Investigations of Suspected Transfusion Reactions by Blood Collection Establishments

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Medical Director
American Red Cross
East Division Blood Services
TYPEFACE DESIGNED
FOR DOCTORS

A B C D E

F G H I J

K L M N O

P Q R S T

U V W X Y

Z
Disclosures

- I have no financial disclosures
- I will not discuss any off label use and/or investigational use in my presentation
Transfusion Reactions

Objectives:

- Recognize the initial signs and symptoms of a transfusion reaction
- Understand the basic work up for a transfusion reaction
- Understand the importance of reporting a suspected transfusion reaction to the Blood Collection Establishment
History of Blood Transfusions

- **1667**
  - Lamb-to-human blood transfusion

- **1816**
  - 1\textsuperscript{st} successful human-to-human transfusion

- **1900**
  - *Discovery of the first blood groups (ABO)*

- **1907**
  - Pre-transfusion cross match
History of Blood Transfusions

- **1930s – 1950s**
  - Blood banks
  - Blood fractionation
  - Plastic blood bags
- **1960s**
  - AABB publishes *Transfusion*
- **1970s**
  - Hepatitis B testing
- **1980s**
  - HIV testing
- **1990s**
  - Hepatitis C testing
- **2000s**
  - “Zero risk” blood (NAT testing)
“Zero Risk” Blood Transfusion-Transmitted Infections

Risk per Unit

1:100

1:1,000

1:10,000

1:100,000

1:1,000,000


Revised Donor Deferral Criteria

HBsAg Screening

HIV Ab Screening

HCV Ab Screening

p24 Ag Testing

HCV and HIV NAT

WNV NAT

T cruzi Ab Screening

HBV NAT

NANB Hepatitis Surrogate Testing

vCJD Deferral Criteria

Perkins et al. Transfusion 2010;50:2080
Transfusion Reactions

- AABB Technical Manual, 19th Edition:
  - Greatest risk of morbidity and mortality is from non-infectious complications of blood transfusions
  - Most commonly reported causes of transfusion-related mortality:
    - Transfusion-related acute lung injury
    - Transfusion-associated circulatory overload
## Transfusion-Associated Fatalities, FY2012-FY2016

<table>
<thead>
<tr>
<th>COMPLICATIONS</th>
<th>FY2012</th>
<th>FY2013</th>
<th>FY2014</th>
<th>FY2015</th>
<th>FY2016</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>5</td>
<td>11 (6%)</td>
</tr>
<tr>
<td>Contamination</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>19 (10%)</td>
</tr>
<tr>
<td>HTR (ABO)</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>14 (8%)</td>
</tr>
<tr>
<td>HTR (non-ABO)</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>19 (10%)</td>
</tr>
<tr>
<td>Hypotensive Reaction</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>TACO</td>
<td>8</td>
<td>13</td>
<td>5</td>
<td>11</td>
<td>19</td>
<td>56 (30%)</td>
</tr>
<tr>
<td>TRALI</td>
<td>17</td>
<td>14</td>
<td>13</td>
<td>12</td>
<td>8</td>
<td>64 (34%)</td>
</tr>
</tbody>
</table>
Transfusion Reactions

- Recognizing signs and symptoms of adverse reactions - with timely lab evaluation - is essential due to the potentially life-threatening nature of acute transfusion reactions

- Assume all reactions are hemolytic until proven otherwise
## Transfusion Reactions

<table>
<thead>
<tr>
<th></th>
<th>Immune</th>
<th>Non-immune</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td>AHTR TRALI*</td>
<td>TACO Septic Hypotensive Non-immune hemolysis Air embolism</td>
</tr>
<tr>
<td>During or &lt; 24 hours</td>
<td>Allergic FNH</td>
<td></td>
</tr>
<tr>
<td><strong>Delayed</strong></td>
<td>DHTR/DSTR TA-GVHD PTP TRALI*</td>
<td>Infection (TTI) Iron Overload</td>
</tr>
<tr>
<td>&gt; 24 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Symptoms?

