Optimal Administration of del Nido Cardioplegia

Richard Ginther, Jr., MBA, CCP, FPP
Faculty Associate, Cardiothoracic Surgery
UT Southwestern Medical Center
Children’s Health Dallas
March 10, 2019

Conflicts of Interest

Zero point zero percent

Art Not Science?

Evidence-based medicine and myocardial protection — where is the evidence?

ZG Ferguson, DE Yarbrough, BL Javine and JL Stein

The Academy Newsletter, Summer 2015
Ashley Risso, CCP, Inova Fairfax Hospital

Cardioplegia Variations (STS)

• Depolarizing cardioplegia: solutions that utilize only a depolarizing agent (e.g. potassium) to arrest the heart.

• Modified depolarizing cardioplegia: solutions that combine a depolarizing agent (e.g. potassium) with additional membrane stabilizing additives (e.g. magnesium or lidocaine) to arrest the heart.

• Hyperpolarizing cardioplegia: solutions that achieve an electrochemical potential that resemble the myocyte at rest (Custodiol HTK); solutions that utilize ATP sensitive potassium channel opening agents (e.g. nicorandil, pinacidil, minoxidil, aprilekalim, loprazolam, adenosine) to arrest the heart.
**Depolarizing Cardioplegia Caveats**

- Left ventricular dysfunction
- [Intracellular Na & Ca overload](#)
- Continued energy expenditure, myocardial stunning, ischemic injury
- Arrhythmia
- Tissue edema
- Free radical production

**Effective Cardioplegia Solutions**

- **Quick diastolic arrest**: keep myocardium relaxed and minimize cellular use of ATP
- **Protect the myocardium**: delay onset of irreversible injury and limit reperfusion injury
- **Reversibility**: quick resumption of heart function upon washout and enable early CPB weaning
- **Low toxicity**: arresting agent should have no toxic effect on heart or other organs after CPB

---

**del Nido Formula**

**Modified Depolarizing Solution**

- 1 L Plasmalyte A – Physiologic/Isotonic solution; *Calcium free
- 13 ml KCl (26 mEq) – Arresting agent
- 13 ml NaHCO₃ 8.4% (13 mEq) - Buffer
- 13 ml Mannitol 25% (3.25 g) – Osmotic agent
- 6.5 ml Lidocaine 2% (130 mg) – Na⁺ channel blocker
- 4 ml MgSO₄ 50% (2 g) – Ca²⁺ antagonist

---

**del Nido Mechanism of Action**
Excitation–Contraction Coupling (ECC)

- **Interrupt Na⁺ Channels**
  A. Depolarize: High K⁺
  B. Polarize: K⁺ channel openers; Adenosine
  C. Na channel blockers: Lidocaine; Esmolol, TTX

- **Inhibit Ca²⁺ Activated Mechanisms**
  A. Ca²⁺ channel blockers: Mg; Esmolol
  B. Zero to low (~0.4mmol/L) extracellular Ca²⁺

Survey

- Survey Monkey survey tool sent to FPP mailing list (125 perfusionists)
- Created February 5, 2019
- Total questions: 30
- Responses collected: 60
- Number of centers using del Nido cardioplegia: **39**

Q4: Who compounds/makes your del Nido solution?

- CAPS: 49%
- Internal Pharmacy: 47%
- Other: 4%

Q5: What source of blood do you use to mix/prime your 1:4 delivery solution?

- The cardioplegia circuit is mixed with pre-bypass circuit volume that contains donor blood or blood components
- The cardioplegia circuit is mixed with patient blood from the circuit once on bypass
Q6: An arresting dose of del Nido cardioplegia is mixed at a 1:4 (blood:crystalloid) ratio, and then delivered cold, antegrade, and at a total volume of 20ml/kg. Is this your standard dose?

- Yes
- No. Please specify your delivery parameters for this patient

Variance
- Most respondents deliver a total volume of 30 ml/kg
- “Our surgeons wanted 30ml/kg fully understanding this was not the recommended dose using standard delNido solution”
- “Blood tinged (Approx 1:4-1:8) per Pedro Del Nido. His original papers specified blood tinged. He visited a few years back and was asked this specific question. He doesn’t know where Perfusionists got 1:4. I believe it’s from Perfusionists just flipping their existing plegia setups for simplicity and cost savings”

Q7: Which parameter is routinely used to guide cardioplegia flow during delivery via the aortic root? (Select all that apply)

- Cardioplegia system pressure
- Aortic root pressure (direct measurement)
- Based on a ml/kg/min calculation
- Other (please specify)

- 110 ml/m²/min (n=3)
- 5 ml/kg/min (n=1)
- 10 ml/kg/min for 3 min (n=1)
- Surges finger manometer (n=1)
- “One surgeon measures Ao root pressure. Target <50mmHg. Admin duration is ~1.5 - 2 min (n=1)"

Q8: If aortic root pressure is not routinely measured, is your cardioplegia system pressure validated against direct aortic root pressure measurement for reference?

