SHOT data 2009
Part 2

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SHOT Annual symposium
July 6th 2010
The Lowry, Manchester
Replica ‘Baby’
Museum of Science and Industry, Manchester
Deaths 2007-2009
where an event or reaction contributed to or was implicated in the death of a patient
Rate per 10,000 components issued
Major morbidity 2007-2009
Rate per 10 000 components issued
SHOT – All cases reviewed

1996-2009 n=6653

2009 n=1279
33% increase in ATR mainly due to increased number of febrile (193) or allergic (84) reactions
### ATR:
Incidence of reactions by component type

<table>
<thead>
<tr>
<th>Component</th>
<th>Febrile reactions, incidence per 100,000 units</th>
<th>Allergic or anaphylactic reactions, incidence per 100,000 units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red cells</td>
<td>7.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Platelets</td>
<td>7.5</td>
<td>20.3</td>
</tr>
<tr>
<td>Plasma</td>
<td>1.6</td>
<td>10.4</td>
</tr>
</tbody>
</table>
ATR: Reactions by component type

Key
- Unclassified
- Mixed/Hypotensive
- Anaphylactic
- Allergic
- Febrile

Each star represents a case of:
- Platelets in suspension medium
- HLA matched platelets
- Solvent Detergent plasma
- Methylene Blue plasma
ATR

• Mortality
  1 death where transfusion possibly contributed

• Major morbidity
  27 cases; 17 anaphylactic

• Anaphylactic reactions

Learning points:

a) manage anaphylaxis according to UK resuscitation council guidelines: www.resus.org.uk/pages/reaction.pdf

b) transfuse patients only when there is a member of staff present who is trained in the management of anaphylaxis and has access to appropriate treatment, particularly IM adrenaline
**Median time to onset of reaction 45 mins (range 1 - 660)**

**Ensure careful observation throughout the transfusion process - SHOT main recommendation 2008 and in 2009 BCSH guideline on blood administration**

[www.bcshguidelines.com](http://www.bcshguidelines.com)

**Investigations**

101 cases (44 moderate and 6 severe reactions) were not investigated

- **Consider possibility of bacterial contamination**
  - Culture unit and inform blood centre
  - If not TTI report as ATR
  - Revised protocol for hospital sampling under development by NHSBT
  - BCSH guidelines on ATR in preparation

- **HLA HNA and HPA studies should only be performed in selected cases after discussion with a blood service consultant**

- **1 ATR case related to IgA deficiency in last 5 years – check IgA**
  - ?common variable immunodeficiency; ?relevance of IgA testing

- **MCT aids in the diagnosis of anaphylaxis; consider referral of pts with anaphylaxis to an allergy clinic**
Haemolytic transfusion reactions (HTR)

AHTR - no deaths, 3 cases major morbidity
DHTR - 2 deaths from underlying disease, 5 major morbidity
Interval between administration of implicated component and signs or symptoms of DHTR
HTR: main findings

- Kidd (Jk) (18/39) and Rh (19/39) alloantibodies most common

- Antibodies not usually associated with HTR identified in several patients following AHTRs e.g. Knops, Bg and weak C\textsuperscript{w}
  - Does not necessarily mean it is the cause of the reaction
  - Consider other causes – bacterial contamination

- Reactions frequently reported in patients with sickle cell disease – these patients are vulnerable to HTR
  - Higher incidence of sensitisation
  - Prone to episodes of hyperhaemolysis – can mask HTR
  - Often move between different treatment centres

- In 3 cases ab specificity was identified in eluate but not in plasma
  Use of eluates in 62% (24/39)
HTR: previous recommendations relevant to 2009 report

2008: Actively seek transfusion history and antibody history for previously unknown patients with sickle cell disease
www.sicklecellsociety.org/pdf/CareBook.pdf

2008: National register of patients with antibodies
Action: Newly formed IT subgroup of NBTC

2005: Appropriate investigation of HTR and ideally refer to a reference laboratory

2005: Reference labs - ensure that ix of DHTRs includes eluate when the DAT is +ve

2001/2: Antibody cards (or similar info) + patient info leaflet
Labs to be informed when these pts admitted

BCSH recommendation (2004)
Action: CMO’s NBTC and equivalents in Scotland, W + NI
TRALI: Main source of HLA/HNA antibodies is donor plasma

A donor with a history of transfusion (excluded since April 2004)

A female donor with history of pregnancy - antibodies in 10-15%
TRALI by year of transfusion
1996-2009 (n=257)
TRALI: cases with concordant donor antibody in FFP or platelet components 2003-2009

Reinforces absolute requirement for provision of 100% male plasma for FFP and for suspension of platelet pools
TRALI: Risks in cases with concordant donor antibody 2009

