Blood Transfusion Guidelines in Clinical Practice

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Introduction

- clinical practice guidelines are necessary for the practice of evidence-based medicine.

- Only over the past 20 years, we have seen a more concerted effort to answer very basic questions regarding the value of transfusion therapy through:
  - randomized, controlled trials
  - Systematic reviews
  - development of clinical practice guidelines
Blood transfusions carry risks, are costly, and the supply of blood is limited.

Patients must be evaluated individually to determine the proper transfusion therapy, taking care to avoid inappropriate over- or under- transfusion.

Transfusion decisions should be based on clinical assessment and not on laboratory values alone.
WHEN WE SHOULD TRANSFUSE?
TO TRANSFUSE
WHEN
NECESSARY
Principles of Clinical Transfusion Practices

- Avoid blood transfusion
- Transfusion is only one part of the patient’s management.
- Prevention and early diagnosis and treatment of Anemia & underlying condition
- Use of alternative to transfusion eg. IV fluids
- Good anesthetic and surgical management to minimized blood loss.
Considerations for Therapy

- Does the patient need blood products.
- What are the alternative options for treatment.
- Using the product that will be most effective in providing the desired outcome.
- Minimum donor exposure.
- What is the patients view of treatment.
Triggers of Component Transfusion

recommendations are made by an American Society of Anesthesiologists Task Force:

1. Transfusion is rarely indicated when the hemoglobin level is above 10 g/dL and is almost always indicated in patients when the hemoglobin level is below 6 g/dL;

2. The determination of transfusion in patients whose hemoglobin level is 6-10 g/dL should be based on: organ ischemia, bleeding, the patient’s intravascular volume status and risk of complications due to inadequate oxygenation.
Triggers of Component Transfusion

The lowest threshold for transfusion of components are:

- Hb level of 6-7g/dl.
- FFP threshold PT & PTT 1.5 times the upper limit of the normal range.
- Platelet threshold of:
  - 10 000/µl- 20 000/µl for prophylactic transfusion.

Consider: Clinical judgment
Triggers of Platelet Transfusion

- 20 000/µl for BMA and Biopsy

- 50 000/µl for surgery, massive transfusion, Liver cirrhosis.

- 100 000/µl for surgery to brain or eye.

  Consider: Clinical judgment
Blood Administration and Documentation

- Documentation used in ordering or administering blood components should include the clinical and laboratory indication and collect standardized data items.

- Documentation of transfusion events including: informed consent
  
  pretransfusion laboratory testing (e.g., hemoglobin, prothrombin time/international normalized ration (INR), and platelet count) should be documented
  
  the clinical indications for transfusion of blood components.
Blood Administration and Documentation

- Patient identification and transfusion order (blood identification number) must be confirmed before the initiation of blood
- Date and time of transfusion
- Blood pressure, pulse, and temperature recorded before, during, and after transfusion
- Adherence to such requirements should be monitored by the hospital's quality department or transfusion committee
Red Blood Cells as a Therapeutic Products
RBCs Indications

Red blood cells are indicated:

- for patients with a symptomatic deficiency of oxygen-carrying capacity or tissue hypoxia due to an inadequate circulating red cell mass.

- for exchange transfusion (e.g., for hemolytic disease of the newborn) and red cell exchange (e.g., for acute chest syndrome in sickle cell disease).
Red Blood Cells as a therapeutic Product:

Proper uses of red Blood cell (RBC) Transfusion

- Treatment of symptomatic anemia
- Prophylaxis in life-threatening anemia
- Restoration of oxygen-carrying capacity in case of Hemorrhage
- PRBC are also indicated to exchange transfusion
  - Sickle cells disease
  - Severe parasitic infection (malaria, babesiosis)
  - Severe methemoglobinemia
  - Severe hyperbilirubinemia of newborn
# Guidelines for RBC transfusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Design (N)</th>
<th>Population</th>
<th>Transfusion threshold</th>
<th>Primary outcome(s)</th>
<th>Secondary outcome(s)</th>
<th>General conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hebert et al&lt;sup&gt;9&lt;/sup&gt; (TRICC)</td>
<td>RCT (838)</td>
<td>Stable, critically ill patients &gt; 16 y of age with Hb &lt; 9 g/dL</td>
<td>Restrictive (Hb &lt; 7 g/dL) vs liberal (Hb &lt; 10 g/dL)</td>
<td>Death within 30 d of randomization</td>
<td>Death at 60 d, assessment of organ dysfunction</td>
<td>Restrictive transfusion strategy is at least as effective and possibly superior to a liberal transfusion strategy with the possible exception of patients with acute myocardial infarction or unstable angina</td>
</tr>
<tr>
<td>Lacroix et al&lt;sup&gt;10&lt;/sup&gt; (TRIPICU)</td>
<td>RCT (637)</td>
<td>Stable, critically ill children with Hb &lt; 9.5 g/dL</td>
<td>Restrictive (Hb &lt; 7 g/dL) vs liberal (Hb &lt; 9.5 g/dL)</td>
<td>Death within 28 d of randomization, development or progression of MODS</td>
<td>Daily assessment of organ dysfunction, sepsis, transfusion reactions, infections, adverse events, length of stay, overall mortality</td>
<td>Restrictive transfusion strategy decreases transfusion requirements without increasing adverse events</td>
</tr>
<tr>
<td>Carson et al&lt;sup&gt;11&lt;/sup&gt; (FOCUS)</td>
<td>RCT (2016)</td>
<td>Adults &gt; 50 y of age with history or risk factors for cardiovascular disease with Hb &lt; 10 g/dL after hip fracture surgery</td>
<td>Restrictive (Hb &lt; 8 g/dL) vs liberal (Hb &lt; 10 g/dL)</td>
<td>Death or inability to walk across a room at 60 d follow-up</td>
<td>In-hospital myocardial infarction, unstable angina, or death</td>
<td>Liberal transfusion strategy did not reduce rate of death or inability to walk at 60 d follow-up</td>
</tr>
<tr>
<td>Villanueva et al&lt;sup&gt;14&lt;/sup&gt;</td>
<td>RCT (921)</td>
<td>Adult patients with severe upper gastrointestinal bleeding</td>
<td>Restrictive (Hb &lt; 7 g/dL) vs liberal (Hb &lt; 9 g/dL)</td>
<td>Death within 45 d of randomization</td>
<td>Rates of further bleeding or hospital complications</td>
<td>Restrictive transfusion strategy was associated with improved outcomes</td>
</tr>
</tbody>
</table>

MODS indicates multiple-organ dysfunction syndrome; FOCUS, Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair; RCT, randomized, controlled trial; TRICC, Transfusion Requirements in Critical Care; and TRIPICU, Transfusion Requirements in Pediatric Intensive Care Unit.

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Outcomes Using Lower vs Higher Hemoglobin Thresholds for Red Blood Cell Transfusion

Jeffrey L. Carson, MD; Paul A. Carless, MMedSc (Clin Epid); Paul C. Hébert, MD, MSc


- **Clinical Question:** Is a lower vs higher hemoglobin threshold best for minimizing both red blood cell use and adverse clinical outcomes when used to trigger red blood cell transfusions in anemic patients in critical care and acute care settings?

- **Bottom Line:** Compared with higher hemoglobin thresholds, a hemoglobin threshold of 7 or 8 g/dL is associated with fewer red blood cell units transfused without adverse associations with mortality, cardiac morbidity, functional recovery, or length of hospital stay.
Guidelines for blood component therapy

<table>
<thead>
<tr>
<th>Haemoglobin (Hb) trigger for transfusion</th>
<th>Indications</th>
<th>NB: Hb should not be the sole deciding factor for transfusion.</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7 g/dL</td>
<td>• If there are signs or symptoms of impaired oxygen transport</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lower thresholds may be acceptable in patients without symptoms and/or where specific therapy is available e.g. sickle cell disease or iron deficiency anemia</td>
<td></td>
</tr>
<tr>
<td>&lt; 7 – 8 g/dL</td>
<td>• Preoperative and for surgery associated with major blood loss.</td>
<td></td>
</tr>
<tr>
<td>&lt; 9 g/dL</td>
<td>• In a patient on chronic transfusion regimen or during marrow suppressive therapy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• May be appropriate to control anaemia-related symptoms.</td>
<td></td>
</tr>
<tr>
<td>&lt; 10 g/dL</td>
<td>• Not likely to be appropriate unless there are specific indications.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Acute blood loss &gt;30-40% of total blood volume.</td>
<td></td>
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</tbody>
</table>
| Guidelines for routine blood leucodepletion | 1. transfusion dependent patients  
2. Bone marrow transplant candidates – either autologous / peripheral blood stem cell transplants (PBSCT) or allogeneic bone marrow transplants  
3. may be for Patients undergoing intensive chemotherapy regimens  
4. Previous repeated febrile reactions to red blood cells |
| Guidelines for blood Irradiation (to prevent TAGVHD) | 1. Intrauterine transfusion (IUT) and neonates received IUT.  
2. One week prior to stem cell collection, and for 12 months post autografting or allografting.  
3. Hodgkin’s disease  
4. Treatment with purine analogues (fludarabine, 2-CdA, deoxycofomycin)  
5. Aplastic anaemia within 6 months of ATG treatment  
6. Products obtained from close relatives or HLA matched donors.  
7. Immunodeficiency patients: congenital or acquired |
General Guidelines For Small-volume (10-15 mL/kg) Transfusion To Infants:

Maintain HCT between:

- 40-45% in Severe cardiopulmonary disease (e.g., mechanical ventilation >0.35 FiO2)

- 30-35% in moderate cardiopulmonary disease (e.g., less intensive assisted ventilation such as nasal CPAP or supplemental oxygen)

- 30-35% in Major surgery

- 20-30% in Stable anemia, especially if unexplained breathing disorder or unexplained poor growth
Accepted Indications for Transfusion in Sickle Cell Disease:

- Severe anemia
- Prevention of stroke in children with abnormal transcranial Doppler studies
- Acute splenic sequestration
- Stroke and Prevention of stroke recurrence
- Transient red cell aplasia
- Chronic debilitating pain
- Pulmonary hypertension
- Anemia associated with chronic renal failure
- Acute chest syndrome
- Acute multi-organ failure
Fresh Frozen Plasma and Cryoprecipitate As a therapeutic Products
Rationale for Use of FFP

1. Prevent bleeding in patients with abnormal coagulation results who require urgent surgery or invasive procedures.

2. Treat bleeding in patients with abnormal coagulation results.
Indications for Plasma Transfusion

the Transfusion Practices Committee of the AABB recommended plasma therapy for only a few clinical indications, based on the available evidence in the literature:

- trauma patients with substantial hemorrhage
- patients undergoing complex cardiovascular surgery
- patients with intracranial hemorrhage or severe bleeding due to warfarin therapy, or urgent reversal of warfarin effect
Indications for Plasma Transfusion

- Active bleeding due to deficiency of multiple coagulation factors, or risk of bleeding due to deficiency of multiple coagulation factors.
- Massive transfusion with coagulopathy bleeding.
- Bleeding or prophylaxis of bleeding for a known single coagulation factor deficiency for which no concentrate is available.
- Thrombotic thrombocytopenic purpura.
- Rare specific plasma protein deficiencies, such as C1-inhibitor.
## Acquired Plasma Coagulopathies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Coagulation Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver disease - mild</td>
<td>Abnormal PT</td>
</tr>
<tr>
<td>Liver disease - moderate to severe</td>
<td>Abnormal PT, PTT, D-Dimer, platelet function</td>
</tr>
<tr>
<td>Acute DIC</td>
<td>PT, PTT, low platelet count, low fibrinogen, elevated D-Dimer</td>
</tr>
<tr>
<td>Postoperative bleeding</td>
<td>Minimal PT &amp; PTT elevation, low platelet count</td>
</tr>
<tr>
<td>Massive Transfusion</td>
<td>Minimal PT &amp; PTT elevation, low platelet count</td>
</tr>
<tr>
<td>Vitamin K deficiency, mild</td>
<td>PT (factor VII)</td>
</tr>
<tr>
<td>Vitamin K deficiency, moderate to severe</td>
<td>PT &amp; aPTT (II, VII, IX, X)</td>
</tr>
</tbody>
</table>
## Warfarin Reversal Guidelines

<table>
<thead>
<tr>
<th>INR</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>Withhold warfarin until INR therapeutic</td>
</tr>
<tr>
<td>&gt;5 &amp; &lt;9</td>
<td>Withhold 1 or 2 doses&lt;br&gt;Give 2.5 mg Vitamin K orally, especially if patient is at high risk of bleeding&lt;br&gt;For rapid reversal for surgery, give 2.5 - 5.0 mg Vitamin K orally</td>
</tr>
<tr>
<td>&gt;9</td>
<td>Hold warfarin &amp; give 5 mg Vitamin K orally</td>
</tr>
<tr>
<td>&gt;20</td>
<td>Hold warfarin &amp; give 10 mg vitamin K SC or IV &amp; PCC or FFP</td>
</tr>
</tbody>
</table>
FFP not indicated in:

- Fluid resuscitation
- ‘Nutritional’ supplementation
Indications for Cryoprecipitate Transfusion

- Cryoprecipitate is indicated for bleeding associated with fibrinogen deficiencies and Factor XIII deficiency.

