

Non-Infectious Transfusion Reactions

(minus TRALI)

Transfusion Medicine

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Transfusion Reactions

- **ANY** unfavorable consequence is considered a transfusion reaction of blood TX
- The **risks** of transfusion must be weighed against the **benefits**

Transfusion Reactions

1. Acute (<24 hours) Transfusion Reactions - Immunologic
 - Hemolytic; Febrile-non hemolytic; Allergic; Anaphylactic; Transfusion Reaction of Acute Lung injury (TRALI)
2. Acute Transfusion Reactions - Nonimmunologic
 - Hemolytic (Physical or Chemical destruction of RBC); Circulatory overload; Air embolus; Hypocalcemia; Hypothermia
3. Delayed (>24 Hours) Transfusion Reaction - Immunologic
 - Hemolytic ; Graft vs. Host Disease; Posttransfusion Purpura
4. Delayed Transfusion Reactions - Nonimmunologic
 - Iron Overload
5. Infectious Complications of Blood Transfusion

Acute (<24 hours) Transfusion Reactions

1. Immunologic

- Hemolytic; Febrile-non hemolytic; Allergic; Anaphylactic; Transfusion Reaction of Acute Lung injury (TRALI)

2. Nonimmunologic

- Volume overload; Hemolytic (Physical or Chemical destruction of RBC); Air embolus; Hypocalcaemia; Hypothermia

Acute Transfusion Reactions

Immunologic

Acute Hemolytic Transfusion Reaction

- Associated with **Intravascular Hemolysis**
- **Etiology:** Antibodies that activate complements in the vasculature: **ABO** antibodies are predominant / not the only ones.
- **Prevention:** Give ABO compatible blood.

Acute Transfusion Reactions

Immunologic

- May also occur due to ABO incompatible plasma in **platelet products**
- Very rare; less than 20 case reports, all involving **group O platelets**
- Usually occurs in group A patients or those with anti-A titers greater than 1:1000
- Can prevent by **removing plasma** from platelets, or limiting number of incompatible group O platelets in a 24 hour period

Intravascular Hemolysis

Characteristics

- Within minutes
- IgM &/or IgG antibody
- Complement activation
- Release of histamine and serotonin

Signs may include:

- Pain along infusion site
- Shock
- Abnormal bleeding/DIC/
Hemoglobinemia/uria
- Release of cytokines: fever, hypotension
- Renal failure/ Oliguria, may progress to...anuria

Acute Transfusion Reactions

Immunologic

Febrile non-hemolytic TX Reactions

- An **INCREASE** in temperature of 1°C during infusion of blood component
 - Usually "mild & benign" = not life threatening
 - Can have more severe symptoms, not usually
- **Non-hemolytic**
- Incidence of 0.1% of RBC transfusions, 0.1-1.0% of platelet transfusions
- **Cause:** Recipient antibodies to donor WBCs & Cytokines in the transfused blood component.

Febrile Transfusion Reactions

Seen in...

- Multiply transfused patients
- Multiple pregnancies
- Previously transplanted

Must rule out...

- Hemolytic transfusion reaction
- Bacterial contamination of unit

Prevention

- **Leukocyte reduction** (pre-storage reduction may be more effective than post-storage reduction) or **plasma removal** is also helpful.

Acute Transfusion Reactions

Immunologic

Allergic (Urticarial-Hives) Transfusion Reactions

- **Etiology:** Form of **cutaneous hypersensitivity** triggered by recipient antibodies directed against:
 - Donor plasma proteins or
 - Other allergens (food, medicines) in donor plasma
- Begins within minutes of infusion
- Characterized by **rash and/or hives** and itching .
- Common (1 per 2000 transfusions)
- Usually involves **release of histamine.**

Allergic (Urticarial) Reactions

- **MUST** be sure that the only reaction is the development of urticaria
- **Must** rule out more severe symptoms that could lead to anaphylaxis:
 - angioneurotic edema
 - laryngeal edema
 - bronchial asthma
- **Prevention:** Can pre-treat recipient with anti-histamines before transfusion.

([Transfus Med Rev 2007;21:1](#), [Br J Haematol 2005;130:781](#)) .

Acute Transfusion Reactions

Immunologic

Anaphylaxis

- Life threatening!!
- Etiology:
 - Recipient is IgA deficient & has anti-IgA in serum
 - Recipient anti-IgA can react to even small amounts of donor IgA in the plasma in any blood component
 - Idiopathic & Haptoglobin deficiency
- Reaction may occur within minutes : Onset of symptoms is SUDDEN
- **Prevention:** Wash cellular components or blood products from IgA deficient

Anaphylaxis

Symptoms

- Burning sensation at infusion site
- Coughing, difficulty in breathing, and bronchospasms can lead to cyanosis
- Nausea, vomiting, severe abdominal cramps, diarrhea
- Hypotension which can lead to shock, loss of consciousness, & death
- **MUST STOP TX IMMEDIATELY**

Acute Transfusion Reactions

Immunologic

TX Reaction of Acute Lung Injury

Etiology:

- Acute onset of hypoxemia and pulmonary edema on CX-RAY within 6 hrs of TX without evidence of cardiac failure.

