Cool Medicine

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Disclosures

<table>
<thead>
<tr>
<th>Category</th>
<th>Disclosures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant/Speakers Bureaus</td>
<td>No Disclosures</td>
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<tr>
<td>Research Funding</td>
<td>No Disclosures</td>
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<td>Stock ownership/Corporate Boards-employment</td>
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<td>Off-label uses</td>
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* I did change a couple of slides since submission.
Objectives

1. History of the origin of cooling patients for HIE
2. Physiological perspective of hypothermia
3. Describe the two different modalities of hypothermia and their outcomes
4. What do we see while the kids are cold
5. What lies in the future?
Hypoxic-Ischemic Encephalopathy

- Definition
- Incidence
  - 1 to 1.5%
    - 9% of all infants younger than 36 weeks
    - 0.5% of all infants older than 36 weeks
- Timing of development
  - Antepartum—20%
  - Intrapartum—30%
  - Antepartum and intrapartum—35%
  - Postpartum—10%
Where did it start??

• It all started in the NICU!!

• The adult Neuro-ICU

• MD’s noticed that some stroke patients had longer stays and worse outcomes.

• What was the cause??
Where is the proof?

- Meta-analysis
  - 24 articles
  - Stroke (embolic, ischemic, traumatic brain injury).
  - Fever vs. Afebrile
  - Worse outcomes
    1. Increased LOS
    2. Increased ICU-LOS
    3. Increased Mortality
    4. Increased Rankin Score—measure degree of disability or dependence with ADL
    5. Worse Barthel index—10 common ADL
The origin of hypothermia

• If hyperthermia is BAD,

• Then Hypothermia = GOOD !
Hypothermia since the 50’s

• 1950’s Hypothermic ischemia on cardiac bypass.
  » No-brainer

• 1960’s
  – Rhesus monkey
  – Puppies
To the animals

- Hypothermia for out-of-hospital cardiac arrest
  - Better outcomes and more patients survived
  - Multiple studies prove safety without adverse events.

- 1990’s
  - Piglets
  - Rats
  - Sheep
Physiology of Cooling

Does shivering count as exercise?
An event

• An event must happen that decreases oxygen delivery to the brain (and body).
  – Blood Clot
  – Hemorrhage
  – Occlusion

• Timing ???
Posthypoxic Brain Injury

• Lack of Oxygen = lack of oxidative phosphorylation of ATP

• Decrease in ATP leads to cell membrane depolarization and disruption of voltage-dependent ion channels
  
  – Failure of Na/K-ATPase membrane pumps result in leakage of Na and CL into the cell with water (cerebral edema).

  – Intracellular and intranuclear calcium causes activation of
    • Endonucleases
    • Proteases
    • Phospholipases
Primary neuronal death

- Increased extracellular acidosis increases free radical formation
- Free radicals cause neuronal necrosis
Aw shucks!!
Secondary Neuronal Death
(this is where the money is)
Secondary Neuronal Death

• This is reperfusion injury!!

• The previous ischemia caused
  – Proinflammatory gene products (leukocyte adhesion molecules and cytokines)
  – Bioactive agents (endothelin, thromboxane A2)
  – Repression of protective gene products (prostacyclin and nitric oxide).

• Apoptosis is the major cause of neuronal cell death

• Occurs 2 to 72 hours after insult

• Goal = Hypothermia

Apoptosis.
Prolonged Hypoxia

PERINATAL ASPHYXIA

(Initially)

Redistribution of blood flow

↑BP

Hypercapnia, hypoxemia, acidemia

Loss of autoregulation

(Continuing)

↑CBF

Hemorrhage

↓BP

↓CBF

Ischemic brain injury
Autoregulation

• Impairment of autoregulation with asphyxia
  – Hypoxemia
  – Hypercarbia

• Pressure passive state
  – Increase CBF with increase MAP.

From Rosenberg AA: Stroke 19:239-244, 1988
Reperfusion chemistry

- Reperfusion/reoxygenation results in formation of toxic reactive oxygen species
  
  \[ \text{XDH} \]
  
  - Hypoxanthine $\rightarrow$ xanthine
  
  - Ischemia causes XDH to become Xanthine-Oxidase
  
  - X-Oxidase + Hypoxanthine (buildup) formation of reactive oxygen species.
  
  - Oxygen radical damage to organelles and cell membranes in addition to disruption of nucleotide metabolism and leads to apoptosis.
So why does hypothermia work?