- Yes
- No

Q9: If aortic root pressure is measured, what is an approximate target root pressure for the 4kg AVSD patient?

- We use the pre-op MAP to determine what root pressure we want to target
- We use the pre-op diastolic pressure to determine what root pressure we want to target
- Target root pressure please specify

9 respondents directly measure root pressure during delivery
- 2 respondents submitted target root pressures that appear to be system pressure (100, 120 mmHg)
- 1 respondent specified a target root pressure <50mmHg
Q10&11 Is cardioplegia delivery temperature routinely measured during the arresting dose?

- Yes: Please specify the temperature (Celsius) of your delivery solution
- No

![Graph showing temperature distribution](image)

- Delivery temp range: 3 - 8 °C
- Respondents who specified “ice water” for water temp were assigned a water temp of 5°C

Q12 Do you routinely measure myocardial temperature?

- No respondents measure myocardial temperature

Q13 Some centers deliver cardioplegia based on time not volume. For the arresting dose, is the time it takes to deliver cardioplegia used to determine a full dose rather than volume (ml/kg)?

Time Parameters:
- We like to get 2 minutes minimum for the arresting dose. Once arrest is achieved, we tend to back down the flow rate to hit dose (20ml/kg) and time together
- Two minutes minimum or total volume up to 30ml/kg
- 2.5 mins with 30ml/kg given
- 30 ml/kg over 3 mins
- 30 ml/kg for 3 min (flow 10 ml/kg/min)
- 20ml/kg delivered over 3 minutes
- Delivered over two to four minutes depending on size of patient

Q14 The optimal calcium level of cardioplegia has been frequently debated. Even at a 1:4 ratio, choosing whether or not to correct calcium at the onset of CPB can significantly impact the calcium concentration of the delivery solution. Do you correct the ionized calcium before mixing and delivering the cardioplegia?

Respondents that correct calcium:
- To clarify, correcting ca++ mostly applies to neonates with blood primed circuits. Corrections are done with calcium gluconate to approximately 0.8 to 1.2 level
- We add calcium to prime but do not have a specific goal before giving cardioplegia
- We expect the Calcium to be around 1.2 since our pump prime is created to be physiologically correct to the patient
- Normal range. Prime is tested
- CaCl in prime if PRBCs in prime; not measured until after CPB finished, goal 1.3mmol/L

Respondents that do NOT correct calcium:
- 0.8 – 1.0 mmol/L (n=3)
- 0.9 – 1.0
- 0.8 – 1.3
- Low calcium no specific number but is usually under 0.8

![Graph showing calcium distribution](image)
Q15 Is your protocol to give del Nido cardioplegia continuously or intermittently?

- Continuous administration
- Intermittent bolus doses
- Both (specify)
- Other (please specify)

Q16 When do you re-dose del Nido cardioplegia? (Check all that apply)

- Determined on a specific time-based protocol: 59% (n=23)
- If there is electrical activity: 74% (n=29)
- Whenever the surgeon determines to re-dose (despite no electrical activity): 49% (n=19)

Q17 If re-dosing is routinely determined on a time-based protocol, how long (in minutes) do you typically wait between maintenance doses? (enter n/a if you do not deliver a routine time-based maintenance dose)

- Maintenance Dose Time (minutes)
- Respondent (n=23)

Q18 Do you have a maximum threshold time in which you at least consider giving another dose of del Nido cardioplegia? In other words, if there is no electrical activity and you do not re-dose based on a time protocol, does your surgeon have a threshold time in which they become uncomfortable with protection and will most likely ask for another dose?

- No threshold time. Re-dosing is based on electrical activity only
- No threshold time. We use a specific time-based protocol
- Threshold time (minutes) to re-dose – please specify

- Max Threshold Time to Re-Dose

No threshold time. Re-dosing is based on electrical activity only
No threshold time. We use a specific time-based protocol
Threshold time (minutes) to re-dose – please specify
Q19 When re-dosing del Nido cardioplegia, how much do you deliver? (For simplicity, the cross-clamp is not about to come off soon)

- 10-20 ml/kg depending on how long we think we’ll go before re-dosing
- I wouldn’t say we have a standard. It changes
- depends on how much longer the aorta will be x-clamped usually 10-15 ml/kg
- 10 to 15 ml/kg
- 5-10 ml/kg

Comments:
- 10-20 ml/kg depending on how long we think we’ll go before re-dosing
- I wouldn’t say we have a standard. It changes
- depends on how much longer the aorta will be x-clamped usually 10-15 ml/kg
- 10 to 15 ml/kg
- 5-10 ml/kg

