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RHD GENE CARRIERS AMONG SEROLOGICALLY D NEGATIVE DONORS: ALLELES AND POPULATION FREQUENCY IN CENTRAL EUROPE

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Background: Lack of the RHD gene is the predominant cause for the D neg. phenotype in Europeans. A much less frequent cause is the absence or very low expression of D antigen albeit the RHD gene is present. The lack of D antigen detectable by routine serological methods may be due to weak D types, to alleles demonstrated as D positive only by adsorption/elution (DEL), to alleles without any D antigen expression or to D chimeras. DEL positive red blood cell (RBC) units are known to pose a potential risk for anti-D immunization in D negative recipients.

Aims: This ongoing study was designed to gather information on the potential risk posed by DEL RBC units among the D neg. RBC units, to clear the D neg. donor pool from DEL carriers and to develop suitable molecular diagnostic strategies.

Methods: From Jan 2002 until Dec 2005 the presence of the RHD gene was investigated in first time donors in Southwestern Germany typing D neg. by serological methods including the indirect antiglobulin test. Samples were tested in pools of 20 donors for RHD intron 4 by PCR-SSP. RHD gene positive samples were further investigated by PCR-SSP and nucleotide sequencing. The DEL phenotype was determined by adsorption/elution.

Results: Among 29,823 first time donors, 61 were RHD gene carriers. New D neg. alleles were: RHcE(1-3)-D(4-10) (n=4), RHD(343delC) (n=2), RHD(IVS3+2T>A) (n=2), RHD(660delG) (n=1), RHD(712delG) (n=1), RHD(785delA) (n=1), RHD(Y269X) (n=1) and RHD(R318X) (n=1). New DEL alleles were: RHD(147delA;IVS1+6delA) (n=2), RHD(93-94insT) (n=1) and RHD(L153P) (n=1). RHD(V56M, W90X) (n=1) was a new allele not tested for DEL. 7 alleles were known: RHD(IVS3+1G>A) (n=11), RHD-CE(8-9)-D (n=11), RHD α (n=8), RHD(M295I) (n=7), RHD(K409K) (n=2), RHD(W16X) (n=2) and RHD(1252-53insT) (n=1). The molecular evaluation of 1 sample is pending. Altogether D negative types comprised 11 different alleles, and the DEL types comprised 7 different alleles. No chimeras were detected.

Conclusions: Among D negative donors in Germany the prevalence of RHD gene carriers was 1:489, of whom 43% were DEL. The potential immunogenicity of DEL RBC units is known and at least the transfusion to girls or women of childbearing age should be avoided. Hence, DEL positive donors are eliminated from the D neg. donor pool at our institution. The serologically D neg. phenotype among RHD gene carriers in Europe may be attributed to a large number of different RHD alleles: 19 different alleles were encountered in this study and more are known. In contrast, the D neg. phenotype in Asians is often associated with the DEL allele RHD(K409K) and in Africans with RHD α and Ccde. As a consequence, different diagnostic approaches may be required if serologically D neg. carriers of the RHD gene are investigated in populations of variant ethnic backgrounds.