7. 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, haemolytic reactions, transfusion-related acute lung injury (TRALI) or those due to bacterial contamination of the component.

Current Category Definitions

- **Isolated febrile**: rise in temperature >1^{0}C with or without minor rigors and chills.
- **Minor allergic**: skin irritation with or without rash.
- **Anaphylactic/anaphylactoid/severe allergic reaction:**
  Anaphylactic/anaphylactoid reaction: Hypotension with one or more of: rash, dyspnoea, stridor, wheezing, angioedema, pruritus, urticaria, during or within 24 hrs of transfusion.
  Severe allergic reaction: A severe allergic reaction with immediate risk to life occurring during or within 24 hours of transfusion, characterised by bronchospasm causing hypoxia, or angioedema causing respiratory distress.
- **Hypotension:** a drop in systolic and/or diastolic pressure of >30mm Hg occurring during or within one hour of completing transfusion, when all other categories of adverse reactions have been excluded together with underlying conditions that could explain hypotension.
- **TACO (Transfusion-associated circulatory overload):** any 4 of the following within 6 hours of transfusion:
  - Acute respiratory distress
  - Tachycardia
  - Increased blood pressure
  - Acute or worsening pulmonary oedema
  - Evidence of positive fluid balance
- **Febrile with other symptoms/signs:** rise in temperature >1^{0}C, with no features of an allergic reaction, but with one or more of myalgia, nausea, change in blood pressure or hypoxia.

Analysis

Ninety-one completed questionnaires were received, plus 1 initially reported as a haemolytic transfusion reaction. Seven were subsequently withdrawn from analysis; 5 where symptoms were due to the underlying disease, 1 that was a haemolytic reaction and 1 in which a patient died from presumed sepsis following ALI (occurring 8 hours following transfusion).

85 questionnaires were therefore analysed.

Gender 43 males, 42 females

Age Range 3 to 91 years; median 72 years

Major Morbidity

There were no deaths, but there were 4 cases of major morbidity, all related to anaphylactic/anaphylactoid reactions (Imputability level 3). One patient suffered a myocardial infarct during a red cell transfusion and 3 patients arrested during transfusion; 1 receiving platelets, 1 FFP and 1 a red cell transfusion.

Table 23

Components Implicated (85 reports)

Reaction	RBC N = 39	Platelets apheresis N = 11	Platelets buffy coats N = 8	FFP* N = 22	Multiple N = 4	Buffy coats N = 1
Isolated febrile	18	1				1
Minor allergic	3	3	1	3		
Anaphylactic/ anaphylactoid/ Severe allergic	11	5	7	15	3	
TACO	1			1	1	
Hypotension				3*		
Febrile with other symptoms/signs	6	2				
Rate per 100,000 units	2.01	11.2	6.6	8.2		

* With the exception of 1 hypotensive reaction to FFP-SD, the remainder were the result of standard FFP

Isolated febrile and minor allergic reactions

There were 30 reports, as shown in table 23.

Anaphylactic/anaphylactoid reactions

There were 22 cases, including 4 with major morbidity.

Case 1 (RBC)

An 83-year-old male had undergone an endovascular aortic aneurysm repair and a unit of red cells was started at the end of surgery. His pre-transfusion BP was 120/55. Within 15 minutes he complained of skin irritation, became hypotensive with a BP of 40/20 and developed chest and back pain. He received adrenaline followed by a noradrenaline infusion. The following day, his troponin had risen from 0.09 to 2.07and his ECG showed ST elevation, confirming a myocardial infarct.

Case 2 (FFP)

A 69-year-old male was bleeding following a coronary artery bypass graft. He was being treated at an NHS site that relied upon the out-of-hours laboratory service of the main hospital 7 miles away. The local policy is to thaw FFP at the first sign of a major bleed and this was initiated. However, the post-operative bleed responded to surgical measures and the patient required only 2 units of red cells throughout both procedures. Despite this, and without coagulation results being available, the FFP was transfused. After receiving 100mL FFP the patient developed severe bronchospasm, and had a respiratory arrest, but was successfully resuscitated.

Case 3 (PLTaph)

A 46-year-old male with alcoholic liver disease and who had a cerebral haemorrhage and a platelet count of 32 x 10^9/l was transfused with a unit of apheresis platelets. After receiving <10mL component, he developed a widespread urticarial rash and a cardiac arrest but was successfully resuscitated.

Case 4 (RBC)

A 32-year-old female with congenital dyserythropoietic anaemia was receiving the second of a 3 unit transfusion. After 15 minutes she developed pruritis, angioedema and nausea. She was given chlorpheniramine but rapidly became dyspnoeic, lost consciousness, had an unrecordable blood pressure and suffered a respiratory arrest. She recovered following mouth-to-mouth resuscitation and hydrocortisone and went on to receive the third unit uneventfully.