- Fever, chills/rigors
  - AHTR
  - FNH
  - Septic
  - TRALI

- Itching, rash/hives
  - AHTR
  - Allergic reaction
  - Anaphylaxis

- Respiratory distress
  - AHTR
  - TRALI
  - TACO
  - Anaphylaxis

- Shock
  - AHTR
  - Sepsis
  - Anaphylaxis
Basics

- **Stop the transfusion!!!**
- Treat symptoms
  - Keep the line open
  - Monitor vital signs and symptoms
- Report the reaction to the physician, transfusion service, and blood center
- Collect appropriate specimens and send to laboratory
  - Return blood product bag with administration tubing set, all attached bags to Blood Bank
Initial Laboratory Evaluation

- Blood Bank
  - Immediate visual checks for hemolysis
  - Clerical check
  - ABO/Rh of patient
  - Direct antiglobulin test (DAT)
  - Examine blood bag, administration set, IV fluid bags
Initial Laboratory Evaluation

- Immediate visual check for hemolysis
  - Can detect free hemoglobin with lysis of as little as 5-10cc red cells
Direct Antiglobulin Test

Antigen

Erythrocyte

In vivo antibody coating of erythrocytes

Anti-IgG AHG reagent added after erythrocytes are washed

AHG reagent causes IgG-coated erythrocytes to agglutinate

Indirect Antiglobulin Test

Antibodies in serum

Reagent erythrocyte

http://crashingpatient.com/wp-content/images/part1/coombs.jpg
Direct Antiglobulin Test

- Compare to pre-transfusion DAT:
  - Positive DAT
    - Change from baseline?
    - Antibody coated RBCs
  - Negative DAT
    - Non-immune mediated hemolysis
    - Transfused cells already destroyed
Acute Hemolytic Transfusion Reaction

- Acute hemolysis of transfused red cells due to presence of preformed antibody
- Usually due to ABO incompatible RBCs
- Majority due to clerical error:
  - *Misidentification of patient/sample*
    - Phlebotomy
    - Blood bank
    - Transfusion administration
AHTR

- Usually occurs *early* in transfusion
- *5 – 10 ml*
- Severity related to amount of blood transfused: value of early recognition/stopping transfusion!
  - Fatality rate 15-20%
  - AHTR rate 1:76,000
  - Fatal AHTR 1:1,800,000
Febrile Non-Hemolytic Reaction

- 0.1 – 1% or all transfusions
  - 1° C or greater temp increase within 4 hours
  - **Must rule out:**
    - AHTR
      - Evidence of hemolysis
    - Septic TR
      - Higher fever, systemic symptoms
    - TRALI
      - Respiratory symptoms
Allergic Reaction

- 1 – 3% or transfusions
  - Usually plasma or platelet products
- Symptoms:
  - Pruritis/hives
  - Localized or widespread
  - Angioedema
- If effective in relieving symptoms, restart component slowly
Anaphylactic Reaction

- 1:20,000 – 1:50,000
- Hypersensitive reaction to allergens in donor plasma
  - IgA deficient recipient with anti-IgA antibodies
  - Haptoglobin (and other plasma proteins) deficiency
- Symptoms:
  - Respiratory distress, laryngeal edema
  - Hypotension/shock
- Order products from IgA-deficient donor
- Wash products
# Reporting Form

## Section I: Clinical Information

<table>
<thead>
<tr>
<th>Recipient ID (patient #):</th>
<th>Age or DOB:</th>
<th>Gender:</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
</table>

**Primary diagnoses:**

<table>
<thead>
<tr>
<th>Attending physician:</th>
<th>Phone:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Transfusion service medical director:</th>
<th>Phone:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Contact for additional information:</th>
<th>Phone:</th>
</tr>
</thead>
</table>

**Date and time evidence of reaction began:**

**Fatality?**

- [ ] No
- [ ] Yes

If yes, will autopsy be performed?  

**Transfusion fatalities must be investigated urgently and are reportable to the Food and Drug Administration (FDA) by the transfusion service.**

### Which of the following developed during or within 6 hours following transfusion? (Note: The signs/symptoms of a septic reaction may be delayed for as long as 24 hours post transfusion). Check all that apply:

- [ ] Fever (≥39°C or ≥2°C rise)
- [ ] Hypoxemia (PaO₂<60, O₂ sat. <90%)
- [ ] Tachycardia (>120/min or >40/min rise)
- [ ] Rapid breathing (>28/min)
- [ ] Rise in systolic BP of >30 mmHg
- [ ] Drop in systolic BP of >30 mmHg
- [ ] Hematuria
- [ ] Hemoglobinuria
- [ ] Nausea or vomiting
- [ ] Bronchospasm/wheezing
- [ ] Jugular venous distension
- [ ] Pulmonary edema
- [ ] Rigors
- [ ] Abdominal pain
- [ ] Lumbar pain
- [ ] Chest pain
- [ ] Cardiac arrhythmia
- [ ] Other:

**Describe reaction in more detail:**

______________________________
### Section II: Transfusion History

Did the patient receive any non-Red Cross-provided products?  
[ ] No  [ ] Yes

Did the Red Cross perform the compatibility testing of record?  
[ ] No  [ ] Yes

#### List transfusions of Red Cross-provided products that are suspected to have been involved with the reaction.

<table>
<thead>
<tr>
<th>Unit number</th>
<th>Product name</th>
<th>Transfusion</th>
<th>Volume transfused</th>
<th>Residual product available</th>
<th><em>Unit Involved</em></th>
<th>Cleared</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Unit involvement recorded by:

(Identity/date)
Reporting Form

Section II: Transfusion History (continued)

<table>
<thead>
<tr>
<th>Previous transfusion history in this patient (summarize, including types of products and nature of prior reactions):</th>
</tr>
</thead>
</table>

Was a post-transfusion chest X-ray performed?  
☐ No  ☑ Yes  
If yes, please attach copy of radiology report.  ☑ Yes  ☐ No  
Result: ____________________________________________

Summary of treatment, response, and patient status at the time of this report:  ______________________________
______________________________________________________________________________________________
______________________________________________________________________________________________
______________________________________________________________________________________________

Were any of the involved products modified by the transfusion service or in the clinical care area?  
(pooled, aliquoted, warmed, irradiated, washed, leukocyte-reduced by filtration, or other):

Routine transfusion reaction workup (or ☑ Not done)

<table>
<thead>
<tr>
<th>Clerical check of transfusion (right unit, right recipient?):</th>
<th>☐ Correct</th>
<th>☑ Incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance of returned blood bag and contents:</td>
<td>☑ Normal</td>
<td>☐ Abnormal</td>
</tr>
<tr>
<td>Appearance of returned solutions, tubing, and filters:</td>
<td>☑ Normal</td>
<td>☐ Abnormal</td>
</tr>
<tr>
<td>Describe any problems:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Confirmation of compatibility

<table>
<thead>
<tr>
<th>Pre-transfusion</th>
<th>Post-transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO/RH type</td>
<td></td>
</tr>
<tr>
<td>Antibody screen</td>
<td></td>
</tr>
<tr>
<td>Crossmatch (if applicable)</td>
<td></td>
</tr>
<tr>
<td>Direct antiglobulin test</td>
<td></td>
</tr>
</tbody>
</table>
How Do We Work Up Reactions?

- **Protect the safety of the blood supply!**
- Temporarily defer all involved donors
- Gain control of all associated products
  - Hemolytic reactions:
    - Check ABO and clerical check of donor/product
    - Check antibody screen – did we miss something?
  - Transfusion-transmitted infections:
    - Donors must provide samples for testing to determine if they have infection – if yes, permanently deferred
# Reporting Form

For potential septic reactions due to bacterial contamination of the blood product:

<table>
<thead>
<tr>
<th>Residual product/blood bag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample source: □ Bag □ Segment □ Infusion set/tubing</td>
</tr>
<tr>
<td>Sample collection: □ Aseptic □ Clean □ Retrieved from trash</td>
</tr>
<tr>
<td>Gram stain: □ Negative □ Not done □ Positive</td>
</tr>
<tr>
<td>Culture: □ Negative □ Not done □ Positive</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient blood cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transfusion □ Not done Date: □ Negative □ Positive for:</td>
</tr>
<tr>
<td>Post-transfusion □ Not done Date: □ Negative □ Positive for:</td>
</tr>
</tbody>
</table>

What other event could explain the findings in this patient other than the transfusion?

- □ Sepsis
- □ Drug reaction □ Volume overload
- □ Heart failure □ Hemorrhagic shock □ Allergic or anaphylactic reaction
- □ Other:

Transfusion Service: Medical Director’s Summary

Suspect Cause: (check appropriate box)

- □ Septic reaction
- □ Hemolytic reaction
- □ Transfusion-related acute lung injury (TRALI)
- □ Electrolyte abnormality (K+, Ca++)
- □ Anaphylaxis
- □ Volume overload
- □ Other: ______________________________________

From your perspective, what is the likelihood that the transfusion caused this event?

