13. DELAYED TRANSFUSION REACTIONS

Definition
Delayed transfusion reactions are defined in this report as those occurring more than 24 hours following a transfusion of blood or blood components. In practice, these are usually delayed haemolytic reactions due to the development of red cell alloantibodies. Simple serological reactions (antibody development without a positive DAT or evidence of haemolysis) are excluded.

This category accounted for 9.6% of non-infectious hazards reported and 9.5% of all hazards.
Forty-six new initial reports were received and 3 were brought forward from the previous year. Five additional reports were received which were not included in the analysis for this chapter. Two of these were withdrawn by the reporters following further investigation, 1 was withdrawn by SHOT staff on review, 1 was an incorrect component transfused and is included in that chapter and 1 was "written off" when it became clear that a completed questionnaire would not be returned by the reporter. Two reports received during the reporting period are still awaiting completion of a questionnaire and will be presented next year.
This chapter highlights the main findings from 47 completed questionnaires (44 from the current reporting year).

Age and sex

Age (46 reports)

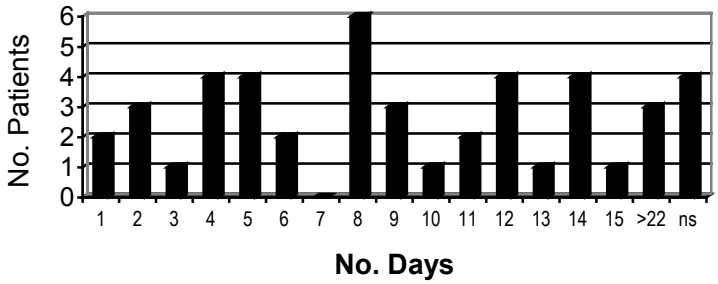
Age range	17 – 91 years
Median age	67 years

Sex (47 reports)

Males	20
Females	27

Figure 25 shows the interval in days between the implicated transfusion and signs or symptoms of a DHTR.

Figure 25
Interval between transfusion and symptoms



Range: 1 to 40
Median: 8

Reactions reported

There were 9 deaths in this group, of which 2 were thought to be definitely due to and 1 probably due to the transfusion reaction. One further patient suffered some renal impairment and another required admission to ICU and renal dialysis. The remaining patients suffered minor or no morbidity.

All reactions were probably caused by the administration of allogeneic red cells, although not all reports fit the classical definition of a delayed haemolytic transfusion reaction. Those where the antibody was detectable retrospectively in the pre-transfusion sample and possibly those where signs of haemolysis were noted within 2 or 3 days of the transfusion may well have had mild, ongoing extravascular haemolysis during or soon after the

transfusion. In 2 cases no antibody was detected pre or post transfusion. One of these (case 45, male) had a clear-cut haemolytic reaction and a positive direct antiglobulin test when tested 4 days after transfusion, but had no known history of previous transfusion. The second was a patient with sickle cell disease (case 27) who had a well-demonstrated haemolytic episode with a negative DAT, and required ICU admission and renal dialysis; this was probably due to hyper-haemolysis associated with SCD, rather than a DHTR, although insufficient detail was provided about the investigations undertaken to be conclusive. In a further 2 emergency cases (46 and 47), no pre-transfusion testing was performed, but antibodies were detected retrospectively in the pre-transfusion sample; again, there was insufficient information provided to determine when signs of haemolysis developed (a fall in Hb and an isolated rise in bilirubin, respectively).

Seventy new antibodies were identified in 42 patients. In one (case 28), the antibody was detected only in the eluate and in a second (case 1) no specificity was assigned.

Four cases had no reported history of previous transfusion or pregnancy. In one of these (case 10) the reaction was probably due to primary sensitisation, the antibody being detected 40 days post transfusion. In the other three cases (all male patients) the antibodies were found within 10 days of the transfusion and it must, therefore, be assumed that these patients had received previous transfusions unknown to the reporter.

