Transfusion Medicine Update and Cases

OAP September 16, 2017
Objectives

1. Explain the rationale for limiting the use of group O negative red cells.
2. List the indications for the use of irradiated and CMV seronegative blood products.
3. Summarize the findings of the PATCH study.
4. After this talk, review your hospital’s contingency plan for the management of blood shortages
5. After this talk, listen to at least one podcast about transfusion medicine.
Disclosures

- No conflicts of interest to declare
- ORBCoN is funded by the Ministry of Health and Long Term Care
Last year Dr. Yulia Lin reviewed:

• Utilisation of: red cells, platelets, plasma, prothrombin complex concentrate
• The Ontario Transfusion Quality Improvement Plan (OTQIP)
• Transfusion reactions
• Management of bleeding patients on direct oral anticoagulants (DOACs)
• Warfarin reversal
• If you missed it, the presentation is on the ORBCoN and OAP websites
Case

A 25 year old male is admitted to the Emergency Department following a motor vehicle accident. He is bleeding from multiple traumatic injuries and requires an urgent blood transfusion. The ordering physician asks for “emergency release” red cells before the group and screen can be completed.

You issue:

A. Group O positive RBC  
B. Group O negative RBC  
C. Group AB positive RBC  
D. Group AB negative RBC  
E. No RBC until the group and screen is completed
9. Don’t transfuse O negative blood except to O negative patients and in emergencies for female patients of child-bearing potential of unknown blood group.
CBS O neg RBC Data

O-neg issues
~11.5% of red cells

CBS O-neg donors
~10.6% (11.2% of donations)

General population
~6-7%

Webert. CBS Blood Brief Sept 2015
Canadian Blood Services

% O-Neg RBC Issues of Total RBC Issues

- 11.4% in 2009/10
- 11.3% in 2010/11
- 11.6% in 2011/12
- 11.8% in 2012/13
- 11.8% in 2013/14
- 11.9% in 2014/15
- 11.5% in 2015/16
- 11.4% in 2016/17
Mandatory Indications for O neg red Cells

- O neg females of child-bearing potential (≤ 45 years of age)
- O neg males and females with anti-D
- Emergency use for females of child-bearing potential (≤ 45 years of age) when blood group is unknown
- Intrauterine transfusions
Highly Recommended Indications for O neg red Cells

- O neg individuals of any age who are expected to receive chronic transfusions e.g. hemoglobinopathies or with chronic transfusion requirement
Generally Acceptable Indications for O neg red Cells

- O neg males or females > 45 years of age requiring non-massive transfusion
  - if no known anti-D and transfusing more than 4-6 units strongly encourage switch to O pos after 4-6 units
- Non-O neg infants less than 1 year of age where group specific units are not available
- Non-O neg patients requiring phenotypically matched or antigen negative units when group specific units are not available
National Advisory Committee on Blood and Blood Products 2017

Likely Unacceptable use of O neg red Cells

• Any O neg male, or O neg female > 45 years of age, without anti-D and requiring > 4-6 units
• Non-O neg patient because unit is approaching expiry date
Suggestions for Management of O neg RBC Supply: Trauma or Hemorrhage

• immediately collect a blood sample for ABO/Rh from all trauma patients
• transfuse male trauma or hemorrhaging patients, regardless of age, with O pos RBC until blood group is known or unless known to have anti-D
• have a policy to switch patients to their own blood group
• have a policy to switch hemorrhaging Rh neg patients to Rh pos RBC unless known to have anti-D
Suggestions for Management of O neg RBC Supply: Trauma or Hemorrhage

• Determine the optimal maternal age restriction for women served by your hospital and transfuse female trauma or hemorrhaging patients above this age with O pos RBC until blood group is known or unless known to have anti-D
Ontario
FY 09-10 to FY 15-16

Cumulative % of births by maternal age

Data for each LHIN is available on the ORBCoN website
Maternal age trend Ontario

Number of births

Ontario

Maternal age trend Ontario

Number of births

FY 09-10
FY 10-11
FY 11-12
FY 12-13
FY 13-14
FY 14-15
FY 15-16

age 40
age 41
age 42
age 43
age 44
age 45

www.transfusionontario.org
Request for Emergency Release of Uncrossmatched Red Cells

Male

Less than or equal to 42 years old

Known anti-D?

No

Issue O positive red cells

Yes

Issue O negative red cells

Female

43 years old or older

Known anti-D?

Yes

Issue O positive red cells

No

When the results of the Group and Screen are available:

1. Rh(D) negative males (any age) or Rh(D) negative females 43 years or older without anti-D: Issue O negative units to a maximum of 4 units and then switch to group specific or O positive red cells.
2. If switching to group specific after 20 units of group O red cells have been given, use only crossmatch compatible red cells if the group is A, B, or AB.
Risk of D alloimmunisation

- In D neg patients who received emergency issue uncrossmatched D pos RBC
  - Range 11 to 30.4%
    - 11% (Dutton. J Trauma 2005;59(6):1445)
    - 11.5% (Tchakarov. Immunohematology 2014;30(4):149)
    - 12.5% (Meyer. Transfusion 2015;55:791)
    - 21.4% (Gonzales. Transfusion 2008;48:1318)
    - 22% (Yazer. Transfusion 2007;47:2197)
    - 20-26% (Selleng. Lancet Haematology 2017;4:218)
    - 30.4% (Frohn. Transfusion 2003;43:893)
- Patients with trauma/hemorrhage do not appear to form anti-D as readily as healthy volunteers (80%)
Why Limit the Use of O Neg?

- O negative red cells are a precious resource, often in short supply
- O negative red cells should be reserved for those who truly need them
Transfusion-associated Graft vs Host Disease and the use of Irradiated Blood Components
Case

Which of the following patients required irradiated cellular blood components?
A. A patient with CLL, no drug treatment
B. A patient with CLL being treated with fludarabine
C. A patient receiving ABO identical platelets
D. A 2 year old child
E. All of the above
Graft vs Host Disease
Billingham Criteria (1966)

1. Viable, immunocompetent cells in a graft (T lymphocytes)
2. The recipient’s tissues express antigens not present in the donor
3. The recipient’s immune system fails to recognise and/or eliminate the immunocompetent cells of the donor
Transfusion Associated Graft vs. Host Disease (TA-GVHD)

