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The mean Frequencies of Blood Group Genes in Sweden with special Regard to the Rh Genes

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Our material consists of paternity cases investigated at the Blood Group Genetical Section of the Blood Group Serological Department, State Laboratory for Forensic Chemistry, Stockholm, and is thus totally free from clinical selection. For technical reasons and to avoid correlations through relationship we use only adults, i.e. the mothers and alleged fathers, for population statistics.

The cases are sent in rather proportionally from all parts of the country and the proportion of rural and urban population and the social groups to which the tested persons belong must, in the main, be regarded as average.

Our material, therefore, may be assumed to give a tolerably good value for the mean blood group composition of the Swedish population.

The Rh System

In *table I* we present our most recent Rh material, consisting of 2,743 adults investigated in 1955 and at the end of 1954 (designated below « material 1955 »). The bloods are tested with anti-C, anti-c, anti-D and anti-E and for all apparent C+D—E—, C—D—E+ and C+D—E+ samples with an antiglobulin test for D^u too. D+^{u} in our material is noted as D+ in table I.

For comparison a Danish (Gürtler and Henningsen 3) and an English material (Race et al. 7) are given, which materials have been of special importance for our routine work.

The differences found in the 3 materials in *table I* are small and not significant.

They may, to some extent, depend upon the technics used. In our material 1955, CcD^u and D^uE are noted as CcD and DE respectively, in contrast to the English and Danish materials, most of which seem to be noted as Cc and E respectively.

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Table 1

« 4-Serum » reactions	Wiener's notation 1936 (11, 12)	Our notation (5)	Absolute Our material 1955 2,743 adults	% Our material 1955 2,743 adults	% Danish mat. (Gurtler et Henningsen) 5,500 adults (3)	% English mat. (Race et al) 2,000 adults (7)
C—c+D—E—	rh	rh—	397	$14.47 \pm \sqrt{0.4512}$	$15.06 \pm \sqrt{0.2326}$	$15.35 \pm \sqrt{0.6497}$
C+c—D+E—	Rh_1Rh_1	CCD	498	$18.16 \pm \sqrt{0.5418}$	$18.35 \pm \sqrt{0.2724}$	$18.65 \pm \sqrt{0.7586}$
C+c+D+E—	Rh_1rh	CcD	944	$34.41 \pm \sqrt{0.8228}$	$34.80 \pm \sqrt{0.4125}$	$34.45 \pm \sqrt{1.1291}$
C+c+D+E+	Rh_1Rh_2	CcDE	407	$14.84 \pm \sqrt{0.4607}$	$14.47 \pm \sqrt{0.2250}$	$13.50 \pm \sqrt{0.5839}$
C—c+D+E+	Rh_2	DE	433	$15.79 \pm \sqrt{0.4848}$	$14.27 \pm \sqrt{0.2224}$	$13.95 \pm \sqrt{0.6002}$
C—c+D+E—	Rh_o	D	37	$1.35 \pm \sqrt{0.0486}$	$1.44 \pm \sqrt{0.0258}$	$2.10 \pm \sqrt{0.1028}$
C+c+D—E—	rh'rh	Cc	14	$0.51 \pm \sqrt{0.0185}$	$0.98 \pm \sqrt{0.0176}$	$0.80 \pm \sqrt{0.0397}$
C—c+D—E+	rh''	E	9	$0.33 \pm \sqrt{0.0120}$	$0.56 \pm \sqrt{0.0101}$	$0.95 \pm \sqrt{0.0407}$
C+c—D+E+	Rh_2Rh_1	CCDE	3	0.11	0.05	0.25
C+c+D—E+	rh'rh''	CcE	1	0.04	0.00	0.00
C+c—D—E—	rh'rh'	CC	0	0.00	0.02	0.00
C+c—D—E+	rh_yrh'	CCE	0	0.00	0.00	0.00

