# Acute Transfusion Reactions (Allergic, Hypotensive and Severe Febrile) (ATR) n=296

# 11

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## 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 an incorrect component being transfused, haemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), transfusion-associated dyspnoea (TAD) or those due to bacterial contamination of the component.**

In contrast to previous years unclassifiable reactions have also been removed. This largely leaves febrile type, allergic and hypotensive reactions for which no other obvious cause is evident. These are classified according to the International Haemovigilance Network/International Society for Blood Transfusion (IHN/ISBT) definitions which can be found in the supplementary information on the SHOT website www.shotuk.org, (ISBT/IHN 2011) and these have been adopted by the British Committee for Standards in Haematology (BCSH Tinegate et al. 2012).

## Key SHOT message

- SHOT data and published studies indicate that the use of platelets suspended in platelet additive solution (PAS) is associated with a reduction in allergic response. Hospitals should consider preferential use of platelets suspended in PAS in patients with a history of this type of reaction. If reactions continue then platelets resuspended in 100% PAS can be supplied

## Number and types of reactions

Total number of reactions n=296

## Deaths n=0

## Major morbidity n=86

| | Moderate | Severe | Total |
|---|---|---|---|
| Febrile | 122 | 20 | **142** |
| Allergic | 64 | 58 | **122** |
| Mixed allergic/febrile | 18 | 7 | **25** |
| Hypotensive | 6 | 1 | **7** |
| **Total** | **210** | **86** | **296** |

*NB: in 25 of the 86 reactions classified as severe this was primarily because the patient was admitted*

**Table 11.1: Classification of reactions**

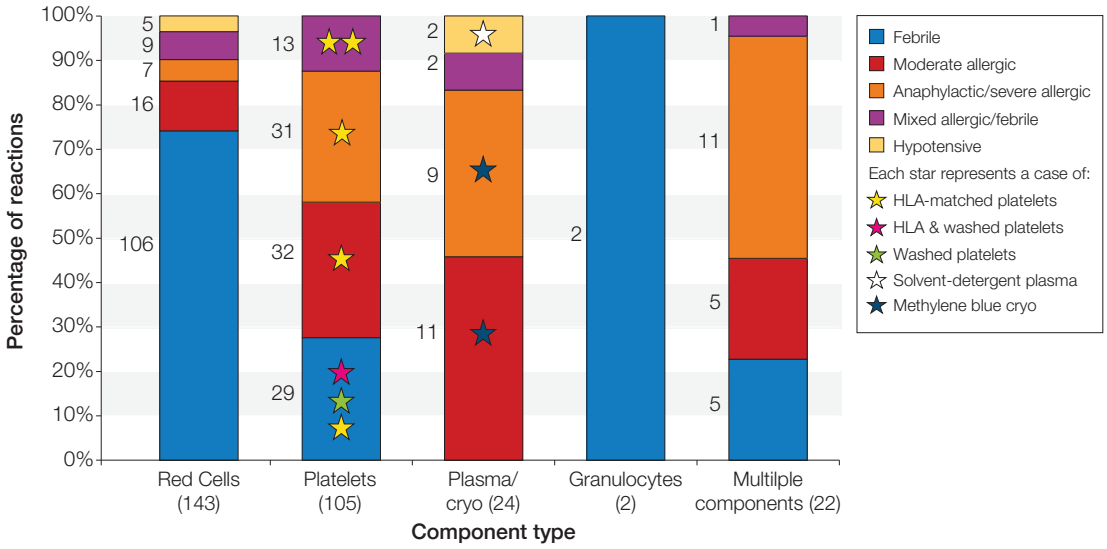
# Comparison with previous Annual SHOT Reports

## Similarities to 2014

### Reactions by component type

These remain similar to previous Annual SHOT Reports: Figure 11.1. Red cells are usually associated with febrile-type reactions (~75%) whereas plasma and platelets more commonly cause allergic reactions (~80% and ~60% respectively). The percentage of severe reactions remains similar to 2014 at 30% and in around 30% of these this was primarily because the patient required admission. As in previous years, many reactions were difficult to classify as a result of insufficient information, the IHN/ISBT grade of reaction severity not being used and because of the difficulty distinguishing true transfusion reactions from symptoms and signs caused by the patient's underlying condition.

**Figure 11.1: Reaction by component type**




*HLA: human leucocyte antigen, SD-FFP: solvent detergent-treated fresh frozen plasma*

**Table 11.2: Analysis of reactions (similar to last year)**

| Characteristic | Occurrence |
|---|---|
| Age distribution | 90% 18 years or over and 1% under 1 year |
| Gender | Similar numbers of male and female cases |
| Urgency of transfusion | 70% were given routinely |
| Timing of transfusion | 50-60% occurred within standard hours |
| Location | 20% in outpatients/day units, 50-60% on wards |

### Treatment of reactions

Similar to last year, where medication was given to treat a febrile-only type of reaction more than 50% were given an antihistamine +/- steroid for which there is no evidence of benefit.

