Blood Product Utilization

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Medical Director
American Red Cross
Northeast Division Blood Services
Blood Product Utilization

- “The appropriate use of blood and blood components with a goal to minimize their use”

- Objectives:
  - Review the safety of current blood product transfusions
  - Review the appropriate utilization of red blood cells, plasma and platelet products
  - Review the current indications for transfusion
Reevaluate role of blood products in patient care

Blood products can be life-saving in the appropriate clinical situations:

- Red blood cells restore oxygen carrying capacity and potentially improve tissue hypoxia
- Platelets maintain endothelial integrity and assist in coagulation
- Plasma provides coagulation factors to ensure adequate clotting
Blood Product Utilization

- Factors driving appropriate use:
  - **Good:**
    - Blood transfusion is considered safer than it has ever been
    - “Zero risk” blood
  - **Bad:**
    - Increased cost (more testing)
    - Decreased supply (more donor deferrals)
Blood Product Utilization

“Zero Risk” Blood

Emerging Infectious Disease Threats

Risk per Unit

1:100

1:1,000

1:10,000

1:100,000

1:1,000,000


Revised Donor Deferral Criteria
HBsAg Screening
HIV Ab Screening
HCV Ab Screening
p24 Ag Testing
HCV and HIV NAT
WNV NAT
T cruzi Ab Screening
HBV NAT

Emerging Disease Threats
ICL
bacteria
vCJD
T cruzi
PTLVs
SFV
WNV
SARS
Monkey Pox
Leishmania
Influenza
DENV
Babesia
CHIKV
XMRV

Perkins et al. Transfusion 2010;50:2080
Blood Product Utilization

Blood Product Utilization

“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”

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Blood Product Utilization

Red Blood Cells (RBCs)

- 15 million units of RBCs transfused annually in the US
  - > 40,000 units per day
  - 3.5 million patients will receive RBC transfusions
- Transfusion practices vary widely
RBC Products

- Made from whole blood or apheresis
- Stored in anticoagulant/preservative solution
- Avg Hct 55-65%, volume 350-400 mL
- 1 unit will raise Hgb by 1 g/dL and Hct by 3%
- Leukoreduction
  - From $1 \times 10^9$ to < $5 \times 10^6$ WBC
  - Decrease in febrile transfusion reactions
  - CMV safe (< 4% vs. 1% for CMV-seronegative)
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When to Transfuse RBC Products?

- Historically, transfusion followed the “10/30” rule:
  - Hgb < 10 g/dL or Hct < 30% indicated a need for RBC transfusion
  - Established in WWII
  - Remained standard of care for over 50 years

Adams RC, Lundy JS. *Surg Gynecol Obstet* 1942;74:1011
Transfusion Requirements in Critical Care (TRICC) Trial

- 838 patients from 22 centers, randomized to transfusion at Hgb < 7 g/dL (restrictive group) vs. < 10 g/dL (liberal group)
  - 2.6 units of RBCs transfused per restrictive patient vs. 5.6 units per liberal patient

- Restrictive group used 54% fewer RBC transfusions (33% required NO transfusions)
Transfusion Requirements in Critical Care (TRICC) Trial

- **No difference in 30-day mortality** *(18.7% restrictive vs. 23.3% liberal, p=0.10)*
- In-hospital mortality lower in restrictive group *(22.2% vs. 28.1%, p=0.06)*
Blood Product Utilization

Transfusion Requirements in Critical Care (TRICC) Trial

<table>
<thead>
<tr>
<th></th>
<th>Restrictive N (%)</th>
<th>Liberal N (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>3 (0.7)</td>
<td>12 (2.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pulmonary Edema</td>
<td>22 (5.3)</td>
<td>45 (10.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>ARDS</td>
<td>32 (7.7)</td>
<td>48 (11.4)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Patients with acute cardiac disease did the same in the two groups*
“A restrictive strategy (Hgb < 7 g/dL) of red-cell transfusion is at least as effective as and possibly superior to a liberal transfusion strategy (Hgb < 10 g/dL) in critically ill patients...with the possible exception of patients with acute myocardial infarction and unstable angina.”
Transfusion in Patients with Cardiovascular Disease

