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Key words: Genetic polymorphism, Blood proteins, Visp valleys, Swiss populations, Population genetics, Gene frequencies.

Genetic polymorphisms in three Alpine populations (Visp valleys, Switzerland)

Phenotype distributions and allele frequencies of 13 blood proteins are presented for the populations of the three Visp valleys, situated in the Swiss Alps. Blood samples of a total of 883 individuals were electrophoretically analysed. The three populations were statistically compared with each other, and with an additional sample from the literature thought to be representative of the entire Swiss population. Statistical differences are revealed and genetic distances are presented. These results are interpreted in connection with differences between the Visp valleys in topological situation.

Introduction

The topography of mountain regions has repeatedly been suggested to influence the gene flow of its populations. "Geographical barriers such as mountains do affect mate selection, marital movement and undoubtedly allelic frequency distributions." (CRAWFORD, 1980). Several human populations in mountain valleys of Italy and Switzerland have been found to show relatively high rates of isonymy (e.g. FRIEDL & ELLIS, 1974; LASKER, 1985; LASKER *et al*., 1972), endogamy (e.g. BIEDERMANN, 1986; FRIEDL & ELLIS, 1974; NETTING, 1981), and consanguineous marriages (e.g. PETTENER, 1980, 1981, 1985). In addition, in comparison with populations of neighbouring valleys or areas at the foot of the mountains, marked differences have been found in their gene frequencies (e.g. KRATZER, 1986; LUCCHETTI & RABINO MASSA, 1984; SCHÜTZ, 1946), surname frequencies (e.g. KAPLAN *et al*., 1978), and anthropological characteristics (e.g. KAUFMANN *et al*., 1958; SCHLEGEL & WEILENMANN-GRIESHABER, 1975, 1976).

In this study, phenotype distributions and allele frequencies of several blood proteins are analysed for the populations of the three Visp valleys. This narrow, Y-shaped river system is situated in the Alpine zone (Canton Valais, Switzerland) and is bounded by high mountain chains (*Figure 1*). The two valleys of the Matter- and the Saas-river merge together and thus form the Visp-river. Only the lower end of the Visp valleys opens into the vast Rhône valley, where the main traffic routes of this Swiss canton are situated. The only direct access to the upper Visp valleys (Matter and Saas valley) leads through the Visp valley itself. Considering this particular geographical situation, one would expect that the population down at the entrance to the Visp valley differs genetically less from the mean of the entire Swiss population than do the populations up in the Matter and Saas valley. The demography of the Saas valley has been studied previously by HUSSELS (1969) and MORTON *et al*. (1973), who felt that it was representative of Alpine isolates.

The main goals of this study are:

1. To determine phenotype distributions and allele frequencies of a larger series of blood protein systems for the three regions: Visp valley, Matter valley and Saas valley.

2. To statistically compare these data between the three Visp samples and a sample of

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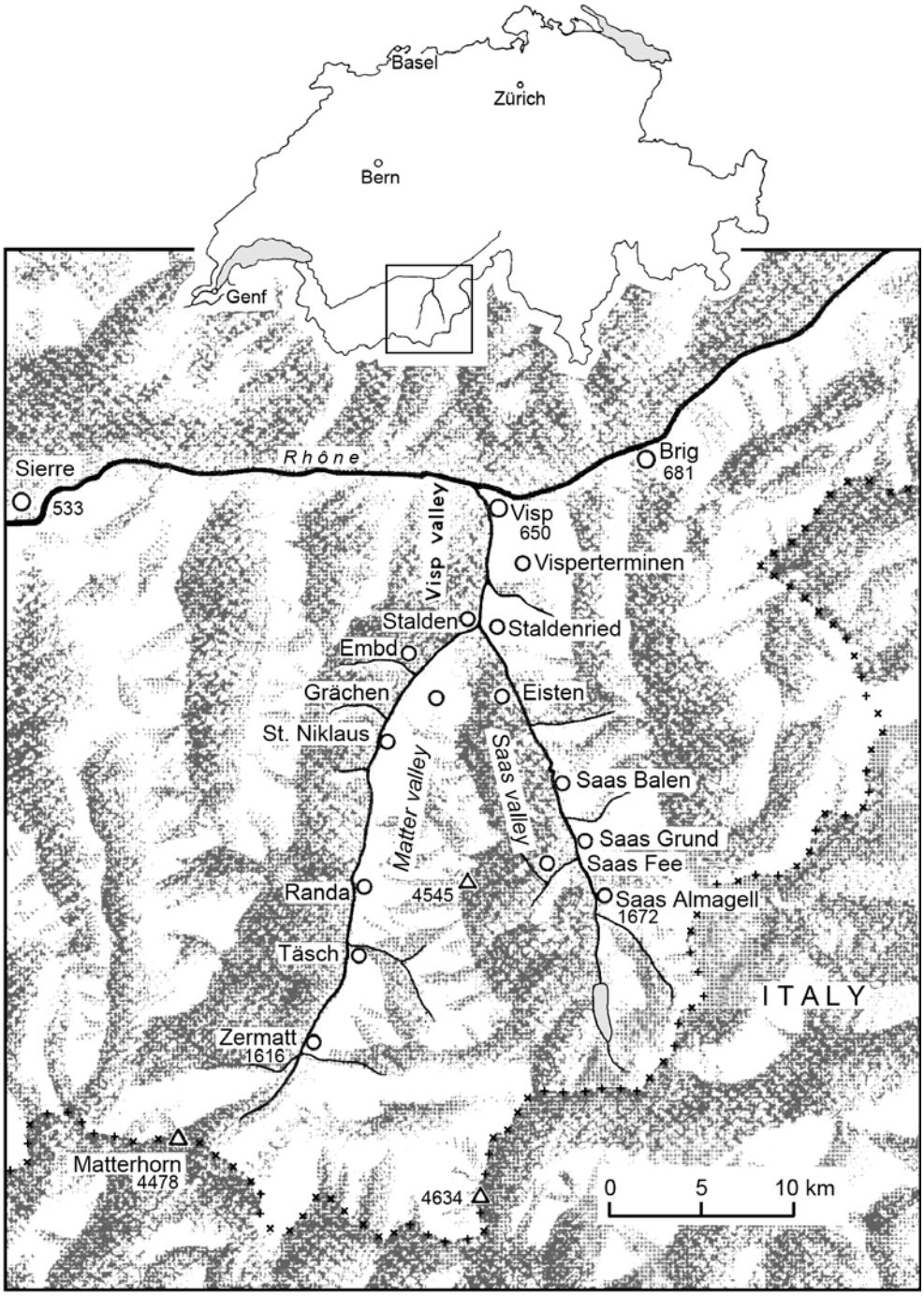

