8. ACUTE TRANSFUSION REACTIONS

Definition

Acute transfusion reactions are 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 11.9% of non-infectious hazards reported.
36 initial reports (34 new) were received. 33 completed questionnaires were received. These included 2 cases for which initial notification forms were received in the previous reporting year.

This chapter highlights the main findings from 33 completed questionnaires.

Overall there were 2 deaths in this group, both of which were felt to be unrelated to the transfusion. One death followed FFP administration in a patient with liver disease on ICU, and the second was a patient with myelodysplastic syndrome who was receiving platelets for gastro-intestinal bleeding and who died due to the haemorrhage. One patient required admission to ICU following an anaphylactic reaction to platelets but subsequently made a good recovery and 4 patients were already on ICU at the time of their adverse event. All the remaining patients suffered minor or no morbidity.

Sex (32 reports)

Males	19
Females	13

Age (32 reports)

Age range	1 month - 88 years
Median	52 years

Components implicated (33 reports)

Red Cells (RBC)	11
Fresh frozen plasma (FFP)	9 (2 concurrently receiving red cells +/- platelets; one patient receiving cryosupernatant rather than FFP)
Platelets	13

Leucocyte-depleted components were being transfused in at least 18/24 patients who were transfused with red cells or platelets. In a number of the earlier reports (prior to universal leucodepletion) the nature of the component is unclear.

1. Reactions in which red cells were implicated

There were 11 cases and all survived without long term sequelae. The following reactions were seen:

Reaction type	Number of cases
Non-haemolytic febrile	2
Anaphylactic[+]	1
Allergic[++]	2
Dyspnoea and chest pain	2
Haemolysis	4

[+]anaphylactic/anaphylactoid (hypotension with one or more of: rash, dyspnoea, angioedema)
[++]allergic (one or more of: 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. However, two reports fell into this category and in both cases the reaction began while the transfusion was in progress.

Anaphylaxis

One patient developed a severe anaphylactic reaction during a red cell transfusion. She recovered following steroid, anti-histamine and adrenaline administration. Subsequent investigations showed that she had IgA deficiency with anti-IgA.

Allergic reactions

There were 2 apparent allergic reactions in this group. In 1 case, a patient receiving an autologous unit of red cells following a bone marrow harvest developed a rash and fever. The reaction was noted during the red cell transfusion and led to the transfusion being abandoned. The cause of the allergic reaction was not determined.

Dyspnoea/chest pain

Two patients developed acute dyspnoeic reactions during their transfusions. TRALI was queried in each case but then discounted, though the reasons for this are unclear. One red cell unit grew micrococcus and coagulase negative staphylococcus which were felt to be contaminants. Otherwise investigations for TRALI were negative in one case and possibly not carried out in the second case.

Haemolytic Transfusion Reactions

There were 4 patients with evidence of acute haemolysis. In three cases this was due to an identified red cell incompatibility while in the fourth the reaction may have been an exacerbation of autoimmune haemolysis. Details of these cases are given below.

Case 1 This 61 year old male with chronic lymphocytic leukaemia was being transfused as an emergency due to cardiac ischaemia secondary to anaemia. He developed symptoms of intravascular haemolysis within the first 50mls of the red cell unit which had been issued before completion of antibody identification because of clinical urgency. The patient was found to have anti-Jkb and this had been known to the Regional Transfusion Centre but not the hospital laboratory as the patient had been transfused in another hospital previously.

Case 2 A 78 year old female patient with heart disease and recent bleeding was transfused 9 days after a previous uneventful transfusion. She developed dyspnoea and fever during her first unit. Pre-transfusion testing had shown anti-c and anti-E but post-transfusion testing showed a further antibody which was later shown to be anti-Jkb which had presumably been evolving following the earlier transfusion.

