Managing patients who experience transfusion reactions
Serious Hazards of Transfusion scheme

- All cases in this talk are from SHOT
- If it were not for SHOT, the content of this talk would be substantially different!
  - What are the true risks of transfusion?
  - How effective are our strategies to manage ATR?
Have you ever managed patients who have experienced an adverse reaction to transfusion?

A. Yes, often
B. Yes, occasionally
C. No
How common are ATRs in the UK?

A. 1 in 30 units?
B. 1 in 100?
C. 1 in 1000?
D. 1 in 10,000?

- SHOT collects reports on moderate and severe ATRs.
- Incidence varies according to component type
- Are all cases reported?
Incidence per 10,000 units issued

- Red cells: 0.9
- Platelets: 3.1
- Plasma components: 0.8
Case History

- An patient with myelodysplasia has a 2 unit red cell transfusion as a day case
- History of complex red cell antibodies
- With the second unit, she complains of feeling unwell, with mild nausea and chills
- Her temperature rises from 37.8 to 39 C, BP and pulse both increase
- The transfusion is stopped and symptoms and signs improve within 30 minutes
What is this most likely to be?

A. A haemolytic transfusion reaction due to complex red cell antibodies

B. A haemolytic reaction due to incorrect component transfused

C. A febrile transfusion reaction

D. Bacterial contamination of the unit
Figure 4.2: Cumulative data for SHOT categories 1996/7-2013
n=13141

- Unclassifiable complications of transfusion
  - Post-transfusion purpura
  - Transfusion-transmitted infection
  - Transfusion-associated dyspnoea
  - Autologous
  - Acute transfusion reaction

- Transfusion-associated graft vs host disease
  - Aloimmunisation
  - Transfusion-associated circulatory overload
  - Transfusion-related acute lung injury
  - Haemolytic transfusion reaction

- Avoidable, delayed or undertransfusion
  - Anti-D immunoglobulin
  - Handling and storage errors
  - Incorrect blood component transfused

Pathological reactions which may not be preventable

Probably or possibly preventable by improved practice and monitoring

Adverse events caused by error
So this is most likely to be a non-haemolytic febrile reaction

BUT
Consider other causes
What clinical features suggest a patient is reacting adversely to a transfusion?

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, chills, rigors</td>
<td>Change in temperature</td>
</tr>
<tr>
<td>Dyspnoea, stridor</td>
<td>Hypoxia</td>
</tr>
<tr>
<td>Itch, rash, swelling of lips</td>
<td>Raised BP, pulse</td>
</tr>
<tr>
<td>Shock, collapse</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Nausea, general malaise</td>
<td>Raised venous pressure, pulmonary signs</td>
</tr>
<tr>
<td>Pain</td>
<td>Reduced urine output, change in urine colour</td>
</tr>
<tr>
<td>Feeling of impending doom</td>
<td>Change in conscious level</td>
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</tbody>
</table>
Patient exhibiting possible features of an acute transfusion reaction, which may include:
- Fever, chills, rigors, tachycardia, hyperventilation, 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

Yes

**SEVERE/LIFE-THREATENING**
- Call for urgent medical help
- Initiate resuscitation-ABC
- Is haemorrhage likely to be causing hypotension? If not, discontinue transfusion (do not discard implicated units)
- 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 associated components
- Perform appropriate investigations (see Table I)

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

No

**Inform medical staff**

**MODERATE**
- Temperature ≥ 38°C or rise ≥ 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

- If consistent with underlying condition or transfusion history consider continuation of transfusion at slower rate and appropriate symptomatic treatment

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

**Transfusion unrelated**
- Continue Transfusion

- Not consistent with condition or history
- Discontinue (do not discard implicated units)
- Perform appropriate investigations (see Table I)
Immediate management

- Recognise patient experiencing adverse reaction
- Stop transfusion, keep line open, retain component
- Airway, Breathing, Circulation and Bag, Band, Blood
- How severe is this reaction?
  - Minor - e.g. itch. Should you restart the transfusion?
  - More serious. Do not restart the transfusion. Establish most likely cause
Fever, chills and rigors during or soon after transfusion: possible causes

- Febrile non-haemolytic transfusion reaction
- Acute haemolytic reaction
- Bacterial contamination
- Underlying condition
Fever 1: Case history from SHOT

- Patient with haematuria being transfused with platelets
- 20 minutes into transfusion:
  - 2.2°C rise in temperature, vomiting, tachycardia, chest pain
- Hypoxia
- Rigors prevented BP measurement
- Urine positive for haemoglobin but patient has haematuria
Which investigations would you do?

