The challenge and paradox in serology RhD typing for blood donors and patients

Catherine A. Hyland

Research and Development, Australian Red Cross Blood Service, Queensland, Australia

Selecting reagents for RhD typing poses an ongoing challenge and is a paradox for transfusion medicine. Red cells from the majority of blood donors and patients are readily defined as D positive or D negative. However, a spectrum of partial D, weak D or very weak (DEL) red cell phenotypes are found in individuals who carry *RHD* genetic variants. The challenge in typing blood donors is to select appropriate typing reagents and testing strategies with sufficient sensitivity to detect these partial and weak D types. Ideally blood donations from such individuals should be labelled as D-positive.

The paradox arises in patient management where individuals whose red cells carry partial and weak D antigen types are managed as D-negative. Hospital serology in these situations is detuned to type these patients as D negative[1-3]. This is potentially important for pregnant women to ensure those with partial D antigen phenotypes receive anti-D prophylaxis to guard against haemolytic disease of the foetus and newborn (HDFN). RhD immunisation has been reported in carriers of partial D phenotypes and can be associated with HDFN.

One further challenge arises because the frequency of partial and weak D types varies for different populations. Indeed, the advent of molecular typing has provided a basis for classification for the range of alleles present in different populations[4-6]. However, molecular typing as an adjunct to serology is resource intensive and, currently restricted to specialised reference laboratories.

In this edition Kulkarni *et al.* report a serological study to resolve 60 cases, in an Indian population, referred because of discrepant RhD serological typing[7]. Extended serological testing using a commercial panel, comprising 12 monoclonal antibodies, defined partial and weak D types present for 93% (56/60) of the samples.

In addition to providing insight into the range of variants present, the authors observed distinct reactivity patterns for a subset of monoclonal antibodies. For all samples one monoclonal antibody consistently typed all samples as D negative and three monoclonal antibodies consistently typed all samples as D positive.

The authors propose that a streamlined testing strategy using this subset of monoclonal antibodies provides a strategy for resolution of samples with D typing discrepancies. For this case series, this strategy provided an evidence base for D assignment required to ensure safe clinical management for both patients and donors. There are partial D and weak D types, not represented in this cohort, which would have been accurately signalled on the basis of reactivity patterns different from the one observed. The authors show these among the patterns in Table II. It would be appropriate to apply extended serological and molecular typing to such samples.

As molecular typing becomes more readily available, a combination of enhanced serological and molecular typing strategies promises to overcome the ongoing challenge and paradox in RhD typing for donors and patients. It is therefore important to document evidence for the range of partial and weak D types in various population groups and document evidence for the performance of typing reagents. Accumulated evidence of the type presented by Kulkarni *et al.*, will contribute to selection of optimised serological and molecular typing strategies in the future.

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Correspondence: Catherine A. Hyland
Australian Red Cross Blood Service
Research and Development Division
Level 1, 44 Musk Avenue, Kelvin Grove
Queensland, 4059, Australia
e-mail: CHyland@redcrossblood.org.au