Case 3 A 56 year old female patient receiving chemotherapy for breast cancer developed haemoglobinuria, nausea, vomiting and abdominal pain during a routine transfusion. She had had no monitoring of vital signs for 4 hours prior to the reaction. The Junior House Officer (JHO), notified by the nursing staff, saw the patient more than an hour later, having advised continuation of the transfusion, and queried a urinary tract infection. Blood tests confirmed a likely haemolytic event. Anti-K was detected 2 months later, although the pre-transfusion and immediate post-transfusion antibody screens were negative.

Case 4 A 68 year old female patient with prolymphocytic leukaemia received a 2 unit red cell transfusion in the community, under the supervision of the Community Rapid Response Team. Two hours after completion of the transfusion she developed chills, fever, haemoglobinuria and back pain. She was brought to A&E where investigations confirmed a probable haemolytic event. Antibiotics were given but blood cultures were negative. Pre-transfusion and post-transfusion testing was negative although she had previously been DAT positive with a non-specific autoantibody. The cause of the haemolytic event remained unclear.

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

There were 9 reports in this group. One patient was concurrently receiving red cells and another was receiving red cells and platelets. One patient died but this was not felt to be related to the transfusion. The remaining patients survived without sequelae. In all cases, the reactions occurred during the transfusion and were of 2 main types:

Reaction type	Number of cases
Anaphylactic	5
Allergic	4

Anaphylactic/anaphylactoid reactions

There were 5 patients in this category and their reactions were characterised by hypotension with respiratory complications in 3 cases and rash in 2 cases. Two patients were investigated for a possible immunological cause. The first was tested only for HLA antibodies (negative) while the second had more comprehensive investigations (HLA, granulocyte and IgA antibodies - all negative in FFP but weak anti-HLA in patient). It should be noted that there is no clear distinction between transfusion-related acute lung injury and anaphylaxis with dyspnoea unless appropriate investigations (performed only in one of these cases) show the presence of potentially implicated antibodies.

One of these patients was given FFP to manage bleeding secondary to a high INR (>20). The guidelines on management of anticoagulation[14] suggest the use of prothrombin complex concentrate may be appropriate in these circumstances but this may not be immediately available in some smaller or more remote hospitals. Currently, only HT-DEFIX (Scottish National Blood Transfusion Service) is licensed for this purpose in the UK.

In the other 4 cases it is difficult to assess whether or not the administration of FFP was appropriate (1 liver disease, 1 prophylaxis before endoscopic retrograde cholangiopancreatography (ERCP), 1 bleeding heavily during cardiac surgery, 1 patient with trauma who had received 3 units of red cells and 2 units of FFP).

Allergic reactions (not anaphylaxis)

Four patients suffered apparent allergic reactions with dyspnoea and rash/pruritis. In one case the patient was receiving cryosupernatant for thrombotic thrombocytopenic purpura (TTP).
Two patients who developed dyspnoea, angioedema and a rash were receiving FFP to reverse a high international normalised ratio (INR) in the absence of bleeding. This is not felt to be an appropriate indication for FFP administration.
A further case appeared to be receiving FFP and red cells in a 1:1 ratio while undergoing re-do cardiac surgery which is generally not considered an appropriate use of this product.
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 13 cases in this group all of which occurred during the transfusion. One patient died due to a recurrent haemorrhage, unrelated to the transfusion reaction while all the other patients survived without ill effects.

Reaction type	Number of cases
Anaphylactic	7
Allergic	3
Hypotension	2
Dyspnoea/chest pain	1

Anaphylactic reactions were common in this group. As noted above, it can be difficult to differentiate these from episodes of TRALI or sepsis, unless appropriate investigations have been performed.
Selected cases are described in some detail below.