Figure 1. - Map of the study area. Blood samples from the following villages are analysed in this study: Visp valley: Visp, Visperterminen, Stalden, Staldenried. Matter valley: Embd, Grächen, St. Niklaus, Randa, Täsch, Zermatt. Saas valley: Eisten, Saas Balen, Saas Grund, Saas Fee, Saas Almagell.

the entire Swiss population and to test if the hypothesis postulated above can be supported by the results.

The importance of the *first* aspect consists in offering the necessary basis for studies of population-genetical and micro-evolutionary processes, of which the *second* aspect represents a simple example. To our knowledge, no previous publication exists which not only presents phenotype distributions and allele frequencies of a relatively large series of blood proteins for several Swiss populations but also an appropriate statistical evaluation of the data.

Material and Methods

All phenotype distributions for our Visp samples have been extracted from ZIGGIOTTI (1985), with the exception of the ABO system (see below). The blood samples come from 15 villages of the Visp valleys indicated in *Figure 1*. The villages lie at altitudes ranging from 650 m (Visp, at the entrance to the Visp valleys) to 1616 m and 1790 m (Zermatt and Saas Fee, respectively, at the two upper ends of the Visp valleys). The donors (n = 883 individuals) are roughly evenly distributed between the three regions constituting the Visp valleys: Visp valley, Matter valley, and Saas valley (*Table 1*). Place of residence of a donor's father was chosen to represent the provenience of the donor.

The blood samples were all taken from healthy individuals. In connection with the project "Hematogenetical and population-genetical investigations on populations of the Valais and of the Walsers of the Grisons" (see SCHEFFRAHN, 1983b; ZIGGIOTTI, 1985), blood samples were obtained during two blood collection campaigns of the Blood Transfusion Service SRC, Berne (April 1981, and April 1983, respectively), during special blood collections carried out in the villages of the Visp valleys in June 1982, and through occasional collections by the district hospitals of Brig, Sion, and Visp.

Four serum proteins (C3, GC, HPA, BF) and 9 polymorphic enzymes (ACP1, ADA, AK1, AMY2, ESD, GALT, GLO, PGM1, PGD) have been electrophoretically analysed for all individuals. The designation of the loci and alleles investigated here follows the nomenclature guidelines of SHOWS *et al.* (1979). Methods for visualization and identification of phenotypes follow those described by SPIELMANN & KÜHNL (1982) for the serum proteins, and by HARRIS & HOPKINSON (1976) and SPIELMANN & KÜHNL (1982) for the enzymes (see also ZIGGIOTTI, 1985).

Data on the phenotype distribution for the ABO system in Switzerland have been published by ROSIN (1956). Because of ROSIN's detailed data presentation, organised according to provenience of the blood-donors, it was possible to extract samples from donors from exactly the same villages as those of this study, and to include these data in our analysis. Allele frequencies for the ABO system were estimated by the method of BERNSTEIN (1930).

In addition, a sample thought to be representative of the entire Swiss population has also been included for comparison. This sample consists mostly of published data collected from the sources given in *Table 2*. From these sources, only the phenotype distributions are used here (listed in *Table 2*), whereas the respective allele frequencies have been re-calculated.