Hebert et al. *Crit Care Med* 2001;29:227

- Subset analysis of TRICC trial of 357 patients with or at risk of cardiovascular disease: 160 restrictive and 197 liberal
  - RBC units transfused – 2.4 vs. 5.2
  - 30 and 60-day mortality rates not significantly different (23% vs 23%; 26% vs. 27%)
  - No difference in complication rates except pulmonary edema (9% vs. 18%, p=0.01)
  - *However a non significant trend (p=0.30) towards better outcome was observed in liberally transfused patients with confirmed ischemic heart disease.*
  - *This was the only patient group where risk tended to favor liberal transfusion strategy*
“A restrictive red blood cell transfusion strategy generally appears to be safe in most critically ill patients with cardiovascular disease, with the possible exception of patients with acute myocardial infarcts and unstable angina.”
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Restrictive vs. Liberal

- McIntyre et al. *Neurocrit Care* 2006;5:4
- 67 patients with moderate to severe head injury: 29 restrictive (Hgb < 7 g/dL) vs. 38 liberal (< 10 g/dL)
  - Units transfused – 1.4 vs. 4.6
  - No difference in 30 or 60-day mortality rates (17% vs. 13%, p=0.64)
  - No difference in incidence of multiple organ dysfunction syndrome (12.1% vs. 10.6%, p=0.35)
  - “Unable to detect significant improvements in mortality with a liberal as compared to restrictive transfusion strategy”
TRIPICU study

- 637 stable, critically ill children: 320 restrictive (Hgb < 7 g/dL) vs. 317 liberal (< 9.5 g/dL)
  - Patients in restrictive arm received 44% fewer transfusions; 174 (54%) received no transfusions
  - New or progressive MODS developed in 39 liberal vs. 38 restrictive (12% in both)
  - 14 deaths in each arm

- No significant differences were found in other outcomes, including adverse events
Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair

- FOCUS trial
- 2016 patients randomly assigned to a transfusion threshold of 10 g/dL, or to receive RBC transfusion with anemia symptoms or Hgb < 8 g/dL
  - Primary outcome: death or the inability to walk across a room without human assistance at 60-day follow-up
- Restrictive group required 65% fewer RBC transfusions (59% received NO transfusions)
# Blood Product Utilization

## FOCUS Trial

<table>
<thead>
<tr>
<th>60-day Period</th>
<th>Liberal N=1007</th>
<th>Restrictive N=1009</th>
<th>Risk Difference</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or Inability to walk</td>
<td>351 (35.2%)</td>
<td>347 (34.7%)</td>
<td>0.5%</td>
<td>1.01</td>
</tr>
<tr>
<td>Inability to walk</td>
<td>275 (27.6%)</td>
<td>281 (28.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>76 (7.6%)</td>
<td>66 (6.6%)</td>
<td>1.0%</td>
<td>1.17</td>
</tr>
</tbody>
</table>

“Symptomatic transfusion conserved blood and had no adverse effects on ability to walk or mortality at 60-day follow-up.”

Blood Product Utilization

American Association of Blood Banks

- Transfusion recommendations:
  - 1) Restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients
  - 2) Restrictive strategy in hospitalized patients with preexisting cardiovascular disease (8 g/dL)
  - 3) Cannot rec. restrictive strategy in patients with Acute Coronary Syndrome
  - 4) Decision to transfuse should be based on symptoms as well as hgb level
Blood Product Utilization

“Spork.”
Blood Product Utilization

Platelet Products

American Red Cross
Platelet Kinetics and Dose

- 2 mechanisms of clearance
  - Lifespan in circulation is 7-10 days
  - Fixed daily loss to maintain vascular integrity – plugging gaps in microvasculature-estimated to be 7.1x10^9 platelets/L/day

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Retrospective analysis of 92 patients with acute leukemia

Days with bleeding
- I = any hemorrhage
- II = excludes skin, epistaxis
- III = visible hemorrhage

Statistically significant increase in bleeding rate at platelet count < 20,000/μL
Blood Product Utilization


- 20 stable aplastic anemia patients
  - Received no transfusions
  - 51Cr stool blood loss
  - Bleeding rate stable at platelet count > 5,000/uL

![Graph showing stool blood loss vs platelet count](image-url)
Prophylactic Platelet Transfusions

- 52-74% of platelet transfusions
- For decades the trigger for transfusions was 20,000/uL
- More recent studies have assessed the bleeding risk for platelet counts of 10,000/uL vs. 20,000/uL
  - None of those studies showed an increase in bleeding risk or need for more RBC transfusions with the 10,000/uL trigger

