Transfusion Medicine Topics & Case Studies

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Transfusion Medicine & Hematology, Sunnybrook Health Sciences Centre
Associate Professor, Dept of Laboratory Medicine & Pathobiology
OAP AGM Oct 1, 2016
12:15 – 13:00 Lecture & 13:15- 14:15 Interactive Case Studies
Disclosures

• Grants/Research Support
  – Canadian Blood Services, Glaxo-Smith Kline, Novartis, University of Toronto

• Consultancy/Advisory Board
  – Genzyme, Boehringer-Ingelheim, Pfizer

• Unrestricted educational grant for Transfusion Camp
  – CSL Behring, Grifols, ORBCoN
Outline

• 12:15-13:00 – Didactic session
  – Where we are moving with transfusion in Ontario
  – Ontario Transfusion Quality Improvement Plan
  – Update on Transfusion Guidelines & Risks

• 13:00-13:15 – Buffet lunch

• 13:15-14:15 – Interactive case studies
  – Work through cases and how to handle them as the TM medical director
  – Review literature with each case
Objectives

At the end of the session, attendees will:

- Be able to provide advice on appropriate indications for blood transfusion
- Be able to consult effectively on management of transfusion reactions
- Seek out more information on transfusion and visit the ORBCoN website at www.transfusionontario.org
- Rate transfusion medicine consultation as an important component for the laboratory services offered by your hospital/institution
The ultimate goal...

Institute of Medicine
High Quality Healthcare = Improves Health Outcomes

Effective
Safe
Patient Centred
Timely
Efficient
Equitable

Health Quality Ontario
A just, patient-centred health system committed to relentless improvement
What is Quality in Transfusion?

- The right sample
- The right test result
- The right equipment
- The right bag
- The right patient
- The right decision to transfusion
So how are we doing?

Inappropriate RBC Transfusion

12-36%
Critical Care Societies

- Don’t transfuse red blood cells in hemodynamically stable, non-bleeding ICU patients with a hemoglobin concentration greater than 70 g/L.

American Society of Hematology

- Don’t transfuse more than the minimum number of red blood cell (RBC) units necessary to relieve symptoms of anemia or to return a patient to a safe hemoglobin range (70 to 80 g/L in stable, non-cardiac in-patients).

American Society of Anesthesiologists

- Don’t administer packed red blood cells (PRBCs) in a young healthy patient without ongoing blood loss and hemoglobin of ≥ 60 g/L unless symptomatic or hemodynamically unstable.

http://www.choosingwisely.org/
Canadian Society for Transfusion Medicine

- Don’t transfuse more than one red cell unit at a time when transfusion is required in stable, non-bleeding patients.
- Don’t transfuse blood if other non-transfusion therapies or observation would be just as effective.

American Association of Blood Banks

- Don’t transfuse more units of blood than absolutely necessary.
- Don’t transfuse red blood cells for iron deficiency without hemodynamic instability.

Pre-transfusion Hb < 80 g/L
(excluding outpatients 20-25%)

ORBCON RBC Audit, 2013, unpublished data
Percent Single Unit Transfusions
(excluding outpatients 20-25%)

A: 25
B: 37
C: 35
D: 33
E: 32
F: 78

ORBCON RBC Audit, 2013, unpublished data
Ontario Transfusion QIP Committee

OTQIP
- Tom Alloway, patient
- Jennifer Bawden, MLT
- Donna Berta, RN
- Chris Campbell, MLT
- Craig Ivany, CEO
- Yulia Lin, MD
- Menaka Pai, MD
- Robert Romans, CBS
- Lisa Ruston, Quality
- Danielle Watson, MLT
- Sophie Yang, MOH
- Sandra Fazari, MLT

Recommendations WG
- Allison Collins, MD
- Michelle Zeller, MD
- Kathryn Webert, MD
- Elianna Saidenberg, MD
- Yulia Lin, MD

Technologist Screening WG
- Lisa Richards, MLT
- Barb Silveri, MLT
- Melanie Tokessy, MLT
- Sandra Baker, MLT
- Krista Walkers, MLT

Health Quality Ontario       Choosing Wisely Canada
Quality Improvement Plan

Title & Information

Ontario Transfusion Quality Improvement Plan Guidance Document for Institutional Implementation

This document was created to provide guidance on how to implement quality improvement activities to reduce unnecessary RBC transfusion at your institution or hospital. It can be used as a template by transfusion medicine committees or institutional (hospital) departments or incorporated in the institution’s corporate quality improvement plan.