Six patients had a positive antibody screen before transfusion. In three emergency situations crossmatch compatible blood was transfused before full investigation of a positive antibody screen was complete. Anti-Jk^a reacting only with Jk(a+b-) cells, at least by the column IAT technique in use (one DiaMed, one BioVue), was missed in the crossmatch in two of these patients (cases 18 and 35). In case 35, a newly developed anti-Fy^b was also identified post transfusion; it is unclear to what extent the missed pre-existing anti-Jk^a and the newly developed anti-Fy^b contributed to the reaction, although no signs of haemolysis were noted until 9 days post-transfusion. In the third of the emergencies (case 38, described in detail later), anti-c+E+Jk^a was retrospectively identified in a pre-transfusion sample by a reference laboratory, but other than a positive DAT, no symptoms of haemolysis were noted. In 2 other cases, appropriately phenotyped blood was transfused but further antibodies developed (cases 25, 36). In one report (case 31), phenotyped blood was selected for the antibody identified, but a 2^{nd} weak antibody was retrospectively identified in the pre-transfusion sample. In addition to case 27, already described, 6 further patients had a negative DAT post-transfusion. All had clear-cut haemolytic reactions (grade 3 or 4) with identifiable red cell antibodies.

Urgency of transfusion requirement

The transfusion was said to be routine in 28 patients and an emergency in 19.

New post transfusion antibodies

Table 34 shows the specificity of all new antibodies detected post-transfusion and table 35 antibodies in individual patients. The data include antibodies missed that should have been detected pre-transfusion, but not those that were undetected because pre-transfusion testing was omitted due to the emergency nature of the request.

Table 34
Specificity of new antibodies detected post-transfusion

Antibody specificity by blood group system	Number of cases	Sole new antibody
Kidd		
Jk^a	17	10
Jk^b	9	6 (1 detected in eluate only)
Rh		
c	11	1*
E	10	1*
D	2	2
C	2	
C^w	2	
e	1	
Duffy		
Fy^a	6	2
Fy^b	1	
$?Fy^3$	1	
Kell		
K	2	1
MNSs		
S	1	
s	1	
Other		
A_1	1	
Bg	1	
P_1	1	
Lu^a	1	

*In addition, there were 4 examples of anti-c+E reported.

Table 35
New post-transfusion antibodies in individual patients
(Cases in bold type indicate those that resulted in mortality)

Case No	Antibody (ies)	Comment
1	UI	
2	Jk^b	
3	D	
4	Jk^a+C^w	Detected by enzyme or enzyme IAT only
5	Jk^b	
6	Jk^a	
7	**c+E**	
8	Jk^a	
9	E	Anti-E detected in eluate
10	Jk^a	
11	Fy^a	
12	c+E	
13	**c+UI+cold reacting Antibody**	Anti-c in eluate
14	Jk^a	
15	c	
16	c+E+K	
17	Jk^a	
18	Jk^a	Pre-transfusion screen positive, ID panel not performed
19	Fy^a+E+Bg	Anti-E + anti-Fy^a detected in eluate
20	**c+E+Jk^b**	
21	K	
22	C+E+s+Jk^b+?Fy^3	
23	Jk^b	
24	c+E	Anti-E detected in eluate
25	c+S	Pre-transfusion anti-Fy^a
26	c+E	Record of anti-c at reference centre, but unknown to hospital
27	none	Negative DAT post-transfusion. SCD patient with probable hyperhaemolysis
28	Jk^b	Detected in eluate only
29	Jk^a+e	
30	Jk^b	
31	Jk^a	Pre-transfusion anti-E. Anti-Jk^a missed pre-transfusion, detectable vs Jk(a+b-) cells only.
32	A_1	? Passively acquired from FFP or platelets.
33	$Jk^b+Fy^a+C^w$	
34	Jk^b	Enzyme only antibody – identified by reference laboratory
35	Fy^b+Jk^a	Pre-transfusion anti-c + other unidentified antibody
36	$C+Jk^a+Fy^a$+UI	Pre-transfusion anti-E
37	Jk^a	
38	$c+E+Jk^a$	Pre-transfusion screen positive with non-specific reactions by CRRS*; negative by DiaMed
39	Jk^a	
40	Fy^a	
41	$c+Jk^a+Lu^a$	
42	D	
43	Jk^a+Fy^a	
44	Jk^a	Missed pre-transfusion by automated technique – detected retrospectively by manual technique
45	none	No known transfusion history
46	none	Pre-existing anti-c+E. No pre-transfusion testing performed.
47	none	Pre-existing anti-K. No pre-transfusion testing performed.

