Transfusion Guidelines: Less is Best (usually)

Nursing Transfusion Medicine Boot Camp
March 26, 2018
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Conflicts of Interest

• No commercial conflicts to declare
• ORBCoN, for which I am a consultant, is funded by the Ministry of Health and Long Term Care
• I acknowledge a preference for a restrictive approach to transfusion whenever possible
Objectives

1. Explain the rationale for using restrictive transfusion practices.
2. Describe the recommendations for transfusing red cells, plasma, and platelets in the Choosing Wisely Canada statements.
3. List the Quality Indicators in the Ontario Transfusion Quality Improvement Plan.
Question 1

What is the recommended red cell transfusion threshold for stable adult inpatients, including patients in the ICU?

1. Hb 60 g/L
2. Hb 70 g/L
3. Hb 80 g/L
4. Hb 90 g/L
5. Hb 100 g/L
Question 2

What are the two quality indicators for red cell transfusion in the Ontario Transfusion Quality Improvement Plan? (choose 2)

1. % transfusions with pre-transfusion Hb < 70 g/L
2. % transfusions with pre-transfusion Hb < 80 g/L
3. % single unit transfusions (1 unit ordered at a time)
4. % transfusions with documented consent on the chart
5. % RBC inventory wasted by the hospital for any reason
Ontario Regional Blood Coordinating Network (ORBCoN)

- Created by the Ministry of Health and Long Term Care in 2006, and funded by the ministry
- Mission: “Inspiring and facilitating best transfusion practices in Ontario”
- Focus is on hospital transfusion practice
- Education for physicians, technologists, nurses, midwives
Transfusion Guidelines

Well-designed, appropriately powered randomised controlled trials → Systematic reviews → Clinical practice guideline (CPG) → CPG endorsed by professional organisations and/or health authorities → Evidence-based medicine → Optimised patient care, Improved patient outcomes
Evaluating Evidence

• Grades of Recommendation Assessment, Development, and Evaluation (GRADE)
• Developed by an international working group starting in 2000, published in the BMJ in 2008
• A system for evaluating the quality of evidence supporting a recommendation, and the strength of the recommendation
<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (randomised controlled trial)</td>
<td>Strong</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Low (observational study)</td>
<td>Weak</td>
</tr>
<tr>
<td>Very low</td>
<td></td>
</tr>
</tbody>
</table>
Randomised Controlled Trial (RCT)

Transfusion Requirements in Critical Care (TRICC) Trial

829 ICU patients with Hb < 90

416 restrictive strategy
Transfused at Hb < 70
Hb maintained at 70-90

413 liberal strategy
Transfused at Hb < 100
Hb maintained at 100-120

Primary End points:
Death from all causes at 30 days
Severity of organ dysfunction

Hebert. NEJM 1999;340:409
TRICC Trial: Results

- Overall 30-day mortality not significantly different

Hebert. NEJM 1999;340:409
Observational Study

Safety of LP for Children with ALL and Thrombocytopenia

Retrospective chart review of 5223 lumbar punctures in children with ALL and thrombocytopenia

- Platelet count <10
- Platelet count 11-20
- Platelet count 21-50

- Serious complications e.g. spinal hematoma

Howard. JAMA 2000;284(17):2222
# Prophylactic PLTs in LP

<table>
<thead>
<tr>
<th>PLT</th>
<th>Number of LPs</th>
<th>95% CI for complications, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 5</td>
<td>6</td>
<td>0-40.19</td>
</tr>
<tr>
<td>6 – 10</td>
<td>23</td>
<td>0-13.21</td>
</tr>
<tr>
<td>11 – 20</td>
<td>170</td>
<td>0-2.05</td>
</tr>
<tr>
<td>21 – 30</td>
<td>234</td>
<td>0-1.49</td>
</tr>
<tr>
<td>31 – 40</td>
<td>235</td>
<td>0-1.48</td>
</tr>
<tr>
<td>41 – 50</td>
<td>273</td>
<td>0-1.27</td>
</tr>
<tr>
<td>51 – 100</td>
<td>858</td>
<td>0-0.40</td>
</tr>
<tr>
<td>&gt; 100</td>
<td>3424</td>
<td>0-0.10</td>
</tr>
<tr>
<td>Total</td>
<td>5223</td>
<td>0-0.07</td>
</tr>
</tbody>
</table>

No serious complications at any platelet count.