Q20 Consider a complex repair that does not require DHCA in which you are certain the cross-clamp time will approach or exceed 120 minutes. Select the hypothermia strategy that you would employ. Based on feedback I received from those of you that conduct CPB mild to normothermic, please describe the temp strategy that you would honestly target in the "other" field

- Typically 28-30 for complex or if pt has multiple collaterals
- 22-25 degrees
- 20-28 depending on procedure and surgeon
- Our surgeons like to operate on the warm side but we will usually sneak a little cooler when we know we will have a long clamp
- 32 degrees

Comments:
- Typically 28-30 for complex or if pt has multiple collaterals
- 22-25 degrees
- 20-28 depending on procedure and surgeon
- Our surgeons like to operate on the warm side but we will usually sneak a little cooler when we know we will have a long clamp
- 32 degrees

Q21 Which other myocardial protection techniques would you use during a long and complex repair? (check all that apply)

- Slush around the heart
- Cold irrigation
- Cold irrigation using del Nido crystalloid solution
- Reduce OR temperature
- Reduce blanket temperature

Q22 Do you have a maximum total cardioplegia dose that you reference when considering lidocaine or magnesium toxicity?

- No respondents reported a specific dose
- Lidocaine (130mg/L in del Nido solution)
  - Toxic dose at ≥4.5 mg/kg
  - A 30 ml/kg dose for our hypothetical 4kg pt would deliver about 12.5 mg of lidocaine (Toxic dose: 18mg)
  - Can lead to: AV block, seizures, hypotension
  - Half life ~ 1.5 hours; hepatically cleared
- Magnesium (2g/L in del Nido solution)
  - Toxic dose at >2g
  - Can lead to: severe respiratory depression (muscle weakness)
  - Treat toxicity with calcium chloride
Q23 In addition to your pump prime, do you re-dose mannitol at any other point during the surgery?

**Comments:**
- 5 respondents specify that they do not add mannitol to their prime solution
- 1 respondent uses mannitol in a 2bufl dialysate throughout case
- 1 respondent gives mannitol @ xC removal but only if 32 deg C

Q24 Do you use del Nido cardioplegia as your cardiac transplant solution?

**Comments:**
- 5 respondents specify that they do not add mannitol to their prime solution
- 1 respondent uses mannitol in a 2bufl dialysate throughout case
- 1 respondent gives mannitol @ xC removal but only if 32 deg C

Q25 Some centers have shared that they deliver a hot-shot solution or use a different solution when re-dosing. Do you use any other cardioplegia formulation in addition to del Nido during the same procedure?

**Comments:**
- Sometimes one of our surgeons will ask us to deliver warm blood to flush out the cardioplegia right before the clamp comes off
- Warm reperfusion with warm blood only
- Straight blood, cold then warm it. Or warm it just blood
- Hot shot using del Nido solution

Q26 Do you modify the del Nido solution in any way? (e.g. extra bicarbonate, different base solution, albumin, additional additives, etc.)

**Comments:**
- One respondent specified that Albumin (3.5% to 4%) is added to their solution

Q27 Do you have any experience using the del Nido formulation as a microplegia (blood cardioplegia with the additives but without the crystalloid base solution)?

**Comments:**
- One respondent specified that they have used the solution as 4:1 or greater using continuous flow
Q28 What is the longest cross-clamp time (in minutes) you can recall when using a single-dose of del Nido?

![Ischemic Time with Single Dose](image)

<table>
<thead>
<tr>
<th>Descriptive Stat</th>
<th># of Centers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>128</td>
</tr>
<tr>
<td>Median</td>
<td>120</td>
</tr>
<tr>
<td>Mode</td>
<td>90</td>
</tr>
<tr>
<td>Standard Dev</td>
<td>55</td>
</tr>
<tr>
<td>Range</td>
<td>280</td>
</tr>
<tr>
<td>Minimum</td>
<td>50</td>
</tr>
<tr>
<td>Maximum</td>
<td>230</td>
</tr>
</tbody>
</table>

Take Home Points & Suggestions

- Reducing variation improves quality and will support better research (Lean Six Sigma)
- Consider a 503b registered outsourcing pharmacy (CAPS)
- A 20 – 30 ml/kg is often used as the arresting dose in small patients
- Delivery flow, volume, pressure, time, and temp does not have to be a “black box”
- Control and understand the importance of calcium management, calcium paradox
- The single dose is nice but speed matters
  - Keep the heart cold, discuss your CPB hypothermia strategy
  - Most centers re-dose every 60 to 90 min
  - Centers that reported lower hypothermia temps were more likely to go 90-120 min

Thank You

RIP
Nick Rappa, CCP
1987 - 2018
Awesome friend
Great pediatric perfusionist
Renaissance man
Even better dad

Memorial Endowment
https://www.upstatefoundation.org/rappa-endowment
Cardioplegia for Pediatric Patients
Is del Nido the right way to go?

