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Rh BLOOD GROUP SYSTEM IN TURKEY*

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Because of the absence of original data concerning the Rh blood group system in Turkey, for the benefit of researchers interested in the human blood groups field, serological results obtained in Hacettepe University Hospitals' Blood Center between 1980 and 1996 have been evaluated for the first time in this paper. During the study, 581,606 people were evaluated for Rho (D) positivity and negativity. In addition, 5,600 people from different parts of Turkey were screened for the five major antigens (D, C, E, c, e) of the Rh blood group system and, according to the results, various gene frequencies and most likely genotypes were calculated. Results clearly show that the Rh blood group system in Turkey is completely, in line with that of the Caucasians.
Key words: Rh blood group system, gene frequencies, most likely genotypes.

The discovery of the Rh blood group by Landsteiner and Wiener[1] in 1940, which must be considered with the work of Levine and Stetson[2] in 1939, was undoubtedly the most important event in the blood group field since the discovery of the ABO system forty years before. After A and B antigens of the ABO system, Rho (D) antigen is without a doubt the most clinically important antigen of the red cell antigens.

The considerable clinical importance of the Rh blood group system arises from the fact Rh negative individuals are at risk of producing anti-Rh antibodies by entering Rh positive red cells into the circulation by either transfusion or transplacental hemorrhage. The formation of anti-Rh antibodies is potentially very serious with respect to hemolytic disease of the newborn and hemolytic transfusion reactions.

Because of the impressive complexity of the Rh blood group system, this paper concentrates on giving precise common information and commonly encountered Rh genotypes and phenotypes in Turkey, without exhaustive theoretical considerations.

Material and Methods

We tested 581,606 people, including volunteer blood donors and patients from the wards requiring blood transfusion for routine ABO and Rh (D) grouping. D positive and D negative frequencies were evaluated in this group.

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We screened 5,600 people, including randomly selected donors, individuals subjected to paternity tests; patients with natural or immune irregular antibodies in their serum; donors for newborn babies suffering from hemolytic disease due to Rh or subgroup incompatibilities, and their parents; and patients with autoimmune hemolytic anemias with warm antibodies for the five major (D, C, E, c, e) Rh antigens.

The regular tube method was employed and both saline-reactive and rapid tube test anti-sera from Dade and Organon Teknika Corp. were used for the screening of Rh_0 (D), rh'(C), rh"(E), hr'(c) and hr"(e) antigens[3].

According to the results and gene frequencies, and due to the complexity of the Rh system, only first guesses were taken under consideration to calculate the most likely genotypes. Results were expressed in accordance with both Wiener[4] and Fisher-Race[5] nomenclatures.

Since our patients and donors were from all regions of the country, we believe that these results reflect data concerning the Rh blood group system in the Turkish population.

Results

From a known gene frequencies in any blood group system, the genotype (or phenotype) frequencies can readily be calculated. As Table II shows, the most common Rh gene complexes in the Turkish population are CDe (R_1) and cde (r). Thus, the three most common Rh genotypes expected are CDe/cde (R_1 r), with a frequency of 2 x (0.4200 x 0.3850) = 0.3234 or 32 percent; CDe/CDe (R_1 R_1) with a frequency of (0.4200 x 0.4200) = 0.1764 or 17.6 percent; and cde/cde (r r) with a frequency of (0.3850 x 0.3850) = 0.1482 or 14.8 percent.

Table I: Major Rh Antigen Frequencies

Antigens	Positivity in Turks %	*Positivity in Caucasians %	**Positivity In Basques %	**Positivity in Orientals %
D	85.3	85	60-8	99-100
C	69.6	70		
E	29.7	30		
c	79.05	80		
e	95.63	98		

* Issit et al.[6]

** Mourant et al.[7]

Table II: Frequencies of Some Rh Genes in Turkey (5,600 people)

Wiener	Fisher-Race	Frequencis %
Allele	Gene Combination	
R_1	CDE	0.42
r	cde	0.385
R_2	cDE	0.16
R_0	cDe	0.0115
R^w_1	c^wDe	0.01
r'	Cde	0.0055
r"	cdE	0.0055
R_2	CDE	0.0025

