Overview of Transfusion Medicine: From A Western World Perspective

Grace Totoe, MBChB, SBB

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Objectives

- Give an overview of role of transfusion medicine in clinical medicine
- Discuss evidence guiding decisions to transfuse
- Complications associated with allogeneic blood transfusions (ABT)
- Quality assurance in transfusion medicine
Blood Banking

- Whole blood collection and component processing
- Infectious disease screening of blood products
- Storage, monitoring, pretransfusion processing
- Distribution of the blood components
- Quality control of the blood components
Whole Blood Collection and Component Processing

Donor

- Plateletpheresis
- Venesection
- Plasmapheresis

Whole blood

Platelet components:
- 1 donation unit, recovered from 1 donation of whole blood
- ‘Pooled’ unit (from 4-6 donation units)
- ‘Single donor’ unit, prepared by apheresis

Red cell components:
- Red cell concentrate
- Red cell suspension (red cells + additive solution)
- Buffy coat depleted red cells
- Leucocyte-depleted (filtered) red cells

Plasma components:
- Fresh frozen plasma
- Liquid plasma
- Freeze-dried plasma
- Cryoprecipitate-depleted plasma
- Viral-inactivated plasma
- Cryoprecipitate

Plasma derivatives:
- Albumin
- Coagulation factors
- Immunoglobulin
Infectious Disease Screening

- At a minimum per WHO
  - Hepatitis B
  - Hepatitis C
  - Syphilis
  - HIV 1 and 2

Also
- Malaria, vCJD, West Nile virus, CMV, HTLV I and II, T cruzi, Babesia
**Laboratory screening for TTIs**

- **Syphilis**
- **HCV**
- **HBV**
- **HIV**

**Number of countries**

- 100%
- <100%
- Not tested

HIV, human immunodeficiency virus; HBV, hepatitis B virus; HCV, hepatitis C virus

Infection Control

- Bacterial cultures

- BacT/Alert bacterial culture technology-relies on CO₂ production by bacteria and detects both anaerobic and aerobic bacteria

- eBDS culture technology- relies on oxygen consumption by bacteria and detects only aerobic bacteria

- Clinical sensitivity is ~50%. (sample volume and time collected). False negative 11%–74% due to low bacteria level in samples.

- Pathogen inactivation for residual risk
  - 4 licensed technologies in Europe-Amotosalen and UV light, Riboflaven and UV light, methylene blue and solvent detergent—all improve blood safety by eliminating residual microorganisms from the plasma
Storage

- RBCs- AS + anticoagulant. Stored at 1-6 °C
- Platelet-AS. Stored at 20-24 °C

FP is stored at -18 °C or less in other countries -30 °C

Monitoring

- Quality measures requires all products to be at the same temperatures, PH->6.2 in 90% of platelets, same WBC count
Leukoreduction

The process of filtering the blood product using special filters that decreases the number of WBCs to $<5 \times 10^6$. (>99.9% in each unit)

- **Benefits**
  - Decrease in febrile reactions
  - Decrease in alloimmunization to leucocytes
  - Decreased in CMV transmission
  - Decreased in TA-GVHD.
  - Irradiators are expensive

**But**

- It is expensive
- ~50% of RBCs with sickle cell trait fail to filter and residual WBC may be higher than allowable limits
Pretransfusion processing

- Washed e.g. IgA deficiency, decreased allergic reactions
- Irradiated e.g. TA-GVHD
- Volume depleted - neonates, CKD patients, chronic CHF
- Deglycerolized - rare blood types, IgA deficiency
**General Guidelines for Hemotherapy**

- **Expected Result:** One unit will increase hemoglobin approximately 1 g/dL and the hematocrit by 3% in a 70 kg adult.

- **Infant/Child Dose:** 2.5-5 mL/kg will increase hemoglobin approximately 1 g/dL; 10-15 mL/kg will increase hemoglobin approximately 2 to 3 g/dL.

