19 Febrile, Allergic, and Hypotensive Reactions (FAHR) n=354

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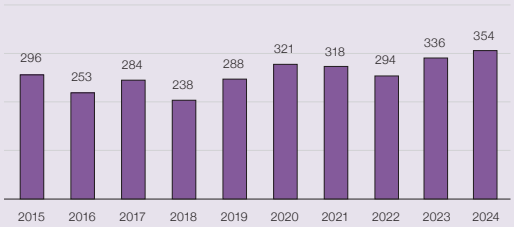
Headline data 2024

Number of reports n=354
Deaths n=0
Major morbidity n=113

FAHR reports by year



Demographic data

Male n=158
Female n=196
Adults n=308
Paediatric n=46

Blood component data

Red cells n=192
Platelets n=121
Fresh frozen plasma (FFP) n=20*
Solvent-detergent FFP n=1
Granullocytes n=4
Cryoprecipitate n=2
Multiple components n=14

1 FFP case also involved SD-FFP

Key findings:

- An increase in reports in 2024 – the highest number in 10 years
- Particular increase in reactions to pooled platelets (febrile and allergic)
- One third of patients with febrile reactions were treated inappropriately with antihistamine and/or steroid
- Red cell serological investigations were commonly performed unnecessarily (for allergic reactions or reactions to platelets/plasma)

Gaps identified:

- Lack of knowledge amongst clinicians about appropriate classification and targeted management and investigation of FAHR reactions
- Laboratory staff not empowered to challenge inappropriate requests for investigation

Good practice:

- Inappropriate use of antihistamine and/or steroid for febrile reactions reduced in both 2023 and 2024

Next steps:

- Check out the new SHOT Bite on appropriate investigation of febrile, allergic, and hypotensive reactions

For all abbreviations and references used, please see the **Glossary** and **Reference list** at the end of the full Annual SHOT Report. Please see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/annual-shot-report-2024/).

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.

Introduction

Reactions are classified according to the International Society of Blood Transfusion (ISBT)/International Haemovigilance Network (IHN) definitions, which are summarised in Table 19.1 and have been adopted by the British Society for Haematology (BSH) (Soutar, et al., 2023). Mild reactions are not reportable to SHOT.

Table 19.1: 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*

The 354 reports submitted in 2024 represents an increase from the 336 in 2023, which itself was the highest number for 10 years. There was a particular increase in reports related to platelets (121 in 2024 compared to 99 in 2023), which included both febrile and moderate allergic reactions.

There were 192 reports related to red cells, 21 fresh frozen plasma (FFP), 2 cryoprecipitate, 4 granulocytes and 14 involving multiple components.

Deaths related to transfusion n=0

There were no FAHR reports in 2024 that resulted in a transfusion-related death.

Major morbidity n=113

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

Reactions are categorised in Table 19.2.

Table 19.2: Classification of reactions in 2024 (n=354)

	Moderate	Severe	Total
Febrile	155	28	**183**
Allergic	58	64	**122**
Mixed allergic/febrile	25	15	**40**
Hypotensive	3	6	**9**
Total	**241**	**113**	**354**

All patients with major morbidity recovered with no sequelae. In 25 of the 113 reactions classified as severe, this was primarily because the patient was admitted, or hospital stay was prolonged.

Reactions in IgA deficient patients n=6

There were 6 reports of reactions in patients who were later identified to have severe IgA deficiency (IgA <0.07g/L). Four were confirmed to have anti-IgA antibodies; results were not available for the other cases. Two of the reactions were febrile-type reactions and 3 were mixed febrile/allergic. All of these involved marked systemic upset. One of the patients reported a history of a similar reaction in 2023, while another experienced recurrence of identical symptoms when transfusion was attempted again in the same admission. One patient had a purely allergic reaction with rash, wheezing and hypoxia, but recovered without needing adrenaline.

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 (Latham, 2019).

Anaphylaxis n=33

There were 33 severe allergic reactions requiring treatment with adrenaline. The components most often responsible were platelets (n=15) and FFP (n=18). Children were disproportionately represented: ten of these reports (30.3%) involved people under 18. This compares to 46/354 (13.0%) reports related to children in the whole FAHR category. Two reactions occurred in outpatient departments, 16 on wards, 1 in the emergency department and 3 on the medical assessment unit. Ten involved transfusions outside of normal working hours.

