Transfusion Reactions

Adverse Effects of Blood Transfusion

- Transfusion-Transmitted Infectious Disease (ie, “aftermath”)
- “Transfusion Reactions” (acute/subacute)

Introduction of ID Testing for Blood

<table>
<thead>
<tr>
<th>Date</th>
<th>Test</th>
<th>Date</th>
<th>Test</th>
</tr>
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<tbody>
<tr>
<td>c. 1910</td>
<td>Syphilis</td>
<td>1987</td>
<td>HIV-2</td>
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<td>1970</td>
<td>HBV by ID</td>
<td>1988</td>
<td>HTLV I &amp; II</td>
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<td>1972</td>
<td>HBV by CIE</td>
<td>1991</td>
<td>HCV</td>
</tr>
<tr>
<td>1975</td>
<td>HBV by RIA</td>
<td>1995</td>
<td>HIV p24 Ag</td>
</tr>
<tr>
<td>1981</td>
<td>HBV by RIA</td>
<td>1995</td>
<td>NAT (HCV/HIV)</td>
</tr>
<tr>
<td>1985</td>
<td>HIV-1</td>
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</table>

Transfusion-Transmitted Agents Not Tested For

- Malaria
- Trypanosoma cruzi
- Babesia
- Miscellaneous bacteria
- Miscellaneous viruses (eg CMV, Parvovirus)

Risk Estimate/Unit Transfused (approximate)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Estimate</th>
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</thead>
<tbody>
<tr>
<td>HAV</td>
<td>1: 1 million</td>
</tr>
<tr>
<td>HBV</td>
<td>1:100,000</td>
</tr>
<tr>
<td>HCV</td>
<td>1:360,000</td>
</tr>
<tr>
<td>HIV</td>
<td>1: 1 million</td>
</tr>
<tr>
<td>Bacteria/platelet</td>
<td>1:10-20,000</td>
</tr>
<tr>
<td>T cruzi</td>
<td>1:42,000</td>
</tr>
<tr>
<td>ABO incompatible</td>
<td>1:12,000</td>
</tr>
</tbody>
</table>

Transfusion Reactions

- Allergic
- Hemolytic (Acute; Delayed)
- Bacterial
- Febrile non-hemolytic
- TRALI
- Volume Overload
Transfusion Reactions: Signs & Symptoms

• Fever
• Hypotension
• Chest Tightness/Dyspnea
• Nausea/Vomiting
• etc

Allergic Transfusion Reactions - Etiology

• Anti-IgA in an IgA deficient patient (18%)
• Antibodies to polymorphic forms of serum proteins (IgG, albumin, haptoglobin, α-1 antitrypsin, transferrin, C3, C4, etc)
• Transfusion of allergen in a sensitized patient (eg Penicillin, ASA, etc consumed by donor)
• Passive transfer of IgE (to drugs, food)
• MOST COMPLETELY UNEXPLAINED

Immunohemolymphatic Transfusion Reactions

• Intravascular vs Extravascular

• Immediate vs Delayed

Immunohematological Testing for Safety

• Imminent Importance – ABO Typing

• Anticipatory/Prophylactic Importance – Rh Typing

RE: Transfusion Safety (Serological)

• “Given the distribution frequency of ABO groups, the chances of major incompatibility are one in three”

Acute Hemolytic Reactions - Etiology

• 1 in 38,000 Red Blood Cell Transfusions
• Usually ABO incompatibility
  • Sample or transfusion error 65%
  • Blood Bank error 35%
• Other red cell antigen – K, Jk-a/b, Fy-a
• Mortality dependent on amount transfused
  • 0% < 500 ml, 25% 500-1000 ml, 44% > 1000 ml
• Non-immune hemolysis – hypotonic fluid, overheating or freezing, cell saver
Acute Hemolytic Reactions - Management

- STOP the transfusion
- Keep IV open
- Report immediately!!!
- Blood samples (T&S, DAT, lytes, creat, PT/aPTT, fibrinogen)
- Support BP
- Transfuse to correct coagulopathy
- ↑K, metabolic acidosis common; dialysis as needed
- Return units to Blood Bank
- Often another patient at risk

Case #2 – Patient History

- 38 year old man with AML admitted with febrile neutropenia post-chemotherapy
- On cefazolin & tobramycin
- Blood cultures negative
- Afebrile
- Tongue swelling since day 2 with airway compromise
- Taken to OR for awake intubation and possible tracheostomy if oral intubation failed
- Pre-intubation:
  - Pt count 7x 10^9/l; Temp 37.4° C, BP 140/80

Case #2 – Patient History Cont’d

- Transfused 5 units of pooled random donor platelets (including the implicated platelet)
  - The pool is infused over 10 minutes
- During platelet transfusion patient is intubated
- Patient develops immediate cardiac ischemia & hypotension
  - BP 95/60, O2 Sat 91% (temp not monitored)
- Patient sedated & paralyzed
- Transfusion reaction not included in the differential diagnosis of the acute clinical change

