Transfusion Reactions and Laboratory Incidents

How do we minimise the damage?
Acute Transfusion Reactions

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Patient exhibiting possible features of an acute transfusion reaction, which may include: Fever, chills, rigors, tachycardia, hyper- or hypotension, collapse, flushing, urticaria, pain (bone, muscle, chest, abdominal), respiratory distress, nausea, general malaise

**STOP THE TRANSFUSION**
Undertake rapid clinical assessment, check patient ID/blood compatibility label, visually assess unit

**Evidence of:**
Life-threatening Airway and/or Breathing and/or Circulatory problems and/or wrong blood given and/or evidence of contaminated unit

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**Yes**

**SEVERE/LIFETHREATENING**
- Call for urgent medical help
- Initiate resuscitation-ABC
- Is haemorrhage likely to be causing hypotension? If not, discontinue transfusion (do not discard implicated unit(s))
- Maintain venous access
- Monitor patient e.g. TPR, BP, urinary output, oxygen saturations

- If likely anaphylaxis/severe allergy-follow anaphylaxis pathway
- If bacterial contamination likely start antibiotic treatment
- Use BP, pulse, urine output (catheterise if necessary) to guide intravenous physiological saline administration
- Inform hospital transfusion department
- Return unit (with administration set) to transfusion laboratory
- If bacterial contamination suspected contact blood service to discuss recall of associated components
- Perform appropriate investigations (see Table 1)

- Review at HTC
- Report to SHOT/MHRA as appropriate

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**No**

**Moderate**
- Temperature ≥ 39°C or rise of ≥ 2°C and/or
- Other symptoms/signs apart from pruritus/rash only

- Consider bacterial contamination if the temperature rises as above and review patient’s underlying condition and transfusion history
- Monitor patient more frequently e.g. TPR, BP, oxygen saturations, urinary output

**Mild**
- Isolated temperature ≥ 38°C and rise of 1-2°C and/or
- Pruritus/rash only

- Continue transfusion
- Consider symptomatic treatment (see text)
- Monitor patient more frequently as for moderate reactions
- If symptoms/signs worsen, manage as moderate/severe reaction (see left)

**Transfusion-related event**
- If consistent with underlying condition or history, transfusion can be continued at same or slower rate with appropriate symptomatic treatment

**Transfusion unrelated**
- Not consistent with condition or history
- Discontinue (do not discard implicated unit(s))
- Perform appropriate investigations (see Table 1)

**Document in notes that no HTA/HTC review/SHOT report necessary**

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**SHOT**

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**SERIOUS HAZARDS OF TRANSFUSION**
Case 1

• A neutropenic patient, post ABO compatible allogeneic stem cell transplant, receives a red cell unit and 30 minutes in, feels unwell
  – temp rise 1.5C
  – some transient rigors,
  – slight rise in blood pressure

• She is known to have anti Jk$^{a}$ and enzyme-only anti E
What should you do next?

- A Get patient seen by doctor
- B Stop the transfusion and triage the patient
- C Continue transfusion as reaction not severe
- D Administer paracetamol
Answer

• The first step is to stop the transfusion
  – Check Airway, Breathing, Circulation
  – Check compatibility label on blood and check patient ID: ask who they are if possible
  – Check condition of blood component
Further management

• You have checked the ID and blood component, and have decided the patient is in no immediate danger.

• Which of these statements would you most agree with?
• **A** Bacterial contamination must be considered

• **B** In view of her antibodies, this could be an acute haemolytic reaction

• **C** This is probably a febrile transfusion reaction

• **D** This may be unrelated to the transfusion
Cases reviewed in 2011 (excluding near miss and instances where the patient received a correct component despite errors having occurred – RBRP)
n=1815

- HSE: 325 (17.9%)
- I&U: 149 (8.2%)
- Anti-D: 249 (13.7%)
- IBCT: 247 (13.6%)
- PTP: 2 (0.1%)
- CS: 42 (2.3%)
- PUCT: 2 (0.1%)
- TAD: 35 (1.9%)
- TACO: 71 (3.9%)
- TRALI: 12 (0.7%)
- HTR: 94 (5.2%)
- ATR: 587 (32.3%)
Likely causes

- Febrile transfusion reactions are common, occurring in 1% of transfusions, commonest reaction with red cells
Reaction by component type

