Reducing Injury to the Brain through TTM

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Disclosure

• Mary Kay Bader
  – Speaker’s Bureau: Integra Neuroscience
Therapeutic Temperature Management

• Temperature Management
  – Normothermia
  – Hypothermia
Neurologic Patient

• Temperature control
  – Avoid hyperthermia
  – Neuro Populations ++
    • Stroke
    • Traumatic Brain Injury
    • Spinal Cord Injury
Normothermia

Hyperthermia exacerbates ischaemic brain injury

C. X. Wang¹,²*, A. Stroink¹, J. M. Casto², and K. Kattner¹,²
**Table 1** Hyperthermia and ischaemic stroke in clinical studies

<table>
<thead>
<tr>
<th>Type</th>
<th>Patient (number)</th>
<th>BT recorded (h post ictus)</th>
<th>Hyperthermia (%)*</th>
<th>Major findings</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(A) Prospective</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>390</td>
<td>6</td>
<td>25</td>
<td>Hyperthermia worsens mortality and outcome. BT correlates with initial stroke severity, lesion size, mortality and outcome in survivors. For 1°C increase in BT, the relative risk of poor outcome rises by 2.2</td>
<td>(17, 19)</td>
</tr>
<tr>
<td></td>
<td>398</td>
<td>12 and 24</td>
<td>N/G</td>
<td>BT correlates to stroke severity and mortality in patients admitted between 6–12 h from stroke onset, but not admitted 12–24 h</td>
<td>(18)</td>
</tr>
<tr>
<td></td>
<td>260</td>
<td>72</td>
<td>60.8</td>
<td>Hyperthermia initiated in 24 h from insult associated with poor outcome and large infarcts. The earlier the hyperthermia occurs, the higher the relation between the BT increase and brain damage.</td>
<td>(14)</td>
</tr>
<tr>
<td></td>
<td>725</td>
<td>24</td>
<td>N/G</td>
<td>At 10–12 h after stroke onset, increased BT relates to stroke severity and poor outcome. Initial increased BT (&lt; 8 h) does not relate to stroke severity and outcome.</td>
<td>(12)†</td>
</tr>
<tr>
<td></td>
<td>183</td>
<td>168</td>
<td>43</td>
<td>Higher BT correlates with poor stroke outcome</td>
<td>(20)†</td>
</tr>
<tr>
<td></td>
<td>229</td>
<td>24</td>
<td>37.6</td>
<td>Hyperthermia correlates with higher infarct volume, poor outcome</td>
<td>(21)</td>
</tr>
<tr>
<td><strong>(B) Retrospective</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>346</td>
<td>72</td>
<td>N/G</td>
<td>Higher BT correlates with larger infarct volume and more severe neurological deficits</td>
<td>(22)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>24</td>
<td>53</td>
<td>Hyperthermia associated with unfavourable outcome following thrombolysis with tPA</td>
<td>(24)</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>72</td>
<td>31</td>
<td>Hyperthermia correlated to mortality</td>
<td>(15)</td>
</tr>
<tr>
<td></td>
<td>3790</td>
<td>N/G</td>
<td>N/G</td>
<td>Hyperthermia correlated to morbidity and mortality</td>
<td>(25)</td>
</tr>
<tr>
<td></td>
<td>509</td>
<td>N/G</td>
<td>N/G</td>
<td>Hyperthermia associated with both short- and long-term mortality. 1°C increase in BT increases relative risk of 1-year mortality by 3.4</td>
<td>(23)†</td>
</tr>
<tr>
<td></td>
<td>119</td>
<td>48</td>
<td>32</td>
<td>Increased BT associated with more severe neurological deficits</td>
<td>(16)</td>
</tr>
</tbody>
</table>

*Hyperthermia occurred in the recording period. †Includes ischaemic and haemorrhagic stroke. N/G, data not given; BT, body temperature.
Fever Burden

Hyperthermia in the Neurosurgical Intensive Care Unit

Megan M. Kilpatrick, B.S., David W. Lowry, M.D.,
Andrew D. Firlik, M.D., Howard Yonas, M.D.,
Donald W. Marion, M.D.