Table 2

« 3-Serum » reactions	Our notation	% Our mat. 1949 2,768 adults	$(o-e)^2/e$ 1949 + $(o-e)^2/e$ Danish	% Danish mat (3) 5,500 adults	% Our mat. 1955 2,743 adults	$(o-e)^2/e$ 1955 + $(o-e)^2/e$ Danish	Absolute Danish mat. (3) 5,500 adults	Absolute our mat. 1955 2,743 adults	$(o-e)^2/e$ 1955 $(o-e)^2/e$ 1949	Absolute Our mat. 1949 2,768 adults
C—D—E—	rh—	14.88	0.0371	15.06	14.47	0.4209	828	397	0.1551	412
C+D+E—	CD	51.99	0.4714	53.15	52.57	0.1181	2,923	1,442	0.0911	1,439
C+D+E+	CDE	14.38	0.0294	14.52	14.95	0.2151	799	410	0.3090	398
C—D+E+	DE	15.61	2.2145	14.27	15.79	2.8164	785	433	0.0289	432
C—D+E—	D	1.41	0.0095	1.44	1.35	0.0994	79	37	0.0337	39
C+D—E—	C	1.08	0.1187	1.00	0.51	5.2826	55	14	5.6738	30
C—D—E+	E	0.58	0.2346	0.56	0.33	1.4259	31	9	2.1729	16
C+D—E+	CE	0.07		0.00	0.04		0	1		2
χ^2			3.1152 6 d.f.			10.3784 6 d.f.			8.4645 6 d.f.	

Table II gives a comparison between our material 1955, an old material of ours from 1949 (« material 1949 », part of which has been published 5, which was not controlled with D^u test and only tested with anti-C, anti-D and anti-E) and the Danish material.

Table II shows a little higher frequency of group DE in both our Swedish materials than in the Danish material and shows that the differences between the C and E group frequencies of our recent Swedish material on the one hand, and the Danish material and our old Swedish material on the other hand can be fully explained by the D^u factor. This can be seen in *table III* too, where both our Swedish materials are compared after neutralizing of the D^u influence.

Table 3

Our notation	Our mat. 1949 2,768 adults	(O-e) ^{2}/e 1949 + (o-e) ^{2}/e 1955	Our mat. 1955 2,743 adults
rh- plus D	451	0.1910	434
CD plus C	1,469	0.0000	1,456
CDE plus CE	400	0.2701	411
DE plus E	448	0.0045	442
		$\chi^2 = 0.4656$ 3 d.f.	

In both our Swedish materials, as well as in the Danish material, there is a somewhat lower frequency of group D (= C—D+E—) than is found in most of the Anglo-Saxon materials.

Table IV gives some gene frequencies calculated directly with the simple formulae:

$$[\varrho] = \sqrt{(\text{rh}—)}; \quad [\gamma] = \sqrt{(\text{rh}—) + (\text{C})} - \sqrt{(\text{rh}—)}; \quad [\varepsilon] = \sqrt{(\text{rh}—) + (\text{E})} - \sqrt{(\text{rh}—)};$$

$$[\delta] = \sqrt{(\text{rh}—) + (\text{D})} - \sqrt{(\text{rh}—)};$$

$$[\gamma\delta] = \sqrt{(\text{rh}—) + (\text{C}) + (\text{D}) + (\text{CD}) - 2[\gamma] \times [\delta]} - \sqrt{(\text{rh}—) + (\text{C}) + (\text{D})};$$

$$[\delta\varepsilon] = \sqrt{(\text{rh}—) + (\text{E}) + (\text{D}) + (\text{DE}) - 2[\varepsilon] \times [\delta]} - \sqrt{(\text{rh}—) + (\text{E}) + (\text{D})};$$

$$[\gamma\delta\varepsilon] = \sqrt{([\gamma\delta] + [\gamma])^2 + (\text{CCDE})} - ([\gamma\delta] + [\gamma]);$$

For the judging of materials, especially as to the panmixia and the quality of the technics used, the differences of the sum of the genes from 1 and the differences of the sum of $\sqrt{\text{CC..}} + \sqrt{\text{cc..}}$ from 1 are of very great importance (comp. i.a. Bernstein 1).