Clarke Thuy CCP FAANCP.

Disclosure
• Nothing to disclose.

Measuring performance:
• There is no consensus on the best tools for myocardial protection assessment.
• There is no way to routinely perform real-time myocardial protection evaluation.
• Myocardial protection is clinically assessed post-operatively via a number of indirect factors such as:
  • troponin I/T or creatine kinase MB levels,
  • ischemic indicators on EKG,
  • myocardial infarction,
  • stroke,
  • time to resumption of sinus rhythm,
  • atrial fibrillation,
  • need to defibrillate post cross clamp removal
  • myocardial function on echo,
  • low cardiac output state,
  • inotropic support,
  • intra-aortic balloon pump,
  • extracorporeal membrane oxygenation,
  • time to extubation,
  • length of stay in intensive care.

Global Cardioplegia Practices: Results from the Global Cardiopulmonary Bypass Survey:
Jason M. Al; Lachlan F. Miles; Yasir Abu Omar; Carlos Galhardo; Florian Falter
JECD. 2018;50:83–93
Quantifying the Effect of Cardioplegia Administration in the Cardiac Surgical Patient
Alfred H. Stammers, MSA, CCP, Eric Tesdahl, PhD Linda Mongero, CCP, Andy Stasko, MS, CCP, Sam Weinstein, MD, MBA
2017 AmSECT Quality and Outcomes

Kardiotechnik February 2014

A survey of practices during cardiopulmonary bypass in India: An Indian association of cardiovascular and thoracic anesthesiologist endeavor.
Deepak Prakash Borde, Shreedhar S Joshi, Murali Chakravarthy, Vishwas Malik, Ranjith B Karthekeyan, Antony George, Thomas Koshy, Uday Gandhe, Suresh G Nair
Annals of Cardiac Anaesthesia 2019; 22(1): 56-66

Cardioplegia practice in pediatric cardiac surgery: a UK & Ireland survey
Miguel E. Devy, Angela Horvaeth, Thomas Ri, Robert G. Milson and Timothy J. Jones; On behalf of the Congenital Heart Trials Network in the UK & Ireland

Custodiol
St Thomas
del Nido
Custodiol HCl
Galamin
Cardioplegia
Current Cardioplegia Practice in Pediatric Cardiac Surgery: A North American Multiinstitutional Survey

Measuring performance:

Cardioplegia Dose Rate:

Table 1. Cardioplegia Tempature by Solution

<table>
<thead>
<tr>
<th>Solution</th>
<th>5-10°C</th>
<th>10-15°C</th>
<th>15-20°C</th>
<th>20-25°C</th>
<th>Median (Interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad-Niko</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>N. Thomas, Pappel, Resto</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customized</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Microlyte</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
</tbody>
</table>

The number in each cell represents the median temperature for the stated option.

Table 2. Cardioplegia Temperature by Solution

<table>
<thead>
<tr>
<th>Solution</th>
<th>5-10°C</th>
<th>10-15°C</th>
<th>15-20°C</th>
<th>20-25°C</th>
<th>Median (Interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad-Niko</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>N. Thomas, Pappel, Resto</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customized</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Microlyte</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
</tbody>
</table>

The number in each cell represents the median temperature for the stated option.

Table 3. Induction Usage by Solution

<table>
<thead>
<tr>
<th>Solution</th>
<th>5 mL/kg</th>
<th>10 mL/kg</th>
<th>15 mL/kg</th>
<th>20 mL/kg</th>
<th>25 mL/kg</th>
<th>Median (Interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad-Niko</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>N. Thomas, Pappel, Resto</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
<tr>
<td>Customized</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
<tr>
<td>Microlyte</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
</tbody>
</table>

The number in each cell represents the median usage for the stated option.

Table 4. Maintenance Usage by Solution

<table>
<thead>
<tr>
<th>Solution</th>
<th>5 mL/kg</th>
<th>10 mL/kg</th>
<th>15 mL/kg</th>
<th>20 mL/kg</th>
<th>25 mL/kg</th>
<th>Median (Interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad-Niko</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Customed</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>N. Thomas, Pappel, Resto</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
<tr>
<td>Customized</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
<tr>
<td>Microlyte</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 (0-0)</td>
<td></td>
</tr>
</tbody>
</table>

The number in each cell represents the median usage for the stated option.