CONCLUSION: Fever is common in critically ill neurosurgical patients, especially those with a prolonged length of stay in the ICU or a cranial disease. If hyperthermia worsens the functional outcome after a primary ischemic or traumatic injury, as has been suggested by several studies of stroke patients, treatment of fever is a clinical issue that requires better management. (Neurosurgery 47:850–856, 2000)
Effects of Poststroke Pyrexia on Stroke Outcome
A Meta-Analysis of Studies in Patients
Cother Hajat, MRCP; Shakoor Hajat, MSc; Pankaj Sharma, PhD

Results—Nine studies were identified totaling 3790 patients, providing our study with 99% power to detect a 9% increase in morbidity and 84% power to detect a 1% increase in mortality for the pyrexial group. The combined odds ratio for mortality was 1.19 (95% CI, 0.99 to 1.43). A heterogeneity test was highly nonsignificant ($P > 0.05$) for mortality, suggesting that the data were sufficiently similar to be meta-analyzed. Combined probability values were highly significant for both morbidity ($P < 0.0001$) and mortality ($P < 0.0000001$).

Conclusions—The results from this meta-analysis suggest that pyrexia after stroke onset is associated with a marked increase in morbidity and mortality. Measures should be taken to combat fever in the clinical setting to prevent stroke progression. The possible benefit of therapeutic hypothermia in the management of acute stroke should be further investigated. (Stroke. 2000;31:410-414.)
**Impact of Fever on Outcome in Patients With Stroke and Neurologic Injury**

A Comprehensive Meta-Analysis

David M. Greer, MD, MA; Susan E. Funk, MBA; Nancy L. Reaven, MA; Myrsini Ouzounelli, MD; Gwen C. Uman, RN, PhD

**Results**—Fever or higher body temperature was significantly associated with worse outcome in every measure studied. Relative risk of worse outcome with fever was: mortality, 1.5; Glasgow Outcome Scale, 1.3; Barthel Index, 1.9; modified Rankin Scale, 2.2; Canadian Stroke Scale, 1.4; intensive care length of stay, 2.8; and hospital length of stay, 3.2.

**Conclusions**—In the pooled analyses covering 14,431 patients with stroke and other brain injuries, fever is consistently associated with worse outcomes across multiple outcome measures. *(Stroke. 2008;39:000-000.)*
Conclusions—Hyperthermia, in acute ischemic stroke, is associated with a poor clinical outcome. The later the hyperthermia occurs within the first week, the worse the prognosis. Severity of stroke and inflammation are important determinants of hyperthermia after ischemic stroke. In patients with acute ischemic stroke, aggressive measures to prevent and treat hyperthermia could improve the clinical outcomes. (Stroke. 2009;40:3051-3059.)
Fever after subarachnoid hemorrhage

Risk factors and impact on outcome

A. Fernandez, MD; J.M. Schmidt, PhD; J. Claassen, MD; M. Pavlicova, PhD; D. Huddleston, MD; K.T. Kreiter, PhD; N.D. Ostapkovich, MS; R.G. Kowalski, MS; A. Parra, MD; E. Sander Connolly, MD; and S.A. Mayer, MD