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- 255 newly diagnosed AML patients, randomized to receive platelet transfusions for thresholds of < 20,000/uL vs. < 10,000/uL
- Patients in the < 10,000/uL threshold group received 21.5% fewer platelet transfusions (p=0.01)
- Episodes of major bleeding occurred in 21.5% vs. 20% (p=0.41)
- Number of RBC transfusions similar in both groups
- “The risk of major bleeding during induction chemotherapy in adolescents and adults with AML...was similar with platelet-transfusion thresholds of 20,000 per cubic millimeter and 10,000 per cubic millimeter”
Blood Product Utilization

Determination of the Optimal Prophylactic PLADo study

- Multi-institutional study sponsored by the National Heart, Lung, and Blood Institute of the National Institutes of Health
- Question addressed: Does the dose of platelets transfused affect hemostasis in thrombocytopenic patients?

- 1272 Patients with thrombocytopenia due to chemotherapy for hematologic malignancy/BMT-expected to have platelet count ≤10,000 for ≥5 days

Slichter, SJ et al. NEJM 2010;362(7):600
PLADO Study

• 1,272 patients randomized to 1 of 3 arms:

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Platelet Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium Dose (MD)*</td>
<td>2.2 x 10^{11}</td>
</tr>
<tr>
<td>Lower Dose (LD)</td>
<td>1.1 x 10^{11} (1/2 MD)</td>
</tr>
<tr>
<td>Higher Dose (HD)</td>
<td>4.4 x 10^{11} (2x MD)</td>
</tr>
</tbody>
</table>

*Medium dose corresponds to standard transfusion dose of 1 SDP

—Primary endpoint: % patients with WHO grade 2-4 bleeding (gross hemorrhage not requiring RBC transfusions—epistaxis, hematuria, etc)

—Transfusion trigger: AM platelet count <10,000

• SURPRISING RESULT: *Everyone bled!*

Slichter, SJ et al. *NEJM* 2010;362(7):600
# Blood Product Utilization

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>LD</th>
<th>HD</th>
<th>MD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>417</td>
<td>423</td>
<td>432</td>
<td>1,272</td>
</tr>
</tbody>
</table>

**Primary Endpoint**

*At least one episode of ≥ Grade 2 bleeding*

<table>
<thead>
<tr>
<th>Secondary Endpoints:</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest grade of bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None or Grade 1</td>
<td>30%</td>
<td>32%</td>
<td>30%</td>
<td>31%</td>
</tr>
<tr>
<td>Grade 2</td>
<td>58%</td>
<td>59%</td>
<td>60%</td>
<td>59%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>9%</td>
<td>7%</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Grade 4</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Hemorrhagic mortality</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Slichter, SJ et al. *NEJM* 2010;362(7):600
Blood Product Utilization

PLADO-Conclusions

- Occurrence of Grade 2 or higher bleeding in thrombocytopenic patients receiving platelet transfusions remains high (70%) regardless of the platelet dose
- Low dose policy reduces total platelet requirements at the expense of a higher number of transfusion events without difference in bleeding outcomes
- Validates smaller pools of RDP, confirms splitting practices and the use of “non standard” low dose SDP
- Models suggest low and medium dose strategies are cost effective (though splitting of SDPs is required)
- High dose strategy may be useful in outpatient settings

Slichter, SJ et al.  *NEJM* 2010;362(7):600
**Blood Product Utilization**

**Strategies for Transfusion of Platelets**

- **STOP trial**
  - Double-blind randomized controlled trial (RCT) performed in 6 sites in 3 countries
  - Comparing low dose vs. standard dose prophylactic platelet transfusions in patients with thrombocytopenia
- 536 thrombocytopenic patients
  - Low dose of $1.5-3.0 \times 10^{11}$ platelets/product vs. standard dose of $3.0-6.0 \times 10^{11}$
- Primary outcome:
  - WHO Grade 2 (or higher) bleeding

ClinicalTrials.gov identifier: NCT00420914
SToP Trial

- Data Safety Monitoring Board stopped study when the difference of Grade 4 bleeding reached the pre-specified threshold of 5%
  - 129 patients had been randomized (goal was to enroll 536 patients); 119 patients analyzed
  - 3 patients in low dose arm vs. none in standard dose arm had Grade 4 bleeds
    - 2 had retinal hemorrhage and 1 had subarachnoid hemorrhage

ClinicalTrials.gov identifier: NCT00420914
Proportion of patients with WHO Grade 2 or higher bleeding was 51.7% (30/58) in low-dose treatment arm & 49.2% (30/61) in standard-dose arm.