- Patients with hemophilia A or von Willebrand’s disease (vWD) should only be treated with cryoprecipitate when appropriate Factor VIII concentrates or Factor VIII concentrates containing FVIII: vWF are not available.
## FFP trigger for transfusion

<table>
<thead>
<tr>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Multiple coagulation deficiencies associated with acute DIC.</td>
</tr>
<tr>
<td>- Inherited deficiencies of coagulation inhibitors in patients undergoing high-risk procedures where a specific factor concentrate is unavailable.</td>
</tr>
<tr>
<td>- Thrombotic thrombocytopenia purpura (plasma exchange is preferred)</td>
</tr>
<tr>
<td>- Replacement of single factor deficiencies where a specific or combined factor concentrates is unavailable.</td>
</tr>
<tr>
<td>- Immediate reversal of warfarin effect in the presence or potentially life-threatening bleeding when used in addition to Vitamin K &amp; / or Factor Concentrate (Prothrombin concentrate)</td>
</tr>
<tr>
<td>- The presence of bleeding and abnormal coagulation parameters following massive transfusion or cardiac bypass surgery or in patients with liver disease</td>
</tr>
</tbody>
</table>

**PT & PTT are more than 1.5 times the upper limit of normal range**

## Cryoprecipitate trigger for transfusion

<table>
<thead>
<tr>
<th>Indications</th>
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<tbody>
<tr>
<td>- Congenital or acquired fibrinogen deficiency including DIC.</td>
</tr>
<tr>
<td>- Hemophilia A, von Willebrand disease (if the concentrate is not available).</td>
</tr>
<tr>
<td>- Factor XIII deficiency.</td>
</tr>
</tbody>
</table>

**Fibrinogen< 1gm/L**
Platelets As a Therapeutic Product
Rationale for Platelet Transfusion

Current guidelines from the European Union and United States recommend a transfusion trigger of of $10 \times 10^9/l$ for platelets transfused prophylactically.

These guidelines are based on outcomes from four randomized clinical trials that compared prophylactic triggers of $10 \times 10^9/l$ versus $20 \times 10^9/l$ in patients with acute leukemia and in autologous and allogeneic hematopoietic stem cell transplant recipients.

A recent trial demonstrated that “low-dose” prophylactic platelet transfusions are equally effective as those with “standard” or “high” dose.
Indications for Platelet Transfusion

- Use to treat bleeding due to critically decreased circulating platelet counts or functionally abnormal platelets.

- Use prophylactically to prevent bleeding at pre-specified low platelet counts. In general, maintain platelet count >10,000/mm3 in stable, non-bleeding patients, >20,000/mm3 in unstable non-bleeding patients and >50,000/mm3 in patients undergoing invasive procedures or actively bleeding.
<table>
<thead>
<tr>
<th>Platelet Count trigger for transfusion</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 x 10⁹/L</td>
<td>• As prophylaxis in bone marrow failure.</td>
</tr>
<tr>
<td>&lt; 20 x 10⁹/L</td>
<td>• Bone marrow failure in presence of additional risk factors: fever, antibiotics, evidence of systemic haemostatic failure. (unstable patients)</td>
</tr>
</tbody>
</table>
| < 50 x 10⁹/L                          | • Massive haemorrhage or transfusion.  
• In patients undergoing surgery or invasive procedures.  
• Diffuse microvascular bleeding-DIC |
| < 100 x 10⁹/L                         | • Brain or eye surgery. |
| Any Bleeding Patient                  | • Appropriate when thrombocytopenia is considered a major contributory factor. |
| Any platelet count                    | • In inherited or acquired qualitative platelete function disorders, depending on clinical features & setting. |
Alternative to Blood Transfusion

- The use of alternative measures to reduce allogeneic red cell use should be considered, including
  - preoperative autologous donation,
  - operative and pharmacologic measures that reduce blood loss.
  - acute normovolemic hemodilution.
  - intra-operative and post-operative autologous blood recovery.
Conclusions

For effective clinical use of blood components:

- Ensure a safe and adequate supply of blood and blood products.

- Establish a national committee on the clinical use of blood to develop national guidelines on the clinical use of blood.

- Establish a national haemovigilance system to monitor, report and investigate adverse events associated with transfusion.
Conclusions

Establish transfusion committees in each hospital in which transfusion takes place to:

- Establish a system to monitor and evaluate blood usage
- Ensure appropriate prescribing of blood and blood products in accordance with national or local guidelines.
- Establish Patient Blood Management Program to improve patient care and optimize blood component usage.
Conclusions

Provide training for all clinicians, nurses, BTS/hospital blood bank staff and other personnel involved in the transfusion process on:

- Prevention, early diagnosis and effective treatment of conditions that could result in the need for transfusion.
- Safe pre-transfusion procedures
- Safe administration of blood and blood products.
- Management of Adverse Reaction

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THANKS
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SCITECH, Alkhobar

Presentation by:
Distinguished International & National Speakers

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