

How easy is it to identify common antibody mixtures using only one antibody screen and panel combination?

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Introduction

35/106 (33%) haemolytic transfusion reactions reported to SHOT (2012-2015)¹ involved mixtures of antibodies.

In March 2017, UK NEQAS (BTLP) distributed a sample containing anti-c+K. 26/353 (7.5%) UK and Republic of Ireland laboratories were unable to complete antibody identification and submitted screen and panel antigrams to support their conclusion; the suitability of these to fully identify anti-c+K varied by supplier. Whilst the antigrams submitted in response to the March exercise were not representative of all suppliers (as submissions were only made by laboratories who could not complete their investigation), interesting differences were noted.

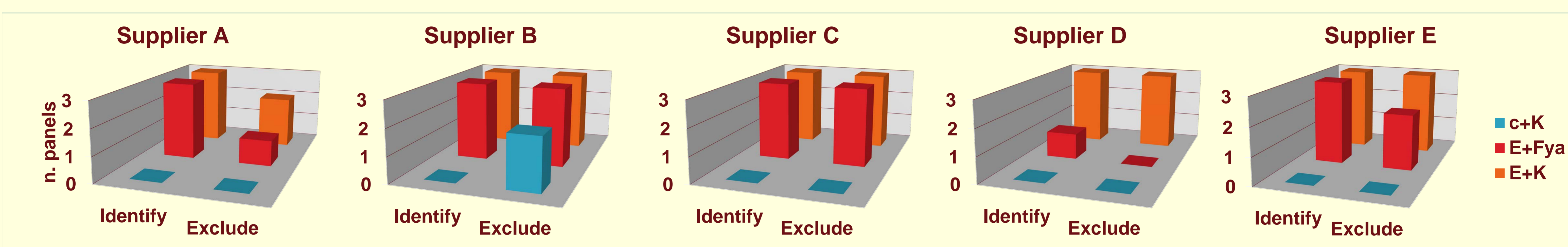
Subsequently, suppliers of reagent red cell panels to the UK were invited to submit antigrams to allow a more representative comparison, and five out of six responded.

Methods

For each supplier, the three most recent antibody panels were paired with a 3-cell screen with the closest expiry. These combinations were used to determine whether some common antibody mixtures (anti-c+K, anti-E+Fy^a, and anti-E+K) could be positively identified by IAT (and enzyme where required), and all common clinically significant antibodies excluded without the requirement for further cells. An enzyme IAT panel was not considered part of a first line panel.

Positive identification and exclusion of antibodies was based on the 2012 BSH guideline on Compatibility Testing².

Results



Anti-c+K

No combination allowed positive identification of anti-K in the presence of anti-c, although all panels had one c-, K+ cell, which would indicate the presence of an additional antibody.

Only 2/15 combinations (both from Supplier B) allowed exclusion of clinically significant antibodies.

Chart legend

Identify = Both antibodies positively identified using BSH criteria
Exclude = All clinically significant antibodies excluded using BSH criteria

Anti-E+Fy^a

All combinations allowed the identification of anti-Fy^a in the presence of anti-E, but 6/15 did not allow exclusion of other clinically significant antibodies, even where enzyme treated cells were used. 9/15 combinations did not allow identification of anti-E, which was masked by anti-Fy^a in 4/9 (3 from one supplier). Anti-E was always identifiable by enzyme where available.

Anti-E+K

All three combinations from each supplier allowed positive identification of anti-E and anti-K.

All combinations allowed exclusion of clinically significant antibodies apart from one from Supplier A which did not allow exclusion of anti-S.

Principles applied (BSH Guideline² section)

Antibody screening cells and antibody panel cells were used together for identification and exclusion. (6.2.2)

Positive reactions vs. two antigen positive cells (negative for antigens corresponding to antibodies not excluded), and negative reactions vs. two antigen negative cells were required for positive identification. (6.2.4)

The antibody investigation was deemed complete if both antibodies could be identified and all clinically significant antibodies could be excluded. Exclusion of antibodies to low frequency antigens (e.g. Kp^a) or those of low clinical significance (e.g. Le^b). (6.2.5)

A homozygous cell was required for exclusion of Jk^a, Jk^b, Fy^a, Fy^b, S, and s antibodies, and only one cell was required. (6.2.6)

Rh antibodies were excluded based on negative reactions with enzyme treated cells. (6.2.7)

Conclusions

This limited study demonstrated variation in effectiveness of screening and 'first-line' panel cells from different suppliers in identifying common antibody mixtures. It may be useful to compare the antibody panel production specifications used by manufacturers, to determine the most suitable reagents for use locally to enable rapid antibody identification, and avoid unnecessary delays in blood issue. A full review of this nature may be beneficial to laboratories prior to selection of a supplier, especially where technology limits the choice of reagent red cells available.

The frequency of antibodies seen in clinical laboratories may be different, depending on patient type and local population. Manufacturers often have to satisfy the requirements of a global market and cannot always tailor their products to the Red Book Guidelines³.

The probability of completing antibody identification is improved with a well designed screen and primary panel combination, and with access to an enzyme panel and/or additional IAT panels; however, it is never possible to guarantee that antibodies will not be masked in some mixtures. The solve rate for anti-E+Fy^a was improved from 6/15 combinations to 13/15 when an enzyme panel was included as part of the testing.

39 antibody identification errors were made due to mis-interpretation during the last 6 UK NEQAS exercises that included antibody mixtures (error rate 1.4%). A full understanding of the characteristics of red cell antibodies/antigens and application of systematic exclusion/inclusion processes, supported by robust training and competency assessment, remain essential for successful antibody identification.

References

- (1) Milkins, C., personal communication by email. 28/04/2017.
- (2) British Committee for Standards in Haematology (BSH) (2012): C Milkins, J Berryman, C Cantwell, C Elliott, R Haggas, J Jones, M Rowley, M Williams, N Win. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. <http://www.b-s-h.org.uk/guidelines/> (Accessed 14/08/17).
- (3) UK Blood Transfusion Services (2013) Guidelines for the Blood Transfusion Services in the UK. URL <http://www.transfusionguidelines.org.uk> (Accessed 14/08/17).