Only around 10% were given paracetamol as treatment for allergic-only symptoms and signs; Table 11.3.

| | Number of reports | Medication stated | Antihistamine +/- steroid |
|---|---|---|---|
| **Febrile** | | | |
| 2015 | 142 | 101/142 (71.1%) | 57/101 (56.4%) |
| 2014 | 144 | 97/144 (67.4%) | 42/97 (43.3%) |
| | **Number of reports** | **Medication stated** | **Paracetamol** |
| **Allergic** | | | |
| 2015 | 122 | 106/122 (86.9%) | 10/106 (9.4%) |
| 2014 | 139 | 112/139 (80.6%) | 14/112 (12.5%) |

**Table 11.3: Treatment of reactions**

### Management to prevent subsequent febrile reactions

Although numbers were small the most common medication stated as prophylaxis to prevent future pure febrile-type reactions was an antihistamine +/- steroid; Table 11.4.

| Prophylaxis | Febrile | Medication stated | Antihistamine +/- steroid |
|---|---|---|---|
| 2015 | 44 | 9 | 7/9 (77.8%) |
| 2014 | 52 | 24 | 9/24 (37.5%) |

**Table 11.4: Management to prevent subsequent febrile reactions**

## Differences from 2014

### Use of platelet additive solution

In 2015 in England PAS was introduced to replace plasma in concentrates made from platelet pools with full implementation by July 2015. Apheresis platelets remained suspended in plasma. Using adult data for England only and corrected for the total number of pooled and apheresis platelets issued, a reduction in allergic reactions to pooled platelets is evident. This has not been observed for allergic reactions linked to apheresis platelets or for febrile-type reactions associated with either component. This is in keeping with published studies (Tobian et al. 2014, Cohn et al. 2014, Cazenave et al. 2011, Yanagisawa et al. 2013). The lack of a demonstrable effect of PAS on febrile-type reactions is likely to be because these are caused by the accumulation of cytokines post storage and not directly related to plasma: see Figures 11.2 and 11.3.