- Reduces ATP consumption
- Reduces cerebral metabolism
- Reduces cerebral blood flow
- Down regulates many intracerebral metabolic processes associated with gene expression!
- Decreases oxygen reperfusion injury.
Development of Inclusion and Methods

- Who??
- What??
- When??
- Where??
- Why??
- How??
Development of Inclusion and Methods

• Who??
• What??
  • When??
  • Where??
• Why??
• How??
Who + What??

• What age??

• Physiologic Criteria

• Neurologic Criteria

• Exclusions???
Who + What??

• **What age??**
  – Term animals = term neonates

• Physiologic Criteria

• Neurologic Criteria

• Exclusions???
Who + What??

• What age??

• Physiologic Criteria
  • Neurologic Criteria
  • Exclusions???
Physiologic Criteria

1. If Blood Gas has pH <7 or base deficit of > 16 than proceed to Neurologic Inclusion

2. If Blood Gas has pH 7-7.15 or base deficit of 10-15.9 or no initial blood gas they must have:

   – A perinatal event (abruption placenta, cord prolapse, severe FHR abnormality: variable or late decels), and either i or ii.

   i. A 10 minute apgar less than 5
   ii. A need for ventilation initiated at birth and continued for at least 10 minutes.
Who + What??

- What age??

- Physiologic Criteria

- **Neurologic Criteria**

- Exclusions???
## Neurologic Criteria (3 of 6)

<table>
<thead>
<tr>
<th></th>
<th><strong>Neuro Exam</strong></th>
<th><strong>Moderate Encephalopathy</strong></th>
<th><strong>Severe Encephalopathy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Level of Consciousness</td>
<td>Lethargic</td>
<td>Stupor or coma</td>
</tr>
<tr>
<td>2</td>
<td>Spontaneous movement</td>
<td>Decreased activity</td>
<td>No activity</td>
</tr>
<tr>
<td>3</td>
<td>Posture</td>
<td>Distal flexion</td>
<td>Decerebrate</td>
</tr>
<tr>
<td>4</td>
<td>Tone</td>
<td>Hypotonia</td>
<td>Flaccid</td>
</tr>
<tr>
<td>5</td>
<td>Primitive reflexes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suck</td>
<td>Weak</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td>Moro</td>
<td>Incomplete</td>
<td>Absent</td>
</tr>
<tr>
<td>6</td>
<td>Autonomic system</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pupils</td>
<td>Constricted</td>
<td>Dilated, nonreactive</td>
</tr>
<tr>
<td></td>
<td>Heart rate</td>
<td>Bradycardia</td>
<td>Variable</td>
</tr>
<tr>
<td></td>
<td>Respiration</td>
<td>Periodic breathing</td>
<td>Apnea</td>
</tr>
</tbody>
</table>
Who + What??

- What age??
- Physiologic Criteria
- Neurologic Criteria
- Exclusions???
Exclusions

• <36 weeks
• <1,800 grams
• > 6 hours after event
• Chromosomal Abnormality
• Congenital Heart Disease
Exclusions

- <36 weeks
- <1,800 grams
- > 6 hours after event
- Chromosomal Abnormality
- Congenital Heart Disease
Exclusions

- <36 weeks
- <1,800 grams
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- Congenital Heart Disease
Exclusions

• <36 weeks
• <1,800 grams
• > 6 hours after event
• Congenital Heart Disease
Exclusions

• <36 weeks

• <1,800 grams

• Congenital Heart Disease
When??

Neonatal Piglets

 Delayed hypothermia and neuronal rescue

- Sham Cooled
- Early (90 min) Cooling
- Delayed (5.5 h) Cooling
- Post Seizure (8.5 h) Cooling

Neuronal Loss %

- Parasagittal Cortex
- Lateral Cortex
- Striatum
- DG
- CA1/2

* Indicates statistically significant difference
Where + Why

• Where
  » Obvious one!!

• Why
  » Patience, that is next.
How

• How long for cooling??
  – 72 hours from studies on reperfusion injury and gene expression of apoptosis.

