Platelet collection by apheresis

Single Donor Platelets (SDP)

3 X 10^{11} plts

(10^4-10^6 WBC)
How much should we transfuse?

- Tricky due to type of product being used
- Most of the time in pediatrics 10 – 20 ml/kg is the dose used primarily based on platelet concentrate studies not apheresis products
- Many places use apheresis products due to an AABB standard (March 2004) to limit and detect bacterial contamination in all platelet components.
- No data to support exactly how much should be given for prophylaxis versus during a time of bleeding
When should we transfuse?

- Platelet count whereby risk of bleeding justifies platelet transfusion is not well established in neonates - least amount of evidence available.

- Different etiologies for thrombocytopenia as mentioned earlier makes this difficult.

- Developmental difference in neonates versus adults does not allow for extrapolation from adult studies when establishing platelet transfusion thresholds
  a) hyporeactive platelets
  b) higher incidence IVH
  c) NAIT – ICH approximately 11%
Neonatal Alloimmune Thrombocytopenia

- Pathogenesis: incompatibility between parental platelet antigens, mother sensitized to fetal platelet antigen.
- First pregnancy can produce affected fetus, no routine screening
- ICH reported in 10 – 15% of cases.
- A systematic review of best practice and review of the literature revealed no RCTs
- A survey of Germany and Canada neonatologists revealed:
  - 60% of Canadian and 32% German Neonatologists tx preterm infants for cts between 30 – 50 x 10^9/L but 25% German Neonatologists tx for 10 – 20 x 10^9/L.
  - In term infants even use lower triggers 5 – 10 x 10^9/L.

Neonatal Alloimmune Thrombocytopenia

- If plt count < 30 \(\times 10^9\)/L give therapy ASAP
  published in uncontrolled studies

- Therapy: 1\(^{st}\) line: Maternal platelets, irradiated and washed

  2\(^{nd}\) line: In Caucasians HPA-1a/HPA-5b antigen-negative platelets

  3\(^{rd}\) line: RDP or SDP
  IVIG (delayed response 1-3 days)

Why should we transfuse?

- Unlike adults, there are very few clinical trials that study neonatal transfusion practices.

- Expert opinion and clinical experience seem to dictate why we should transfuse certain infants at certain platelet counts and during certain stages of treatment in the NICU.

- In adults etiologies for thrombocytopenia are better understood due to more rigorous study.

- In adults, length of time in hypoproliferative state is far more predictable in most cases.
# Platelet Transfusion Trigger Trials

## Adults

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Design</th>
<th>Plt Trigger</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gil-Fernandez et al., 1996</td>
<td>190</td>
<td>BMT, Non-randomized</td>
<td>10 versus 20</td>
<td>No diff bleeding, Fewer plt tx 10K group</td>
</tr>
<tr>
<td>Heckman et al., 1997</td>
<td>78</td>
<td>Acute Leukemia, randomized</td>
<td>10 versus 20</td>
<td>No diff bleeding</td>
</tr>
<tr>
<td>Rebuella et al., 1997</td>
<td>255</td>
<td>New dx AML, randomized multi-instit</td>
<td>10 versus 20</td>
<td>No diff major bleeding, No diff RBC tx</td>
</tr>
<tr>
<td>Wandt et al., 1998</td>
<td>105</td>
<td>AML, Prospective Comp.</td>
<td>10 versus 20</td>
<td>No diff bleeding, Fewer plt tx in 10K grp.</td>
</tr>
<tr>
<td>Lawrence et al., 2001</td>
<td>144</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zumberg et al., 2002</td>
<td>159</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Approximately 25% of thrombocytopenic neonates in the U.S. (35,000 neonates per year) have platelet counts that reach levels thought to increase the risk of hemorrhage (< 50 x 10^9/L). (Murray, 2002)

Largest number of donor exposures for neonates in U.S. NICUs is due to platelet transfusions. (Del Vecchio, 2001 and Chevuru, 2002)

No clear correlations have been established between degree of thrombocytopenia and risk of bleeding.
Neonatal Transfusion Practice Studies

- Over past 10 yrs worldwide disparity in use of platelet transfusions in thrombocytopenic neonates
  - Mexico – 2%
  - UK - 3%
  - US - 8.2%

- No correlation between platelet useages and severity of illness or incidence of thrombocytopenia in each NICU

- NICU with lowest platelet use had lowest incidence of IVH suggesting no correlation between platelet transfusion and thrombocytopenia and preventing IVH

Neonatal Transfusion Practice Studies

- Andrew M et al. 1993. is the only multi-center RCT in neonates examining prophylactic platelet transfusion triggers.

