Northern Ireland Blood Transfusion Service

POLICY DOCUMENT

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Document Title: INVESTIGATION OF A SUSPECTED TRANSFUSION REACTION

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This policy has been screened for equality implications as required by Section 75 and Schedule 9 of the Northern Ireland Act 1998.

CROSS REFERENCES

This Policy refers to the following documents:

Doc Type	Doc. No.	Title
SOP	QA:070	Procedure for Reporting and Management of Quality Incidents
SOP	QB:012	Bacteriological Investigation of Adverse Reactions associated with Transfusion
SOP	QB:013	Procedure for Treatment of Culture Positive Single Donor Platelets or Red Cells
SOP	QB:005	Procedure for Culture Positive Pooled Blood Components
SOP	BG:022	Serological Investigation of Transfusion Reactions
SOP	BG:046	Minimum Specifications for the Labelling of Blood Samples and Accompanying Documentation received for Antibody Identification and Cross-Matching
SOP	QA:002	Blood Component Recall Procedure
POL	MP:011	Policy for receipt of samples which do not conform to NIBTS sample labelling or request form requirements
POL	MP:009	Investigation of a suspected transfusion related acute lung injury (TRALI) case policy.
FORM	DD:1013	Approval to Test Non-Conforming Sample(S)
FORM	DD:1040	Recall record form
FORM	DD:046	Recall notification and component fate record
APP	1	Algorithm for Managing a Transfusion Reaction
APP	2	Transfusion Reaction Investigation Form
APP	3	Hospital Initiated Recall for Transfusion Reactions

Key Change from Previous Revision:
Updating the whole policy in line with BSH 'Guidelines on the investigation and management of acute transfusion reactions' 2022 and updated data from SHOT annual reports 2022. Section 5: Equality statement updated.

1 STATEMENT

A suspected transfusion reaction may occur in any patient who has been transfused with any blood component e.g. red cells, platelets, plasma or cryoprecipitate, or blood product e.g. intravenous immunoglobulin.

Acute Transfusion Reactions (ATR) are defined by the UK Serious Hazards of Transfusion group (SHOT) as those occurring within 24 hours of the administration of blood or blood components. Patients should be asked to report symptoms which develop within 24 hours of completion of the transfusion.

Acute Transfusion Reactions vary in severity from minor febrile reactions to life-threatening allergic, haemolytic or hypotensive events. Allergic and febrile non-haemolytic transfusion reactions (FNHTR) are those most commonly reported.

The initial clinical picture is often obscured by factors related to the patients underlying medical condition, such as febrile septic episodes in neutropenic patients who also happen to be receiving a blood component transfusion.

The purpose of this policy is to provide guidance to both NIBTS and Hospital staff on how to appropriately investigate a suspected transfusion reaction.

2 POLICY

This policy provides guidance on investigation of a suspected transfusion reaction. Hospital staff should be aware of, and comply with, the policies and practices associated with their individual Hospital Trust. Responsibility for reporting of clinical incidents by hospital staff should be through their Trust's Incident Reporting System, in addition to reporting to statutory bodies (e.g. MHRA /HTA) and/or SHOT.

Some of the appendixes included in this policy are indicative to help medical team and hospital clinical staff on the intended information required to gather, in order to help managing these reactions.

Any suspected transfusion reaction which requires further investigation at NIBTS must have a Quality Incident raised as per SOP:QA:070, Procedure for Reporting and Management of Quality Incidents.

3 OVERVIEW

The purpose of this policy is to provide guidance on the recognition, investigation and management of possible transfusion reaction. It is based on BSH 'Guidelines on the investigation and management of acute transfusion reactions' 2022 and data from SHOT annual reports. It recognises that transfusion reactions can have extremely variable clinical presentations and disparate aetiology.

Acute Transfusion Reactions (ATR) vary in severity from minor febrile reactions to life-threatening allergic, haemolytic or hypotensive events. ATR rates of 0.5-3% of transfusions are commonly quoted (Fry JL *et al*, 2010). Data from 2022 SHOT annual report suggests that the risk of death related to transfusion in the UK is 1 in 63,563 (1.57 per 100,000) components issued and the risk of serious harm is 1 in 15,449 (6.47 per 100,000) components. The incidence of febrile, allergic or hypotensive reactions is around 1/7,378, where haemolytic transfusion reaction incidence was 1/48,033. Although red cells are the most common blood component transfused, platelets account for the highest number of reactions reported per 10,000 components.

Reporting ATR to the Northern Ireland Blood Transfusion Service (NIBTS). See Appendix 3:

The Hospital Blood Transfusion Laboratory must ensure that NIBTS is informed when an ATR is suspected to be caused by Bacterial Contamination, or if TRALI is suspected, or there is severe neutropenia or thrombocytopenia associated with an ATR. This is to ensure that all associated components from the implicated donation are removed from the blood supply.

Reporting ATR to National Surveillance Schemes (MHRA & SHOT):

The Hospital Blood Transfusion Team should ensure that all transfusion reactions, except mild febrile and/or allergic reactions are reported when necessary to the appropriate regulatory and haemovigilance organisations (MHRA and SHOT).

