COMPLICATIONS AND MANAGEMENT OF BLOOD TRANSFUSION REACTIONS

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Prevention is Better than Cure

- Clerical Error Accounts for 85% of all transfusion reaction
- Identify risk factors
  - Previous reactions/History of Allergy
  - Heart Failure/Renal Failure
  - Cold Blood
  - Emergency Transfusion
  - Massive transfusion (>10 units)
- Prepare for Complications (Drugs/Resuscitation)
Classification

- **Serious Reactions**
  - Rare→very rare
  - Severe anaphylaxis
  - Severe hemolysis
  - Causes death/morbidity
  - Requires aggressive treatment

- **Mild reactions**
  - Common
  - Non hemolytic fever/Reaction to WBC antigens
  - Mild allergy to plasma proteins

- Long-term risk (HIV/Hepatitis)
Transfusion reactions

Mild & Common

- Nonhemolytic febrile reactions
- Mild allergic reactions
- Volume overload

Serious but rare

- Acute intravascular hemolysis (very rare)
- Anaphylactic reaction (very rare)
- Acute lung injury (rare)
- Sepsis/Infections (rare)
- Alloimmunisation (rare)
- Transfusion Associated-Host versus Graft Disease (TA-GVHD)
Other reactions/complications

- Electrolyte Abnormalities (Ca++, Mg+2 or K+)
- Coagulation Disorders/Thrombocytopenia
- Hypothermia
<table>
<thead>
<tr>
<th>Risks of Transfusion Complications</th>
<th>Frequency, Episodes/Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reactions</strong></td>
<td></td>
</tr>
<tr>
<td>Febrile (FNHTR)</td>
<td>1–4:100</td>
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<tr>
<td>Allergic</td>
<td>1–4:100</td>
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<tr>
<td>Delayed hemolytic</td>
<td>1:1000</td>
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<tr>
<td>TRALI</td>
<td>1:5000</td>
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<tr>
<td>Acute hemolytic</td>
<td>1:12,000</td>
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<tr>
<td>Fatal hemolytic</td>
<td>1:100,000</td>
</tr>
<tr>
<td>Anaphylactic</td>
<td>1:150,000</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1:63,000</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:1,600,000</td>
</tr>
<tr>
<td>HIV-1</td>
<td>1:1,960,000</td>
</tr>
<tr>
<td>HIV-2</td>
<td>None reported</td>
</tr>
<tr>
<td>HTLV-I and -II</td>
<td>1:641,000</td>
</tr>
<tr>
<td>Malaria</td>
<td>1:4,000,000</td>
</tr>
<tr>
<td><strong>Other complications</strong></td>
<td></td>
</tr>
<tr>
<td>RBC allosensitization</td>
<td>1:100</td>
</tr>
<tr>
<td>HLA allosensitization</td>
<td>1:10</td>
</tr>
<tr>
<td>Graft-versus-host disease</td>
<td>Rare</td>
</tr>
</tbody>
</table>


*Note:* FNHTR, febrile nonhemolytic transfusion reaction; TRALI, transfusion-related acute lung injury; HTLV, human T lymphotropic virus; RBC, red blood cell; HLA, human leukocyte antigen.
Detection of Transfusion Reactions

- **Symptoms**
  - Restlessness, vomiting, headache, dizzy
  - SOB/chest pain
  - Pain over IV site
  - Itchiness
  - Fever
  - Chills & Rigor
  - Abdominal pain
  - Dark urine

- **Signs**
  - Hypotension/hypertension
  - High/Low Temp
  - Hypoxaemia
  - tachycardia
  - Lung crackles
  - Low Hb
  - Hematuria/dark urine
  - Hypocalcemia/hypoK+
  - Pink plasma
  - Abnormal PT or APTT
  - Low haptoglobin
Complications of Acute Transfusion

- **Acute intravascular hemolysis.** Incidence 1/240,000-760,000 units transfused)
  - Cause-
    - ABO incompatibility (Rarely other RBC antigens; Rh, Kell, Duffy)
    - > 85% (clerical error)

- Renal Failure occurs in <1/250,000 units transfused.

