16 Febrile, Allergic and Hypotensive Reactions (FAHR) n=318

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Definition:

The reactions assessed are isolated febrile-type (not associated with other specific reaction categories), allergic and hypotensive reactions occurring up to 24 hours following a transfusion of blood or components, for which no other obvious cause is evident.

Abbreviations used in this chapter

ATD	Adult therapeutic dose	**IV**	Intravenous
BSH	British Society for Haematology	**MB**	Methylene blue treated
FAHR	Febrile, allergic and hypotensive reactions	**PAS**	Platelet additive solution
FFP	Fresh frozen plasma	**PICC**	Peripherally inserted central catheter
Hb	Haemoglobin	**SABRE**	Serious adverse blood reactions and events
IHN	International Haemovigilance Network	**SD**	Solvent detergent treated
ISBT	International Society for Blood Transfusion		

Key SHOT messages

- Use the patient's symptoms and signs to differentiate allergic from febrile reactions, as they require different investigation and treatment
- Do not give antihistamine or a steroid to treat or prevent febrile reactions
- Anaphylactic transfusion reactions are unpredictable and can occur in any setting. All staff involved in administering transfusions should be trained in recognition and management of severe allergic reactions
- The possibility of a febrile or allergic reaction should be explained to patients/guardians when taking consent for transfusion

Recommendations

- Give appropriate targeted treatment and if needed, use preventative cover for future transfusion (BSH Tinegate et al. 2012), as indicated below:

Table 16.1: Targeted treatment for febrile and allergic transfusion reactions

Reaction	Treatment	Prevention of recurrent reactions
Febrile	Paracetamol	Paracetamol 60 minutes before anticipated time of reaction
Allergic	Antihistamine (steroid should not be used routinely); If anaphylaxis, adrenaline is essential	If previous reaction with apheresis platelets try pooled platelets in PAS; If reactions continue, give pre-transfusion antihistamine; If reactions continue, consider washed platelets/red cells; for FFP try a pooled component e.g. SD-treated plasma

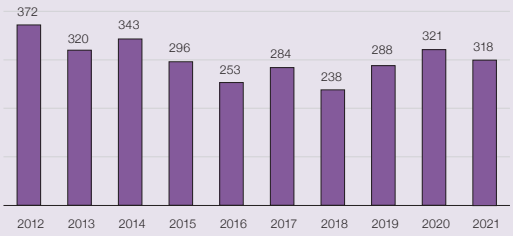
- Transfusion teams should audit appropriateness of treatment given for acute transfusion reactions and take relevant actions

Action: Hospital transfusion teams

Headline data 2021

Number of reports n=318
Deaths n=0
Major morbidity n=74

FAHR reports by year



Demographic data

Male n=145
Female n=173
Adults n=272
Paediatric n=42
Unknown n=4

Blood component data

Red cells n=179
Platelets n=96
Plasma n=19
Multiple components n=23
Granulocytes n=1

Introduction

Reactions are classified according to the ISBT/IHN definitions, which are summarised below in Table 16.2, available online (ISBT/IHN 2011) and have been adopted by the BSH (BSH Tinegate et al. 2012). Mild reactions are not reportable to SHOT.

