8. ACUTE TRANSFUSION REACTIONS

Definition
Acute transfusion reactions were defined in this report as those occurring at any time up to 24 hours following a transfusion of blood or components, excluding cases of acute reactions due to incorrect component being transfused as these are covered in Chapter 7

This category accounted for 13.9% of non-infectious hazards reported.

Forty three initial reports (40 new) were received, but of these, 4 were not, in fact, thought to be reactions to blood components (1 to desferrioxamine, 1 to intravenous immunoglobulin, 1 to prostaglandin E2 and 1 not stated). After careful consideration a further 3 were withdrawn (including 1 from last year) because insufficient information could be obtained. 34 completed questionnaires were received. These included 2 cases for which initial notification forms were received in the previous reporting year. 2 reports are outstanding and will be analysed next year.

This chapter highlights the main findings from 34 completed questionnaires.

Overall there were 3 deaths in this group, 1 following red cells, 1 following FFP and 1 in a patient who received both FFP and platelets. In two cases the deaths were thought possibly related to the transfusion reaction (one patient with acute liver failure who developed angio-oedema and one patient with a massive gastro-intestinal bleed who developed dyspnoea) while in the third the death was unrelated to the transfusion (gastrointestinal haemorrhage). In all three cases the patients were severely ill and the deaths seemed primarily related to their underlying disease. One patient required admission to ITU following an anaphylactic reaction to FFP but subsequently made a good recovery. All the remaining patients suffered minor, or no, morbidity.

Sex (42 reports)

Males	24
Females	18

Age (38 reports)

Age range	17 months - 92 years
Median	56 years

Components implicated (34 reports)

Red Cells (RBC)	17 (1 including concomitant FFP)
Fresh frozen plasma (FFP)	10
Platelets	7 (1 including concomitant FFP)

1. Reactions in which red cells were implicated

There were 17 cases (including 1 case receiving red cells and FFP) and all but 1 survived without long term sequelae. The following reactions were seen:

Reaction type	Number of cases
Non-haemolytic febrile	8
Anaphylactic[1]	3
Allergic[2]	3
Dyspnoea/chest pain/rigors	1
Jaundice	1
Haemoglobinuria	1

[1]anaphylactic/anaphylactoid (defined as: hypotension with one or more of: rash, dyspnoea, angioedema)
[2]allergic (defined as: one or more of the following - rash, dyspnoea or angioedema **without** hypotension)

Non-haemolytic febrile transfusion reactions (NHFTR)

Most NHFTRs are not regarded as serious sequelae and therefore SHOT does not set out to collect reports of these types of reactions. Nevertheless, 8 reports fell into this category and in all cases the reaction started while the transfusion was in progress.
In one case a mixed growth of *Staphylococcus epidermidis* was obtained from the pack but the patient had no blood cultures drawn (and received no antibiotics) and so it is assumed that this was not a bacterial reaction and that the *Staph* was a laboratory contaminant. In one case HLA antibodies were demonstrated. No diagnostic investigations were carried out in the remaining patients.
In 2 cases a pre-existing red cell antibody was missed in the pre-transfusion testing (see below). It is not known what role, if any, the antibody may have had in the transfusion reaction.

- *a 76 year old female with multiple myeloma, admitted with a fractured neck of femur suffered fever and rigors during transfusion of 1 unit of red cells. The blood had been issued after grouping by tile technique and no antibody screen had been performed (the hospital's "routine" out-of-hours practice). A LISS-IAT cross-match in tube did not detect any incompatibility. Retrospective antibody screen revealed the presence of anti-K in the pre-transfusion sample but the K status of the unit is not known.*

- *a 42 year old female with gastrointestinal bleeding developed fever and rigors after the transfusion of 50ml of red cells. A pre-transfusion antibody screen and identification panel (10 cells) showed the presence of anti-E. However, a second sample, drawn only 30 minutes later showed both anti-E and anti-s. There was no laboratory evidence of haemolysis.*

Anaphylactic/anaphylactoid reactions

Three patients developed hypotension in association with fever or rigors and a rash or dyspnoea.