Each star represents a case of:
- HLA matched platelets
- Solvent detergent plasma
- Methylene blue plasma

Component type

<table>
<thead>
<tr>
<th>Component type</th>
<th>Percentage of reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cells</td>
<td>284</td>
</tr>
<tr>
<td>Platelets</td>
<td>67</td>
</tr>
<tr>
<td>Plasma</td>
<td>26</td>
</tr>
<tr>
<td>Multiple components</td>
<td>3</td>
</tr>
</tbody>
</table>
Likely causes

- Febrile transfusion reactions are common, occurring in 1% of transfusions, commonest reaction with red cells
- Need to consider other causes
  - Unrelated to transfusion, e.g. infected long line?
  - Consider haemolytic reaction, bacterial contamination
Investigations of a moderate febrile reaction (assuming “standard” FBC, U&E and LFTs done)

- **A:** Repeat patient group, antibody screen and Direct antiglobulin test
- **B:** Patient blood culture and culture the unit
- **C:** Both A and B
- **D:** Neither A nor B
Guideline:

- Appropriate to check FBC, U & E, LFTs, inspect urine (rule out frank haemolysis)
- Other investigations as indicated by clinical features
Question

• What would most influence your decision to investigate possible transfusion transmitted infection?
• **A:** Bacterial TTI is much less common with red cell units

• **B:** I would only worry about bacterial contamination if the clinical features were more severe than this

• **C:** It is our policy to do local culture of the patient’s blood and the unit in all but the mildest reactions. We will involve NHSBT if the picture worsens or if we get a positive result

• **D:** I think we should discuss this case with a blood service consultant
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from 10/1998)
Strategy to reduce bacterial TTI

- Donor screening
- Post donation information
- Arm cleaning
- Diversion pouches
- Bacterial screening
- Withdrawing associated components when adverse reactions reported
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Clinical features of bacterial transfusion transmitted infection

- Temperature rise >2C and/or severe shivering, rigors
- Back or abdominal pain
- Severe hypotension, shock
- Tachycardia
- Occasionally symptoms are milder
  - Pathogenicity, number of bacteria, underlying clinical state
Clinical features of acute haemolysis

- Fever
- Pain in back, chest, occasionally cannula site
- Hypotension, shock
Symptoms settle. You decide this is an ATR. How would you continue the transfusion?

A: I would discard this unit and try another one crossmatched for this patient

B: I would restart this unit if within time limits, at the same rate

C: I would restart this unit at a slower rate

D: I would re-crossmatch the patient
Next case: Keep it local?

- A patient experiences febrile reaction to apheresis platelets
- Local sampling and culture is performed
- Two days later (a Saturday) the hospital micro lab identifies a gram positive coccus: type not available yet
- The SpR contacts NHSBT consultant for advice.
A patient experiences febrile reaction to apheresis platelets
NHSBT bacterial screen was negative
Local sampling and culture is performed
Two days later (a Saturday) the hospital micro lab identifies a gram positive coccus: type not available yet
The SpR contacts NHSBT consultant for advice.
  - Immediately try to withdraw any associated components
  - Send us the pack please
There was one other unit from this apheresis donation.

Hospital contacted: the platelet has been transfused and the patient died the next day.

The hospital did not consider bacterial TTI and that unit has been discarded.

The unit associated with the reaction reaches NBL 3 days later.
Continued

• Cultured coagulase negative staphylococcus in the unit: Propionibacterium acnes
• Was this a contaminant introduced at the time of sampling?
• Or was it present in the transfused platelet and did it contribute to the other patient’s death?
Cultured coagulase negative staphylococcus in the unit: Propionibacterium acnes

Was this a contaminant introduced at the time of sampling?

Or was it present in the transfused platelet and did it contribute to the other patient’s death?

In fact, P acnes is of low pathogenicity.

Bacterial screening was negative.

In this case it was a likely contaminant introduced at sampling.
Local or NBL bacterial testing

- Pro local
  - Speedy results

- Pro NBL
  - Controlled sampling conditions
  - Ability to compare component and donor isolates
  - ensures withdrawal of associated components if necessary
Take Home Message

• Whether you are considering sampling the component in a hospital lab or referring to a blood service laboratory
  – Discuss with blood service consultant to determine whether other components need to be withdrawn
Third case

- A 49 year old woman with thrombotic thrombocytopenic purpura is receiving regular plasma exchange with solvent detergent plasma.
- On the last treatment, 2 days ago, she had a rash 20 minutes post-exchange.
- Today, at the end of the exchange procedure, she complains of tingling around her mouth, then she develops swelling of her lips and eyelids, and has an audible wheeze.
What is the likely cause?