Prophylactic transfusion is not necessary if platelet count >10 in this population.

Howard. JAMA 2000;284(17):2222
Some Studies Are Not Done

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Problem – no control group

Smith. BMJ 2003;327:1459
Evolution of Approach to Red Cell Transfusion

Liberal (pre-TRICC trial 1999)
- the transfusion threshold is higher; Hb 90 or 100
- routine order may be for 2 units
- MORE blood is transfused

Restrictive
- the transfusion threshold is lower; Hb 70 or 80
- routine order is for 1 unit
- LESS blood is transfused
Why Restrictive Transfusion?

- Evidence supports the safety of restrictive practice
- Risk of adverse events is often dose dependent
- Blood supply is limited (volunteer donors)
- Costs:
  - blood products
  - transfusing them
  - adverse events
![Diagram showing study results with risk ratios and confidence intervals.]

Carson. NEJM 2017;377:1261
Restrictive vs liberal transfusion. Outcome: 30 day mortality same.

Risk of receiving a transfusion ↓43% with restrictive strategy.

Carson. NEJM 2017;377:1261
AABB Red Cell Recommendations 2016

1. Hb threshold 70g/L for:
   - hospitalized adult patients
   - hemodynamically stable
   - including critically ill patients

2. Hb threshold 80 g/L for:
   - cardiac surgery
   - orthopedic surgery
   - pre-existing cardiovascular disease

3. Excluded conditions:
   - acute coronary syndrome
   - severe thrombocytopenia
   - chronic transfusion-dependent anemia
   - insufficient evidence

"...standard practice should be to initiate a transfusion with 1 unit of blood rather than 2 units".
Red Cells

1. Don’t transfuse blood if other non-transfusion therapies or observation would be just as effective.
   • e.g. hemodynamically stable patients with iron deficiency anemia should be treated with iron therapy

2. Don’t transfuse more than one red cell unit at a time when transfusion is required in stable, non-bleeding patients.
   • 1U RBC raises the Hb by about 10 g/L in the non-bleeding patient
Ontario Transfusion Quality Improvement Plan (launched April 2016)

- Narrative template
- Quality improvement plan template (spreadsheet)
- Clinical Practice Recommendations for Blood Component Use in Adult Inpatients
  - red cells, plasma, platelets
- Order Set template
- Technologist Screening Tools
- Tracker Tool for reporting audit results

See ORBCoN website →
## Ontario RBC Recommendations:
### Adult Inpatient

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb &lt;60 g/L</td>
<td>Transfusion likely appropriate. <strong>1 unit</strong> and re-check patient and Hb (healthy/younger patients may tolerate lower Hb)</td>
</tr>
<tr>
<td>Hb &lt;70 g/L</td>
<td>Consider transfusion. <strong>1 unit</strong> and re-check patient and Hb</td>
</tr>
<tr>
<td>Hb &lt;80 g/L</td>
<td>Consider transfusion if pre-existing cardiovascular disease or evidence of impaired tissue oxygenation. <strong>1 unit</strong> and re-check patient and Hb</td>
</tr>
<tr>
<td>Hb 80-90 g/L</td>
<td>Likely inappropriate unless evidence of impaired tissue oxygenation.</td>
</tr>
<tr>
<td>Hb &gt;90 g/L</td>
<td>Likely inappropriate. Clearly document rationale for transfusion and discuss with patient.</td>
</tr>
</tbody>
</table>
| Bleeding patient | • Maintain Hb >70 g/L  
                  | • If pre-existing cardiovascular disease maintain Hb >80 g/L |
### Blood Product Order Set Template RBC/PLT/ FP - Adult

<table>
<thead>
<tr>
<th>Allergies/Sensitivities</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ none known</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Admitting Diagnosis:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Informed consent completed as per institutional guidelines</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date of transfusion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ today</td>
</tr>
<tr>
<td>□ STAT (call blood bank at XXXXX)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-transfusion laboratory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ group and screen</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous transfusion within 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous pregnancy within 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Previous transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If no existing IV initiate IV 0.9% NaCl to keep vein open</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ disconnect peripheral IV after transfusion complete</td>
</tr>
</tbody>
</table>

