Cardiopulmonary Bypass:
Current State-of-the-Art & New Development

Congenital Cardiac Anesthesia Society
Las Vegas, NV
March 2013

Colleen Gruenwald
PhD, MHSc, RN, CCP, CPC
Toronto, Canada
I have no disclosures to declare.
Objectives… with the focus on infants

- Current trends in pediatric CPB management
  “BLOODLESS PEDIATRIC HEART SURGERY”

- Therapeutic interventions that ameliorate the adverse effects of CPB

- New and evolving CPB technologies & techniques
Bloodless Pediatric Heart Surgery

THE CHALLENGE

Complex operations on small hearts

- Significant risk independent of blood conservation
- Cyanotic heart lesions

Consequences of cardiopulmonary bypass

- Dilution
- Anticoagulation
- Inflammatory response
- Coordination of multiple disciplines
- Legal, ethical and medical bias issues
Bloodless Pediatric Heart Surgery

TEAM EFFORT – 1st STEP

- Family
- Cardiology
- Surgeon
- Anesthesiology
- Perfusion
- Nursing
- Laboratory-Blood Bank
- Intensive Care Unit
- Administrative/Program

Communication
Coordination
Commitment
Bloodless Pediatric Heart Surgery

**Diagnosis (pre-op)**
- Timing of procedure (pt size vs circuit volume)
- Iron supplementation

**Surgery (intra-op)**
- Antifibrinolytics (tranexamic acid, amicar)
- Pre-bypass (phlebotomy)
- Bypass techniques .....  
- Surgical techniques (meticulous)

**ICU (post-op)**
- Continued program goals
- Blood sampling, non-invasive monitors
Transfusion-free surgery in neonates is usually not possible due to hemodilution.

- Large prime volume
- Pt Small blood volume
- Immature hemostatic system (50% proteins)
- ↑ Inflammatory response to surgery
Bloodless Pediatric Heart Surgery

Transfusion in neonates…

Results in:
Higher rates of morbidity and mortality in neonates than in older children and adults…
Reasons to Avoid Blood Transfusion

- Risks of transfusions
- Unclear efficacy of transfusions to attain goals of reduced morbidity & mortality in certain settings
- Blood is a rare, expensive resource
- Personal, ethical, religious beliefs
Adverse effects of Blood Transfusion

- Infectious transmission
  - Bacterial, viral
- Transfusion related acute lung injury
- Inflammatory response
- Immunologic compromise
- Graft vs host disease
- Volume overload
- Stroke
  (Major or minor transfusion reaction)
Bloodless Pediatric Heart Surgery

Predictors of:
Red Cell (RC) Transfusion
- Pre-operative hematocrit
  - Low hemoglobin **
  Redlin, JTCVS, 2011
- Longer CPB and x-clamp times, DHCA
  - complex surgical repairs
- Age and weight at time of surgery
  Szekely, ATS 2009
  Miyaji, Int Heart J 2009
  Hornykewycz Ped Anaes 2009
  Ootaki, JTCVS 2004

Predictors of:
Platelet Transfusion
- Pre-operative hematocrit
  - High hemoglobin
- Longer CPB and x-clamp times, DHCA
  - complex surgical repairs
- Age and weight at time of surgery
- Larger doses of heparin
  Petaja, JTCVS 1995
Bloodless Pediatric Heart Surgery

Red Cell Transfusion

Indications
- “Ideal” hemoglobin
  - Specific value, target
- Acute hemorrhage/anemia
- Evidence of inadequate tissue $O_2$ delivery with normovolemia

Goals
- ↑ Patient’s hemoglobin
- Improve oxygen delivery and tissue perfusion

Objective = ↓ morbidity and mortality

HOWEVER....
Bloodless Pediatric Heart Surgery

Morbidity and Mortality of Blood Transfusion

“Potential detrimental effects of allogeneic blood transfusion is increasingly understood”