Symptoms to consider during an ATR include:

Fever, chills, rigors, myalgia, nausea or vomiting and a temperature rise of >1-2 ºC above baseline is significant. A smaller rise is more often due to a cause other than transfusion reaction. Pyrexia is typical of Febrile Non-Haemolytic Transfusion Reaction (FNHTR) but differentiation from other causes is not always straight forward. Pyrexia may occur in acute haemolysis due to ABO incompatibility, TRALI and Bacterial Transfusion Transmitted Infections (TTI).

Skin lesions, flashing, rashes, urticaria, pruritis, angio-oedema Localised, non-pitting, oedema of the subcutaneous or sub mucosal tissues is indicative of an allergic reaction. If this happens the transfusion must be stopped immediately and the patient promptly assessed and treated.

Respiratory symptoms and signs including dyspnoea, stridor, wheeze, hypoxia and anaphylaxis. Presenting as severe, life-threatening, generalised hypersensitivity reaction and rapid airway and/or breathing and/or circulation problems, accompanied by skin and mucosal changes. Possible transfusion reaction causes include allergy, TRALI, TACO and TAD.

Hypotension/tachycardia. Drop of systolic or diastolic blood pressure that is > 30mm Hg. This can be indicative of acute ABO haemolysis, severe allergic reaction, bacterial contamination or TRALI. The patient's underlying condition, especially haemorrhage is also a cause for hypotension and careful clinical risk assessment is required when deciding to stop the transfusion for this indication.

Bleeding diathesis with generalised oozing from wounds or puncture sites, can be suggestive of Disseminating Intravascular Coagulation (DIC) secondary to ABO incompatibility or bacterial contamination.

Pain at the venepuncture site, in the abdomen, flank or chest. Febrile reactions often cause generalised muscular and bone aches. Acute haemolytic reactions, particularly those due to ABO incompatibility, may be characterised by pain at the infusion site, abdomen, chest and loins. Chest pain can also be an occasional feature of anaphylactic reactions, possibly due to myocardial ischemia.

Severe anxiety or feeling of impending doom. Reported in serious transfusion reactions such as acute haemolysis, bacterial TTI and should always initiate urgent review of the patient. Mild anxiety is common in patients transfused for the first time.

The aetiology of a transfusion reaction is specific to the type of reaction observed. Patients often present with an overlapping complex of signs and symptoms, the differential diagnosis of which includes acute and delayed transfusion reactions.

Acute transfusion reactions

Acute haemolytic transfusion reaction (e.g. ABO incompatibility, Allogeneic RBC Antibody), where the presence of preformed recipient antibodies to donor antigens results in complement activation, leading to intravascular haemolysis and its associated severe acute inflammatory cascade, which may ultimately progress to disseminated intravascular coagulation, shock, and/or acute renal failure, and ultimately death. The risk of death correlating with the amount of incompatible blood transfused. In 2022 SHOT report, there were 2 deaths attributed to ABO-incompatible red cell transfusions, both of which were totally preventable.

Most cases of ABO incompatible red cell transfusion are caused by failures in the sampling process or at the bedside. These are always totally preventable and often resulting from failure to identify the patient at the time of blood sampling (wrong blood in tube) or administration to the wrong patient. Pre-transfusion administration safety checks using a patient side checklist can prevent incorrect transfusions in most cases. Very occasionally an error can occur at the transfusion laboratory /blood bank, although, the two-sample policy helped the laboratory staff to detect any discrepancy where the results don't match with a previous sample.

All Hospitals will have in place a policy on investigation and management of suspected incompatible blood transfusion. In addition, NIBTS may provide advice on serological investigation of a reaction. Acute haemolysis may also be caused by antibodies other than ABO e.g. Rh group, Kell etc. (which can also cause delayed reactions). Significant haemolysis may also occur in platelet transfusion where crossing of groups is not uncommon. Group O platelets should only be transfused to group O patients, unless they have been tested and labelled as 'High Titre negative' (even then, caution should be exercised, especially in children).

Any case of inadvertent transfusion of RhD positive red cells to an RhD negative female of child-bearing age should be immediately referred to the Hospital Transfusion Lead for consideration for anti-D Ig to prevent RhD alloimmunization.

Non-immune haemolysis may occasionally mimic a transfusion reaction. Possible examples are transfusion of red cells which have been inadvertently exposed to very high or very low temperatures, mixing of drugs /hypotonic iv solutions with transfused blood in the same iv-line, transfusion under pressure through a small-bore needle, or medical device related (e.g. Cell saver, blood warmer). All can cause haemolysis *in vitro* and result in transfusion of free haemoglobin to the patient.

Allergic/anaphylaxis transfusion reaction. Allergic reactions are common in blood transfusion, and particularly with plasma-containing products (FFP or platelets). Allergic reactions may be categorised as mild, moderate or severe (SHOT definitions):
MILD: transient flushing, urticaria (hives) or rash
MODERATE:Wheeze or angioedema with or without flushing /urticaria /rash but without respiratory compromise or hypotension
SEVERE: Bronchospasm, stridor, angioedema or circulatory problems with require urgent medical intervention or anaphylaxis

The majority of allergic reactions are mild and do not requires further investigation. The transfusion should be interrupted, patient's vital signs checked, compatibility details checked and the unit restarted only if the patient has no additional symptoms or signs*, and there is no evidence of clerical or other error. The patient should be given anti-histamines and the transfusion cautiously recommenced.
*defined as: hypotension, dyspnoea/cough, tachycardia, generalised flushing or anxiety, nausea/vomiting, widespread rash >2/3 of body

For moderate to severe allergic reactions, the transfusion should not be restarted and the transfusion lead should be contacted for further advice. The vast majority of allergic reactions are unexplained but in a small number of patients, the cause may be evident from the history (e.g. peanut allergy – check recent dietary history with the donor), or IgA deficiency may be suspected.

