Whittington Health NHS

Acute Transfusion Reactions - Management and Investigation

Subject:	Acute transfusion reactions
Policy Number	N/A
Ratified By:	Hospital Transfusion Committee
Date Ratified:	October 2009, reviewed November 2015
Version:	2.0
Policy Executive Owner:	Clinical Director, Medicine, Frailty and Networked Service ICSU
Designation of Author:	Transfusion Practitioner
Name of Assurance Committee:	As above
Date Issued:	November 2015
Review Date:	3 years hence
Target Audience:	Clinical teams involved in blood component transfusion
Key Words:	Acute, Delayed, Minor reactions and Major transfusion reactions

Version Control Sheet

Version	Date	Author	Status	Comment
1.0	Oct 2009	Mr J Dalton – Transfusion Laboratory Manager	Off Line	New guideline approved at Hospital Transfusion Committee
2.0	Nov 2015	Mr Abdul Adamu Transfusion Practitioner	Live	Reviewed. Insertion of Appendix 2. Agreed at Hospital Transfusion Committee

➢ Criteria for use

Symptoms / signs of an acute transfusion reaction:

Fever
Chills
Tachycardia
Hyper- or hypotension
Collapse
Rigors
Flushing
Urticaria
Bone, muscle, chest and / or abdominal pain
Shortness of breath
Nausea
Generally feeling unwell
Respiratory distress

NB: Reactions can occur after the blood has been discontinued or may be caused by a previous unit

➢ Background/ introduction

There are eight types of Acute Transfusion Reaction:
(see appendix 2 for algorithm for recognition and management of acute transfusion reactions)

- Mild fever - febrile non-haemolytic transfusion reaction
- Mild allergic reaction – urticaria
- Severe allergic - anaphylactic
- Suspected ABO haemolytic reaction
- Other haemolytic reaction / bacterial contamination of unit
- Fluid overload – transfusion associated circulatory overload (TACO)
- Transfusion related acute lung injury (TRALI)
- Transfusion Associated Dyspnoea(TAD)

➢ Inclusion/ exclusion criteria

See appendix 2 - Recognition and management of acute transfusion reactions

➢ Clinical management

STOP the transfusion and call a doctor

Measure:

- Temperature
- Pulse
- Blood pressure
- Respiratory rate
- O_2 saturation

Check the details on the compatibility bag tag with:

- the identity of the patient
- the details of the unit

Minor reactions where the transfusion may be continued

Mild allergic reaction (Urticarial rash only)

Urticaria and/or itching within minutes of starting a transfusion are quite common, particularly with components including large volumes of plasma, e.g. platelet concentrates and fresh frozen plasma (FFP). Symptoms usually subside if the transfusion is slowed and antihistamine is given (e.g. chlorpheniramine 10 mg, by slow intravenous injection or intramuscular injection in patients who are not thrombocytopenic).

Management: The transfusion may be continued if there is no progression of symptoms after 30 minutes. Chlorpheniramine should be given before transfusion if the patient has previously experienced repeated allergic reactions. If signs and symptoms fail to respond to this, seek advice from clinical haematologist. For severe cases saline-washed blood components should be considered.

Febrile non-haemolytic transfusion reactions (FNHTR) (mild fever only)

Fever or rigors during red cell or platelet transfusion affect 1−2% of recipients, mainly multi-transfused or previously pregnant patients. These reactions are probably less frequent with current leucodepleted components. Features are fever (> 1.5°C above baseline), usually with shivering and general discomfort occurring towards the end of the transfusion or up to two hours after it has been completed.

***Management*:** Most febrile reactions can be managed by slowing or stopping the transfusion and giving an antipyretic e.g. paracetamol (not aspirin). These reactions are unpleasant but not life threatening, but it is important to remember that the fever or rigors could be the first warning of a severe acute reaction

NB: If symptoms do not settle or they recur once the transfusion is resumed contact the duty clinical Haematologist
If in doubt treat and investigate as a major transfusion reaction.
Send all necessary samples to the laboratory including the 1st urine passed and a completed **Acute Transfusion Reaction Report** – see Appendix 1

Major reactions where the transfusion must be discontinued

Suspected ABO incompatibility

If red cells are mistakenly administered to the 'wrong' patient, the chance of ABO incompatibility is about one in three. Even a few millilitres of ABO incompatible blood may cause symptoms within a few minutes that will be noticed by a conscious patient. However, if the patient is unconscious or cannot communicate, the first signs of the reaction may be bleeding, tachycardia, hypotension or hypertension. Acute haemolysis may also occur following infusion of plasma-rich components, usually platelets or FFP, containing high-titre anti-red-cell antibodies, usually anti A or B.