<table>
<thead>
<tr>
<th></th>
<th>Admission $T_{\text{max}}$ ($&gt;37.0 \text{ °C}$)</th>
<th>Mean $T_{\text{max}}$ ($&gt;37.0 \text{ °C}$)</th>
<th>Mean extreme $T_{\text{max}}$ ($&gt;38.3 \text{ °C}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (mRS 6)</td>
<td>$1.67 (0.90–3.12)$; $p = 0.106$</td>
<td>$8.70 (3.32–22.80)$; $p &lt; 0.001^*$</td>
<td>$22.47 (5.68–88.94)$; $p &lt; 0.001^*$</td>
</tr>
<tr>
<td>Death or moderate to severe disability (mRS 4–6)</td>
<td>$1.01 (0.62–1.65)$; $p = 0.97$</td>
<td>$3.01 (1.58–5.75)$; $p &lt; 0.001^*$</td>
<td>$6.88 (2.18–21.73)$; $p &lt; 0.001^*$</td>
</tr>
<tr>
<td>Dependence in IADLs (Lawton IADL ≥9)</td>
<td>$1.39 (0.78–2.48)$; $p = 0.265$</td>
<td>$2.55 (1.16–5.59)$; $p &lt; 0.020^*$</td>
<td>$9.06 (1.35–60.83)$; $p &lt; 0.023^*$</td>
</tr>
<tr>
<td>Cognitive impairment (TICS ≤30)</td>
<td>$1.14 (0.67–1.93)$; $p = 0.637$</td>
<td>$2.53 (1.19–5.14)$; $p &lt; 0.015^*$</td>
<td>$6.58 (1.27–34.18)$; $p &lt; 0.025^*$</td>
</tr>
<tr>
<td>Poor quality of life (SIP ≥ 15.5)</td>
<td>$1.06 (0.63–1.78)$; $p = 0.839$</td>
<td>$1.33 (0.63–2.79)$; $p &lt; 0.452$</td>
<td>$2.86 (0.49–16.59)$; $p &lt; 0.242$</td>
</tr>
</tbody>
</table>

Values are reported as adjusted OR per °C (95% CI) and $p$ value after controlling for baseline predictors of poor outcome. Baseline predictors: death and death or moderate to severe disability: admission Hunt-Hess grade, age, aneurysm size ≥10 mm; dependence in IADLs: admission Hunt-Hess grade, race, education; cognitive impairment: admission Hunt-Hess grade, nonwhite race/ethnicity, education, age; poor quality of life: admission Hunt-Hess grade, nonwhite race/ethnicity, years of education. In 75 patients (21% of the total sample), a day 90 evaluation was not available and the day 14 mRS score was used, according to the principle of last observation carried forward.

* Significant ($p < 0.05$).
Fever after subarachnoid hemorrhage
Risk factors and impact on outcome

A. Fernandez, MD; J.M. Schmidt, PhD; J. Claassen, MD; M. Pavlicova, PhD; D. Huddleston, MD; K.T. Kreiter, PhD; N.D. Ostapkovich, MS; R.G. Kowalski, MS; A. Parra, MD; E. Sander Connolly, MD; and S.A. Mayer, MD

stronger when extreme $T_{\text{max}}$ was analyzed. Conclusion: Treatment-refractory fever during the first 10 days after subarachnoid hemorrhage (SAH) is predicted by poor clinical grade and intraventricular hemorrhage, and is associated with increased mortality and more functional disability and cognitive impairment among survivors. Clinical trials are needed to evaluate the impact of prophylactic fever control on outcome after SAH.

NEUROLOGY 2007;68:1013–1019
Induced Normothermia Attenuates Cerebral Metabolic Distress in Patients With Aneurysmal Subarachnoid Hemorrhage and Refractory Fever

Mauro Oddo, MD; Suzanne Frangos, RN; Andrew Milby, BS; Isaac Chen, MD; Eileen Maloney-Wilensky, APRN; Eileen Mac Murtrie, RN; Michael Stiefel, MD; W. Andrew Kofke, MD; Peter D. Le Roux, MD; Joshua M. Levine, MD

Results—Compared to fever, induced normothermia resulted in lower LPR (40±24 versus 32±9, P<0.01) and a reduced incidence of cerebral metabolic crisis (13% versus 5%, P<0.05) at normal ICP. During episodes of high ICP, induced normothermia was associated with a similar reduction of LPR, fewer episodes of cerebral metabolic crisis (37% versus 8%, P<0.01), and lower ICP (32±11 versus 28±12 mm Hg, P<0.05).