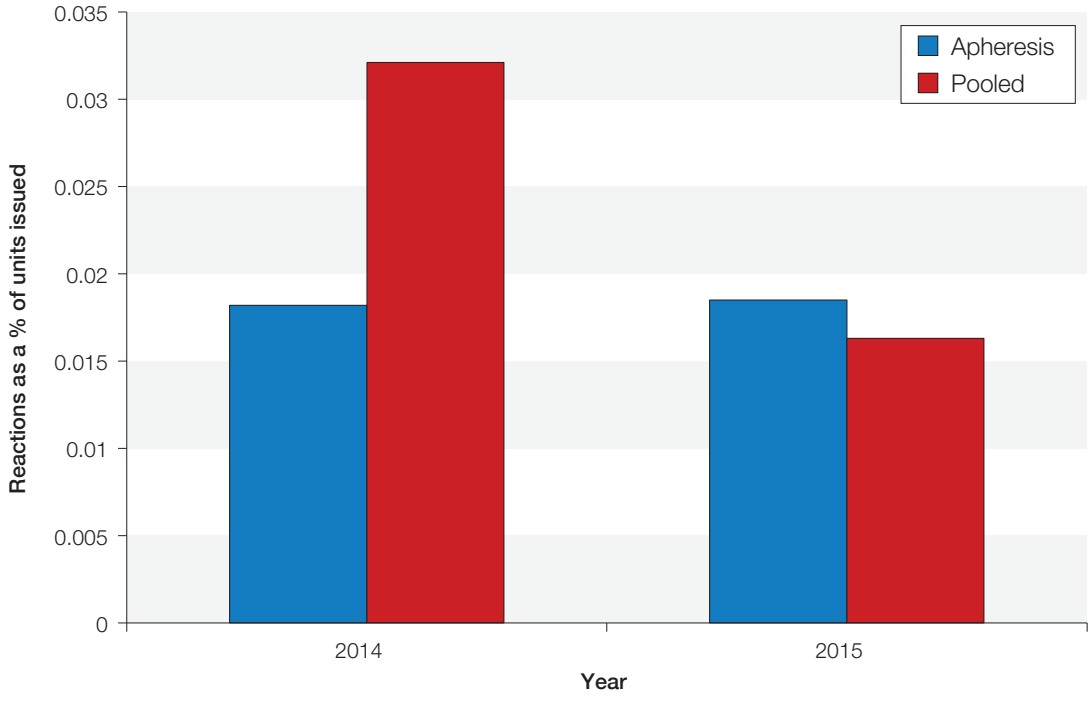
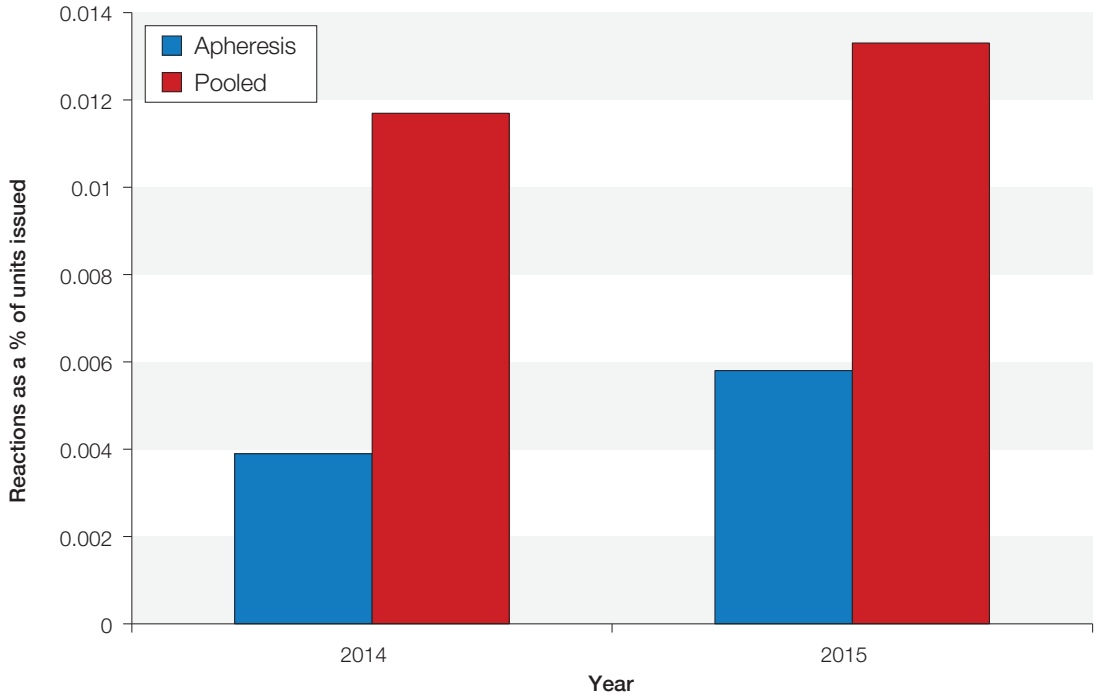



**Figure 11.2: Percentage of moderate/severe allergic reactions 2014 compared with 2015**

**Figure 11.3: Percentage of moderate/severe febrile-type reactions 2014 and 2015**

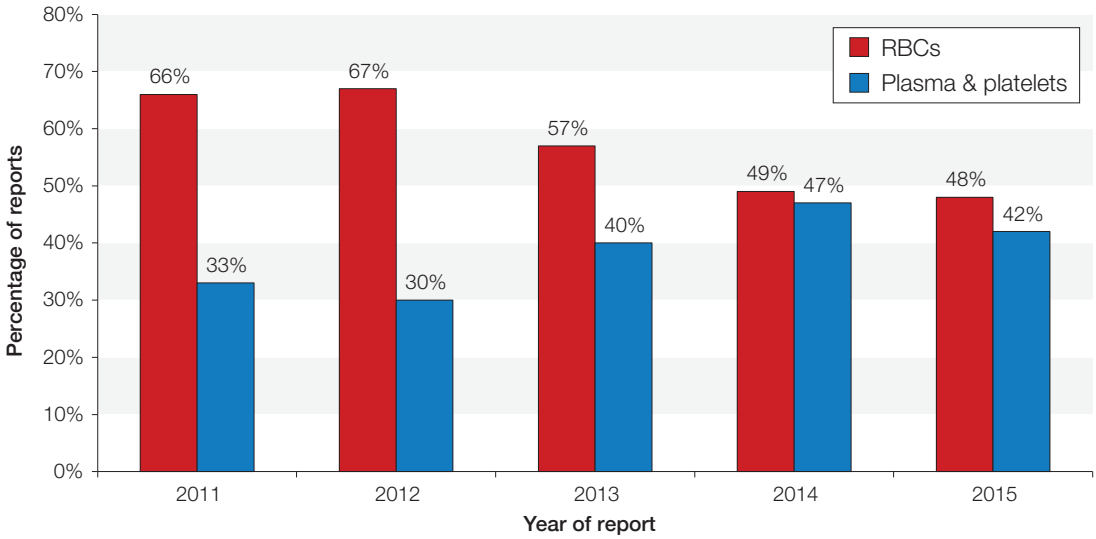



## Percentage of reactions associated with each component

The percentage of reactions associated with plasma and platelets has reduced from 48% to 42%. This is entirely due to a reduction in reactions to FFP from 39 (13%) in 2014 to 20 (7%) this year. Out of the 20 reported 19 were linked to standard FFP and only one to pooled solvent detergent (SD)-treated plasma. Pooled plasma is known to cause fewer reactions and its increased use is likely to have contributed to the observed reduction: Figure 11.4.