• How low of temperature??
Cool Cap
Cool Cap Study

Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial

Peter D Gluckman, John S Wyatt, Denis Azzopardi, Roberta Ballard, A David Edwards, Donna M Ferriero, Richard A Polin, Charlene M Robertson, Marianne Thoresen, Andrew Whitelaw, Alistair J Gunn, on behalf of the CoolCap Study Group

- 7/1999 through 1/2002
- Randomized, non-blinded
- Central to 34 degrees, body 36.5 degrees
Inclusion--Biological

• >36 weeks

• Ten minute Apgar of 5 or less
  OR

• Need for resuscitation at 10 minutes of age
  OR

• Severe acidosis
  – pH < 7.0
  – Base deficit >16 mmol/L
Inclusion--Neurological

- Lethargy, Stupor, or Coma

- Hypotonia, abnormal reflexes, abnormal suck, seizures

- aEEG of moderate or severe encephalopathy or seizures
Exclusion

- >5.5 hours of age
- Anticonvulsants
- Severe growth restriction
- <1,800 grams
- Too critically ill for NICU support
What they found

<table>
<thead>
<tr>
<th></th>
<th>Cooling</th>
<th>Control</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died or severe disability at 18 months</td>
<td>59/108 (55%)</td>
<td>73/110 (66%)</td>
<td>0.61 (0.34–1.09)</td>
<td>0.10</td>
</tr>
<tr>
<td>Died</td>
<td>36/108 (33%)</td>
<td>42/110 (38%)</td>
<td>0.81 (0.47–1.41)</td>
<td>0.48</td>
</tr>
<tr>
<td>Severe neuromotor disability</td>
<td>14/72 (19%)</td>
<td>21/68 (31%)</td>
<td>0.54 (0.25–1.17)</td>
<td>0.12</td>
</tr>
<tr>
<td>Bayley MDI† &lt;70</td>
<td>21/70 (30%)</td>
<td>24/61 (39%)</td>
<td>0.66 (0.32–1.36)</td>
<td>0.27</td>
</tr>
<tr>
<td>Bilateral cortical visual impairment</td>
<td>7/72 (10%)</td>
<td>11/64 (17%)</td>
<td>0.52 (0.19–1.39)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

**Secondary outcomes**

<table>
<thead>
<tr>
<th></th>
<th>Cooling</th>
<th>Control</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-organ dysfunction</td>
<td>97/116 (84%)</td>
<td>95/118 (81%)</td>
<td>1.24 (0.64–2.40)</td>
<td>0.61</td>
</tr>
<tr>
<td>Multiple disabilities</td>
<td>15/70 (21%)</td>
<td>20/65 (31%)</td>
<td>0.61 (0.29–1.32)</td>
<td>0.24</td>
</tr>
<tr>
<td>Bayley PDI &lt;70</td>
<td>21/69 (30%)</td>
<td>23/56 (41%)</td>
<td>0.63 (0.30–1.31)</td>
<td>0.26</td>
</tr>
<tr>
<td>Bilateral sensorineural Hearing loss</td>
<td>5/64 (8%)</td>
<td>3/55 (6%)</td>
<td>1.47 (0.37–5.84)</td>
<td>0.72</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>11/72 (15%)</td>
<td>11/67 (16%)</td>
<td>0.92 (0.38–2.24)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Continuous BSID II scores, median (range)**

<table>
<thead>
<tr>
<th></th>
<th>Cooling</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayley MDI §</td>
<td>84.5 (49–116)</td>
<td>77.0 (49–121)</td>
<td>0.11</td>
</tr>
<tr>
<td>Bayley PDI</td>
<td>87.0 (49–127)</td>
<td>79.5 (49–125)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

†Nine surviving patients did not have Bayley MDI scores at 18 months; four of the nine were also missing bilateral cortical visual impairment data. However, all nine had unfavourable primary outcome due to GMF ≥3 (GMF=3 for all nine and GMF=4 for the other one). §Incidence compared by Fisher’s exact test. Continuous BSID II scores compared by Cox regression analysis including baseline aEEG parameters. Data are number of patients (%) unless otherwise stated.
### Intermediate aEEG group, n=172

<table>
<thead>
<tr>
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<th>Cooled</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died or severe disability at 18 months</td>
<td>40 (48%)</td>
<td>58 (66%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Died</td>
<td>24 (29%)</td>
<td>34 (39%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Severe neuromotor disability</td>
<td>7 (12%)</td>
<td>15 (28%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Bayley MDI† &lt;70</td>
<td>15 (25%)</td>
<td>20 (40%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Bilateral cortical visual impairment</td>
<td>4 (7%)</td>
<td>7 (14%)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

### Secondary outcomes

<table>
<thead>
<tr>
<th></th>
<th>Cooled</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple disabilities</td>
<td>8 (14%)</td>
<td>14 (28%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Bayley PDI &lt;70</td>
<td>14 (24%)</td>
<td>18 (39%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Bilateral sensorineural hearing loss</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>8 (13%)</td>
<td>8 (15%)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

