9. DELAYED TRANSFUSION REACTIONS

Definition

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

This category accounted for 13% of non-infectious hazards reported.

27 initial reports were received and 27 completed questionnaires were returned. Due to the change in reporting of cases by date when the initial report was received rather than the date of incident (for an explanation please refer to Chapter 6), three cases reported in the 1996/97 Annual Report are also reported here. The data retrieved from the returned questionnaires are shown in Appendix 9. This chapter highlights the main findings from the 27 completed questionnaires.

Sex	
Males	9
Females	18

Age	
Age range	27 - 91 years (1 unknown)
Median age	71

Components implicated	No. of cases
Red cells (rbc)	27

In all cases allogeneic red cells were implicated. The development of 46 newly detectable red cell allo-antibodies was recorded in 27 patients who suffered delayed haemolytic transfusion reactions (DHTR).

There were 2 deaths in this group of patients, 1 from underlying disease and 1 from the combined effects of underlying disease and transfusion complications.

Five patients were noted to have pre-transfusion red cell allo-antibodies and were assumed to have received red cells lacking the appropriate antigen. In 1 of these it cannot be ruled out that pre-existing anti Kna, an antibody not considered to be of clinical significance, may have masked the presence of other allo-antibodies in a multiply transfused patient.

In one patient, a pre-transfusion antibody screen was omitted and immediate-spin cross-match only performed, despite the fact that the transfusion was not an emergency. Multiple red cell allo-antibodies were detected post-transfusion.

In another patient an unspecified antibody to a low frequency antigen was apparently detected pre-transfusion and it was unclear from the records whether this was in fact the anti Jka detected post-transfusion and responsible for the DHTR.

Two patients were previously known to have clinically significant red cell antibodies some years earlier. However, these were not detectable immediately prior to the transfusion, were not disclosed by the patient and the information was not available in blood bank records to guide the selection of appropriate red cells.

In 20 patients the transfusion was said to be routine and in 7 urgent. At least 1 patient and possibly 2 were transfused for iron deficiency anaemia.

Table 15 shows the breakdown of new post-transfusion red cell allo-antibodies according to antigen specificity and Table 16 gives details of these antibodies for individual patients.

Table 15

New post-transfusion red cell allo-antibodies in 27 patients: according to antigen specificity

Antibody group	Number	Sole antibody
Kidd (Jk)		
Jka	17**	9
Jkb	1	
Duffy (Fy)		
Fya	4	2
Kell		
K	3*	
Rhesus		
D	2	2
C	2	
c	3*+	2
E	8+	1
e	1	
MNSs		
M$	1	
S	1	
Lutheran		
Lua	1	
Lewis		
Lea	1	
Weak cold agglutinin$	1	
Total	**46**	**16**

* 1 each previously known but not disclosed

+ 1 each enzyme-only in presence of multiple antibodies, not responsible for DHTR

** 2 possibly present pre-transfusion

$ Unlikely to be of clinical significance

Table 16

New post-transfusion red cell allo-antibodies in individual patients

ID	Antibody(ies)	Comment
1	K + Jka	Anti K known 10 years previously, not disclosed
2	Jka + E	? masked by pre-existing anti Kna
3	E + Jka + Fya	Antibody screen omitted pre-transfusion
4	Jka	? missed as antibody to "low frequency" antigen pre-transfusion
5	Jka	
6	Fya	
7	E + wk cold agglutinin	
8	E + Jka	
9	Jka	Hospital unable to detect post-transfusion (presumed found at reference centre)
10	Jka	
11	Jka	
12	C + E	Pre-transfusion anti S
13`	Jka	
14	D	Primary sensitisation to Rh D in an RhD negative male
15	E + Jka + Lua + Lea	Sequential development of antibodies
16	Jka (+ K later)	Responsible antibody = Jka
17	c	Known 1980, not disclosed
18	Jka	
19	Fya	Pre-transfusion anti K
20	Jka (+ M)	Responsible antibody = Jka. Pre-transfusion anti E + Fya
21	Jka + c + E	Enzyme-only anti c + E
22	Jka + K	
23	Jka	
24	E + Fya + Jkb	Pre-transfusion anti K
25	D	? Primary sensitisation to RhD in a RhD negative male
26	c (+ HLA)	
27	C + e + S	

Clinical sequelae

Symptoms and signs could be divided into 4 categories as follows:

- **Group 1** Asymptomatic (± positive direct antiglobulin test (DAT) ± spherocytes)
- **Group 2** Falling haemoglobin (↓Hb) / positive DAT/ spherocytes (2 of these parameters)
- **Group 3** ↓Hb + jaundice ± positive DAT ± spherocytes
- **Group 4** As group 3 + renal impairment

Group 1
There were 3 patients in this group (cases 1, 19, 22). All survived without sequelae.

Group 2
There were also 3 patients in this group (cases 6, 8, 26) and again all survived without sequelae.

Group 3
There were 17 patients in this group (cases 2, 3, 4, 7, 10, 11, 13, 15, 16, 17, 18, 20, 21, 23, 24, 25, 27) of whom 15 survived without sequelae, 1 died from underlying causes and the outcome in 1 was not stated.

Group 4
There were 4 cases in this group (cases 5, 9, 12, 14) of whom 2 survived with renal failure, 1 died from the combined effects of underlying disease and DHTR and 1 survived without sequelae.