- **Diagnosis - One or more of the following:**
  - Shortness of breath
  - Chest pain not due to cardiac problems OR pulmonary oedema
  - Back pain
  - Loin tenderness
  - Profound hypotension
  - Unexplained bleeding / tachycardia in unconscious patient

- **Action:**
  - Disconnect blood and put up saline infusion
  - Monitor urine output / catheterize
  - Maintain urine output >100ml/hour
  - Give furosemide if urine output falls / absent
  - Treat any disseminated intra-vascular coagulopathy (DIC) with appropriate blood components
  - Contact clinical haematologist / transfusion laboratory immediately

Take essential samples:
- 6ml EDTA - Direct Coombs test
- 6ml EDTA - repeat cross-match
- 4ml EDTA – full blood count
- 4 ml Citrate - coagulation screen

- U & E's
- Take blood cultures and samples for culture from blood component pack
- First urine passed
- Send unit with giving set, plus previous units and samples to blood transfusion laboratory with a completed **Acute Transfusion Reaction Report** – see Appendix 1

***Management*:** Stop the transfusion. Maintain venous access. Resuscitate with crystalloid fluid. Consider inotrope support if hypotension is prolonged. Take blood cultures and samples for culture from component pack. Inform the blood bank. Seek urgent critical care and advice from the clinical haematologist. Admit to ICU if possible

Haemolytic Gram negative shock.

NB: It is often difficult to distinguish between the two in acute situations.

Infusion of a blood pack contaminated by bacteria

This is likely to cause a very severe acute reaction with rapid onset of hyper- or hypotension, rigors and collapse. The signs and symptoms may be similar to acute haemolytic transfusion reactions or severe acute allergic reactions. Bacterial contamination of blood components is rare but is more often reported with platelet concentrates (stored at +22°C) than with red cells (stored at +4°C).

Examination of the pack (discolouration, smell and gram stain) may rapidly confirm the diagnosis. Organisms associated with contamination include *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus cereus*, Group B streptococci, *E. coli*, *Pseudomonas* species and other gram-negative organisms.

- **Diagnosis - One or more of the following:**
  - Shortness of breath
  - Chest pain not due to cardiac problems OR pulmonary oedema
  - Back pain
  - Loin tenderness
  - Profound hypotension

- **Action:**
  - Disconnect blood and put up saline infusion
  - Check documentation that the right patient has been given the right unit

  Take essential samples:
  - 6ml EDTA - Direct Coombs test
  - 6ml EDTA - repeat cross-match
  - 4ml EDTA – full blood count
  - 4 ml Citrate - coagulation screen

- U & E's
- Blood culture
- First urine passed
- Send unit with giving set, plus previous units and samples to blood transfusion laboratory with a completed **Acute Transfusion Reaction Report** – see Appendix 1

***Management*:** As for acute haemolytic reaction – see Page 5, DIC and acute renal failure and administer a combination of antibiotics that will be active against the range of bacteria that may be involved. In the absence of expert microbiology advice it would generally be appropriate to follow the local protocol for antibiotic management of sepsis in neutropenic patients. If this is not available, a combination of the following antibiotics may be considered to provide activity against gram-positive and gram-negative bacteria:

Gram-negative bacteria

Piperacillin/tazobactam (Tazocin) 4.5 g tds iv **OR**
Ceftriaxone 1 g once daily iv (2 g if 'severe' infection) **OR**
Meropenem 1 g tds iv

Gram-positive bacteria including most MRSA

Teicoplanin 400 mg bd iv x 2 doses then once daily (non-nephrotoxic) **OR**
Vancomycin − 1 g bd iv then adjusted according to levels − equally effective but potentially adds to any renal impairment **OR**
Ceftriaxone/teicoplanin has the advantages of once daily dosing, low renal toxicity

Anaphylactic.

Anaphylactic is a rare but life threatening complication usually occurring in the early part of a transfusion. Rapid infusion of plasma is one cause. Signs consist of hypotension, bronchospasm, periorbital and laryngeal oedema, vomiting, erythema, urticaria and conjunctivitis. Symptoms include dyspnoea, chest pain, abdominal pain and nausea.

Anaphylaxis occurs when a patient who is pre-sensitised to an allergen producing IgE antibodies is re-exposed to the particular antigen.