### Continuous BSID II scores (median, range)

<table>
<thead>
<tr>
<th></th>
<th>Cooled</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayley MDI</td>
<td>85 (49–116)</td>
<td>77 (49–119)</td>
<td>0.04</td>
</tr>
<tr>
<td>Bayley PDI</td>
<td>84.5 (49–127)</td>
<td>84.5 (49–125)</td>
<td>0.047</td>
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</tbody>
</table>

### Severe aEEG group, n=46

<table>
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<th>Cooled</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died or severe disability at 18 months</td>
<td>19 (79%)</td>
<td>15 (68%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Died</td>
<td>12 (50%)</td>
<td>8 (36%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Severe neuromotor disability</td>
<td>7 (58%)</td>
<td>6 (43%)</td>
<td>0.70</td>
</tr>
<tr>
<td>Bayley MDI† &lt;70</td>
<td>6 (55%)</td>
<td>4 (36%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Bilateral cortical visual impairment</td>
<td>3 (25%)</td>
<td>4 (31%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

### Secondary outcomes

<table>
<thead>
<tr>
<th></th>
<th>Cooled</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple disabilities</td>
<td>7 (58%)</td>
<td>6 (43%)</td>
<td>0.70</td>
</tr>
<tr>
<td>Bayley PDI &lt;70</td>
<td>7 (64%)</td>
<td>5 (50%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Bilateral sensorineural hearing loss</td>
<td>2 (22%)</td>
<td>2 (17%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>3 (25%)</td>
<td>3 (21%)</td>
<td>1.00</td>
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</table>
Moderate vs. Severe

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Hypothermia Events</th>
<th>Hypothermia Total</th>
<th>Normothermia Events</th>
<th>Normothermia Total</th>
<th>Risk ratio (95% CI)</th>
<th>Weight (%)</th>
<th>Risk ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Infants with moderate encephalopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoolCap</td>
<td>28</td>
<td>62</td>
<td>39</td>
<td>69</td>
<td>37.9</td>
<td>0.80</td>
<td>0.57 to 1.13</td>
</tr>
<tr>
<td>NICHD</td>
<td>22</td>
<td>69</td>
<td>30</td>
<td>66</td>
<td>31.5</td>
<td>0.70</td>
<td>0.45 to 1.08</td>
</tr>
<tr>
<td>TOBY</td>
<td>20</td>
<td>66</td>
<td>30</td>
<td>67</td>
<td>30.6</td>
<td>0.68</td>
<td>0.43 to 1.06</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>197</td>
<td>202</td>
<td></td>
<td></td>
<td>100.00</td>
<td>0.73</td>
<td>0.58 to 0.92</td>
</tr>
<tr>
<td>Total events</td>
<td>70</td>
<td>99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants with severe encephalopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoolCap</td>
<td>28</td>
<td>40</td>
<td>32</td>
<td>35</td>
<td>28.6</td>
<td>0.77</td>
<td>0.61 to 0.96</td>
</tr>
<tr>
<td>NICHD</td>
<td>23</td>
<td>32</td>
<td>34</td>
<td>40</td>
<td>25.4</td>
<td>0.85</td>
<td>0.66 to 1.09</td>
</tr>
<tr>
<td>TOBY</td>
<td>53</td>
<td>98</td>
<td>54</td>
<td>95</td>
<td>46.0</td>
<td>0.95</td>
<td>0.74 to 1.23</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>170</td>
<td>170</td>
<td></td>
<td></td>
<td>100.00</td>
<td>0.87</td>
<td>0.75 to 1.01</td>
</tr>
<tr>
<td>Total events</td>
<td>104</td>
<td>120</td>
<td></td>
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</tr>
</tbody>
</table>
Whole Body Cooling
Whole-Body Hypothermia for Neonates with Hypoxic–Ischemic Encephalopathy


