Quality Improvements in Transfusion Medicine

Transfusion Medicine Education Videoconference Symposium

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Faculty/Presenter Disclosure

- **Faculty**: Allison Collins

- **Relationships with commercial interests**:)
  - none
  - ORBCoN is funded by the Ministry of Health and Long Term Care
Objectives

1. List evidence and data supporting a policy for single unit transfusion
2. Identify strategies to improve red blood cell utilization
Restrictive Transfusion Practice

• Two-pronged approach:
  – restrictive transfusions thresholds ("triggers")
  – single unit transfusions

• This presentation will focus on single unit transfusions

• But…both are important
### Historical Reviews of Single Unit Transfusions

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N (Tx)</th>
<th>% single unit Tx</th>
<th>Surgery % of single unit Tx</th>
<th>% all single unit Tx questionable or inappropriate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morton</td>
<td>1960</td>
<td>475</td>
<td>36</td>
<td>100</td>
<td>72</td>
</tr>
<tr>
<td>King</td>
<td>1960</td>
<td>1761</td>
<td>30</td>
<td>74</td>
<td></td>
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<tr>
<td>Crispen</td>
<td>1962</td>
<td>1243</td>
<td>38</td>
<td>86</td>
<td>65</td>
</tr>
<tr>
<td>Reece</td>
<td>1962</td>
<td>2912</td>
<td>29</td>
<td>93</td>
<td>67</td>
</tr>
<tr>
<td>Micolonghi</td>
<td>1963</td>
<td>583</td>
<td>38</td>
<td>80</td>
<td>38</td>
</tr>
<tr>
<td>Walz</td>
<td>1963</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diethrich</td>
<td>1964</td>
<td>217</td>
<td>30</td>
<td>57</td>
<td>68</td>
</tr>
<tr>
<td>Fadell</td>
<td>1965</td>
<td>633</td>
<td>26</td>
<td>61</td>
<td>68</td>
</tr>
<tr>
<td>Morton</td>
<td>1967</td>
<td>604</td>
<td>24</td>
<td>100</td>
<td>51</td>
</tr>
<tr>
<td>Domen</td>
<td>1985</td>
<td>50</td>
<td>100</td>
<td>98</td>
<td>63</td>
</tr>
</tbody>
</table>

Majority of single unit transfusions ordered by surgeons (or maybe by anesthesiologists).
“Appropriate” in the 1960s

<table>
<thead>
<tr>
<th>OK</th>
<th>Not OK</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Children</td>
<td>- “Routine” pro-op in surgery to achieve an arbitrary Hb</td>
</tr>
<tr>
<td>- Maintain blood volume e.g. massive transfusion, shock, burns</td>
<td>- “Routine” in obstetrics</td>
</tr>
<tr>
<td>- Significant symptoms of anemia e.g. hypotension, chest pain, dyspnea, tachycardia, pre-syncope, nausea, clamminness</td>
<td>- “Routine” post-op to hasten convalescence, wound healing</td>
</tr>
<tr>
<td>- Exchange transfusion</td>
<td>- Nutrition, iron deficiency</td>
</tr>
<tr>
<td>- Fluid challenge</td>
<td>- A tonic to “make the patient feel better”</td>
</tr>
<tr>
<td></td>
<td>- Palliative patients unless anemia is the cause of symptoms</td>
</tr>
<tr>
<td></td>
<td>- Any single unit in adults</td>
</tr>
</tbody>
</table>
Early Guidelines (1960)

• Hospital/expert-opinion-based e.g.
• “Single-pint transfusions should not be given to adults”
• “Single-pint transfusions should not constitute more than 5% of the blood used in any hospital”

Graham-Stewart. The Lancet 1960;7147:421
Early Guidelines (1962)

• Joint Blood Council (AABB, AHA, AMA, ANRC, ASCP)

• “A predominance of single unit transfusions (more than 50%) in any hospital implies a need for critical reassessment…with the recognition, however, that there are indications for the single transfusion”.
Early Guidelines (1963)

- National Academy of Sciences/National Research Council (U.S.)
- “A high percentage of single-unit transfusions cannot be justified...There are cases, however, in which the requirement for transfusion is clear and the requirement is obviously satisfied by a single unit...The use of a single unit in such circumstances reflects sound judgement and good practice...”
All before screening tests for viruses