Type of reaction by component

Types of reaction by component reported in 2024 remain consistent with previous Annual SHOT Reports; see Figure 19.1. Red cells were most often associated with febrile-type reactions, 147/192 (76.6%), whereas plasma components and platelets more commonly cause allergic reactions, 21/23 (91.3%) and 70/121 (57.9%) respectively.

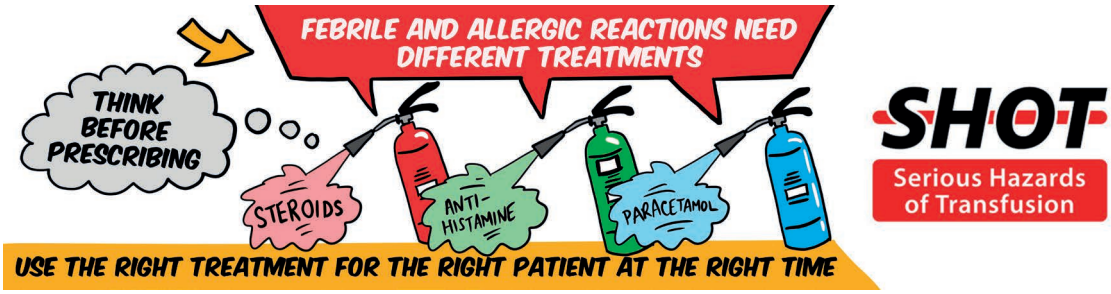
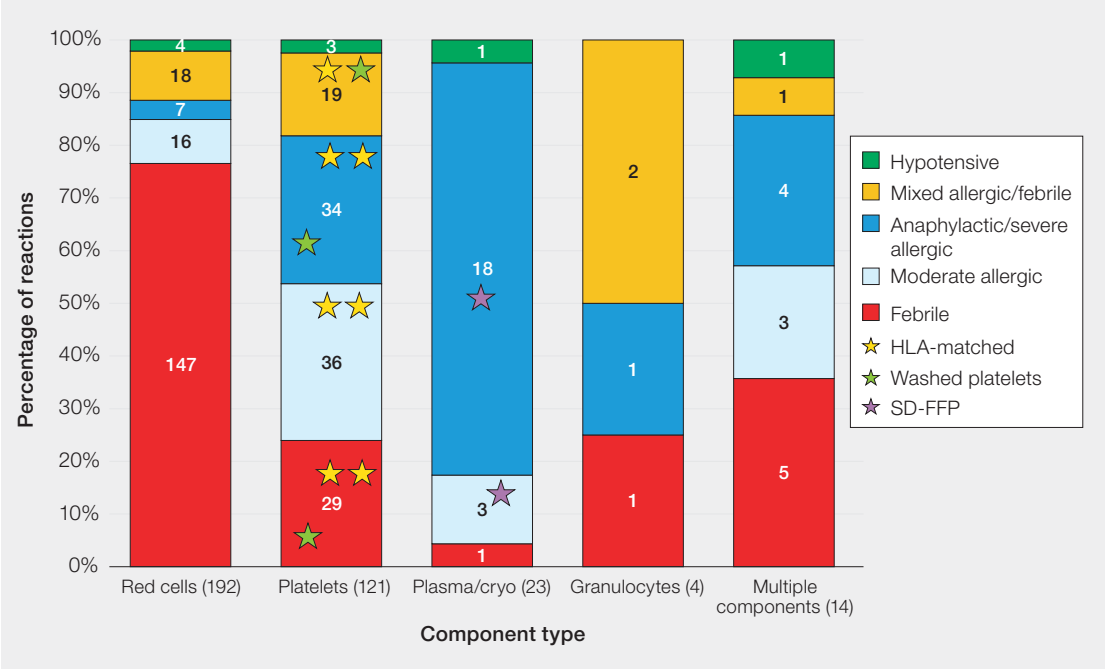


Figure 19.1: FAHR reactions by component type in 2024 (n=354)