***** Capture R Ready Screen

Severity of reaction/ clinical sequelae

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

- Group 1 Asymptomatic (with positive DAT only)
- 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 8 patients in this group. Two had falling Hb levels but this was probably related to their underlying condition. All survived with no sequelae.

Group 2
There were 11 patients in this group, of whom 4 survived with no long-term complications. Three required further transfusion due to their falling Hb (attributable to the DHTR), and the other four died from unrelated causes.

Group 3
There were 24 patients in this group, of whom 11 survived with no sequelae. One death (case 13) was definitely related to the transfusion and is described below. Two required admission to the High Dependency Unit, but suffered no long-term ill effects. One had his planned operation postponed. Six required further transfusion as a result of a falling Hb (attributable to the DHTR), but otherwise survived with no ill effects. The remaining two died of unrelated causes. One further case (47) remained on ICU at the time of reporting due to his underlying condition.

Group 4
There were four patients in this group. Two of them died, one definitely and one probably as a result of the DHTR and these cases are described below. The third required ICU admission and dialysis and the fourth patient had his discharge delayed by eight days, but both survived with no long-term ill effects.

Table 36
Individual new antibodies grouped by severity
(Cases in bold type are those that resulted in mortality)

Group 1		Group 2		Group 3				Group 4	
Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity
10	Jk^a	2	Jk^b	1	UI	21	K	7	**c+E**
12	c+E	9	E	3	D	22	$C+E+s+Jk^b+?Fy^3$	20	**c+E+Jk^b**
28	Jk^b	11	Fy^a	4	Jk^a+C^w	23	Jk^b	25	c+E
29	Jk^a+e	14	Jk^a	5	Jk^b	24	c+E	27	none
38	$c+E+Jk^a$	30	Jk^b	6	Jk^a	26	c+E		
39	Jk^a	31	Jk^a	8	Jk^a	33	$Jk^b+Fy^a+C^w$		
41	$c+Jk^a+Lu^a$	32	A_1	13	**c+UI**	34	Jk^b		
44	Jk^a	40	Fy^a	15	c	35	Fy^b+Jk^a		
		42	D	16	c+E+K	36	$C+Jk^a+Fy^a$+UI		
		43	Jk^a+Fy^a	17	Jk^a	37	Jk^a		
				18	Jk^a	45	none		
				19	Fy^a+E+Bg				

Case reports of deaths attributable to the DHTR

Case 7
A 65 year old male patient had an anterior resection for carcinoma of the colon and was later taken back to theatre for removal of an intra-abdominal haematoma. He had been transfused with several units of red cells, FFP and platelets over a 3 day period. Eight days following his first transfusion the patient had a fever, jaundice and red urine and his Hb fell to 40g/L. He underwent a third laparotomy for presumed internal bleeding and was transfused 5 units of red cells.

Pre-transfusion antibody screening performed by routine BioVue IAT on plasma samples taken on days 3 and 6 following the initial transfusion were negative. The day 6 sample is believed to have been used for an immediate-spin crossmatch for his third laparotomy. Post-operatively, the patient was admitted to ICU and required renal dialysis, but died three days later with metabolic acidosis, acute renal failure, episodes of bradycardia and hypotension. Meanwhile post transfusion serology on day 9 revealed anti-c+E by BioVue IAT and 2-stage enzyme and a positive DAT with anti-IgG. Retrospective testing of the pre-transfusion samples still showed negative antibody screens, although it was not stated in the report by which techniques this result was obtained or whether it was confirmed by the reference laboratory.