Quality Improvement Plan Tools

http://transfusionontario.org
Guidance Document

How to develop a formal Quality Improvement Plan
(Narrative and QIP template)

Module 1

How to do a simplified RBC transfusion audit

Module 2

How to implement local transfusion guidelines

Module 3

How to implement MLT prospective transfusion order screening

Key role of the Transfusion Medicine Medical Director
# Clinical Practice Recommendations (Adult Inpatient - RBC)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb less than 60 g/L</td>
<td>Transfusion likely appropriate*. Transfuse 1 unit and re-check patient symptoms and Hb before giving second unit.</td>
</tr>
<tr>
<td>Hb less than 70 g/L</td>
<td>Consider transfusion. Transfuse 1 unit and recheck patient symptoms and Hb before giving second unit.</td>
</tr>
<tr>
<td>Hb less than 80 g/L</td>
<td>Consider transfusion in patients with pre-existing cardiovascular disease or evidence of impaired tissue oxygenation. Transfuse 1 unit and recheck patient symptoms and Hb before giving second unit.</td>
</tr>
<tr>
<td>Hb 80 to 90 g/L</td>
<td>Likely inappropriate unless evidence of impaired tissue oxygenation.</td>
</tr>
<tr>
<td>Hb greater than 90 g/L</td>
<td>Likely inappropriate. If transfusion is ordered clearly document indication in patient’s chart and discuss reason with patient.</td>
</tr>
<tr>
<td>Bleeding patient</td>
<td>- Maintain Hb greater than 70 g/L</td>
</tr>
<tr>
<td></td>
<td>- If pre-existing cardiovascular disease – maintain Hb greater than 80g/L</td>
</tr>
</tbody>
</table>

http://transfusionontario.org
TRICC – Critical Care

838 ICU pts

Transfuse 1 unit at a time and measure Hb

Restrictive Hb < 70 g/L

Liberal Hb < 100 g/L

<table>
<thead>
<tr>
<th></th>
<th>Restrictive</th>
<th>Liberal</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 d mortality</td>
<td>19%</td>
<td>23%</td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>2.6 units</td>
<td>5.6 units</td>
</tr>
</tbody>
</table>

P=NS

P<0.01

Hebert PC et al. NEJM 1999;340:409-17
FOCUS – Elderly & Cardiac

2016 Hip fracture pts
Average 81 yrs
Cardiac or RF for Cardiac

Transfuse if Hb < 80 g/L or symptoms
Transfuse if Hb < 100 g/L

<table>
<thead>
<tr>
<th></th>
<th>Transfuse 1 unit at a time and measure Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or unable to walk</td>
<td>34.7%</td>
</tr>
<tr>
<td>60 d death</td>
<td>6.6%</td>
</tr>
<tr>
<td>Total RBC units</td>
<td>652</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Transfuse 1 unit at a time and measure Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or unable to walk</td>
<td>35.2%</td>
</tr>
<tr>
<td>60 d death</td>
<td>7.6%</td>
</tr>
<tr>
<td>Total RBC units</td>
<td>1866</td>
</tr>
</tbody>
</table>

No difference
P<0.001

Carson JL et al. NEJM Dec 29, 2011; 365:2453-62
Acute UGI Bleeding

921 pts with severe UGIB

Noted increased portal pressure gradient in liberal group

Transfuse 1 unit at a time and measure Hb

Restrictive
Hb < 70 g/L

Liberal
Hb < 90 g/L

<table>
<thead>
<tr>
<th></th>
<th>Restrictive</th>
<th>Liberal</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 week survival</td>
<td>95%</td>
<td>91%</td>
<td>0.02</td>
</tr>
<tr>
<td>Further bleeding</td>
<td>10%</td>
<td>16%</td>
<td>0.05</td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>1.5 units</td>
<td>3.7 units</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Villanueva et al. NEJM Jan 2013;368:11-21
TRISS – Septic Shock

998 ICU pts
70% on Mech Ventilation

Transfuse 1 unit at a time

Restrictive
Hb < 70 g/L

Liberal
Hb < 90 g/L

<table>
<thead>
<tr>
<th></th>
<th>Restrictive</th>
<th>Liberal</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 d mortality</td>
<td>43%</td>
<td>45%</td>
<td>P=NS</td>
</tr>
<tr>
<td>RBC transfusion</td>
<td>1 (IQR 0-3)</td>
<td>4 (IQR 2-7)</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

Holst al. NEJM 2014
AABB RBC Guideline 2012

Endorsed by National Advisory Committee on Blood and Blood Products | Comité consultatif national sur le sang et les produits sanguins

• In hospitalized, hemodynamically stable patients, at what hemoglobin should a RBC transfusion **be considered**?
  – In adult and pediatric ICU patients, transfusion should be considered at 70 g/L or less.

• In hospitalized, hemodynamically stable patients with preexisting cardiovascular disease, at what hemoglobin should a RBC transfusion **be considered**?
  – Transfusion should be considered at 80 g/dL or less or for symptoms (chest pain, hypotension or tachycardia, or CHF).

Why 1 unit at a time?

Evidence-based
Hemodynamically stable pts

Common!
1 in 100 RBC transfusions

TACO
Transfusion-associated circulatory overload

33%
of serious adverse transfusion reactions reported to TTISS 2006-2012

Most common cause of
life-threatening transfusion reactions
TTISS 2006-2012
Clinical Practice Recommendations (Adult Inpatient - Platelets)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Platelet Count ( \times 10^9/\text{L} )</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-immune thrombocytopenia</td>
<td>Less than 10</td>
<td>1 dose</td>
</tr>
<tr>
<td>Procedures not associated with significant blood loss, including percutaneous</td>
<td></td>
<td>1 dose</td>
</tr>
<tr>
<td>procedures other than epidural anesthesia or lumbar puncture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic anticoagulation that cannot be stopped</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Epidural anesthesia or lumbar puncture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Procedures with expected blood loss greater than 500ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Major non-neuraxial surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Significant bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Neuraxial surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Head trauma or CNS hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Life-threatening hemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Platelet dysfunction and significant bleeding e.g. ASA, clopidogrel therapy,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• post cardiopulmonary bypass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Immun thrombocytopenia (ITP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>holemologist</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RCT – 20 vs. 10 in AML