- Occurs in immunosuppressed and immunocompetent recipients of cellular blood products (RBC, PLT, granulocytes)
- rare
- onset 3-30d post transfusion
- fever, rash, hepatitis, watery diarrhea, jaundice
- pancytopenia (bone marrow failure), multi-organ failure
- death from infection, bleeding (BM failure), in 3 wks +/-
- mortality > 90%, no effective treatment
- diagnosis by skin or liver biopsy, BM exam
- demonstration of donor lymphocytes in recipient tissue, HLA typing/molecular studies to confirm Dx

Agbaht. Transfusion 2007;47:1405
GVHD – morbiliform rash
Starts on trunk, moves to limbs, resembles a drug rash
Components Requiring Irradiation to Prevent TAGVHD

- red cells
- platelets (whole blood or apheresis)
- granulocytes
- not FP, cryoprecipitate or fractionated plasma products (e.g. IVIg, PCC)
- if blood is needed urgently use oldest inventory
  - 94% of GVHD in one review involved RBCs 10 days old or less

Kopolovic. Blood 2015;126(3):406
Factors Affecting Probability of TA-GVHD

- **Patient Factors**
  - Neonate

- **Product Factors**
  - Fresh blood with WBC, including dose

- **HLA Factors**
  - Homozygous donor

These may be the most important.
Immunocompetent Recipients at risk for GVHD

- Transfusions from family members
- Transfusion of HLA matched platelets
- Transfusion of HLA haploidentical blood products
TA-GVHD in Immunocompetent Recipients

Blood donor

A1
B8
DR3

A1
B8
DR3

Donor responds against the recipient

Blood recipient

A1
B8
DR3

A3
B40
DR5

Recipient does not recognise the donor cells as foreign
Estimates of Frequency of HLA
Homozygous to Heterozygous Transfusion

<table>
<thead>
<tr>
<th>Nation</th>
<th>%</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sardinia</td>
<td>11.4</td>
<td>1:4,300</td>
<td>1:440</td>
</tr>
<tr>
<td>Japan</td>
<td>8.3</td>
<td>1:8,000</td>
<td>1:1,600</td>
</tr>
<tr>
<td>Canada</td>
<td>5.2</td>
<td>1:21,000</td>
<td>1:2,800</td>
</tr>
<tr>
<td>Germany</td>
<td>4.8</td>
<td>1:48,500</td>
<td>1:6,900</td>
</tr>
<tr>
<td>USA</td>
<td>6.4</td>
<td>1:39,000</td>
<td>1:17,700</td>
</tr>
</tbody>
</table>

Frequency is higher in island populations e.g. Japan, Sardinia

Wagner. Transfusion 1995;35:284
Leukoreduction vs. Gamma Irradiation

Dzik. Transfusion 1993;33:493
TA-GVHD Reported to SHOT

Universal LR late 1999 (vCJD)

In the 13 cases 1996-2001:
• 11 were not leukoreduced
• 2 were leukoreduced
• 2 involved blood < 7d old

2012 case:
Fetus given 2 IUTs of maternal blood, neither irradiated nor LR

None 2002 to 2011
None 2013 to 2016
Indications for Irradiated Products

- Directed donations from first-and second-degree relatives
- HLA matched platelets
- Granulocyte transfusion
- Potent immunosuppression (past or present):

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Trade name</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludarabine</td>
<td>Fludara</td>
<td>Purine analogue</td>
</tr>
<tr>
<td>Cladribine or 2-CDA</td>
<td>Leustatin</td>
<td>Purine analogue</td>
</tr>
<tr>
<td>Deoxycoformicin</td>
<td>Pentostatin or Nipent</td>
<td>Purine analogue</td>
</tr>
<tr>
<td>Clofarbine</td>
<td>Clolar</td>
<td>Purine analogue</td>
</tr>
<tr>
<td>Alemtuzumab (anti-CD-52)</td>
<td>Campath</td>
<td>T-cell inhibitor</td>
</tr>
<tr>
<td>Anti-thymocyte globulin</td>
<td></td>
<td>T-cell inhibitor</td>
</tr>
<tr>
<td>Bendamustine</td>
<td>Treakisym, Ribomustin, Levact, Treanda</td>
<td>Purine antagonist</td>
</tr>
</tbody>
</table>
Indications for Irradiated Products (2)

- Intrauterine, fetal transfusion
- Neonatal exchange transfusion
- Neonatal top-up transfusion
- NOT neonatal emergency transfusion
- Congenital cardiac anomalies
  - until 22q11.2 deletion has been excluded
  - confirmed 22q11.2 deletion (DiGeorge syndrome)
Indications for Irradiated Products (3)

- Acute leukemia ONLY IF:
  - HLA-selected platelets
  - Donations from first- or second-degree relatives
- Aplastic anemia IF treated with anti-thymocyte globulin and/or alemtuzumab
- Hodgkin lymphoma
- Non-Hodgkin lymphoma IF treated with purine analogues and related drugs
Indications for Irradiated Products (4)

• Allogeneic hematopoietic stem cell or bone marrow transplant
  – from time of initiation of conditioning therapy
  – while the patient continues to receive GVHD prophylaxis i.e. usually 6 months post transplant or until the lymphocyte count is greater than $1 \times 10^9$/L
Why Don’t We Just Irradiate Them all?

- RBC hemolysis over time is greater with gamma irradiation than with normal aging of RBC
  - release of free Hb
  - release of potassium
  - release of LDH

Use irradiated blood only if indicated.
Evidence of hemolysis in irradiated RBCs on days 0, 14, 28.

Council of Europe Guideline

- RBCs may be irradiated up to 28 days after collection
- Irradiated cells must be transfused ASAP but no later than 14 days post irradiation and no later than 28 days post collection
- Intrauterine transfusions: within 5 days of donation and within 24 hours of irradiation

How does the Blood Bank know if these products are needed?

- It is the ordering physician’s responsibility to order it
- Blood bank may be informed by patient, physician, referring hospital, history check for LIS flags
- Sometimes the blood bank is not told
- SHOT report 2016 (UK): irradiation was missed in 95 cases, and in 77% the clinical area was responsible, but no TAGVHD was reported
- If history suggests that special products may be needed, blood bank staff should check with the Charge Technologist, Medical Director, or ordering physician
Irradiated Products

This list is also on page 71 of Bloody Easy 4
If your patient has special blood requirements he/she should carry a wallet card and wear a MedicAlert bracelet to alert first responders.
Which of the following is true about irradiation of blood products?