As a result of this episode, there has been a recommended change in practice, relating to increased awareness of DHTR causing red urine, jaundice and falling Hb. The case was also reported to the National Confidential Enquiry into Perioperative Deaths (CEPOD). Current BCSH guidelines[13] recommend testing a sample taken within 24 hours of the intended transfusion if the patient has been transfused within the previous 3-14 days. A sample taken on day 7 or 8 may have revealed the antibodies before the transfusion of the subsequent 5 units on day 8. Such a sample would presumably have been sent if the symptoms of DHTR had been recognised.

Case 20

A 77 year old female patient with ischaemic heart disease and atrial fibrillation was admitted with gastrointestinal bleeding secondary to excessive warfarinisation. She was transfused with 4 units of red cells as an emergency. Pre-transfusion antibody screening by routine BioVue IAT was negative (DAT not performed) and was followed by a routine BioVue IAT crossmatch. Eight days post-transfusion the patient developed a fever, chills, jaundice and a falling Hb. Post-transfusion testing by BioVue IAT and enzyme and by the blood service reference laboratory, revealed anti-c+E+Jk^a and a positive DAT with anti-C3 only. Retrospective testing of the pre-transfusion sample by both the hospital laboratory and the reference laboratory gave negative results. The patient was monitored on the ward awaiting a supply of compatible red cells from the NBS, but de-compensated, suffered a cardiac arrest and died before blood was available. Although the patient had pre-existing cardiac disease, the reporter felt that the anaemia caused by the DHTR probably contributed to the death.

The blood service had a previous record of anti-E for this patient and the reporter feels that having this information would have meant that antigen-negative blood would have been selected. The patient was presumably R_1R_1 and therefore R_1R_1 may have been selected had the history of anti-E been known. Blood selected for Rh-compatibility would not, of course, have prevented the development of anti-Jk^a. Although the positive DAT was caused by C3 only (suggesting coating with anti-Jk^a rather than anti-c or anti-E), one cannot be certain which specificity or combination of specificities contributed to the DHTR. Another point to be highlighted by this case was the lack of appreciation of the severity of the anaemia which, had it been realised, pre-transfusion testing could have been accelerated.

Case 13

A 51 year old female patient with vaginal bleeding had been transfused with four units of red cells on Day 1 and three units on Day 4. Pre-transfusion antibody screening on Day 4 by BioVue IAT (rapid/urgent technique) using a plasma sample was negative (DAT not performed) and was followed by a routine BioVue crossmatch. On Day 6 a new sample was received for pre-op hysterectomy and it was noted that the patient had received two recent transfusions.

There was a delay in processing the Day 6 specimen, due to the details being typed into the computer with the wrong hospital number. On testing the following day, the antibody screen was positive; manual BioVue testing using several panels of cells revealed possible anti-c and what appeared to be a cold auto-antibody. A subsequent sample suggested anti-c and anti-P_1 and although the DAT was positive, so was the negative control, and the patient's red cells typed positive for the c and P_1 antigens. The phenotypes were repeated at 37^{o}C (as it was thought that the cold agglutinins were interfering with the results) and were still positive. Further samples were requested and kept at 37^{o}C for testing the following morning. On Day 8, following repeat testing at 37^{o}C, a further sample was requested for referral to the blood service reference laboratory.

On Day 8 the ward and the blood bank were informed by the haematology laboratory that the patient's Hb was 40g/L. At this point the surgeon was unsure whether the patient was bleeding but queried a transfusion reaction. By this time the patient's circulation had shut down and she was transferred to ICU where a central line was inserted and fresh samples taken for referral and repeat Hb. Two hours later, and following a discussion between the blood service haematologist and the surgeon, it was agreed that uncrossmatched ABO/RhD identical red cells should be transfused. However, during these discussions the patient died.

The blood service reference laboratory later reported anti-c plus further unidentified reactions by IAT and a pan-reacting antibody at 16^{o}C. There was some indication of anti-c in the eluate. As a result of this incident, the laboratory is reviewing its antibody investigation and reporting mechanisms.