IgA deficiency, defined as IgA level <0.07g/l, is seen in approximately 1 in 700 individuals. However, severe anaphylactic transfusion reactions are very rare (approximately 1 in 40,000 transfusions), and may be predicted by the presence of a high titre of anti-IgA antibodies in the patient. If a patient has suffered a severe allergic or anaphylactic type reaction to blood transfusion, then they should be investigated for possible IgA deficiency. Testing for IgA should be completed initially locally, & then if an isolated IgA deficiency is detected, the medical team in NIBTS would liaise with clinical team & discuss case with NHSBT RCI Colindale regarding further testing.

In patients with confirmed IgA deficiency and a history of reaction to blood should be transfused with components from IgA-deficient donors (first choice) or washed red cells (second choice) if time allows. Life-saving transfusion should not be denied or delayed if these are not immediately available but the facilities and skills to manage severe allergic reactions must also be present. Patients with known IgA deficiency and no history of reactions to blood must be assessed on an individual basis, taking into account the urgency of transfusion, the indication for IgA testing, the anticipated frequency of transfusion, and history of allergy/anaphylaxis in other settings.

Patients who have experienced an anaphylactic reaction associated with transfusion must be discussed with an allergist or immunologist, in keeping with UKRC guidelines.

Transfusion management of an IgA deficient patient with or without anti-IgA should be discussed with the NIBTS consultant. Current NHSBT guidelines on 'Investigation and Clinical Management of Suspected Reactions to IgA' are available at: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/28765/inf486.pdf. Most patients can be managed with standard blood products but occasional patients may require washed products. Stocks of IgA deficient plasma can be obtained from NHSBT (Barnsley and Filton).

Febrile non-haemolytic transfusion reaction (FNHTR), may result in part from interaction between recipient antibodies directed against leukocytes present in the red-cell or platelet unit transfused. The formation of antigen-antibody complexes may result in complement binding and release of endogenous pyrogens. FNHTR may also result from the transfusion of proinflammatory substances including cytokines, complement fragments, and lipid compounds that are contained in the transfused unit's plasma supernatant. Leucodepletion reduces the risk but does not remove it entirely and some patients seem to be particularly prone to reactions. Common symptoms are chills, mild temperature rise (usually <38.5^{o}C), headache and general malaise. These may persist for up to 8 hours post transfusion. If there are more significant symptoms or signs such as hypotension, significant temperature rise, chest or back pain, shortness of breath, this is unlikely to be a FNHTR and a more serious AHTR or bacterial contamination should be suspected.
The majority of mild FNHTR can be managed by temporarily stopping the transfusion, administering paracetamol and cautiously restarting the transfusion. Further investigation is usually necessary only where there is any doubt as to the aetiology of the reaction, the main 'differential diagnosis' being acute haemolytic reaction or bacterial contamination (**Transfusion-associated bacterial contamination)**. The transfusion should be discontinued until a haemolytic reaction has been ruled out. If no clinical concern for haemolysis exists, transfusion may be resumed. Alternatively, the patient may be transfused with a new component. **If febrile symptoms of moderate severity are sustained, implicated units should be returned to the laboratory for further investigation, the Blood Service contacted immediately so that associated components from the implicated donation can be withdrawn, and the patient sampled for repeat compatibility and culture (BCSH).**

For patients with recurrent febrile reactions, BSH guidelines recommend a trial of premedication with oral paracetamol given one hour before the reaction is anticipated. In patients who continue to react, a trial of washed blood components may be indicated.

Transfusion-Transmitted Infection (TTI), is defined when following investigation, the recipient had evidence of infection post transfusion and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection, AND, either at least one component received by the infected recipient was donated by a donor who had evidence of the same infection, Or, at least one component received by the infected recipient was shown to contain the agent of infection.

Current BSH guidance recommends that patients are advised to report any symptoms that occur within 24 hours of transfusion (BSH Tinegate et al. 2012) although patients with confirmed bacterial TTI generally become unwell very rapidly, often during transfusion.

TTI is clinically difficult to distinguish from immune-mediated transfusion reaction and is caused by bacterial contamination of transfused component. Clinically significant transfusion of bacterially contaminated blood components is a rare but serious event and is particularly associated with platelets (as they are stored at room temperature). To reduce the risk, all UK Blood Services have introduced automated bacterial screening of platelet components.

Bacterial reactions may present as a severe febrile acute transfusion reaction and a high index of suspicion is important. There is usually a sustained reaction with a rise in temperature of 2^{o}C or more and/or rigors. Nausea, severe hypotension leading to shock, back, chest or transfusion site pain often occur. Visual inspection of the component for discolouration, abnormal clumps or signs of leakage is important, but many contaminated units appear normal.