In 2015 there were only 3 reactions associated with methylene blue (MB)- or SD-treated plasma components compared to 10 last year. The reaction to SD-FFP was a severe hypotensive reaction in a 9 day old cardiac surgery patient coming off extracorporeal membrane oxygenation. There were two reactions to MB-cryoprecipitate: a severe allergic reaction in a 16 year old and a moderate allergic reaction in an 18 year old.

**Figure 11.4: Percentage of cases reported by component**



## Illustrative cases

**Case 11.1: A severe febrile reaction**

*An adult male with chronic bone marrow failure was transfused standard red cells and within 30 minutes he developed severe rigors with dyspnoea, hypertension and tachycardia. Symptoms and signs resolved on cessation of the transfusion. Culture of the implicated unit was negative. Screening for HLA antibodies was also requested and prophylaxis with hydrocortisone and chlorphenamine planned for future transfusions.*

**Comment:** It is unclear how the presence of HLA antibodies would alter management or why hydrocortisone and chlorphenamine would prevent similar reactions.

**Case 11.2: A moderate febrile reaction resulting in admission**

*A girl receiving treatment for a brain tumour attended hospital for a platelet transfusion. At the end of the infusion her temperature had increased from 37.6°C pre transfusion to 40.1°C. Other observations remained stable. Blood cultures were taken; she was given paracetamol, started on intravenous antibiotics and admitted. Within three hours post transfusion her temperature had returned to normal. Blood cultures were negative.*

**Comment:** Febrile-type reactions can be indistinguishable from more severe reactions at presentation and thus requiring admission for investigation and treatment.

**Case 11.3: An anaphylactic reaction with classic rise in mast cell tryptase**

*An adult male with chronic bone marrow failure who was refractory to standard platelets, with HLA antibodies, was transfused with HLA-matched platelets. He rapidly developed hypotension with collapse and hypoxia. Resuscitation with adrenaline, hydrocortisone, chlorphenamine, intravenous fluids and high flow oxygen was successful. Serial samples for mast cell tryptase identified a high level at 84 picograms (pg)/L in the first sample taken post reaction, 121pg/L 30 minutes later and a normal level of 9pg/L the following day.*

**Comment:** SHOT reporting has previously shown similar rates of allergic reactions to both HLA-matched and standard platelets.

**Case 11.4: An allergic reaction following plasma infusion to reverse warfarin**

*An adult male was given FFP prior to cystoscopy to reverse a raised international normalised ratio (INR) of 7 associated with warfarin. After the first bag had been infused he developed an itchy rash with shortness of breath and chest tightness. The transfusion was discontinued and adrenaline and hydrocortisone given. He made a complete recovery.*

**Comment:** This was an inappropriate transfusion. The treatment of choice to reverse the effect of warfarin is prothrombin complex concentrate.

**Case 11.5: A severe reaction in a patient with IgA deficiency**

*An adult female presented with acute myeloid leukaemia (AML). She had been found to be IgA-deficient, with IgA antibodies, during investigation for chronic fatigue several years previously but had never received blood. She was transfused a unit of standard red cells and experienced a severe reaction with nausea, rigors, wheeze and a feeling of impending doom. She subsequently received washed red cells and platelets without problems, achieved remission and underwent a successful allogeneic stem cell transplant. The stem cells were washed to remove donor plasma.*

**Comment:** Reactions associated with IgA deficiency are rare despite a prevalence of IgA deficiency of around 1 in 200. In this case symptoms of allergy were present, which are considered standard, but in addition rigors occurred which are typical of a febrile-type reaction.

## Recommendation

- SHOT data and published studies indicate that the use of platelets suspended in platelet additive solution (PAS) is associated with a reduction in allergic response. Hospitals should consider preferential use of platelets suspended in PAS in patients with a history of this type of reaction. If reactions continue then platelets resuspended in 100% PAS can be supplied

**Action: UK Blood Services, Hospital Transfusion Teams (HTT)**

**Key recommendations from previous years** can be found in the supplementary information on the SHOT website www.shotuk.org

## References

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