- *Case 1 This 41 year old male patient with immune thrombocytopenic purpura (ITP) received three pools of platelets to manage bruising. He developed an anaphylactic reaction requiring the administration of steroids, antihistamine and adrenaline and required admission to ICU. It is generally felt that platelets should not be administered in ITP other than to manage significant bleeding.*

- *Case 2 This 43 year old female patient with acute lymphoblastic leukaemia (ALL) had a cardiac arrest during an anaphylactic reaction to a leucocyte-depleted platelet pool. She made a full recovery following resuscitation. Blood cultures drawn from the patient were negative. No cultures of the pack were performed although the reporter queried a bacterial cause of the reaction.*

- *Case 3 This 68 year old male patient with Waldenstrom's Macroglobulinaemia developed dyspnoea and chest pain during the transfusion of the first 10mls of an apheresis unit of platelets (leucocyte-depleted). Bacterial cultures of the pack grew coagulase-negative staphylococcus but blood cultures were not performed on the patient. The patient appears to have made a good recovery without antibiotic administration and has subsequently received platelets in Platelet Storage Medium(PSM).*

- *Case 4 This neonate, thrombocytopenic due to Gram-negative sepsis, developed hypotension and tachycardia with platelet transfusions on 2 consecutive days. No cause for the reactions were identified.*

Response times

In general patients were seen within 5-10 minutes of the reaction developing (24 cases, 72%) and the local haematologist was contacted for advice in 24 cases (72%). The haematologist was not, apparently, contacted in some of the more severe cases, however, and this may contribute to the under-investigation of many of these events.

Observations

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

Table 25
Frequency of nursing observations

Frequency of observations	Number of cases
5 minutes	1
15 minutes	4
20 minutes	1
30 minutes	5
40-60 minutes	5
>1 hour	1
No information	16
Total	**33**

Reporting to Blood Centres and Hospital Transfusion Committees

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

Table 26
Reporting of reactions to the local Transfusion Centre, the Hospital Transfusion Committees (HTC) and the Hospital Laboratory

Reported to	Number
HTC	20
Hospital Laboratory	32
Transfusion Centre	20
Not stated	1

In 5 cases the reporter stated that practice had been changed as a result of the incident. This included 2 patients who were subsequently provided with platelets in PSM, one patient who had a haemolytic transfusion reaction due to an antibody known to the Regional Transfusion Centre (communication with the Centre has been changed) and one patient (Case 2, above) whose pre-transfusion sample was felt to have been drawn too long before the transfusion ("more than 24 hrs"), resulting in haemolysis due to a developing anti-Jkb.

COMMENTARY

- Fresh frozen plasma and platelets are both "over-represented" in the acute transfusion reaction group, compared to red cells which are administered much more frequently. 7-10 units of red cells are transfused for every unit of platelets or FFP and yet FFP and platelets appear to be a more common cause of acute transfusion reactions.

- The SHOT scheme does not specifically attempt to assess the appropriateness of transfusion but it is clear from the details provided that patients are experiencing life-threatening reactions to components which they perhaps did not require.

- Reactions are under-investigated and it is generally unclear why they have occurred. Some of these acute reactions may, in fact, have been due to bacterially-infected components or may have been episodes of transfusion-related acute lung injury.

- Although the local haematologist has been informed (or initially involved) in most instances it is surprising that some severe reactions appear not to have been notified to him/her.

RECOMMENDATIONS

- **Clinicians involved in transfusion should be made aware that FFP and platelets carry a relatively high risk of inducing a severe adverse event.**

- **National guidelines are available relating to anticoagulant management[14] and the appropriate use of FFP[15] and also platelets[16] (FFP guidelines currently being updated) but many staff prescribing these may not be aware of their content. Summaries of the more relevant points could usefully be included in hospital transfusion guidelines or Transfusion Laboratory Handbooks in order to improve accessibility and compliance with these.**

- **A national guideline on the appropriate investigation of transfusion reactions is required and is currently under preparation within the NBS and SNBTS**

- **The local haematologist should be contacted regarding all serious adverse events arising from the transfusion of blood components. These events may have implications for other potential recipients and require timely and appropriate investigation if the cause of the event is to be clarified.**