Disclosures: None Relevant

- Honoraria for speaking:
  Alexion, Novartis, Shire, Bard
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  Alexion, Ablynx, Shire
- Clinical trials:
  Ablynx, Bioverativ, CSL Behring, Octapharma
- Research funding:
  CSL Behring, Ortho Clinical Diagnostics
Learning Objectives

1. When should platelets be transfused?
2. What platelets should be selected for transfusion?
   1. Role of ABO and Rh
   2. Apheresis vs. buffy coat pool platelets
   3. HLA matched platelets
   4. Irradiated
   5. CMV negative
WHEN SHOULD PLATELETS
BE TRANSFUSED?
Hypoproliferative Thrombocytopenia

- Transfusion guidelines:
  - **Prophylactic** platelet transfusions should be given
  - A threshold of $\leq 10 \times 10^9 / L$ should be used for prophylactic platelet transfusion
  - Patients with **clinically significant bleeding** attributed to thrombocytopenia should probably receive platelet transfusions even if the platelet count is **above $10 \times 10^9 / L$**
Beyond Hypoproliferative Thrombocytopenia...

- Evidence is poor and recommendations are based on consensus opinion.
- Preoperative platelet count is not significantly associated with intraoperative or postoperative bleeding (Bishop et al 1987).

Check out recent AABB platelet guidelines...Kaufman et al 2015.
## Other Indications for Platelet Transfusion

<table>
<thead>
<tr>
<th>PLT</th>
<th>Clinical Setting</th>
<th>Suggest</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>Procedures not associated with significant blood loss (e.g. Central line placement)</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Patients on anticoagulants that should not be stopped</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>20-50</td>
<td>Procedures not associated with significant blood loss</td>
<td>1 adult dose on hold, transfuse only if significant bleeding</td>
</tr>
<tr>
<td>&lt;50</td>
<td>Significant bleeding</td>
<td>Transfuse 1 pool immediately before procedure</td>
</tr>
<tr>
<td></td>
<td>Pre-major surgery, lumbar puncture, epidural anaesthesia</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>Immune thrombocytopenia</td>
<td>Transfuse platelets only with life-threatening bleeding</td>
</tr>
<tr>
<td>&lt;100</td>
<td>CNS surgery, ICH, TBI</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>Any</td>
<td>Platelet dysfunction and marked bleeding (e.g. post cardiopulmonary bypass, aspirin, or other antiplatelet agents)</td>
<td>Transfuse 1 adult dose</td>
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</tbody>
</table>
WHAT PLATELETS SHOULD BE SELECTED FOR TRANSFUSION?
Does ABO Matter?

- ABH antigens are expressed on platelets
- Platelet concentrate = Platelets + Plasma
- Minor incompatibility
  - Plasma is incompatible with recipient (ex. Group O platelets to group A recipient)
  - Potential for hemolytic transfusion reaction
- Major incompatibility
  - Platelets are incompatible with recipient (ex. Group A platelets to group O recipient)
  - Potential for reduced post-transfusion platelet count increment
    - But there is no definitive evidence that adverse events or mortality are different (with exception of rate of refractoriness)
Does ABO Matter?

• ICTMG recommends:
  • Platelet concentrates that are ABO identical should probably be used in patients with hypoproliferative thrombocytopenia, if available
  • But…We have limited platelet inventory, shelf-life of platelets is short and the clinical need for platelets is often urgent
    • About 50% of platelet transfusions are non-identical
• How to mitigate risk?
  • Platelet substitution guidelines
  • Titration of group O platelets
  • Plasma reduction
  • Future: platelet additive solution

Nahirniak et al 2015; Pavenski et al Transfusion 2010
Does ABO Matter?

Algorithm for ABO/Rh Decision – Platelet Infusions

Order for platelets received for appropriate clinical indication

- Issue ABO, RhD-identical platelets

  Issue available platelets according to patient group:
  1. Group RhD neg gets RhD neg wherever possible
  2. Group O gets O>B>A>AB
     Group A gets A>AB>B>O
     Group B gets B>AB>A>O
     Group AB gets AB>A>B>O

- ABO, RhD-identical platelets available

  Is clinical requirement urgent

    YES
    1. RhD group takes precedence over ABO in choice of product for RhD Negative recipients
    2. Each institution should have a policy to address use of RhIg when RhD neg. patients receive RhD pos. platelets, particularly when the patient is a female of child-bearing potential

    NO
    Contact CBS – are ABO, RhD-identical platelets available in time

    NO
    YES
Does Rh Matter?