Mechanism's

- **Primary Suspect: Donor antibodies** to recipient WBCs
- Another cause: **Biologically active lipids** in the lungs causing edema

Transfusion Reaction of Acute Lung Injury (TRALI)

- Symptoms

- Chills, fever, cough, cyanosis, **hypotension**, increased difficulty breathing
- **Prevention:** For recipients : give male products- For donors: watch/defer.

Acute Transfusion Reactions

NONimmunologic

Circulatory Overload

- **Etiology:** Rapid increases in blood volume to patient. **Risk factors:** compromised cardiovascular function, current volume overload, small intravascular volume (elderly, young children), severe chronic anemia.

Signs and Symptoms

- Dyspnea, cyanosis, severe headaches, **hypertension** or CHF (congestive heart failure). Chest Xray: pulmonary edema, distended pulmonary artery, cardiomegaly
- Laboratory: elevated B-natriuretic peptide (BNP) is 81% sensitive and 89% specific ([Transfusion 2005;45:1056](#))
- **Prevention:** Slow Tx. **Treatment:** Stop infusion and place patient in sitting position.

Acute Transfusion Reactions

NONimmunologic

Physically or Chemically Induced
Red Cell Destruction

Etiology:

- Destruction of red blood cells in the collection bag and infusion of free hemoglobin, etc.

Improper temperatures: High or Low

- Microwave blood bag, malfunctioning blood warmer or water bath, inadvertent freezing of blood.

Physically or Chemically Induced Red Cell Destruction

Osmotic Hemolysis

- Addition of drugs or hypotonic solutions (5% dextrose, deionized water, etc.) to transfusion.

Mechanical Hemolysis

- Caused by rollers in blood pump
- Pressure infusion pumps
- Small bore needles
- **Prevention:** Adherence to procedures for all aspects of procuring, processing, issuing and administering red blood cell transfusions.

Acute Transfusion Reactions

NONimmunologic

Hypocalcemia

- **Excess citrate:** When infused at rate >100 mL/minute or individuals with impaired liver function:
 - Citrate is broken down by liver.
- Seen more in pediatric and elderly patients
- **Signs and Symptoms:** Facial tingling, nausea, vomiting.
- **Prevention:** Slowing or discontinuing infusion.

Acute Transfusion Reactions

NONimmunologic

Hypothermia

- **Etiology:** Drop in core body temperature due to rapid infusion of large volumes of cold blood.
- **Symptoms:** Decreased body temperature and ventricular arrhythmias.
- **Seen** in small infants or massive transfusion
- **Prevention:** Reduce rate of infusion or use blood warmers.

Acute Transfusion Reactions

NONimmunologic

Air Embolism

- **Etiology:** If blood in an open system is infused under pressure or if air enters the system while container or blood administration sets are being changed.
- **Treatment:** Place patient on left side with head down to displace air bubble from pulmonic valve.

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Delayed (>24 Hours) Transfusion Reaction -

1. Immunologic

- Hemolytic ; Graft vs. Host Disease;
Posttransfusion Purpura

2. Nonimmunologic

- Iron Overload

Delayed Transfusion Reactions

Immunologic

Delayed Hemolytic Transfusion Reaction (Red blood cell alloimmunization)

- Onset within days (>24 hours)
- Associated with Extravascular Hemolysis
- **Etiology:** Antibodies that usually do **NOT** activate Complements : **Rh, Kell, etc.**
- **Prevention:** Give antigen negative blood.

Extravascular Hemolysis

Characteristics

- Reaction within days
- Antibody attaches to RBC: RBC destroyed in spleen or liver, etc.
- Commonly IgG
- May or may not activate Complement

Signs may include:

- No release of free Hgb, or enzymes into circulation
- May be **immediate** (hours) or **delayed** (days)
- Bilirubinemia or bilirubinuria

Extravascular Hemolysis

Signs & Symptoms continued...

1. Fever or fever & chills
2. Jaundice
3. Unexpected anemia
 - Some may present as an **ABSENCE** of an anticipated increase in Hemoglobin and hematocrit.

Delayed Transfusion Reaction

Immunologic

Graft vs Host Disease (GVHD)

- **Etiology:** Donor CD8+ T-Lymphocytes attack recipient (host) tissues. Very rare in blood stored 4+ days due to WBC inactivation ([Br J Haematol 2000;111:146](#))
- **Groups at risk:**
 - Immunocompromised patients (Cancer, fetus, neonatal, bone marrow transplant).
- **Signs:** Fever, dermatitis, or erythroderma, hepatitis, diarrhea, pancytopenia, etc.
- **Prevention:** Irradiation of blood products.