When TTI is suspected, the following should be performed by the referring hospital as a minimum:

- Take blood cultures from a peripheral vein and any central lines
- Seal the component and return immediately to the hospital blood bank
- Trusts will do their own bacteriology investigation. If they grow an organism, it will be discussed with the NIBTS medical team to see if appropriate to send the implicated unit to bacteriology in NIBTS.
- **In all cases, NIBTS must be contacted immediately as recall /quarantine of other components from this donation may be required**.
- DO NOT wait for the results of blood culture prior to starting antibiotic treatment.

When TTI is suspected, NIBTS will arrange the following investigations:
(*see also SOP: QB:012, Bacteriological Investigation of Adverse Reactions associated with Transfusion)*

- Any components from the same donation must be identified and quarantined if still in NIBTS, or recalled if already issued (SOP:QA:002 Blood Component Recall Procedure, FORM:DD:1040 Recall record form, and FORM:DD:046 Recall notification and component record fate)
- If an associated component has already been transfused, then, the NIBTS medical team should contact the patient's clinician to ascertain if that patient developed any reaction to the transfusion, and to give appropriate advice.
- A quality incident should be reported as per SOP:QA:070.
- If this has been discussed and agreed with the NIBTS medical team, the affected component should be sent to the Bacteriology lab of the hospital, and if necessary, or confirmation is needed, the affected component can be referred to NIBTS bacteriology laboratory.
- As part of the incident, a letter/email should be sent to the patient's clinician, with a copy to Haemovigilance report, indicating if any bacterial growth was detected, and the nature of any organism(s) grown.
- Follow up of the donor may be required, depending on organism detected and donor history.
- Follow up of donor arm cleansing technique on session may also be relevant to the investigation.

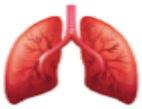
If a blood component is flagged positive on BacT/ALERT system at NIBTS, then SOP: QB:013 (Procedure for Treatment of Culture Positive Single Donor Platelets or Red Cells) and SOP: QB:005 (Procedure for Culture Positive Pooled Blood Components) should be followed.

Transfusion Associated Acute Lung Injury (TRALI) (See also SOP MP:009 'Investigation Of A Suspected Transfusion Related Acute Lung Injury (Trali) Case Policy'). TRALI is characterised by symptoms and signs of acute dyspnoea, cyanosis, hypotension, fever and pulmonary oedema. There is no definitive clinical test or sign for TRALI and other causes of acute lung injury should be considered. The features are often indistinguishable from TACO or from other lung conditions, such as Acute Respiratory Distress Syndrome (ARDS), or Acute Lung Injury (ALI). The onset of TRALI is usually within 6 hours of the transfusion episode. Clinically, TRALI is thought to result from activation and damage to the pulmonary endothelial/epithelial interface by systemic inflammatory stimuli. Epithelial and endothelial injury occurs and the alveolar spaces are filled with fluid and proteinaceous debris. However, the main differential diagnosis is acute pulmonary oedema due to fluid overload or left ventricular failure (TACO). Distinction between cardiac failure and TRALI may be aided by measurement of the left atrial pressure (LAH) which is typically normal or low in TRALI. The following table may be of help in differentiating between TRALI and TACO.

Transfusion associated Cardiac Overload (TACO): TACO is defined as acute or worsening respiratory compromise and/or acute or worsening pulmonary oedema during or up to 24 hours of transfusion, with additional features including cardiovascular system changes not explained by the patient's underlying medical condition; evidence of fluid overload and a relevant biomarker. TACO continues to be the major cause of harm and the number of cases reported in the 2022 Annual SHOT Report is the highest to date, at 160, a 22% increase on the previous year. Included in these were 8 deaths and 25 cases of major morbidity. TACO is more commonly reported in elderly and non-bleeding patients with severe euvolaemic anaemia (e.g. Hb < 50g/l, such as seen in B_{12} deficiency). Clinical presentation includes dyspnoea, cyanosis, tachycardia and signs of cardiac overload. The main differential diagnosis is TRALI but in TRALI there is no evidence of cardiac overload or positive fluid balance.

It's recommended that a formal pre-transfusion risk assessment for TACO is undertaken whenever possible for all patients receiving blood transfusion (especially if older than 50 years or weighing less than 50kg) and mitigating actions taken. See Table 1.

Table 1: TACO Checklist

TACO Checklist	Red cell transfusion for non-bleeding patients	If 'yes' to any of these questions
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic? Does the patient have severe anaemia?	1 • Review the need for transfusion (do the benefits outweigh the risks)?
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?	2 • Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?
	Is the fluid balance clinically significantly positive? Is the patient on concomitant fluids (or has been in the past 24 hours)? Is there any peripheral oedema? Does the patient have hypoalbuminaemia? Does the patient have significant renal impairment?	3 • Consider body weight dosing for red cells (especially if low body weight) • Transfuse one unit (red cells) and review symptoms of anaemia • Measure the fluid balance • Consider giving a prophylactic diuretic • Monitor the vital signs closely, including oxygen saturation

Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.

TACO=transfusion-associated circulatory overload

Actions to prevent TACO are to transfuse over longer periods (maximum 4 hours), and use of pre-emptive diuretics. There are no specific investigations required for suspected TACO at the Transfusion Laboratory level – the diagnosis is clinical and/or radiological.