- The decision to transfuse should be supported by the need to relieve clinical signs of anemia and improve tissue hypoxia to improve morbidity and mortality. Benefit > risks at all times.
Symptomatic anemia
Acute loss of >25% whole blood volume
Acute loss with inadequate response to volume resuscitation
Hgb < 7g/dl (~8g in certain populations)
Preoperative hgb <8g/dl
May use higher trigger in setting of acute MI
Adult RBC Transfusion Triggers

- TRICC - NEJM 1999 randomized critical care patients (n=838) to transfusion trigger of Hb 7 vs 9 mg/dl

- The mortality rate overall during hospitalization and the 30 day mortality rates for the younger (<55y) and less critically ill were significantly lower in the more restrictive (Hb =7) group.

- FOCUS –NEJM 2011-Functional outcomes in cardiovascular patients undergoing surgical hip fracture repair-No difference in restrictive and liberal group. Hb-8 vrs 10

- TRACS - 2010-Transfusion requirement after cardiac surgery. Hb7 vrs 9. Non inferiority in the restrictive group vrs the liberal group
Mortality in patients refusing Tx: Jehovah’s Witnesses (Carson-Transfusion 42:812)

<table>
<thead>
<tr>
<th>Post op Hb (g/dl)</th>
<th>Total study N</th>
<th>30d mortality: N (%)</th>
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</thead>
<tbody>
<tr>
<td>1.1-2.0</td>
<td>7</td>
<td>7 (100)</td>
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<tr>
<td>2.1-3.0</td>
<td>24</td>
<td>13 (54)</td>
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<tr>
<td><strong>3.1-4.0</strong></td>
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<td><strong>7 (25)</strong></td>
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<tr>
<td>4.1-5.0</td>
<td>32</td>
<td>11 (34)</td>
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<td>5.1-6.0</td>
<td>54</td>
<td>5 (9)</td>
</tr>
<tr>
<td>6.1-7.0</td>
<td>56</td>
<td>5 (9)</td>
</tr>
<tr>
<td>7.1-8.0</td>
<td>99</td>
<td>0 (0)</td>
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Pediatric /NICU RBC Transfusion Trigger

- TRIPICU - RCT. NEJM- 2007 (N-637) - Transfusion requirements in pediatric ICU, a non inferiority trial, patients were randomly assigned Hgb- 7 vs 9.5g. No difference in both groups.

- PINT - The premature infants in Need of transfusion Infants <1kg were randomized to a low or high hemoglobin transfusion threshold. The "low threshold" transfusion group had cutoffs for transfusion that were on average 15-20 g/L.

- Superiority trial: Hypothesis = restrictive tx were superior. 451 neonate 10 NICUs, Canada, US, Australia.

*J Pediatr 2006;149:301-7*
• Inclusion criteria: BW <1kg, < 31 wk, <48hr old
  Groups were similar, with mean birth weight of 770 g and gestational age of 26 weeks

• Outcomes: Death before home discharge or survival with either severe retinopathy, bronchopulmonary dysplasia, or brain injury on cranial ultrasound

• Fewer infants received one or more transfusions in the low threshold group (89% low versus 95% high, P = .037)

• Combined rates of death/severe morbidity were NOT different in low vs. high groups
CONCLUSIONS

In extremely low birth weight infants, maintaining a higher hemoglobin level results in more infants receiving transfusions but confers little evidence of benefit.
Adult Platelet Guidelines

- One platelet concentrate will raise count \( \sim 7-10 \times 10^5 \) per ul. Hence pool of 5-6 or one apheresis (3x \( 10^{11} \)) is typical adult dose.

- Platelet <10K in non-bleeding patient.

- Platelet <50K in surgical patient.

- Diffuse microvascular bleeding-platelet dysfunction.

- Qualitative platelet defect (antiplatelet drug).
Platelet Transfusion Trigger

- PLADO - RCT of prophylactic platelet transfusions in patients with hypoproliferative thrombocytopenia to determine
  - the effects of the dose of platelets on clinical signs of bleeding, the use of platelet and red cell transfusions, changes in the recipient's post-transfusion platelet count, days to next transfusion and adverse events
  - The primary end point of the study was one episode of bleeding of WHO grade 2

- Conclusion-The dose of platelets transfused had no significant effect on the incidence of bleeding in patients with hypoproliferative thrombocytopenia and platelet counts no greater than $10 \times 10^9/l$. 
Adult Plasma Guidelines

- Given to correct multiple deficiencies of plasma coagulation factors

- Inappropriate when PT or PTT < 1.5 X normal

- Diffuse micro vascular bleeding in patient transfused > 1 blood volume (e.g. massive transfusion with >10 units of RBCs in 24 hours)