- 16 Centers in US
- July 2000 to May 2003
- 239 eligible patients
- 102 cooled, 106 controls
- Follow-up at 18 to 22 months.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypothermia Group (N=102)</th>
<th>Control Group (N=106)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or moderate or severe disability‡</td>
<td>45 (44)</td>
<td>64 (62)</td>
<td>0.72 (0.54–0.95)</td>
<td>0.01</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>24 (24)</td>
<td>38 (37)</td>
<td>0.68 (0.44–1.05)</td>
<td>0.08</td>
</tr>
<tr>
<td>Death or disability§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Among infants with moderate encephalopathy</td>
<td>22 (32)</td>
<td>30 (48)</td>
<td>0.69 (0.44–1.07)</td>
<td>0.09</td>
</tr>
<tr>
<td>Among infants with severe encephalopathy</td>
<td>23 (72)</td>
<td>34 (85)</td>
<td>0.85 (0.64–1.13)</td>
<td>0.24</td>
</tr>
<tr>
<td>Survival</td>
<td>78 (76)</td>
<td>68 (66)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bayley Mental Development Index score†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥85</td>
<td>39 (52)</td>
<td>25 (40)</td>
<td>1.24 (0.83–1.83)</td>
<td>0.27</td>
</tr>
<tr>
<td>70–84</td>
<td>17 (23)</td>
<td>13 (21)</td>
<td>1.08 (0.57–2.05)</td>
<td>0.81</td>
</tr>
<tr>
<td>&lt;70</td>
<td>19 (25)</td>
<td>24 (39)</td>
<td>0.71 (0.43–1.17)</td>
<td>0.18</td>
</tr>
<tr>
<td>Bayley Psychomotor Developmental Index score‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥85</td>
<td>46 (62)</td>
<td>34 (55)</td>
<td>1.10 (0.82–1.48)</td>
<td>0.53</td>
</tr>
<tr>
<td>70–84</td>
<td>8 (11)</td>
<td>6 (10)</td>
<td>1.19 (0.38–3.76)</td>
<td>0.77</td>
</tr>
<tr>
<td>&lt;70</td>
<td>20 (27)</td>
<td>22 (35)</td>
<td>0.80 (0.48–1.33)</td>
<td>0.39</td>
</tr>
<tr>
<td>Disabling cerebral palsy**</td>
<td>15 (19)</td>
<td>19 (30)</td>
<td>0.68 (0.38–1.22)</td>
<td>0.20</td>
</tr>
<tr>
<td>Blindness††</td>
<td>5 (7)</td>
<td>9 (14)</td>
<td>0.50 (0.17–1.44)</td>
<td>0.20</td>
</tr>
<tr>
<td>Severe hearing impairment **</td>
<td>3 (4)</td>
<td>4 (6)</td>
<td>0.54 (0.10–3.02)</td>
<td>0.47</td>
</tr>
</tbody>
</table>
So in Summary:

- Potential for HIE needs to be recognized early.
- Cooling helps when started earlier, don’t be afraid to ask for help/advice early.
- Improved combined outcomes of death or severe neurodevelopmental disability.
- Intermediate HIE better results than severe
- Hypothermia is a preventive strategy for further damage, it is not a curative treatment.
What happens when they cool?
Vital Signs

A

B

Esophageal Temperature (°C)

Skin Temperature (°C)

Control

Hypothermia

Hours

0 10 20

0 10 20

30 31

30 31

32 32

33 33

34 34

35 35

36 36

37 37

38 38
Vital Signs

![Graph showing heart rate changes over hours]

- Control
- Hypothermia
Other things we see

• **Brain**
  – Seizures

• **Lungs**
  – PPHN \(\text{Yes}\)
  – RDS (surfactant inactivation)

• **Heart**
  – Bradycardia \(\text{Yes}\)
  – Hypotension requiring inotropinc support \(??\) \(\text{Yes}\)

• **Kidneys**
  – Oligouria
  – Hematuria \(\text{Yes}\)
Other things we see

• Electrolytes
  – Hypokalemia
  – Hyponatermia
  – Hypocalcemia
  – Hypoglycemia

• Heme
  – Thrombocytopenia  Yes
  – Coagulopathy
  – Leukocytosis
  – Anemia

• Skin
  – Subcutaneous fat necrosis  Yes
What we do

• Not all kids need AED.

• aEEG with EEG to follow

• MRI

• Neurology consult

• Close developmental follow-up
Parting thoughts

• If concerned get a blood gas (venous is fine, capillary will work)

• Would consider cooling if gas is bad and infant is great!

• If it’s a possibility, call referral center early

• Moderate kids have better outcomes than severe

• Counseling keys
Horizons
Horizons

1. A preferred method??
   • Hot topics in December
2. Cooling after 6 hours??
   • Ongoing NRN research
3. Cooling after Code??
   • Interesting thought
4. Preemies??
   • In the queue for NRN—interesting that 9% of preemies have HIE?
5. Cooling on transport??
   • Many places do it, anecdotal but no randomized trial
6. Is 72 hours of cooling correct??
7. Are they cold enough??
8. Longer follow-up??
Thank you
References


References


References


• Rosenberg AA. Regulation of cerebral blood flow after asphyxia in neonatal lambs. *Stroke* 1988;19;239-244.