Case #2 – Patient History Cont’d

- On arrival to the Critical Care Unit
  - Temp 40°C
  - BP 70/58
- Blood cultures taken at admission to ICU grow Serratia marcescens within 24 hours despite Cipro/tobramycin administered pre-transfusion
- Renal & hepatic failure ensue
  - Death within 18 hours of transfusion
- Platelet pool discarded; no cultures performed
- RBC positive culture for Serratia marcescens

Bacterial Contamination Etiology

- Donor bacteremia, skin plug, processing
- Organisms PRBC = Yersinia enterocolitica, Serratia marcescens, Serratia liquefaciens
- Organisms PLTs = Staph aureus, Klebsiella pneumoniae, Serratia marcescens, Staph epidermidis

Incidence of Bacterial Contamination and Septic Transfusion Reactions

- Incidence of bacterial contamination
  - 1 in 2000-3000 platelet units
  - 1 in 30,000 RBC units
- Prevalence of severe episodes of transfusion-associated bacterial sepsis not clearly established; estimated to occur in about 1/6 contaminated units
Febrile Transfusion Reactions
Differential Diagnosis

- Bacterial contamination/septic transfusion reaction
- Acute hemolytic transfusion reaction
- Febrile non-hemolytic transfusion reaction (although such a reaction may actually occur without fever!)

Transfusion Related Acute Lung Injury - Definition

- A syndrome of acute respiratory distress with hypoxia and bilateral pulmonary edema, without evidence of congestive heart failure
  - Within 6 hours of transfusion
  - May be indistinguishable from ARDS (from other causes)
  - Usually resolves in 24-72 hours

Case #1 – Reaction Details

- Transferred to ICU
- Intubated & ventilated
- Temperature 38.4°C (37.9°C pre-transfusion & normal 6 hours later)
- Antihistamines, acetaminophen, antibiotics
- CXR
- Patient and product culture negative
- Extubated 6 hours later
- Up walking 2 days later

Case #1 – Transfusion Details

- Patient transfused 5 units pooled platelets over 30 minutes
- 15 minutes after completion of platelet transfusion:
  - Not feeling well
  - Rigors
  - Rapidly progressive dyspnea
  - Tachycardic (pulse 170/min)
  - Reduced level of consciousness – Cardiac arrest code called
Transfusion Reaction

Manifestation

Pulmonary Edema

- Circulatory Overload
- TRALI

Suspected Transfusion Reaction

Clinical Management

1. STOP THE TRANSFUSION
2. Maintain IV access; administer 0.9% saline
3. Treat reaction symptoms
4. Report reaction to transfusion service
5. Perform bedside clerical check
6. Continue to monitor vital signs
7. Obtain blood and urine samples, if indicated
8. Complete transfusion reaction form
9. Send transfusion reaction form, patient specimens, and blood bag with attached administration set to the Blood Bank
10. Document the transfusion reaction in the patient's chart

Risks of Transfusion Complications

Frequency per million units transfused

<table>
<thead>
<tr>
<th>Frequency (per million units transfused)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>500</td>
</tr>
<tr>
<td>1000</td>
</tr>
<tr>
<td>1500</td>
</tr>
<tr>
<td>2000</td>
</tr>
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</table>

BMJ 1999 “SHOT” [Serious Hazards of Transfusion] Study

Acute Transfusion Reactions

<table>
<thead>
<tr>
<th>Type</th>
<th>Signs and Symptoms</th>
<th>Therapy</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune Incompatibility</td>
<td>Urticaria, rarely hypotension</td>
<td>Stop transfusion; give antihistamine (PO or IM); if severe, epinephrine and/or steroids</td>
<td>Check paper work to ensure correct blood component was transfused to the right patient; Evaluate patient for hemoglobinuria; Perform direct antiglobulin test; Repeat compatibility testing (crossmatch); Repeat other serologic testing as needed (ABO, Rh); Analyze urine for hemoglobinuria</td>
</tr>
<tr>
<td>Antibody to leukocytes or plasma proteins; rule out hemolysis; consider sepsis. Commonly due to patient's underlying condition</td>
<td>Fever, chills, rarely hypotension</td>
<td>Stop transfusion; give antipyretics, acetaminophen (or aspirin, if not thrombocytopenic)</td>
<td>Pretransfusion antipyretic; leukocyte-reduced blood components, if recurrent</td>
</tr>
<tr>
<td>Antibodies to plasma proteins including antibodies to IgA</td>
<td>Urticaria (hives), rarely hypotension</td>
<td>Stop transfusion; give antihistamine (PO or IM); if severe, epinephrine and/or steroids</td>
<td>Check paper work to ensure correct blood component was transfused to the right patient; Evaluate patient for hemoglobinuria; Perform direct antiglobulin test; Repeat compatibility testing (crossmatch); Repeat other serologic testing as needed (ABO, Rh); Analyze urine for hemoglobinuria</td>
</tr>
<tr>
<td>Intravascular Hemolysis</td>
<td>Fever, malaise, indirect hyperbilirubinemia, increased urine urobilinogen, falling hematocrit</td>
<td>Avoid clerical errors; ensure proper sample and recipient identification</td>
<td>Stop transfusion; hydrate, support blood pressure and respiration, induce diuresis, treat shock &amp; DIC</td>
</tr>
</tbody>
</table>

