9. DELAYED TRANSFUSION REACTIONS

Definition
Delayed transfusion reactions were defined in this report as occurring more than 24 hours following a transfusion of blood or blood components. In practice these are almost invariably haemolytic due to the development of red cell allo-antibodies.

This category accounted for 17% of non-infectious hazards reported.

27 initial reports were received (2 fatal) and 23 completed questionnaires were returned.
The data retrieved from the returned questionnaires are shown in Appendix 5.iii.
This chapter highlights the main findings from the 23 completed questionnaires.

Sex	
Males	7
Females	16
Age	
Age range	25 - 87 years
Median age	68 years
Components implicated	No. of cases
Red cells (rbc)	23

In all cases donor (allogeneic) red cells were implicated. The development of 33 newly detectable post-transfusion red cell allo-antibodies was reported in 21 patients.

4 patients were noted to have pre-transfusion red cell allo-antibodies.

In one patient the same antibody (anti Jk^b) found post-transfusion was detected retrospectively in the pre-transfusion sample. Its presence had been suspected pre-transfusion but the urgency of the transfusion left insufficient time for antigen -negative blood to be selected.

A further patient on α-Interferon treatment and with autoimmune haemolytic anemia (AIHA) had pre and post transfusion anti S but it was not clear whether S-negative red cells were selected for the transfusion.

In 2 other patients with pre-existing red cell allo-antibodies (anti E, anti Cw) in whom new allo-antibodies developed it is presumed that appropriate antigen-negative red cells were selected.

Table 12 shows the breakdown of new post-transfusion red cell allo-antibodies according to antigen specificity and Table 13 gives details of these antibodies for individual patients.

Table 12. New post-transfusion red cell allo-antibodies in 21 of 23 patients

Antibody group	Number	Sole antibody
Kidd (Jk)		
Jka	6	5
Jkb	2	
Duffy (Fy)		
Fya	1	
Fy3	1	
Kell		
K	4	1
Kpa	1	
Rhesus		
D	2	1
C	3	1
c	2	1
E	5	1
e	2	1
MNSs		
M	1	
S	2	
Unspecified pan-agglutinin	1	
Total	33	11

Table 13. New red cell allo-antibodies in individual patients

Patient no.	Antibody(ies)
1	D +Jka
2	Jka
3	S+Jkb+Fy3
4	E
5	K+Jkb+Kpa
6	K
7	Jka
8	C+E
9	Jka
10	e
11	Fya+E
12	E+M
13	D
14	E+K
15	Jka
16	C
17	K+C
18	Jka
19	Unspecified pan-agglutinin
20	C+e+S
21	c

Clinical sequelae

Symptoms and signs fell into 3 categories:

- **Group 1** Asymptomatic (± positive direct antiglobulin test(DAT)/spherocytes)
- **Group 2** Falling haemoglobin (↓Hb)/positive DAT/spherocytes (2 of these)
- **Group 3** Jaundice/↓Hb/dark urine ± positive DAT/spherocytes/renal impairment

Information about symptoms and signs was not complete in all cases so only broad conclusions can be drawn.

Group 1

There were 4 patients in this group. Antibody specificities were all Rhesus (E, C+E, e, c). All survived without sequelae.

Group 2

There were 3 patients in this group. Antibody specificities were D+Jka, Jka and c. All survived without sequelae.

A fourth patient reported solely with a positive DAT and spherocytes developed anti Jka and died from underlying trauma.

Group 3

Of the 14 patients in this group, 13 were recorded with jaundice and of these 6 had evidence of intravascular haemolysis. Five of the 14 patients suffered deterioration in renal function. A total of four patients in this group died, two as a result of combined factors of underlying disease and delayed haemolytic transfusion reaction (DHTR) and two as a result of their underlying condition. The antibody distribution and outcome in this group is shown table 14.

Table 14. Antibody distribution and outcome in Group 3 patients

Patient no.	Antibody(ies)	Outcome
3	S+Jkb+Fy3	Survived
5	K+Jkb+Kpa	Died. Haematological malignancy, AIHA and DHTR
6	K	Died. Underlying immunosuppression
7	Jka	Survived
9	Jka	Survived
11	Fya+E	Survived
13	D	Died. Underlying trauma
14	E+K	Died. Trauma and DHTR
15	Jka	Survived
17	K+c	Survived. Mild renal impairment recovered.
19	Panagglutinin and HLA	Survived
20	C+e+S	Survived
22	Pre-existing S and AIHA	Survived
23	Pre-existing Jkb	Survived

No firm conclusions can be drawn but the more severe DHTRs associated with the development of jaundice, including intravascular haemolysis, and renal dysfunction appeared to be associated with non-Rhesus (particularly Kell and Kidd) and/or multiple antibodies. The 2 deaths in which a DHTR was implicated were in this group.

Summary

- There was no evidence of widespread poor practice. In general delayed reactions as a result of the development of new red cell allo-antibodies could not have been prevented as the antibodies were undetectable at the time of the original crossmatch. In one case where an antibody was suspected pre-transfusion there was insufficient time to investigate and crossmatch-compatible, unselected red cells were transfused. Procedural changes recommended in individual hospitals included access to off-site computer records to enable checking of transfusion history (1 case) and increased emphasis on reporting transfusion and obstetric histories (2 cases)

- The onset of DHTRs ranged from 2 to 15 days (median 7 days) and is similar to that reported in the literature[25].

- The antibody types encountered are similar to those previously reported[25].

- There was marked variation in the data given for symptoms and signs and the types of samples taken suggesting a need for standardisation.

- One haematologist was keen to draw attention to the association of AIHA and treatment with α-Interferon, recommending that the DAT should be monitored in patients receiving this treatment.

- The crossmatch sample was usually taken within 48 hours of the transfusion and timing did not appear to be relevant to the development of the reaction.

- Over 50% of reactions were reported to the local Blood Centre but there was a low level of reporting to hospital transfusion committees. As with acute transfusion reactions it is not clear whether this reflects simple lack of reporting or the absence of a suitable forum for discussion of transfusion-related matters.

Recommendations

- A national review of the requirements for samples and investigation of delayed transfusion reactions is recommended.

- The importance of taking full transfusion and obstetric histories should be stressed.

- Access to off-site computer records may alert to pre-existing antibody(ies) not detectable at the time of crossmatch.