Screening tests and emerging agents


- Syphilis 1938
- HBsAg
- Anti-HIV
- Anti-CMV
- Anti-HBc
- ALT
- Anti-HTLV
- Anti-HCV
- HIV Ag
- HIV/HCV/(HBV) NAT
- WNV NAT
- Anti-T.cruzi

Potential additional screening tests

- Malaria
- HHV-8
- Babesia
- Leishmania
- Foamy viruses
- CHIKV
- Dengue

Dr. Dana Devine, CBS, 2015
“…rather than criticize the surgeons for their single-unit transfusions, we ought to realize that it takes extraordinarily good surgery to carry out many of these procedures using but one unit of blood.”

(Cleveland Clinic)
“The man who estimates the patient’s lack at 500 cc and orders 1,000 cc ‘because the front office is checking on single unit transfusions’ has permitted administrative pressure to convert him to a charlatan.”

William H Crosby
1914-2005
RCT Evidence to 1997

• MEDLINE search from 1966 to July 1996
• Only 6 randomized controlled trials (RCTs) evaluating ‘restrictive’ vs. ‘liberal’ RBC transfusion strategies
• Only 1 of them was large enough to identify clinically significant differences between strategies (sickle cell disease)
Guidelines for red blood cell and plasma transfusion for adults and children

Expert Working Group*

• The routine transfusion of multiple units in less urgent situations appears to be common and should be re-evaluated
• Physicians should consider transfusing one unit at a time with assessment after each unit
• Did not specify Hb thresholds

*www.transfusionontario.org
## Randomised Trials of Restrictive vs. Liberal RBC Transfusion 1999-2015

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Res/Lib Hb/Hct</th>
<th>1 unit?</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRICC (ICU)</td>
<td>838</td>
<td>70/100</td>
<td>Yes</td>
</tr>
<tr>
<td>TRACS (cardiac surgery)</td>
<td>502</td>
<td>.24/.30</td>
<td>Yes</td>
</tr>
<tr>
<td>FOCUS (hip #, cardiac risk factors)</td>
<td>1999</td>
<td>80/100</td>
<td>Yes</td>
</tr>
<tr>
<td>UGIB</td>
<td>889</td>
<td>70/90</td>
<td>Yes</td>
</tr>
<tr>
<td>TRISS (sep. shock)</td>
<td>998</td>
<td>70/90</td>
<td>Yes</td>
</tr>
<tr>
<td>Major abdominal cancer surgery</td>
<td>198</td>
<td>70/90</td>
<td>Yes</td>
</tr>
<tr>
<td>TITRe2 (cardiac surgery)</td>
<td>2003</td>
<td>75/90</td>
<td>Yes</td>
</tr>
</tbody>
</table>
British Committee for Standards in Haematology (BCSH) 2012

- Guideline on the Administration of Blood Components updated 2012
- 2012 Addendum states: “single unit transfusions are recommended where possible, especially in non-bleeding patients”
- This Addendum specifically addresses the avoidance of TACO
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

Routine practice should be to start with 1 unit instead of 2 units

Carson. JAMA. 2016;316(19):2025
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 (7 to 8 g/dL in stable, non-cardiac in-patients).

Transfusion of the smallest effective dose of RBCs is recommended because liberal transfusion strategies do not improve outcomes when compared to restrictive strategies. Unnecessary transfusion generates costs and exposes patients to potential adverse effects without any likelihood of benefit. Clinicians are urged to avoid the routine administration of 2 units of RBCs if 1 unit is sufficient and to use appropriate weight-based dosing of RBCs in children.

avoid the ‘routine’ 2U RBC transfusion
Choosing Wisely Canada (2014)

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 average-sized patient and more than that in smaller patients.
Why Restrictive Transfusion?

- Patients should receive evidence-based transfusion therapy at all hospitals.
- Evidence and guidelines are available.
- Ontario audits have showed marked variability in transfusion practice.
- Liberal transfusion practice may harm patients.
- Iron deficiency in blood donors: 24% repeat blood donors have ferritin less than 25 µg/L.
- Blood products are costly (acquisition cost about $450/RBC unit).