A. Blood cultures of the patient, send the platelet unit for culture
B. Repeat group and antibody screen the patient
C. Both the above
D. Neither of the above
Culturing the platelet unit:

A. Perform culture in hospital lab, refer to blood service if positive result

B. Refer to blood service for culture

C. Perform culture locally but at the same time inform blood service
With a severe febrile reaction such as this, the most important step is to **contact the blood service**

- Any associated components can be withdrawn from issue
- Unit sampling and culture requires expertise
Patient with AML received a unit of apheresis platelets
Developed chills, nausea and feeling of impending doom
Recall: one other apheresis unit
- Transfused to young male with ALL
- Had moderate allergy-like symptoms
Patient with AML received a unit of apheresis platelets
Developed chills, nausea and feeling of impending doom
Recall: one other apheresis unit
  - Transfused to young male with ALL
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Packs sent to NBL
Both packs and donor showed Lancefield group G streptococcus
Febrile reactions are more commonly seen with red cell transfusions. The incidence has been reduced since universal leucodepletion. Less severe reactions can be treated with paracetamol or anti-inflammatory medication. In severe reactions, the most important differential diagnosis is transfusion-transmitted infection although very uncommon.
No reports in 2012 or 2013
Fever 2: SHOT 2012

- Patient receiving red cell transfusion
- Felt unwell with temperature rise of 2.8°C to 39.4°C
  - Rigors
  - Increased respiratory rate
  - Tachycardia
  - $O_2$ fell from 97% to 75%
What do you think this is?

A. Severe febrile transfusion reaction
B. Bacterial contamination
C. Severe haemolytic reaction
D. I don’t know!
ABO incompatibility

- Post-transfusion group not interpretable
- DAT positive
- Patient was group O pos, unit was A pos
- Failure of two person bedside check
- Both staff already competency assessed
A young female patient with a history of multiple transfusions
Admitted with menorrhagia and Hb 78g/L
Transfused 7 days earlier
Bilirubin and creatinine both raised
Known to have anti-s and anti-Fyb
DAT positive: no other antibodies found
Given 2 units negative for these antigens
Patient had rigors and difficulty breathing during the second unit
Reaction

- Admitted to ITU
- Creatinine rose
- Bilirubin already raised
- DAT still positive
- Found to have weak anti Jka-an antibody that can be difficult to identify on screening cells
- Thought to have an acute haemolytic reaction and also delayed haemolysis
Patient with myelodysplasia reacted 100 ml into a day case red cell transfusion

Electronic issue as no history of antibodies
- Negative antibody screen

Diarrhoea, vomiting, hypotension

Subsequently jaundiced

Some evidence of DIC
What is this likely to be?

A. Acute haemolytic reaction
B. Bacterial TTI
C. Delayed transfusion reaction
D. Febrile ATR
Patient with myelodysplasia reacted 100 mls into a day case red cell transfusion. Electronic issue as no history of antibodies. Negative antibody screen. Diarrhoea, vomiting, hypotension. Subsequently jaundiced. Some evidence of DIC. Anti-Wra found in pre- and post-transfusion samples (not present on commercial antibody screening panels). Donor Wra positive.
Wr<sup>a</sup> and anti- Wr<sup>a</sup> in the North of England 1996

- 54/5098 blood donors shown to have anti- Wr<sup>a</sup> (1 in 94)
- 88/1199 patient samples had anti-Wr<sup>a</sup> (1 in 13)
- 2/5253 blood donor specimens were Wr<sup>a</sup> positive (1 in 2626, 95% CI: 1 in 1136 to <1 in 10,000)
What do we learn from this?

A. Donors should be screened for Wr

B. Patients should be screened for anti-Wr

C. This is a small, but acceptable risk of electronic issue
Many reports in the HTR section are likely to be delayed haemolysis presenting as further transfusion need.

Be particularly careful with patients with sickle cell disease.

- Risk of hyperhaemolysis
Respiratory symptoms
Case from SHOT 2013

- 67 year old female with myelodysplasia
- Transfused 3 units as a day case
- Felt ill on her journey home and returned immediately to A and E
- Had respiratory arrest
Most likely cause?

A. Transfusion Related Acute Lung Injury (TRALI)
B. Allergic reaction
C. Transfusion Associated Circulatory Overload (TACO)
D. Unrelated to transfusion
Outcome

- Chest X Ray appearances consistent with left ventricular failure
- Probable TACO
- Given diuretics
- Patient made a full recovery
TACO

- Acute respiratory distress, tachycardia, hypertension, acute or worsening pulmonary oedema, evidence of positive fluid balance
  - At least 4 of the above features
  - Occurring within 6 hours of transfusion
- Tends to be seen in over 70s
- Almost certainly under-reported
  - Recent series of 8/247 transfusions in this age group (3%) Bartholomew and Watson, 2014
Age and gender distribution: national figures

3% of all those to the right of the line!!
Teenage boy with history of liver disease transfused with female apheresis platelets for an elective surgical procedure.

Developed hypoxia, hypotension and pyrexia within 30 minutes of transfusion. Hb increased from 8g/dl before procedure to 18 after.

Required cardio-respiratory support on ITU.

When ET tube inserted, developed fountain like pulmonary oedema.
30 mins post transfusion

supine 85/3.2
What is the most likely diagnosis?

