Bacterial Screening of NHSBT Platelet Components

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NHS Blood and Transplant
Overview

• Impact of bacterial transmission
• Why PCs are the greatest risk
• NHSBT Strategy
• Impact diversion and improved donor arm disinfection
• NHSBT protocol Bacterial Screening
• NHSBT results Bacterial Screening
• Added value Bacterial Screening
• Future development
# Bacterial Mortality Worldwide

<table>
<thead>
<tr>
<th>Country</th>
<th>Period</th>
<th>Deaths</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>2005-2015</td>
<td>38</td>
<td>(FDA)</td>
</tr>
<tr>
<td>France</td>
<td>1994-2015</td>
<td>36</td>
<td>(Haemovigilance)</td>
</tr>
<tr>
<td>Germany</td>
<td>1997-2014</td>
<td>14</td>
<td>(Haemovigilance)</td>
</tr>
<tr>
<td>U.K.</td>
<td>1994</td>
<td>3</td>
<td>(Pre-SHOT)</td>
</tr>
<tr>
<td>U.K.</td>
<td>1996-2016</td>
<td>11</td>
<td>(SHOT)</td>
</tr>
</tbody>
</table>
Platelet Components Are The Greatest Risk!

- USA: (FDA) 2005 – 2015 platelet components comprised 87% (33/38) bacterial fatalities
- UK: (SHOT) 1996 – 2016 platelet components comprised 84% (37/44) cases
Klebsiella oxytoca
NHSBT Strategy

- Improved donor arm disinfection
- Diversion
- Bacterial Screening
Interventions Introduced

• Improved Donor Arm Disinfection – implemented nationally 2007
• Diversion – implemented nationally 2003
• In combination 77% reduction in contamination

Post Implementation Improved Donor Arm Disinfection and Diversion (2006 – 2010)

- 7 contamination incidents in PC
- 10 patients affected
- 3 deaths
- 5 near misses
NHSBT
Bacterial Screening
Bacterial Screening of Platelet Components in NHSBT

- NHSBT Board Meeting in January 2010
- Decision was made to implement bacterial screening within 12 months
- February 2011 rolled out
- July 2011 all components screened
BacT/ALERT System
Bacterial Screening Laboratory
Bacterial Screening Laboratory
Bacterial Screening Laboratory
NHSBT Test Protocol
(1 test, Extension Shelf Life to 7 Days)

1. Platelet components held for > 36hrs – 48hrs after collection
2. Platelet components sampled and tested
3. Held for 6hrs
4. Released with a 7 day shelf life
5. Monitored for the component shelf life
6. Positives recalled
What Happened?
Quarterly Bacterial Screening Rates (February 2011 - Sept 2017)
# Initial Reactive and Confirmed Positive Rates (Cumulative Feb 2011 – Sept 2017)

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Initial Reactive Rate</th>
<th>Confirmed Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apheresis*</td>
<td>1,285,959</td>
<td>0.33%</td>
<td>0.02%</td>
</tr>
<tr>
<td>Pooled*</td>
<td>530,804</td>
<td>0.25%</td>
<td>0.07%</td>
</tr>
<tr>
<td>Total</td>
<td>1,816,763</td>
<td>0.31%</td>
<td>0.04%</td>
</tr>
</tbody>
</table>

*Apheresis platelets screened from Feb 2011
*Pooled platelets screened from May 2011
## Initial Screen: Bottle Reactivity

(February 2011 – Sept 2017)

<table>
<thead>
<tr>
<th>Bottle Type</th>
<th>Initial Reactive</th>
<th>False Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic</td>
<td>73.8%</td>
<td>77.9%</td>
</tr>
<tr>
<td>Aerobic</td>
<td>21.3%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Both</td>
<td>4.8%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>
Confirmed Positives - Bottle Type (February 2011 – Sept 2017)

- Anaerobic bottle 65%
- Aerobic bottle 7%
- Both bottles 28%
Confirmed Positives (February 2011 – Sept 2017)

- 666 confirmed
- 640 Gram positives
- 26 Gram negatives
Confirmed Organisms
(February 2011 – Sept 2017)