- *a 16 year old boy undergoing spinal surgery developed hypotension, fever, rash and respiratory problems after receiving only around 5-10ml of red cells. He had a history of previous transfusion. He responded to adrenaline and steroids and was subsequently shown to have IgA deficiency with IgA antibodies. Subsequent transfusion with washed red cells was tolerated without incident.*

- *An 18 year old male receiving a transfusion of laboratory-leucodepleted red cells for thalassaemia developed hypotension, rash and fever. He responded to IV colloid and crystalloid with steroids and an antihistamine. The patient had increased the speed of his red cell transfusion in order to attend a social event. No other cause was identified.*

- *a 42 year old woman with a post-partum bleed developed hypotension, rigors and dyspnoea after receiving 100ml of red cells through a bedside filter. She responded to antihistamines, steroids and oxygen. Although TRALI was suspected, investigation of donor and recipient revealed no white cell antibodies. The patient was known to be allergic to penicillin but the donor unit was not tested for the presence of this drug.*

Allergic reactions

There were three allergic reactions in this group, characterised by a rash or angioedema without hypotension. Two of these appertained to one patient:

- *a 45 year old woman being transfused because of a haematological malignancy developed rash, rigors and chest pain during transfusion of buffy-coat depleted red cells. She was subsequently shown to have IgA deficiency but with no detectable anti-IgA. Subsequent transfusions were of washed red cells but she reacted again about six weeks later. It was felt that the red cells had been inadequately washed on that occasion.*

- *a 16 month old girl being treated for acute myeloid leukaemia (AML) developed facial oedema during a laboratory-leucodepleted red cell transfusion. She had developed a similar reaction to leucocyte-depleted platelets a few weeks previously.*

Other reactions

- *a 92 year old woman became jaundiced a few hours after a post-operative transfusion. There was no evidence of acute haemolysis and no other cause was found. The role of the transfusion in this event was not clear.*

- *an 89 year old woman developed dyspnoea, chills, rigors and hypertension with peripheral cyanosis after receiving 100ml of non-leucodepleted red cells. Donor and patient were tested for granulocyte and HLA antibodies but this was negative. The patient subsequently died but this was not thought to be related to the transfusion reaction.*

- *an 82 year old female developed isolated haemoglobinuria during the transfusion of two units of red cells. No cause was identified and the Hb rose by 40g/l as a result of the two unit transfusion.*

2. Reactions in which fresh frozen plasma (FFP) was implicated

There were 10 reports in this group. Two patients, who were very ill due to bleeding varices or gastrointestinal bleeding at the time of component administration, died and the reaction may have contributed to their deaths. The remaining 8 patients survived without sequelae. Reactions occurred during (8 cases) or within 2 hours of stopping the transfusion (2 cases) and were of 2 main types:

Reaction type	Number of cases
Anaphylactic	6
Allergic	4

Anaphylactic/anaphylactoid reactions

There were 6 patients in this category and their reactions were characterised by hypotension with respiratory complications in 5. Two of these also had rash/pruritis with angioedema and anti-Gm1,3 was detected in one of these cases. The final patient, who was receiving angiotensin-converting enzyme (ACE) inhibitors had hypotension with bradycardia/systemic collapse and it is not clear if this was an anaphylactic response or somehow related to his medication. It should be noted that there is no clear distinction between transfusion-related acute lung injury and anaphylaxis in the absence of a rash or angioedema unless appropriate investigations (performed only in one of these cases) show the presence of potentially implicated antibodies.

Four patients were treated with steroids and a antihistamine, one received only a diuretic and one received steroids and adrenaline.

Allergic reactions (not anaphylaxis)

Four patients suffered apparent allergic reactions with dyspnoea and rash/pruritis. In three cases steroids and an antihistamine were given and two patients received adrenaline.

In the majority of cases investigations to identify the cause of the reactions had not been carried out.

3. Reactions in which platelets were implicated

There were 7 cases in this group (including 1 case in which FFP was also administered), 5 of which occurred during the transfusion and two within 2 hours after completion of infusion. All patients survived without ill effects.

Reaction type	Number of cases
Haemolytic	1
Anaphylactic	3
Allergic	2
Hypotension	1

- *A 36 year old woman, group A RhD positive received an apheresis unit of group O platelets for a post-partum haemorrhage. She developed evidence of intravascular haemolysis and a positive DAT within 2 hours of completing the transfusion. The donor had been tested to exclude high titre haemolysins (saline, 37^{o}C) but retrospective testing by IAT methods for IgG anti-A showed a titre of 1 in 20,000.*

- *Three patients experienced anaphylaxis, 2 with rash, dyspnoea and hypotension and one with rash and hypotension. In one case a bedside filter was in use. Only one patient was tested for IgA antibodies (negative) and although Gm3 antibodies were found in this patient, the platelet donation was Gm3 negative. One patient had multiple HLA antibodies.*

- *Two patients experienced allergic reactions with rash and dyspnoea. One of these, a 16 year old boy being treated for acute lymphoblastic leukaemia and who was receiving platelets through a bedside filter, also developed angioedema. In one case it was suggested that the patient's penicillin allergy may have been the cause although no donor or pack testing for this drug was carried out.*

- *A 64 year old female being treated for acute myeloblastic leukaemia developed hypotension and syncope within 15 minutes of completing a transfusion of a pool of laboratory-leucodepleted platelets. She was not on ACE inhibitors and there was no evidence of infection.*

Response times

In general patients were seen within minutes of the reaction developing and the local haematologist was contacted for advice in 21 cases (60%).