A. All patients with HIV should receive irradiated components
B. At-risk patients should receive irradiated plasma
C. Life-saving transfusions should not be delayed while waiting for irradiated blood
D. Prevents sepsis due to bacterial contamination of RBC or PLT
E. Has no adverse effects on RBC
Cytomegalovirus
NAC Recommends CMV seronegative products for:

A. Allogeneic bone marrow transplant recipients
B. Pregnant women
C. Neonates
D. Fetuses undergoing intrauterine transfusion
E. All of the above
Recommendations regarding CMV ‘safe’ vs. CMV seronegative blood components:
1. That CMV safe (leukoreduced) and CMV IgG seronegative products be considered equivalent except for intrauterine transfusions
2. That CBS stop testing for and providing CMV seronegative components
3. That CBS provide a small inventory of CMV dually tested (seronegative and NAT) products for the sole purpose of intrauterine transfusion
Rationale behind NAC Recommendations

• Both leukoreduction (LR) and the use of CMV seronegative components are both very effective at reducing transfusion-transmitted CMV (TT-CMV)
• using both methods limits the donor pool and costs $$
• leukoreduction filter failures are rare (about 0.2%)
• the most infective donors are seronegative and within the first year of seroconversion after acute 1° infection
• there is good data on the safety of LR products for hematopoietic stem cell transplant patients
• infants are at greater risk of contracting CMV from breast milk than from transfusion
Failures of both leukoreduction and serologic testing

Leukoreduction does not eliminate plasma CMV CMV DNA in 44% of newly seropositive donors

Window period before seroconversion is 6 to 8 weeks

Ziemann. Transfusion 2007;47:1972
Ziemann. Transfusion 2013;53:2183
Roback. Transfusion 2013;53:2112
Optimal Approach?

- Optimal approach may be leukoreduction plus NAT testing
Prevalence of CMV DNA in Plasma post seroconversion

Ziemann. Transfusion 2007;47:1972
Are the safest donors seropositive?

CMV DNA IU/mL
Leukoreduced blood to HSCT recipients

- 166 CMV seronegative HSCT recipients
- 89 received LR and seronegative products (pre Jan 2007)
- 79 received leukoreduced products only (post Jan 2007)

<table>
<thead>
<tr>
<th></th>
<th>CMV viremia</th>
<th>CMV disease</th>
<th>2° outcomes*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR and CMV seronegative</td>
<td>3</td>
<td>2</td>
<td>same</td>
</tr>
<tr>
<td>LR only</td>
<td>1</td>
<td>0</td>
<td>same</td>
</tr>
</tbody>
</table>

* total hospital LOS, admissions to ICU, acute and chronic GVHD, 100-day non-relapse mortality
Transfusion vs Breast Milk in VLBW Infants

• 539 VLBW infants (≤ 1500 g) born to 462 mothers at 3 Atlanta hospitals 2010-2013
• followed for up to 12 weeks after birth
• serial testing of serum, urine, breast milk by CMV serology and CMV NAT
• 76% of the mothers were CMV seropositive
• 29 infants became CMV seropositive, all had CMV seropositive mothers (CMV transmission rate 9.1%)
• source of the 29 CMV infections: 27/29 from breast milk, 1 congenital, 1 unknown
Transfusion vs Breast Milk in VLBW Infants

- 24/29 CMV infections asymptomatic
- 5/29 developed symptomatic CMV disease or died
  - 1 pneumonia following NEC, 2 NEC, 2 survived
- 1038 blood products transfused to 310 infants
- Cellular products were LR and CMV seronegative
- Filter failure rate .11% (1 apheresis platelet), which did not result in CMV transmission
- Conclusions: breast milk is the primary cause of postnatal CMV infection in VLBW infants
- Limitations include: the study did not compare LR vs. LR and CMV seronegative blood products

Josephson. JAMA Paedr 2014;168(11):1054
Pilot Study in VLBW Infants

- Compared TT-CMV rates at 2 hospitals that use different approaches to CMV
  - Seattle: LR only
  - Atlanta: LR and CMV seronegative
- Seattle: 20 infants born to 17 mothers, 8 received transfusions, none developed CMV seropositivity
  - CMV seropositivity rate of mothers was 69%
  - overall TT-CMV rate 0% (95% CI 0 – 25.3%)
- Atlanta CMV seropositivity rate 0 (95% CI 0 – 0.9%)
- Would need a large study (6000 patients) to detect a 1% difference between these 2 approaches
  - is this ever going to happen?
Residual Risk of TT-CMV

- **Australian study of leukoreduced only**
  - used a mathematical model
  - RBC and PLT 1:13,575,000
  - RBC only 1:7,790,000
  - PLT only zero

- **Canada leukoreduced only**
  - 1:680,000 RBC
  - 1:186,000 PLT

https://professionaleducation.blood.ca
Current Practice

• The use of CMV seronegative blood was stopped in:
  – 2001 at Sick Kids and Sunnybrook for children
  – 2009 in Ottawa, for HSCT patients
  – 2012 at SHSC
  – 2015 at the 27 hospitals overseen by SHSC/UHN

• YouTube video on this topic by Dr. Callum
  – https://www.youtube.com/watch?v=Cw746m78X3U&feature=youtu.be
Current Standards

  - Cellular blood components should be selected from CMV negative donors or processed e.g. by leukoreduction for:
    - all intrauterine transfusions
    - infants less than 1200 g at birth and CMV status of infant or mother is CMV negative or unknown

- CSTM Standards version 4: 5.4.4.2.1 (2017)
  - there shall be a policy defining when CMV seronegative cellular components are required
  - refer to the most recent NAC recommendations
Contingency Planning for Blood Shortages
Ontario Contingency Plan for the Management of Blood Shortages
Version 3

October 31, 2016
Contingency Planning for Blood Shortages

- the National Plan was updated October 7, 2015
- the Emergency Framework for rationing blood for massively bleeding patients during a red phase of a blood shortage was not changed
- the Ontario Plan, version 3, was published in February, 2017
- an exercise to test the Ontario contingency plan is planned for early 2018, with all hospitals strongly encouraged to participate
Changes to Ontario Plan v3

• Shortage may be regional or provincial in scope
• Small/rural hospitals to maintain inventories on site until redistribution is needed
• Hospital inventories may be adjusted based on Hospital Inventory Index (HII) to ensure equitable distribution
Changes to Ontario Plan v3

- with short-term platelet shortage CBS staff will communicate with hospital staff to negotiate platelet orders for the next morning
- platelet shortages will be communicated as early in the morning as possible, before induction of anesthesia or initiation of CPB
- Appendix F: platelet guidelines
- toolkit updated: checklists, forms, memos, training materials, one-page summaries for hospital and medical staff
Key Elements of a Hospital Emergency Blood Management Plan (HEBMP)