Table 16.2: Classification of reactions

CURRENT IHN/SHOT/B(C)SH CLASSIFICATION OF ACUTE TRANSFUSION REACTIONS				SABRE classification
	1=Mild	**2=Moderate**	**3=Severe**	
Febrile type reaction	A temperature > 38°C and a rise between 1°C and 2°C from pre-transfusion values, but no other symptoms/ signs	A rise in temperature of 2°C or more, or fever 39°C or over and/or rigors, chills, other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion	A rise in temperature of 2°C or more, and/or rigors, chills, or fever 39°C or over, or other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion, prompt medical review AND/OR directly results in, or prolongs hospital stay	**Other/febrile FAHR**
Allergic type reaction	Transient flushing urticaria or rash	Wheeze or angioedema with or without flushing/urticaria/ rash but without respiratory compromise or hypotension	Bronchospasm, stridor, angioedema or circulatory problems which require urgent medical intervention AND/OR, directly result in or prolong hospital stay, or **Anaphylaxis** (severe, life-threatening, generalised or systemic hypersensitivity reaction with rapidly developing airway AND/OR breathing AND/OR circulation problems, usually associated with skin and mucosal changes)	**Anaphylaxis/ hypersensitivity/ allergic/FAHR**
Reaction with both allergic and febrile features	Features of mild febrile **and** mild allergic reactions	Features of both allergic and febrile reactions, at least one of which is in the moderate category	Features of both allergic and febrile reactions, at least one of which is in the severe category.	*__Other/mixed febrile/allergic FAHR__
Hypotensive reaction		Isolated fall in systolic blood pressure of 30 mm Hg or more occurring during or within one hour of completing transfusion **and** a systolic blood pressure 80 mm or less in the absence of allergic or anaphylactic systems. No/ minor intervention required	Hypotension, as previously defined, leading to shock (e.g., acidaemia, impairment of vital organ function) without allergic or inflammatory symptoms. Urgent medical intervention required	**Other/ hypotensive FAHR**

**This category may include mild symptoms/signs of one reaction type providing the other category is either moderate or severe*

As the reporting categories on SABRE can cause confusion, the SHOT definitions document has been updated for 2022 to clearly map which category to select when submitting a report.

Total number of FAHR reactions n=318

Although the number of reactions reported is similar to 2020, this was still more than 10% higher than in previous years. This is due to an increase in the reports of febrile reactions, while allergic reactions remain stable.

Deaths related to transfusion n=0

There were no deaths related to the transfusion reactions in 2021.

Major morbidity n=74

The ISBT/IHN classification of a severe reaction has been used to define major morbidity.

Reactions are categorised in Table 16.3.

	Moderate	Severe	Total
Febrile	158	16	174
Allergic	58	50	108
Mixed allergic/febrile	20	6	26
Hypotensive	8	2	10
Total	**244**	**74**	**318**

Table 16.3: Classification of FAHR in 2021

NB: in 20 of the 74 reactions classified as severe this was primarily because the patient was admitted or kept in overnight or re-presented to the hospital after discharge

Excluded reports n=150

There were 468 cases initially reported as FAHR. Of these, 140 cases were withdrawn, and 10 cases were transferred to other SHOT reaction categories. This resulted in 318 FAHR cases for analysis and inclusion in the Annual SHOT Report. Of the withdrawn cases, 65/140 (46.4%) were withdrawn as they were mild reactions, which have not been reportable to SHOT since 2012. The remaining reports were withdrawn as clinical details suggested the reaction was not related to the transfusion, or did not fit the criteria for reporting to SHOT (for example, reactions to anti-D Ig which are only reportable to the MHRA yellow card scheme).

Reactions in IgA deficient patients n=4

There were 4 reactions reported in patients who on subsequent investigation were discovered to have severe IgA deficiency with anti-IgA antibodies. All occurred within the first 15 minutes of transfusion. Of these, 3 were febrile reactions; 2 of these patients had marked systemic upset, with other features including hypertension, breathlessness, myalgia and vomiting. The 4th case was an anaphylactic reaction involving bronchospasm and hypotension in a patient under anaesthesia.

It is recommended that these patients receive washed components for future red cell or platelet transfusions, provided this does not risk delaying an urgent transfusion. Transfusion should be carried out in a setting where there is immediate access to skilled clinical help (Latham 2019).

Anaphylactic reactions n=32

Anaphylaxis is a serious systemic hypersensitivity reaction that is usually rapid in onset. It is characterised by potentially life-threatening compromise in airway, breathing and/or the circulation, with or without typical skin features or circulatory shock (Resuscitation Council UK 2021).