Observations

There was a wide range of frequency of nursing observations prior to the onset of the reaction:

Table 14
Frequency of nursing observations

Frequency of observations	Number of cases

5 minutes	2
10 minutes	3
15 minutes	6
30 minutes	6
60 minutes	2
Continuously monitored	6
Nil	2
No information	7
Total reporting	**34**

Reporting to Blood Centres and Hospital Transfusion Committees

This was highly variable, reflecting, perhaps, the wide range of reactions reported.

Table 15
Reporting of reactions to the local Blood Centre (BC) and the Hospital Transfusion Committees (HTC)

Reported to	Number
HTC only	2
BC only	10
HTC and BC	17
Neither	5
Total	**34**

COMMENTARY

- In two cases of acute reactions to red cells a pre-existing antibody was not identified, in the first instance because no antibody screen was carried out on a non-urgent, out-of-hours sample and in the second case a second antibody appears to have been missed (detected in a sample drawn 30 minutes later). In the first case the procedures for handling out-of-hours samples have been reviewed and altered.

- It is not the intention of SHOT to seek reports of non-haemolytic febrile transfusion reactions but 8 such reports were received. It is notable that some acute reactions due to undetected red cell antibodies are indistinguishable from febrile, non-haemolytic transfusion reactions if the patient has received only a small volume of blood. Clinicians should therefore be encouraged to report all reactions which they regard as serious.

- The reported use of laboratory leucocyte-depleted components was low (3 units of red cells, 3 units of platelets) and there was no clear association between laboratory leucodepletion or the use of bedside filters and the nature of the adverse event. Nevertheless, continued vigilance is recommended in order to detect any unexpected adverse reactions to this new technology.

- Two adverse events followed the administration of FFP to reduce the INR in warfarinised patients who were not bleeding. The BCSH Guidelines on Oral Anticoagulation[7] recommend that patients who have been anticoagulated with warfarin and who require reversal of anticoagulation should be managed by omitting the drug, administering vitamin K or, in cases of life-threatening haemorrhage by giving prothrombin complex concentrate(PCC). FFP is indicated only if PCC is unavailable and life-threatening bleeding is occurring[8].

- One platelet reaction seemed to be related to a high titre anti-A which was not detected by standard screening methods for high-titre agglutinins/haemolysins. It is recognised that the use of IAT methods for isoagglutinin detection will yield a result which may be five-fold higher than that obtained by direct techniques.

- Reactions, other than haemolytic reactions, to all components were, in general, not investigated to determine the cause of the reaction. However, in one case which was likely to be due to anti-IgA a second event followed inadequate washing of red cells, emphasising that some of these patients are extremely sensitive to very small residual amounts of plasma.

RECOMMENDATIONS

- Clinicians should continue to report all serious adverse events even if these are not currently recognised as "classical" acute transfusion reactions as this may act as an early alert to unusual adverse effects of novel techniques and processes (e.g. laboratory leucodepletion, virus inactivation, drug/product interactions).

- Reactions to platelets and FFP may be similar to TRALI but this diagnosis cannot be confirmed without appropriate investigations for donor and recipient white cell antibodies. It is recommended that such investigations are performed whenever respiratory symptoms are prominent.

- Administration of FFP and platelets should conform to published guidelines[8,9]. The use of FFP to reverse warfarin effect is rarely justified.

- If group O plasma (or platelets in plasma) is to be used for non-O recipients then those administering the unit should ensure that it does not contain high-titre ABO antibodies.

- Transfusion Services should re-examine their current screening methods for detection of potentially haemolytic titres of isohaemagglutinins to assess whether or not more sensitive methodology might be indicated in order to minimise the risk of haemolysis of recipient red cells.

- There remains a need for guidelines on the appropriate investigation of acute transfusion reactions and the British Committee for Standards in Haematology should consider this as a suitable topic for development of national guidelines.