• Communication strategy; identifying key individuals to notify

• Guide to stepwise reduction of blood use including tools to document decisions

• Processes to allow for transfer of blood products between sites

• Plan for recovery
# Blood Shortage Phases

<table>
<thead>
<tr>
<th>Phase</th>
<th>Inventory Level</th>
<th>Hospital Action</th>
</tr>
</thead>
</table>
| **Green**        | Normal                                 | • Practice good blood management, report inventory levels to CBS  
| (includes Advisory) |                                        | • Establish Hospital Emergency Blood Management Committee (HEBMC), maintain emergency blood management plan (EBMP)                                   |
| Amber            | Reduction of inventory by up to 50%    | • Reduce stock inventory (50-75% of Green level) and report inventory to CBS  
|                  |                                        | • Notify HEBMC and convene if prolonged shortage  
|                  |                                        | • Notify internal stakeholders (follow EBMP)  
|                  |                                        | • Screen blood requests (for RBC, transfuse 1 unit and reassess) and consider deferral or alternative therapy (document)  
|                  |                                        | • Review elective OR cases, consider deferral (document) |
| Red              | Shortage is severe and anticipated to be prolonged | • Reduce inventory to critical levels (25% of Green level) and report to CBS  
|                  |                                        | • Convene EBMC and initiate and monitor reduction of blood use (blood issued only for life threatening need)  
|                  |                                        | • Notify internal stakeholders (follow EBMP)  
|                  |                                        | • Document all decisions to defer or cancel blood orders |
| Recovery         | CBS inventory improves                 | • Ensure return to normal operations occurs at a gradual and controlled pace  
|                  |                                        | • Review event and revise plan as needed  
|                  |                                        | • Notify internal stakeholders |
Inventory Management

- Total inventory = CBS inventory + hospital inventory
- CBS knows its own inventory but depends on hospitals to report their:
  - inventory (what they have as a snapshot in time) and
  - disposition data (where it went - either transfused, redistributed, transferred, discarded, etc.)
- Web-based reporting to CBS of hospital inventory and disposition data has been available since May 12, 2014
- Hospitals are asked to report by ABO/Rh where applicable
Inventory Reporting at www.blood.ca
Completeness of Inventory Reporting

242 hospitals, Jan 6-23 2015 inclusive, daily reporting by noon EST

49-86% nationally
Inventory Index (II)

• To improve on “days on hand” as a blood system inventory indicator

• Inventory Index takes into account red cell demand (RCD) as well as inventory
  – red cell demand = RBCs transfused + outdated + wasted

• II can be used nationally, provincially, regionally, and by hospitals

• Could be used to show trends, compare users and balance inventory in shortages
## Inventory Index Calculation

<table>
<thead>
<tr>
<th>Calculation step</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital totals all RBC transfused, outdated and wasted for the past 12 months = average yearly RBC demand</td>
<td>3650</td>
</tr>
<tr>
<td>Hospital divides by 365 to calculate average daily RBC demand (ADRD)</td>
<td>3650/365=10</td>
</tr>
<tr>
<td></td>
<td>ADRD=10</td>
</tr>
<tr>
<td>Hospital notes average total Green phase inventory</td>
<td>90 units</td>
</tr>
<tr>
<td>Inventory Index = Inventory/ADRD</td>
<td>90/10=9</td>
</tr>
<tr>
<td></td>
<td>Hospital Inventory Index=9</td>
</tr>
</tbody>
</table>
### Inventory Index Calculation

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<tr>
<td>Hospital notes average total inventory</td>
<td>90 units</td>
</tr>
<tr>
<td>Inventory index = Inventory/ADRD</td>
<td>90/10=9</td>
</tr>
</tbody>
</table>

**Hospital Inventory Index = 9**

**What is your hospital inventory index?**

Ideal is unknown; “lean” is 6-8
Hospital Average Daily Red Cell Demand (transfused+outdated+wasted/365)
Sourced from disposition data provided by hospitals

National ADRD = 2100
Ontario ADRD = 1050 (50%)
Example hospital ADRD = 10
Total National Inventory RBC

CBS = 25,372 U
Hospitals = 24,994 U
(86% of hospitals reporting)
Total (CBS+hosp) = 50,366

National II = 11.88
Provincial II = 10.42 to 13.4

ON inventory 12,500
ON ADRD (from previous slide) = 1050

Total National Inventory RBC

ON inventory 12,500
ON ADRD (from previous slide) = 1050
<table>
<thead>
<tr>
<th>National # units – Hospitals</th>
<th>Inventory Index</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>25,000</td>
<td>11.9</td>
<td>Green</td>
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<tr>
<td>20,000</td>
<td>9.5</td>
<td>Green</td>
</tr>
<tr>
<td>19,000</td>
<td>9.04</td>
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<td>18,000</td>
<td>8.57</td>
<td>Green</td>
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<tr>
<td>17,000</td>
<td>8.09</td>
<td>Green Advisory &lt;8.0</td>
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<tr>
<td>16,000</td>
<td>7.62</td>
<td>Green Advisory</td>
</tr>
<tr>
<td>15,000</td>
<td>7.14</td>
<td>Amber = &lt; 7.0</td>
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<tr>
<td>14,000</td>
<td>6.67</td>
<td>Amber</td>
</tr>
<tr>
<td>10,000</td>
<td>4.76</td>
<td>Red &lt;5</td>
</tr>
<tr>
<td>5,000</td>
<td>2.38</td>
<td>Red</td>
</tr>
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</table>

Fiscal 2014/2015
National ADRD = 2100 units

Slide credit: C. Doncaster, CBS
“Red Line” Inventory in Rural Sites

For example, in 73 Ontario small hospitals

<table>
<thead>
<tr>
<th></th>
<th>O positive RBC</th>
<th>O negative RBC</th>
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</thead>
<tbody>
<tr>
<td>Green phase</td>
<td>404</td>
<td>303</td>
</tr>
<tr>
<td>Red phase</td>
<td>163</td>
<td>147</td>
</tr>
</tbody>
</table>

Some other groups are also stocked in 21 hospitals in the central and southwest regions of the province.

Small = fewer than 100 beds
Documentation Log: Deferred/Cancelled Surgeries During Blood Shortage

(Use this form if no facility specific form is available)

Instructions for completion: Use this log sheet to record any surgeries deferred or cancelled as a result of blood shortage.

