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Vox Sanguinis

RHD DNA screening for weak D, DEL and D+/– 'chimeras'

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Three recent publications on the presence of weak D and DEL among apparently D-negative individuals and the existence of D+/– chimeras with minute D-expression [1–3] have rekindled the discussion on their immunogenicity that resulted in a comprehensive survey among transfusion specialists published in *Vox Sanguinis* [4].

As the definition of weak D is mainly important for the typing of blood donors, most statements in the *Vox Sanguinis* survey reassure us that the currently used routine serological methods for weak D determination are satisfactory, given the low prevalence of immunizations caused by small amounts of D antigen as found in donor blood from weak D, DEL or D+/– chimeric individuals, and given the cost/benefit ratio of molecular *RHD* screening methods.

To satisfactorily resolve the uncertainties that have arisen, however, studies that have already been performed will most likely not be sufficient. Most of these studies have only focused on the Central European Caucasian population. As already stated by Gassner *et al*., more extensive population genetic data will have to be taken into consideration, which can only be delivered by a series of geographical spot checks [2]. Such pilot studies are planned by the transfusion centres of Amsterdam, Warsaw, Bern and Shanghai (personal communication with Hustinx Hein, Schweizerisches Rotes Kreuz, Bern, Switzerland; and Li Qin and Zhu Zi Yan, Shanghai Blood Centre, PR China).

Gassner *et al*. did not make a claim for mandatory *RHD* screening of D-negative donor samples, simply because not enough is currently known [2]. What is known, on the other hand, is that a small percentage of all Ds may well be positioned in between clear-cut D positivity and negativity, primarily depending on the number of D molecules on the red blood cell surface. Although small in percentage terms, this 'in-between segment' is highly heterogenous consisting of most D categories, partial Ds and all weak Ds and DELs [1–3,5]. These Ds cannot be serologically characterized by using available routine anti-D antibodies, which leaves some of them (deliberately) 'overseen' and – scientifically spoken – misinterpreted as D-negative. Accepting these facts, the only way to accurately characterize the 'in-between segment' is via the *RHD* DNA screening and typing and by the employment of finest serological methods.

The knowledge resulting from population studies will show if the call for mandatory *RHD* DNA screening and typing in routine procedures is legitimate. The decision will finally also depend on economic aspects, and with respect to these, it should be considered that DNA typing will play an important role in future standard diagnostic workflow in general. The addition of various genotypic parameters (e.g. other polymorphisms relevant for blood groups, platelet and granulocyte antigens and immune response) seems inevitable and it will probably reduce the costs of singular tests dramatically, which could open new opportunities for high throughput diagnostic typing in blood transfusion services.

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