Proportion without Major Bleeding

Threshold, 20,000 platelets/mm³

Threshold, 10,000 platelets/mm³

P = 0.54

Rebulla et al. NEJM 1997;337:1870-5
AABB Platelet Guideline 2015

- **Plt < 10 x 10⁹/L**: Prophylactic transfusion in hypoproliferative thrombocytopenia
- **Plt < 20 x 10⁹/L**: Central venous catheter placement
- **Plt < 50 x 10⁹/L**: Major elective surgery, Lumbar puncture
- **No specific recommendation**: Antiplatelet agents and ICH

Clinical Practice Recommendations (Adult Inpatient - Plasma)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>INR</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant bleeding</td>
<td>Greater than 1.7</td>
<td>3-4 units</td>
</tr>
<tr>
<td>Liver disease with coagulopathy and invasive procedure planned (see Notes below)</td>
<td>Greater than 1.5 to 2.0 or unknown and cannot wait for result</td>
<td>3-4 units</td>
</tr>
<tr>
<td>Microvascular bleeding</td>
<td>Greater than 1.5 to 2.0 or unknown and cannot wait for result</td>
<td>3-4 units</td>
</tr>
<tr>
<td>Massive transfusion</td>
<td>Greater than 1.5 to 2.0 or unknown and cannot wait for result</td>
<td>3-4 units</td>
</tr>
</tbody>
</table>

http://transfusionontario.org
Why?

A mildly elevated INR is not predictive of an increased risk of bleeding.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Studies</th>
<th>AbN</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchoscopy</td>
<td>2</td>
<td>42</td>
<td>No difference</td>
</tr>
<tr>
<td>Angiography</td>
<td>3</td>
<td>104</td>
<td>No difference</td>
</tr>
<tr>
<td>Liver biopsy</td>
<td>2</td>
<td>122</td>
<td>No difference</td>
</tr>
<tr>
<td>- Hi risk + plug</td>
<td>3</td>
<td>147</td>
<td>No difference</td>
</tr>
<tr>
<td>- Transjugular</td>
<td>5</td>
<td>421</td>
<td>No difference</td>
</tr>
<tr>
<td>Kidney biopsy</td>
<td>2</td>
<td>19</td>
<td>No difference</td>
</tr>
<tr>
<td>Mixed procedures</td>
<td>2</td>
<td>30+</td>
<td>No difference</td>
</tr>
<tr>
<td>CV cannulation</td>
<td>3</td>
<td>735</td>
<td>No major bleeding except 1 arterial puncture</td>
</tr>
</tbody>
</table>

Segal JB, Dzik WH et al. Transfusion 2005;45:1413-25
Some procedures do NOT require plasma regardless the INR!

- 1,100 paracenteses
- Setting: no ultrasound guidance, no transfusion of platelets or plasma for any count abnormality
- Lowest platelet count was 19 (IQR 42-56)
- Highest INR was 8.7 (IQR 1.4-2.2)
- No significant bleeding in any patient
For INR 1.3-1.8, plasma does not change INR

Median Decrease = -0.07

## Clinical Practice Recommendations (Adult Inpatient - Plasma)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>INR</th>
<th>Recommendation and dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significant bleeding</td>
<td>Greater than 1.7</td>
<td>3-4 units</td>
</tr>
<tr>
<td>• Liver disease with coagulopathy and invasive procedure planned (see Notes below)</td>
<td>Greater than 1.5 to 2.0 or unknown and cannot wait for result</td>
<td>3-4 units</td>
</tr>
<tr>
<td>• Microvascular bleeding</td>
<td></td>
<td>3-4 units</td>
</tr>
<tr>
<td>• Massive transfusion</td>
<td></td>
<td>3-4 units</td>
</tr>
<tr>
<td>• Urgent warfarin reversal and</td>
<td>Greater than 1.5</td>
<td>Do not use plasma unless prothrombin complex concentrate (PCC) is not available or is contraindicated (e.g. history of heparin-induced thrombocytopenia). Administer 10 mg IV Vitamin K with the PCC or plasma.</td>
</tr>
<tr>
<td>o Serious bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>o Urgent surgical procedure required within 6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Congenital coagulation factor deficiency where a factor concentrate is not available and</td>
<td>any</td>
<td>Consult a hematologist</td>
</tr>
<tr>
<td>o Serious bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>o Urgent surgical procedure required</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Asymptomatic high INR on Warfarin

- Hold warfarin or small dose of vitamin K

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>INR</th>
<th>Vitamin K Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCP 2012</td>
<td>INR &gt; 10</td>
<td>oral (no dose stated)</td>
</tr>
<tr>
<td>BCSH 2011</td>
<td>INR &gt; 8</td>
<td>oral 1-5 mg</td>
</tr>
<tr>
<td>Aus/NZ 2013</td>
<td>INR &gt; 10</td>
<td>oral/IV 3-5 mg</td>
</tr>
<tr>
<td></td>
<td>INR 4.5-10 + high risk for bleeding</td>
<td>oral 1-2mg or IV 0.5-1mg</td>
</tr>
</tbody>
</table>