- □ Certain
- □ Likely
- □ Possible
- □ Cannot exclude
- □ Unlikely
How Do We Work Up Reactions?

- Septic/Bacterial contamination:
  - Determine the causative organism
    - Was in-house sample positive
    - Did it match with patient/blood product result
  - Interview donor
    - Health issues – possible transient bacteremia
    - Arm issues – unable to get adequate arm scrub
  - Review processing records to locate source
    - Collections – inadequate arm scrub/break sterility
    - Manufacturing – accidently create an open system
How Do We Work Up Reactions?

- TRALI (vs TACO):
  - Donor allo-immunization risk
    - Prior transfusions, transplants or pregnancies
    - If yes to any, order HLA and HNA workup
  - Recipient HLA typing
  - Test results
    - Positive for HLA antibodies – defer if match with recipient
    - Positive for HLA antibodies, no match – defer from plasma (may redirect to RBC)
    - Positive for HNA antibodies – defer
The End
Investigation of Suspected Septic Transfusion Reactions by Blood Collection Establishments

Dr. F. Bernadette West MD
Medical Director
American Red Cross
East Division Blood Services
Disclosures

- Fenwal
- Cerus
- No commercial support was received for this activity.
Septic Transfusion Reactions

- Objectives:
  - List the initial signs and symptoms of a suspected septic transfusion reaction.
  - State why a suspected septic transfusion reaction should be reported (to the Blood Center).
  - Name the most common causes of fatal septic reactions as reported to the FDA in 2016.
  - Summarize the approach to a septic transfusion reaction by our Blood Center.
Septic Transfusion Reaction

AABB Standards 31st Ed. Effective April 1, 2018 (Glossary)

Transfusion-Transmitted Infection: A disease or condition caused by a virus, bacteria, fungus, parasite, or agent of transmissible spongiform encephalopathy that may be transmitted by transfusion of blood or blood components or by tissue implantation or transplantation or administration of derivatives.

- Septic Transfusion Reaction (AABB TM 19th Ed.)
  - **Fever** > or = 38.5C (101F)
  - Chills
  - Rigors
  - Hypotension (but could see hypertension)
  - Shock
  - Renal failure
  - DIC
  - DIC

Esp. gram negative organisms
Implicated Bacteria in STRs

- Coag-neg staphylococcus: 52%
- Staphylococcus aureus: 22%
- Streptococcus spp.: 9%
- Enterococcus faecalis
- Enterobacter spp.
- Klebsiella spp.
- Acinetobacter spp
- Pseudomonas fluorescens
- Bacillus spp.
- Clostridium perfringens
- Ralstonia pickettii

March 1, 2004 to December 31, 2014
> 8 million distributed Apheresis Platelets

Eder et al. Transfusion, 2014;54:857-862
### FY2012-FY2016 Fatalities Reported to FDA

#### Table 3: Transfusion-Associated Fatalities by Complication, FY2012 – FY2016

<table>
<thead>
<tr>
<th>Complication</th>
<th>FY12 No.</th>
<th>FY12 %</th>
<th>FY13 No.</th>
<th>FY13 %</th>
<th>FY14 No.</th>
<th>FY14 %</th>
<th>FY15 No.</th>
<th>FY15 %</th>
<th>FY16 No.</th>
<th>FY16 %</th>
<th>Total No.</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>2</td>
<td>5%</td>
<td>-</td>
<td>0%</td>
<td>2</td>
<td>7%</td>
<td>2</td>
<td>5%</td>
<td>5</td>
<td>12%</td>
<td>11</td>
<td>6%</td>
</tr>
<tr>
<td>Contamination</td>
<td>3</td>
<td>8%</td>
<td>5</td>
<td>13%</td>
<td>1</td>
<td>3%</td>
<td>5</td>
<td>14%</td>
<td>5</td>
<td>12%</td>
<td>19</td>
<td>10%</td>
</tr>
<tr>
<td>HTR (ABO)</td>
<td>3</td>
<td>8%</td>
<td>1</td>
<td>3%</td>
<td>4</td>
<td>13%</td>
<td>2</td>
<td>5%</td>
<td>4</td>
<td>9%</td>
<td>14</td>
<td>8%</td>
</tr>
<tr>
<td>HTR (non-ABO)</td>
<td>5</td>
<td>13%</td>
<td>5</td>
<td>13%</td>
<td>4</td>
<td>13%</td>
<td>4</td>
<td>11%</td>
<td>1</td>
<td>2%</td>
<td>19</td>
<td>10%</td>
</tr>
<tr>
<td>Hypotensive Reaction</td>
<td>-</td>
<td>0%</td>
<td>-</td>
<td>0%</td>
<td>1</td>
<td>3%</td>
<td>1</td>
<td>3%</td>
<td>1</td>
<td>2%</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>TACO</td>
<td>8</td>
<td>21%</td>
<td>13</td>
<td>34%</td>
<td>5</td>
<td>17%</td>
<td>11</td>
<td>30%</td>
<td>19</td>
<td>44%</td>
<td>56</td>
<td>30%</td>
</tr>
<tr>
<td>TRALI*</td>
<td>17</td>
<td>45%</td>
<td>14</td>
<td>37%</td>
<td>13</td>
<td>43%</td>
<td>12</td>
<td>32%</td>
<td>8</td>
<td>19%</td>
<td>64</td>
<td>34%</td>
</tr>
</tbody>
</table>