For testing the goodness of fit with the Hardy-Weinberg equilibrium and also for evaluating inter-group differences among the populations, the G-test (log likelihood ratio test) has been used, with the significance level at 5% ($\alpha = 0.05$). For details of the G-test

TABLE 1 - Distribution of the analysed blood samples within the three populations from the Visp valleys

Region	Actual population size in 1980	Sample size			In % of actual population
		Men	Women	Total	
Visp valley	9381	165	141	306	3.26
Matter valley	7024	169	151	320	4.56
Saas valley	2910	141	116	257	8.83
Visp valleys together	19315	475	408	883	4.57

[1] Data from Kantonales Statistisches Amt (1982)

TABLE 2 - Phenotype distribution and sources for the sample of the entire Swiss population

ABO	ROSIN (1956)	
A		130201
B		23263
AB		8327
O		113873
Total		275664
C3	**PFLUGSHAUPT *et al.*(1973, 1975)**	
S		1865
S-F		939
F		129
S-'R'		24
F-'R'		4
'R'		0
Total		2961
GC	**SCHEFFRAHN (1983a)**	
1S		324
1S-1F		154
1F		23
1S-2		310
1F-2		88
2		89
1F-1C20		1
Total		989
HPA	**combined data from BÜTLER *et al.* (1959) and BERINGER (1967)[1]**	
1	140+ 431=	571
1-2	449 + 1376 =	1825
2	331 + 970 =	1301
Total	920 + 2777 =	3697

(continued Table 2)

ACP1	PFLUGSHAUPT *et al*. (1970)	
A		147
AB		604
B		486
AC		41
BC		82
C		5
Total		1365
ADA	PFLUGSHAUPT *et al*. (1976)	
1		5828
1-2		763
2		12
4-1		1
Total		6604
AK1	PFLUGSHAUPT *et al*. (1971)	
1		2079
1-2		187
2		3
Total		2269
AMY2	SCHEIL & SCHEFFRAHN (1984, and pers. comm.)	
1		556
1-2		49
2		0
Total		605
ESD	combined data from PFLUGSHAUPT *et al.* (1976) and SCHERZ *et al*. (1983)[2]	
1	558 + 543 =	1101
1-2	174 + 154 =	328
2	12+ 14=	26
Total	744 + 711 =	1455
GALT	PFLUGSHAUPT *et al*. (1976)	
1		926
1-2		166
2		5
1-R		1
Total		1098
GLO	PFLUGSHAUPT *et al*. (1978)	
1		120
1-2		309
2		190
Total		619

(continued Table 2)

PGM1	SCHERZ *et al.* (1981)	
1		202
1-2		115
2		18
1-3		82
2-3		31
3		5
1-4		28
2-4		12
3-4		7
4		1
Total		501
PGD	Unpublished data collected between 1979 and 1986 in the course of paternity analysis at the Gerichtl. Medizin. Inst. Zürich, and compiled by one of us (TG).	
A		1268
AB		53
B		1
A-var		3
Total		1325

[1] Data from BÜTLER *et al.* (1959) and BERINGER (1967) can be combined, as the latter were collected after 1959, see BERINGER (1967).
[2] Data from PFLUGSHAUPT *et al.* (1976) and SCHERZ *et al.* (1983) do not overlap and can be combined (SCHERZ, pers. comm.).

and its advantages see SOKAL & ROHLF (1969). A minor problem arose in those few (N = 7) tests of the goodness of fit, in which one of the observed frequencies was 0 and no pooling was possible, because the degree of freedom was already 1. As the logarithm of 0 is not defined, no direct application of the G-test was then possible. In these cases, we used the following simple correction: 10^{-8} was added to the observed frequency of 0, and G was then calculated as usual. Other, unproblematical distributions were also tested and found to give identical G-values with or without such correction.

The calculation of the number of degrees of freedom in the test for goodness of fit still seems to deserve a few comments: As the parameters for the null hypothesis (expected frequencies) are not based on an extrinsic hypothesis but have been extracted from the sample data themselves, the number of degrees of freedom is less than N – 1, in contrast to most G-tests (and chi-square tests). Thus, many papers on allele frequencies of blood proteins contain incorrect degrees of freedom in their analyses (for instance all publications quoted in *Table 2*, with the exception of ROSIN, 1956, BÜTLER *et al*, 1959, and SCHEIL & SCHEFFRAHN, 1984, but in the latter two publications, agreement with the Hardy-Weinberg equilibrium was not tested). In general, the number of degrees of freedom can be calculated as

$$^1/_2\,(n^2\text{-}n)$$

where n is the number of alleles (Ferguson, 1980, p. 165), or: "the degrees of freedom are the number of phenotypic classes minus the number of alleles" (CAVALLI-SFORZA & BODMER, 1971, p. 58).

As a measure of genetic distance, the formula of PREVOSTI (1974) and PREVOSTI *et al.* (1975) was used. To equalize both size and variablity of the raw data, Gower's method of ranging (cited in SNEATH & SOKAL, 1973) was applied.

Results

Phenotype distributions for each blood protein system and for each sample are shown in *Table 3*. In neither population is there significant departure from the Hardy-Weinberg equilibrium in the majority of systems (G- and p-values are given in *Table 3*). One exception consists of the properdin factor B (BF) for all samples separately and in combination. We suspect that this may be attributable to a systematic error in interpretation of the BF-plates during the earliest electrophoresis-runs. A significant elevation of homozygotes was also found for the GALT locus in the Visp sample and for the GLO locus in the combined Visp samples, whereas a significant elevation of heterozygotes was found for the ADA locus in the Matter sample. These deviations do not reveal a consistent pattern and may be chance findings in view of the number of tests (N = 56) carried out on our samples from the Visp valleys.

