8. ACUTE TRANSFUSION REACTIONS

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

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

27 initial reports were received (1 fatal) and 24 completed questionnaires were returned.
The data retrieved from the returned questionnaires are shown in Appendix 5.ii.
This chapter highlights the main features of the 24 completed questionnaires received.

Sex	
Males	8
Females	16
Age	
Age range	1 month - 80 years
Median age	64 years
Components implicated	No. of cases
Red cells (rbc)	18 (1 also FFP)
Platelets	5
Fresh frozen plasma (FFP)	2 (1 also rbc)

A. Reactions in which red cells were implicated

There were 18 cases including 1 case where FFP was also implicated.

Reactions could be broken down into the following categories:

Reaction type	**Number of cases**
Haemolytic	6
Non-haemolytic febrile	7
Hypotensive	2
Due to anti IgA antibodies	1
Other	2

Haemolytic reactions and their clinical sequelae.
In 4 cases red cell allo-antibodies were detected for the first time post-transfusion. In 2 of these cases crossmatching was performed on a sample taken four or more days prior to the transfusion in a previously transfused patient. In one case this was undoubtedly a contributory factor but was less clear in the second case. In one case the development of anti-D in a Rhesus D negative patient being transfused with RhD positive red cells was unrecognised because free anti-D was not detected in the pre-transfusion serum. A further case developed a non-haemolytic febrile transfusion reaction and was also found to have red cell allo-antibodies and a positive direct antiglobulin test. In this case the presence of red cell antibodies pre-transfusion had been suspected but transfusion with crossmatch-compatible, unselected red cells was allowed to proceed because it was considered urgent.

Clinical sequelae included one case of exacerbation of pre-existing auto-immune haemolysis (AIHA) and one case of haemolysis presumed to be caused by a cephalosporin-dependent red cell antibody.

Non-haemolytic febrile reactions
Note that the initial SHOT information package did not seek reports of febrile non-haemolytic reactions.
Seven of these were reported. HLA (histocompatibility locus associated) antibodies were found in 4 cases and suspected, but not identified at the time of the report, in 2 cases. In another case the cause was not established. Such reactions are known to be common and not usually serious. The fact that these cases were reported may reflect reactions which were considered more severe than usual.

Hypotensive reactions
There was one reported case in which autologous whole blood, filtered through a negatively charged leucocyte-depleting filter and transfused to a bone marrow donor, was clearly associated with an immediate hypotensive reaction. The transfusion was terminated. The patient was not receiving ACE (angiotensin converting enzyme) inhibitor drugs. Hypotensive reactions to platelets, associated with the use of negatively charged filters and treatment with ACE inhibitors, has been recently recognised (see below) but to our knowledge has not been reported in patients receiving red cell transfusions.

IgA antibodies
The one case reported in this category is worthy of mention because the sole manifestation was pruritis and a skin rash. The patient was subsequently found to be IgA deficient with high titre anti- IgA antibodies. This is the likely cause of the reaction, since such patients are well recognised to experience anaphylaxis during transfusion.

Others
A further three cases were hypertransfusion (1 case), clinical anaphylaxis, cause unknown (1 case) and dyspnoea/restlessness, cause unknown (1 case). In the last case, subsequent transfusion with washed red cells was well tolerated.

B. Reactions in which platelets were implicated

There were 5 cases which fell into 2 groups:

Hypotension/flushing
There were 4 cases in this group, 3 of which involved the use of negatively charged leucodepletion filters as previously described[24] . In 1 of the cases, the patient was receiving treatment with an ACE inhibitor. A fourth case involved neither the use of a filter nor ACE inhibitor.

Haemolysis
One patient (group A) receiving pooled, buffy coat-derived, group O platelets for a haematological malignancy developed a haemolytic reaction. The group O platelet unit could not be shown retrospectively to have high titre anti A and exacerbation of autoimmune haemolysis could not be ruled out.

C. Reactions in which fresh frozen plasma was implicated

There were only 2 reports in this group, one also involving the use of red cells and resulting in hypertransfusion and the second resulting in pruritis and dyspnoea, cause unknown and probably not fully investigated.

Outcome
The majority of patients reported with acute transfusion reactions survived without sequelae. There was only 1 transfusion-related death, in an elderly female with underlying haematological malignancy and AIHA in whom haemolysis as a result of passive transfer of anti A from group O platelets was thought to be a contributory factor. A further patient, who suffered a reaction as a result of platelet/filter interaction, subsequently died of underlying disease. One patient who was hypertransfused remained seriously ill.

Summary

- In general the reported reactions do not reflect poor practice and cannot be predicted. Procedures for reporting reactions to attendant medical staff and for subsequently seeking more expert advice are generally adhered to although in some cases retraining and/or tightening up of procedures was deemed necessary by hospitals.

- This group of patients who experience acute reactions is commonly treated with a combination of hydrocortisone and antihistamine. Such patients may experience repeated reactions and thus be prescribed repeated doses of hydrocortisone.

- There is wide variation in the frequency with which nursing observations are recorded during transfusions. It is not clear what the optimum type and frequency of such observations should be and this area would benefit from audit and standardisation.

- There is marked variability in the number and types of post-transfusion investigation performed. This may reflect the type of component implicated and the perceived seriousness and cause of the reaction. Lack of data in some cases made it difficult to draw firm conclusions about the cause of the reaction. This is another area which would benefit from standardisation.

- There were four cases where the crossmatch sample was taken four or more days prior to the transfusion. In one case this clearly contributed to the development of acute haemolysis in a patient with an unrecognised delayed haemolytic transfusion reaction. In a second case it was not clear whether the time lag was a contributory factor. In two further cases the delay was not a relevant factor. Recommendations for safe intervals between sampling and transfusion are given in BCSH guidelines for pre-transfusion compatibility testing[6].

- The majority of reactions were reported to the local Blood Centre but only about 50% of reactions was reported to a hospital transfusion committee. It is not clear whether this reflects simple lack of reporting or the absence of an appropriate forum for reporting.

- There is a new type of reaction, only recently recognised, in which hypotension and flushing is associated with the use of negatively charged bedside leucodepleting platelet filters in patients with reduced ability to break down bradykinin, for example during treatment with angiotensin converting enzyme (ACE) inhibitors[24]. In this report, a similar reaction occurred in the absence of ACE inhibitor treatment and also in response to filtered whole blood, a feature which to our knowledge has not been previously reported.

Recommendations

- Consider the use of paracetamol rather than hydrocortisone for the treatment of recurrent non-haemolytic febrile transfusion reactions.

- A national review of standards for the type and frequency of nursing observations during transfusion is recommended.

- A national review of the requirements for samples and investigations following acute transfusion reactions is recommended.

- Hospitals should review crossmatch sampling intervals in the light of BCSH guidelines for pre-transfusion compatibility testing[6].

- A hospital transfusion committee or other appropriate forum for discussion of transfusion-related matters should be set up where one does not exist.

- Clinicians should consider the possibility of platelet/filter interactions in patients receiving ACE inhibitor treatment. Reporting of future cases is encouraged so that a complete picture can emerge.