Based on study being stopped, no conclusion can be reached about the non-inferiority of low dose platelets related to bleeding.

Even though 3 patients in low dose arm experienced Grade 4 bleeding, all 3 remained in study and suffered no long-term morbidity related to the bleeding events.

ClinicalTrials.gov identifier: NCT00420914
Therapeutic vs. Prophylactic

  - 396 patients undergoing either chemotherapy for AML or autologous stem cell transplant for hematologic cancer
  - Randomized to receive platelet transfusions for bleeding (therapeutic strategy) or for platelet counts < 10,000/uL (prophylactic strategy)
  - Therapeutic strategy resulted in 33.5% decrease in transfusions
  - No increased risk of major bleeding observed in the autologous stem cell transplant group
  - However, there was an increased risk of WHO grade 4 bleeds (CNS) in the AML group

- “The therapeutic strategy could become a new standard of care after autologous stem cell transplantation”
- “However, prophylactic platelet transfusion should remain the standard for patients with acute myeloid leukemia”
- “The new strategy should be used...only if the staff are well educated and experienced...and can react in a timely way to the first sign of CNS bleeding”
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**Trial of Platelet Prophylaxis**

- **TOPPS** trial
- RCT to evaluate the safety and efficacy of therapeutic vs. prophylactic platelet transfusions (platelet count < 10,000/uL)
  - 600 adult thrombocytopenic patients with hematologic malignancy undergoing myelosuppressive therapy
  - 300 patients randomized to each group
  - WHO Grade 2 or higher
  - Therapeutic group received 38% fewer platelets (41% received no transfusions)

WHO grade 2-4 bleeding occurred in 151/300 patients (50%) in the therapeutic group compared to 128/298 (43%) in the prophylaxis group (p=0.06)

The time to the first grade 2-4 bleed was significantly shorter in the therapeutic group

Patients in the therapeutic group averaged 1.7d (SD 2.9) with a WHO grade 2-4 bleed during follow-up, vs. 1.2d (SD 2.0) in the prophylactic group [rate ratio 1.52, 95% CI 1.14 to 2.03]

“the results of our study support the need for the continued use of prophylaxis with platelet transfusion and show the benefit of such prophylaxis for reducing bleeding, as compared to no prophylaxis”
Platelet Transfusion Guidelines

- <10,000/uL in presence of marrow failure with NO bleeding
- <50,000/uL in patients who are bleeding or with invasive procedures
- <100,000/uL for neuro/eye surgery
- Patients with qualitative platelet abnormalities—bleeding/prophylaxis
- Dosage appropriate for body mass:
  - 1 unit/10 kg (6 RDP or 1 SDP)
  - Increase platelet count by 20,000–60,000/uL
“You’ll be awake during the entire procedure. The anesthesiologist is on vacation.”
Blood Product Utilization

Plasma Products

- Fresh Frozen Plasma (FFP)
- Plasma Frozen Within 24 Hours (FP24)
- Thawed Plasma
- Plasma, Cryoprecipitate-Reduced
  - Cryo Poor Plasma
FFP vs. FP24

- **Fresh Frozen Plasma**
  - Prepared from whole blood or apheresis
  - Separated and frozen at -18° C within 6 - 8 hours of collection
  - Store for 12 months at -18° C
  - After thaw store for 24 hours at 1-6° C

- **Plasma Frozen 24 Hrs**
  - Prepared only from whole blood
  - Separated and frozen at -18° C within 24 hours of collection
  - Store for 12 months at -18° C
  - After thaw store for 24 hours at 1-6° C
FFP vs. FP24