Figure 1: The majority of papers in this search consisted of mixed surgical procedures, with no particular type of procedure being favored over any other. This does not support the report that the majority of congenital maladies consisted standard A1 blood cardioplegia, which correlates to the widespread usage.
Comparison Studies: Cardioplegia Dose Rate

<table>
<thead>
<tr>
<th>Study</th>
<th>Del Nido initial dose</th>
<th>ST Thomas/Other initial dose</th>
<th>Redose DN rate (interval mins)</th>
<th>Redose ST rate (interval mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matte 2012</td>
<td>20mg/kg (10mg/kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buel 2016</td>
<td>20mg/kg</td>
<td>40mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talwar 2017</td>
<td>20mg/kg</td>
<td>30mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talwar 2018</td>
<td>20mg/kg</td>
<td>40mg/kg/mix ( Custodiol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim 2011</td>
<td>30mg/kg</td>
<td>50mg/kg/4h (HTK)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pourmoghadam 2017</td>
<td>20mg/kg</td>
<td>20mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gorjipour 2018</td>
<td>20mg/kg</td>
<td>30mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gorjipour 2018</td>
<td>20mg/kg</td>
<td>30mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persson 2019</td>
<td>20mg/kg</td>
<td>Blood 4:1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charette 2012</td>
<td>20mg/kg</td>
<td>15mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O'Brien 2009</td>
<td>20mg/kg</td>
<td>Blood 4:1. Modified Buckberg Blood 4:1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sur 2018</td>
<td>?</td>
<td>?</td>
<td>(40)</td>
<td>(24)</td>
</tr>
</tbody>
</table>

Comparison Studies: Results

Buel – 6 fold decrease in rate of defibrillation post cross clamp removal compared to modified St Thomas No 2 (Plegisol) • Talwar 2017 – Cardiac indices were significantly higher in the del Nido group than in the St Thomas group 2 hours after termination of cpb. less duration of mechanical ventilation, ICU and hospital stay, lower inotropic scores, lower occurrence of low cardiac output state. • Talwar 2018 - Compared to Custodial, del Nido was associated with better preservation of cardiac index, less duration of mechanical ventilation, ICU and hospital stay, lower inotropic scores, lower occurrence of low cardiac output state and less release of Troponin-I. • Kim - HTK cardioplegic solution is related to hyponatremia during CPB. Fluctuation of sodium concentration was associated with postoperative seizure. • Pourmoghadam - The early postoperative clinical outcome measures showed little difference between the del Nido and conventional cardioplegia.

Comparison Studies

- Gorjipour - We were not able to find significant advantages for del Nido cardioplegic solution over St Thomas in terms of inflammatory response.
- Charette - Multiple doses of cardioplegia do not add significant amounts of time to the overall cross clamp period. Glucose levels were reduced in the del Nido group.
- Smigla – adult congenital - if a dose of del Nido CPS is given soon before the XC is taken off, the heart rate may be slow and contractility diminished. 9% defibrillation after cross clamp removal.
- O’Brien – reduced Troponin for del Nido but no difference in outcome as documented by early death, inotrope score, and ICU and hospital length of stay.
- Gur – del Nido cardioplegia, reduces inotropic need and duration of operation as well as significantly reduce extubation and discharge times.

Modified del Nido?

Cardioplegia in Surgery for Adult Acquired Heart Disease.

"Hypothesis: We retrospectively compared a lidocaine containing “modified del Nido” solution with our standard whole blood cardioplegia to investigate its safety and efficacy in adult cardiac surgery.”
Issues with del Nido Cardioplegia

- Do you need to recalcify?
- What about haemodilution?
- Redosing?
- Short Cross clamp?

Does the Type of Cardioplegia Solution Affect Intraoperative Glucose Levels? A Propensity-Matched Analysis.

Evidence-based medicine and myocardial protection: where is the evidence?
ZG Ferguson, DE Yarborough, BL Jarvis and JJ Sistino
Perfusion 2015, Vol. 30(5) 415–422

Cardioplegia in paediatric cardiac surgery: a systematic review of randomized controlled trials.
Nigel E. Drury, Ivan Yim, Akshay J. Patel, Nicola K.Oswald, Cher-Rin Chong, John Stickley and Timothy J. Jones
Interactive CardioVascular and Thoracic Surgery 28 (2019) 144–150

Patient Matched Cardioplegia?

Cardioplegia in paediatric cardiac surgery: a systematic review of randomized controlled trials.
The published studies show del Nido clearly works, and works well, but there is insufficient high quality evidence to conclude that it is better than other forms of cardioplegia.

It isn’t the right way or wrong way to go.
It is just another way to go.
Neuromonitoring for the Pediatric Cardiac Surgery Patient
Perfusion Considerations and Modern Team Approach

John Miller CPC
Lead Pediatric Perfusionist
Children’s Hospital Foundation Heart Center
Children’s Hospital of Richmond at VCU Health

Disclosure

No affiliations, financial relationships, or conflicts of interest, either actual or perceived, to declare

Obviously I’m in the wrong line of work…
No claims of expertise in neuromonitoring instrumentation or interpretation
The Importance of Neuromonitoring

The reported incidence of neurologic complications (subtle to severe) following congenital heart surgery in children still ranges from 1–25% (with associated 20% mortality) - Jafri et al; J Pediatr Neurosci. 2017 Oct-Dec 12(4):328–331

Infants with congenital heart disease have higher incidence of CNS dysgenesis (particularly in HLHS and chromosomal anomalies)

Multifactorial etiology of neurologic injury:
- Embolic (particulate or gaseous)
- Hypoxic
- Ischemic/hyperperfusion or hyperemia
- Reperfusion injury, inflammatory mechanism

Any of these insults may go undetected by standard monitoring techniques!