Table III: Comparison of Some Gene Frequencies in Different Countries

Wiener	Fisher-Race	Turkey	England*	Sweden**	USA***			
					Whites	Blacks	Orientals	Indians
R_1	cDE	0.42	0.4076	0.40356	0.42	0.17	0.7	0.44
r	cde	0.385	0.3886	0.38205	0.37	0.26	0.03	0.11
R_2	cDE	0.16	0.1411	0.16701	0.14	0.11	0.21	0.34
R_0	cDe	0.0115	0.0257	0.01855	0.04	0.44	0.03	0.02
R^w_1	C^wDe	0.01	0.0129	0.011983	—	—	—	—
r'	Cde	0.0055	9.0098	0.00498	0.02	0.02	0.02	0.02
r"	cdE	0.0055	0.0119	0.00295	0.01	0	0	0.01
R_2	CDE	0.0025	0.0024	0.00082	0	0.01	0.01	0.06
r^w	C^wde	—	—	0.00034	—	—	—	—

* Race et al.[6]
** Heiken and Rasmuson[8]
*** Mourant et al.[7]

The similarity of frequencies seen in Turkey, England, Sweden and in the whites of the USA is quite impressive.

Because of the complexity of the Rh system and the gradual multiplicity of probable genotypes, there might be some slight differences between the expected frequencies calculated from gene frequencies and those observed in the population.

The overall frequencies of the most likely Rh genotypes and phenotypes calculated in 5,600 people are shown in Table IV.

Table IV: Frequencies of Rh Genotypes (Phenotypes) in 5,600 Turkish People

Reactions with anti-								
D	C	E	c	e	Cw	Fisher-Race	Wiener	Frequencies %
+	+	o	+	+	o	CDe/cde	R_1 r	34.48
+	+	o	o	+	o	CDe/CDe	R_1 R_1	17.7
o	o	o	+	+	o	cde/cde	r r	14.7
+	+	+	+	+	o	CDe/cDE	R_1 R_2	14.06
+	o	+	+	+	o	cDE/cde	R_2 r	11.96
+	o	+	+	o	o	cDE/cDE	R_2 R_2	3.45
+	o	o	+	+	o	cDe/cde	R_0 r	0.85
+	o	o	+	+	+	C^wDe/cde	R^w_1 r	1.17
o	+	o	+	+	o	Cde/cde	r' r	0.28
o	o	+	+	+	o	cdE/cde	r" r	0.14
+	+	+	+	o	o	CDE/cDE	R_2 R_2	0.14

As can be seen in the table, the, frequency of the most common genotype or phenotype, CDe/cde (R1 r), is 34.48 percent; frequencies of the next most common phenotypes in order are: CDe/CDe (R1 R1) 17.70 percent; cde/cde (r r) 15.22 percent (including Cde/cde and cdE/cde); CDe/cDE (R1 R2) 14.06 percent; cDE/cde (R2 r) 11.96 percent and cDE/cDE (R2 R2) 3.45 percent. These together account for approximately 96.87 percent of the total Rh phenotypes of the screened Turkish population.

Frequencies of some common Rh genotypes in Turks and some Caucasians are shown in Table V.

Discussion

The complex nature of the Rh blood group system has become even more complicated by the discovery of apparent "compound antigens", "deleted antigens" and numerous variants. These clear and detailed accounts will not be repeated here. But, it is convenient to consider the antigens 'C' and 'c', 'E' and 'e' and 'D' and 'd' as alternatives or antithetical expressions of genetic determinants which appear to reside within a single locus or genetic region of chromosome 1[12,13].

Table V: Some Common Rh Genotypes in Turks and Caucasians

Fisher-Race	Wiener	Turks (%)	English* (%)	USA Whites** (%)
CDe/cde	R_1 r	34.48	34.89	35
CDe/CDe	R_1 R_1	17.7	18.51	19
cde/cde	r r	14.7 (15.22)	15.1	15
CDe/cDE	R_1 R_2	14.06	13.34	13
cDE/cde	R_2 r	11.96	12.67	12

** Mollison, et al.[10]

** Harmening[11]

Accordance of frequencies between Turks and Caucasians is remarkable.