IgG antibodies to infused allergens can also cause severe reactions.

A few patients with severe IgA deficiency develop antibodies to IgA and may have severe anaphylaxis if exposed to IgA by transfusion. If the patient who has had a reaction has to have further transfusion, it is essential to seek advice from the blood bank as there is a real risk of a repeat reaction unless blood components are specially selected.

- **Diagnosis:**

  - Acute bronchospasm
  - Oedema
  - Circulatory collapse

- **Action:**

  Disconnect blood, put up saline infusion and investigate as in Haemolytic or Gram negative shock (see page 6)

  - Give oxygen by mask
  - Adrenaline 0.5 ml of 1:1000 every 10 minutes as necessary
  - Piriton 10mg IV slowly

  Take essential samples:
  - 6ml EDTA - Direct Coombs test
  - 6ml EDTA - repeat cross-match
  - 4ml EDTA – full blood count
  - 4 ml Citrate - coagulation screen
  - U & E's
  - Blood culture
  - First urine passed
  - Send unit with giving set, plus previous units and samples to blood transfusion laboratory with a completed **Acute Transfusion Reaction Report** – see Appendix 1

Management:

Fluid overload (transfusion-associated circulatory overload, TACO)

When too much fluid is transfused or the transfusion is too rapid, acute left ventricular failure (LVF) may occur with dyspnoea, tachypnoea, non-productive cough, raised JVP, basal lung crackles, frothy pink sputum, hypertension and tachycardia.

***Management*:** The transfusion should be stopped and standard medical treatment, including diuretic and oxygen, given.

Note: Patients with chronic anaemia are usually normovolaemic or hypervolaemic, and may have signs of cardiac failure before any fluid is infused. If such a patient must be transfused, each unit should be given slowly with diuretic (e.g. frusemide 20−40 mg), and the patient closely observed. Restricting transfusion to one unit of red cells in each 12-hour period should reduce the risk of LVF. Circulatory overload is a special risk with 20% albumin solutions.

Transfusion-related acute-lung injury (TRALI)

Typically within six hours of a transfusion, the patient develops breathlessness and non-productive cough. The chest X-ray characteristically shows bilateral nodular infiltrates in a batwing pattern, typical of acute respiratory distress syndrome. Loss of circulating volume and hypotension are common. The patient may or may not have fever or chills. Monocytopenia or neutropenia may be seen.

Differential diagnosis: It may be very difficult to distinguish TRALI from other non-cardiogenic pulmonary oedema or cardiac failure.

***Management*:** Seek urgent critical care and advice from the clinical haematologist and/or intensive care team. Admit to ICU if possible. Treatment is that of adult respiratory distress syndrome from any cause. Diuretics should be avoided. Steroids are of uncertain benefit.

It is often found that plasma of one of the donors contains antibodies that react strongly with the patient's leucocytes. The implicated donors are almost always parous women. It is important to report any case of TRALI to the blood service so that an implicated donor can be contacted and, if appropriate, taken off the donor panel.

➢ Further information

Delayed haemolytic transfusion reaction (DHTR)

DHTR is a haemolytic reaction occurring more than 24 hours after transfusion, in a patient who has been immunised to a red cell antigen by previous transfusion or pregnancy. The antibody may be undetectable by routine blood bank screening. However, red cell transfusion can cause a secondary immune response that boosts the antibody level. Antibodies of the Kidd (Jk) and Rh systems are the most frequent cause of such delayed haemolytic reactions. Features, occurring usually within 1−14 days of transfusion, may include falling haemoglobin concentration, unexpectedly small rise in Hb, jaundice, fever and rarely haemoglobinuria or renal failure.

Management: Investigations include haemoglobin level, blood film, LDH, direct antiglobulin test, renal profile, serum bilirubin, haptoglobin and urinalysis for haemoglobinuria. Renal function should be closely monitored. The group and antibody screen should be repeated and the units should be re-crossmatched using both pre- and post-transfusion samples. Specific treatment is rarely required, although further transfusion may be needed.

Transfusion associated graft-versus-host disease (TA-GvHD)

This is a rare but serious complication, due to the engraftment and proliferation of transfused donor lymphocytes. These damage recipient

cells that carry HLA antigens. The skin, gut, liver, spleen and bone marrow are affected, usually one to two weeks following a transfusion, initially causing fever, skin rash, diarrhoea and hepatitis. The condition is usually fatal. Patients at risk are immunocompromised or those who receive transfusion from a first- or second-degree relative (due to the sharing of an HLA haplotype).