Non-urgent procedure or bleed

- Non-major bleeding
  - Determine if reversal is necessary
  - BCSH 2011: Vitamin K 1-3mg IV
  - Auz/NZ 2013: Vitamin K 1-2 mg PO or 0.5-1 mg IV

- Non-emergency surgery within 24 hours
  - Determine if reversal is necessary
  - Vitamin K 5-10 mg IV if complete reversal desired
Emergent reversal

- Limb or life-threatening bleeding requiring reversal within 6 h
- Urgent surgery that cannot be delayed for 6 h

- All patients receive vitamin K 10 mg IV and Prothrombin Complex Concentrates (PCC)
<table>
<thead>
<tr>
<th>PCC</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contains factors II, VII, IX, X</td>
<td>Contains all clotting factors</td>
</tr>
<tr>
<td>Pooled, virally inactivated</td>
<td>Not virally inactivated</td>
</tr>
<tr>
<td>Prion reduction process</td>
<td></td>
</tr>
<tr>
<td>Lyophilized</td>
<td>Needs ABO group (10min)</td>
</tr>
<tr>
<td>Needs to be reconstituted</td>
<td>Needs to be thawed (30min)</td>
</tr>
<tr>
<td>Volume 40-80mL</td>
<td>Volume 15mL/kg (~1000mL)</td>
</tr>
<tr>
<td>Infused over 15-30min</td>
<td>Infused over hours</td>
</tr>
<tr>
<td>Less risk of transfusion reactions</td>
<td>Risk of transfusion reactions:</td>
</tr>
<tr>
<td></td>
<td>TRALI, TACO, anaphylaxis</td>
</tr>
<tr>
<td>$560 for 1000 units$¹</td>
<td>$156 for 4 units plasma²</td>
</tr>
</tbody>
</table>

4F-PCC vs. Plasma: Major Bleed

- Major bleed, INR ≥ 2 on warfarin

<table>
<thead>
<tr>
<th>Results</th>
<th>PCC</th>
<th>Plasma</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemostatic efficacy at 24 h from start of infusion</td>
<td>72%</td>
<td>65%</td>
<td>No difference</td>
</tr>
<tr>
<td>INR ≤ 1.3 at 0.5 h after end of infusion</td>
<td>62%</td>
<td>10%</td>
<td>PCC faster</td>
</tr>
</tbody>
</table>
4F-PCC vs. Plasma: Major Bleed

Sarode et al. Circulation 2013;128:1234-43
# 4F-PCC vs. Plasma: Major Bleed

- Major bleed, INR ≥ 2 on warfarin

<table>
<thead>
<tr>
<th>Results</th>
<th>PCC</th>
<th>Plasma</th>
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<td>65%</td>
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</tr>
<tr>
<td>INR ≤ 1.3 at 0.5 h after end of infusion</td>
<td>62%</td>
<td>10%</td>
<td>PCC faster</td>
</tr>
<tr>
<td>Thrombotic Events</td>
<td>8%</td>
<td>6%</td>
<td>No difference</td>
</tr>
<tr>
<td>Fluid Overload</td>
<td>5%</td>
<td>13%</td>
<td>PCC fewer events</td>
</tr>
</tbody>
</table>

Sarode et al. Circulation 2013;128:1234-43
# How to implement local guidelines

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prepare</strong></td>
<td>Baseline audit results showing need for improvement</td>
</tr>
<tr>
<td></td>
<td>Clinical practice recommendations for blood component use</td>
</tr>
<tr>
<td><strong>Engage Transfusion Committee</strong></td>
<td>Committee reviews and modify recommendations, if needed</td>
</tr>
<tr>
<td><strong>Disseminate</strong></td>
<td>Disseminate widely to medical and surgical departments, professional practice committees, transfusion medicine laboratory staff, etc.</td>
</tr>
<tr>
<td></td>
<td>Educate staff</td>
</tr>
<tr>
<td><strong>Incorporate Feedback</strong></td>
<td>Transfusion committee reviews and approves final recommendations</td>
</tr>
<tr>
<td><strong>Final Approval</strong></td>
<td>Present to MAC for final approval</td>
</tr>
</tbody>
</table>


WHY GIVE TWO WHEN ONE WILL DO?