*Note: FY2015-FY2016 only includes cases with an imputability of *Definite/Certain, Probable/Likely, or Possible.*

FY2012-FY2014 only include cases classified as transfusion-related.

*FY2012-FY2016 numbers combine both TRALI and Possible TRALI cases.*

2223
### Table 6: Contamination by Implicated Organism, FY2012 - FY2016

<table>
<thead>
<tr>
<th>Organism</th>
<th>FY12</th>
<th>FY13</th>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Babesia microti</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Coagulase-negative staphylococci</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas fluorescens</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Acinetobacter species</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>West Nile virus</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>3</strong></td>
<td><strong>5</strong></td>
<td><strong>1</strong></td>
<td><strong>5</strong></td>
<td><strong>5</strong></td>
<td><strong>19</strong></td>
</tr>
<tr>
<td>Product</td>
<td>Organism</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td><em>Enterobacter aerogenes</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma (TPE)</td>
<td>Coagulase-negative staphylococci</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Red Blood Cells</td>
<td><em>Pseudomonas fluorescens</em></td>
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</tr>
<tr>
<td>Red Blood Cells</td>
<td><em>Babesia microti</em></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Red Blood Cells</td>
<td><em>Babesia microti</em></td>
<td></td>
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</tr>
</tbody>
</table>
Figure 4: Contamination by Implicated Blood Product, FY2012 – FY2016

<table>
<thead>
<tr>
<th>Blood Product</th>
<th>FY12</th>
<th>FY13</th>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Blood Cells</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Pooled Platelets</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Platelets Pheresis</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Plasma</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Red Blood Cells microorganisms: B. microti (4), P. fluorescens (2), E. faecium (1)
Pooled Platelets microorganisms: S. Marcescens (2)
Plasma (TPE): coagulase-negative staphylococci (1)
Platelets Pheresis microorganisms: S. aureus (4), S. epidermidis (1), coagulase-negative staphylococci (1), West Nile virus (1), Acinetobacter sp. (1), E. aerogenes (1)
Focusing on Platelets
morbidity and mortality from septic risk

- Greater risk of sepsis than other blood products
- Platelets in:
  - 100% plasma
  - Platelet additive solution
  - Pools of 5-6
- Stored at 20C-24C
- Continuous, gentle agitation
- Oxygen-permeable bag
- 5-7d storage

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**Title 21: Food and Drugs**
PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS
Subpart F—Dating Period Limitations

<table>
<thead>
<tr>
<th>Platelets</th>
<th>Between 20 and 24°C</th>
<th>5 days from date of collection.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelets</td>
<td>Other temperatures</td>
<td>As specified in the instructions for use by the blood collection, processing and storage system approved or cleared for such use by FDA.</td>
</tr>
</tbody>
</table>

---

American Red Cross
Reducing Risk *Pre-collection: protecting the patient*

- **Donor**
  - Reading materials
  - Health history
  - Mini-physical
  - Chlorhexidine-based
  - Iodine-based
  - Diversion pouch
  - Routine ID testing
§606.145 Control of bacterial contamination of platelets.