The above results are detailed in Table 17.

Table 17 Grouping of cases by clinical sequelae of DHTR

Group 1		Group 2		Group 3		Group 4	
ID	**Antibody**	**ID**	**Antibody**	**ID**	**Antibody**	**ID**	**Antibody**
1	K + Jka	6	Fya	2	Jka + E	5+	Jka
19	Fya	8	E + Jka	3	E+Jka+Fya	9$	Jka
22	Jka+K	26	c	4	Jka	12$	C+E
				7	E	14	D
				10	Jka		
				11	Jka		
				13	Jka		
				15	E+Jka+Lua+Lea		
				16*	Jka (+K)		
				17	c		
				18	Jka		
				20	Jka (+M)		
				21	Jka (+c+E)		
				23	Jka		
				24	E+Fya+Jkb		
				25	D		
				27	C+e+S		

* Died of underlying illness
+ Died of combined effects of underlying illness and DHTR
$ Survived with renal failure

Analysis of serological information

Limited information could be obtained from analysing the questions on serological methods and in some cases the questions were incompletely answered. The limitations of the current questionnaire have been recognised and the design of serological questions has been revised for the 1998/99 reporting year. Although it is not the intention of SHOT questionnaires to attempt to "police" the methodology used, and whilst no direct links can be established between NEQAS and SHOT data, it is hoped that by improving the quality of the questionnaire design, useful information can be obtained which will complement that obtained by NEQAS exercises.

Antibody screening

Table 18 gives information on the serological methods used for antibody screening in 22 of the 27 reported cases. The data is incomplete for the remaining 5 cases.

Table18
Summary of serological methods used for antibody screening

Screening Method	2 cell screen	3 cell screen	Total
Tube	3	6	9
Column	3	7	10
Tube and column		2	2
Microtitre		1	1
Total	**6**	**16**	**22**

Details of some of the antibody investigations were as follows:

Case 1 Historical anti K not detected pre-transfusion but detected by the same methodology post-transfusion.

Case 2: Anti Kna pre-transfusion could have masked pre-transfusion anti E+Jka in a multi-transfused patient (not shown in above matrix). The anti Kna had been detected previously by the Blood Centre and least incompatible units issued with no ill effects. It is presumed that this practice continued until a change in the strength of some serological reactions alerted the hospital to the possibility of additional red cell allo-antibodies.

Case 9: Anti Jka not detected by hospital post-transfusion despite positive DAT. The case was referred to the local Blood Centre which presumably detected and identified the antibody.

Case 17: Historical anti c not detected pre-transfusion but detected post-transfusion by the same method.

Without knowing more about the panels used it is not possible to draw any conclusions on the adequacy of the methodology.

Cross-matching

Interval between sampling and cross-matching

The interval between sampling and cross-matching is shown below for the 27 reports.

Interval between cross-matching and sampling (hrs)	No. of cases
0-47	22
48-71	2
72-96	1
> 96	0
Not known	2

There appears to be adherence to British Committee for Standards in Haematology guidelines[14]. However since the questionnaire did not ask about previous transfusion history this conclusion cannot be verified. This inadequacy in the questionnaire has subsequently been corrected for the 1998/99 reporting year.

Cross-matching methodology

No useful information could be elicited due to the current design of this section of the questionnaire. The format has been modified for the 1998/99 reporting year.

Reporting to Blood Centres and Hospital Transfusion Committees

20/27 (74%) cases were reported to local Blood Centres whereas only 12/27 (44%) were reported to Hospital Transfusion Committees. The design of the questionnaire was such that it was not possible to know whether the latter figure represents lack of reporting per se or lack of a Hospital Transfusion Committee. This question has been re-designed for the 1997/98 reporting year.

Comments

- There was little evidence of poor laboratory practice. In the majority of cases DHTRs occurred as a result of the development of new red cell allo-antibodies and could not have been prevented, as the antibodies were undetectable at the time of the original antibody investigation in previously sensitised patients. Exceptions to this were 1 case where the pre-transfusion antibody screen was omitted and limited cross-matching performed, one case of possible mis-identification of an antibody to a low frequency antigen and 1 case where the hospital failed to detect anti Jka post-transfusion despite a positive DAT. In the first case the hospital took immediate steps to review procedures and instigate re-training.

- The antibody specificities encountered as causes of DHTRs were as expected from the literature[15] and showed a preponderance of anti Jka (17/46 or 37% of all antibodies, 17/27 or 63% of patients).

- The onset of DHTRs ranged from 1 to 28 days (median 7 days). A delay of 28 days is unusual for DHTRs which are normally the result of re-stimulation to an antigen to which the patient was previously sensitised. In this case the antibody was a result of primary sensitisation to Rh D in a RhD negative male who received a massive transfusion of RhD positive blood, a well accepted practice under defined circumstances.

- In 2 cases historical clinically significant antibodies were undetectable pre-transfusion, were not disclosed by the patient and the previous records were not available to guide the selection of suitable blood.

- Only 44% of cases were reported to Hospital Transfusion Committees.

Recommendations

- Access to previous transfusion records may alert to historical clinically significant antibodies which are undetectable at the time of cross-match

- Careful questioning of patients regarding previous transfusion and the possible existence of patient antibody cards should be stressed

- There should be greater utilisation of Hospital Transfusion Committees as a forum for discussion of such cases.