<table>
<thead>
<tr>
<th>Reference</th>
<th>Measurement</th>
<th>Factor</th>
<th>FP24</th>
<th>FFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardigan^5</td>
<td>Median activity U/mL (range)</td>
<td>Factor V</td>
<td>0.80 (0.53-1.12)</td>
<td>0.94 (0.35-1.48)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor VIII</td>
<td>0.77 (0.38-1.40)</td>
<td>1.00 (0.48-1.85)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vWF protease activity</td>
<td>0.97 (0.30-1.85)</td>
<td>1.01 (0.57-1.63)</td>
</tr>
<tr>
<td>Smith^6</td>
<td>Mean percent of activity relative to time zero ±1SD</td>
<td>Factor V</td>
<td>98.6 ± 3.2</td>
<td>101.4 ± 2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor VIII</td>
<td>89.8 ± 1.9</td>
<td>75.9 ± 2.4</td>
</tr>
<tr>
<td>O’Neill^7</td>
<td>Mean percent of activity relative to time zero ±1SD</td>
<td>Factor V</td>
<td>100 ± 14</td>
<td>102 ± 14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor VIII</td>
<td>64 ± 13</td>
<td>84 ± 16</td>
</tr>
<tr>
<td>Thibault^8</td>
<td>Mean activity U/mL ±1SD</td>
<td>Factor V</td>
<td>0.87 ± 0.13</td>
<td>0.88 ± 0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor VIII</td>
<td>0.82 ± 0.17</td>
<td>0.90 ± 0.18</td>
</tr>
</tbody>
</table>

- Levels of FVIII are significantly lower in FP24 than FFP but within normal range
- No significant difference in other factors, ATIII, Protein C and S

http://www.aabb.org/development/education/material/Pages/resourceguide.aspx
Thawed Plasma

- FFP or FP24 stored at 1-6°C for up to 5 days after thaw
- Used primarily in trauma and transplantation settings

<table>
<thead>
<tr>
<th>Factor</th>
<th>Day 1</th>
<th>Day 5</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIII* (%)</td>
<td>89±22</td>
<td>52±12</td>
<td>41</td>
</tr>
<tr>
<td>II (%)</td>
<td>81±9</td>
<td>80±10</td>
<td>1</td>
</tr>
<tr>
<td>V (%)</td>
<td>79±7</td>
<td>66±9</td>
<td>16</td>
</tr>
<tr>
<td>VII (%)</td>
<td>90±18</td>
<td>72±15</td>
<td>20</td>
</tr>
<tr>
<td>X (%)</td>
<td>85±13</td>
<td>80±11</td>
<td>6</td>
</tr>
<tr>
<td>I (mg/dL)</td>
<td>225±12</td>
<td>225±12</td>
<td>0</td>
</tr>
</tbody>
</table>

Downes et al. Transfusion 2001;41:570
One unit = 250-400 mL = 100% coagulation factor activity

1 mL/kg increases coagulation factors by 1%

Usual therapeutic dose is 10-20mL/kg (more for warfarin reversal)

<table>
<thead>
<tr>
<th>Factor</th>
<th>Normal</th>
<th>Hemostatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>200-400</td>
<td>50-100</td>
</tr>
<tr>
<td>Factor V</td>
<td>1 U/mL</td>
<td>5-25%</td>
</tr>
<tr>
<td>Factor VII</td>
<td>1 U/mL</td>
<td>5-25%</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>1 U/mL</td>
<td>15-25%</td>
</tr>
</tbody>
</table>
Clinical Indications for Plasma

- Treat/prevent bleeding and/or pre-operatively
  - Deficiency of multiple coagulation factors
  - Specific factor deficiency & no concentrate available
- Replacement of Multiple Coagulation Factors
  - Liver disease
  - Disseminated intravascular coagulation (DIC)
  - Massive transfusion
  - *Reversal of warfarin*
- Plasmapheresis therapy
  - TTP (Cryo Poor Plasma)
Reversal of Warfarin

- Indicated for *immediate* reversal of anticoagulation
  - Life threatening bleeding
  - Urgent need for surgical intervention
  - Dose 30 mL/Kg (lower doses ineffective)
- Withholding drug & vitamin K therapy safer options in patients who did NOT need urgent correction
  - Baker et al. *Br J Haematol* 2006;133:331
# Blood Product Utilization