• Platelet concentrate may contain residual RBC
  • Number of RBCs in apheresis platelets: less than 0.0002 mL per unit
  • Number of RBC in PRP WBD platelets: 0.4 to 0.6 mL of RBCs per unit
  • Number of RBC in BC WBD platelets: ?
• Risk of D alloimmunization is very low
  • ADAPT (Cid et al)
    • 7 (1.44%) of 485 D− recipients developed anti-D after transfusion of D+ platelets (no difference in the type of platelet product was observed)
• RhIg can prevent alloimmunization and is safe
• Single dose of RhIg may cover multiple platelet exposures
  • Half-life is 21 days
  • 300μg dose eliminates 15mL of RBC
• Consider risks and benefits for each individual patient
Does Rh Matter?

- ICTMG recommends:
  - Female children and females of child-bearing age/potential, with hypoproliferative thrombocytopenia, who are RhD negative should probably receive RhIg before, immediately after, or within 72 hours of receiving an RhD-positive platelet component (unless antibody testing demonstrates the persistence of anti-D from a previous dose of Rh immunoglobulin)
  - Males and females who are not of child-bearing age/potential, with hypoproliferative thrombocytopenia, who are RhD-negative and are transfused with RhD-positive platelet components probably do not require RhIg
# Apheresis vs. Buffy Coat Platelets

<table>
<thead>
<tr>
<th></th>
<th>Apheresis PLT</th>
<th>Buffy Coat PLT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Method of production</strong></td>
<td>Collected by apheresis</td>
<td>Whole blood derived</td>
</tr>
<tr>
<td><strong>Donor exposure</strong></td>
<td></td>
<td>45% increase in donor exposure</td>
</tr>
<tr>
<td><strong>Clinical efficacy</strong></td>
<td>Better corrected count increment without proven improved hemostatic efficacy</td>
<td></td>
</tr>
<tr>
<td><strong>HLA alloimmunization risk</strong></td>
<td>same</td>
<td>same</td>
</tr>
<tr>
<td><strong>Bacterial contamination risk</strong></td>
<td>same</td>
<td>same</td>
</tr>
<tr>
<td><strong>Transfusion safety</strong></td>
<td>Increased reactions</td>
<td>TRALI risk – same</td>
</tr>
<tr>
<td></td>
<td>TRALI risk – same</td>
<td>Hemolysis risk - same</td>
</tr>
<tr>
<td><strong>Cost of production</strong></td>
<td>Expensive to produce</td>
<td>Allows for production of other components</td>
</tr>
<tr>
<td><strong>Donor safety</strong></td>
<td>Increased donor reactions</td>
<td></td>
</tr>
<tr>
<td><strong>Product quality</strong></td>
<td>?lower pH, donor dependent</td>
<td></td>
</tr>
</tbody>
</table>

Apheresis vs. Buffy Coat Platelets

• ICTMG recommends:
  • When leukoreduced platelet products are available, WBD platelets should be used as equivalent products to apheresis platelets

• When are apheresis platelets specifically indicated?
  • HLA and/or HPA selected
  • IgA deficient
National Platelet Demand

Platelet Demand

Month of Date

- Grand Total
- Apherisis PLTS
- Platelets Pooled

Product Type
- Apherisis PLTS
- Platelets Pooled
- Grand Total
Nova Scotia Platelet Demand

The graph illustrates the platelet demand in Nova Scotia from May 2016 to September 2018. The data is divided into three categories:

1. **APHERESIS PLTS**
2. **PLATELETS POOLED ED**
3. **Grand Total**

The graph shows fluctuations in demand over the specified period, with peaks and troughs indicating periods of higher and lower demand. The month of date is indicated at the bottom of the graph.
HLA Matching

- Platelet refractoriness is a persistent lack of post-transfusion platelet count increment

Platelet Refractoriness

Immune factors (<20%)
- Alloimmune to HPA (10-20%)
- Alloimmune to HLA Class I (80-90%)
- Alloimmune to both HLA and HPA (5%)
- Autoimmune (unknown)

Non-immune factors (>80%)
- Sepsis, fever, disseminated intravascular coagulation, splenomegaly, active bleeding, drugs, etc.
Before Looking for HLA Match...