Table 24

Clinical features of remaining 18 cases of anaphylactic/anaphylactoid reactions

Case No.	Component Type	Rash	Angioedema	Dyspnoea O_2 sats (%) where recorded	BP	Impaired conscious-ness or collapse	Interval from starting transfusion in minutes
5	RBC/FFP	√		√	?		10
6	FFP	√		√ 83	60/30		80
7	FFP	√		√	100/60 (30mm Hg drop)		30
8	FFP	√			70/30		5
9	FFP	√		√ 92	97/55 (40mm Hg drop)		60
10	Multiple	√	√		90/60	anaesthetised	<5
11	PC-BC	√	√		50/30	√	15
12	PC-Aph	√			?	√	30
13	PC-BC	√	√	√	75/40	√	15
14*	FFP			√ 65	97/45	√	15
15	FFP	√	√		78/40		30
16	RBC/FFP	√		√ 84	60/30	anaesthetised	?
17	PC-?	√		√ 72	87/52		40
18**	RBC				?		?
19	RBC	√	√	√ 91	90/40		15
20	RBC	√		√ 88	65/40		60
21	FFP	√	√	√ 74	86/53		15
22	RBC	√	√		90/50 (20mm Hg drop)		170

* Classified as anaphylactic/anaphylactoid on the basis of a raised mast cell tryptase (56.2)

** Classified as anaphylactic/anaphylactoid on the basis of wheezing

Investigations

Eleven of the 22 patients with an anaphylactic/anaphylactoid reaction were investigated.

Eight were investigated for IgA deficiency, of which 7 had normal levels and 1 detectable but low levels.

In 4, mast cell tryptase was measured, with 3 found to be elevated.

One case was noted to have HPA antibodies.

Severe Allergic Reactions

Nineteen severe allergic reactions were reported; 5 due to red cells, 7 to platelets and 7 due to FFP.

Table 25
Clinical features of severe allergic reactions

Case No.	Component	Fever	Rigors	Rash	Dyspnoea	Hypoxia	Angioedema
23	FFP			√			√
24	FFP			√			√
25	PC-Aph			√	√		
26	FFP			√	√		√
27	RBC			√	√		
28	PC-Aph			√	√	√	√
29	RBC			√	√		
30	PC-Aph			√	√		√
31	FFP	√		√			√
32	PC-BC			√	√		
33	RBC						√
34	PC-BC	√	√		√ (wheeze)		
35	PC-Aph			√	√		√
36	RBC				√		√
37	RBC	√		√	√		
38	FFP			√	√		
39	FFP	√			√		√
40	FFP			√	√		√
41	PC-BC				√ (wheeze)		

Investigations

Nine out of the 19 patients were investigated.

In 8, IgA levels were measured and found to be normal and 1 of 2 patients for HLA antibodies had a positive result.

Hypotension

Three cases of hypotension were reported during FFP transfusions. One occurred during a plasma exchange for TTP (using SD-FFP) and was accompanied by symptoms of hypocalcaemia, and a second during plasma exchange for HUS.

The third occurred after the transfusion of 100mL FFP over 10 minutes prior to insertion of a pericardial drain in a patient with septicaemia and DIC. The patient's baseline systolic pressure was 70mm Hg on inotropes, but rapidly fell to 40mm Hg during the FFP transfusion.

Transfusion-Associated Circulatory Overload (TACO)

SHOT will study transfusion-associated circulatory overload (TACO) in more detail in future reports. However, three reports from this year fitted well into this category.

Case 42

An 85-year-old lady who was bleeding following an aortic abdominal aneurysm repair had received 2 units of red cells, 1 unit of platelets and 4 units of FFP over 4 hours. Her fluid balance was > 2.5 litres positive, she developed dyspnoea and a tachycardia but a CXR was not performed.

Case 43

A 38-year-old lady had a post-operative haemoglobin of 8.4g/dL and a CVP +4cm, but was nevertheless prescribed 4 units of red cells. The following day she developed dyspnoea and was recorded to have a 7 litre positive fluid balance, to which the unnecessary transfusion had contributed.

Case 44

An 83-year-old lady undergoing an abdominal aortic aneurysm repair received salvaged red cells, 1 unit of allogeneic red cells and 10 units of FFP during surgery. She developed a rash over her abdomen and bilateral lung infiltrates. The FFP had been derived from male donors and the mast cell tryptase (MCT) was normal. Given the volume of components given over a short period, TACO would appear to be the most likely explanation for the CXR changes.

Febrile reactions with other symptoms or signs

An increasing number of febrile reactions have been reported this year due to the blood safety and quality regulations requirement to report these to MHRA. Whilst the majority of patients are either asymptomatic or have rigor and chills, there is a proportion who develop additional symptoms that make the reactions difficult to classify.