Transfusion associated dyspnoea (TAD) is defined by SHOT as "Transfusion associated dyspnoea that is characterised by respiratory distress within 24 hours of transfusion that does not meet the criteria of transfusion related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO) or allergic reaction. There were 10 cases of TAD associated with major morbidity reported in SHOT annual report in 2022.

Respiratory distress should be the most prominent clinical feature, and should not be explained by the patient's underlying condition or any other known cause. There are currently no other known distinguishing features to aid diagnosis of TADs

TRALI must essentially be excluded to diagnose TAD.TRALI's investigation and management is also covered in Medical Policy POL:MP:009, 'Investigation of a suspected transfusion related acute lung injury (TRALI) case policy'. An absence of typical CXR appearances of TRALI (i.e. bilateral pulmonary infiltrates /ARDS type picture) and absence of features of pulmonary oedema or cardiac overload (i.e. TACO) would strongly suggest a diagnosis of TAD should be considered.

Table 2: differential diagnosis between TRALI and TACO

Indicators	TRALI	TACO
Patient characteristics	More frequently reported in haematology and surgical patients	May occur at any age, but characteristically age > 70
Type of component	Usually plasma or platelets	Any
Speed of onset	During/ within 6 hours of transfusion, usually within 2 hours	Defined as occurring within 6 hours of transfusion
Oxygen saturation	Reduced	Reduced
Blood pressure	Often reduced	Often raised
JVP	Normal	Raised
Temperature	Often raised	Usually unchanged
CXR findings	Often suggestive of pulmonary oedema with normal heart size: may be a 'whiteout'	Cardiomegaly, signs of pulmonary oedema
Echo findings	Normal	Abnormal
Pulmonary wedge pressure	Low	Raised
Full Blood Count	May be fall in neutrophils and monocytes followed by neutrophil leucocytosis	No specific changes
Response to fluid load	Improves	worsens
Response to diuretics	Worsens	Improves

Delayed transfusion reactions

Delayed haemolytic transfusion reactions (DHTR), occur more than 24 hours following a transfusion and are associated with a fall in Hb or failure to increment, rise in bilirubin and LDH and an incompatible crossmatch not detectable pre-transfusion. However, the transfusion seems boosting the low/undetectable level of antibody and results in haemolysis of the transfused cells. The antibody will be readily identifiable in a post-transfusion sample. Commonly implicated antigens (in order of frequency) are: Jk^a , Fy^a , Jk^b, Fy^b , E, c, C.

If the reaction is manifested by a brisk haemolysis, treatment should be rendered as for an acute haemolytic reaction. In the majority of cases, the haemolysis observed is extravascular and relatively mild. Some patients develop jaundice. The fact that haemolysis is primarily extravascular explains why acute renal failure and disseminated intravascular coagulation rarely occur. Delayed haemolysis often occurs in the absence of symptoms. The diagnosis may be made when a new positive direct antiglobulin test and/or positive antibody screen is identified during the preparation of a subsequent transfusion. Usually no specific treatment is required.

Investigation of a possible DHTR requires the following samples/tests as a minimum:

- FBC, Bilirubin, LDH, blood film (spherocytosis seen), reticulocyte count
- DAT, antibody screen
- Referral of sample to blood bank for serological investigation +/- onward referral to NIBTS reference lab.
- If antibody is detected it may be possible to retest the donor sample /unit for that antigen

Transfusion-associated graft-versus-host disease, occurs 8-10 days after a transfusion and is primarily observed in immunodeficient patients in which transfused white cells react with recipient antigens, though it can occur in non-immunosuppressed patients if the blood components transfused are derived from a human leukocyte antigen (HLA) haplo-identical donor. This is characterised by:

- Maculopapular rash
- Fever
- Diarrhoea
- Bone marrow aplasia and rapid progress towards death in some patients
- Occurrence in immunocompromised patients
- Skin biopsy of the affected area, which is diagnostic.

Treatment is supportive. Many immunosuppressive regimens have been tried. Corticosteroids, antithymocyte globulin, methotrexate, cyclosporine, Azathioprine, serine protease inhibitors, chloroquine, and OKT3 have all yielded poor results.

Post-transfusion purpura, occurs as a result of prior sensitisation to foreign platelet antigen, often during pregnancy. This is characterised by:

- Bleeding from mucous membranes, gastrointestinal tract, and urinary tract
- Associated thrombocytopenia, usually severe (less than 10 x 10^9/L)
- Platelet antibody screen, which confirms diagnosis.

High-dose intravenous immune globulin (immunoglobulin) is the therapy of choice and should correct the associated thrombocytopenia in a matter of days

4 MANAGEMENT

Management of mild ATR

For patients with mild reactions, such as pyrexia (temperature of >38 °C OR a rise of 1-2°C from baseline), and/or pruritus or rash but WITHOUT other features, the transfusion may be continued with appropriate treatment and direct observation. When managing a mild transfusion reaction, consider underlying patient condition, mild febrile and allergic reactions. In both cases, medical staff should be informed and the transfusion may be restarted if there is no progression of symptoms after 30 minutes. The total transfusion time for red cells must still not exceed 4 hours (in adults) from the commencement of transfusion. The patient should be closely monitored for onset of anaphylaxis, which may progress rapidly. In such severe cases, the transfusion should not be resumed. Investigations are not indicated. No Hospital Transfusion Team/Hospital Transfusion Committee review/SHOT report is necessary.