- N=152 patients studied and investigators concluded:
  a) No difference observed in frequency or severity of ICH between the cohort receiving transfusions for < 150 x10⁹/L vs. control grp. transfusions for < 50 x 10⁹/L grp.
  b) non-bleeding premature infants with plt cts > 60 x 10⁹/L should not receive prophylactic platelet transfusions.
Neonatal Transfusion Practice Studies

- Murray *et al.* 2002 over a 3 year period.
- Small retrospective study N= 53 patients.
- Group 1 transfuse plts if < 30 x 10⁹/L.
- Group 2 transfuse plts if between 30-50 x 10⁹/L with previous IVH and or clinically unstable.
- Observed no major hemorrhage among neonates no matter platelet transfusion threshold.
- Concluded that a prophylactic platelet transfusion trigger of < 30x10⁹/L probably represents a safe practice for clinically stable NICU patients.
Neonatal Transfusion Practice Studies

- Paucity of scientific evidence

- Platelet transfusion practice based on
  a. physician preference
  b. expert or consensus recommendations
  c. guidelines
# Summary of Platelet Transfusion Triggers Recommended for Neonates

(platelet counts $\times 10^9/L$)

## Table 2

Summary of platelet transfusion triggers recommended for neonates (platelet counts $\times 10^9/L$)

<table>
<thead>
<tr>
<th>Author</th>
<th>Nonbleeding sick preterm</th>
<th>Nonbleeding stable preterm</th>
<th>Nonbleeding term</th>
<th>Before invasive procedure</th>
<th>Active bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blanchette et al, 1991$^a$ [60]</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
<td>&lt;50 if failure of production</td>
<td>&lt;50 if failure of production</td>
</tr>
<tr>
<td>Blanchette et al, 1995 [56]</td>
<td>&lt;50</td>
<td>&lt;30</td>
<td>&lt;20 if stable</td>
<td>&lt;100 if DIC</td>
<td>&lt;100 if DIC</td>
</tr>
<tr>
<td>Roberts et al, 1999 [55]</td>
<td>&lt;50 if DIC</td>
<td>&lt;50</td>
<td>&lt;30</td>
<td>&lt;50 for minor procedure</td>
<td>&lt;50 in all cases</td>
</tr>
<tr>
<td>Calhoun et al, 2000 [57]</td>
<td>&lt;50</td>
<td>&lt;25</td>
<td>Same as preterm</td>
<td>&lt;100 for major surgery</td>
<td>&lt;100 if DIC</td>
</tr>
<tr>
<td>Strauss, 2000 [58]</td>
<td>&lt;100</td>
<td>&lt;20</td>
<td>&lt;20</td>
<td>&lt;100 if major organ bleeding</td>
<td>&lt;100 if DIC</td>
</tr>
<tr>
<td>Murray, 2002 [52]</td>
<td>&lt;50</td>
<td>&lt;30</td>
<td>&lt;30</td>
<td>&lt;50 if minor bleeding</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Gibson et al, 2004$^b$ [86]</td>
<td>&lt;30</td>
<td>&lt;20</td>
<td>Same as preterm</td>
<td>Not addressed</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>

$^a$ Guidelines from the Pediatric Hemotherapy Committee of the American Association of Blood Banks for the conduct of pediatric blood transfusion audits.

$^b$ Guidelines from the British Committee for Standards in Haematology Transfusion Task Force.

Platelet Transfusion Practice Among Neonatologists in the U.S. and Canada: Results of a Survey

- Survey designed to understand current neonatal platelet transfusion practices of neonatologists

CD Josephson, LL Su, RD Christensen, CD Hillyer, M Castillejo, MR Emory, Y Lin, HA Hume, M Sola-Visner

Emory University, GA; Intermountain Healthcare, UT; Canadian Blood Services, Ontario and Ottawa, ON; Drexel University, PA

Josephson et al., Pediatrics (in press) 2008
Hypothesis

There will be significant variability in the following platelet transfusion practices in neonates:

1) platelet transfusion triggers
2) platelet product selection
3) platelet dosing among U.S. and Canadian neonatologists

Josephson et al., Pediatrics (in press) 2008