<table>
<thead>
<tr>
<th>Component</th>
<th>Risk of TRALI</th>
</tr>
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<tbody>
<tr>
<td>Female FFP</td>
<td>1: 6884</td>
</tr>
<tr>
<td>Male FFP</td>
<td>0</td>
</tr>
<tr>
<td>Platelets</td>
<td>1: 88,771</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>1: 121,555</td>
</tr>
<tr>
<td>RBC</td>
<td>1: 736,384</td>
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Transfusion-associated circulatory overload (TACO)

- 34 cases (18 last year)
- 4 deaths (2 probably, 2 possibly)
- 9 transferred to ITU, further 3 in ITU, 2 needed CPAP
- TACO relatively common especially in elderly (can occur after ≤1 unit of RBC) and those with additional risk factors: cardiac failure, renal impairment, hypoalbuminaemia, fluid overload
- Can occur after 6 hours and up to 24 hrs after tx (5 cases)

Learning points
- TACO often potentially avoidable. Consider a) whether transfusion appropriate; b) risk factors for TACO; c) diuretic
  
  *not addressed in 2009 BCSH guidelines on blood administration*
- Monitor patient during and after transfusion; monitor rate of transfusion and fluid balance
# Thrombotic thrombocytopenic purpura (TTP): 2 case studies

## Case 2: Highly likely TRALI
- Patient with TTP given 4 units of FFP prior to transfer to another hospital
- Respiratory distress 2-6 hours later in ambulance:
  - Increasingly hypoxic and hypotensive: chest “bubbly, CXR ‘bilateral whiteout’
  - Cardio-respiratory arrest, resuscitated, ventilation for 2 days. Full recovery.
- One female donor had multiple HLA class I concordant abs

## Case 25: Probable TACO
- Woman 65 yrs diagnosed to have TTP
- MB-FFP 12 units (~2640mL) daily for 3 days. No plasma exchange
- Became SOB and wheezy
- Hypertensive, positive fluid balance. Improved following furosemide
Pathophysiology of TTP

Normal Subject
- Cleaved unusually large multimers of von Willebrand factor

Patient with Thrombotic Thrombocytopenic Purpura
- Adhesion and aggregation of platelets
- Uncleaved unusually large multimers of von Willebrand factor

ADAMTS 13
- Binding site

Endothelial cell
- Secretion of multimers from Weibel–Palade body
Peripheral blood film from patient with TTP showing fragmented red cells and thrombocytopenia
Survival of patients with Thrombotic Thrombocytopenic Purpura

Rock GA et al NEJM 1991:325:393-397
Methylene Blue Photoinactivated Plasma vs Fresh Frozen Plasma in TTP: A Multicentre Prospective Cohort Study

<table>
<thead>
<tr>
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<th>MB-FFP N=38</th>
<th>FFP N=25</th>
</tr>
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<tbody>
<tr>
<td>No of PEX (P=0.004)</td>
<td>16 +/-13</td>
<td>9 +/-7</td>
</tr>
<tr>
<td>Volume of plasma to remission (mls/Kg) (P=0.02)</td>
<td>763 +/-678</td>
<td>413 +/-326</td>
</tr>
<tr>
<td>Recurrences on treatment (p=0.02)</td>
<td>21/38</td>
<td>6/25</td>
</tr>
</tbody>
</table>

• MB-FFP
  • reduced remission rates by day 8 (OR 5.1 95% CI 1.6-15.9)
  • Increased recurrence rate (OR 4.2 95% CI 1.3-13.5)

_del Río-Garma BJH 2008_
TTP

- DH recommended SD-FFP for plasma exchange 2006

- **New recommendation (TACO)**
  Patients with TTP should have plasma exchange at presentation (and ideally within 24 hours of presentation) with plasma infusion alone prior to transfer to a unit or hospital that can offer plasma exchange and appropriate management.

**Action:** consultant haematologists and SHAs
Transfusion associated dyspnoea (TAD)

- 4 cases reported in 2009, with no mortality or major morbidity
- TAD is a heterogenous entity and cases likely to have varying physiological mechanisms.
2 cases demonstrating diagnostic difficulty

TRALI Case 1
- Rectal ca, cardiac failure
- 3 units RBC OA
- 6 hrs later during 3rd unit, chills, SOB, JVP raised
- Died one hr later
- PM: severe pulmonary oedema, no MI or PE; ↑ neutrophils in interstitial fluid
- 3rd unit: female donor had multiple HLA class I and class II abs concordant abs
- Blood pack: enterobacter sp, pantoea sp and enterococcus faecalis – likely contaminants

Probable TRALI – cardiac failure may have also been contributory

TACO Case 5
- 62 yr old with AML became acutely SOB after 1 unit of RBC over 2 hrs and 1 pool plts over 30 mins
- 4 kg weight gain over previous few days and positive fluid balance >3L in 24 hrs prior to tx
- Responded to furosemide
- Developed fever and was restarted on tazocin and vancomycin following positive cultures
- Appeared highly likely TACO but based on ISBT criteria classified as probable TACO