Make Choosing Wisely your next improvement project.
Join the campaign to prevent 10 million unnecessary tests and treatments by 2020.
Transfusion Order Set - Adult

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

| □ informed consent completed as per institutional guidelines |

| Date of transfusion: □ today □ other (DD/MM/YYYY) _________ □ STAT (call blood bank at XXXXX) |

<table>
<thead>
<tr>
<th>Pre-transfusion laboratory tests □ group and screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous transfusion within 3 months □ yes □ no</td>
</tr>
<tr>
<td>Previous pregnancy within 3 months □ yes □ no</td>
</tr>
</tbody>
</table>

| □ if no existing IV initiate IV 0.9% NaCl to keep vein open |
| □ discontinue peripheral IV after transfusion complete |

<table>
<thead>
<tr>
<th>Pre-transfusion medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ furosemide _____ mg po prior to transfusion or _____ mg IV prior to transfusion</td>
</tr>
</tbody>
</table>

| □ irradiated product required as per hospital guidelines, specify reason: |

| □ specially matched product required as per hospital guidelines, specify reason: |

<table>
<thead>
<tr>
<th>Red Blood Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-transfusion Hb: _____ g/L</td>
</tr>
<tr>
<td>Indication: □ low Hb □ significant bleeding □ symptomatic □ other</td>
</tr>
<tr>
<td>□ Transfuse 1 unit, over _____ hours (e.g. 1 unit over 2-3 hours, maximum 4 hrs)</td>
</tr>
<tr>
<td>□ Transfuse _____ units, each over _____ hours</td>
</tr>
</tbody>
</table>

**Note:** consider IV iron instead of red blood cells for patients with stable iron deficiency anemia
# Technologist Prospective Screening

<table>
<thead>
<tr>
<th>Manual</th>
<th>Transfusion Medicine</th>
<th>PROCEDURE TEMPLATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section</td>
<td>Inventory Management</td>
<td></td>
</tr>
<tr>
<td>Title:</td>
<td>Prospective Screening Blood Product Orders</td>
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<td>Issued by</td>
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<tr>
<td>Effective Date</td>
<td>Revised Date</td>
<td>Version: 1</td>
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</table>

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<table>
<thead>
<tr>
<th>Manual</th>
<th>JOB AID TEMPLATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section</td>
<td></td>
</tr>
<tr>
<td>Title:</td>
<td>Screening Blood Product Orders for Technologists</td>
</tr>
<tr>
<td>Issued by</td>
<td>Ontario Regional Blood Coordinating Network</td>
</tr>
<tr>
<td>Approved by</td>
<td>Project Sponsor</td>
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http://transfusionontario.org
**Order Received: RBC**

**SCREEN ORDER IF:**
- Nor-Bleeding Adult Inpatient
- Non-Bleeding Adult ER patient

**DO NOT SCREEN ORDER IF:**
- Trauma Room (Massive Transfusion Protocol)
- Operating Room
- Recovery Room or Post Anesthetic Care Unit (PACU)
- Outpatient including Cancer Care and Medical Day unit

- **Hb less than 60 g/L**
  - Transfusion likely appropriate
  - Transfuse 1 unit and re-check patient symptoms and Hb before giving second unit

- **Hb less than 70 g/L**
  - Consider Transfusion.
  - Transfuse 1 unit and re-check patient symptoms and Hb before giving second unit

- **Hb less than 80 g/L**
  - Consider transfusion in patients with pre-existing cardiovascular disease
  - Transfuse 1 unit to patient if experiencing elevated heart rate, dizziness or fainting, or cardiac symptoms like chest pain
  - Re-check patient symptoms and Hb before giving second unit

- **Hb 80 g/L to 90 g/L**
  - Likely inappropriate unless evidence of impaired tissue oxygenation
  - Transfuse 1 unit to patient if experiencing elevated heart rate, dizziness or fainting, or cardiac symptoms like chest pain or shortness of breath.
  - For all other patients, or if more than 1 unit ordered, inform the patient care area that the request is outside the hospital guidelines and refer the request to the Transfusion Medicine Physician

- **Hb greater than 90 g/L**
  - Likely inappropriate.
  - Request is outside of hospital guidelines.
  - Refer the request to the Transfusion Medicine Physician
Partnership with Academic Teaching Hospital Collaborative

Education on Guidelines
9-5 Prospective Order Screen
MAC Approval & 24/7 Screen

RBC Units Transfused

Jan 2012 to Dec 2013:
Mean 5.38 RBC/100 AIPD

↓31%

July 2014 to June 2015:
Mean 3.71 RBC/100 AIPD

Lin et al. Transfusion 2016. in press
Transfusion Risks

- **Common:** fever, hives, alloimmunization
- **Serious:** TACO, TRALI, BaCON, Major allergic, AHTR
- **Rare:** Viral infections (Hepatitis B/C, HIV, etc)

Callum & Pinkerton et al. BloodyEasy4 coming soon.
Reporting Transfusion Reactions is Important!

- Why?
  - To determine the risks of transfusion
  - To prevent another transfusion reaction from happening: TRALI, BaCoN (quarantine of dangerous companion components), TACO (making recommendations for the future)
  - To identify potential issues in the blood system
Reporting Transfusion Reactions is Important!

• What?
  – Wards: Report all suspected transfusion reactions to the blood bank

• To whom?
  – Trackers: Ontario Transfusion Transmitted Injuries Surveillance System
  – Manufacturer: Canadian Blood Services
  – Regulator: Canada Vigilance Program (reaction due to activity done at the hospital)
TTISS-ON Resources

Ontario Guide for Reporting Transfusion Reactions
A tool for the Transfusion Medicine Laboratory/Blood Bank (or designate) used to determine reporting requirements when a recipient experiences a transfusion reaction. Notification of various blood agencies and programs may be required. Canadian Blood Services, Health Canada, Manufacturers of Plasma Derivatives and Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON).