Table 4

Chromosome	*Gene Wiener's notation* 1956 (11, 12)	Gene Our notation	Swedish Our material 1955 2,743 adults	Swedish Our material 1949 2,768 adults	Danish Gurtler et Henningsen (3) 5,500 adults	British Race et al (7) 2,000 adults	U.S.A. Unger New York (10) 2,438 whites	Swedish Our material 1955 2,743 adults Proportionally equalized frequencies
cde	r	[ρ]	0.380395	0.385746	0.388072	0.391791	0.380789	0.380777
Cde	r′	[γ]	0.006646	0.013754	0.012677	0.010080	0.014179	0.006653
cDe	R^0	[δ]	0.017349	0.017863	0.018130	0.025941	0.030307	0.017366
cdE	r′′	[ε]	0.004313	0.007446	0.007149	0.011942	0.009083	0.004317
CDe	R^1	[γδ]	0.425836	0.415753	0.421932	0.417785	0.414843	0.426264
cDE	R^2	[δε]	0.163196	0.158918	0.146462	0.139291	0.157018	0.163360
CdE	r^y	[γε]						
CDE	R^z	[γδε]	0.001262	?	0.000627	0.001908	?	0.001263
		1 —		(1 —	1 —	1 —	(1 +	
	Σ		0.001003	0.000520)	0.004951	0.001262	0.006219)	1.000000
	$\sqrt{\overline{CC..}}$		0.427434		0.429185	0.434741		
	$\sqrt{\overline{cc..}}$		0.565155		0.559732	0.568771		
		1 —			1 —	1 +		
	Σ		0.007411		0.011083	0.003512		

Our material 1955, the Danish material (Gürtler and Henningsen 3) and the English material (Race et al. 7) in table IV give in this respects sums, which have a highly satisfactory equivalence to 1.

The equalizing of the gene-sum to 1 can, by such small differences, easily be carried out by the simple proportional division of the differences. The more complicated methods may be necessary in case of somewhat larger differences but an equalizing where too large differences occur may almost be considered a falsification of the material.

CD^u and *D*^{u}*E*.

CD^u and D^{u}E respectively, indicate in the following bloods which, by routine tests, reacts as C (usually Cc) and E (usually Ee) but give positive antiglobulin test for D^u, i.e. D^u indicates only a markedly low grade D^u. Even with this limitation the concept D^u is a little vague.

D^u is by Wiener indicated by the use of a German capital ℜ in different combinations.

By direct calculation on differences between our two materials 1949 and 1955 we get the gene frequencies:

$[\gamma$ actual$] = 0.6646\%$, $[\gamma\delta^u] = 0.7319\%$, $[\varepsilon$ actual$] = 0.4313\%$, $[\delta^u\varepsilon] = 0.3227\%$.

The latitude of error of these figures is, of course, very large.

In a paternity material of 78 non-selected, non-related adults, apparent C or E, investigated 1955-1956 (about half of this material is included in material 1955) we found:

Apparent	C	55	Apparent	E	23
Actual	C	27	Actual	E	16
	CD^u	28		D^{u}E	7

Calculation of these figures in comparison with the gene frequencies of our material 1949 gives:

$[\gamma$ actual$] = 0.675\%$, $[\gamma\delta^u] = 0.700\%$, $[\varepsilon$ actual$] = 0.518\%$, $[\delta^u\varepsilon] = 0.226\%$.

Non-clinical D^u materials are rare.

Rosenfield et al. (9) have a material of white donors in New York:

Apparent C	161	Apparent E	92
Actual C	89	Actual E	73
CD^u	72	D^{u}E	19

Of 628 apparent rh— (= C—c+D—E—) 3 were D^u (= C—c+D^u+E—).

Renton and Stratton (8) have material from Manchester:

Apparent C	34	Apparent E	46
Actual C	23	Actual E	41
CD^u	11	D^{u}E	5

The results arrived at by calculations of the materials above are given in *table V*. Rosenfield's material is compared with the gene frequencies of Unger's material (10)

and Renton and Stratton's material with the gene frequencies of Race's material (7) see table IV.