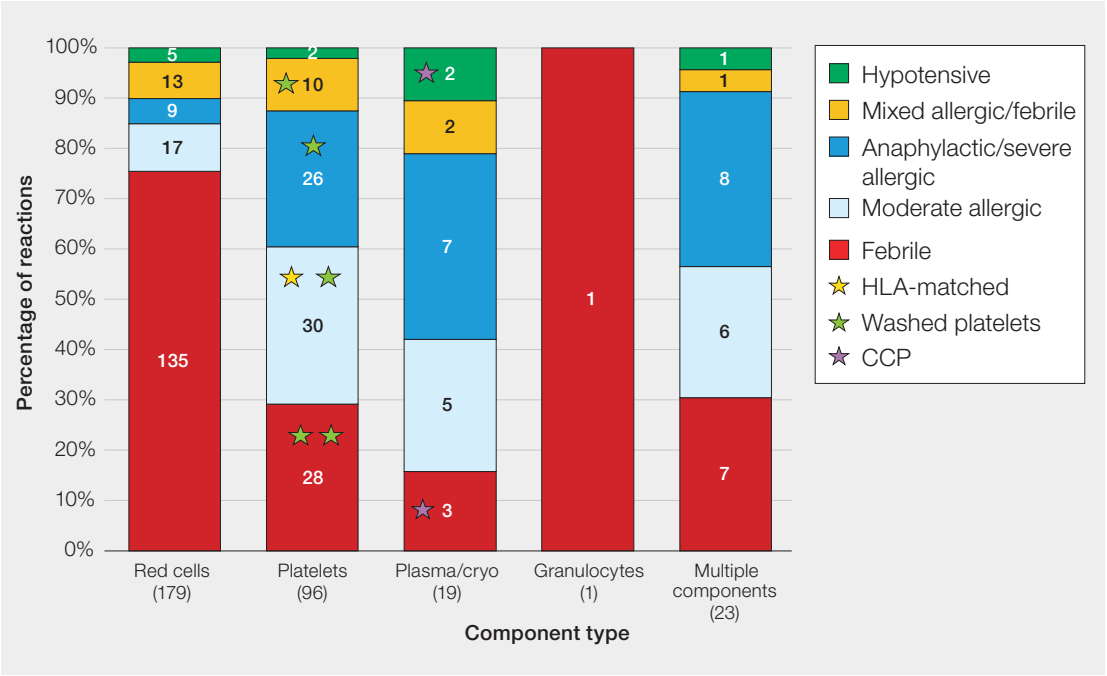
There were 32 reactions reported which required the use of adrenaline. In 15 cases the transfusions were routine, and 5 occurred in an outpatient or day care setting. Children were disproportionately represented: 10/32 (31.3%) cases were in patients under 18 years. There was 1 unnecessary transfusion (a fourth unit of platelets given to a patient with an intracranial haemorrhage who was taking aspirin), and 1 patient was subsequently discovered to have IgA deficiency (see above).

This highlights the importance of close monitoring and observation of patients receiving transfusions. Staff should be able to recognise any complication and act promptly.

Type of reaction by component

This remains similar to previous Annual SHOT Reports; see Figure 16.1. Red cells are usually associated with febrile-type reactions, 135/179 (75.4%), whereas plasma components and platelets more commonly cause allergic reactions, 12/19 (63.2%) and 56/96 (58.3%) respectively. There were 2 reactions reported with the use of COVID-19 convalescent plasma. None were reported in association with solvent-detergent treated FFP or methylene blue treated components.