Transfusion Reaction Chart Version 2.1 Pocket and Poster
The reaction chart provides guidance for nurses, physicians and Blood Transfusion Laboratory personnel on how to identify, investigate and treat transfusion reactions. Version 2.1 allows hospitals to add their hospital logo and contact information for guidance on handling.
Investigate and identify type of transfusion reaction**

**Refer to this document as Adverse Transfusion Event (ATE) and in the Blood Regulations as Adverse Recipient Reaction (ARR)

No Further Reporting Required

Is the ATE one of the following?
- Minor Allergic
- Febrile Non-Hemolytic
- Delayed Serological

COMPLETE the Canadian Transfusion Adverse Event Reporting Form (CTAERF) excluding patient name and OHIP No.

Is the ATE the result of transfusion practice or due to an error at the bedside?

Examples: Transfusion associated circulatory overload (TACO); Incompatible transfusion due to mislabeled sample; Transfusing the wrong patient
Note: ATEs resulting from device malfunction (e.g. blood warmer, infusion pump) are also reportable to Health Canada - Medical Devices Regulations

Is the ATE attributable to an activity at the hospital that affected the safety/efficacy of the component?

Examples:
- ATEs due to mislabeling of the component by the TML (e.g. unirradiated blood labelled as irradiated)
- Bacterial contamination due to pooling of component at the hospital or storing of blood in a malfunctioning fridge
- REPORT TO BOTH the Canadian Blood Services and the Canada Vigilance Program if it is not clear whether an ATE is due to a hospital activity that affected the component or the component itself (e.g. contamination)

Report ATE to Canada Vigilance Program (Health Canada Blood Regulations)
FAX or mail CTAERF within 24 hours of a fatality, otherwise within 15 days (see Instructions p.1)
Final report is required once investigation is complete

Is the ATE one of the following?
- Transfusion-Related Acute Lung Injury (TRALI or Possible TRALI)
- Severe allergic reaction/anaphylaxis
- Bacterial contamination
- Post transfusion infection (e.g. HIV, Hepatitis, Chagas, Malaria, West Nile)
- Adverse events due to suspected CBS mislabelling
- Unexplained new acute severe neutropenia or thrombocytopenia (transfusion-related alloimmune neutropenia or thrombocytopenia)
- Other unusual reaction where the hospital is concerned the blood component is the cause

Report ATE to Canadian Blood Services (CBS)
FAX the CTAERF to local Medical Office (see Instructions p.1)
Report the ATE immediately if fatality or if suspected to be attributable to quality of component (e.g. bacterial or viral contamination). Otherwise as soon as possible.
Note: CBS reports as required to the Canada Vigilance Program

Report ATE to Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON)
Enter data directly into the TTISS-ON web database or send CTAERF by FAX within 3 months (see Instructions p.1)
# Transfusion Reactions

**TTISS-ON Transfusion Reaction Chart**

<table>
<thead>
<tr>
<th>Immediate Actions!</th>
<th>Signs &amp; Symptoms</th>
<th>Usual Timing</th>
<th>Possible Etiology</th>
<th>Recommended Investigations</th>
<th>Suggested Treatment and Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. STOP the transfusion</td>
<td>Fever (at least 38°C and an increase of at least 1°C from baseline) and/or Shaking Chills/Rigors</td>
<td>38°C to 38.9°C but NO other symptoms</td>
<td>During or up to 4 hours post transfusion</td>
<td>Febrile non-hemolytic transfusion reaction</td>
<td>No testing required</td>
</tr>
<tr>
<td>2. Maintain IV access</td>
<td>Less than 39°C but with other symptoms (e.g., rigors, hypotension) or 39°C or more</td>
<td>Usually within first 15 minutes but may be later</td>
<td>Febrile non-hemolytic transfusion reaction</td>
<td>Group &amp; Screen, DAT</td>
<td>Antipyretic</td>
</tr>
<tr>
<td>3. Check vital signs</td>
<td></td>
<td></td>
<td>Infection contamination</td>
<td>Patient blood culture(s)</td>
<td>With physician approval transfusion may be resumed cautiously if product still viable</td>
</tr>
<tr>
<td>4. Re-check patient ID band and product label</td>
<td></td>
<td></td>
<td>Acute hemolytic transfusion reaction</td>
<td>Urinalysis</td>
<td>Antipyretic</td>
</tr>
<tr>
<td>5. Notify physician</td>
<td></td>
<td></td>
<td></td>
<td>If hemolysis suspected (e.g., red urine or plasma)</td>
<td>Consider Meperidine (Demerol®) for significant rigors</td>
</tr>
<tr>
<td>6. Notify Transfusion Laboratory</td>
<td>Urticaria (hives)</td>
<td>Less than 2/3 body but NO other symptoms</td>
<td>During or up to 4 hours post transfusion</td>
<td>Anaphylactoid reaction/Anaphylaxis</td>
<td>If bacterial contamination suspected, antibiotics should be started immediately</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2/3 body or more but NO other symptoms</td>
<td>Usually early in transfusion</td>
<td></td>
<td>Monitor for hypotension, renal failure and DIC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Accompanied by other symptoms (e.g., dyspnea, hypotension)</td>
<td>Usually early in transfusion</td>
<td></td>
<td>Return blood product to Transfusion Laboratory</td>
</tr>
<tr>
<td></td>
<td>Itching or Rash</td>
<td></td>
<td>Anaphylactoid reaction/Anaphylaxis</td>
<td>Group &amp; Screen, DAT</td>
<td>For additional assistance, contact</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chest X-Ray (if dyspneic)</td>
<td>Place text</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Blood gases (if dyspneic)</td>
<td>Do not restart transfusion</td>
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<td></td>
<td>Haptoglobin</td>
<td>Do not restart transfusion</td>
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<td></td>
<td></td>
<td>Anti-IgA testing</td>
<td>Do not restart transfusion</td>
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<td>Antihistamine</td>
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<td></td>
<td>With physician approval transfusion may be resumed cautiously if product still viable</td>
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<td></td>
<td>May require steroid</td>
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<td></td>
<td></td>
<td>Epinephrine</td>
</tr>
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<td></td>
<td></td>
<td>Washed/plasma depleted blood products pending investigation</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Return blood product to Transfusion Laboratory</td>
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<td>For additional assistance, contact Place text</td>
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*Ontario Transfusion Transmitted Injuries Surveillance System (TTISS-ON)*

