Cardiopulmonary Bypass in infants and children

The impact of priming solutions and volumes

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The Ideal Cardiopulmonary Bypass Prime...

- Would be physiologic
  - mild hypocalcemia
- Would not trigger:
  - inflammation
  - immune response
- Would prevent macro or microthrombosis
- Would protect end-organ function
Prime volumes in Pediatric Patients

- Start at about 200-300ml generally
- Circulating volume of neonates is 80ml/kg (240ml)
- Dilution of RBC, platelets, coagulation factors
- Dilution of plasma proteins, drug levels
- Significant electrolyte changes
Realistic Prime Solutions

• At least physiologic:

• Blood Prime:
  • Age of blood
  • Impact of Red Cell transfusions
  • Hematocrit values

• Crystalloid/colloid Solutions:
  • Colloid osmotic pressure and outcomes
  • Small volume circuits
Blood Products and Cardiopulmonary Bypass

- Age of RBCs and outcomes
- Use of whole blood vs component products
- Target hematocrit
- Dilutional Coagulopathy
- Metabolic Consequences
Age of RBCs and Clinical Effects in Pediatric Patients


Studies of Blood Products, Bleeding and Outcomes Are Confounded By:

- Storage Solutions
- Leucocyte Depletion
- Legislation
- Transfusion Protocols and adherence
- Surrogate end points and relevant findings
  - Lactate during CPB?
  - Definition of old vs new
Reconstituted Fresh Whole Blood vs Stored Blood Component Therapy for Neonates Undergoing Cardiac Surgery

*Study Design*

♥ single center, prospective RCT

**Entrance criteria:**
- neonates less than one month of age undergoing CPB for elective open heart surgery

**Exclusion criteria:**
- emergency surgery
- known pre-existing coagulopathy
## Study Protocol

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<tr>
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<th><strong>Treatment Group</strong></th>
<th><strong>Control Group</strong></th>
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<tbody>
<tr>
<td></td>
<td>Reconstituted Fresh Whole Blood (RFWB)</td>
<td>Component Blood Therapy</td>
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<tr>
<td><strong>CPB Prime</strong></td>
<td>• RFWB to achieve HCT 22-24% on CPB</td>
<td>• RBC to achieve HCT 22-24% on CPB</td>
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| **During CPB**       | • RFWB to achieve HCT >28% prior to termination of CPB | • 1 unit FFP prior to cross clamp removal  
• RBC to achieve HCT >28% prior to termination of CPB |
Conclusions

*RFWB is associated with improved clinical outcomes:*

- Reduced chest tube loss at 24 hours in CCCU
- Reduced markers of systemic inflammation
- Reduced ventilation time
- Reduced inotropic support at 24 hours
- Reduced hospital LOS

*It is unclear if this is a result of age of product or donor exposures or both or something else entirely!*
**Independent effect on post-operative outcomes**

**Chest tube loss 24 hours**
- Lower platelet count, \( p<0.0001 \)
- Older age of blood, \( p<0.0001 \)
- Higher number of exposures, \( p=0.06 \)

**Longer ventilation**
- Lower platelet count, \( p<0.0001 \)
- Older age of blood, \( p<0.0001 \)
- Higher number of exposures, \( p<0.0001 \)

**Blood product exposures**

<table>
<thead>
<tr>
<th>Exposures</th>
<th>RFWB</th>
<th>Control</th>
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<tr>
<td>3.2</td>
<td>6.9</td>
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Outcomes and Storage of RBCs

- Retrospective review of 192 children
- Centrifugal pump
- Older blood >4 days

**Results**
- Risk of major morbidity only if blood prime
- Increased risk of postoperative complications
  - Pulmonary
  - Renal

Ranucci M, et al.
Hemostatic Consequences of Blood Prime

- 30 patients <1yr old
- Prime volumes 340/465mL
- Target Hct .30
- Leukoreduced product
  - Whole blood 2-7days (CPDA1)
  - pRBC (CPDA1) plus FFP

Results

- No difference between whole blood and component therapy
- Significant thrombocytopenia
- Significant reduction in:
  - Fibrinogen
  - AT III
  - Plasminogen
  - II, V, VII, VIII, X
Maybe *Fresh* Whole Blood?

- Less inflammation and less bleeding?
- 200 patients<1yr
- Single OR team
- Intention to treat and comparable groups
- Whole blood CPD/pRBC Adsol or Optisol

Results

- Fresh whole blood has no advantage over component therapy
- In fact...
  - Increased LOS in CCU
  - Increased perioperative fluid overload
- Fewer (by one!) donor exposures
Maybe No Blood?

- Limits of hemodilution?
- Hematocrit
- Dilutional Coagulopathy
- Thrombocytopenia
Hematocrit


  No difference between Hct 25% and 35%

- Wypij D, et al. J Thorac Cardiovasc Surg. 2008 Feb;135(2):347-54, 354.e1-4. A hematocrit level at the onset of low-flow cardiopulmonary bypass of approximately 24% or higher is associated with higher Psychomotor Development Index scores and reduced lactate levels.....

This study cannot ascertain a universally "safe” hemodilution.
Asanguinious Prime

- Is Beneficial?
  - Less inflammation
  - Less blood transfusion
  - Similar outcomes?

- Is Achievable
  - 120-200mL
  - Increased complexity
  - New oxygenators/filters
  - Remote pump

Koster A, et al. A new miniaturized cardiopulmonary bypass system reduces transfusion requirements....

Miyaji K, et al. The influences of red blood cell transfusion on perioperative inflammatory responses...

Golab HD, Bogers JJ. Small, smaller, smallest....

Durandy Y. The impact of vacuum-assisted venous drainage and miniaturized bypass circuits...
No Transfusion?

- Not often….it is heart surgery after all!!
  - 13 neonates 1.7-4kg
  - 11/13 transfused but only 2/13 given platelets

 Delayed RBC transfusion reduces inflammatory markers
  - CRP
  - Neutrophils
  - Body water gain


No Intra-operative transfusion:

- Prime volume 110mL
- VAD
- Acceptable Hgb 7g/dL during CPB
- NIRS
- 6/13 neonates had no perioperative transfusion
  - All corrective procedures (TGA, HAA, IAA, TAPVD)

Delayed Transfusion

- 54 patients 4-10kg
- 41% received RBC transfusion (leucocyte depleted)
  - Weight
  - CPB time
- NIRS and rSO2 and SVO2 plus lactate
- No platelets or FFP administered
- Elevated cRP and WCC in patients transfused on bypass

Myaji et al. (Int Heart J 2009; 50: 581-589)
Asanguinous Prime

• Composition
  • Crystalloid Prime
    • What solution?
  • Colloid
    • Albumin
    • Starch
Hypertonic Hyperoncotic Solutions Improve Cardiac Function

- Post CPB single infusion of 6% HES vs 0.9%NaCl 4ml/kg
- Increased CI
- Decreased SVRI
- Decreased extravascular lung water

Schroth M, et al
High Colloid Pressure is helpful during CPB

- 25% albumin vs FFP
- Improved hemofiltration rates
- Decreased weight gain
- Comparable effects on renal function
In Summary

• Cardiopulmonary prime solutions are partly driven by technological limitations.

• The ideal CPB prime is probably an
  • asanguinous
  • low volume
  • high colloid osmotic pressure solution

• The freshest blood possible should be acquired
Looking into the far(?) distance...

**Therapeutic quandaries:**
- RIPC
- Superhydrophobic surfaces
- Bonded circuits
- Endothelium