CBS Notification Phase: _ Amber _ Red _ Recovery

Blood Component:

Date of notification of blood shortage received:

<table>
<thead>
<tr>
<th>Date/time</th>
<th>Patient name/ID &amp; location</th>
<th>Procedure</th>
<th>Elective or emergency</th>
<th>Component &amp; estimated # units/dose</th>
<th>Rescheduled</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>
### Documentation of Blood Orders (non-surgery) During a Blood Shortage

Instructions for completion: Record all orders, indicate if order was filled, reduced or deferred. Use the comment field to note any remarkable events including blood group substitutions if ABO/Rh type specific blood is not available. Use new page each day.

**CBS Notification Phase:**  
- Green Advisory  
- Amber  
- Red  
- Recovery  

**Blood Component:** 

**Date of notification of blood shortage received:** 

<table>
<thead>
<tr>
<th>Patient name/ID &amp; location</th>
<th>Products ordered</th>
<th>Time</th>
<th>Products issued</th>
<th>Relevant laboratory results (e.g., hgb, plt)</th>
<th>Comments - alternative therapy or adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### Documentation Log: Platelet Orders During Blood Shortage

(Use this form if no facility specific form is available)

Instructions for completion: Use this log sheet to record any platelet use or deferral due to a blood shortage.

**CBS Notification Phase:**  
- Amber  
- Red  
- Recovery

**Blood Component:** PLATELETS

**Date of notification of blood shortage/advisory received:** 

<table>
<thead>
<tr>
<th>Date/time</th>
<th>Patient name/ID &amp; location</th>
<th>Location</th>
<th>Ordering MD Specialty</th>
<th>Pit Count</th>
<th>Indication for use</th>
<th>No. of doses ordered/transfused</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green Phase</td>
<td>Amber Phase</td>
<td>Red Phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow Failure/</td>
<td>Adhere to a maximum threshold PC of 10 x 10^9/L for prophylactic platelet</td>
<td>Eliminate all prophylactic transfusions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematopoietic Stem Cell Transplantation/</td>
<td>transfusions; consider lowering this threshold for routine prophylactic</td>
<td>All requests for platelet transfusions in non-bleeding patients must be</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>transfusions to 5 x 10^9/L. Transfuse patients undergoing autologous</td>
<td>reviewed by designated medical personnel.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>stem cell transplant only if symptoms of bleeding.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All requests for a platelet transfusion in non-bleeding patients with a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC &gt; 10 x 10^9/L must be reviewed by designated medical personnel.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Split PC doses and use half doses in non-bleeding patients if necessary.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Lowering the Platelet Dose in Amber

Adults, prophylactic PLT transfusions at low, medium or high doses
Days with Bleeding of WHO Grade 2 or higher same at all doses

Slichter. NEJM 2010;362:600 (PLADO trial)
Modified WHO Bleeding Scale

• Grade 2
  – bad nosebleed
  – deep tissue hematoma, joint bleeding
  – melena
  – hematuria
  – vaginal bleeding more than spotting
  – hemoptysis
  – bleeding at venepuncture sites, IV lines

• Grade 3 - requires RBC transfusion

• Grade 4 – hemodynamic instability, death
Lowering Prophylactic PLT Threshold from 10 to 5 in Amber

- retrospective review of all patients with aplastic anemia treated for at least 3 months between 1973 and 1996 (19,000 patient days)
- to evaluate feasibility of platelet threshold of ≤ 5 in stable patients (afebrile, not bleeding), also increased the transfusion interval to ≥ 7 days
- 88% of transfusions occurred at a platelet count of ≤ 10, 57% at a platelet count of ≤ 5
- 3 major nonfatal bleeds (GIB with angiodysplasia, retinal bleed with blurred vision, hemoperitoneum), platelet count at the time of bleed not given
Prophylactic versus Therapeutic-only Platelet Transfusion

Adults with AML or HSCT, prophylactic (< 10) vs. therapeutic PLTs

Days with Bleeding of WHO Grade 2 or higher

Days with bleeding WHO grade 2 or higher

Grade 4 bleeding more common in the therapeutic group, (18 vs. 7)

Wandt. Lancet 2012;380:1309
Prophylactic versus Therapeutic-only Platelet Transfusion

- Randomised multi-centre non-inferiority trial of 600 patients undergoing chemotherapy or HSCT
- 2006 to 2011, UK and Australia
- Randomised to prophylaxis at platelet count of $10 \times 10^9$/L versus no prophylaxis
- Outcome: bleeding of grade 2, 3, or 4 within 30 days

Stanworth. NEJM 2013;368:1771 (TOPPS trial)
Prophylactic versus Therapeutic-only Platelet Transfusion

<table>
<thead>
<tr>
<th></th>
<th>no prophylaxis</th>
<th>prophylaxis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2-4 bleeding</td>
<td>50%</td>
<td>43%</td>
<td>0.06</td>
</tr>
<tr>
<td>Number of bleeding episodes</td>
<td>1.7 +/- 2.9</td>
<td>1.2 +/- 2.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Time to first bleeding episode</td>
<td>17.2 +/- 12.8</td>
<td>19.5 +/- 12.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Platelet transfusions</td>
<td>1.7 +/- 2.6</td>
<td>3.0 +/- 3.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Deaths due to bleeding</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions:
- prophylactic platelet transfusions reduce rates of bleeding in patients with hematologic cancers
- even with prophylaxis, the rate of bleeding is high
Accuracy/Precision of Platelet Counts?

• Ontario: IQMH 2011 to present, no challenges at PLT count below approximately 60

• UK NEQAS (H)
  – accuracy: 40-80% within target range for PLT count 7 +/- 3, depending on analyser
  – precision: CVs for platelet counts of 5-10 range from 15-43%
Platelet count accuracy  UK NEQAS

Target value 7 +/- 3. The greater the proportion of the curve that falls between the 2 red lines, the more accurate the analyser