### Red Blood Cells

**Pre-transfusion Hb:** _____ g/L  
**Indication:** □ low Hb  □ significant bleeding  □ symptomatic  □ other

- **Transfuse 1 unit, over _____ hours** (e.g. 1 unit over 2-3 hours, maximum 4 hrs)

**Pre-transfusion Hb:** _____ g/L  
**Indication:** □ low Hb  □ significant bleeding  □ symptomatic  □ other

- □ Transfuse 1 unit, over _____ hours (e.g. 1 unit over 2-3 hours, maximum 4 hrs)
- □ Transfuse ____ units, each over ____ hours

**Note:** Consider IV iron instead of red blood cells for patients with stable iron deficiency anemia
Blood Order Screening

- Orders screened by the blood bank technologists
- Similar to pharmacy screening of drug orders
- To ensure that orders comply with institutional guidelines
- To clarify the reason for the order e.g. patient has signs or symptoms of impaired tissue oxygenation or a relevant clinical history that would justify transfusion
- To enable a discussion between the ordering physician and the blood bank physician if necessary
Significant Signs and Symptoms of Anemia?

- Dyspnea, chest pain
- Syncope, presyncope
- Dizziness upon walking/standing
- HR >100 bpm, systolic BP < 90 mmHg
  - unresponsive to fluid challenge
- ST changes on ECG, positive troponin
- not fatigue, pallor or decreased exercise tolerance alone
Technologist Screening in an Ontario Community Hospital

Events per 100 acute inpatient days (AIPD)

RBC units transfused

hospital deaths

RBC/100 AIPD: 5.38 to 3.71

month 2012-2015
OTQIP Indicators

1. % RBC transfusions with a pre-transfusion Hb < 80 g/L
   - eventual goal 80%
   - justification: matching best performance

2. % RBC transfusions which are single unit
   - prescribe 1 unit at a time and reassess the patient (preferably including Hb) before second unit
   - eventual goal 80%
   - justification: matching best performance
Ontario hospitals: % pre-Tx Hb < 80
How soon can the post-transfusion CBC be drawn?

15 minutes

Acute anemia, normovolemic GI patients

Elizade. Transfusion 1997;37:573

General medicine ward, not bleeding

4. Don’t routinely transfuse platelets for patients with chemotherapy-induced thrombocytopenia if the platelet count is greater than $10 \times 10^9$/L in the absence of bleeding.
<table>
<thead>
<tr>
<th>Indication</th>
<th>Threshold PLT count</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy-induced thrombocytopenia</td>
<td>≤ 10</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Elective central venous catheter</td>
<td>&lt; 20</td>
<td>Low</td>
<td>Weak</td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>&lt; 50</td>
<td>Very low</td>
<td>Weak</td>
</tr>
<tr>
<td>Major surgery</td>
<td>&lt; 50</td>
<td>For perioperative bleeding only</td>
<td>Weak</td>
</tr>
<tr>
<td>Cardiopulmonary bypass</td>
<td>For perioperative bleeding only</td>
<td>Very low</td>
<td>Weak</td>
</tr>
<tr>
<td>Intracranial bleed and anti-platelet therapy</td>
<td>cannot recommend for or against</td>
<td>Very low</td>
<td>Uncertain</td>
</tr>
</tbody>
</table>

## AABB Platelet Guideline 2014

<table>
<thead>
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<th>Indication</th>
<th>Threshold PLT count</th>
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</tr>
</tbody>
</table>

**Prophylactic PLTs before Lumbar Puncture?**

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Recommended PLT count</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Plan for the Management of Blood Shortages (Canada)</td>
<td>50 in Green Phase 20 in Amber Phase</td>
</tr>
<tr>
<td>AABB (U.S.)</td>
<td>50</td>
</tr>
<tr>
<td>Use clinical judgment for 20-50</td>
<td></td>
</tr>
<tr>
<td>British Committee for Standards in Haematology</td>
<td>40</td>
</tr>
<tr>
<td>C17 Guidelines (Children’s Oncology Group, Canada)</td>
<td>20</td>
</tr>
<tr>
<td>Cardiovascular and Interventional Radiology Society of Europe</td>
<td>50</td>
</tr>
<tr>
<td>American Society of Clinical Oncology</td>
<td>Discusses evidence for 20 More research needed</td>
</tr>
</tbody>
</table>
References for Previous Slide