*Goldman. CSTM 2015*
Red Blood Cell Units Issued by Canadian Blood Services Per 100 Active Adult Treatment Days to 62 Ontario Community Hospitals for Fiscal Year 2015-2016.

Range 1.81 to 11.71, a 6-fold difference

Source: Dr. P. Pinkerton
% single units, Ontario

3.5% to 78%, a 22-fold difference
## Risks of Transfusion (non-viral)

<table>
<thead>
<tr>
<th>RISK OF EVENT</th>
<th>EVENT</th>
<th>The serious ones with RBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 in 13</td>
<td>RBC sensitization (↑ risk hemolytic reaction, HDFN)</td>
<td></td>
</tr>
<tr>
<td>1 in 100</td>
<td>Transfusion-associated circulatory overload (TACO)</td>
<td>★★</td>
</tr>
<tr>
<td>1 in 7,000</td>
<td>Delayed hemolytic transfusion reaction</td>
<td></td>
</tr>
<tr>
<td>1 in 10,000</td>
<td>Transfusion related acute lung injury (TRALI)</td>
<td>★★</td>
</tr>
<tr>
<td>1 in 40,000</td>
<td>ABO-incompatible transfusion per RBC transfusion</td>
<td>★★</td>
</tr>
<tr>
<td>1 in 40,000</td>
<td>Serious allergic reaction per unit of component</td>
<td>★★</td>
</tr>
</tbody>
</table>
Ontario Transfusion Transmitted Injuries Surveillance System 2008-2014 (n=1226)

Transfusion associated circulatory overload 27%

- TRALI 33, 3%
- TAD, 45, 4%
- Acute Hemolytic Reaction, 72, 6%
- Anaphylactic Shock, 3, 0%
- Aseptic Meningitis, 16, 1%
- Bacterial Infection, 29, 2%
- Other pain/unknown, 74, 6%
- Delayed Hemolytic Reaction, 222, 18%
- Hypotensive Reaction, 37, 3%
- IVIG Headache, 58, 5%
- IVIG pain/reaction, 66, 5%
- Severe Allergic/Anaphylactic/Anaphylactoid, 190, 15%
- PTP, 3, 0%
- Possible TRALI, 51, 4%
- Other Infection, 1, 0%
TACO: 1 Unit will do it

- incidence 1:708 patients transfused with RBC
- in 9 patients a single RBC unit precipitated circulatory overload (35%)
- not called TACO at that time

Popovsky. Transfusion 1985;25(5):469
TACO: 1 Unit will do it

• Review of 98 consecutive patients with TACO at 2 Toronto hospitals.
• 81 received red cells:

<table>
<thead>
<tr>
<th># RBC units transfused per order</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37 (45.7)</td>
</tr>
<tr>
<td>2</td>
<td>33 (40.7)</td>
</tr>
<tr>
<td>3</td>
<td>3 (3.7)</td>
</tr>
<tr>
<td>≥ 4</td>
<td>8 (9.9)</td>
</tr>
</tbody>
</table>
Evolution of Practice

1966

now
Interventions to Change Practice

- Education (rounds, memos, one-to-one discussions)
- Guidelines
- Order sets, order forms
- Reminders e.g. screen savers on hospital computers
- Audit and feedback
- Screening of orders (real time)
- Computerized provider order entry (CPOE)
- Clinical decision support (CDS)
- Many challenges: practitioner knowledge (prescriber and TM Medical Director), hospital culture, financial and human resources, patient preferences, etc.
Suspect inappropriate RBC transfusion
  – *How to do a simplified RBC transfusion audit*

Inappropriate RBC transfusion and practitioner variability
  – *How to implement local transfusion guidelines*

Have guidelines but not being followed
  – *How to implement MLT prospective transfusion order screening*
Ontario Transfusion Quality Improvement Plan: Indicators