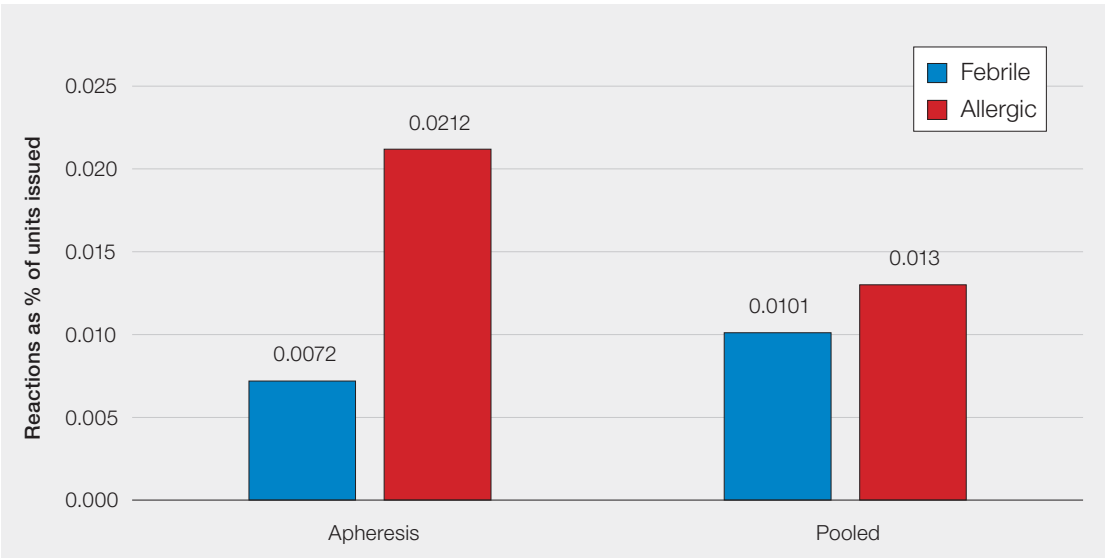
Figure 16.1: Reactions by component type



HLA=human leucocyte antigen; CCP=COVID-19 convalescent plasma; cryo=cryoprecipitate

The overall incidence of reactions of all types combined is greater for apheresis 48/145,920 (0.03%) than for pooled 35/137,932 (0.025%) platelet components (there were 13 cases that did not specify the type of platelets). Fewer allergic reactions continue to be reported in association with pooled platelets in PAS than apheresis platelets, which is linked to the lower plasma content (Figure 16.2) (Estcourt et al. 2017).

Figure 16.2: Incidence of reactions as a percentage of platelet units issued



Analysis of reactions remains comparable to previous years in the following characteristics (Table 16.4):

Table 16.4: Characteristics of FAHR

Recipient or transfusion characteristic	Percentage
Age distribution	84% of patients were aged 18 years or over
Gender	46% male and 54% female cases
Urgency of transfusion	63% were given routinely
Timing of transfusion	73%* occurred within standard hours
Location	62% were on wards and 17% in outpatient/day case units

**Higher % of cases than previous years likely associated with fewer cases reported as unknown*

Treatment of reactions

An antihistamine with or without steroid continues to be used inappropriately to treat reactions with only febrile/inflammatory type symptoms and/or signs; see Table 16.5. In addition to no evidence of benefit, the repeated use of steroids may further suppress immunity in already immunocompromised patients and increase the risk of side effects such as infection.

	Number	Medication stated	Antihistamine and/or steroid
2021	174	155/174 (89.1%)	61/155 (39.4%)
2020	166	140/166 (84.3%)	58/140 (41.4%)
2019	146	130/146 (89.0%)	62/130 (47.7%)
2018	103	88/103 (85.4%)	39/88 (44.3%)
2017	140	121/140 (86.4%)	46/121 (38.0%)
2016	124	102/124 (82.3%)	51/102 (50.0%)
2015	142	101/142 (71.1%)	57/101 (56.4%)
2014	144	97/144 (67.4%)	42/97 (43.3%)

Table 16.5: Reported treatment of febrile reaction

In 2023, as part of the annual participation benchmarking exercise for 2022, SHOT will provide feedback on the proportion of reactions from each Trust/Health Board where the SHOT working experts judged that alternative treatment might have been more beneficial. This will give a means of benchmarking and can be used to target local quality improvement initiatives.

SHOT have produced a quick-reference guide to aid classification and immediate management of febrile and allergic reactions (Figure 16.3), which can also be found in SHOT Bite No. 5: FAHR (see 'Recommended resources').

