Ortho Clinical Diagnostics

A Transfusion Reaction
What Do I Do Now?

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Objectives

• Describe the four types of adverse reactions to blood and blood products
• Identify the most common symptoms of transfusion reactions
• Describe immediate treatment recommendations
• List some of the Transfusion Transmitted Diseases
• Describe prevention practices for each type of reaction
Definitions

• Immune – stimulation of immune system
• Non-immune – reactions do not involve recipient’s immune system
• Immediate – reactions begin in minutes
• Delayed – reactions occur months after transfusion event
Regulatory Requirements

- College of American Pathologists (CAP)
- The Joint Commission
- AABB
- COLA
- FDA
# Summary of Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Immediate</th>
<th>Delayed</th>
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</thead>
<tbody>
<tr>
<td><strong>Immune</strong></td>
<td>• Acute hemolytic reaction</td>
<td>• Delayed hemolytic reaction</td>
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<tr>
<td></td>
<td>• Febrile, non-hemolytic</td>
<td>• Graft-versus-host disease (GvHD)</td>
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<td></td>
<td>• Allergic</td>
<td>• Alloimmunization</td>
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<td></td>
<td>• TRALI</td>
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<tr>
<td><strong>Non-Immune</strong></td>
<td>• Bacterial Sepsis</td>
<td>• Viral infections</td>
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<td></td>
<td>• Massive Transfusion</td>
<td>• Parasitic infections</td>
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<tr>
<td></td>
<td>• Volume Overload</td>
<td>• Iron overload</td>
</tr>
<tr>
<td></td>
<td>• Citrate Toxicity</td>
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<td></td>
<td>• Non immune hemolysis</td>
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# Reaction Statistics in the United States

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Hemolytic Transfusion Reactions</td>
<td>One/40,000 transfused units of packed RBC’s</td>
</tr>
<tr>
<td>Non-hemolytic febrile and minor allergic reactions</td>
<td>Three to four percent of all transfusions</td>
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<tr>
<td>GvH disease</td>
<td>&lt; 0.15 percent</td>
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## Reaction Statistics in the United States

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<tr>
<td>TRALI</td>
<td>0.1-0.2% of all transfusions</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 per 200,000-500,000 units</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1 per 2-4 million units</td>
</tr>
<tr>
<td>HIV Infection</td>
<td>1 per 2-4 million units</td>
</tr>
</tbody>
</table>

Morbidity and Mortality

- Transfusion-related Hepatitis C causes chronic Hepatitis 50% of infected recipients
- Cirrhosis develops in 10% Hepatitis patients
- Transfusion-associated GvH disease 80-90% mortality rate
- Transfusion-related acute lung injury-mortality rate 5%

Immune: 
Acute Hemolytic Transfusion Reactions

• Overall – occurs in 1/40,000 transfusions

• Misidentification causes majority of hemolytic transfusion reactions (HTR)

• Clerical errors occur 1:6,000 to 1:10,000 units

• Mistaken hospital identification occurs approximately 1:33,000

Acute Hemolytic Reaction Symptoms

Fever
- Oppressive chest pain and dyspnea after start

Chills
- Hemoglobinemia

Anxiety
- Hemoglobinuria and oliguria, followed by renal failure

Back Pain

Shock
- Jaundice - several hours to develop
- Abnormal bleeding - disseminated intravascular coagulation (DIC)

Acute Hemolytic Reaction
Immediate Treatment

• Stop transfusion
• Maintain IV access
• Supportive care
• Fluids to maintain urine flow and support blood pressure
• Diuretics and low dose dopamine
• Monitor coagulation for DIC
• Monitor for renal failure

Source: Primer of Blood Administration, Bethesda, MD™ AABB, 2012
Acute Hemolytic Reaction Follow-up

- Return unit and associated tubing to transfusion service
- Include freshly collected patient blood and urine samples

Initial Laboratory Testing

- Clerical sample and patient ID
- Repeat ABO/Rh
- Direct Antiglobulin Test (DAT)
- Check for hemolysis

Laboratory Testing

• Subsequent Laboratory Testing
• Repeat of antibody screen and crossmatch
• Urine Hb
• Serum LDH
• Bilirubin
• Haptoglobin

Hemoglobinuria
Prevention – Acute Hemolytic

- Patient identification
  - Samples
  - Transfusion Administration
- Laboratory testing
  - Performed on properly labeled sample
- Product retrieval from Blood Bank
  - Retrieval form has correct patient identification
  - Product tag matches with retrieval form and computer information
- Bedside verification
  - 2 person verification that the product is correct for patient

Immune – Febrile Non-hemolytic Reaction

• Most common adverse effect of transfusion
• 3-4% of transfusions
• Begins within minutes to hours of transfusion

Febrile Non-hemolytic Reaction Symptoms

- Increase in temperature of greater than 1°C or 2°Fahrenheit
- Symptoms include: fever, chills, rigor