Five antigenic determinants (D, C, E, c, e), which are the products of genes, are situated at three distinct but closely linked loci on the chromosome. The three loci are so closely linked that crossing-over would very rarely occur. They are codominantly inherited as a unit or gene complex, and a pair of chromosomes may be heterozygous or homozygous according to the genes inherited from each parent. Both the gene and the red cell antigens are given the same symbol, and the 'd' gene is considered to be a "silent" gene or amorphous.

As seen in Table I, the frequency of the different Rh antigens varies widely in different parts of the world. For example, the frequency of Rh negatives (D negative) varies from 20-40 percent in Basques to 0-1 percent in Orientals, American Indians and Eskimos.

There are now several different theories to explain the genetic control under which Rh antigens are synthesized. Two of these theories were introduced at the time of early discoveries in the Rh system. One postulated by Wiener is that genetic control is under the influence of a single gene, producing an antigenic complex of alleles. The other, Fisher-Race's theory, suggest that Rh antigens were produced under the control of three sets of allelic genes at very closely linked loci. A third theory with numerical terminology was introduced in 1962[14]. Because of their basic differences, each employed a different terminology to describe the antigens and antibodies of the system.

The net result is that today most workers use a hybrid terminology that is based on three distinct original suggestions and on new theories of genetic control. However, since the hybrid terminology is so well established, despite the objections, it is likely to remain in use for many years.

As mentioned before, Rho (D) antigen, due to its strong antigenicity and high frequency, is the most clinically important antigen and, despite being thirty times

weaker than the D antigen, the hr' (c) is the second most clinically important antigen of the Rh system.

As for the antibodies of the Rh system, they are immune antibodies in general. Because of the antigenic potency and the population frequencies of the antigens, the anti-D antibody is of major importance with respect to hemolytic disease of the newborn and hemolytic transfusion reactions.

After anti-D, anti-c is the most important immune Rh antibody from the clinical point of view. Anti-c is often involved, especially in delayed hemolytic transfusion reactions and the hemolytic disease of the newborn.

Anti-C alone, i.e. without anti-D, is quite rare.

Anti-E is more common than anti-c, and is frequently a naturally occurring antibody. Rare examples of anti-e, like anti-c, are found only as an immune antibody[10].

In our study, due to the inadequate number of fully screened people for Rh genotypes (phenotypes), rare Rh deleted red cells, such as -D-, cD- and Rh since the D^u phenotypes, arising from either a weakly reactive antigen or suppression of a completely normal gene by the other alleles, are encountered rarely, frequency of this Rh variant has not been calculated.

Some rare Rh genotypes were also encountered during the screening. C^wDe/cde (R_1^w r) genotypes were evaluated from two cases of hemolytic disease of the newborn, due to anti-C^w.

Human blood groups could be evaluated as reliable anthropological markers. The cDE/cde (R_0, r) genotype and cDe (R_0) gene complex, which are common in Blacks as African markers, quite rare (0.85%) in the native Turkish population. But, in Eti Turks, a small group living in Southern Anatolia, besides some African blood group markers, such as Fy (a- b-), Le (a- b-), jk^a and P_1, R_0 marker was found quite high (6.89%), addition to the high frequency of Hb S[15].

The relation of autoimmune hemolytic anemias with warm autoantibody and the Rh blood group system is well documented[10]. One of the cDe/cde (R_0, r) genotypes was encountered during the studies of an autoimmune hemolytic anemia due to auto anti-D[15].

Thus, in conclusion the Rh blood group system in Turkey bears a great similarity with the Caucasian population in Europe and the USA, according to the data evaluated from 5,600 native Turkish people. No relation has been observed with the other populations, including Blacks, American Indians, Orientals and Eskimos.

We believe this original data will be a beneficial guide to researchers interested in human blood groups in Turkey.

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