Conclusions—Fever control is associated with reduced cerebral metabolic distress in patients with SAH, irrespective of ICP. (Stroke. 2009;40:1913-1916.)
Normothermia

- Maintaining temperature at 36-37 degrees C

Induced Normothermia Attenuates Intracranial Hypertension and Reduces Fever Burden after Severe Traumatic Brain Injury

Results Mean (±SD) or median [range] demographics did not differ between groups [total N = 42 (6 female, 36 male, age 36.4 ± 14.8 years and initial GCS 7 [3–8], median and range]. Fever burden in the first 3 days (time >38°C) in the induced normothermia versus control group was significantly less at 1.6% versus 10.6%, respectively (P = 0.03). Mean ICP for patients with induced normothermia versus control was 12.74 ± 4.0 and 16.37 ± 6.9 mmHg, respectively. Furthermore, percentage of time with ICP > 25 mmHg was significantly less in the induced normothermia group (P = 0.03).

Conclusion Induced normothermia (fever prophylaxis via intravascular cooling catheter) is effective in reducing fever burden and may offer a means to attenuate secondary injury, as evidenced by a reduction in the intracranial hypertension burden.
Normothermia

- Maintaining temperature at 36-37 degrees C

**Metabolic Impact of Shivering During Therapeutic Temperature Modulation**

**The Bedside Shivering Assessment Scale**

Neeraj Badjatia, MD, MSc; Evangelia Strongilis, RD; Errol Gordon, MD; Mary Prescutti, RN; Luis Fernandez, MD; Andres Fernandez, MD; Manuel Buitrago, MD, PhD; J. Michael Schmidt, PhD; Noeleen D. Ostapkovich, MSc; Stephan A. Mayer, MD, FCCM

**Results**—Fifty consecutive cerebrovascular patients underwent indirect calorimetry between January 2006 and June 2007. Fifty-six percent were women, and mean age 63±16 years. The majority underwent fever control (n=40 [80%]) with a surface cooling device (n=44 [87%]) and had signs of shivering (Bedside Shivering Assessment Scale >0, 64% [n=34 of 50]). Low serum magnesium was independently associated with the presence of shivering (Bedside Shivering Assessment Scale >0; OR, 6.8; 95% CI, 1.7 to 28.0; *P*=0.01). The Bedside Shivering Assessment Scale was independently associated with the hypermetabolic index (*W*=16.3, *P*<0.001), oxygen consumption (*W*=26.3, *P*<0.001), resting energy expenditure (*W*=27.2, *P*<0.001), and carbon dioxide production (*W*=18.2, *P*<0.001) with a high level of interobserver reliability (*κ*=0.84, 95% CI, 0.81 to 0.86).

**Conclusion**—The Bedside Shivering Assessment Scale is a simple and reliable tool for evaluating the metabolic stress of shivering. *(Stroke. 2008;39:3242-3247.)*
Normothermia

- Maintaining temperature at 36-37 degrees C

| Metabolic Impact of Shivering During Therapeutic Temperature Modulation
| The Bedside Shivering Assessment Scale
| Neeraj Badjatia, MD; Evangelia Strongili, RD; Errol Grenon, MD; Mary Prescuiti, RN; Luis Fernandez, MD; Andres Fernandez, MD; Manuel Buitrago, MD, PhD; J. Michael Schmidt, PhD; Noeleen D. Ostapkovich, MSc; Stephan A. Mayer, MD, FCCM