## Recommended management of a supratherapeutic INR

<table>
<thead>
<tr>
<th>INR</th>
<th>Bleeding present</th>
<th>Recommended action</th>
</tr>
</thead>
</table>
| >Ther to 5.0 | No               | Lower warfarin dose, or  
Omit a dose and resume warfarin at a lower dose when INR is in therapeutic range, or  
No dose reduction needed if INR is minimally prolonged |
| >5.0 to 9.0 | No               | Omit the next 1 to 2 doses of warfarin, monitor INR more frequently, and resume treatment at a lower dose when INR is in therapeutic range, or  
Omit a dose and administer 1 to 2.5 mg oral vitamin K1* |
| >9.0      | No               | Hold warfarin and administer 2.5 to 5 mg oral vitamin K1. Monitor INR more frequently and administer more vitamin K1 as needed,  
Resume warfarin at a lower dose when INR is in therapeutic range |
| Any       | Serious or life-threatening | Hold warfarin and administer 10 mg vitamin K1 by slow IV infusion; supplement with prothrombin complex concentrate, fresh frozen plasma, or recombinant human factor VIIa, depending on clinical urgency. Monitor and repeat as needed. |

INR: International Normalized Ratio; Ther: therapeutic INR range for the patient in question.  
* This option is preferred in patients at increased risk for bleeding (e.g., history of bleeding, stroke, renal insufficiency, anemia, hypertension). Adapted from Ansell, J, Hirsh, J, Hylek, E, et al. Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008; (6 Suppl):160s.
## Blood Product Utilization

<table>
<thead>
<tr>
<th>Non-urgent</th>
<th>Urgent (not bleeding)</th>
<th>Urgent (bleeding)</th>
</tr>
</thead>
</table>
| - Stop 5 days prior to procedure  
- Check INR 1-2 days prior  
- If INR>1.5 Vit K 1-2mg PO | - Plasma or PCC prior to procedure. Repeat in 6-12 hours if INR high and  
- Vit K 5-10mg PO/IV if sustained reversal is desired | - Vit K 5-10mg IV; repeat every 12 hours as needed  
- PCC or Plasma; repeat every 6 hours as needed |
“Routine minimally invasive critical care procedures can be safely performed by experienced clinicians in the setting of mildly abnormal coagulation test results”

“There is no evidence that FFP transfusion alters the risk of bleeding”

- Stanworth et al. *Br J Haem* 2004;126:139
- Segal et al. *Transfusion* 2005;45:1413
- Gajic et al. *Crit Care Med* 2006;34:S170
Blood Product Utilization

Prophylaxis in Non-Bleeding Patients

Elevated INR/PT increases risk of bleeding

Transfusing FFP will correct the INR/PT

Correcting the INR/PT will reduce bleeding

Segal JB, Dzik WH. Transfusion 2005;45:1413
**Conclusion:**
There is insufficient evidence to conclude that abnormal test results predict bleeding.

Segal JB, Dzik WH. *Transfusion* 2005;45:1413
Does Plasma Transfusion Correct Prolonged INR in Patients with Mild Coagulation Abnormalities?

- 121 patients with pre-transfusion INR from 1.1 to 1.85
- 1091 plasma transfusions
  - Only 1 patient (0.8%) INR corrected with plasma
  - 15% showed partial correction of INR
  - Median decrease in PT= 0.20 seconds (INR 0.07)

INR of FFP/PF24 may be as high as 1.3

- “Available studies do not support the efficacy of FFP in treating bleeding or as prophylaxis for invasive procedures in patients with mild coagulopathy (INR < 2.0).”

Abdel-Wahab et al. Transfusion 2005; 46:1279
Blood Product Utilization

Relationship between the PT and INR, and levels of clotting factors

Dzik WH. Transfusion 2012;52:45S
Blood Product Utilization

Plasma Required to Maintain Target INR for >3 hours after Transfusion

<table>
<thead>
<tr>
<th>Init. INR</th>
<th>1.3 Target</th>
<th>1.5 Target</th>
<th>1.7 Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vol.* (L)</td>
<td>Dose (ml/kg)</td>
<td>Vol.* (L)</td>
</tr>
<tr>
<td>6.0</td>
<td>4.5</td>
<td>64</td>
<td>3.5</td>
</tr>
<tr>
<td>5.0</td>
<td>4.3</td>
<td>61</td>
<td>3.0</td>
</tr>
<tr>
<td>4.0</td>
<td>4.0</td>
<td>57</td>
<td>2.5</td>
</tr>
<tr>
<td>3.0</td>
<td>3.5</td>
<td>50</td>
<td>2.0</td>
</tr>
<tr>
<td>2.0</td>
<td>2.5</td>
<td>36</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Vol. necessary for 70 kg. person