Among the samples thought to be representative of the entire Swiss population, a significant deviation from the Hardy-Weinberg equilibrium was found for ROSIN's (1956) ABO data ($G = 230.652$, $df = 1$, $p < 0.0005$). As has already been noted by MORTON *et al.* (1968, 1973) and ROSIN (1956), phenotype B is in excess at the expense of phenotype AB. It has been suggested that this indicates a common error, whereby *ABO*A/ABO*B* genotypes (and especially *ABO*A2/ABO*B*) are misclassified as phenotype B (MORTON *et al.*, 1968). Therefore, according to the recommendation of MORTON *et al*. (1968), we have pooled the phenotypes B and AB in the following comparisons.

Statistical comparisons (G-test) were conducted for all possible pairs of samples. In addition, all samples were compared with the entire Swiss sample. The G-values and error probabilities of these tests are presented in *Table 4*. No comparisons were carried out with the BF system, as these phenotype distributions were found to be unreliable (see above).

The allele frequencies found for the study area (the combined Visp valleys) as well as for its three sub-regions (Visp valley, Matter valley, and Saas valley) and for the entire Swiss sample are given in *Table 5*. Due to the probable error in ROSIN's (1956) ABO data for the sample of the entire Swiss population, we used the corrected allele frequencies from MORTON *et al.* (1968) in this case. As the ABO phenotype distributions did not reveal a significant departure from the Hardy-Weinberg equilibrium for the Visp samples (see *Table 3*), we did not apply any corrections on the latter samples.

Only the most striking of the statistically significant differences will be individually mentioned here: In each of the three samples from the Visp valleys, we found high frequencies of *C3*S* and low frequencies of *C3*F*, in combination with high frequencies of *GLO*1* and low frequencies of *GLO*2*, as compared to the entire Swiss sample. These characteristics seem to be typical of the Visp valleys, although they may be common to other regions as well. Visp valley and Saas valley share relatively high *HPA*1* and low *HPA*2* frequencies, as compared to the entire Swiss sample, whereas the Matter and Saas valley share low *ACP1*A* and high *ACP1*B* frequencies, as well as high *PGM1*1* and low *PGM1**2 frequencies. The Matter sample shows, in comparison with the entire Swiss sample, especially low frequencies of *ABO*A* and high frequencies of *AB*O* o as well as a low frequency of *GC*1S*. An especially low frequency of *AK1*1* (and therefore a high frequency of *AK1**2) has been found in the Saas valley, as compared to all our other samples.

TABLE 3 - *Distribution of phenotypes of 14 blood protein systems in the Visp valleys, with tests on agreement with the Hardy-Weinberg equilibrium (G-test). df = degree of freedom, * = pooled in the G-test.*

Pheno-type	Visp valleys together		Visp valley		Matter valley		Saas valley		
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	
ABO-system:									
A	433	427.10	121	119.91	218	217.52	94	90.90	
B	148	141.53	17	15.77	82	81.42	49	45.77	
AB	36	42.90	6	7.28	22	22.66	8	11.43	
O	568	573.70	100	101.04	321	321.40	147	149.84	
Total	1185	1185.23	244	244.00	643	643.00	298	297.94	
G		1.052		0.340		–0.021		1.635	
df		1		1		1		1	
p		>0.05		>0.05		>0.05		>0.05	
Complement factor 3 (C3):									
S	628	628.79	221	221.12	232	232.63	175	175.03	
S-F	199	199.57	69	69.45	79	77.84	51	52.29	
F	17	15.83	6	5.45	6	6.51	5	3.91	
S-F0.5	16	13.57	5	4.28 *			11	9.30	
F-F0.5	0	2.15 *	0	0.67 *			0	1.39	*1
F0.5	0	0.07 *	0	0.02 *			0	0.12	*1
S-F1.2	0	0.88 *					0	0.83	*2
F-F1.2	1	0.14 *					1	0.12	*1
S-S0.35	2	1.77					2	1.70	
S-S0.5	2	1.77			1	0.87 *	1	0.83	*2
F-S0.5	0	0.28 *			0	0.15 *	0	0.12	*1
S0.5	0	0.00 *			0	0.00 *	0	0.00	*1
others	0	0.33 *					0	0.34	*1
pooled 1	1	3.86	5	4.97	1	1.02	1	2.09	
pooled 2							1	1.66	
Total	865	865.15	301	300.99	318	318.00	246	245.98	
G		3.187		0.057		0.039		1.663	
df		1		1		1		1	
p		>0.05		>0.05		>0.05		>0.05	

(Table 3 continued)