- Children undergoing cardiac surgery are the greatest paediatric users of RC transfusions
  Keung, Ped Anes 2009
- RC transfusion in critically ill children is independently associated with prolonged mechanical ventilation, inotropic requirement, ICU stay and increased mortality
  Kneyber, Intensive Care Med 2007
- Effect of blood transfusion on long-term survival after cardiac operation
  Engoren, Ann Thorac Surg 2002
Bloodless Pediatric Heart Surgery

Interventions: Age of Blood

Infants
- RFWB <48 hours old used in prime & 24 hours in neonates significantly improves clinical outcomes
  Gruenwald, JTCVS 2008

Children
- RCs >4 days old used in prime – increased morbidity
  Ranucci, Critical Care 2009

Adults
- RCs >14 day old is associated with significant increased risk of postoperative complications including mortality
Age of Blood

“RBC Storage Lesions” occur in both.....

Supernatant

- Inflammatory mediators (cytokines, iron, micro-particles containing lipids)

Within RBC

- Loss of 2,3 DPG, ATP
- Deformability
- Diminished oxygen transport
- Increased adhesiveness
- Decreased overall viability

Therefore, washing blood does not remove all of these concerns...
Bloodless Pediatric Heart Surgery

Age of Blood – Effect on Chest Tube Volume Loss

Retrospective review of 1225 consecutive cardiac surgeries at SickKids from 2004 to 2007

Manlhiot, Soc of Thorac Surg 2011
# Association Between Average Age of RBC Transfusion and Surgical Outcomes

(Patients transfused either >4 units of RBC’s or >150ml/kg RBC’s)

<table>
<thead>
<tr>
<th></th>
<th>EST (SE)</th>
<th>OR (95% CI)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inotrope scores 6-12 hrs</td>
<td>+0.067 (0.022)</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Inotrope scores 12-24 hrs</td>
<td>+0.081 (0.021)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Inotrope scores 24-48 hrs</strong></td>
<td><strong>+0.068 (0.018)</strong></td>
<td></td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Chest tube loss (ml/kg)</td>
<td>+1.499 (0.340)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intubation (days)</td>
<td>+0.263 (0.086)</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>+0.192 (0.109)</td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>+0.303 (0.132)</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Major bleeding complications</td>
<td>1.029 (0.998-1.062)</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Renal insufficiency/failure</strong></td>
<td><strong>1.085 (1.034-1.138)</strong></td>
<td></td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Liver insufficiency/failure</td>
<td>1.087 (0.999-1.184)</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Early unplanned reoperation</td>
<td>1.040 (1.000-1.082)</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>In hospital mortality</td>
<td>1.054 (1.005-1.106)</td>
<td></td>
<td>0.03</td>
</tr>
</tbody>
</table>
Bloodless Pediatric Heart Surgery

Percent Survival with Age of Blood

- 100 ml/kg, average age: 10 days
- 100 ml/kg, average age: 25 days
- 100 ml/kg, average age: 40 days

$\text{p < 0.001}$
FRESH WHOLE BLOOD (FWB)

RCT Infants < 2 years

- Use of FWB - less post-operative bleeding than component therapy [Manno CS, Blood 1991]

HOWEVER...

- FWB generally not available today
Bloodless Pediatric Heart Surgery

Reconstituted Fresh Whole Blood Study

Neonates < 1 month, Single center, RCT 2001-2005

RFWB group - significant results

- Fewer donor exposures (study design)
- Lower chest tube losses over first 24 hours
- Shorter ventilation time and hospital LOS
- Lower inotropic support scores at 24 hours

Gruenwald, JTCVS 2008
Bloodless Pediatric Heart Surgery

Independent effect on post-operative outcome

Factors associated with higher chest tube loss 24 hours
- Lower platelet count: $-0.0026 (0.0004)$, $p<0.0001$
- Older age of blood: $0.0120 (0.0010)$, $p<0.0001$
- Higher number of exposures: $0.0241 (0.0024)$, $p=0.06$