In cases of patients with recurrent febrile and allergic reactions, premedication and/or component manipulation by washing or plasma removal is usually considered although the evidence base is weak.

The 'traffic light' illustrated table (see Appendix 1) provides a practical guide to the recognition and initial management of a suspected ATR.

Management of moderate ATR

When managing a moderate transfusion reaction, consider underlying condition, bacterial contamination, haemolytic reaction or IgA deficiency, these are defined as sustained febrile signs or symptoms, which can include a temperature > 39°C OR a rise of > 2°C from baseline AND/OR systemic symptoms such

Symptoms are as chills, rigors, myalgia, nausea or vomiting, AND/OR angioedema and dyspnoea, but not sufficiently severe to be life-threatening.

For patients with moderate reactions, urgent medical advice should usually be sought before the transfusion is restarted, after full clinical evaluation. In most cases it is prudent to discontinue or switch to an alternative unit. Exceptions to this would include reactions where there is an obvious alternative explanation for the symptoms/signs or the patient has a history of similar, previously investigated, non-serious transfusion reactions.

If symptoms are consistent with an underlying condition or transfusion history, consider continuation of transfusion at a slower rate and appropriate symptomatic treatment with oral Paracetamol (500-1000 mg in adults) +/-antihistamine such Chlorphenamine (10 mg by slow intravenous injection), oxygen therapy and a short-acting inhaled beta-2 agonist such as Salbutamol may be useful for respiratory symptoms.

If symptoms are not consistent with patient history and conditions, consider bacterial contamination or a haemolytic reaction. Discontinue implicated unit and perform appropriate investigations. (see Table 3)

If bacterial contamination is suspected, then immediately notify blood transfusion and return the implicated unit to the laboratory. The laboratory will then inform NIBTS so that the associated components from the implicated donation can be withdrawn.

A repeat Group &Save (G&S) and Blood Culture sample should be taken from the patient, along with a completed Transfusion Reaction Form (see Appendix 2)

For patients with recurrent moderate, other than those in which the patient is IgA deficient, consider antihistamine prophylaxis. This may be the only option when further transfusion is urgent and withholding blood is a greater risk. Transfusion of washed red cells or platelets may be required.

Patients who experience moderate allergic reaction should have IgA levels measured (2-3ml EDTA blood sample) - if <0.07g/L, and no generalised hypogammaglobinaemia, check for IgA antibodies. Patients who have experienced an anaphylactic reaction associated with transfusion or found with IgA deficiency after an ATR should be discussed with an allergist or immunologist regarding further management.

Management of Severe Transfusion Reactions

The usual presentation of a severe transfusion reaction:

- Shock/severe hypotension associated with wheeze or stridor, suggestive of anaphylaxis or IgA deficiency.
- Shock/severe hypotension without signs of anaphylaxis or fluid overload, suggestive of Bacterial contamination, ABO incompatibility or Haemorrhage.
- Severe dyspnoea without shock, suggestive of TRALI or TACO
- Transfusion Associated Dyspnoea (TAD)

For patients with severe or life-threatening reactions, contact medical staff responsible for the patient's care immediately and request urgent assessment. Initiate Early Warning Scoring (EWS) System.

Patients with a clinically significant haemolytic transfusion reaction should be managed in an intensive care unit. Depending on the severity of the patient's condition, airway support with intubation and mechanical ventilation, haemodynamic invasive monitoring, vasopressor administration, and renal replacement therapy with dialysis may be warranted.

Prompt initiation of crystalloid resuscitation should be instituted to support the circulation and maintain renal cortical perfusion. Urine output goal is >0.5-1 ml/kg body weight per hour to prevent oliguric renal failure. Should fluid resuscitation fail to meet the urine output goal, forced diuresis should be considered, and renal dialysis may be needed. Prior to initiating a forced diuresis, intravascular volume depletion should be excluded by evidence of central venous pressure or pulmonary artery catheter monitoring.

In case of severe anaphylactic or severe allergic reaction, symptoms often occur within minutes of the initiation of transfusion, though reactions can present much later, even up to hours after finishing a transfusion. Anaphylaxis with hypotension, dyspnoea, wheezing and stridor, or angio-oedema, may follow urticaria.

Anaphylaxis requires immediate administration of intramuscular epinephrine (adrenaline). Maybe repeated every 5 minutes as necessary to alleviate stridor and improve blood pressure. Intravenous epinephrine (adrenaline) infusion may be administered in the setting of cardiac arrest or profound hypotension refractory to intramuscular injection of epinephrine (adrenaline).

The airway should be secured with intubation and initiation of mechanical ventilation if symptoms do not immediately respond to epinephrine (adrenaline) injection. Crystalloid administration should be performed to support circulation. Antihistamines may also be administered as an adjunct to epinephrine (adrenaline). Corticosteroid administration (such as methylprednisolone) is not routinely recommended as evidence is lacking for clear benefit in anaphylaxis, however it may be considered after initial resuscitation.