Pheno-type	Visp Valleys together		Visp valley		Matter valley		Saas valley	
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected
Group specific component (GC):								
1S	247	244.59	88	92.53	86	81.52	73	70.92
1S-1F	153	150.58	69	55.64	52	56.01	32	38.88
1F	24	23.18	4	8.36	12	9.62	8	5.33
1S-2	265	271.71	90	93.07	93	98.94	82	79.33
1F-2	79	83.64	23	27.98	33	33.99	23	21.75
2	83	75.46	27	23.40	34	30.02	22	22.18
1F-1C1	6	4.69	1	0.67*	2	1.56*	3	2.30*
1S-1C1	13	15.23	1	2.22*	5	4.55	7	8.40
2-1C1	6	8.46	2	1.12*	2	2.76*	2	4.70
1C1	2	0.24*	0	0.01*	0	0.06*	2	0.25*
1S-1C3	4	2.14*			1	0.52*	3	1.57
others	0	1.92*			0	0.50*	0	1.41
pooled	6	4.3	4	4.02	5	5.40	8	5.53
Total	882	881.84	305	305.00	320	320.04	257	257.02
G		3.587		7.584		1.958		5.820
df		5		3		3		4
p		>0.05		>0.05		>0.05		>0.05
Haptoglobin (HPA):								
1	188	181.77	63	63.10	43	43.19	82	80.68
1-2	423	435.44	151	150.80	148	147.64	124	126.63
2	267	260.79	90	90.10	126	126.18	51	49.69
Total	878	878.00	304	304.00	317	317.01	257	257.00
G		0.652		–0.018		–0.038		0.096
df		1		1		1		1
p		>0.05		>0.05		>0.05		>0.05

(Table 3 continued)

Pheno-type	Visp valleys together		Visp valley		Matter valley		Saas valley	
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected
Properdin factor B (BF):								
S	642	605.75	218	208.07	237	221.94	187	182.38
S-F	148	216.38	57	78.62	52	81.60	39	50.53
F	51	19.32	19	7.43	22	7.50	10	3.50*
S-S0.7	15	19.87	3	2.46*	3	3.36*	9	758
F-S0.7	9	3.55*	0	0.47*	1	0.62*	0	1.05*
S0.7	0	0.16*	0	0.01*	0	0.01*	0	0.08*
S-F1.0	14	13.30	7	5.78	4	4.16	11	10.09
F-F1.0	2	2.37*	0	1.09*	1	0.76*	1	1.40*
S0.7-F1.0	0	0.22*	0	0.03*	0	0.03*	0	0.21*
S1.0	0	0.07*	0	0.04*	0	0.02*	0	0.14*
pooled	11	6.37	3	4.10	5	4.80	11	6.38
Total	881	880.99	304	304.00	320	320.00	257	256.96
G		66.162		20.134		31.683		6.113
df		2		1		1		1
p		<0.0005		<0.0005		<0.0005		<0.025
Acid phosphatase (ACP1):								
A	79	74.96	43	43.22	20	19.13	16	15.93
AB	341	352.38	138	136.80	109	113.58	94	94.86
B	421	414.11	107	108.26	172	168.53	142	141.19
AC	15	11.67*	6	6.76*	7	4.17	2	1.24*
BC	25	27.42	12	10.70	10	12.36	3	3.70*
C	0	0.45*	0	0.26*	0	0.23*	0	0.02
pooled	15	12.12	6	7.02	7	4.40	5	4.96
Total	881	880.99	306	306.00	318	318.00	257	256.94
G		1.511		0.316		2.061		0.119
df		2		2		2		1
p		>0.05		>0.05		>0.05		>0.05

(Table 3 continued)

Pheno-type	Visp valleys together		Visp valley		Matter valley		Saas valley	
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected
Adenosine deaminase (ADA):								
1	775	777.40	277	277.68	265	267.39	233	232.63
1-2	107	102.24	29	27.63	55	50.25	23	23.77
2	1	3.36	01	0.69	01	2.36	1	0.61
Total	883	883.00	306	306.00	320	320.00	257	257.01
G		2.449		1.427		5.155		0.197
df		1		1		1		1
p		>0.05		>0.05		<0.025		>0.05
Adenylate kinase (AK1):								
1	748	747.70	276	274.83	273	273.80	199	199.61
1-2	129	129.68	28	30.33	46	44.40	55	53.77
2	6	5.62	2	0.84	1	1.80	3	3.62
Total	883	883.00	306	306.00	320	320.00	257	257.00
G		–0.044		1.317		0.462		0.126
df		1		1		1		1
p		>0.05		>0.05		>0.05		>0.05
Amylase-2 (AMY2):								
1	769	769.62	261	261.80	277	276.59	231	231.42
1-2	91	89.76	30	28.43	41	41.83	20	19.18
2	2	2.62	01	0.77	2	1.58	01	0.40
Total	862	862.00	291	291.00	320	320.00	251	251.00
G		0.106		1.608		0.098		0.818
df		1		1		1		1
p		>0.05		>0.05		>0.05		>0.05

(Table 3 continued)