Gram Positives (n=640):
- Propionibacterium spp. = 346
- Staphylococcus spp. = 163
- Streptococcus spp. = 105
- Gemella spp. = 6
- Listeria monocytogenes = 4
- Corynebacterium spp. = 3
- Enterococcus spp. = 3
- Lactobacillus casei = 2
- Bacillus cereus = 2
- Granulicatella adaciens = 2
- Lactococcus lactis = 1
- Peptostreptococcus micros = 1
- Finegoldia magna = 1
- Misc. Gram Positive bacilli = 1

Gram Negatives (n=26):
- Escherichia coli = 9
- Serratia marcescens = 5
- Klebsiella spp. = 5
- Enterobacter spp = 2
- Pseudomonas aeruginosa = 1
- Haemophilus aphrophilus = 1
- Bacteroides vulgatus = 1
- Proteus mirabilis = 1
- Campylobacter lari = 1
### Confirmed Positive Gram Positive ‘Pathogenic’ Organisms (Feb 2011 – Sept 2017)

<table>
<thead>
<tr>
<th>Organisms</th>
<th>n</th>
<th>Detection Time Range (hours)</th>
<th>Total Contaminated Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptococcus dysgalactiae (Group G/C)</strong></td>
<td>24</td>
<td>2-19</td>
<td>32</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>17</td>
<td>2-21</td>
<td>21</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>12</td>
<td>10-13</td>
<td>16</td>
</tr>
<tr>
<td><strong>Streptococcus agalactiae (Group B)</strong></td>
<td>6</td>
<td>6-16</td>
<td>5</td>
</tr>
<tr>
<td><strong>Listeria monocytogenes</strong></td>
<td>4</td>
<td>14-20</td>
<td>5</td>
</tr>
<tr>
<td><strong>Bacillus cereus</strong></td>
<td>2</td>
<td>11-14</td>
<td>2</td>
</tr>
</tbody>
</table>

Total cases with pathogenic organisms: 65  
Total number of contaminated components: 81
Confirmed Positive Gram Negative ‘Pathogenic’ Organisms (Feb 2011- Sept 2017)

<table>
<thead>
<tr>
<th>Organisms</th>
<th>n</th>
<th>Detection Time Range (hours)</th>
<th>Total Contaminated Components</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em></td>
<td>9</td>
<td>3-14</td>
<td>19</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>5</td>
<td>3-13</td>
<td>8</td>
</tr>
<tr>
<td><em>Klebsiella oxytoca</em></td>
<td>3</td>
<td>3-10</td>
<td>4</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>2</td>
<td>4-11</td>
<td>3</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>1</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td><em>Campylobacter lari</em></td>
<td>1</td>
<td>32</td>
<td>1</td>
</tr>
</tbody>
</table>

Total cases with pathogenic organisms: 22
Total number of contaminated components: 37
### Number of Splits Contaminated in Confirmed Positive Apheresis Donations (Feb 2011 – Sept 2017)

<table>
<thead>
<tr>
<th>Splits per donation</th>
<th>Total number of splits positive per investigation</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>47.9% (69)</td>
<td></td>
<td>52.1% (75)</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>50% (16)</td>
<td>18.8% (6)</td>
<td>31.2% (10)</td>
<td></td>
</tr>
</tbody>
</table>

NB: when all components returned for confirmatory/reference testing
Near Misses and Transmissions
Transmissions and Near Misses

• 1 transmission: 1 x *Staphylococcus aureus*

• 4 near misses: 3 x *S. aureus*
  1 x *Serratia marcescens*
Near Miss 1: 2013

- Apheresis platelet donation (2 splits)
- Large clumps reported in pack 2 by Hospital A
- Pack 1 issued to Hospital B but not transfused. No clumps present
- Both units received by NBL
Near Miss 1: 2013 (cont’d)

- No clumps visible in pack 2, but were present in pack 1
- BacT/ALERT cultures for both units positive in 3.8hr
- *Staphylococcus aureus* isolated
- Investigation of donor found *S. aureus* colonisation
- Strain typing of PC and donor isolates were indistinguishable
Near Miss 3
BacT/ALERT Culture Bottles
Near Miss 4: 2015