<p>| Table 4. Characteristics of Shivering as Determined by the BSAS |
| BSAS |</p>
<table>
<thead>
<tr>
<th>0 (n=18)</th>
<th>1 (n=14)</th>
<th>2 (n=10)</th>
<th>3 (n=8)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years, mean±SD</td>
<td>62±16</td>
<td>55±18</td>
<td>65±16</td>
<td>60±13</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25±4</td>
<td>24±6</td>
<td>26±3</td>
<td>27±2</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.8±0.3</td>
<td>1.8±0.3</td>
<td>1.8±0.2</td>
<td>1.9±0.2</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>18 (72)</td>
<td>19 (80)</td>
<td>10 (63)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Therapeutic normothermia, n (%)</td>
<td>19 (84)</td>
<td>19 (79)</td>
<td>14 (88)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Surface cooling, n (%)</td>
<td>20 (80)</td>
<td>23 (96)</td>
<td>14 (88)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Sedative use, n (%)</td>
<td>12 (48)</td>
<td>8 (33)</td>
<td>10 (63)</td>
<td>10 (100)</td>
</tr>
<tr>
<td><strong>Laboratory values</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium, mg/dL</td>
<td>2.4±0.5</td>
<td>2.2±0.5</td>
<td>1.8±0.0</td>
<td>1.7±0.2</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>151±9</td>
<td>154±10</td>
<td>149±12</td>
<td>148±11</td>
</tr>
<tr>
<td>White blood cell count, 10⁹/L</td>
<td>12.2±4.5</td>
<td>12.7±4.5</td>
<td>14.9±4.3</td>
<td>16.3±3.9</td>
</tr>
<tr>
<td><strong>IDC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMI</td>
<td>1.0±0.1</td>
<td>1.2±0.1</td>
<td>1.6±0.2</td>
<td>2.4±0.5</td>
</tr>
<tr>
<td>REE, kcal/d</td>
<td>1390±383</td>
<td>1730±481</td>
<td>2303±688</td>
<td>3686±960</td>
</tr>
<tr>
<td>O₂ consumption, mL/min</td>
<td>198±62</td>
<td>251±74</td>
<td>337±119</td>
<td>568±152</td>
</tr>
<tr>
<td>CO₂ production, mL/min</td>
<td>165±36</td>
<td>200±61</td>
<td>233±55</td>
<td>325±93</td>
</tr>
</tbody>
</table>
Fever control and its impact on outcomes: What is the evidence?

Venkatesh Aiyagari a,*, Michael N. Diringer b,1

Although there is a body of experimental data and clinical experience that relate fever to more substantial neurologic injury and worse outcome, the answer to the critical question: “Does fever control improve outcome?” is not known. This is not to indicate that absence of proof is proof of absence. The definitive study has not been performed.
Summary

**Fever control in the neuro-ICU: why, who, and when?**
Neeraj Badjatia

**Recent findings**
Meta-analyses have demonstrated that fever at onset and in the acute setting after ischemic brain injury, intracerebral hemorrhage, and cardiac arrest have a negative impact on morbidity and mortality. There are data to support that the impact of fever is sustained for longer durations after subarachnoid hemorrhage and traumatic brain injury. However, there are currently no prospective randomized trials demonstrating the benefit of fever control in these patient populations.

**Summary**
The negative impact of fever after neurologic injury is well understood. Prospective randomized trials are needed to determine whether the beneficial impact of secondary injury prevention is outweighed by the potential infectious risk of prolonged fever control.
Hypothermia

• What is the evidence in the neuro population?
Hypothermia Treatment for Traumatic Brain Injury: A Systematic Review & Meta-Analysis

• Updated meta-analysis
  – effects of HT therapy on:
    • Mortality
    • favorable Neuro outcome
    • associated adverse effects
  – To develop evidence-based treatment guidelines

• 13 trials met eligibility criteria: 1339 randomized patients
  – Outcomes influenced by variations in methodology
  – Therefore, main analysis on 8 trials with lowest potential for bias
  – N=781

Hypothermia Treatment for Traumatic Brain Injury: A Systematic Review & Meta-Analysis