Development of Neuromonitoring

The electroencephalogram in patients undergoing open intracardiac operations with the aid of extracorporeal circulation.

The Role of Neuromonitoring in Cardiovascular Surgery

Hennes, L., Edmonds, J., PhD, Rosenblum, A. Rodriguez, MD, PhD, Stone, M., Anderson, MD, Ed, H. Austin, S., MD, Samuel, B., Pollock, Jr., MD, and Brian, L., Garfath, MD


Improved Outcomes


- Retrospective cohort 250 Pts
- 76% showed significant change in cerebral perfusion or neurologic function
- Perfusionist directly involved in 52% of interventions
- Neuromonitoring guided care resulted in ¼ neurologic complications vs. unmonitored group
Improved Outcomes

Protective Effect of Neuromonitoring during Cardiac Surgery

Retrospective review of 332 Pts 
Imbalances were detected in 59% of the cases and successfully corrected in all but 2%. In the absence of neuromonitoring, the expected incidence of serious brain injury is 6.1%. With neuromonitoring, the actual observed incidence was 3.0%.

Neuromonitoring in CHoR Ped CVOR

Incorporated as a standard of practice in pediatric CV surgery in 2015
Included modalities of
- Cerebral NIRS
- 8-channel EEG
- Trans-cranial Doppler (TCD) of middle cerebral artery
Private contract neuromonitoring group with technician in OR
- limited experience in pediatric congenital cardiac surgery

Neuromonitoring in CHoR Ped CVOR

- Recently progressed to in-house specialty service
- Neurophysiologist (MD) with over 20 years experience
- Multi-modality neuromonitoring also now includes somatosensory evoked potentials, and brainstem auditory evoked potentials

Multidisciplinary team approach – neurophysiologist, anaesthesiologist, surgeons, perfusionists

Neuromonitoring Modalities - NIRS

- 4-channel near infrared spectrometry – cerebral, spinal, and somatic rSO2
- Alerts to alterations in cerebral oxygenation supply vs. demand (DO2/VO2)
- Spinal cord ischemia, renal, hepatic
- Sensitive, but not specific...so we need more
Transcranial Doppler

Sensitive, real-time monitoring of bilateral middle cerebral artery blood flow velocities, and microemboli counts

- CPB flow
- PaCO2 levels
- Arterial or venous cannula position
- Embolic count - HITTS

EEG Monitoring

- 8-channel EEG is a relatively simple set-up (raw and digitally processed signals)
- Exquisitely sensitive to deficiencies of cortical oxygen delivery
- Displays regional physiologic imbalance in neural function
- Helps guide rate and duration of cooling and rewarming
- Can guide anaesthetic depth and technique

Evoked Potentials – SSEP + Brainstem

Auditory evoked potentials monitor brainstem neural function

- Particularly useful during cooling and rewarming phases of DHCA or low-flow cerebral perfusion
- Deep brainstem cooling

Somato-sensory EP's monitor functional neural integrity in cerebral watershed zones and spinal cord

© A. Sefc

© A. Sefc

© A. Sefc
Perfusion Considerations

Unhappy brain shows progressive changes in:
- TCD
- NIRS
- EEG
- EP

Sensitivity and specificity remove the trial and error guesswork

Optimal flowrates
PaCO2 levels -- pH Stat
Blood pressure targets
Safe hemoglobin levels -- transfusion & DO2
Cannula position!!

Temperature management

Textbook 8-10°C gradients...
- Not every patient has read the textbook!
- COOLING: EEG and EP's detect disparities with rapid cooling
- REWARMING: regional mismatch of supply and demand
  (disabled autoregulation and vasoconstriction + increased CMRO2)
- TCD low flow velocity, NIRS, and EEG slowing
- 6-8°C gradient often works better
DHCA management

**Induction:**
- EEG and auditory EP quiescence – deep brain structures may not be adequately cooled based on EEG alone
- NP temp or time-limited cooling is often insufficient
- Target NIRS 85-90%

**Maintenance:**
- Only NIRS is relevant
- If rSO2 < 50% from pre-arrest baseline, then reperfuse to replenish cerebral O2 reserves

What microemboli??

Real-time correlation of microemboli (HITTS) to specific CPB/surgical events or conditions

- Vent and sucker pump speeds
- Venous reservoir level
- VAVD
- Volume and drug additions
  *not picked up by HLM bubble detector!