- Therapeutic apheresis for TTP
Risks of Transfusion

- **Infectious**
  - (HIV, Hep B and Hep C, CMV, Babesia, Anaplasmosis, Malaria)

- **Non-infectious**
  - Volume related- TACO
  - Immunologic-TRIM
  - Allergic transfusion reactions
  - TRALI, ABO, other hemolytic, allergic, febrile

- **Other-age of blood**
Figure 1: Transfusion-Related Fatalities by Complication, FY2007 through FY2011

<table>
<thead>
<tr>
<th>Complication</th>
<th>TRALI</th>
<th>HTR (non-ABO)</th>
<th>HTR (ABO)</th>
<th>Microbial Infection</th>
<th>TACO</th>
<th>Anaphylaxis</th>
<th>Other</th>
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<td>FY07</td>
<td>34</td>
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<td>3</td>
<td>4</td>
<td>4</td>
<td>2</td>
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TRALI

BEFORE Transfusion

AFTER Transfusion
Transfusion Associated Complications

- **Non-Infectious Complications**
  - **Acute < 24 hours**
    - 1 in 100: Febrile non-hemolytic reaction with universal leukocyte reduction
    - 1 in 100: Minor Allergic reactions (urticaria )
    - <1 in 100: Transfusion associated circulatory overload
    - 1 in 5000: Transfusion-related acute lung injury (TRALI)
    - 1 in 33,000-1:20,000: Hemolysis associated with ABO/Rh incompatibility
    - 1 in 100,000-1 in 600,000: Fatal HTR
    - 1 in 20,000-1:500000: Anaphylaxis

- **Delayed >24hours**
  - 1:10: Alloimmunization, HLA antigens
  - 1:100: Alloimmunization, RBC antigens
  - 1 in 2500: Delayed hemolytic transfusion reaction
  - 1 in 200,000: Post Transfusion Purpura
  - 1 in 400,000: TA-GVHD
Infectious Complications of Transfusion

Infectious Complications-Bacterial

RBCs

- 1 in 31,385  Incidence of bacterial contamination in RBCs
- 1 in 500,000  Clinically relevant septic reaction with RBCs transfusion
- 1 in 10,000,000  Risk of fatal septic reaction in RBCs

Platelets

- 1 in 5000  Incidence of bacterial contamination in platelets
- 1 in 75,000  Clinically relevant septic reaction with platelets transfusion
- 1 in 500,000  Risk of fatal septic reaction in platelets
Infectious Complications - Viral

- 1 in 20,000  
  Transmission of Parvovirus
- 1 in 250,000  
  Transmission of Hepatitis B
- 1 in 3,000,000  
  Transmission of HTLV-I
- 1 in 7,000,000  
  Transmission of West Nile Virus
- 1 in 1,200,000  
  Transmission of hepatitis C virus
- 1 in 1,200,000  
  Transmission of HIV

Infectious Complications – Parasites

- 1 in 4,000,000  
  Transmission of Plasmodium spp (falciparum, malariae, ovale, vivax)

Unknown rate of Transmission

- Transfusion transmission of Babesiosis (1:1000 in CT)
- Transmission of trypanosome Cruzi
- Transfusion transmission of Erlichia chaffeensis
- Transfusion transmission of Anaplasma phagocytophila
- Transfusion transmission of HHV8
- Transfusion transmission of CMV(HHV5)
Transfusion-associated infections: 50 years of relentless challenges and remarkable progress

Herbert A. Perkins and Michael P. Busch

Fig. 2. Declining incidence of transfusion-associated hepatitis in transfusion recipients monitored prospectively at the NIH Clinical Center. Incidence of hepatitis, traced from 1969 to 1998, demonstrated a decrease in risk from 33% to nearly zero. Arrows indicate main interventions in donor selection and screening that effected this change. Reproduced from Alter, with permission from the American Society of Hematology.
Blood transfusion practice in a rural hospital in Northern Ghana, Damongo, West Gonja District

Chrysantus Kubio, Geraldine Tierney, Theophilus Quaye, James Wewoli Nabilisi, Callistus Ziemah, Sr Mary Zagbeeb, Sandra Shaw, and William G. Murphy