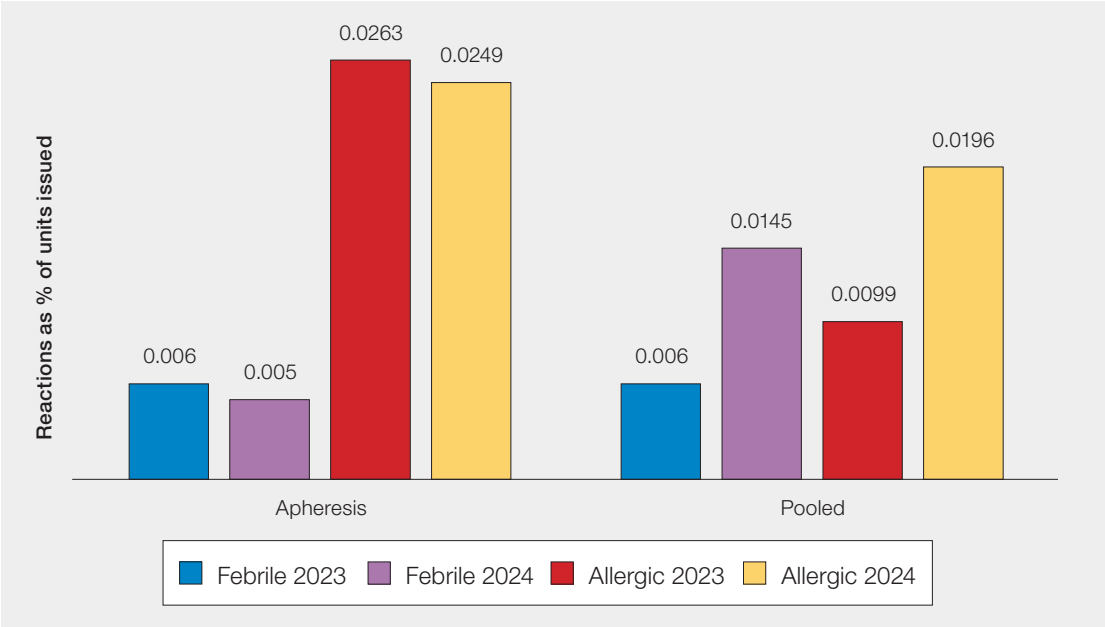


HLA=human leucocyte antigen; cryo=cryoprecipitate; SD-FFP=solvent detergent-treated fresh frozen plasma

In comparison to 2023 data, the incidence of reactions to apheresis platelets remains similar, for both allergic and febrile reactions. The overall increase in platelet reactions was related to pooled platelet components. The incidence of both febrile and allergic reactions roughly doubled in comparison to 2023 (Figure 19.2). SHOT will continue to monitor this.

The incidence of allergic reactions remains higher in apheresis platelets compared to pooled platelets, which relates to their higher plasma content (Estcourt, et al., 2017). The first step for subsequent transfusions for a patient experiencing a mild to moderate allergic reaction to apheresis platelets should be to switch to a pooled component.

Figure 19.2: Incidence of platelet reactions as a percentage of units issued 2023-2024



Management of reactions

Of the 179 reactions with only febrile features where treatment was stated, 63/179 (35.2%) were managed inappropriately with an antihistamine and/or steroid. This represented a further small improvement on previous years (Table 19.3).

Table 19.3: Inappropriate management of febrile reactions 2020-2024

Year	Number of febrile reactions	Medication stated	Antihistamine and/or steroid
2024	183	179/183 (97.8%)	63/179 (35.2%)
2023	163	163/163 (100%)	61/163 (37.4%)
2022	132	130/132 (98.5%)	61/130 (46.9%)
2021	174	155/174 (89.1%)	61/155 (39.4%)
2020	166	140/166 (84.3%)	58/140 (41.4%)

Table 19.4 summarises appropriate treatment targeted to the reaction type, and preventive cover for future transfusion, if needed (Soutar, et al., 2023).