It is essential that all patients at risk of GvHD receive only blood components that have been irradiated to inactivate any donor lymphocytes.

Post-transfusion purpura (PTP)

This is a rare but potentially lethal complication of transfusion of red cells or platelets. It is more often seen in female patients. It is caused by platelet-specific allo-antibodies. Typically five to nine days after transfusion, the patient develops an extremely low platelet count with bleeding.

***Management*:** Seek specialist advice from the clinical haematologist. High-dose intravenous immunoglobulin is the current treatment of choice with responses in about 85% of cases; there is often a rapid and prompt increase in the platelet count. Steroids and plasma exchange were the preferred treatments before the availability of IVIgG, and plasma exchange in particular appeared to be effective in some but not all cases. Platelet transfusions are usually ineffective in raising the platelet count, but may have to be given in large doses in the attempt to control severe bleeding in the acute phase, particularly in patients who have recently undergone surgery, before there has been a response to high-dose IVIgG. There is no evidence that platelet concentrates from HPA 1a negative platelets are more effective than those from random donors in the acute thrombocytopenic phase, and the dose of platelets may be more important than the platelet type of the donor platelets. There is no evidence to suggest that further transfusions in the acute phase prolong the duration or severity of thrombocytopaenia.

Iron overload

Patients with beta thalassaemia are the most likely to have iron overload problems, but patients with sickle cell disease and those with other transfusion-dependent conditions may also be affected. Each unit of red cells contains about 250 mg of iron. Since iron excretion is very limited, accumulation in the body causes toxic effects after 10−50 units have been transfused. These patients require life-long iron chelation therapy from the age of two or three years. Those who can comply well with iron chelation

therapy have a 90% chance of surviving into the fourth decade of life; those who comply poorly have a high mortality rate in the third and fourth decade of life, usually due to complications of iron overload (cardiac disease, cirrhosis and diabetes mellitus).

Iron chelation therapy: A conventional regime would be desferioxamine 30−50 mg subcutaneously by slow infusion overnight using a syringe driver at least five times per week.

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

Clinical haematologist bleep 3060 or 3037. Transfusion practitioner ext. 5192, bleep 2953 Blood transfusion laboratory ext 5766. Out of hour bleep 2686

➢ References (evidence upon which the guideline is based)

Handbook of Transfusion Medicine. 2013 5th edition. Blood Transfusion Services of the United Kingdom ED.B. McClelland. http://www.transfusionguidelines.org.uk/

Handbook of Transfusion Medicine. 2013 4th edition. Blood Transfusion Services of the United Kingdom ED.B. McClelland. http://www.transfusionguidelines.org.uk/

British Committee for Standards in Haematology. Guideline on administration of blood components 2009 http://www.bcshguidelines.com/4 HAEMATOLOGYGUIDELINES.html?dpage=0&dtype=transfusion&sspage=0 &ipage=0

➢ Compliance with this guideline (how and when the guideline will be monitored e.g. audit and which committee the results will be reported to)

Generic monitoring through DATIX reporting of incidents pertaining to acute transfusion reactions

Appendix 1: - Acute Transfusion Reaction Report

See clinical guideline: Acute Transfusion Reactions - Management and Investigation for guidance

Notify clinical haematologist (bleep 3060/3037), transfusion practitioner (bleep 2953), or senior staff in the transfusion laboratory (ext 5766) and out of hours bleep 2686.

Surname: Hospital Nos:

Forenames: DOB:

M/F: Consultant:

Ward: Bed location:

Date of reaction: Time:

Blood unit nos: Volume of blood given:
Date of reaction: Time:

Reporter Name: Signature:

Component donation number	Volume given (mLs)

(Record the numbers of all the units given during the current transfusion)

Type of reaction (tick where applicable)

Fever - sudden rise in temp >1.5^{o}C (specify rise from baseline) …….. ºC
Chills
Tachycardia
Hyper - or hypotension (specify) ……
Collapse
Rigors
Flushing
Urticaria
Bone, muscle, chest and / or abdominal pain (specify) ……
Shortness of breath
Nausea
Generally feeling unwell
Respiratory distress
Other (specify) ……..