Lines for Sysmex and Coulter Overlay each other
<table>
<thead>
<tr>
<th></th>
<th>5-10</th>
<th>11-20</th>
<th>21-35</th>
<th>36-65</th>
</tr>
</thead>
<tbody>
<tr>
<td>All methods CV (%)</td>
<td>31.6</td>
<td>20.2</td>
<td>15.1</td>
<td>9.5</td>
</tr>
<tr>
<td>Mean CV (%) by instrument</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beckman Coulter (Miami, FL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ac*T 5 Diff</td>
<td>42.8</td>
<td>24.5</td>
<td>14.9</td>
<td>9.9</td>
</tr>
<tr>
<td>Ac*T Diff</td>
<td>34.4</td>
<td>21.0</td>
<td>12.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Gen-S</td>
<td>20.1</td>
<td>17.2</td>
<td>11.5</td>
<td>8.3</td>
</tr>
<tr>
<td>HmX</td>
<td>34.8</td>
<td>23.6</td>
<td>17.6</td>
<td>10.4</td>
</tr>
<tr>
<td>LH 500</td>
<td>29.1</td>
<td>12.1</td>
<td>11.4</td>
<td>5.7</td>
</tr>
<tr>
<td>LH 750</td>
<td>15.3</td>
<td>12.6</td>
<td>11.5</td>
<td>5.5</td>
</tr>
<tr>
<td>LH 780</td>
<td>18.8</td>
<td>9.9</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>Abbott (Santa Clara, CA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CELL-DYN 3200</td>
<td>33.8</td>
<td>23.3</td>
<td>17.3</td>
<td>10.0</td>
</tr>
<tr>
<td>CELL-DYN 3700</td>
<td>33.1</td>
<td>27.0</td>
<td>19.9</td>
<td>10.9</td>
</tr>
<tr>
<td>CELL-DYN 4000</td>
<td>27.1</td>
<td>19.2</td>
<td>14.4</td>
<td>8.8</td>
</tr>
<tr>
<td>CELL-DYN Sapphire</td>
<td>26.5</td>
<td>17.2</td>
<td>14.2</td>
<td>9.6</td>
</tr>
<tr>
<td>Horiba ABX (Montpellier, France)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DX 120</td>
<td>30.3</td>
<td>18.4</td>
<td>10.7</td>
<td>7.3</td>
</tr>
<tr>
<td>Pentra 120</td>
<td>32.5</td>
<td>21.0</td>
<td>13.9</td>
<td>8.2</td>
</tr>
<tr>
<td>Pentra 60</td>
<td>33.2</td>
<td>20.8</td>
<td>16.5</td>
<td>8.0</td>
</tr>
<tr>
<td>Pentra 80</td>
<td>39.7</td>
<td>19.3</td>
<td>14.7</td>
<td>8.5</td>
</tr>
<tr>
<td>Siemens (Tarrytown, NY)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADVIA 120</td>
<td>21.8</td>
<td>13.1</td>
<td>10.9</td>
<td>7.8</td>
</tr>
<tr>
<td>ADVIA 2120</td>
<td>21.9</td>
<td>13.1</td>
<td>11.5</td>
<td>7.8</td>
</tr>
<tr>
<td>Sysmex (Kobe, Japan)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KX-21</td>
<td>37.1</td>
<td>22.7</td>
<td>14.9</td>
<td>10.2</td>
</tr>
<tr>
<td>poch-100i</td>
<td>31.6</td>
<td>23.6</td>
<td>13.8</td>
<td>9.9</td>
</tr>
<tr>
<td>SF-3000</td>
<td>31.8</td>
<td>19.4</td>
<td>13.2</td>
<td>6.7</td>
</tr>
<tr>
<td>XE-2100</td>
<td>17.3</td>
<td>15.3</td>
<td>9.5</td>
<td>5.2</td>
</tr>
<tr>
<td>XT-1800i</td>
<td>18.2</td>
<td>12.2</td>
<td>10.6</td>
<td>5.1</td>
</tr>
<tr>
<td>XT-2000i</td>
<td>25.0</td>
<td>17.6</td>
<td>9.2</td>
<td>4.6</td>
</tr>
<tr>
<td>CV range (%)</td>
<td>15-43</td>
<td>10-27</td>
<td>9-20</td>
<td>5-11</td>
</tr>
</tbody>
</table>

Platelet Count Precision
UK NEQAS
CV range 15 – 43%
at platelet count 0f 5-10

De la Salle. AJCP 2012;137:65
### Platelet Guidelines

<table>
<thead>
<tr>
<th><strong>Green Phase</strong></th>
<th><strong>Amber Phase</strong></th>
<th><strong>Red Phase</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Hemorrhage</strong></td>
<td>For head trauma or CNS bleeding maintain a PC &gt; 80 x 10⁹/L.</td>
<td>Same as Amber phase.</td>
</tr>
<tr>
<td>Immune thrombocytopenia and life- or limb-threatening bleeding maintain PC &gt; 10 x 10⁹/L.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other significant bleeding, or acute promyelocytic leukemia at acute presentation, maintain a PC &gt; 50 x 10⁹/L.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Invasive Procedures/Surgery</strong></td>
<td><strong>Invasive Procedures/Surgery</strong></td>
<td><strong>Invasive Procedures/Surgery</strong></td>
</tr>
<tr>
<td>For non-surgical invasive procedures maintain a PC &gt; 20 x 10⁹/L (central venous catheter insertion, paracentesis, thoracentesis).</td>
<td>Urgent² and emergency³ surgery in consultation with HEBMC. In presence of active bleeding or surgical procedure maintain a PC &gt; 50 x 10⁹/L or if CNS trauma/surgery a PC &gt; 80 x 10⁹/L.</td>
<td>Emergency surgery in consultation with HEBMC. All requests for platelet transfusion must be reviewed by designated medical personnel.</td>
</tr>
<tr>
<td>For lumbar maintain a PC &gt; 50 x 10⁹/L.</td>
<td>For non-surgical invasive procedures (other than bone marrow aspiration or biopsy) maintain a PC &gt; 10 x 10⁹/L with image guidance.</td>
<td></td>
</tr>
<tr>
<td>For CNS surgery maintain a PC &gt; 100 x 10⁹/L.</td>
<td>For lumbar puncture, maintain a PC &gt; 20 x 10⁹/L.</td>
<td></td>
</tr>
</tbody>
</table>

[www.transfusionontario.org](http://www.transfusionontario.org)
Prophylactic PLTs in LP

• National Plan Guideline (Canada) states threshold of 50 in Green Phase, 20 in Amber, consult in Red
• AABB (2015) – 50 (and use clinical judgment for 20-50)
• BCSH (2017) – 40
  – or 20/40/50 in children depending on clinical situation (2016)
• C17 Guidelines Committee (Children’s Oncology Group, Canada) (2010) – 20 (Grade 2B)
• Cardiovascular and Interventional Radiological Society of Europe (CIRSE, 2012) – 50 (this is our challenge)
• Am Society of Clinical Oncology (2001) – discusses studies that used 20, says more research needed
2. Estcourt. BJH 2017;176:365
3. New. BJH 2016;175:784
4. www.C17.ca
Prophylactic PLTs in LP (1)

- 5223 LPs in children with ALL
- 941 (18%) had platelet count ≤ 50
- 199 (3.8%) had platelet count ≤ 20
- For the 199 with PLTs ≤ 20, 95% CI for serious complications was 0 – 1.75%
- no serious complications (neurologic, infectious, hemorrhagic) after any LP
- concluded that children with ALL do not require prophylactic PLTs if count > 10
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>

3.8% PLT count ≤ 20.