The results are in rather good agreement with a theory, that D^u partial gene corresponds to an aliquote part of the D partial gene, about the same part of $[\gamma\delta]$ and $[\delta\varepsilon]$ (and probably of $[\delta]$ too). The combination $[\gamma\delta^u] \times [\delta\varepsilon]/[\delta^u\varepsilon] \times [\gamma\delta]$ in the different materials ought, therefore, to be near 1, which in view of the rather small number of samples is tolerably the case. No clear connection to the $[\gamma]$ and $[\varepsilon]$ frequencies is found.

It may perhaps be of some interest to mention that of 4 apparent CC persons (phenotype C+c—D—E—) we found 3 to be CCD^u and 1 actual CC, and that of 3 apparent CcE persons (phenotype C+c+D—E+) we found 1 to be CcD^uE and 2 actual CcE. These bloods were from non-selected, non-related adults. The findings correspond much better to our suppositions of the gene frequencies than could be expected.

From the Clinical Department of our laboratory there is laid forth (Broman 2) a very large *clinical* D^u material:

Apparent C	526	Apparent E	240
Actual C	362	Actual E	224
CD^u	164	D^uE	16

Its CD^u frequency is rather low and its D^uE is extremely low. A coming division of this material in unselected parts and parts of different clinical or technical selection will probably throw light on some D^u problems.

The C^w factor

On the blood group genetical section we do not as a routine-test treat the bloods with pure anti-C^w. In spite of that we have a rather large C^w tested material, but it is in the main a material with large and complicated selection. Only one part of this material is quite free from C^w selection: *all* cases with child homozygous CC.. and alleged father homozygous cc.. or vice versa (« homozygous C paternity exclusions ») are tested with pure anti-C^w too. Our routine anti-C is anti-C+anti-C^w. This part of our material is thus free from C^w selection vis-à-vis the CCD bloods in the population and as the children and these men are non-related one can count them together.

In 256 « homozygous C paternity exclusions » (1950-1955) we found 232 actual CCD men or children and 24 CC^wD men or children (a few of the latter 24 may possibly be C^wC^wD). This gives a frequency of C^w at C locus of about 2.1%, which is of the same order of magnitude as Gürtler and Henningsen's (3) frequency 1.66% and Race et al's (7) frequency 1.29, which are obtained in quite another ways.

That means in our material about 1/20 of the partial gene C. We have not yet

found any bloods of the group C^wc, ($C^w+c+D—E—$) but it is supposed probably that the gene-frequencies $[\gamma^w\delta]$, $[\gamma^w]$ and even $[\gamma^w\delta\varepsilon]$ and $[\gamma^w\varepsilon]$ have the same proportion to $[\gamma\delta]$, $[\gamma]$ and even $[\gamma\delta\varepsilon]$ and $[\gamma\varepsilon]$ respectively (by δ I here mean both actual δ and δ^u).

The CDE chromosome (the $[\gamma\delta\varepsilon]$ gene) and other rare Rh genes

In our basis material of 2,743 bloods there were only 3 cases of CCDE bloods. The calculation of the frequency of the $[\gamma\delta\varepsilon]$ gene to 0.1262% thus has a very limited security, but the value found lies about in the middle between Gürtler and Henningsen's (3) frequency 0.0627% (unequalized) and Race et al's (7) frequency 0.1908% (unequalized). The order of magnitude corresponds well to our experiences in other respects.