This case highlights several points:

- A need to recognise a DHTR at both laboratory and ward level
- A need to appreciate that phenotyping patients' red cells post transfusion may be of little value
- A need to involve the hospital haematologist earlier
- A need to understand limitations of in-house serological investigations and refer sooner

Analysis of serological information

Table 37 gives information on the techniques used for antibody screening in the 47 reported cases. An IAT crossmatch was performed in 35 cases, an immediate spin crossmatch in 5 cases and electronic issue in 5 cases. No pre-transfusion crossmatching was performed in 2 emergency cases.

Table 37
Techniques used for antibody screening and crossmatching

IAT screening technology	Number of cases
BioVue	17
DiaMed	20*
LISS tube	3
CRRS+DiaMed	2
LP microplate	1
Solid Screen	1
Scangel	1
None	2
All techniques	47

*In one case a CRRS screen was also performed and found to be positive

The IAT technology used for antibody screening broadly reflects that being used in the UK with approximately 82% of antibody screens in non-reference laboratories being performed using Column Agglutination Technology (DiaMed ID 54%, Ortho BioVue 28%) and 13% solid phase technology (data from UK National External Quality Assurance Scheme (NEQAS) questionnaire, February 2003).

In only 5 cases (11%) was there a report of an eluate being performed. In one case the anti-Jk^b was only detected in the eluate, highlighting the importance of this test when investigating suspected DHTRs.

In 24 (53%) cases the pre-transfusion sample was retested and the same result was obtained in 22 (92%) of them. This was reported as being confirmed by a reference laboratory in only two cases. The remaining reports did not state who repeated the testing or by what techniques. In two patients (cases 31 and 44, described below), a weak anti-Jk^a was missed by automated pre-transfusion testing but detected retrospectively using a manual technique.

In 34 cases (77%) plasma was used and in 10 cases serum (1 not stated and 2 no pre-transfusion testing performed). This appears to be a higher proportion of plasma samples than would be expected from the proportion of laboratories employing automated grouping and screening techniques. However, recent data obtained from a UK NEQAS questionnaire shows that approximately 86% of antibody screens undertaken in UK hospitals are performed using plasma rather than serum, reflecting the data presented in this report.

The post transfusion DAT was reported to be negative in 7 cases and was not performed in 4 cases.

Interval between drawing the crossmatch sample and transfusion

Table 38
Interval between drawing the crossmatch sample and transfusion

Interval between crossmatch and sampling (hrs)	No. cases
<48	33
48-71	1
72-96	1
>96	5
Not stated	5

As far as it is possible to tell from the questionnaire the vast majority of the samples were taken within the time limits recommended in the BCSH guidelines[13]. In one case described below (case 36) a 4-week old pre-assessment sample was used, despite the fact that the patient had received a very recent transfusion (probably unknown to the reporting hospital at the time). In a second patient, already described (case 7) a 48 hour old sample was used, following transfusion 5 days previously. In this case, BCSH guidelines would recommend a fresh sample, however, it was thought that the patient was bleeding and transfusion was presumably requested urgently.

Reporting to Blood Centres and Hospital Transfusion committees

A total of 26 (58%) incidents were reported to the local Blood Centre and 33 (73%) to the Hospital Transfusion Committee, with a further 5 indicating that they would report to a future meeting. Three respondents said that they had not reported to either and 2 did not answer the question.

Details of some of the interesting cases are given below:

Case 42
An 80 year old male patient, underwent emergency vascular surgery for an aortic aneurysm. No previous transfusion history was known. Pre-transfusion testing typed the patient as A RhD negative, antibody screen negative by DiaMed IAT (rapid/urgent technique) using plasma (DAT not performed). The patient was transfused with 28 units of A RhD negative red cells, followed by 12 units of A RhD positive (after depletion of local stocks of A RhD negative). Ten days post-transfusion, the patient's Hb fell and spherocytes were noted on the blood film. Post-transfusion serology revealed anti-D in the patient's plasma, but a DAT was not performed. The patient was already on ICU but required further red cell transfusions. He survived with no further ill effects. As a result of this incident there have been recommended changes in practice with respect to investigation of a suspected transfusion reaction, particularly performance of a DAT. Although there was no previous transfusion history known, it is impossible that this was due to a primary immune response.