Fig. 1. Infections and coinfections in the 2009 donor population. The underlying rates were 7.5% (64/853) for HBsAg, 6.1% (50/819) for HCV, 3.9% (33/846) for HIV, and 4.7% (22/468) for syphilis. The accuracy for the incidence of coinfection rates is compromised by the variations in testing rates among donors, due to unavailability of some test kits at some times.
Transfusion associated metabolic complications

- Hyperkalemia - more in patients with renal failure
- Hyperglycemia/hypoglycemia - pediatrics (paradoxical)
- Hypocalcemia
- Metabolic Alkalosis
- Iron overload - chronic anemia with recurrent transfusion eg Patients with aplastic anemia, hemoglobinopathies, etc. (? After >100 RBC transfusions)
The purpose of quality assurance is to maximize patient care and minimize risk. The most risk-free transfusion is the one never given. Minimizes transfusion risks, cost effective and saves products for those recipients who most need them.
Quality Assurance in Transfusion Medicine

- Organizations that have policies that guide the industry to ensure standardization and ensure processes work as intended to.

- Reduces variations in practice and works to optimize patient safety ultimately.

- Voluntary - AABB, CAP, Joint commission

- Government regulatory bodies - FDA, AMS-CLIA, DHHS
Relevant to Physicians

- **Proper documentations and record keeping**
  
  - SOPS for blood banks, sickle cell transfusions, transfusion guidelines, transfusion reaction forms available and accessible to all. - Organization website
  
  - *Chart documentation*: e.g. Two units of RBCs to be transfused. Consent taken from patient, risks and benefit of transfusion discussed with the patient. Questions and concerns addressed.
Monitoring and Assessing

- Quality indicator e.g. turn around time when blood products are ordered
- Blood utilization assessment
- Internal assessments
- External evaluation
- Proficiency testing for laboratories
Process Improvement

- Identification of problems and their causes
  - Root cause analysis
- Identification and evaluation of solutions
- ISBT Bar coding technology to identify patients.
Process Improvement

Fatal Transfusion Reaction

- **Laboratory based error** - wrong blood drawn/typing error/improper documentation
- **Physician error** - proper indication/proper forms filled with clear legible writing/premedicated if needed
- **Systems Error** - inadequate equipment for resuscitation/lack of trained personnel for resuscitation/lack of guidelines/standardization

Process Improvement
Summary

- Obtain Informed consent prior to transfusion and document clearly the indication for transfusion.

- Hemotherapy should be based on national guidelines as well as hospital-developed guidelines approved by the medical staff and the Transfusion committee → research

- Blood transfusion should be supported by the need to relieve clinical signs of anemia and improve tissue hypoxia to improve morbidity and mortality not based on the Hb level

- Adverse outcomes should be reported to the blood bank

- Benefit > risk

- Cost
Guidelines for Patient Blood Management and Blood Utilization

Quality Assurance and Patient Safety

Blood Management

Nonsurgical and Preoperative
- Anemia screening
  - Maximize hemoglobin
    - erythropoietin
    - iron therapy
  - Optimize coagulation
    - discontinue herbal and vitamin supplements
    - discontinue anti-coagulants and antiplatelet drugs
  - address genetic coagulation abnormalities
- Minimize crystalloids in acute bleeding
- Limit phlebotomy
- Autologous donation

Intraoperative Strategies
- Wound drainage
  - Tolerate low hemoglobin
  - Limit phlebotomy
  - Monitor bleeding
  - Replacement fluids
    - crystalloid
    - colloid
    - Hyperbaric oxygen
  - Iron therapy
  - Erythropoietin
  - Intraoperative blood recovery
    - devices available
    - trained, dedicated operators
    - wash or not?

Postoperative Strategies
- Coagulation management
- Acute normovolemic hemodilution
- Component sequestration
- Surgical techniques
  - harmonic scalpel
  - rinse swabs
  - suction control
- Point-of-care testing/microsampling
- Hemostatics
  - platelet gel
  - fibrin sealant
  - topical thrombin
  - Tolerate low blood pressure
  - Avoid hypothermia
  - Tolerate low hemoglobin
  - Small volume in bypass circuit
  - Monitor acute bleeding
  - Positioning

Blood Utilization Review
- Thresholds
- Indications
- Transfusion Safety Officer
- Transfusion Committee
- Auditing
References

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