Workup of an Acute Intravascular Hemolytic Transfusion Reaction

If an acute transfusion reaction occurs:
1. Stop blood component transfusion immediately.
2. Maintain IV access with an appropriate crystalloid or colloid solution
3. Maintain blood pressure, pulse
4. Maintain adequate ventilation
5. Give a diuretic and/or institute fluid diuresis
6. Obtain bloodborne for transfusion reaction workup
7. Perform blood bank workup of suspected transfusion reaction
   - Check paper work to ensure correct blood component was transfused to the right patient
   - Evaluate patient for hemoglobinuria
   - Perform direct antiglobulin test
   - Repeat compatibility testing (crossmatch)
   - Repeat other serologic testing as needed (ABO, Rh)
   - Analyze urine for hemoglobinuria

If intravascular hemolysis is confirmed:
8. Monitor renal status
9. Monitor coagulation status (prothrombin time, partial thromboplastin time, fibrinogen, platelet count)
10. Monitor for signs of hemolysis (LDH, bilirubin, haptoglobin, plasma hemoglobin)
11. If sepsis is suspected, culture and treat as appropriate
Table 1-11. Common signs and symptoms of acute transfusion reactions

<table>
<thead>
<tr>
<th>Symptom</th>
<th>AHTR</th>
<th>DAT</th>
<th>FNTHR</th>
<th>TRALI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>+</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>+</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Nausea and Vomiting</td>
<td>+</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Abdominal cramps</td>
<td>+</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Faintness</td>
<td>-</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Shock</td>
<td>-</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Respiratory Distress</td>
<td>-</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Hypotension, SOB</td>
<td>-</td>
<td></td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Acute Hemolytic Reaction</td>
<td>-</td>
<td></td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Types of Acute Transfusion Reactions

AHTR, acute hemolytic transfusion reaction; DAT, direct antiglobulin test; DIC, disseminated intravascular coagulation; FNTHR, febrile non-hemolytic transfusion reaction; Hgb-emia, hemoglobinemia; Hgb-uria, hemoglobinuria; N/V, nausea and vomiting; SOB, shortness of breath; TRALI - transfusion related acute lung injury.

*Hypotension is associated with hypotension and signs of congestive heart failure

Case #1

At 11:40 pm on January 7, 1975 a unit of blood was requisitioned from the blood bank for patient A, who was being prepared for plastic surgery the following day. A cross-matched specimen compatible Group A Rh negative was released to be picked up by the requisitioning physician (Dr. X).

This unit of blood was (incorrectly) administered to patient B, for whom no blood had been ordered, by Dr. X, who signed the mandatory bedside identification documents for the blood and the patient (patient B was Group B Rh positive). Patient B's hospital record reveals that the transfusion ran from 12:30 am to 4:00 am on January 8. During this period the patient complained of fever and abdominal cramps. At approximately 5:30 am the patient voided urine which was dark Coca-Cola in color. Shortly thereafter his blood pressure dropped markedly. Despite numerous efforts at resuscitation, the patient was pronounced dead at 6:45 am.

A blood specimen taken from the patient after resuscitation had begun showed visible evidence of marked hemolysis. Additionally, the dark-colored urine already mentioned was demonstrated to be due to the presence of free hemoglobin. Blood bank serologic investigations revealed a positive direct antiglobulin (Coombs) test (normally negative) and an AB blood grouping.

Case #2

A 74 year old female had undergone aortic valve replacement for aortic stenosis when she was 68 years old. Seven units of blood were utilized during this open heart surgery, which was accomplished with the use of the heart-lung machine (extracorporeal circulation).

The patient required reoperation for a leak which developed in the replacement valve. This procedure was carried out on 6/3/91 without any complications. The patient received multiple units of several, completely compatible blood components (packed red cells, platelets, and fresh frozen plasma) with no untoward effects in the course of the surgery. Her hematocrit immediately following surgery was 35, and remained at approximately that level for the next ten days.

Her post-operative course was uneventful until 6/14/91, when it was noted that her hematocrit had abruptly fallen to 25. A blood transfusion was ordered, and her physician requested a type and crossmatch for four units. At that time both the direct and indirect antiglobulin tests (Coombs tests) were found to be positive (they were both negative at the time of surgical transfusion). This prompted additional testing and it was discovered that her total bilirubin had risen to 4.0 (normal 1.3), with 90% of this being of the indirect reacting type. In addition, her serum lactic dehydrogenase enzyme level had risen to 2390 units (from 750 at time of surgery) (normal up to 625).

Additional testing in the blood bank then revealed that an antibody of specificity "little s" could be eluted from the patient's circulating red cells. Moreover, an indirect Coombs test disclosed that the patient now had two "irregular" antibodies in her circulating plasma (of specificities "little f" and "Kidd-B").

Testing on 6/18/91 showed that the direct antiglobulin test on the red cells had become negative, but the indirect Coombs test remained positive. At that time also, the patient's reticulocyte count was reported as 5.8% (normal < 1.6%).