- Confirm refractoriness on the basis of at least 2 post-transfusion count increments
- Consider patient factors: rule out/consider non-alloimmune causes of platelet refractoriness
- Consider platelet factors
  - **Older** platelet concentrate age (>48 hrs) and **ABO** platelet incompatibility is associated with worse post-transfusion platelet count increments
- **Dose**

  Transfuse fresh, ABO identical PLT and measure post-transfusion platelet increment at 10-60 min

Slichter et al 2005; Triulzi et al 2012
Diagnostic Workup

- HLA alloimmunization = IgG antibodies against HLA Class I antigens, namely A and B antigens
- Test for presence of HLA antibodies and determine their specificity if present
  - flow cytometric immunofluorescence, multiplex flow cytometric bead-based assays
- Determine patient’s HLA type
  - genotyping
HLA-matched Platelet Transfusions in Patients with Hypoproliferative Thrombocytopenia

• Systematic review: 1 RCT, 15 prospective and 14 retrospective observational studies (1600 patients)
  • Old studies using old methods (62% published prior to 1990)
  • Small and of poor methodological quality
  • +++ Heterogeneity, not amenable to meta-analysis
• RCT:
  • Patients receiving HLA-matched PLT transfusion had fewer bleeding episodes than patients receiving nonmatched PLTs (p = 0.095)
  • Similar results were found for refractoriness (p value was not stated), alloimmunization (p value was not stated), and the number of PLT transfusions
HLA-matched Platelet Transfusions in Patients with Hypoproliferative Thrombocytopenia

- Observational studies
  - Not enough data to make conclusions re: mortality and bleeding
  - HLA-matched platelets associated with improved platelet increments/recovery at 1 hour
    - Findings on 18-24 hour CCR or PPR variable suggesting that HLA-matched PLT do not survive normally
    - Better increment with closer matches
    - Presence of HLA antibodies associated with better increment
Guidance on Platelet Transfusion for Patients with Hypoproliferative Thrombocytopenia

• Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions:
  • AND have class I HLA antibodies
    • should probably receive class I HLA-selected or crossmatch-selected platelet transfusion to increase the platelet count (weak level of evidence, weak recommendation).

• Due solely to nonimmune factors
  • should probably not receive HLA-selected or crossmatch-selected platelets (weak level of evidence, weak recommendation).
Who Needs Irradiated Platelets?

- Irradiation prevents **transfusion-associated graft versus host disease** (destroys lymphocytes)
- Platelets may be irradiated at any stage during storage and then stored as per their normal shelf life
- At risk: immunocompromised patients OR immunocompetent patients receiving a haploidentical blood component

348 unique cases identified in literature
The first symptom occurs at median 11 days (IQR, 8-14 days; range, 1-198 days) from the implicated transfusion
Who Needs Irradiated Platelets?

- Everyone receiving:
  - Components donated by first- or second-degree relatives
  - HLA selected platelets
  - Intrauterine transfusions (IUT)
- At risk patients:
  - Patients undergoing allogeneic hematopoietic stem cell transplantation: from the time of initiation of conditioning chemoradiotherapy for the duration of GVHD prophylaxis
  - Patients undergoing autologous bone marrow or peripheral blood stem cell transplant: from initiation of conditioning chemoradiotherapy until 3 months post-transplant (6 months if total body irradiation was used in conditioning).
  - Patients with severe congenital T-cell immunodeficiency
  - Patients with Hodgkin lymphoma
  - Patients with non-Hodgkin lymphoma and who received purine analogues or other drugs
  - Patients with aplastic anemia and treated with ATG or alemtuzumab
  - Neonates who have received IUT and those with very low birth weight
Who Needs CMV Negative Platelets?

- Transfusion-transmitted CMV may lead to organ and/or life-threatening CMV disease in vulnerable, CMV seronegative patients
- Risk of CMV is reduced by universal pre-storage leukoreduction (CMV safe)
  - Residual risk is 1 in 13,575,000!
- National Advisory Committee on Blood and Blood Products (NAC)
  - Recommends that CMV safe (leukoreduced) and CMV IgG seronegative products be considered equivalent except for intrauterine transfusion

[http://www.nacblood.ca/resources/guidelines/CMV.html](http://www.nacblood.ca/resources/guidelines/CMV.html), February 2017; Seed et al Vox Sanguinis 2015
Questions?

Everything I ever wanted/needed to know about platelets, I learned from the ICTMG…Check out https://www.ictmg.org/about-ictmg