Coexistent ARDS and probable TACO initially reported as TRALI
SHOT main recommendation: pulmonary complications of transfusion

• Always additional cases reported affecting respiratory system and likely to be transfusion-related which are hard to categorise within current definitions
• Cases which occur after the 6 hour cut-off not reported to EU
• True rate of pulmonary complications – high morbidity and mortality
• New SHOT database collects all pulmonary complications
• For haemovigilance to identify new patterns of complications, important to include atypical data

Recommendation

All pulmonary complications of transfusion should be recorded and reported to haemovigilance systems even if they do not fully fit existing criteria. Research should be initiated to evaluate the current inclusion and exclusion criteria, especially for TRALI and TACO. A register of possibly implicated donors should be kept by the blood services.

Action: SHOT and its reporters, UK blood services and their R&D directorates
Post-transfusion purpura

Further information about PTP is available in Practical Transfusion Medicine
Transfusion-associated graft-versus-host disease

- In the last 7 years 596 cases of pts receiving non-irradiated components
- 300,000 irradiated components were issued from UKBS 2008-2009
- Irradiation is a proven, effective intervention to prevent TA-GvHD
Transfusion-transmitted infection

- 39 suspected TTIs reported in 2009
- 3 reports bacterial TTI, from 2 incidents
- 4 undetermined (2 bacterial, 1 HIV) and 3 pending complete investigation

Confirmed incidents: 3 cases of bacterial TTI
- Expired apheresis pack was contaminated with *strep pneumoninae*: associated units had been transfused to an adult with AML and 3 neonatal units administered to a baby. Both pts suffered reactions, including a fever of 39.8 in the adult and 40.5 in the baby
- Elderly patient receiving palliative care for ca rectum and liver cirrhosis received RBCs contaminated with *Pseudomonas koreensis*. ~2hrs into transfusion, hypotension, pyrexia of 39.6, abdo pain and vomitiong; died later the same day of transfusion-transmitted sepsis.

Most likely source environmental contamination: cold storage room or processing area at blood service or hospital

MHRA’s ‘Orange Guide’ does not cover acceptable levels of cleanliness within cold storage areas. Cleaning protocols for such areas should be reviewed regularly and compliance should be audited
Bacterial TTI incidents by year of report and type of unit transfused (n=40) (Scotland from 10/98)

If moderate or severe pyrexia following blood component transfusion – suspect bacterial sepsis and treated appropriately.
Viral and parasitic TTI incidents, by year of report and infection type (n=22) (Scotland from 10/98)

Current estimated risks of transmission:
HBV 1.09/million donations, HCV 0.01, HIV 0.19, HTLV-1 0.04
Autologous transfusion

14 cases in 2009

- 6 intraoperative cell salvage
  - 3 hypotensive reaction related to reinfusion of intraoperatively cell-salvaged blood
- Common factors in 2 cases:
  - Use of ACD as an anticoagulant
  - Use of a leucodepletion filter (LDF) during reinfusion of autologous washed cells
- 8 postoperative cell salvage
  - 5 related to postoperative, unwashed autologous transfusion
Autologous transfusion

- Other clinical issues
  - Use of bedside LDF, known to cause hypotension with allogeneic blood
  - These pts may be hypovolaemic and therefore more susceptible to the effect of reinfused vasoactive cytokines
  - All pts had transient but clinically significant hypotension – no long term sequelae

- SHOT is continuing to collect all cases related to autologous transfusion, including those collected in collaboration with the UK Cell Salvage Action Group
Paediatric cases

• 110 cases (9% of all SHOT reports in 2009) related to pts under 18; 34 cases 1 year
• 58% (64) reports (compared with 42% of adult reports) error related: IBCT, handling and storage, inappropriate and unnecessary transfusion
• ‘Paediatric–related’:
  • errors relating to dose and rate of transfusion for small children
  • correct use of ‘flying squad’ red cells
  • Special requirements frequently missed (25 cases) – indications for irradiation and MB-FFP for children <16 yrs
• ATR: striking increase in number of paediatric ATRs reported particularly from platelets: (7% of all ATR but 16% of platelet ATR)
Number of paediatric cases in each reporting category
Paediatric cases: new recommendations

New recommendations from this year

- The correct prescription of paediatric transfusions is vital and an area of recurrent errors. Local consideration should be given to the design of paediatric prescription charts in order to facilitate the correct prescription of both blood component volumes/rates and clinical special requirements.

  **Action: HTC, HTT, pharmacists**

- Nursing staff involved in paediatric transfusion must be sufficiently skilled and competent in the use of pumps/blood infusion devices, appropriate transfusion volumes/rates, and the need for special requirements in order to reduce these types of errors. These aspects should be included in their transfusion training as required by the BCSH (2009) guidelines on the administration of blood components.\(^9\)

  **Action: HTC, HTT, RCN, RCM, NMC**
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