The management of TRALI is supportive, and may range from supplemental oxygen by mask for a brief period to mechanical ventilation for a period of days, depending on the severity of the patient's respiratory insufficiency. Resolution of the syndrome generally occurs rapidly, typically within fewer than 7 days following transfusion.

Specimen requirements

This will depend on the nature of the investigation. As the requirements can vary from case to case, for moderate and above transfusion reaction, the investigation team can seek advice from the NIBTS medical team and /or NIBTS reference laboratory, the same for where the transfusion reaction is difficult to classify, as described in SOP:BG:022 'Serological Investigations of Transfusion Reactions'

In all moderate and severe transfusion reactions, standard investigations, including full blood count, renal and liver function tests and assessment of urine for haemoglobin should be performed. Patients with respiratory symptoms not due to allergy should also have a chest X-ray (BCSH).

Sample labelling should conform to SOP:BG:046, 'Minimum Specifications for the Labelling of Blood Samples and Accompanying Documentation received for Antibody Identification and Cross-Matching'.

Sampling should also follow any relevant hospital Trust policies or procedures.

Where samples do not meet relevant requirements but there is a compelling clinical indication to investigate, the NIBTS medical team may elect to allow concessionary testing of the samples as per Medical Policy POL:MP:011, Policy for receipt of samples which do not conform to NIBTS sample labelling or request form requirements, and using for FORM:DD:1013, 'Approval to Test Non-Conforming Sample(S)'.

Table 3: Investigation of Moderate or Severe Acute Transfusion

Take samples from a vein other than the infusion site used to administer blood:

- Coagulation screen (PT, APTT, fibrinogen): (Green Top)
- FBC: (Red Top)
- U&E's, LDH, Haptoglobin: (Brown Top)
- Repeat G&S samples, including DAT: (Red Top)
- Retain the patient's next urine to test for haemoglobinuria.

If febrile type reaction, send also:

- Patient Blood cultures to the microbiology laboratory

If moderate/severe allergic reaction, send also:

- Brown top sample for IgA level
- Purple top for serial mast cell tryptase levels (immediate, 3 hour and 24 hour)

If **TRALI/TACO** suspected:

➢ Check oxygen saturation or blood gases.

➢ Request a Chest X-ray (CXR)

If samples are referred to NIBTS Reference Lab, investigations will be completed as described in SOP:BG:022 'Serological Investigations of Transfusion Reactions'

Typically, Reference Lab staff are made aware of transfusion reactions by a NIBTS Medical Officer. On occasion when completing laboratory investigations, laboratory staff will encounter serological findings indicative of a transfusion reaction. Where red cell antibodies are detected in a pre-transfusion sample, and weakened or absent in the post-transfusion sample, or where red cell alloantibodies are detected in an eluate prepared from the post transfusion sample, then a serological transfusion reaction is indicated. The results of testing must be referred to a NIBTS Medical Officer. If no RBC antibody is implicated in the transfusion reaction, the patient's serum/plasma may be further investigated for white cell and platelet antibodies, at the discretion of the co-ordinating Medical Officer.

5 RESPONSIBILITY

The medical team caring for the patient, supported by their hospital transfusion and haemovigilance teams are responsible for providing clinical advice on investigation and management of suspected transfusion reactions. These have also the responsibility to inform immediately their blood bank and NIBTS on any moderate and severe transfusion reaction so all other components of the implicated units are recalled, quarantined and withdrawn if appropriate, the same where the transfusion reaction is difficult to classify.

The NIBTS medical team will be available to provide advice on the choice of components for future transfusion and the need for investigation of donors.

6 EQUALITY SCREENING OUTCOME

This policy has been drawn up and reviewed in the light of the statutory obligations contained within Section 75 of the Northern Ireland Act (1998). In line with the statutory duty of equality, this policy has been screened against particular criteria. If at any stage of the life of this policy there are any issues within the policy which are perceived by any party as creating adverse impacts on any of the groups under Section 75, that party should bring these to the attention of the Head of HR & Corporate Services.

The Northern Ireland Blood Transfusion Service is committed to the promotion of equality of opportunity of staff, donors and service users. We strive to ensure that everyone is treated fairly and that their rights are respected at all times. We believe that it is important that our policy is understood by all those whose literacy is limited, those who do not speak English as a first language or those who face communication barriers because of a disability. On request it may be possible to make this policy available in alternative formats such as large print, Braille, disk, audio file, audio cassette, Easy Read or in minority languages to meet the needs of those not fluent in English.

7 TRAINING REQUIREMENTS

Hospital Services staff, medical team and any Biomedical Scientist undertaking on-call work should have read and understood this policy. This policy may also be circulated to Heads of Hospital Blood Bank