Additional CPB considerations...

- MUF pump speeds, duration – TCD velocity and NIRS detect cerebral steal, TCD detects changes in volume status
- Anaesthetic administration during CPB – enough, but just enough
  *Too much:* neurotoxicity, excessive EEG burst suppression, EP signal blunting
  *Too little:* awareness, stress response, O2 demand

"Despite continued fibrillatory arrest, cerebral air embolism of uncertain cause was detected by means of transcranial Doppler Ultrasonography... cerebral oxygen saturation declined precipitously and artifacts appeared in the EEG."

"At sternal closure, the asymmetries had nearly disappeared. A neurologic examination the following day revealed no new focal neurologic or EEG abnormality."
It's a Team Sport!

- Neurophysiologist monitors continuously from pre-induction baseline, reports changes in status throughout procedure (post-op period)
- Communication between Neurophysiologist, Perfusionists, Anaesthesiologist, and Surgeons
- Problems quickly identified, corrective action agreed on

How Does This Affect Me??

WHAT IT ISN'T...
- Micromanaging
- Someone else telling you how to run your case
- Finger pointing
- Blame ‘n’ shame

WHAT IT IS...
- High-functioning team with a common goal
- Measurement-driven, co-operative decision-making
- Collaborative problem-solving

“So what did you learn??”

- 15 month experience with neuromonitoring for Peds CPB cases vs. 18 years prior
- Enhanced my practice – similar to NIRS, or CDI 500®
  - not having it on "other" cases is like driving in the dark
- Reward (or negative feedback) of seeing immediate physiologic response to CPB interventions and management
- CPB optimization specific to each patient’s needs (Goal-directed*)
Vacuum Assist: Yes or No?

Tami Rosenthal CCP, MBA, FPP
Chief Perfusionist
Children’s Hospital of Philadelphia

Disclosures

• Current user of

Challenges and Solutions

• Vacuum from the beginning
• Safety survey
• Advantages
• Anecdotes of catastrophic events
• Concerns/complications
• Considerations for safe use

Laboratory work preceding the first clinical application of cardiopulmonary bypass
Table 5. Institutional checklist items pertaining to VAVD.

<table>
<thead>
<tr>
<th>Item</th>
<th>Compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuum reservoir operational*</td>
<td>93.7</td>
</tr>
<tr>
<td>Cardiogram positive pressure relief valve present*</td>
<td>93.1</td>
</tr>
<tr>
<td>Negative pressure relief valve(s) uncontested*</td>
<td>93.8</td>
</tr>
<tr>
<td>Severe has been engaged and tested</td>
<td>94.4</td>
</tr>
<tr>
<td>Reservoir pressure monitoring correlates with vacuum regulator's set</td>
<td>92.8</td>
</tr>
<tr>
<td>Absence access and means access protocols</td>
<td>86.5</td>
</tr>
</tbody>
</table>

VAVD: vacuum-assisted venous drainage.
*Checklist item recommended by AntiECT (54)

Table 6. Reported VAVD-related incidents.

<table>
<thead>
<tr>
<th>Incident</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressurized venous reservoir activating PRV (71)</td>
<td>23.8</td>
</tr>
<tr>
<td>Premature venous reservoir leaking to concomitant outside the venous line</td>
<td>23.6</td>
</tr>
<tr>
<td>Air pulled across the membrane during priming</td>
<td>21.4</td>
</tr>
<tr>
<td>Leak in vacuum system resulting in unsuccessful injection</td>
<td>42.4</td>
</tr>
<tr>
<td>Vacuum regulator malfunction</td>
<td>33.3</td>
</tr>
<tr>
<td>Vacuum source (real vacuum) malfunction</td>
<td>33.3</td>
</tr>
<tr>
<td>Over-administration of drugs or fluids due to increased siphon</td>
<td>18.1</td>
</tr>
</tbody>
</table>
Conclusion: “is likely that a comprehensive approach to renal protection, with specific attention to the containment of hemodilution during CPB and the maintenance of adequate oxygen delivery may represent an effective strategy to limit cardiac operation-induced AKI.”

VAVD Advantages

- Smaller venous cannulae
- Easier cannulation
- Maximizing surgical visibility
- Cardiac decompression
- Eliminates risk of air locks in venous line
- Optimal venous return
- Reduce damaging effects of pump suction
- Decrease prime volume
Miniaturization of CPB Circuitry

Decreases prime volume
• Smaller sized circuit tubing
• Remote mounting of pumps
• Reduction of tubing lengths
• Smaller surface area

“In light of our findings, this would suggest that the practice of using VAVD to commence CPB with an unprimed venous return line in both adult and pediatric circuits would result in a significant number of arterial line emboli being delivered to the patient’s circulation.”