In one case of our total paternity material we found the rare $[\gamma\varepsilon]$ gene, the CdE chromosome. It was a secondary finding to an alleged CcE father. The man's mother was rh- and his father CCDE. The child's mother was CcD and the child CCD. The investigation thus gave an exclusion of the alleged father's paternity. The statistical confirmation of the alleged paternal « grandfather's » paternity to the alleged father however was magnificant. This secondary finding of $[\gamma\varepsilon]$ gives no valuable possibility of judging the frequency of this gene. In spite of that a rather tolerable statistical judging of the « grandfather's » relative paternity probability to his son can be made with help of the known frequency of CCDE in the population. The group CCDE can be calculated to give about 42% of the $[\gamma\varepsilon]$ genes, and as the frequency found of CCDE in our material is 1/917 the « relative probability of paternity » for the « grandfather » in comparison with a random man can be supposed to be about 385/1.

Some diverging types of the C factor have been found in isolated cases also in our material. For population statistics they have not yet any great importance. They make however special technical precautions in cases of « homozygous C paternity exclusions » necessary, i.e. the use of several anti-C, antiglobulin tests for c and single and double dosage tests.

We have not seen any certain cases of diverging E factors in our paternity materials.

The Rh gene frequencies as used in practice

As most probable values for the mean frequencies of the Rh genes in Sweden we use the following figures, calculated on our material 1955 (2,743 adults). The genes are proportionally equalized to a sum of 100%.

$[\varrho]$ = 38.078%
$[\gamma]$ = 0.665%
$[\delta]$ = 1.737%
$[\varepsilon]$ = 0.432%

Table 6

	Absolute Our mat. 1932-35 4,000 adults	Frequency Our mat. 1932-35 4,000 adults	$(o-e)^2/e$ old mat. + $(o-e)^2/e$ new mat.	Absolute Our mat. 1954-55 1,677 adults	Frequency Our mat. 1954-55 1,677 adults	
o	1,509	0.37725	0.0023	634	0.3780	
A_1	1,472	0.36800	0.1959	604	0.3602	
A_2	422	0.10550	0.7681	191	0.1139	
B	422	0.10050	0.0014	168	0.1002	
A_1B	138	0.03450	0.0546	60	0.0358	$\chi^2 = 1.4777$
A_2B	57	0.01425	04554	20	0.0119	5 d.f.
Bernstein's gene-sum	1 + 0.00065			1 + 0.00020		
M	1,359	0.33975	2.0962	529	0.3154	
MN	1,925	0.48125	0.5834	833	0.4968	$\chi^2 = 3.1838$
N	716	0.17900	0.5042	315	0.1878	2 d.f.
$1/\sqrt{M} + 1/\sqrt{N}$	1 + 0.00597			1 − 0.00504		
$2 \times 1/\sqrt{M} \times 1/\sqrt{N}$	0.49322			0.48675		

$[\gamma\delta]$ = 42.626%
$[\delta\varepsilon]$ = 16.336%
$[\gamma\delta\varepsilon]$ = 0.126%

$[\gamma\delta]$ resp. $[\delta\varepsilon]$ we divide approximatively:

$[\gamma\delta$ actual],	about 40%	42.626%
$[\gamma^{w}\delta]$,	about 2%	
$[\gamma\delta^{u}]$,	about 0.7%	
$[\delta\varepsilon$ actual],	about 16%	16.336%
$[\delta^{u}\varepsilon]$,	about 0.25%	

Regarding the A_1A_2BO system and the MN system we have a large and in detail statistically analyzed material from the years 1932-1935. For particulars of this material e.g. the calculation and equalizing of the gene frequencies I refer to Jonsson (4, 5).

In consequence of the latest war a rather large number of refugees have settled in Sweden and a certain degree of change as to the actual blood group frequencies in the population could be suspected. For this reason I worked up new material from the end of 1954 and the first part of 1955. *Table VI* gives our old and our new material.

The differences according to the A_1A_2BO system are of no importance at all. In the MN system the differences are a little greater but not significant.

It must thus be justifiable still to use the following equalized gene frequencies, calculated on our material 1932-1935, 4,000 adults.

		Our notation:	
O gene	r	$[\omega]$	61.421% ± 0.624%
A_1 gene	p_1	$[\alpha_1]$	22.756% ± 0.526%
A_2 gene	p_2	$[\alpha_2]$	8.059% ± 0.375%
B gene	q	$[\beta]$	7.764% ± 0.305%

$[\alpha_1]/[\alpha_2] = 2.824 \pm 0.138$.