Appendix 1: Algorithm for Managing a Transfusion Reaction

Symptoms	Mild	Moderate	Severe
Temperature (ºC)	≥38ºC & or rise of 1-2 ºC from baseline.	≥39ºC OR rise of ≥2ºC from baseline.	As moderate and any new unexplained pyrexia in addition to clinical signs/symptoms
Rigors/ shaking	None	Mild chills	Obvious shaking/rigors
Pulse HR	Minimal or no change in baseline	Rise from baseline ≥ 10bpm without bleeding	Raise from baseline of ≥ 20 bpm without bleeding
Respiratory Rate (RR)	Minimal or no change	Rise in RR ≥10 from baseline	Raise in RR ≥10 from baseline with dyspnoea/ wheeze
Blood Pressure (BP)	Minor or no change in baseline	Change in systolic/ diastolic of ≥30mmHg without bleeding	Change in systolic/diastolic of ≥30mmHg , shock without bleeding
Skin	Mild pruritus/rash	Facial flushing, rash, urticaria, pruritis	Rash, urticarial AND peri-orbital oedema/ conjunctivitis
Pain	None	General discomfort or myalgia. Pain at drip site	Acute pain in back, chest or abdomen
Urine	Clear, normal output	Clear, normal input	Haematuria, haemoglobinuria Oliguria/anuria
Bleeding	No new bleeding	No bleeding	Uncontrolled oozing
Nausea	None	Nausea	Nausea and vomiting
All green Mild TR	**STOP transfusion but leave unit connected:** Consider symptomatic treatment (antipyretic +/- antihistamine). If better, **Continue Transfusion** at reduced rate and monitor more frequently. If another reaction occurs, **discontinue transfusion and return unit and administration set to transfusion Lab.**		
1 or more amber Moderate TR	**STOP transfusion but leave unit connected:** Consider underlying condition, bacterial contamination or haemolytic reaction. If consistent with underlying condition, **consider continuing transfusion at slower rate** following appropriate symptomatic treatment. If not **discontinue transfusion and return unit and administration set to transfusion Lab.**		
1 or more red Severe TR	**STOP transfusion and disconnect unit:** Consider Anaphylaxis, ABO incompatibility, Bacterial Contamination, TRALI, TACO, TAD, Haemorrhage **Return unit and administration set to Transfusion Lab,** unless haemorrhage is suspected.		

Investigation and management:

➢ Request urgent medical help and Re-check identity unit/patient.

➢ Initiate resuscitation ABC and maintain IV fluids

➢ Inform transfusion Lab immediately and Transfusion Practitioner and if necessary consultant haematology.

Take following samples

- FBC, Coagulation screen, U&Es, LDH, Haptoglobin
- Repeat compatibility tests, including DCT
- Retain the patient's next urine to test for haemoglobinuria**.**

If febrile type reaction, send also: Patient Blood Cultures to the Microbiology laboratory

If TRALI/TACO suspected: Check oxygen saturation or blood gases, and request a Chest X-ray.

If moderate/severe allergic reaction, send a sample for IgA and serial Mast Cell Tryptase levels (immediate, 3 h and 24 h). Document the reaction in the case notes.

Fully complete and return a Transfusion Reaction Form to the Transfusion Lab, along with the implicated unit.

Appendix 2: Transfusion Reaction Investigation Form

Please complete all details in full and send the form with appropriate samples and implicated bag with administration set to the Transfusion laboratory **as soon as possible.**

IMPORTANT – inform the Transfusion Laboratory **immediately of any reaction suspected to be due to bacterial contamination, as other blood products may need to be urgently recalled.**

Date of incident…….. Time of incident (approximate)……

Patient information Hospital …… Ward ……
Patient Name …… Reason for Transfusion ……..
Date of Birth …… Blood Group ……..
Hospital Number …… Known antibodies ……..
NHS Number ……. Previous transfusion and when……
Gender …… Previous transfusion reaction ……
Consultant ……. Clinical diagnosis ……

Medical condition of patient:

Septicaemia □ Hickman/central line in situ □ Ventilated/ on ITU □
Other (please specify) □ ……

Blood component information

Product type: RBC □ Platelets □ FFP □ Other (please specify) □ ……
Blood component group …….. Unit number/numbers ……
Blood component expiry date …….
Time delay from blood removed from fridge to transfusion commenced ……
Reason for transfusion ……
Does the patient need to be re-transfused within the next 24/48 hours Yes □ No □
Pre-transfusion Haemoglobin ……. Post transfusion haemoglobin……

Incident Information: Signs/symptoms of transfusion reaction

Fever □ Chills □ Tachycardia □ Collapse □
High/low BP □ Rigors □ Flushing □ Urticaria □
Bone/muscle/chest/abdominal pain □ SOB □ Nausea □

Pre-Transfusion reaction	Transfusion reaction	Post Transfusion reaction
BP ……..	BP ……..	BP …….
Temp …….	Temp ……..	Temp …….
RR …….	RR ……	RR ……..
O2 sats ……. ..	O2 sats ……	O2 sats ……
HR ……	HR ……	HR ……...

Actions

Transfusion stopped Yes □ No □
Patient identity checked Yes □ No □
Volume transfused before onset of symptoms ……
Time transfused before onset of symptoms ……
Visual appearance of implicated unit/s …….
Blood cultures taken post-incident from patient Yes □ No □
Blood cultures taken: ……..
Peripheral access □ Central access □
Implicated unit sent to local transfusion department Yes □ No □
Antibiotics given pre-reaction …… Antibiotics given post reaction ……
Fluids given …….. Other drugs given ……

Person completing the form
Doctor/nurse/laboratory staff ……..……Signature …… Date…….

Laboratory staff only – NIBTS informed Yes/No
Haemovigilance Team informed Yes □ No □

Appendix 3: Hospital Initiated Recall for Transfusion Reactions