- **Mortality**
  - Hypothermia reduced mortality by 20% vs. conventional therapies
  - Variations in cooling duration & ICP management strategy had significant influences on risk of mortality
  - Benefits of HT were greatest when cooling was maintained for more than 48hr

- **Favorable Neurological Outcome**
  - Hypothermia was associated with 25% in improved Neuro outcome, measured by GOS although NOT Statistically significant
  - Variations in cooling duration, & ICP management strategy had significant influences on risk of mortality
  - Benefits of HT were greatest when cooling was maintained for more than 48hr

- **Adverse Events** (reported in very few trials)
  - Significantly more cases of pneumonia reported within 12 months following HT
    - Risk threefold greater with trials involving barbiturate administration
Hypothermia in Stroke

- Limited studies
Endovascular Cooling for Moderate Hypothermia in Patients With Acute Stroke
First Results of a Novel Approach

D. Georgiadis, MD; S. Schwarz, MD; R. Kollmar, MD; S. Schwab, MD

Conclusions—Induction and maintenance of hypothermia with an intravenous cooling device are feasible. The safety of this approach remains to be evaluated. (Stroke. 2001;32:2550-2553.)

Reduction of Diffusion-Weighted MRI Lesion Volume After Early Moderate Hypothermia in Ischemic Stroke

Christian Berger, MD; Peter Schramm, MD; Stefan Schwab, MD

Results—The initially large DWI deficit of the whole MCA territory contrasted to the relatively small final lesion restricted to the basal ganglia on MRI and computed tomography scan.

Conclusion—This case describes an unexpected reduction of a DWI lesion after early moderate hypothermia and spontaneous recanalization 3 days after stroke onset. We discuss potential reasons for the unexpected DWI lesion reduction. (Stroke. 2005;36:e56-e58.)
Induced Hypothermia for Acute Stroke

Thomas M. Hemmen, MD, PhD; Patrick D. Lyden, MD

Abstract—Induced hypothermia is one of the most promising neuroprotective therapies. Technological limitations and homeostatic mechanisms that maintain core body temperature have impeded the clinical use of hypothermia. Recent advances in intravascular cooling catheters and successful trials of hypothermia for cardiac arrest and neonatal asphyxia renewed interest in hypothermia for stroke, resulting in early phase clinical trials and plans for further development. This review elaborates on the clinical implications of hypothermia research in stroke and technical and logistical issues associated with the application of hypothermia. (Stroke. 2007;38[part 2]:794-799.)
Hypothermia as a neuroprotective strategy in subarachnoid hemorrhage: a pathophysiological review focusing on the acute phase

Claudius Thomé, Gerrit A. Schubert and Lothar Schilling

In various experimental studies during the past decade, hypothermia has been shown to reduce neuronal damage after ischemia, traumatic brain injury and other cerebrovascular diseases. Clinically, only some of these encouraging results could be reproduced. This review analyses results of studies on the effects of hypothermia on SAH with special respect to the acute phase in an experimental setting. Based on the available data, some considerations for the application of mild to moderate hypothermia in patients with subarachnoid hemorrhage are given. [Neurol Res 2005; 27: 229–237]
The use of mild hypothermia for patients with severe vasospasm: a preliminary report

S. Nagao MD, K. Irie MD, N. Kawai MD, T. Nakamura MD, K. Kunishio MD, Y. Matsumoto MD

Department of Neurological Surgery, Kagawa Medical University, Kagawa, Japan

Summary The purpose of this study was to determine the effect of mild hypothermia on cerebral ischaemia due to severe vasospasm, which was refractory to medical and intravascular treatments and to assess the brain protection of this treatment in patients who underwent delayed aneurysm clipping after presenting with ischaemic neurological deficits. Mild hypothermia (32–34 °C of brain temperature) was employed in two groups: (1) Patients (Hunt and Kosnik grades I to II) who showed progressive neurological deficits due to vasospasm and did not respond to conventional therapy (Group 1) and (2) Patients who received delayed aneurysm clipping after presenting with ischaemic neurological deficits due to vasospasm (Group 2). Seven of 8 patients in both Groups showed a favorable outcome with mild hypothermia (good recovery in 5 and moderate disability in two patients). Mild hypothermia is considered to be effective on critical cerebral ischaemia due to vasospasm even after failure to response the conventional therapies and to provide brain protection in delayed aneurysm clipping.