Febrile Non-hemolytic Initial Treatment

- Antipyretics are effective treatment
- Acetaminophen (Tylenol, Panadol)
- Reduces fever

Febrile Non-hemolytic Clinical Follow-up

- Clerical check
- Plasma evaluation
- ABO/Rh
- DAT

Prevention – Febrile Reaction

- Use of leukoreduced blood products
- Pre-medicate patient with history of febrile reactions
- Antipyretics
- Acetaminophen

Immune – Allergic Reactions

- Minor allergic reaction
  - Rash/Hives (Urticaria)/Itching (pruritus)
  - With febrile reactions – 3-4% of all transfusions

- Anaphylactic
  - Respiratory distress
  - Vascular instability
  - Shock
Allergic Reactions Initial Treatment

• Antihistamines – generally effective treatment
• If symptoms resolve, no need to stop transfusion

Severe Allergic Reactions

Severe (i.e. anaphylaxis) usually in IgA deficient

- Facial edema
- Dyspnea
- Tight itching throat
- Bronchoconstriction including cough
- Nausea, vomiting, diarrhea, hypotension, arrhythmia

Severe Allergic Reactions Treatment

- Stop transfusion
- Volume expanders
- Epinephrine
- Corticosteroids
- Oxygen

Prevention – Allergic Reactions

- Severe allergic
  - Wash all cell products to remove plasma
  - IgA deficient plasma donors
- Less severe
  - Pre-medicate with antihistamines

Immune – Transfusion Related Acute Lung Injury (TRALI)

- Non-cardiogenic pulmonary edema
- First described in 1985
- True incidence is unknown
  - Estimates vary widely
  - 1:432 - 1:88,000/platelet transfusion
  - 1:4,000 to 1:557,000/red blood cell unit
  - Most literature supports 1:5,000
  - Increased plasma = increased risk

TRALI Symptoms

- Pulmonary edema with hypoxia
- Bilateral infiltrates on frontal chest radiograph
- ≤ 6 hours after transfusion; no other cause identified
- Symptoms of pulmonary edema with normal left ventricular filling pressure

TRALI Symptoms

• Mimic Acute Respiratory Distress Syndrome
  • Severe pulmonary distress
  • Ventilation/BP support required
  • White-out on chest X-ray

• Resolution without sequela in a couple of days
TRALI Example
TRALI Initial Treatment

- Diuretics
  - Not indicated – even deleterious
- Steroids
  - Not clearly helpful
- Antibiotics – for high fever and/or circulatory collapse

- Supportive care
  - Supplemental oxygen
  - Mechanical ventilation
- Circulatory support
  - Fluids
  - Inotrope support
- ICU care if needed

TRALI Prevention

• Best Treatment
• Blood Center Activities
• Reduce plasma products collected from multiparous females
• HLA testing

Immune – Delayed Hemolytic Reaction

- Hemoglobin concentration drops unexpectedly
- Fever
- Jaundice appears 5-10 days post transfusion
- Sensitized through transfusion or pregnancy
- Antibodies cause destruction
  - Starts 4-7 days post transfusion

Delayed Hemolytic Reaction

• Treatment
  • Monitor the patient’s urine output and renal function

• Laboratory Testing
  • Fresh blood sample
  • ABO/Rh, DAT
  • Antibody Screen and ID

• Prevention
  • Provide antigen negative blood for future transfusions

Immune – Transfusion Associated Graft vs. Host Disease (TA-GvHD)

• TA-GvHD is rare <0.15%
• Donor lymphocytes can’t be eliminated by the recipient
• Minimum number of lymphocytes required for TA-GvHD unknown

Treatment of GvHD

• Suppress the immune response
  • Methotrexate
  • Cyclosporine
  • Corticosteroids

Prevention of GvHD Gamma Irradiation

• Irradiation damages DNA in donor lymphocytes rendering them incompetent

• Pathogen reduction
Non-immune – Hemolysis

- Mechanical
- Use of roller pumps (cardiac bypass surgery)
- Pressure infusion pumps
- Small bore needle

Non-immune – Hemolysis

- Thermal
- Unit exposed to improper temperatures
- Malfunctioning blood warmers
- Hypotonic Solutions
- Addition of drugs or hypotonic solutions
- Inadequate deglycerolization

Prevention – Non-immune Hemolysis

- Proper administration
- Blood warmers work properly
- No “creative warming”
- No drugs or hypotonic solutions used with transfusion
- Proper storage and thawing of frozen blood

Non-immune – Transfusion Associated Cardiac Overload (TACO)

- Elderly and infants are most susceptible
- Dyspnea
  - Protruding neck veins
  - Pulmonary edema
  - Systolic hypertension
  - Cardiac failure
- Treatment
  - Diuretics

TACO Prevention

- Slow infusion
- Split units

Non-immune – Transfusion Transmitted Diseases (TTD)

• Bacterial
• Viral
• Parasitic
• Prion
Immediate – Bacterial Sepsis

- Caused by gram-negative and gram-positive bacteria
- Occurs most often with platelet transfusion

Bacterial Sepsis Symptoms

- Hyperpyrexia
- Red body rash
- Chills
- Acute shock

Most common infectious source of morbidity and mortality related to transfusion.