Pheno-type	Visp valleys together		Visp valley		Matter valley		Saas valley	
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected
Esterase D (ESD):								
1	714	713.96	256	257.14	258	255.64	200	201.38
1-2	160	160.07	49	46.73	56	60.75	55	52.23
2	9	8.97	1	2.12	6	3.61	2	3.39
Total	883	883.00	306	305.99	320	320.00	257	257.00
G		–0.071		0.850		1.698		0.807
df		1		1		1		1
p		>0.05		>0.05		>0.05		>0.05
Galactose-1-phosphate uridyltransferase(GALT):								
1	760	760.50	257	258.88	282	280.25	221	221.32
1-2	117	116.07	48	44.23	34	37.49	35	34.34
2	4	4.43	01	1.89	3	1.25	1	1.33
Total	881	881.00	305	305.00	319	318.99	257	256.99
G		–0.022		4.085		2.097		0.106
df		2		1		1		1
p		>0.05		>0.05		>0.05		>0.05
Glyoxalase-1 (GLO):								
1	289	274.15	90	82.62	114	109.29	85	82.94
1-2	406	435.72	138	152.76	146	155.44	122	126.12
2	188	173.13	78	70.62	60	55.27	50	47.94
Total	883	883.00	306	306.00	320	320.00	257	257.00
G		4.042		2.842		1.160		0.259
df		1		1		1		1
p		<0.05		>0.05		>0.05		>0.05

(Table 3 continued)

Pheno-type	Visp valleys together		Visp valley		Matter valley		Saas valley	
	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected	Ob-served	Ex-pected
Phosphoglucomutase-1 (PGM1):								
1	445	438.87	137	141.37	178	172.59	130	125.35
1-2	136	147.29	67	68.64	35	42.58	34	34.93
2	16	12.36	10	8.33	3	2.63*	3	2.43*
1-3	171	169.20	60	51.66	62	64.63	49	53.09
2-3	34	28.39	12	12.54	15	7.97	7	7.40
3	11	16.31	1	4.72	4	6.05	6	5.62
1-4	48	50.80	15	12.90	17	17.63	16	20.25
2-4	7	8.52*	2	3.13*	2	2.17*	3	2.82*
3-4	13	9.79	2	2.36*	3	3.30*	8	4.29
4	2	1.47*	0	0.29*	1	0.45*	1	0.82*
Pooled	9	9.99	4	5.78	9	8.55	7	6.07
Total	883	883.00	306	305.94	320	320.00	257	257.00
G		6.121		7.173		7.442		4.201
df		5		4		3		2
p		>0.05		>0.05		>0.05		>0.05
6-Phospogluconate-dehydrogenase (PGD):								
A	846	845.44	300	300.03	313	313.06	233	232.63
AB	34	35.25	6	5.94	5	4.94	23	23.77
B	1	0.37*	0[1]	0.03	0	0.02*	1	0.61
A-Rich	2	1.90			2	1.96		
B-Rich	0	0.04*			0	0.02*		
Rich	0	0.00*			0	0.00*		
Pooled	1	0.41			01	0.04		
Total	883	883.00	306	306.00	320	320.00	257	257.01
G		0.578		0.038		0.058		0.197
df		1		1		1		1
p		>0.05		>0.05		>0.05		>0.05

[1] A correction on this frequency of 0 was made to enable calculation of G (explanation of the correction see section on material and methods).

TABLE 4 - Comparison between the phenotype distributions in the three Visp valleys and the sample of the entire Swiss population (G-test). G-values, degrees of freedom and error probabilities are given for all possible pairs of samples.

Blood protein system	Comparison						
	Visp valley/ Matter valley	Visp valley/ Saas valley	Saas valley/ Matter valley	Visp valleys/ Entire Swiss	Visp valley/ Entire Swiss	Matter valley/ Entire Swiss	Saas valley/ Entire Swiss
ABO[2]	19.942 2 p<0.0005	21.891 2 p<0.0005	1.293 2 p>0.05	16.864 2 p<0.0005	–40.050 2 p>0.05	7.288 2 p<0.05	–6.640 2 p>0.05
C3	1.335 2 p>0.05	7.827 3 p<0.05	11.352 2 p<0.005	48.518 3 p<0.0005	13.193 2 p<0.001	15.487 2 p<0.0005	14.850 2 p<0.001
GC	12.285 7 p>0.05	22.428 7 p<0.005	6.871 7 p>0.05	43.891 6 p<0.0005	16.508 6 p<0.025	28.060 6 p<0.0005	49.541 6 p<0.0005
HPA	9.545 2 p<0.01	12.099 2 p<0.005	40.979 2 p<0.0005	18.925 2 p<0.0005	6.823 2 p<0.05	2.413 2 p>0.05	50.539 2 p<0.0005
ACP1	27.250 4 p<0.0005	29.733 4 p<0.0005	4.821 4 p>0.05	42.833 4 p<0.0005	6.085 4 p>0.05	38.412 4 p<0.0005	47.528 4 p<0.0005
ADA	8.090 1 p<0.005	–0.036 1 p>0.05	7.627 1 p<0.010	–0.624 1 p>0.05	0.810 1 p>0.05	6.963 1 p<0.01	0.747 1 p>0.05
AKI	3.445 1 p>0.05	17.296 1 p<0.0005	5.871 1 p<0.025	30.409 1 p<0.0005	0.442 1 p>0.05	11.600 1 p<0.001	41.251 1 p<0.0005
AMY2	1.386 1 p>0.05	0.849 1 p>0.05	4.364 1 p<0.05	2.874 1 p>0.05	1.096 1 p>0.05	6.339 1 p<0.025	–0.061 1 p>0.05
ESD	4.078 2 p>0.05	3.048 1 p>0.05	2.531 2 p>0.05	9.237 2 p<0.01	12.194 2 p<0.005	3.949 2 p>0.05	1.748 2 p>0.05
GALT	2.228 1 p>0.1	0.291 1 p>0.05	0.704 1 p>0.05	1.291 2 p>0.05	–0.113 1 p>0.05	3.289 1 p>0.05	0.338 1 p>0.05
GLO	5.057 2 p>0.05	3.000 2 p>0.05	0.378 2 p>0.05	38.431 2 p<0.0005	11.594 2 p<0.01	33.958 2 p<0.0005	22.747 2 p<0.0005
PGM1	21.390 6 p<0.005	21.121 6 p<0.005	7.458 6 p>0.05	31.756 8 p<0.0005	10.789 7 p>0.05	38.691 8 p<0.0005	28.163 8 p<0.0005
PGD	–0.007 1 p>0.05	15.713 1 p<0005	14.681 1 p<0.0005	–0.180 1 p>0.05	4.140 1 p<0.05	3.371 1 p>0.05	9.439 1 p<0.005