Delayed Transfusion Reaction

Immunologic

Post-transfusion Purpura

- **Etiology:** Antibodies to platelet antigens (HP1a) causes abrupt onset of severe thrombocytopenia (platelet count $<10,000/\mu\text{l}$) 5-10 days following transfusion. Usually affects multiparous women .
- **Signs:** Purpura, bleeding, fall in platelet count
- **treatment:** IVIG, plasmapheresis or corticosteroids; platelet transfusions usually NOT recommended

Delayed Transfusion Reaction

NONimmunologic

Iron Overload

- **Etiology:** Excess iron resulting from chronically transfused patients such as hemoglobinopathies, chronic renal failure, etc.
- **Signs:** Muscle weakness, fatigue, weight loss, mild jaundice, anemia, etc.
- **Treatment:** Infusion of deferoxamine - an iron chelating agent has been useful.

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Infectious Complications
of
Blood Transfusion
(Viral is rare)

Infectious Complication of Blood Transfusion

Bacterial Contamination

- **Etiology:** At time of collection: either from the donor or the venipuncture site.
 - During component preparation, etc.
- Usually involves **endotoxins**
 - *Staph, Pseudomonas, E.coli, Yersinia*

Bacterial Contamination

- **Components:** Most often from platelet components (room temp). Red cell units will look dark.
- **Symptoms:** **Rapid onset**
 - Fever, hypotension, shaking chills, muscle pain
 - Vomiting, abdominal cramps, bloody diarrhea, hemoglobinuria, shock, renal failure, & DIC.

Bacterial Contamination

Transfusion must be stopped immediately

- **Gram stain & blood cultures** should be done on the unit, patient and all infusion sets .
- **Broad-spectrum antibiotics** should be given immediately intravenously
- **Prevention:** Maintain standards of donor selection, blood collection and proper maintenance of collected blood components.

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Transfusion Reaction Follow-up

Clinical Information Needed:

- Recipient diagnosis
- Medical history of pregnancy &/or transfusion
- Current medications
- Signs & symptoms during transfusion reaction
- How many mL's of RBC's or plasma were transfused?

Clinical Information Needed

- Were rbc's cold or warm when transfused?
- Were red cells infused under pressure?
- What was the size of the needle used?
- Were other solutions given through the IV line at the same time? If so what?
- Were any other drugs given at the time of transfusion? If so, what?
- What were pre- & post- transfusion vital signs?

Transfusion Reaction Follow-up

Post Transfusion Reaction blood samples to be collected from the recipient:

- Clotted specimen
- EDTA specimen
- Clotted specimen
- 1st voided urine specimen post-tx'n
- Repeat ABO, Rh, IAT and Crossmatch. Visual check for hemolysis and compare with pre transfusion sample.
- DAT (Direct Antiglobulin Test)
- Collect 5-7 hours post transfusion to check for bilirubin
- Free hemoglobin determination

Transfusion Reaction Workup

CLERICAL CHECKS

1. Correct identification of patient, specimen, and transfused unit.
2. Agreement of records and history with current results
3. Correct labeling of transfused unit

SPECIMEN CHECKS

- Visual inspection of post-transfusion specimen
- Visual inspection of blood bag and lines

Post Transfusion Lab Testing

Direct Antiglobulin Test (DAT)

- Recipient post-tx'n spec.
- **Positive:** Perform eluate and identify antibody if the pre-TX spec negative.

ABO Grouping and Rh Typing

- **Recipient** pretransfusion and posttransfusion specimen
- **Donor** bag.

Post Transfusion Lab Testing

Indirect Antiglobulin Test (IAT)

- Recipient Pre- & post-transfusion reaction specimens
- **Pre neg and post pos:** Identify antibody and compare results of serum panel with eluate panel.

In Summery:

1-Allergic: Minor **VS** Serious

2-Febrile: Minor **VS** Serious

3-Onset<15 Mints,Temp>1C with other symptoms orTemp>39C, BP↓↑, Shock,SOA, Rigors, Back/Chest Pain,Bleeding from IV site, Tachy/Arrhythmia, Nausea/Vomiting and Generalized Flushing

In Summary:

- 1- **Stop TX immediately** and keep an IV open with 0.9 Saline
- 2-Contact the clinician
- 3-Check vital signs every 15 minutes
- 4-Check **labels, forms, and Ids**
- 5-Send bags & patient's blood to BB
- 6-**Minor**(allergic-febrile non-hemolytic)
VS **Serious** (hemolytic & febrile)

Questions?

Thank You