Overall 95% CI for serious complications at PLT count ≤ 20 = 0-1.75%
Prophylactic PLTs in LP (2)

<table>
<thead>
<tr>
<th>PLT</th>
<th># LPs</th>
<th>% of LPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>25</td>
<td>0.27</td>
</tr>
<tr>
<td>10 – 20</td>
<td>67</td>
<td>0.74</td>
</tr>
<tr>
<td>20 – 30</td>
<td>88</td>
<td>0.96</td>
</tr>
<tr>
<td>30 – 40</td>
<td>92</td>
<td>1.00</td>
</tr>
<tr>
<td>40 – 50</td>
<td>107</td>
<td>1.18</td>
</tr>
<tr>
<td>50 – 100</td>
<td>729</td>
<td>8.0</td>
</tr>
<tr>
<td>&gt; 100</td>
<td>7980</td>
<td>87.8</td>
</tr>
<tr>
<td>total</td>
<td>9088</td>
<td>100</td>
</tr>
</tbody>
</table>

- 440 children, 9088 LPs
- 83% had ALL.
- excluded first (diagnostic) LP.
- 1% PLT count ≤ 20.
- no spinal hematomas.
Prophylactic PLTs in LP (3)

- 195 LPs in 66 adult patients with acute leukemia over 6 yrs
- no serious hemorrhagic complications
- significant trend towards traumatic LP at lower PLT counts
- recommended a threshold of not less than 20 in these patients

<table>
<thead>
<tr>
<th>Platelet count ($\times 10^9$/L)</th>
<th>No. of LPs</th>
<th>95% CI for complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–30</td>
<td>35</td>
<td>0.00–10.0</td>
</tr>
<tr>
<td>30–50</td>
<td>40</td>
<td>0.00–8.81</td>
</tr>
<tr>
<td>50–100</td>
<td>43</td>
<td>0.00–8.22</td>
</tr>
<tr>
<td>&gt;100</td>
<td>77</td>
<td>0.00–4.68</td>
</tr>
<tr>
<td>Total</td>
<td>195</td>
<td>0.00–1.87</td>
</tr>
</tbody>
</table>
Rationing Blood for Massively Bleeding Patients during a Red Phase of a Blood Shortage
Emergency framework for rationing of blood for massively bleeding patients during a red phase of a blood shortage

Working group on emergency disposition of blood during a red phase blood shortage

2012-04-14

Approved by CBS Provincial/Territorial Blood Liaison Committee January 2012

www.nacblood.ca
Purposes of the Emergency Framework

• To guide health care professionals in triaging patients requiring massive transfusion during a red phase blood shortage
  – when demand for blood greatly exceeds supply
  – when all other measures to increase the blood supply have been exhausted

• To standardize care across jurisdictions

• To allow for fair and just distribution of blood

• Massive transfusion: one blood volume/24 hr, half blood volume/3 hr, ≥ 4U RBC/1 hr
massive transfusion?

is there enough?

> 1 eligible patient?

supplemental Inclusion criteria

re-assess q24h/q10U

general exclusion criteria

specific exclusion criteria
Triage Tool – General Exclusion Criteria

• Severe burns with
  – Age > 60 yrs, or > 60% body surface affected, or
  – Inhalation injury requiring mechanical ventilation

• Cardiac arrest

• Advanced progressive baseline cognitive impairment

• Metastatic cancer with life expectancy < 6 mo.

• Immunocompromised, advanced and irreversible

• Acute neurological condition, severe and irreversible

• End-stage organ failure (with certain criteria)
Specific Exclusion Criteria

• Trauma
• Ruptured AAA
• ECMO/VAD
• Organ transplantation
• Gastroenterology
• Obstetrics ("specific" in that it’s *not* excluded)
• Other massively bleeding patients
Legal Considerations

Emergency Framework/Triage Tool

• There is an altered standard of care during a Red Phase, when access is limited by supply
• Patients must have access to all other available therapies short of transfusion
• Providers who use the Triage Tool competently and in good faith should not be found negligent for decisions dictated by it
• So far none of the Canadian triage frameworks for allocation of limited resources (e.g. ventilators, ICU beds) has been tested in court
Validation of Emergency Framework

- Done as part of the 2013 National Plan validation exercise
- Study sites:
  - Royal Columbian Hospital, BC
  - Sunnybrook Health Sciences Centre, ON
  - Alberta Health Services – Edmonton, AB
- Nov 14-18 2013 all patients in whom a massive hemorrhage was identified evaluated for:
  - fulfillment of triage stopping criteria for the particular clinical situation
  - total number of RBC units transfused
  - survival outcomes
## Validation of Emergency Framework Exclusion Criteria

<table>
<thead>
<tr>
<th>Pt</th>
<th>Indication</th>
<th>Triage stopping criteria met?</th>
<th>RBC units transfused</th>
<th>Survival outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ruptured AAA</td>
<td>No</td>
<td>8</td>
<td>No. Died within 24 hrs</td>
</tr>
<tr>
<td>2</td>
<td>Trauma MVC</td>
<td><strong>Yes</strong></td>
<td>3</td>
<td>No. Died on day 12</td>
</tr>
<tr>
<td>3</td>
<td>Post op bleeding</td>
<td>No</td>
<td>21</td>
<td>Yes.</td>
</tr>
<tr>
<td>4</td>
<td>RBC exchange for hemoglobinopathy crisis</td>
<td>No</td>
<td>6</td>
<td>Yes.</td>
</tr>
<tr>
<td>5</td>
<td>Perforated colon while on rivaroxaban</td>
<td>No</td>
<td>34</td>
<td>Yes.</td>
</tr>
<tr>
<td>6</td>
<td>Ruptured AAA</td>
<td>No</td>
<td>29</td>
<td>No. Died within 24 hrs</td>
</tr>
</tbody>
</table>

Nahirniak et al CSTM 2014
Results and Conclusions

• Only one of six met ‘stopping’ criteria
• Of the two ruptured AAA neither met stopping criteria, they used 8 and 29 units of RBC and both died within 24 hours
• Simulation exercises of longer duration are needed
• Maybe the ruptured AAA stopping criteria can be revised
Case Scenario