[1] References see *Table 2*.
[2] Based on phenotype frequencies in ROSIN (1956)

TABLE 5 - *Allele frequencies in the populations from the Visp valleys and in a sample representing the entire Swiss population.*

Blood protein system	Allele	Visp valleys together	Visp valley	Matter valley	Saas valley	Entire Swiss [1]
ABO [2]	A	0.2232	0.3081	0.2085	0.1897	0.2982
	B	0.0811	0.0484	0.0845	0.1011	0.0590
	0	0.6958	0.6435	0.7070	0.7091	0.6427
C3	S	0.8526	0.8571	0.8553	0.8435	0.7925
	F	0.1353	0.1346	0.1431	0.1260	0.2028
	var	0.0121	0.0083	0.0016	0.0305	0.0047
GC	is	0.5266	0.5508	0.5047	0.5253	0.5622
	IF	0.1621	0.1656	0.1734	0.1440	0.1461
	2	0.2925	0.2770	0.3063	0.2938	0.2912
	var	0.0187	0.0066	0.0156	0.0370	0.0005
HPA	1	0.4550	0.4556	0.3691	0.5603	0.4013
	2	0.5450	0.5444	0.6309	0.4397	0.5987
ACP1	A	0.2917	0.3758	0.2453	0.2490	0.3440
	B	0.6856	0.5948	0.7280	0.7412	0.6073
	C	0.0227	0.0294	0.0267	0.0097	0.0487
ADA	1	0.9383	0.9526	0.9141	0.9514	0.9403
	2	0.0617	0.0474	0.0859	0.0486	0.0596
	var	0.0000	0.0000	0.0000	0.0000	0.0001
AK1	1	0.9202	0.9477	0.9250	0.8813	0.9575
	2	0.0798	0.0523	0.0750	0.1187	0.0425
AMY2	1	0.9449	0.9485	0.9297	0.9602	0.9595
	2	0.0551	0.0515	0.0703	0.0398	0.0405
ESD	1	0.8992	0.9167	0.8938	0.8852	0.8694
	2	0.1008	0.0833	0.1062	0.1148	0.1306
GALT	1	0.9291	0.9213	0.9373	0.9280	0.9194
	2	0.0709	0.0787	0.0627	0.0720	0.0801
	var	0.0000	0.0000	0.0000	0.0000	0.0005
GLO	1	0.5572	0.5196	0.5844	0.5681	0.4435
	2	0.4428	0.4804	0.4156	0.4319	0.5565
PGM1	1	0.7050	0.6797	0.7344	0.6984	0.6277
	2	0.1183	0.1650	0.0906	0.0973	0.1936
	3	0.1359	0.1242	0.1375	0.1479	0.1297
	4	0.0408	0.0310	0.0375	0.0564	0.0489
PGD	A	0.9785	0.9902	0.9891	0.9514	0.9781
	B	0.0204	0.0098	0.0078	0.0486	0.0208
	var	0.0011	0.0000	0.0031	0.0000	0.0011

[1] References see Table 2.

[2] Based on phenotype frequencies in ROSIN (1956), but for the entire Swiss sample, the corrected allele frequencies of MORTON *et al.* (1968) were used.

TABLE 6 - *Matrix of genetic distances (Prevosti distances) between the three populations from the Visp valleys and a sample of the entire Swiss population. The distances were calculated from the allele frequencies of 13 blood protein systems given in Table 5.*

	CH	VI	SA	MA
CH	0			
VI	0.57	0		
SA	0.92	0.78	0	
MA	0.95	0.72	0.70	0

Abbreviations:
CH = Entire Swiss population, VI = Visp valley, SA = Saas valley, MA = Matter valley.

Between the three Visp samples and the entire Swiss sample, genetic distances were calculated from the allele frequencies; the distance matrix is given in *Table 6*. The lowest value of genetic distance (0.57) was found between the Visp sample and the entire Swiss sample, the highest values (0.95 and 0.92) between the Matter sample and the entire Swiss, and between the Saas sample and the entire Swiss sample, respectively.