Use of Prolonged Hypothermia to Treat Ischemic and Hemorrhagic Stroke

Crystal L. MacLellan, Darren L. Clark, Gergely Silasi, and Frederick Colbourne

of cooling, in each condition. We contend that TH provides considerable protection after global and focal cerebral ischemia, especially when cooling is prolonged (e.g., >24h). However, there is presently insufficient evidence to support the clinical use of TH for ICH and SAH. In any case, further animal work is needed to develop optimized protocols for treating cardiac arrest (global ischemia), and to maximize the likelihood of successful clinical translation in focal cerebral ischemia.
Evidence Based Literature

• Very few published studies on efficacy of hypothermia in the stroke population but . . .
  – Experimental animal studies ++
  – What do you do with the
    • impending stroke pt with impending hemiation . . . refractory increased ICP
    • Refractory vasospasm from aneurysmal SAH
The Brain at Risk:
Initial Anoxia event and reperfusion injury
Pathophysiology of Neurologic Injury

- Trigger cardiac arrest or stroke or increased ICP
- Decreased perfusion → Cell death & almost death

Dead cells are dead

The penumbra is mostly dead
And mostly dead is not “dead”
Development of Ischemic Brain Edema

• Ischemic brain edema is a combination of two major types of edema:
  – Cytotoxic (cellular): edema evolves over minutes to hours and may be reversible
  – Vasogenic: occurs over hours to days, and is considered an irreversibly damaging process
Brain at risk
Ischemia

• Cells exposed to ischemia can either become:
  – Necrotic
  – partially or fully necrotic, recover
  – Enter a path leading to programmed cell death (apoptosis)

• This process occurs over a period minutes to many days after injury
Cell death following ischemia/reperfusion

Two types of cell death following ischemia/reperfusion

• Necrosis: characterized by cell swelling and membrane rupture allowing the contents of the cell to leak into the surrounding tissue
  – Contents of the cell include: oxygen radical, proteases, other inflammatory mediators which further damages the surrounding tissue
Cell death following ischemia/reperfusion

Neuronal Apoptosis aka “bad ju ju”

- 2nd mechanism for cell death
  - Decreased oxygen $\rightarrow$ Decreased ATP/Increased Lactate
  - Decreased sugar $\rightarrow$ Decreased ATP
  - Decreased ATP $\rightarrow$ reduced neurotransmitter uptake
  - Decreased ATP $\rightarrow$ dysfunction of sodium-potassium pump
  - Decreased ATP $\rightarrow$ increased cell membrane permeability

“... But wait... There’s more...”
Cell death following ischemia/reperfusion

Cell death by suicide

- **Apoptosis**: Non-necrotic cell suicide – programmed cell death which includes:
  - Cell shrinkage, membrane blebbing
  - Chromatin condensation, and DNA fragmentation
  - The cells split into plasma membrane bound vesicles known as apoptotic bodies.

- Following brief ischemic episode apoptosis usually prevails as the dominate cause of cell death in injured cells.
Ischemia

Activation of anaerobic glycolysis

↑ inorganic phosphate, lactate, and H+

Intra/extracellular acidosis

Failure of Na⁺-K⁺ pumps

Failure of K⁺, Na⁺ and Ca²⁺ channels

Loss of Cellular Na⁺

Mitochondrial dysfunction

↓ ATP and phosphocreatine

Failure of Na⁺-K⁺ pumps

Influx of Ca²⁺

Neuroexcitory cascade

Depolarization of neurocell membranes

Release of excitatory neurotransmitter glutamate

Impaired reuptake and ↑ extracellular glutamate

Prolonged and excessive activation of membrane glutamine receptors

Neurotoxic Neuron are in hyperexcitable state

Additional injury and cell death

Mitochondrial dysfunction

Activates membrane phospholipases and protein kinases

Production of Free Fatty Acids including arachidonic acids (AAA)