Five out of 8 in this group became breathless, in the absence of wheezing or other clinical features of an allergic reaction, and in 4 of these transient oxygen desaturation was evident. Seven of the 8 developed either chest or loin pain or described aching in their limbs. Significant changes in blood pressure were documented in 5 of the 8; 3 of which became hypertensive.

In 4 out of 8 cases, bacterial culture of the unit was not performed.

Table 26
Febrile reactions with additional features

Case number	Dyspnoea (sats%)	Myalgia/ chest pain	Change in blood pressure	Nausea and/or vomiting	Unit bacterial culture	Other Investigation	Time to recovery (hr)
45 platelets	√ 85		Increase		Neg	IgA normal MCT normal	6
46 platelets		√	Increase		Not done	None	0.2
47 RBC		√	Fall		Not done	None	?
48 RBC	√	√		√	Neg	IgA normal	0.5
49 RBC	√ 82	√	Fall	√	Not done		1.5
50 RBC		√	Increase		Not done	HLA antibodies detected	6
51 RBC	√ 72	√		√	Neg		4
52 RBC	√ 87	√			Neg	MCT normal	6

MCT = mast cell tryptase

Paediatric cases

There were 5 reports of acute transfusion reactions in patients aged less than 18. Three were allergic reactions. There was 1 isolated febrile reaction, and there was 1 report of an anaphylactic/anaphylactoid reaction in a 15-year-old patient, who had received appropriate treatment with FFP (case 15 in table 24).

Appropriate use of FFP and platelets

Table 27

Category	Number of patients	Indication given
Indicated	13	3 plasma exchange 1 DIC 4 urgent reversal of warfarin 4 massive transfusion with raised INR 1 intervention with raised INR
Not indicated	9	4 non-urgent warfarin reversal 1 PPH requiring 4 units red cells with normal INR 3 post-operative with normal INR 1 post-operative bleed requiring surgical intervention

Use of FFP

In 9 out of 22 patients, the use of FFP was not justified according to current guidelines (table 27).

Use of platelets

There were 12 reports of anaphylactic/anaphylactoid or severe allergic reactions to platelets, and 2 reports of febrile reactions with other symptoms or signs. In 10 of these cases, platelets were given appropriately. In 2 cases the use of platelets appeared to be outside guidelines, and in 2 cases insufficient information was available.

COMMENTARY

- Acute transfusion reactions continue to be an important and largely unpredictable hazard of transfusion.
- For the second consecutive year, there has been an increase in the number of allergic or anaphylactic/anaphylactoid or severe allergic reactions reported due to red cells. A sustained increase merits investigation by the UK blood services.
- Only one third of the anaphylactic/anaphylactoid reactions occurred within 15 minutes of commencement of the transfusion. This highlights the need for transfusions to be administered at times and in locations permitting careful observation of the patient. Out-of-hours transfusions should be avoided if possible.
- A higher proportion of patients with significant febrile reactions, 18/26 (69%) compared with 9/17 (52%) in 2005, had bacterial cultures performed.
- There is still inappropriate prescription of FFP, particularly with respect to the reversal of anticoagulation.
- The classification of acute transfusion reactions is often problematic and, with increasing reporting, there is awareness that not all of them fall into existing categories. A new classification of transfused reactions has been developed by ISBT, which if fully utilised would allow international comparison of data. It includes several additional categories such as transfusion-associated dyspnoea. Another recent reclassification has included an 'inflammatory' group covering reactions with rigors, myalgia, hypotension and shock in the absence of allergic symptoms[21].
- An elevated mast cell tryptase, as a marker of mast cell activation and degranulation, will confirm an anaphylactic/anaphylactoid or allergic reaction. However a normal result does not exclude these diagnoses. MCT levels should be measured between 15 minutes and 3 hours after the reaction and should be repeated at 24 hours to establish whether levels are returning to baseline[22].

RECOMMENDATIONS

- All prescriptions for blood components must be clinically justified and in line with current guidelines to ensure that the benefits exceed the risks[23,24,25,26].

  Action: Consultant haematologists with responsibility for transfusion should ensure that BCSH guidelines are incorporated into local protocols

- Junior doctors should be educated, trained and competency assessed in transfusion medicine before being permitted to prescribe.

  This is discussed in detail in the Key Message and Recommendations of the Year (pp. 17, 19).

- Anaphylactic/anaphylactoid reactions may occur at any stage during the transfusion, emphasising the need to keep all patients receiving a transfusion visible and accessible to nursing staff. Out-of-hours transfusions should be avoided unless essential.

  Action: Hospital Transfusion Teams

- All serious transfusion reactions must be investigated. Bacterial cultures must be taken in a febrile reaction when the rise in temperature exceeds 1.5°C or the reaction is otherwise sufficiently severe to merit discontinuing the transfusion[12]. An update of BCSH guidelines is in progress.

  Action: Consultant haematologists with responsibility for transfusion should implement current best practice.