2. Estcourt. BJH 2017;176:365
3. New. BJH 2016;175:784
4. www.C17.ca
## Recommended PLT Transfusion Thresholds

Dose is 1 pool of 4 single-donor platelets or 1 apheresis unit

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>PLT</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-immune thrombocytopenia</td>
<td>&lt;10</td>
<td>1 dose</td>
</tr>
<tr>
<td>Procedures not associated with significant blood loss</td>
<td>&lt;20</td>
<td>1 dose</td>
</tr>
<tr>
<td>Therapeutic anticoagulation that cannot be stopped</td>
<td>&lt;30</td>
<td>1 dose, consult thrombosis expert</td>
</tr>
<tr>
<td>• Epidural anesthesia, LP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• major surgery (EBL &gt;500 mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Significant bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Head trauma, neuraxial surgery</td>
<td>&lt;50</td>
<td>1 dose immediately before procedure and check platelet count before starting procedure</td>
</tr>
<tr>
<td>• Life threatening hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet dysfunction (e.g. anti-platelet drugs, post CPB) with significant hemorrhage</td>
<td>any</td>
<td>1 dose</td>
</tr>
<tr>
<td>Immune thrombocytopenia (ITP)</td>
<td>any</td>
<td>Transfuse for life-threatening bleeding only, consult hematologist</td>
</tr>
</tbody>
</table>
Plasma

- Dose is 15 mL/kg
  - = 3-5 units for an adult (250 mL/unit)
- Each dose increases coagulation factor levels by 20%
3. Don’t transfuse plasma to correct a mildly elevated (<1.8) INR or aPTT before a procedure.

- a mildly elevated INR is not predictive of bleeding risk
- transfusion of plasma has not been demonstrated to significantly change the INR value when the INR was only mildly elevated (<1.8)
Effect of FP with Mild Elevation of INR
(121 patients with INR 1.1 to 1.9)

Failed to correct the INR in 99% of patients
<table>
<thead>
<tr>
<th>Diagnosis/Indication</th>
<th>INR</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significant bleeding</td>
<td>greater than 1.7</td>
<td>Plasma 15 mL/kg (3-5 units) Note: Plasma transfusion is not required before minor procedures (IV, arterial line, PICC, thoracentesis, paracentesis, bone marrow procedure).</td>
</tr>
<tr>
<td>• Liver disease AND planned invasive procedure associated with blood loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Massive transfusion</td>
<td>greater than 1.5-2.0 or unknown and cannot wait for INR result</td>
<td>Plasma 15 mL/kg (3-5 units) For massive transfusion: 2U plasma for every 4U red cells</td>
</tr>
<tr>
<td>• Microvascular bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin reversal/Vitamin K deficiency AND</td>
<td>greater than 1.5</td>
<td>DO NOT USE PLASMA unless PCC unavailable or contraindicated (e.g. history of heparin-induced thrombocytopenia). Administer 10 mg IV Vit K with the PCC or plasma.</td>
</tr>
<tr>
<td>• Emergency surgery (in &lt; 6 hrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Significant bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ontario Recommendations 2016</strong></td>
</tr>
</tbody>
</table>
Dosing Plasma: Less May Not Be Better Here!

2U is dose for 33 kg (73 lb) pt
Dose I 15 mL/kg, 3-5 units for adult
Why Restrictive Transfusion?

- Evidence supports the safety of restrictive practice
- Blood supply is limited (volunteer donors)
- Risk of adverse events is often dose dependent
- Costs:
  - blood products
  - transfusing them
  - adverse events
# Risks of Transfusion (non-viral)

<table>
<thead>
<tr>
<th>Risk of Event</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 in 100</td>
<td>Transfusion-associated circulatory overload (TACO)</td>
</tr>
<tr>
<td>1 in 10,000</td>
<td>Transfusion related acute lung injury (TRALI)</td>
</tr>
<tr>
<td>1 in 40,000</td>
<td>ABO-incompatible transfusion per RBC transfusion</td>
</tr>
<tr>
<td>1 in 40,000</td>
<td>Serious allergic reaction per unit of component</td>
</tr>
<tr>
<td>1 in 200,000</td>
<td>Death from bacterial sepsis per pool of platelets</td>
</tr>
</tbody>
</table>