- Features: hypotension, tachypnea, tachycardia, fever, chills, hemoglobinemia, hemoglobinuria, chest and/or flank pain, and discomfort at the infusion site
Nonhemolytic febrile reaction.

- Usually mild, fever, chills, rigors, mild dyspnea. Cause: Reaction to donor white cells (HLA) and more common in patients who have had

- Incidence: ≅2–3:100 units transfused

- Due to donor WBC antigens (HLA)

- Risk factors: multiple transfusions or multigravida
- Mild allergic reaction.

- Urticaria or pruritus can be caused by sensitization to plasma proteins in transfusion product. ($\approx 1/100$ units transfused)
- **Anaphylactic reaction.**
  - Acute hypotension, hives, abdominal pain and respiratory distress;
  - seen mostly in IgA-deficient recipients. (<1/1000 units transfused)

- **Sepsis.**
  - <1/500 000 RBC transfused
  - 1/12,000 PLTs transfused
  - Transfusion of bacteria infected blood
  - Common bacteria: E.coli, pseudomonas, serratia, salmonella, yersinia
- **Acute Lung Injury**
  - 1/10, 000 units transfused
  - Fever, chills, respiratory failure
  - Donor against recipient WBC

- **Volume overload.**
  - Usually due to excess volume infusion; can exacerbate CHF.
  - Multiple units/whole blood
  - Observe for lung oedema
TRANSFUSION-ASSOCIATED INFECTIOUS DISEASE RISKS

- **Hepatitis**
  - Incidence: HBV 1:63,000 and HCV 1:103,000 units transfused.
  - Anicteric hepatitis is much more common than hepatitis with jaundice.
  - Screening of donors has greatly reduced these forms of hepatitis.
  - Historically, the greatest risk is with pooled factor products (concentrates of Factor VIII).
  - Use of albumin and globulins involves no risk of hepatitis.

- No HCV screening done in PNG
HIV

- Incidence is <1:600,000 units transfused.

- Rapid HIV Screen test has reduced incidence

- Window period when no antibody detected despite infection is up to 6 weeks

- DNA test required during window period

- Screened in PNG
CMV

- Incidence in donors is very high (approaches 100% in many series),

- Clinically major risk mostly for immuno-compromised recipients, transplant and neonates.

- Leukocyte filters can reduce the risk of transmission if procedures are strictly followed.

- Not screened in PNG
- **HTLV-I, II**
  - Very rare (<<1/641,000 units transfused).
  - Use of leukocyte filters can decrease risk of transmission of HTLV.
  - Not screened in PNG

- **Bacteria and Parasites**
  - Sepsis due to bacteria, malaria & Parasites are very rarely transmitted

  - Careful donor screening is necessary, especially in endemic regions (eg, Chagas’ disease in Central America).

  - Screening for VDRL/RPR done in PNG
- Large Volume Transfusions (eg >10 units PC):
  - Monitor coagulation, Mg2+, Ca2+, and lactate levels.
  - PLT and FFP transfusion is usually necessary
  - Calcium replacement is sometimes needed (citrate)
  - Hypothermia should be avoided
  - Observe for cardiac arrhythmia
Volume Overload

- 1/100 units transfused
- Due to excess volume transfused
- More common with WB/FFP transfusion
- Can worsen heart failure
- Cause pulmonary oedema
Electrolytes Problems

- **Hypocalcemia:**
  - Preservative used (Citrate) in the blood is a calcium binder and hypocalcemia can result after large amounts of blood are transfused.
  - Calcium replacement is sometimes needed.

- **Hyperkalemia** - leakage of K+ out of old RBCs
Hypothermia

- Cold Blood Bags (4 oC RBCs or -18 oC Frozen Blood Products)

- Also, for massive transfusions (usually >50 mL/min in adults and 15 mL/min in children)

- Blood should be warmed to prevent hypothermia and cardiac arrhythmias.
Coagulation Problems

- When transfusing large volumes of packed red cells (>10 units), monitor coagulation.