- **A**: Mild allergic reaction
- **B**: Anaphylaxis
- **C**: Moderate allergic reaction, (angioedema)
- **D**: Fluid overload: TACO
What investigation would be most helpful here?

- **A:** Haptoglobin level
- **B:** IgA level and antibodies
- **C:** Mast cell tryptases
- **D:** HLA antibodies
Many patients who have repeated reactions to blood components have history of reactions to other allergens

**Haptoglobin** deficiency is a relatively common cause of ATRs in the Far East but rare in the UK

It is worth checking patients for **IgA deficiency**: incidence 1 in 500 and if associated with ATRs, would merit use of IgA deficient plasma. However, if found incidentally, may not require special components

**Mast cell tryptase** not indicated here: characteristic rise and fall (immediate, 1-3 hrs, baseline or 24 hrs) in anaphylaxis.

**HLA studies** NOT indicated.
   - Except in patients who are refractory to platelets
   - They will be present in 25% of parous females, and are unlikely to contribute to allergic reactions
Further management

- Results of investigations (when received) are all normal. She still requires therapeutic exchange. How will you manage this?
• A: Change to methylene blue FFP

• B: Premedicate with antihistamine

• C: Premedicate with antihistamine and hydrocortisone

• D: Change to standard plasma
Answers

- Methylene Blue FFP should not be used in TTP (new BCSH guidelines: more plasma exchanges needed)
- No evidence of efficacy for prophylaxis but many would use antihistamine for repeat reactors
Case Studies – Laboratory Incidents

Debbie Asher
TLM, Norfolk and Norwich University Hospitals Trust
Member, SHOT Working Expert Group
Patient has frank haematemesis and 4 units of red cells are required urgently. There are records on the LIMS for this patient who was transfused one week previously. A new sample was requested. The doctor sent the sample and request, recording the blood group as A positive on the request form. There was a delay in the sample reaching the laboratory and before testing was begun the ward rang again stating that red cells were required immediately.
What should the BMS do next?

A. Issue group A positive red cells, as group specific, as the doctor has written the group clearly on the request form.

B. Check the LIMS records, perform a rapid group on the sample and issue red cells as group specific.

C. Issue emergency group O red cells as there is no time for any pre-transfusion testing.

D. Insist that full pre-transfusion testing is carried out, before blood is issued, as the patient may have produced red cell antibodies to the red cells transfused last week.
BCSH Guidelines for Compatibility Procedures in Blood Transfusion Laboratories state:

- The ABO and D group must, wherever possible, be verified against previous results for the patient.
- Emergency groups performed in these circumstances MUST include a test against anti-A, anti-B and anti-D with appropriate controls or a reverse group.
- If there is insufficient time to complete this level of testing, group O red cells MUST be issued.
Case Study 2 – Positive or Negative?

A paediatric sample taken pre-operatively for elective surgery, from an 11 year old girl, was placed on the automated analyser in the transfusion laboratory. It was too small to allow complete testing.

The partial grouping results obtained from the analyser gave the D type as D negative. The sample was then tested manually. D typing results of +1 and +2 were obtained.

One unit of D positive red cells were issued and transfused.
Did BMS staff do the right thing?

A. No, the sample should have been rejected as ‘insufficient’, a new sample obtained and testing performed on the automated analyser before any blood was issued.

B. No, although the sample should have been accepted and tested manually the results obtained were equivocal and therefore D negative red cells should have been given until the RhD status was confirmed.

C. Yes, there is a constant shortage of RhD negative red cells, positive results were obtained therefore RhD positive red cells should have been issued in this case.
Recommendations:

**BCSH Guidelines for Compatibility Procedures in Blood Transfusion Laboratories:**
Where there is a discrepancy in grouping the patient should be treated as D negative until the D status is resolved.

**SHOT Annual Report 2010:**
It is important that the D type is determined by the most robust routine method available.

**UKTLC Recommended minimum standards for hospital transfusion laboratories:**
Recommend the use of 24/7 automation for ABO/D grouping.
A patient was brought to A+E late in the evening with a two day history of melaena, fatigue, jaundice and increased shortness of breath.