Discussion

In this study, 14 blood protein systems were analysed. For statistical calculations, only 13 systems could be used. Comparison among our samples from the Visp valleys revealed significant differences in several systems, and significant differences have also been found between the samples here under study and the sample of the entire Swiss population (*Table 4*). Matter and Saas samples seem to differ more from the entire Swiss sample (in 9 and 8 systems, respectively) than does the Visp sample (in 6 systems). The relationships between these samples, as revealed by the G-tests, are shown schematically in *Figure 2a*. Here, the scaled percentage of differing blood protein systems between two samples has been used as a rough measurement of genetical dissimilarity and then subtracted from 1 so that the figure actually shows similarity.

These results suggest, in line with expectation, that the Visp population at the entrance of the valley is, in its genetical composition, more similar to the entire Swiss sample, than each of the two populations (Matter and Saas) at the upper ends of the valleys.

Calculation of the genetic distances (*Table 6*) gave a similar and more convincing result (as shown in *Figure 2b*), thus supporting the G-tests: The sample from the Visp valley shows the smallest distance from the entire Swiss sample; Matter valley and Saas valley show distinctly higher distances from the entire Swiss sample as well as between each other.

These findings are again in agreement with our initial expectations and suggest that the populations from the Matter valley and the Saas valley are not only geographically more peripheral to, but also genetically more remote from, the entire Swiss population than the population of the Visp valley. The villages up in the Matter and Saas valley are more distant from the main traffic routes and industrial zones in the vast Rhône valley than the villages down in the Visp valley. This situation may have enhanced gene flow from and to

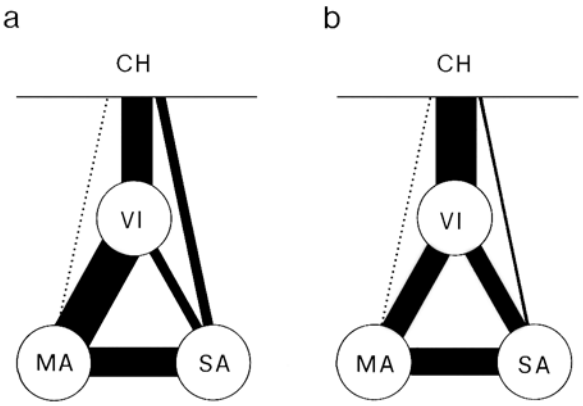

Figure 2. - Visualized genetical relationship between the three populations from the Visp valleys and the sample of the entire Swiss population, based on:
a. the number of blood protein systems which were found to show statistically significant differences between any two populations, of a total of 13 systems analysed here (G-test).
b. the genetic distances from *Table 6*.
For this figure, the percentage of significant differences and, separately, the genetic distances have been ranged with Gower's method (cit. in SNEATH & SOKAL, 1973). As the largest value then becomes 1, and the smallest becomes zero, the two different data sets are now more easily comparable. In order to represent them as measurements of similarity, each value has been subtracted from 1. In the figure, similarity corresponds to the thickness of the lines connecting the samples, and the dotted lines correspond to a similarity value of 0.
Abbreviations: CH = Entire Swiss population, VI = Visp valley, SA = Saas valley, MA = Matter valley.

the Visp valley, whereas the Matter and Saas populations seem to have been more isolated.

Although the striking differences in the genetic composition of our samples thus correspond, to a certain degree, to our expectations, this is not so in every respect. Whereas the number of statistically significant differences in both the Matter-Swiss and the Saas-Swiss comparisons is actually larger (9 and 8 differences in 13 systems, respectively) than in the Visp-Swiss comparison (6 differences), this numerical difference is not very pronounced.

In the upper part of Val Varaita in the Italian Alps, KAPLAN *et al*. (1978) analysed the communality of surnames in three communities situated in a "Y" patern similar to the three valleys of the present study. These authors found that the communities adjacent by road were about twice as closely related to each other as those separated by a high mountain ridge. By analogy, we would also have expected to find a larger number of differences and a larger genetic distance between the Matter and Saas samples than between each of them and the Visp sample, due to the topographical separation of the Matter and Saas valleys and the connection of both of them to the Visp valley. This expectation is, however, not supported by the results of our study (see *Figure 2*). At present we cannot account for this deviation from expectation. We suspect that the population within a valley might be less homogeneous than assumed by our simple model. This could be tested by separately analysing the villages of each valley. Further, CRAWFORD (1980) suggested that population structures in Alpine regions may also be strongly influenced by factors other than geographical barriers, such as economic and other cultural variables.

ACKNOWLEDGEMENTS – The research project "Hematogenetical and population-genetical investigations on populations of the Valais and of the Walsers of the Grisons" (Project leader: Dr. W. SCHEFFRAHN) was supported by the JULIUS KLAUS-STIFTUNG. The typing of the AMY2 protein system has been carried out by Dr. H.-G. SCHEIL, Düsseldorf. Dr. G. BÄCHLI kindly gave access to the computer program used here. We wish to express our thanks to Dr. G. BÄCHLI, Dr. M. GAGLIARDI, A. KRATZER and Dr. D. WYLER for reading the draft and for offering helpful comments, and to Mrs. B. ANDREW for polishing the English of this manuscript.

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Received: Aug., 10, 86. Accepted: Feb., 10, 87.