Table 19.4: Targeted treatment for febrile and allergic 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 (suspended in platelet additive solution) If reactions continue, give pre-transfusion antihistamine; If reactions continue, consider washed platelets/red cells; for FFP try a pooled component e.g., solvent-detergent treated plasma

Laboratory investigation of reactions

There were continued high rates of investigations, many of which were not tailored to the clinical situation. In 78 cases, repeat group and screen was sent inappropriately. This included serological testing in:

- 49/121 (40.5%) of the reactions to platelets
- 10/23 (43.5%) of the reactions to FFP/cryoprecipitate
- 51/122 (41.8%) of the reactions with only allergic features

In 1 report, samples were sent to the Blood Service reference laboratory following a febrile platelet reaction. This constitutes an avoidable burden on laboratories and could have led to unnecessary delays in providing further components to the patient.

Mast cell tryptase was sent unnecessarily in 6 patients with febrile reactions. In 29 allergic reactions, patient blood cultures were sent, and in 11 cases the unit was cultured. All cultures were negative.

A new SHOT Bite is available to support appropriate use of investigations in FAHR (see 'Recommended resources').

Case 19.1: Mismanagement of a febrile reaction to a platelet transfusion given outside of guidelines

A patient with pancytopenia, receiving an adult therapeutic dose of platelets to cover a bone marrow biopsy on the haematology ward, developed rigors and a temperature rise to 38°C after completion of transfusion. They were treated with an antihistamine and hydrocortisone and repeat group and screen was sent. No blood cultures were performed. The patient recovered completely within 4 hours.

It is concerning to see inappropriate treatment and investigation of this febrile platelet reaction, particularly as the patient was under the care of haematology. Giving paracetamol and taking blood cultures would

have been more appropriate. As prophylactic platelet transfusion is not recommended prior to bone marrow biopsy, the transfusion itself was outside of guidelines (Estcourt, et al., 2017).

Case 19.2: Mixed febrile/allergic reaction to granulocytes in a patient with an allergic predisposition

A patient post allogeneic bone marrow transplant for aplastic anaemia received granulocytes in the evening for neutropenic sepsis. The patient developed facial oedema, urticaria and dyspnoea. Temperature increased from 37 to 38.5°C. There was a mild blood pressure drop from 136/81 to 114/57mmHg. The patient had known allergy to banana and peanuts and carried an EpiPen. They were treated with their own EpiPen 300µg intramuscular (IM) whilst waiting for the emergency drug bag and then received a further 500µg IM dose of adrenaline after 5 minutes. They were transferred to intensive care for overnight observations but made a full recovery.

Learning points

- Treatment of febrile and allergic reactions should be targeted to the patient's symptoms and signs (Soutar, et al., 2023)
- Antihistamines are of no benefit in the absence of allergic features, and even in allergic reactions, steroids should not be used routinely
- Red cell serological investigations are only required for febrile or hypotensive reactions to red cells, and where the reaction is severe enough to warrant discontinuing transfusion
- All clinical areas giving transfusion must be equipped and staff trained to manage anaphylaxis, and transfusion should only be given overnight when clinically necessary

Conclusion

Febrile, allergic, and hypotensive reactions to transfusion are unpredictable and largely unpreventable. This emphasises the importance of avoiding transfusion where it is not clinically essential and discussing the possibility of these reactions with patients when taking their consent. Harm can be minimised by ensuring that treatment given, and investigations performed are correctly targeted to the type of reaction. This means using the patient's symptoms and signs to distinguish febrile from allergic reactions. This should be covered in clinical education and training, but also supported by resources within hospitals which are readily accessible and user-friendly.

Recommended resources

SHOT Bite No. 05(a): Febrile, Allergic, and Hypotensive Reactions (FAHR) – getting the diagnosis right
https://www.shotuk.org/resources/shot-bite-no-5/

SHOT Bite No. 05(b): Investigating FAHR
https://www.shotuk.org/resources/shot-bite-no-05b/

SHOT Video: FAHR – Febrile, Allergic, and Hypotensive Reactions
https://www.shotuk.org/resources/fahr-febrile-allergic-and-hypotensive-reactions/

JPAC Consent for Blood Transfusion - Guidance for Healthcare Practitioners in the UK
https://www.transfusionguidelines.org/transfusion-practice/consent-for-blood-transfusion/guidance-for-healthcare-practitioners-involved-in-this-role