http://transfusionontario.org
Case #1

- The MLT calls you with the following case.
- 70M admitted to the ICU with pneumonia 3 d ago.
- Hb 85 g/L.
- The internist has ordered 2 RBC units.
- The MLT wonders if this order is appropriate?

- What additional questions would you want to ask?
Case #2

- 27M with new diagnosis of leukemia awaiting transfer to tertiary centre
- Platelet count is $17 \times 10^9/L$.
- The MLT contacts you as the clinician has ordered 1 pool of platelets.

- What additional questions would you want to know?
Case #3

- 68F with atrial fibrillation, comes to the Emergency department.
- INR 4.5
- Order is for 4 units plasma.
- The MLT calls you with questioning the order as the patient is on warfarin.

- What additional questions do you ask?
Case #4

- 72M motor vehicle collision, driver, blunt trauma
- Hemodynamically unstable with pelvic fracture
- Clinical team discovers the patient is on dabigatran.
- The clinical team calls the Blood Bank and is directed to you.
Oral Anticoagulant Drugs

Intrinsic Pathway
- XII
- XI
- IX
- VIII

Extrinsic Pathway
- VII

Common Pathway
- X
- V
- II

Fibrinogen

Oral Xa inhibitors
- rivaroxaban
- apixaban
- edoxaban

Oral Ila inhibitors
- dabigatran

Fibrin Clot
Patient with bleeding on dabigatran

- When was last dose?
- CBC, creatinine
- aPTT*

If aPTT ≥ 40 sec, consult TE or Transfusion Medicine

Mild bleeding
- Local hemostatic measures
- Hold 1 or more doses of dabigatran

Moderate-severe bleeding\(^1\)
- Manage bleeding (compression, surgery)
- Fluid → diuresis
- Transfuse RBCs or platelets if needed (follow Sunnybrook guidelines)
- Oral charcoal if overdose <2 hrs before

Life-threatening bleeding\(^1\)
- Contact Transfusion Medicine
- Tranexamic acid (1 g iv followed by 1 g infusion over 8 hours)
- Urgent hemodialysis might be helpful
- Consider idarucizumab (Praxbind\(^\circledR\))^2

If idarucizumab not available, FEIBA 50 units/kg
Idarucizumab

- Prospective cohort study: pts with serious bleeding or required urgent procedure
  - Interim analysis: 90 patients (Target 300 pts)
  - Received 5g as two 2.5 mg (50mL) infusions within 15 min
- Reversed dTT, ECT and ↓ dabi concentration but possible wearing off effect at 24 h
- Bleeding pts: median time to hemostasis: 11.4 h
- Procedure pts: 33 of 36 had “normal” hemostasis
- Thrombosis: 5 pts (1 pt < 72 h)
- Deaths: 18 deaths (6 pts < 96 h due to index event)

Pollack Jr et al. NEJM August 6, 2015;373:511-20
What is life-threatening bleeding?

Patient is experiencing one of the following (please check off applicable indications):

a) Life-threatening hemorrhage
   - Hemorrhage resulting in airway compromise
   - Hemorrhage with drop in Hgb ≥ 20 g/L or transfusion of ≥ 2 units RBCs
   - Intracranial hemorrhage
   - Major trauma
   - Other (specify): __________________________

   (Requires approval of Transfusion Medicine physician)

b) Critical site hemorrhage
   - Intra-articular
   - Intra-ocular
   - Intra-spinal
   - Limb – compromising vascular supply and limb viability
   - Retroperitoneal
   - Other (specify): __________________________

   (Requires approval of Transfusion Medicine physician)

c) Emergency surgery
   - Bowel obstruction
   - Cardiac surgery (urgent)
   - Cord compression
   - Ischemic bowel
   - Open fracture
   - Ruptured AAA (abdominal aortic aneurysm)
   - Ruptured spleen
   - Other (specify): __________________________
Case #5