M gene	m	$[\mu]$	58.0375% ± 0.7802%
N gene	n	$[\nu]$	41.9625% ± 0.7802%

As the misuse of α and β as names of agglutinines has now fortunately almost been given up to the advantage of the anti-A and anti-B type of nomination, it seems convenient to use the corresponding Greek letters as nomination for the genes in the A_1A_2BO system too. The old p q r nomenclature is in any case very unsatisfactory nowadays.

The P system

In *table VII* there is given an older and a newer P material. All bloods are tested for agglutinability with one human anti-P and one horse anti-P and *all* bloods are controlled with an absorption test too.

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The differences between the two materials are quite insignificant. We use the gene frequencies obtained on the sum of the materials, 2,682 adults:

Table 7

	Absolute Our mat. 1946-49 1,005 adults	Frequency Our mat. 1946-49 1,005 adults	Absolute Our mat. 1954-55 1,677 adults	Frequency Our mat. 1954-55 1,677 adults	Absolute Our mat. Σ 2,682 adults	Frequency Our mat. Σ 2,682 adults
P+	753	0.7493	1,288	0.7680	2,041	0.7610
p—	252	0.2507	389	0.2320	641	0.2390

		Our notation: (provisional)	
P+ gene	P	[π+]	51.11% ± 0.842%
P— gene	p	[π—]	48.89% ± 0.842%

A certain idea of the variation in strength as to the P+ reaction is obtained by the following division of our older material in regard to agglutinability with a good horse anti-P:

p—	25.07%.
P+ negative agglut.	1.89%.
P+ weak agglut.	2.49%.
P+ medium agglut.	29.05%.
P+ strong agglut.	41.49%.

Total 1,005 adults.

As to the variation in strength of the P+ reaction in a material of twins compare Jonsson (6).

We have not yet any unselected Kell, Lewis, Duffy or (MN) Ss materials large enough for population statistical use.

Summary

Mean frequencies of the Swedish blood group genes of the A_1A_2BO, MN, P and Rh(CcDE) systems are given with special regard to the C^w and D^u factors. The frequencies are calculated from materials of non-related, adult persons, mothers and alleged fathers in paternity cases, which materials must be regarded as free from any clinical or other influencing blood group selection.

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RIASSUNTO

Sono riportate le frequenze medie in Svezia dei geni dei gruppi sanguigni dei sistemi A_1A_2BO, MN, P ed Rh (CcDE) con particolare riguardo per i fattori C^w e D^u. Le frequenze vengono calcolate in base a materiali di persone adulte non consanguinee, madri e supposti padri in casi di discussa paternità, materiali che vanno considerati esenti da qualsiasi selezione clinica o che comunque influenzi i gruppi sanguigni.

RÉSUMÉ

L'Auteur rapporte les fréquences moyennes en Suède des gènes des groupes sanguins des systèmes A_1A_2BO, MN, P et Rh (CcDE), avec regard spécial aux facteurs C^w e D^u. Les fréquences sont calculées sur la base de matériels composés de personnes adultes non-consanguines, (mères et pères en cas de parentage disputé), matériels que l'on peut considérer non-sélectionnés par aucun facteur clinique ou autre qui puisse influencer les groupes sanguins.

ZUSAMMENFASSUNG

Es werden die Durchschnittshäufigkeiten der Gene der Blutgruppensysteme A_1A_2BO, MN, P und Rh (CcDE) in Schweden aufgeführt unter besonderer Berücksichtigung der Faktoren C^w und D^u. Die Häufigkeiten wurden auf Grund eines Materials nicht blutsverwandter erwachsener Personen berechnet, d.h. Mütter und vermutliche Väter bei umstrittenen Vaterschaftsfällen; es handelt sich also um ein Material, das jegliche klinische oder andere die Blutgruppen beeinflussende Auslese ausschliesst.