- Apheresis unit – 2 splits
- Clumps observed in split 1 by SHU
- Packs and BacT/ALERT screening bottles sent to NBL
Near Miss 4: 2015

Pack 1

Pack 2
Near Miss 4: 2015 (cont’d)

- Gram from pack 1 – Gram negative rods
- Gram from pack 2 – negative
- Clotted pack 1 – positive on BacT/ALERT 3.7h
- Unclotted pack 2 – negative on BacT/ALERT
- *S. marcescens* identified from pack 1
Near Miss 4: 2015

Inoculated  Uninoculated
Near Miss 4: 2015 (cont’d)

• BacT/ALERT bottles – Gram stain negative (both packs)

• BacT/ALERT bottles subcultured into new bottles – negative

• Screening bottles inoculated *S. marcescens* – positive
Near Miss 4: Conclusion

- Not a BacT/ALERT failure
- Insufficient bacteria at sampling time?
- Contamination post screening?
Growth Kinetics of *S. marcescens* in Platelets Suspended in Plasma

**Graph:**
- **X-axis:** Time (Hours)
- **Y-axis:** Bacterial Concentration (cfu/ml)
- The graph shows the bacterial concentration over time, with a peak at around 48 hours followed by a decrease and a plateau, indicating growth kinetics.
Confirmed Transfusion-Transmitted Infection (TTI) 2015

• Pooled platelet unit transfused into AML patient
• After 15 mins, the patient became agitated and suffered rigors, tachycardia and pyrexia
  – Temperature rose to 38.7°C, then 40°C overnight
• Patient cultures grew *Staphylococcus aureus*
Confirmed TTI: 2015 (cont’d)

- Platelet unit received by NBL
- Unit was leaking through open port, sealed with a capped needle
- Remaining contents (~3ml) appeared ‘cloudy’
- Gram stain showed heavy contamination with GPC
- BacT/ALERT cultures positive in 3.8h
Confirmed TTI: 2015 (cont’d)

- *S. aureus* isolated, strain type matched the patient isolate
- All 4 associated red cells units were cultured by NBL and remained negative after 7 days incubation
- 2/4 Donors investigated – both had *S. aureus* in multiple sites
- Strain typing of 1st donor isolates showed a distinct strain (no match)
- Strain typing of 2nd donor showed closely-related Spa type and matching DNA fingerprint
Bacterial Screening: Added Value
Donor Healthcare Benefits

Bacterial Screening

• *Streptococcus bovis* (n=4): donor’s colonic polyps

• *Streptococcus constellatus* (n=3) and *P. micros*: dental

McDonald, C. et.al., Transfusion, 2013,53:2117-2119

Lee, CK. et.al., Transfusion, 2013,53:2205-2208
Bacterial Screening Provides Insight into Possible Source of Contamination

• Pseudomonas spp. – poor hygiene facilities
• Staphylococcus spp. – inadequate donor arm disinfection
Future
BacT/ALERT Virtuo
Virtuo Advantages

• Superior performance to BacT/Alert 3D
  – Faster detection times
  – Potentially lower false positive rates
  – Automated loading and unloading
NHSBT Screening
(February 2011 to March 2017)

• 1 transmission in >1.8million PC screened (S.aureus)

• 4 near misses (3 S. aureus and S. marcescens)

• False negative rate 1 in 360,000 (0.0003%)

• 1 CP in 6015 TE platelets screened (S. pneumoniae)
Success NHSBT
Bacterial Screening

• Delayed sampling
• High volume tested (5-7%)
• Screening of apheresis splits
• Use of a two bottle system
Conclusion

Bacterial Screening within NHSBT has proven to be extremely successful risk reduction intervention!
Bacterial Screening of Platelet Components by National Health Service Blood and Transplant, an Effective Risk Reduction Measure

C. McDonald, J. Allen, et al.,

Transfusion 2017;57;1122-1131
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