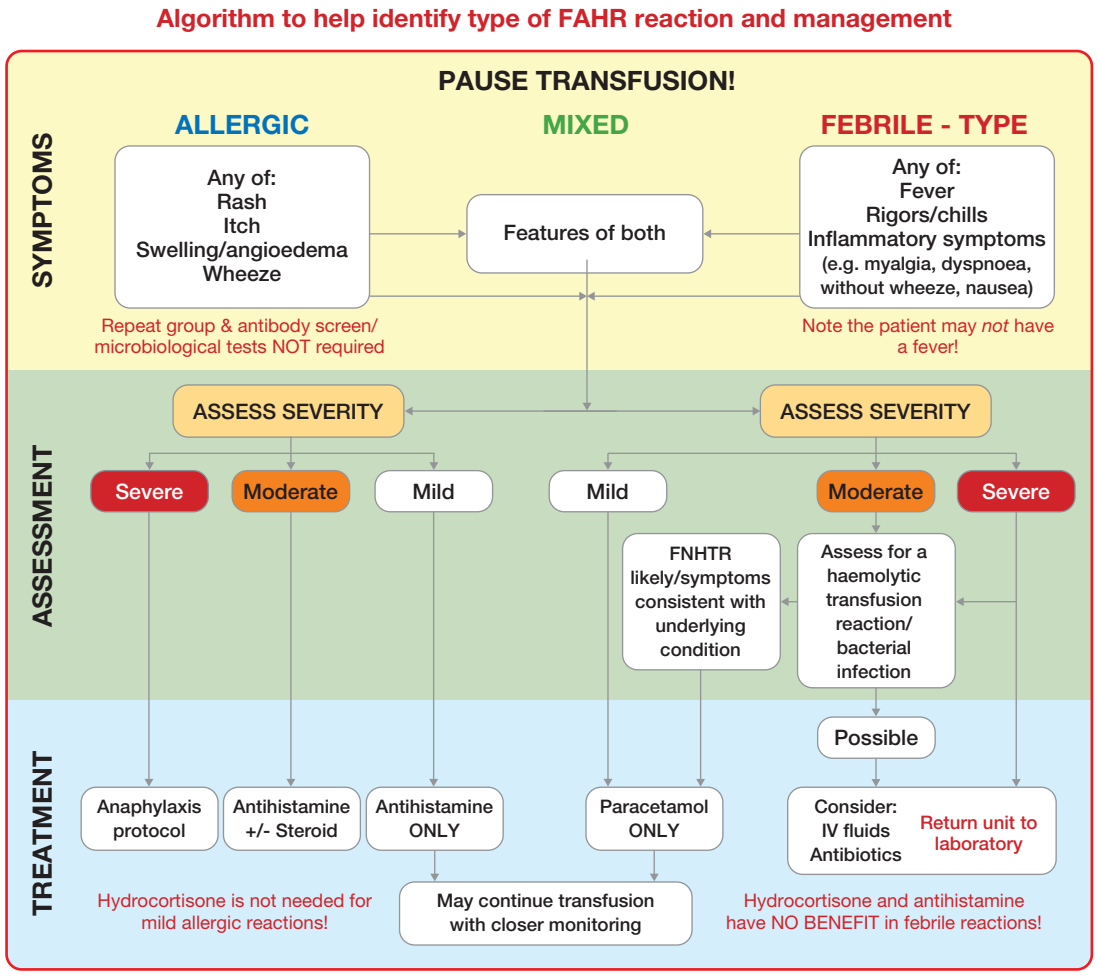


Figure 16.3: Algorithm for classification and management of febrile and allergic reactions

Subsequent management

A plan for subsequent treatment of febrile reactions was only given in 18 cases, likely reflecting that many patients are not expected to need further transfusion. While only 3 reports explicitly gave a plan to use antihistamine with or without steroids to treat a subsequent pure febrile reaction (Table 16.6), a further 4 stated 'premedication'. The use of washed blood components in 9/18 (50.0%) was the most frequently chosen management for future transfusions.