1. Percent of all RBC transfusions with a pre-transfusion Hb of less than 80 g/L

2. Percent of all RBC transfusions which are single unit transfusions
   - prescribe 1 unit at a time and reassess the patient (preferably including Hb) before prescribing a second unit
   - eventual goal 80%
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>

| □ informed consent completed as per institutional guidelines |

<table>
<thead>
<tr>
<th>Date of transfusion:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ today</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>Preceding 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>

| □ 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>
</table>

**Red Blood Cells**

<table>
<thead>
<tr>
<th>Pre-transfusion Hb: ______ g/L</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Indication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ low Hb</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Pre-transfusion Hb: ______ g/L</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Indication:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ low Hb</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transfuse 1 unit, over _____ hours (e.g. 1 unit over 2-3 hours, maximum 4 hrs)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Transfuse _____ units, each over _____ hours</th>
</tr>
</thead>
</table>

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

**SCREEN ORDER IF:**
- Non-Bleeding Adult Inpatient
- Non-Bleeding Adult Emergency patient

**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 if experiencing elevated heart rate, dizziness or fainting or is experiencing 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
  - Issue 1 unit to patient if experiencing elevated heart rate, dizziness or fainting, or is experiencing cardiac symptoms like chest pain or shortness of breath.
  - For all other patients, or for order of more than 1 unit, inform the patient care area that the request is outside the recommendations and refer the request to the Transfusion Medicine Physician

**Hb greater than 90 g/L**
- Likely inappropriate.
  - Request is outside of recommendations.
  - Refer the request to the Transfusion Medicine Physician

**DO NOT SCREEN ORDER IF:**
- Trauma Room (Massive Transfusion Protocol)
- Operating Room
- Recovery Room or Post Anesthetic Care Unit (PACU)
- Outpatient are including Cancer Care and Medical Day unit
I ordered 1 unit and may order a second unit. How soon can the post-transfusion CBC be drawn?

Acute anemia, normovolemic GI patients

Elizade. Transfusion 1997;37:573

General medicine ward, not bleeding

Can interventions work?

WHY GIVE TWO WHEN ONE WILL DO?

Help reduce unnecessary red blood cell transfusions in our hospital
Single Unit Transfusions

Stay Single
... prescribe single units

Prescribing a single unit of blood may reduce the risk of an adverse event.

In accordance with the NHMRC Guidelines:
- Only one unit of blood can be ordered if a patient is not actively bleeding.
- Only one unit will be issued at a time.
- If the unit is not issued, a new request must be made.
- Each unit transfused is an independent clinical decision.

Indications for second unit are:
- Active blood loss
- Hypotension
- Organ failure
- Less than 8g/L, rise in Hb following transfused unit

If requested, the Haematology Department will be happy to provide advice on the appropriate management of patients.

Freemantle, Western Australia

Leahy. Transfusion 2014;54:1133
Ratio of 1 unit to 2 unit orders with Point of Care Clinical Decision Support

Mean 1:2 unit ratios shown for each period of the study

Baseline 0.34
Guidelines 0.50
CPOE 1.20

McKinney. Transfusion 2015;55(9):2086
Effect of Lower Threshold vs. Single Units

- Analysis of RBC utilization data at 3 community hospitals before and after implementation of a PBM program
- Tools: guidelines, education (newsletters, screen savers), “report cards” to physicians, “pop-up” alert when transfusion order received with Hb ≥ 70 g/L
- Evaluated the impact on overall RBC use of the “Why give 2 when 1 will do?” campaign and simultaneous efforts to promote Hb thresholds of 70 g/L or 80 g/L
- Univariate and multivariate analyses to identify the independent effects of these 2 interventions
Effect of Lower Threshold vs. Single Units

- Pre-PBM Baseline
- PBM Implementation period
- Post-PBM Period

- 7/13
- 7/14
- 7/15
- 7/16

Harmonize Guidelines (PBM Begins)

4/15

“Why Give 2” campaign begins
1st report cards sent w/ Hb trigger and 1 vs. 2 unit orders

9/15

Best Practice Advisory (Hb trigger and single-unit advisory)

Effect of Lower Threshold vs. Single Units
### Effect of Lower Threshold vs. Single Units