Anecdotes of Catastrophic Events

Cerebrovascular Accident After Vacuum-Assisted Venous Drainage in a Fontan Patient: A Cautionary Tale

Marjan Jahangiri, FRCS, Alan Rayner, BS, Brian Kergh, FRCS, and Christopher Lincoln, FRCS
Department of Cardiac Surgery, Anesthesia, and Perfusion, Royal Brompton Hospital, London, England

Vacuum-assisted venous drainage was used in a 26-year-old woman who underwent a redo Fontan procedure. She developed a hemiparesis, which is thought to be caused by cerebral air embolism.

© 2001 by The Society of Thoracic Surgeons

• Induces blood trauma if vacuum pressure is too high
• Potential to draw air into the venous line
• Retrograde flow in the venous line
• Complicates circuit
• Cost
Anecdotes of Catastrophic Events

Vasoarterial Air Embolism: A Complication of Vacuum-Assisted Venous Drainage
Richard W. DeBakey, MD,1 Thomas Kestin, DCF,2 and Michael J. Mack, MD
Cardiovascular Research Institute
Dallas, Texas

A “Perfect Storm”...er than expected can be a complication of vacuum-assisted venous drainage. Inadvertent positive pressure ventilation of the vena cava resulting in a paradoxical air embolism across a patent arterial vessel can occur. Reports of the mortality associated with this complication are discussed.

Sources of Gaseous Microemboli

200-um diameter upper limit separating micro from macro

• Aortic and venous cannulation
• CPB initiation
• Non-occlusive purse strings or caval snares
• Excessive cardiotomy suction
• Circuit components
• Perfusionist interventions

Cerebral Microemboli During Cardiopulmonary Bypass: Increased Emboli During Perfusionist Interventions

Baird L. Taylor, MD, Michael S. Bybee, MD, Richard D. Pintilie, MD, Ludwig Tadele, MD, PhD, and Christopher T. Frates, MD

Drs. Taylor, Bybee, Pintilie, Tadele, and Frates (from left) examine the number of microemboli crossing the perfusionist's neck during cardiopulmonary bypass surgery. The data show a significant increase in emboli during perfusionist interventions. The study suggests that these interventions may need to be minimized to mitigate the risk of cerebral microemboli.
Findings

1. How air enters on venous side
   - Majority of microemboli during CPB consist of air
   - Enter at manifold
   - Transported to oxygenator before able to rise to top

2. Gaseous emboli able to traverse arterial filter
   - Average arterial filter is 32um
   - "Distortion of the bubbles into a sausage shape to fit through the pores or coalescence of fragmented bubbles distal to the filter"

Conclusion(s):

1. VAVD at -40mmHg did not significantly increase gaseous microemboli
2. High levels of vacuum and increased pump flow rates should be avoided
3. Air should not be introduced into the venous line

Air Happens...What do you do?

- Retrograde cerebral perfusion- clear air from cerebral circulation
- Cooling to 18 degrees-decrease cerebral metabolic rate
- Vent aortic root
- Intermittent pressure on carotid arteries-facilitate air removal from vertebral arteries
- Steroid- anti-inflammatory
- Epi-aortic echocardiogram-show clearance of air from carotid arteries
- Hyperbaric oxygen therapy-reabsorption and clearance
**VAVD Considerations**

- Sealed venous reservoir
- Positive pressure relief valve
- Negative pressure relief valve
- 0 to -40 mmHg
- Vacuum regulator
- Vacuum source
- VAVD kit; tubing, moisture trap
- Pressure monitor

**Applying VAVD**

- Initiate CPB (VAVD off)
- Increase in blood flow until equilibrium –flow rate vs level
- Turn on VAVD at -10mmHg to -20mmHg
- Monitor return and increase flow rate until ideal
  - Calculated rate
  - Venous saturations
  - NIRS
  - MAP
- Ideal to use minimum vacuum necessary

---

**VAVD Disposable “Kit”**

- Traditional disposable Y
- VavPac

---

Many refinements in perfusion during VAVD are of minimal importance in limiting the number of variables. A technique with a benefit/drawback ratio of 1:0 is utopian, but if we believe that the advantages of VAVD, namely reduction in prime volume and blood transfusion, improved heart decompression and constant optimization of effective negative pressure, far outweigh any potential drawbacks, when applied properly.
In Conclusion

- VAVD offers many benefits for adult and pediatric perfusion
- Incorporate safest equipment and disposables
- Correct, Safe use (Wang, JECT 2008)

Future possibilities
- An effective method for removing air from venous line before it enters the reservoir (Willcox, JECT 2002)
- Removal of micro air from arterial line (Willcox, JECT 2002)
Poll: How low will you go? What is your maximum setting?

Poll: Do you use a scavenger for anesthetic gases?

Poll: Have you ever had a negative incident with the use of VAVD?