(a) Blood collection establishments and transfusion services must assure that the risk of bacterial contamination of platelets is adequately controlled using FDA approved or cleared devices or other adequate and appropriate methods found acceptable for this purpose by FDA.
Options

Standards for Blood Banks and Transfusion Services, 31st edition, effective April 1, 2018

5.1.5.2 The BB/TS shall have methods to detect bacteria or use pathogen reduction technology in all platelet components.*

*21 CFR 606.145.
Reducing Risk *Post-collection:* protecting the patient

- **Blood Center**
  - Visual inspection
  - Environment
  - **Product sampling and volume**
  - **Culture samples since 2004**
    - Rest 24hrs
    - Sample culture
    - 12hr hold prior to release
    - False negatives and false positives
Reducing Risk **Post-collection:** protecting the patient

- Blood Center
- Pathogen reduction technology
  Chemical, UV, both
  - Currently only 1 FDA approved device
  - PAS-collected unit
  - Amotosalen +UVA technology
  - Reduces risk of TTI from many organisms
  - (Not all bacteria are detectable)

Intercalates into DNA and RNA, inactivates a broad spectrum of organisms
Reducing Risk *Post-collection: protecting the patient*

- **Hospital**
  - Visual inspection
  - Environment
  - **Point of issue testing**
    - High false positive rate
    - Possible false negatives
    - Not effective with all bacterial strains
    - Challenge for some hospitals to adopt
Blood Component Visual Inspection Guide
Septic Transfusion Reaction

- Septic Transfusion Reaction (AABB TM 19th Ed.)
  - **Fever** > or = 38.5C (101F)
  - Chills
  - Rigors
  - Hypotension
  - Shock
  - Renal failure
  - DIC
Why Report the Reaction?

- Prevent transfusion of any other co-components.
- Donor is temporarily deferred during investigation.

§606.145 Control of bacterial contamination of platelets.

(c) In the event that a transfusion service identifies platelets as bacterially contaminated, the transfusion service must not release the product and must notify the blood collection establishment that provided the platelets. The transfusion service must take appropriate steps to identify the organism; these steps may include
How We Work Up A Suspected Septic Transfusion Reactions

- Hospital Blood Bank calls Donor Client Support Center
  - Donor is immediately temporarily deferred.
  - Products are recalled/quarantined, disposition determined.
- Hospital BB Medical Director → ARC Medical Director
- Review reaction paperwork and hospital lab. results
  - In-house modifications?
  - Gram stain, culture of donor and product.
- Request additional information as needed.
- Write an initial report within 24 hours of receipt.
Positive Results

- Both blood center and hospital attempt to determine the causative organism
- Original sample (in bottle) from parent bag
  - If positive then determine organism
  - Gram stain
  - Sample ‘daughter’ bags.
    - Confirmatory test is positive (with the same organism).
- Review hospital reports of patient blood cultures pre/post.
- Hospital may also culture the product bag(s).

**True Positive:** A positive result on both the initial test and the confirmatory test. Specifically for bacteria detection, a confirmatory test is a culture-based test performed on a different sample than the blood culture bottle or other sample used for the initial test. For example, a sample source for the confirmatory test could be the original platelet component. A subculture of the initial positive culture is not an adequate sample for this purpose. If initial testing was culture based, the confirmatory test can use the same method applied to the alternate sample source.
Donor

- Talk with donor to determine risk factors.
  - Any remarkable issues during donation?
  - Recent illness or symptoms of illness
  - Recent procedures
  - Contact with soil, certain animals, water, etc.
Donor

- Review donor records from day of donation.
- Review history of donations.
- Look for medical or other previous deferrals.
Review Processing Records

Review of:

- Apheresis or other collection records.
- Instrumentation or lab equipment.
- Observation of staff.
- Manufacturing records.
Fatalities 21CFR Sec 606.170(b)

- The transfusion service (who performed the compatibility testing) must report fatalities to FDA.
  - As soon as possible after confirming the fatality as being linked to the transfusion.
  - Submit a written report within 7 days.
    - Full report may take longer.
- The Blood Establishment can assist with information as needed.
- **fatalities2@fda.hhs.gov** and other methods of contact on FDA website.
Finalizing the Process

- Internal report
- Hospital report
- Letter to donor
- Call to donor
- Call to hospital
- Health Department or any other entity as required by law
Thank you