Return this form with fresh blood samples, unit(s) transfused, including giving set, to the blood transfusion laboratory

Appendix 2: Transfusion reactions for – For Guidance

Symptoms /Signs	*Mild*	*Moderate*	*Severe*
Temperature	Temperature of >38ºC **AND** rise of 1-2ºC from baseline temperature	Temperature of >39ºC **OR** a rise of >2ºC from baseline temperature	Sustained febrile symptoms or any new, unexplained pyrexia ***in addition*** to clinical signs. Temp 37ºC to 38ºC
Rigors/shaking	None	Mild chills	Obvious shaking/rigors
Pulse	Minimal or no change from baseline	Rise in heart rate from baseline of 10 bpm or more NOT associated with bleeding	Rise in heart rate from baseline of 20 bpm or more NOT associated with bleeding
Respirations	Minimal or no change from baseline	Rise in respiratory rate from baseline of 10 or more	Rise in respiratory rate from baseline of 10 or more accompanied by dyspnoea/wheeze
Blood Pressure (Hypo/hypertension	Minor or no change to systolic or diastolic pressure	Change in systolic or diastolic pressure of >30 mm/Hg NOT associated with bleeding	Change in systolic or diastolic pressure of >30 mm/Hg NOT associated with bleeding
Skin	No change	Facial flushing, rash Urticaria, pruritis	Rash, urticaria ***and*** Peri-orbital oedema Conjunctivitis
Pain	None	General discomfort or myalgia Pain at drip site	Acute pain in chest, abdomen, back
Urine	Clear Normal output		Haematuria / haemoglobinuria Oliguria, Anuria
Bleeding	No new bleeding		Uncontrolled oozing
Nausea	None		Nausea or vomiting
All Green	**STOP the transfusion but leave connected.** Re-check identity of the unit with the patient, inform doctor. If all well, continue at reduced rate **for the next 30 minutes and then** resume at prescribed rate. Continue to monitor the patient carefully and be alert for other symptoms or signs of a transfusion reaction. Anti-pyretics may be required.		
1 or more Amber	**STOP the transfusion but leave connected**, request **URGENT** clinical review, re-check identity of the unit with the patient, give IV fluids. If symptoms stable or improving over next 15 minutes consider restarting the unit. Antihistamines and/or anti-pyretics may be required.		
1 or more Red	**STOP the transfusion and disconnect,** request immediate clinical review, re-check identity of the unit with the patient, give IV fluids, inform the transfusion laboratory, send the unit with the giving set and group and save sample, complete the acute transfusion reaction form.		

➢ Further information

	Please see Whittington Hospital NHS Trust Guideline: ***'Blood Policy'***

Appendix A

Plan for Dissemination and implementation plan of new Procedural Documents

To be completed and attached to any document which guides practice when submitted to the appropriate committee for consideration and approval.

Acknowledgement: University Hospitals of Leicester NHS Trust

Title of document:	**Acute Transfusion Reactions - Management and Investigation**		
Date finalised:	**Nov 2015 (re-issue)**	**Dissemination lead: Print name and contact details**	**Mr Abdul Adamu ext 5192**
Previous document already being used?	**Yes**		
If yes, in what format and where?	**Intranet**		
Proposed action to retrieve out-of-date copies of the document:	**Version replacement on intranet**		
To be disseminated to:	**How will it be disseminated/implemented, who will do it and when?**	**Paper or Electronic**	**Comments**
All staff	**Intranet uploading**	**E**	
Is a training programme required?	**No**		
Who is responsible for the training programme?	**N/A**		

Appendix B

Equality Impact Assessment Tool

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval.

Impact (= relevance) 1 Low 2 Medium 3 High	Evidence for impact assessment (monitoring, statistics, consultation, research, etc	Evidential gaps (what info do you need but don't have)	Action to take to fill evidential gap	Other issues
Race	**1**	**N/A**	**N/A**	**N/A**
Disability	**1**	**N/A**	**N/A**	**N/A**
Gender	**1**	**N/A**	**N/A**	**N/A**
Age	**1**	**N/A**	**N/A**	**N/A**
Sexual Orientation	**1**	**N/A**	**N/A**	**N/A**
Religion and belief	**1**	**N/A**	**N/A**	**N/A**

Once the initial screening has been completed, a full assessment is only required if:

- The impact is potentially discriminatory under equality or anti-discrimination legislation
- Any of the key equality groups are identified as being potentially disadvantaged or negatively impacted by the policy or service
- The impact is assessed to be of high significance.

If you have identified a potential discriminatory impact of this procedural document, please refer it to relevant Head of Department, together with any suggestions as to the action required to avoid/reduce this impact.