Holland LL, Brooks JP. *Am J Clin Pathol* 2006;126:133
80% reduction in plasma use when they initiated guidelines against transfusing plasma for INR < 2.0 in non-bleeding patients

Observed NO episodes of bleeding due to withholding plasma

“A program...using evidence-based guidelines can successfully decrease the use of FFP without any observable increase in unexpected bleeding”
Blood Product Utilization

Trauma/Massive Blood Loss

- Massive blood loss:
  - ≥10 units RBCs/24 hrs
  - 1 total blood volume/24 hrs
  - 4 units RBCs/1 hr with expectation of more needed

- **Anyone** can receive type O- RBCs
- **Anyone** can receive type AB plasma

- Resuscitation with reconstituted whole blood
  - 1:1 mix of RBCs, plasma
  - Platelets & cryo at set intervals (e.g. 1 SDP:5 RBCs)
    - Ketchum et al. *J Trauma* 2006;60:S51
    - Burtelow et al. *Transfusion* 2007;47:1564
Blood Product Utilization

Type AB Plasma

- Type AB plasma is RARE
- Donor base is limited (4%)
- Demand often exceeds supply
- Hospitals need to work with blood supplier to make sure type AB plasma use is prioritized for patients who need it most

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>Prevalence in U.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>O+</td>
<td>38%</td>
</tr>
<tr>
<td>O−</td>
<td>7%</td>
</tr>
<tr>
<td>A+</td>
<td>34%</td>
</tr>
<tr>
<td>A−</td>
<td>6%</td>
</tr>
<tr>
<td>B+</td>
<td>9%</td>
</tr>
<tr>
<td>B−</td>
<td>2%</td>
</tr>
<tr>
<td>AB+</td>
<td>3%</td>
</tr>
<tr>
<td>AB−</td>
<td>1%</td>
</tr>
</tbody>
</table>
Premise: Group A plasma is acceptable to use in MTPs when AB plasma availability is limited.

Rationale:

- Population distribution:
  - ~85% Group A or Group O
  - ~15% Group B or Group AB

- Supply of AB plasma limited
  - 4% population Group AB, but distribution of AB plasma ranged from 7%-25%

- TRALI mitigation will reduce available supply of AB plasma
Blood Product Utilization

Group A Plasma in Massive Transfusion

- Problem: ~15% of potential trauma patients would receive incompatible plasma; potential for hemolysis
- Mitigating factors:
  - Patients also getting O RBCs
  - Group A donors have low anti-B titers
  - Severe complications with Anti-B hemolysis are not common (as opposed to anti-A)
Blood Product Utilization

Group A Plasma in Massive Transfusion

- Zielinski et al. *J Trauma Acute Care Surg* 2013;74: 69
  - Reported the use of Group A plasma in MTP
  - “Of the 254 patients, 35 (14%) received ABO-incompatible and 219 (86%) received ABO-compatible transfusions. None of the patients who received incompatible plasma had a hemolytic reaction. There were no differences in clinical outcomes between the two groups.”

- AABB Annual Meeting 2013-4 trauma centers reported their experience
  - Mayo Clinic, Penn State-Hershey, University of Florida, Dartmouth
  - All had similar % of ABO-incompatible patients (14%-16%)
  - None of the patients had a hemolytic reaction
Blood Product Utilization

Group A Plasma in Massive Transfusion

- Antibody titers
  - Mayo data: 120 male group A WB donors were titered
    - Median titer was 1:16
    - 91.7% were 1:64 or less; none above 1:512
  - Karafin et al. *Transfusion* 2012;52:2087
    - Anti-B titers in 228 group A apheresis platelets
    - Median titer was 1:8 in group A platelets
    - 98.7% were 1:64 or less; none above 1:128
    - A “critical titer” did not predict risk of a hemolytic reaction
Blood product usage can be life-saving

- Transfusions are not without risk

Limit overuse of blood products and improve patient safety:

- Following the AABB recommendations for RBC transfusions
- Adhering to the standard of care threshold for prophylactic platelet transfusions
- Following the accepted clinical guidelines for plasma transfusions
Blood Product Utilization

THE END

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