Her haemoglobin was 5.4g/dl and four units of blood were requested but the clinician was willing to wait for fully tested units.

The lone BMS on call was busy. He looked up the patient history and found a historic record of anti-c+E+S.
What should the BMS do next?

A. Get the sample on to the analyser for group and antibody screen and order some c-E-S blood from the local centre
B. Start crossmatching and hope to find some compatible units
C. Request advice from local support staff eg Haematologist, senior BMS
D. Request samples for despatch to the local RCI laboratory
What did happen?

The BMS phoned the ward to ask for two more samples for despatch to the blood service and informed them that there would be a delay in blood availability. He phoned the blood service to inform them that samples were being sent.

The reference lab asked the BMS to screen the sample and let them know the result.
What is your understanding of the RCI laboratory’s instruction to screen the sample?

A. If the antibodies are no longer detectable then ABO/D compatible units can be crossmatched at the hospital and compatible units issued.

B. We are busy and think the staff at the hospital should deal with this case without bothering us.

C. If the antibodies are no longer detectable let us know and we will provide you with antigen negative units which you can then crossmatch without the need for any further work. If the antibody screen is positive then contact us again for further instructions.
The doctor then phoned the BMS to inform him that the patient’s blood pressure was falling and to enquire ‘what the backup scenario was’. The BMS informed him that he could cross match some blood and issue the most compatible if that was required. The BMS completed the antibody screen and crossmatched the blood. The antibody screen was negative and all units were compatible. Four units of blood were issued.
Was this the right course of action?

A. No, the patient has red cell antibodies and transfusion must be delayed until antigen negative red cells are available and crossmatched.

B. Yes, if the patient is bleeding it is important to get red cells into them and worry about possible transfusion reactions later.

C. Before taking this course of action the BMS should have asked for advice either from the RCI laboratory or a Haematologist.
Opinion Poll:

How many of you feel you get good support from your local RCI laboratory?

How many of you have good clinical support ‘out of hours’?

How many of you have good technical support ‘out of hours’?
Take home messages:

- In an emergency issue group O red cells until minimum testing as per BCSH guidelines can be achieved.
- Use ALL the data available to you when authorising results/issuing components.
- Practice good communication.
- Ask for and use appropriate support – it’s tricky out there!
Final ATR case
A teenage girl requires 6 units of red cells during major orthopaedic surgery.
She is also given 2 units of MB-FFP
She develops urticaria, oxygen sats fall, and she becomes severely hypotensive
What is the likely reaction?
• A: TACO
• B: Anaphylaxis
• C: TRALI
• D: Any of these
Suspected anaphylaxis

- A precise definition is not important for emergency management and there is no universally agreed definition
- A severe, life-threatening, generalised or systemic hypersensitivity reaction
  - Characterised by rapidly developing life-threatening airway and/or breathing and/or circulation problems
  - Usually associated with skin and mucosal changes
Anaphylaxis

- First line treatment is adrenaline 0.5 mg IM for adults, 0.3 mg for children.
- IV only if administered where there is expertise.
- Second line antihistamine and hydrocortisone may shorten duration and prevent recurrence.
Which of these statements do you most agree with?

- A: Reactions are commoner with Methylene Blue rather than standard or SD FFP
- B: Reactions are less common with MB-FFP compared to standard or SD FFP
- C: I would refer this girl to an allergist for consideration of skin testing for potential allergens
- D: This may not be related to the transfusion
Reactions associated with MB-FFP

- The French haemovigilance organisation, AFSSAPS, has noted increased anaphylactic reactions to MB-FFP.
- This has not been noted in the UK, or in other European countries.
- However, in view of the French findings, SHOT will proactively monitor severe reactions to FFP in young people.
- Patients who experience severe reactions to MB-FFP should be referred to a clinical allergist or immunologist for assessment.
  - Some may react to similar dyes e.g. methyl violet.
ATRs and lab incidents: what resource do we most need to minimise the damage?

- A: Thorough understanding of red cell serological techniques
- B: The ability to communicate
- C: Access to NHSBT document MPD 1179
- D: Common sense
Thanks

• To all of you who have entered SHOT reports
• To the SHOT steering group and working expert group
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  – Janet Birchall
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