Table 16.6: Planned treatment of subsequent febrile reactions

	Number where treatment stated	Antihistamine +/- steroid stated
2021	18	3/18 (16.7%)
2020	33	7/33 (21.2%)
2019	42	7/42 (16.7%)
2018	27	8/27 (29.6%)
2017	22	5/22 (22.7%)
2016	21	9/21 (42.9%)
2015	9	7/9 (77.8%)
2014	24	9/24 (37.5%)

Illustrative cases

Case 16.1: Allergic reaction to an unnecessary platelet transfusion

A man in his 50s was transfused one ATD of apheresis platelets to cover a PICC insertion in interventional radiology. He developed peri-orbital and lip swelling and a rash. He was treated with IV hydrocortisone and chlorphenamine with resolution of his symptoms.

BSH guidelines (BSH Estcourt et al. 2017) recommend that platelet transfusions should not be used routinely prior to PICC insertion, regardless of the patient's platelet count.

Case 16.2: Future transfusion plan fails to account for reaction type

A woman in her 80s with transfusion-dependent anaemia required one unit of red cells following two large nose bleeds. Her Hb was 68g/L with a stated target Hb of >90g/L. Midway through transfusion she developed pyrexia (temperature 38°C from baseline 36.5°C), rigors and vomiting. The transfusion was stopped. Investigations revealed no evidence of a serological reaction. On review, frequent transfusion reaction investigations had been performed previously due to similar symptoms. The patient was given a plan for premedication with paracetamol, chlorphenamine, hydrocortisone and furosemide for future transfusions.

The choice of premedication appears to be a scatter-gun approach to cover all possible eventualities. This patient suffered recurrent febrile-type reactions, which would be best managed by premedication with paracetamol. If reactions persist, this might be an indication for washed red cells. The history suggests numerous abandoned transfusions, causing wastage of a precious resource, inconvenience to the patient and additional workload for both clinical and laboratory teams.

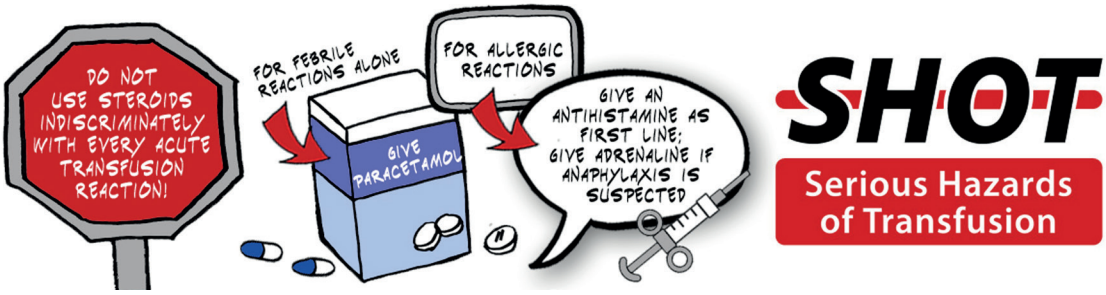
Learning points

- The risk of an acute reaction to transfusion should be a part of the evaluation process when making the decision to transfuse. Patients should be warned of the possibility of a reaction during consent
- 'Premedication' is not a one-size-fits-all cocktail suitable for all eventualities. Treatment of transfusion reactions and prophylaxis for those with recurrent reactions must be tailored to the type of reaction (allergic versus febrile) and its severity

Conclusion

Febrile, allergic and hypotensive reactions are an unavoidable and largely unpredictable risk of transfusion. While most are minor, anaphylaxis can be life-threatening and this underlines the need to ensure that transfusion is only given when clinically indicated and there is fully informed patient consent. There is continuing suboptimal management of acute transfusion reactions, particularly the inappropriate use of antihistamine and/or steroids to treat febrile reactions (in 39.4% of cases). The key message remains the need to use the patient's symptoms and signs to distinguish febrile from allergic reactions and to tailor management accordingly.

SHOT is planning to feedback on appropriateness of reaction management in the annual participation summary to all Trusts/Health Boards, beginning at the next Annual SHOT Report (2022 cases). This will provide benchmarking data and can be used to target local quality improvement initiatives.



Recommended resources

SHOT Bite No. 5: FAHR
https://www.shotuk.org/resources/current-resources/shot-bites/

SHOT Video: FAHR
https://www.shotuk.org/resources/current-resources/videos/

References

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