In a similar case (case 3) a 75 year old, RhD negative, female patient (with an uncertain transfusion history but with previous pregnancies) was electively transfused with 2 units of RhD positive red cells. An unspecified number of days later her Hb fell and she became jaundiced. Her DAT was positive and anti-D was detected in her serum. She required admission and further transfusion.

Case 36
A 43 year old female patient with sickle cell disease was exchange transfused with 10 units of red cells prior to a total hip replacement on Day 1 (in hospital 1), followed by four units of red cells in theatre (in hospital 2) on Day 3. Pre-transfusion testing for the latter transfusion was performed using a sample taken at least three weeks earlier at a pre-assessment clinic in hospital 2. The antibody screen on the pre-assessment sample was positive by routine BioVue IAT and anti-E was identified by BioVue IAT. E negative blood was crossmatched for Day 3 by routine BioVue IAT on the stored plasma sample. On Day 10, the patient was admitted with dark urine, jaundice and a falling Hb (from 84g/L to 35g/L). This was initially assumed to be due to a sickle cell crisis and IvIg was prescribed. On Day 12 a sample was taken for serological testing. Anti-C+E+S+Jk^a+Fy^a were identified by the reference laboratory, plus a further unidentified antibody, but the DAT was negative. The patient required admission to the ward, folic acid, oxygen and further transfusion. She survived with no further ill effects.

This case highlights the potential problems associated with having care shared between hospitals. The patient was seen in outpatients by a visiting consultant with specialist interest in SCD, who recommended transfusion with Rh and K matched blood, however as an in-patient she was seen by the consultant from the host hospital and E negative blood only, was ordered by a junior doctor. It is implied that although the host hospital has a policy of transfusing Rh and K matched blood for patients with SCD, they were unaware that the patient had SCD. Although some details are unknown, it is clear that there was confusion and lack of communication between the hospitals, leading to an old sample being used for crossmatching and the protocol for selecting blood for transfusion to patients with SCD not being followed.

Case 38

A 27 year old female patient received red cells and plasma on ICU post splenectomy. The pre-transfusion screen was performed by manual DiaMed IAT simultaneously with the IAT crossmatch as it would have been too late to wait for the next automated Capture R batch. The screen was negative, the crossmatch was compatible and the blood transfused. Later that day, the antibody screen was found to be positive by the routine Capture R technique, but non-specific reactions were obtained and no further action was taken. New samples were taken and sent to the reference laboratory. Four days later a fresh sample was sent with a request for further crossmatching. The blood was found compatible by DiaMed, but the auto was positive and the antibody screen weakly positive. Simultaneous testing by an automated Capture R technique gave a positive screen. Anti-E was identified by DiaMed IAT and anti-c+E by DiaMed papain. Testing with Capture R revealed anti-c+E plus another unidentified specificity. The reference laboratory gave the results of the original pre-transfusion sample as anti-c+E+Jk^a (techniques not specified by the reporter). In-house retrospective testing of the pre-transfusion sample gave the same results as previously. The patient had no symptoms and survived with no ill effects.

This case raises questions about the investigation of positive antibody screens. When the initial Capture R screen was found to be positive, a DiaMed panel performed by an enzyme technique may have been helpful. An IAT using enzyme treated cells may also be considered when positive reactions fail to give a clear specificity.

Case 44

A 79 year old female patient received 7 units of blood for knee arthroplasty. The antibody screen was negative using a routine automated DiaMed technique and blood was compatible using an 'immediate spin' crossmatch. Another sample taken 14 days later revealed a positive DAT and anti-Jk^a in the plasma. Retrospective testing of the pre-transfusion sample by manual DiaMed testing revealed a weak positive antibody screen with the Jk(a+b-) screening cell, whilst automated testing was still negative. The patient had no symptoms of haemolysis and survived with no ill effects. As a consequence of this event, this laboratory started visually checking all cards processed by the automation and DiaMed were asked to increase the sensitivity of the camera.