Bacterial Sepsis Initial Treatment

- Immediately discontinue transfusion
- Save transfusion materials for cultures
- Preserve venous access
- Collect appropriate blood cultures
- Treat with intravenous broad-spectrum antibiotics
- Treat for shock, renal failure and DIC, as needed

Prevention – Bacterial Sepsis

• Donor Selection
  • Donors well and healthy
  • Off of antibiotics for 3 days prior to donation
• Collection of blood
  • Arm scrub
• Component Preparation
  • Use of properly maintained sterile connecting devices
• Bacterial Detection
  • Platelet products
• Pathogen reduction

Viral Diseases –
Occurs 1 in 2-4 million units

Hepatitis
Hepatitis C
HIV

Viral Diseases

• CMV
  • Normal healthy individuals
  • Immune compromised
• Prevention
  • Leukoreduction
  • Sero-negative

Other Transfusion Transmitted Diseases

- **Viral**
  - HTLV-I/II
  - West Nile
  - Zika
- **Prion – CJD**
- **Parasitic –**
  - Babesiosis
  - Chagas
  - Malaria

West Nile Virus

• Mosquito bite
• Mild illness – West Nile fever
• Over 50 years of age – higher risk of serious illness
• WNV encephalitis or meningitis
• Prevention strategies
  • Cover up
  • Insect repellant

Babesiosis – Malaria Like Illness

- Caused by *Babesia microti*, from the bite of an infected deer tick
- More common in the Northeast and upper Midwest; appears to be spreading
- Currently, there is no licensed test for blood screening

Malaria

• Caused by several species of the *Plasmodium* genus; risk in the U.S. is estimated at 0.25 cases per million transfusions

• Donors with a history of travel to malarial endemic areas are deferred.

Chagas’

• Caused by *Trypanosoma Cruzi* infection
  • Endemic to portions of Mexico, Central and South America
  • Relatively high frequency in Texas and California reflecting patterns of immigration
  • Infection with *T Cruzi* may be asymptomatic for years, but can eventually progress to presentation of cardiac or gastrointestinal disease.

• Testing of blood donors was initiated in January 2007, following FDA licensure of a new screening assay.

Zika

- FDA recently approved tests for blood donations
- Travel related and endemic
- FDA Guidance
  - Testing
  - Pathogen Reduction

Source: Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components  FDA, August 2016
Infectious Disease Clinical Follow-up

• Evaluation of the unit
• Evaluation of the doctor
• Evaluation of the recipient
TTD – Reducing the Risk

U.S. Blood units are routinely tested for

• Hepatitis B (HBV) and C (HCV)
• HIV 1 and 2
• Human T-cell Lymphotropic Virus (HTLV) I and I
• West Nile Virus (WNV)
• Syphilis
• *Trypanosoma Cruzi*, the parasite that causes Chagas’ Disease
• Zika (ongoing)

TTD – Reducing the Risk

• Donor screening policies risk factors for infectious disease
  • Travel to malarial endemic areas
  • Travel to Zika areas
  • Travel-related exposure to New Variant Creutzfeldt-Jakob disease (CJD or “mad cow disease”)

• Platelets are now cultured for bacterial contamination prior to release

• Pathogen reduction of platelets a reality

• All of these measures and more continue to reduce the risk of acquiring transfusion transmitted diseases
Best Practices – What the Transfusionist Must Do

• Two-person bedside verification – EVERY TRANSFUSION!
  • Ensures right product to right patient
• Rate of infusion should initially be slow
• Observe patient for first 15 minutes
• Record patient’s vital signs periodically

Source: Primer of Blood Administration, Bethesda, MD” AABB, 2012.
Immediate Actions
When You Suspect a Transfusion Reaction

Do this for ALL suspected transfusion reactions

• Stop the transfusion
• Limit the amount of blood infused
• Maintain IV access

Source: Primer of Blood Administration, Bethesda, MD" AABB, 2012.
Immediate Actions – Notification

• Notify patient’s physician

• Notify Blood Bank

An order from the patient’s physician is NOT required to investigate a suspected transfusion reaction.

Source: Primer of Blood Administration, Bethesda, MD” AABB, 2012.
Immediate Actions – Reporting and Documenting

Follow facility’s requirements

• Signs and symptoms
• Notification
• Vital signs
• Clerical check

Source: Primer of Blood Administration, Bethesda, MD” AABB, 2012.
In Summary

• 40,000 units of blood transfused daily

• Prompt recognition of transfusion effects will keep our patients safe
Questions?
Thank You