- It is usually necessary to also transfuse platelets and FFP.
Post-transfusion Purpura

- Thrombocytopenia 7–10 days after post-platelet transfusion
- Predominantly women with Positive Platelet-specific antibodies
- The most frequently recognized antigen is HPA-1a on platelet glycoprotein IIIa receptor.
- Delayed thrombocytopenia is due to the production of antibodies that react to both donor and recipient platelets.
- Avoid further PLT transfusions — can worsen thrombocytopenia
- Treatment: IVI immunoglobulin, or plasmapheresis.
Iron Overload

- Each unit contains 200–250 mg iron; hemochromatosis may develop after 100 U of RBCs (less in children),

- In absence of blood loss; iron chelation therapy with deferoxamine indicated;.
Alloimmunization

- Reaction to RBC antigens (D, c, E. Kelle, Duffy, ) and leukocyte or platelet antigens or plasma proteins
- Detected pre-transfusion testing
- Women at childbearing age are risk----------
  ➔ hemolytic disease of the newborn.
Matching for D antigen is the only pre-transfusion selection test to prevent RBC allo-immunization.

Allo-immunization to antigens on leukocytes and platelets can result in refractoriness to platelet transfusions.

Prevention:
- Removal of leukocytes reduces
- Giving matched RhD blood to pregnant mothers
Graft-versus-Host Disease

- Frequent complication of allogeneic stem cell transplantation

- Lymphocyte from Donor attack HLA antigen and cannot be eliminated by an immunodeficient host.

- Onset: 8–10 days, and death occurs at 3–4 weeks posttransfusion.

- which is manifested clinically by the development of fever, a characteristic cutaneous eruption, diarrhea, and liver function abnormalities

- Marrow aplasia and pancytopenia
- Patients at risk for TA-GVHD include:
  - Fetuses receiving intrauterine transfusions,
  - Selected immunocompetent (e.g., lymphoma patients)
  - Immunocompromised recipients,
  - Recipients of donor units known to be from a blood relative, &
  - Recipients who have undergone marrow transplantation.

- Directed donations by family members should be discouraged (they are not less likely to transmit infection);

- Lacking other options, the blood products from family members should always be irradiated.
Treatment of TA-GVHD

- TA-GVHD is highly resistant to treatment with immunosuppressive therapies, including glucocorticoids, cyclosporine, antithymocyte globulin, and ablative therapy followed by allogeneic bone marrow transplantation.

- Prevention: by irradiation of cellular components (minimum of 2500 cGy) before transfusion to patients at risk.
Managing transfusion reaction

1. Give Stop transfusion
2. Notify Dr/Senior Nurse
3. Notify Blood Bank/Laboratory
4. Continue vitals Measurement
5. Give paracetamol/ibuprofen/diclofenac
6. Give phenergan 12.5-25mg or diphenhydramine 25-50mg IM/IV/PO
Managing transfusion reaction

- If severe reaction: (restless/severe itch/hypotension)
  - Methylprednisolone 125mg IV, 2mg/kg paediatrics
  - Epinephrine/adrenaline 1:1000; 0.1ml/kg (0.3-0.5mls adults) (**Beware – don’t use 1:100**)

- Identify cause & Treat
  - ?infection/?Fluid overload/hemolysis/Pulm Oedema etc

- Future transfusions – premedication/washed cells
Treat cause

- **Nonhemolytic febrile reactions**
  - Antipyretic and continue transfusion
  - Use leucocyte-washed products in future

- **Mild allergic Reaction**
  - Give phenergan/diphenhydramine 25-50mg IV/IM/PO resume transfusion if symptoms improve

- **Anaphylactic Reaction**
  - Washing to remove donor plasma reduces risk of allergic reactions
  - Terminate transfusion
  - Give phenergan, methylpred, adrenaline
  - Use premed in future, or use wbc-washed cells
Treat cause

- **Acute Lung Injury**
  - Ventilation Support & oxygen
  - Use WBC-washed cells in future

- **Sepsis**
  - IV broad spectrum antibiotics

- **Volume overload**
  - Slow infusion (3-4 hours PRBC)
  - Diuretics (lasix)
  - Oxygen
Treat Cause

- **Acute intravascular hemolysis**
  - Place IDC
  - Monitor urine output
  - Ensure diuresis (D5W, mannitol)
  - Diuretics (lasic)
  - +/- dopamine
  - Monitor DIC
  - Consult experienced Specialist /haematologist
References:

1. LG Gomella. Clinician’s Pocket Reference 11th Edition