#### Multivariate analysis: Impact of single-unit RBC orders and Hb thresholds on RBC use

<table>
<thead>
<tr>
<th>Hospital</th>
<th>% single-unit RBC orders</th>
<th>%RBC orders with Hb ≥ 80 g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.0014</td>
<td>0.81</td>
</tr>
<tr>
<td>B</td>
<td>0.033</td>
<td>0.35</td>
</tr>
<tr>
<td>C</td>
<td>0.0024</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Negotiating for a single unit may be helpful…
Northumberland Hills Hospital

% Single Units

<table>
<thead>
<tr>
<th>Period</th>
<th>% Single Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>July-Sep 2014</td>
<td>25</td>
</tr>
<tr>
<td>Oct-Dec 2014</td>
<td>32</td>
</tr>
<tr>
<td>Jan-Mar 2015</td>
<td>44</td>
</tr>
<tr>
<td>Apr-Jun 2015</td>
<td>42</td>
</tr>
<tr>
<td>Jul-Sep 2015</td>
<td>34</td>
</tr>
<tr>
<td>Jan-Mar 2016</td>
<td>56</td>
</tr>
<tr>
<td>Sept-Nov 2016</td>
<td>54</td>
</tr>
<tr>
<td>Jan-Mar 2017</td>
<td>78</td>
</tr>
</tbody>
</table>
## Units saved with 1-unit policy

Assumes 1U raises Hb by 10 g/L

<table>
<thead>
<tr>
<th>Transfusion threshold (Hgb) (g L⁻¹)</th>
<th>No. of patients below threshold</th>
<th>No. of patients predicted to surpass threshold with a minimum 1 U, 2 U, 3 U or &gt;3 U transfusion</th>
<th>No. of patients actually received 1 U or 2 U</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70</td>
<td>51</td>
<td>50 1 0 0</td>
<td>8 43</td>
</tr>
<tr>
<td>&lt;75</td>
<td>114</td>
<td>104 9 1 0</td>
<td>22 92</td>
</tr>
<tr>
<td>&lt;80</td>
<td>196</td>
<td>156 35 3 2</td>
<td>45 151</td>
</tr>
<tr>
<td>&lt;85</td>
<td>252</td>
<td>152 81 11 8</td>
<td>57 195</td>
</tr>
<tr>
<td>&lt;90</td>
<td>293</td>
<td>123 122 30 18</td>
<td>68 225</td>
</tr>
</tbody>
</table>
Units saved with restrictive thresholds and single unit policy
The Ontario Transfusion Quality Improvement Plan suggests this approach to improving transfusion practice:

A. Practice audits with annual feedback
B. Monthly memos to medical staff
C. Practice audits, transfusion guidelines, and order screening
D. Approval of all red cell orders by the transfusion service medical director
E. Educational posters on all nursing units
The Ontario Transfusion Quality Improvement Plan suggests this approach to improving transfusion practice:

A. Practice audits with annual feedback
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C. Practice audits, transfusion guidelines, and order screening
D. Approval of all red cell orders by the transfusion service medical director
E. Educational posters on all nursing units
Transfusion-associated circulatory overload (TACO) can occur after the transfusion of this minimum number of red cell units:

A. One
B. Two
C. Three
D. Four
E. Five
Transfusion-associated circulatory overload (TACO) can occur after the transfusion of this minimum number of red cell units:

A. One  
B. Two  
C. Three  
D. Four  
E. Five
How soon after transfusing a single unit of red cells can an accurate post-transfusion hemoglobin be measured?

A. 5 minutes  
B. 15 minutes  
C. 30 minutes  
D. 1 hour  
E. 24 hours
How soon after transfusing a single unit of red cells can an accurate post-transfusion hemoglobin be measured?

A. 5 minutes  
B. 15 minutes  
C. 30 minutes  
D. 1 hour  
E. 24 hours
Acknowledgements

• Members of the Ontario Transfusion Quality Improvement Committee
• Dr. John Freedman (ONTraC)
• Recommendations Working Group
• Technologist Screening Toolkit Working Group
• External reviewers
• Bracken Library staff, Queen’s University
Thank you. Questions?
2. King. Transfusion 1962;2(5):344
4. Reece. JAMA 1966;195(10):113
6. Walz. JAMA 1964;189(9):86
References: RBC RCTs

2. Hajjar. JAMA 2010;304(14):1559
6. de Almeida. Anesthesiology 2015;122:29