Factors associated with longer duration of ventilation
- Lower platelet count: $-0.0041 (0.0002)$, $p<0.0001$
- Older age of blood: $0.0129 (0.0005)$, $p<0.0001$
- Higher number of exposures: $0.0206 (0.0012)$, $p<0.0001$
Bloodless Pediatric Heart Surgery

Technologies & Techniques:
Minimized CPB Circuit

Smaller devices available today
- remote/pump heads close to patient
- oxygenator with integral arterial filter

Techniques:
ANH - acute normovolemic hemodilution
VAD - vacuum-assisted drainage
VAP - venous antegrade prime
RAP - retrograde arterial prime
Hemoconcentration & Cell Salvage
Diameter and length of tubing?

Olshove JECT 2010
Bloodless Pediatric Heart Surgery

Berlin Heart Centre – neonates

1st series (n=13)  Koster JTCVS 2009
2nd series ASO (n=23)  Redlin JTCVS 2011

- Asanguineous prime (1st series: 200ml, 2nd series: 100ml)
- Hypothermia 26-28°C
- Flow rates of 2.5 – 3.0L/min/m² with VAD
- Transfusion trigger (lower than current practice)
  - Hgb 7g/dl CPB, 8-10g/dl post-CPB, 12-16g/dl cyanotic
- Controlled monitoring (NIRS)
  - regional oxygenation of brain & lower body
- Circuit volume processed post CPB (cell-saver)
Bloodless Pediatric Heart Surgery

Minimized CPB Circuit – 100ml Prime

It can be done with a team approach…

Achieved (23 neonates 2.7 – 3.2 kg - ASO)

- 6 patients – intra and post-op transfusion
- 11 patients – no intra-op but ICU transfusion
- 6 patients – no transfusion
- 3 patients – FFP also transfused

Outcome (similar between groups)

- ICU stay & ventilation
- Post-op & wound infection
- Inflammatory response
- Mortality
Bloodless Pediatric Heart Surgery

Other Recent Investigators

- Perfusion strategies for blood conservation in pediatric cardiac surgery
  - Durandy, World J Cardiol 2010

- Specific requirements for bloodless cardiopulmonary bypass in neonates and infants
  - Golab, Perfusion 2010

- Pediatric cardiac surgery without homologous blood transfusion, using a miniaturized bypass system in infants with lower body weight
  - Myaiji, JTCVS 2007
**Benefits of minimized primes…**

- Dilution of hemoglobin, platelets & coagulation factors

- Reduction priming volume – ameliorate inflammatory response independent from blood transfusion
  
  *Myaiji, Int Heart J 2009,  
  Fukumura, J Art Organs 2004*

- Reduced need for blood transfusion while maintaining tissue oxygenation and patient safety
  
  *Redlin, JTCVS 2011*
Bloodless Pediatric Heart Surgery

The effect of hematocrit during hypothermic cardiopulmonary bypass in infant heart surgery: Results from the combined Boston hematocrit trials

Conclusions: hemodilution may vary with diagnosis, age at operation, CPB strategies (pH, flow, temperature etc.) Therefore, the study could not recommend a universally “safe” hemodilution level.....

Linear correlation between psychomotor development and HCT between 15-24% (low flow, 18°C CPB)
Bloodless Pediatric Heart Surgery

Considerations

The **most** important outcome measure for parents and their child...

NORMAL MENTAL & PSYCHOMOTOR DEVELOPMENT
Bloodless Pediatric Heart Surgery

Future…

- Debate continues – **Optimal Perfusion**
  - Further investigation is required to assess the “critical HCT as well as other perfusion variables” as a trigger for transfusion (with current practice)
  - Follow-up studies are needed – Does reduced transfusion result in better long-term outcomes?

- We should advocate for the freshest blood
  - Whole blood may be the best option if available

- We should challenge ourselves
  - Mini bypass circuitry/reduce transfusion
  - Encourage technology development and innovation

- And finally…work as a TEAM!
Bloodless Pediatric Heart Surgery

Thank you