- 58F postop hip replacement
- Hb 65 g/L
- Transfused 1 unit RBC
- RN calls the Blood Bank as patient developed chills and then fever at 1 hour into RBC transfusion – 50% of unit transfused
- The doc wants to speak with you to find out what he should do next?
Fever

• What is a fever?
  – > 1°C rise in temperature AND temperature > 38°C during or up to 4 hr post-transfusion
  – May present with chills/rigors alone

• What is the DDx?
  – Acute hemolytic transfusion reaction (AHTR)
  – Bacterial Contamination (BaCon)
  – Febrile non hemolytic transfusion reaction (FNHTR)
  – Fever due to underlying illness
Acute Hemolytic Transfusion Reaction (AHTR)

• Mechanism
  – Due to incompatibility between donor and patient
  – ABO incompatibility
    • most often due to clerical error
  – Less common: other minor blood group incompatibility (failure to detect/error)

• Manifestation
  – Fever, chills
  – Hemoglobinuria, pain, hypotension, nausea, vomiting, dyspnea, renal failure, DIC
Bacterial Contamination (BaCon)

- Blood components can be contaminated by
  - Normal skin flora from the donor
  - Unrecognized bacteremia in the donor
  - Contamination during handling (rare)

<table>
<thead>
<tr>
<th>Gram-positive</th>
<th>Gram-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td><em>Serratia marcescens</em></td>
</tr>
<tr>
<td><em>Bacillus cereus</em></td>
<td><em>Klebsiella pneumonia</em></td>
</tr>
<tr>
<td></td>
<td><em>Pseudomonas species</em></td>
</tr>
<tr>
<td></td>
<td><em>Yersinia enterocolitica</em></td>
</tr>
</tbody>
</table>

- Most often occur with platelets due to room temperature storage
Febrile Non-hemolytic Transfusion Reaction (FNHTR)

- Mechanism
  - Cytokines in the transfused product
  - Recipient antibodies (to white blood cells or platelets) in the transfused product

- Manifestation
  - Fever
  - May be associated with chills, rigors, nausea, vomiting, hypotension
  - Diagnosis of exclusion
Case #6

- 88M postop hip replacement
- Hb 65 g/L
- Transfused 1 unit RBC
- RN calls the Blood Bank as patient developed SOB at the end of a 2 hour RBC transfusion – 100% of unit transfused
- What information will help you discern the cause of this transfusion reaction?
Dyspnea

- What is dyspnea?
  - Shortness of breath
  - May be associated with drop in oxygen saturation

- What is the DDx?
  - Transfusion associated circulatory overload (TACO)
  - Transfusion related acute lung injury (TRALI)
  - Major allergic transfusion reaction
  - Dyspnea not related to transfusion
TACO

- Mechanism
  - Volume overload $\rightarrow$ too much, too fast
  - Risk factors: known history of congestive heart failure (CHF), elderly, renal dysfunction

- Manifestation
  - Orthopnea, cyanosis, $\uparrow$HR, $\uparrow$BP, $\uparrow$JVP
  - CXR findings: volume overload
  - NT-proBNP from normal to elevated after transfusion
TACO

- Management
  - Stop the transfusion!
  - Chest X-ray (may help discern other causes)
  - Supportive care: oxygen and diuretics

- Prevention is key
TACO Prevention

Transfuse one unit at a time for prophylactic transfusions

Not bleeding
Below Hb trigger
No severe symptoms

Transfuse slowly over 3.5 hours for prophylactic transfusions

Consider the use of furosemide in patients > 60 yrs or hx of CHF
TRALI

- What is it?
- Non-cardiogenic pulmonary edema
- Definition
  - Onset during or within 6 hrs of transfusion
  - New acute lung injury
  - Bilateral infiltrates on CXR
  - No evidence of circulatory overload
  - No preexisting acute lung injury

Kleinman et al. Transfusion 2004;44:1774-89
TRALI - Mechanism

Antibody Hypothesis

Recipient WBC

Donor
-Anti-HNA
-Anti-HLA I
-Anti-HLA II

Release of substances causing pulmonary endothelial damage and capillary leak

2nd event: Transfusion of BRM or antibodies

Activation

1st event
Underlying condition of recipient

Two-Event Hypothesis
TRALI

• Manifestations
  – Dyspnea, hypoxia, fever, hypotension

• Management
  – Stop transfusion and assess patient
  – Inform the Transfusion Medicine Lab
    • Quarantine other products that might have dangerous antibodies
  – Chest X-ray
  – Supportive care: oxygen, fluids, mechanical ventilation in 75%
Reporting Transfusion Reactions is Important!

• What?
  – Wards: Report all suspected transfusion reactions to the blood bank

• To whom?
  – Trackers: Ontario Transfusion Transmitted Injuries Surveillance System
  – Manufacturer: Canadian Blood Services
  – Regulator: Canada Vigilance Program (reaction due to activity done at the hospital)
Summary

I hope, that when you return home, you will:

• Be able to provide advice on appropriate indications for blood transfusion
• Be able to consult effectively on management of transfusion reactions
• Seek out more information on transfusion and visit the ORBCoN website at www.transfusionontario.org
• Rate transfusion medicine consultation as an important component for the laboratory services offered by your hospital/institution