be closer to those of the original inhabitants. As mentioned before, when including frequencies of Slovenia, region 6 clusters with these.

The closeness of Slovenes with the people of region 6 appears at first to be difficult to explain on geographic and historical grounds unless one accepts that original elements are present in the two populations, which would be remnants of the Alpine population in periods predating the immigration of Germanic tribes into the Tyrol and Slavonic tribes into Slovenia. Wopfner (1933), in discussing the prehistory of Tyrol, points out that (on the basis of linguistic studies) Celtic tribes did not reach the western north Tyrol, so the Illyric settlers remained fairly undisturbed. Also, the later German immigrations into these regions were less intense than immigrations further east.

The separation of the people of the Ötz and Pitz valleys from the neighboring large groups may reflect their relative isolation from outside populations.

The apparent paradox that closely neighboring people, such as the inhabitants of the regions in our study, appear more distant from each other than from various European populations deserves comment. The fairly small genetic distances among the European populations result from the stability of average values from many observations, whereas the larger genetic distances among neighboring regions reflect fairly strong isolation and thus genetic drift. Workman et al. (1978) reported similar observations from Sardinia. Cavalli-Sforza and Feldman (1990), using a stepping-stone model of isolation, showed that F_{ST} values decrease linearly with increasing size of neighborhoods.

Although our sample includes a rather large proportion of the population of two valleys, only 17 marker alleles (haplotypes) at 3 loci were determined. The probability of inferring a correct tree increases with the number of traits investigated (Kidd and Cavalli-Sforza 1971), and 17 alleles from 3 loci is certainly less than desirable. However, some studies are based on similar or even fewer loci [e.g., Nei and Imaizumi (1966)] or on similar numbers of genes or haplotypes at only one locus (Roberts et al. 1981). Cavalli-Sforza and Feldman (1990) based their investigation of F_{ST} and neighborhood size on the ABO, MN, and RH loci with fewer haplotypes, and a recent study on genetic polymorphism in Hong Kong is based on the ABO locus only (Yip et al. 1995).

For the four localities in the Ötz valley anthropometric results were available and principal components were computed (Mager 1980; Mager and Janetschek 1986). Graphs were constructed that agreed reasonably well with those developed from blood group gene frequencies.

The relationship derived from genetic information between the people in the various regions of the Ötz and Pitz valleys should be compared with the relationship based on pedigree and migration analysis. Similar studies in other Alpine valleys would be highly desirable for investigating the connection to other European populations.

The present data indicate considerable genetic heterogeneity in the investigated population, and differentiation among villages appears to be somewhat greater than in the northern Appenines. However, gene frequencies seem to be typical of central European populations in general.

Received 10 February 1995; revision received 4 December 1995.

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