Most common causes of death from transfusion: TACO, TRALI, wrong ABO, anaphylaxis, sepsis
8 Rights of Transfusion

- Patient (hemolysis)
- Product (PCC vs plasma)
- Dose (volume overload)
- Route (hemolysis)
- Time (volume overload)
- Documentation (consent, vital signs)
- Reason (within guidelines)
- Response (adverse reactions, lab results)
Transfusion Associated Circulatory Overload

- Pulmonary edema in at-risk patients
  - older (>70 yrs), renal insufficiency
  - LV dysfunction, heart failure
  - severe anemia but normal blood volume

- Volumes of blood components:
  - RBC 300 mL, platelets 350 mL, FP 250 mL/unit (adult dose 3-5 units)

- Slower infusion rate, over 3-3½ hrs

- Pre-transfusion furosemide, monitor vital signs
Blood Supply: CBS Inventory Report Feb 14, 2018

Daily Red Cell and Platelet Inventory Status

CBS Site: Brampton
Current Date: 2018-02-14
Time: 03:00 Hrs EST

If you require this report in an accessible format, please contact your local Hospital Liaison Specialist.

RED BLOOD CELL INVENTORY

Days On Hand Local Inventory

- O Pos
- A Pos
- B Pos
- AB Pos
- O Neg
- A Neg
- B Neg
- AB Neg

www.transfusionontario.org
Costs of Transfusion

• CBS acquisition cost RBC $423
  – total cost to transfuse it about $670 (Alberta 2014)
• One US review $760 USD per RBC transfused (2008)

Ellingson. Transfusion 2017;57:1588
Shander. Transfusion 2010;50:753
Costs of Transfusion Reactions

- Conservative estimate of cost of investigation of a febrile non-hemolytic transfusion reaction $160 (Toronto 2013-2015)
- Every transfusion carried an embedded cost of $2.16 for the cost of reactions (Netherlands 2016)
  - CBS issued 735,000 red cells in 2017/2018, so maybe $1.6M in reaction costs for red cells only

Cohen. Transfusion 2017;57:1674

Janssen. Vox Sanguinis 2018;113:143
Summary

• Restrictive transfusion practices address the issues of evidence-based practice, patient safety, preservation of the blood supply, and costs

• The Ontario Transfusion Quality Improvement Plan quality indicators are: % transfusions with pre-transfusion Hb less than 80 g/L, and % single unit transfusions
Summary

• The Hb threshold for stable adult inpatients, including ICU patients, is 70 g/L
• The platelet threshold for prophylactic platelet transfusion in therapy-induced thrombocytopenia is $10 \times 10^9$/L
• Plasma transfusion in the non-bleeding patient is unlikely to be effective if the INR is 1.7 or less
Question 1

What is the recommended red cell transfusion threshold for stable adult inpatients, including patients in the ICU?

1. Hb 60 g/L
2. Hb 70 g/L
3. Hb 80 g/L
4. Hb 90 g/L
5. Hb 100 g/L
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What is the recommended red cell transfusion threshold for stable adult inpatients, including patients in the ICU?

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Question 2

What are the two quality indicators for red cell transfusion in the Ontario Transfusion Quality Improvement Plan? (choose 2)

1. % transfusions with pre-transfusion Hb < 70 g/L
2. % transfusions with pre-transfusion Hb < 80 g/L
3. % single unit transfusions (1 unit ordered at a time)
4. % transfusions with documented consent on the chart
5. % RBC inventory wasted by the hospital for any reason
Question 2

What are the two quality indicators for red cell transfusion in the Ontario Transfusion Quality Improvement Plan? (choose 2)

1. % transfusions with pre-transfusion Hb < 70 g/L
2. % transfusions with pre-transfusion Hb < 80 g/L
3. % single unit transfusions (1 unit ordered at a time)
4. % transfusions with documented consent on the chart
5. % RBC inventory wasted by the hospital for any reason
Thank you. Questions?

Please consider donating blood or bone marrow
www.blood.ca