• Canada is currently in a Red Phase of a red blood cell (RBC) shortage
• Multiple patients present to your hospital and you have enough RBC for one patient only
• Which of the following patients will be transfused as part of their therapy?...
Case Scenario

A. Transfusion dependent aplastic anemia patient age 12. PLT 17 and Hb 76
B. Male staff member age 56 with ruptured AAA found without pulse or BP in hospital parking lot
C. Female pedestrian age 25 struck by car, unconscious, bleeding 100 mL/min from head wound, partial amputation of leg, distended abdomen suggestive of internal bleeding
D. Male age 63 on the organ transplant waiting list for 5 years, deceased donor organ available
Case Scenario

A. Transfusion dependent aplastic anemia patient age 12. PLT 17 and Hb 76

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C. Female pedestrian age 25 struck by car, unconscious, bleeding 100 mL/min from head wound, partial amputation of leg, distended abdomen suggestive of internal bleeding

D. Male age 63 on the organ transplant waiting list for 5 years, deceased donor organ available

A. Hb > 70 g/L
Case Scenario

A. Transfusion dependent aplastic anemia patient age 12. PLT 17 and Hb 76

B. Male staff member age 56 with ruptured AAA found without pulse or BP in hospital parking lot

C. Female pedestrian age 25 struck by car, unconscious, bleeding 100 mL/min from head wound, partial amputation of leg, distended abdomen suggestive of internal bleeding

D. Male age 63 on the organ transplant waiting list for 5 years, deceased donor organ available

B. Ruptured AAA with preoperative cardiac arrest
D. Male age 63 on the organ transplant waiting list for 5 years, deceased donor organ available

D. Deceased donor organ harvested without transfusion of donor; transplant may proceed but without RBC transfusion, informed consent to state this
Case Scenario

C. Meets trauma criteria for receipt of RBC: transfuse and re-assess

C. Female pedestrian age 25 struck by car, unconscious, bleeding 100 mL/min from head wound, partial amputation of leg, distended abdomen suggestive of internal bleeding

D. Male age 63 on the organ transplant waiting list for 5 years, deceased donor organ available
Platelet Transfusion in Patients on Anti-platelet Drugs
Platelet Transfusion after Spontaneous Intracerebral Hemorrhage (PATCH)

190 patients randomised (Netherlands, France, UK)
Supratentorial ICH, on antiplatelet agent(s) for ≥ 7 days

97 standard care
plus platelet transfusion

93 standard care

Primary outcome: difference in functional outcome (death or dependency) at 3 months based on modified Rankin Score (mRS)

Subgroup analyses by: type of antiplatelet therapy, country, hematoma volume

Baharoglu. Lancet 2016;387(10038):2605
Odds Ratio of death or dependency (mRS score 4-6) = 2.05 (95% CI 1.18-3.56, p=0.0114)
Platelet Transfusion after Spontaneous Intracerebral Hemorrhage (PATCH)

Subgroup analysis: difference in death/dependency according to type of antiplatelet therapy, country, intracerebral hemorrhage volume

![Graph showing subgroup analysis results]

Baharoglu. Lancet 2016;387(10038):2605
Platelet Transfusion after Spontaneous Intracerebral Hemorrhage (PATCH)

Subgroup analysis: difference in death/dependency according to type of antiplatelet therapy, country, intracerebral hemorrhage volume.

“CONCLUSION: PLATELET TRANSFUSION CANNOT BE RECOMMENDED FOR THIS INDICATION IN CLINICAL PRACTICE”
Limitations of this study

• Small sample size
  – 19% met at least one exclusion criterion
  – took 6 years to enroll 190 patients
  – inclusion bias could not be excluded

• Most patients were on aspirin alone (73%)
  – generalizable to all antiplatelet drugs?

• Mechanism of apparent adverse effect of platelet transfusion unknown
  – pro-inflammatory effects?
Neurosurgical Patients on Anti-platelet Drugs

• 72 patients on antiplatelet drugs with intracranial hemorrhage requiring neurosurgical intervention
• All received 2 doses of platelets preoperatively, some received more intraoperatively
• 1° outcome arterial thrombotic complications (acute coronary syndrome, stroke)
• 2° outcome re-bleeding
• No ACS, 1 stroke (1.4%), 19 (26.4%) had recurrent intracranial bleed
• Conclusion: use of pre-op platelets showed low risk for arterial thrombotic complications
Platelet Transfusion in GI Bleed

Retrospective cohort study of ER patients with acute GI bleeds, PLT > 100, on anti-PLT agent(s)

- 204 patients received platelets
- 204 consecutive matched control patients

Multivariate regression analysis performed to adjust for differences in baseline characteristics between cases and controls

Primary outcome: recurrent GI bleed
Platelet Transfusion in GI Bleed: Results

- univariate analysis showed greater rates of re-bleeding, major adverse cardiovascular events, myocardial infarction, mortality, and prolonged length of stay with PLT transfusion
- but multivariate analysis showed a significant difference only in mortality
  – adjusted OR 5.57; 05% CI 1.52 – 27.1
  – higher mortality with PLT transfusion (mechanism?)
Platelet Transfusion in GI Bleed: Results

- Univariate analysis showed greater rates of re-bleeding, major adverse cardiovascular events, myocardial infarction, mortality, and prolonged length of stay with PLT transfusion.
- Multivariate analysis showed a significant difference only in mortality.
  - Adjusted OR 5.57; 05% CI 1.52 – 27.1
  - Higher mortality with PLT transfusion (mechanism?)

“CONCLUSION: WE DO NOT SUPPORT THE USE OF PLATELET TRANSFUSIONS IN PATIENTS WITH GIB WHO ARE TAKING ANTIPLATELET AGENTS”
Podcasts

• Blood Bank Guy [www.bbguy.org](http://www.bbguy.org)
  – 10 minute ‘podlets’ and 60 minute podcasts
  – #016 plasma, #033 ER MD interview, #035 platelets
• Emergency Medicine Cases [https://emergencymedicinecases.com](https://emergencymedicinecases.com)
  – #65: IV iron in the ER, #36: transfusions, anticoagulants and bleeding
• EMCrit (Emergency Department Critical Care and Resuscitation) [https://emcrit.org](https://emcrit.org)
  – search “transfusion”, “PROPPR” etc.
How’s Your TMQIP Doing?
Here’s mine (full disclosure)

- ER, surgery, OB, ICU. 130 beds, about 30 ALC
- have had guidelines for years
- have order sets (nobody uses them yet)
- technologists started screening blood orders December 2016