Case 31

A 63 year old multi-transfused female patient with pre-existing anti-E received 2 units of E negative blood for melaena. The pre-transfusion screen and crossmatch were performed using an automated DiaMed technique. Two days later there was evidence of haemolysis with dark plasma and a falling Hb. A new sample revealed a positive DAT and anti-Jk^a in addition to the anti-E. Retrospective testing of the pre-transfusion sample revealed a weak anti-Jk^a reactive by manual DiaMed but not automated DiaMed.

COMMENTARY

- In two out of the three cases resulting in mortality, the delayed haemolytic transfusion reactions were overlooked and in one case, an incorrect assumption that the drop in haemoglobin was due to bleeding, led to an unnecessary further laparotomy.

- In two out of these three cases, there were critical delays in obtaining red cells for transfusion to correct the anaemias, which in turn led to cardiac decompensation.

- Kidd and/or c antibodies were implicated in approximately 75% of all cases, in over 90% of all patients in whom antibodies were found and 100% of deaths related to the transfusion.

- There were two cases of anti-D where elderly RhD negative patients (one female, one male) were transfused with RhD positive blood, one because of policy and the other because of an emergency. It is worth noting that RhD negative women whose pregnancies occurred before routine post-natal anti-D prophylaxis may have been previously sensitised to the D antigen.

- There is insufficient information from the questionnaires to be sure that sufficient investigation is being undertaken to investigate DTRs. Only 11% reported that a red cell eluate had been performed, 4 did not perform a DAT, and only 2 stated that the pre-transfusion sample had been tested retrospectively by a reference centre. Without detailed information about *how* retrospective testing was performed (where and by what techniques) it is impossible to know whether any of the implicated antibodies could or should have been detected pre-transfusion.

- There were 2 examples of Kidd antibodies that were missed pre-transfusion, only detectable (by the technique used) using red cells bearing homozygous (double-dose) expression of the relevant antigen.

- The 7 patients in whom the DAT was negative all fell into severity categories 3 and 4. Although an important part of the investigation of a DHTR, a negative result must not be regarded as conclusive lack of evidence for a DHTR.

- There is no evidence that laboratories are not following guidelines with respect to timing of samples in relation to the transfusion. There were only two cases, where an inappropriate sample was obviously used for pre-transfusion testing; in one case the laboratory were unaware of a recent transfusion and in the other case the transfusion was required urgently. The majority of DHTRs were evenly spread between 1 and 14 days following the implicated transfusion, confirming the need to follow the BCSH guidelines[13] with respect to sampling and previous transfusion.

RECOMMENDATIONS

- **Investigation of a suspected DHTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. This may involve referral to a reference centre.**

- **If no antibody is detected in a case of suspected DHTR, more sensitive techniques should be considered, e.g. enzyme or enzyme antiglobulin techniques.**

- **Serum (+ plasma, if used routinely) should preferentially be used for investigation of suspected DHTRs, to give the maximum potential for identifying all specificities present, including weak complement binding antibodies.**

- **It is recommended that patients with SCD are phenotyped prior to transfusion and that blood is selected for Rh and K[13].**

- **Automated systems or changes to IAT technology should be validated using a range of weak antibodies to ensure appropriate sensitivity.**

- **Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies. These should be accompanied by patient information leaflets, explaining the significance of the antibody and impressing that the card should be shown in the event of a hospital admission or being crossmatched for surgery.**

- **When the care of patients with haematological disorders requiring transfusion support is shared, there is a risk that not all pertinent transfusion history will be available to both sites. In the absence of networked pathology information systems, it is essential that local procedures are devised for adequate communication between laboratories as well as clinical teams.**

- **When the laboratory cannot supply compatible red cells within the time-frame requested, there should be communication between the haematologist and the responsible clinician to determine whether the risk of delaying the transfusion outweighs the risks of a transfusion reaction and whether potentially incompatible units should be given.**