A. TACO (Transfusion Associated Circulatory Overload)
B. Chest infection
C. Acute myocardial infarction
D. TRALI (Transfusion-Related Acute Lung Injury)
TRALI

- Serious complication of transfusion, almost always with plasma rich components
- Donor has antibody to recipient leucocytes
  - HLA or HNA
- Reduced incidence
  - Universal leucodepletion
  - Male donors for FFP and the plasma used to resuspend platelet pools
  - Female apheresis donors screened for HLA and HNA antibodies
- Dyspnoea, hypoxia (pyrexia) usually within 6 hours
- Commoner in certain groups of patients- “two-hit” hypothesis
LD marks the date when universal leukodepletion was introduced (during 1999). M marks the date (from September 2003) when National Health Service Blood and Transplant (NHSBT) introduced use of male donor plasma only for FFP and preferential use of male plasma for suspending pooled platelets. Hospital stocks of female FFP were not recalled.
# Features of TACO and TRALI

<table>
<thead>
<tr>
<th></th>
<th>TRALI</th>
<th>TACO</th>
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</thead>
<tbody>
<tr>
<td><strong>Type of component</strong></td>
<td>Usually plasma or platelets</td>
<td>Any</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>Often reduced</td>
<td>Often raised</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>Often raised</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Echo</strong></td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td><strong>Diuretics</strong></td>
<td>Worsen</td>
<td>Improve</td>
</tr>
<tr>
<td><strong>Fluid loading</strong></td>
<td>Improves</td>
<td>Worsens</td>
</tr>
</tbody>
</table>
Patient with PPH received a unit of FFP

Previously, 3 units red cells and 1 FFP transfused without problems

8 minutes into transfusion, she began to cough and had swollen eyes, lips and throat

Bronchospasm

Oxygen saturation dropped

Blood pressure unrecordable and briefly lost consciousness

Responded well to treatment
What was the reaction likely to be?

A. TRALI
B. TACO
C. Moderate allergic reaction
D. Anaphylaxis
What is the immediate management?

A. Call the haematologist
B. Hydrocortisone and antihistamine
C. Dopamine
D. Adrenaline
Anaphylaxis is characterised by rash and/or mucous membrane involvement followed rapidly by respiratory and/or circulatory distress.

A medical emergency.

Initial treatment is adrenaline: IM unless you are an anaesthetist or intensivist.

- Steroids and antihistamine may help reduce period of anaphylaxis and prevent recurrence.
Learning point

- Although anaphylaxis is rare, patients should only be transfused when and where there is the ability to recognise and manage a reaction.

Cases of anaphylaxis reported to SHOT since 2005

<table>
<thead>
<tr>
<th>Year of Report</th>
<th>Number of Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>24</td>
</tr>
<tr>
<td>2006</td>
<td>41</td>
</tr>
<tr>
<td>2007</td>
<td>27</td>
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<td>2010</td>
<td>34</td>
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<td>2011</td>
<td>33</td>
</tr>
<tr>
<td>2012</td>
<td>30</td>
</tr>
<tr>
<td>2013</td>
<td>30</td>
</tr>
</tbody>
</table>
Investigation of suspected anaphylaxis 1

- Serial Mast Cell Tryptase
  - Immediate
  - 1-3 hours
  - 24 hours plus for baseline
- Samples rarely taken correctly
- Rise and fall pattern in anaphylaxis
- Does not indicate causative agent
Investigation of suspected anaphylaxis 2

- Immunoglobulin A level plus IgA antibodies
- Patients who are IgA deficient said to be at increased risk of anaphylaxis
  - Evidence is weak
- A positive result in a patient with a history of severe allergic or anaphylactic reaction will guide future transfusion management
  - Standard components for emergency transfusion
  - Washed red cells, platelets in PAS
  - IgAD plasma is available for planned plasma transfusions
Management of patients who have reacted before

- A female patient with bone marrow failure and epistaxis has regular (appropriate) platelet transfusions
- With last two transfusions, she complained of itch
- Now has urticaria
How can you avoid future reactions?

A. Give HLA matched platelets
B. Give hydrocortisone premied
C. Give platelets washed and resuspended in PAS
D. Give antihistamine premied
Learning points

- 25% of women, and at least 10% of multitransfused male patients have HLA antibodies
- No evidence that reactions are reduced with HLA matched platelets
- Washed platelets/platelets in PAS do reduce reactions
- IV Hydrocortisone takes 8 hours to act!!
- Little evidence for or against antihistamine but if washed platelets do not work, worth trying
- Appropriate use underpins everything we do!
Internal reporting

- How well was the incident managed?
- Appropriately documented?
- Review investigations
- Is there a management plan for future transfusions in this patient?
- Was the transfusion appropriate?
- Does the incident need to be reported externally?
External reporting: the benefits of SHOT reporting are:

- Learn about unexpected or undesirable effects from transfusion
- Identifying trends in reactions and events, including effects of new components
- Identifying areas for improvement
- Informing transfusion policy