Damages cell membrane

Biochemical Cascade (thromboxane and leukotrienes)

Platelet aggregation, clotting, vasospasm, and edema

Cerebral Edema

Proinflammatory mediators (TNFa and IL-1) are released from astrocytes, microglia and endothelial cells

Adhesion molecules on leukocytes and endothelial cells

Accumulation of inflammatory cells in the brain

Cerebral edema

Disruption in the blood-brain barrier

Excessive leukocyte infiltrations

↑ risk and extent of cell damage and infarction through their phagocytic actions

Ischemia/Reperfusion

The Brain at Risk:
Mechanisms of Heat Destruction in CNS
Scientific Overview
Physiologic Effects - Hyperthermia

• Increased metabolic rate
• Increased blood velocity
• Increased cerebral blood volume
• Increased oxygen consumption
Scientific Overview
Physiologic Effects - Hyperthermia

- AMPA-mediated
  - AMPA mimics glutamate and is inhibited by lower temperatures
  - Setting up for secondary brain injury
  - AMPA-mediated influx of calcium triggers programmed cell death

- Heat Shock Proteins
  - Increased release of heat shock proteins in the setting of hyperthermia
    - Increase in cell injury – release of neurotoxins
Scientific Overview
Physiologic Effects - Hyperthermia

- Oxygen Radical
  - Hyperthermia increases free radical formation
  - Radical steal electrons from the lipid membrane of a cell
  - The cell membrane breaks down
Free Radicals

The ground state of an atom requires an even number of electrons in the outer shell spinning in opposite directions.

Free radicals are atoms with unpaired electrons in the outermost shell

Free radicals (i.e. oxygen) must steal an electron from another atom.
Temperature and the Cell Membrane
Can lowering the temperature help?

- Decreased cellular demand for oxygen
  - Decrease in metabolic rate (brain & body)
- Stabilize the blood-brain barrier
  - Primarily endothelial cells which are packed tightly together and respond to temperature by expanding and contracting
- Stabilize the cell membrane
How does hypothermia reduce injury?

• Hypothermia
  – Lowers metabolic rate (5-7% per 1 degree Celsius)
  – Decrease in oxygen consumption
    • Especially in highly aerobic organs such as brain tissue
  – Decrease in carbon dioxide production
  – Decrease in Cerebral blood flow

Source: Bernd W. Böttiger, MD
Clinical Hypothermia

Mechanism of Action

• There are three distinct stages of cerebral injury after hypoxic insult
  – Early
  – Intermediate
  – Late

• Therapeutic hypothermia is considered to be neuroprotective by acting at each of the three stages of injury
Ischemia/Reperfusion Injury

Hypothermia Blocks

Reactive oxygen species (ROS)

Inflammatory cascades

Mitochondrial dysfunction

Ischemia/Reperfusion
Use of mild hypothermia to ameliorate cascade of ischemic insult

Temperature Regulation in the Body
Hypothalamus: Thermal Balance

• Complex feedback system:
  – *Sensory input* is transmitted to preoptic-anterior area of hypothalamus from central and peripheral thermoreceptors found in brain and spinal cord
  – *Hypothalamic integration* and comparison
  – *Output* via effector systems to activate compensatory warming and cooling mechanisms
Thermoregulation

- Thermoregulation consists of a complicated network of:
  - Temperature sensitive neurons
  - Temperature insensitive neurons
  - Effector neurons
    - Heat loss
    - Heat production
- Activation and inhibition of these neurons are the foundation of the model of set-point temperature
- Responsible for the ability of the body to regulate one’s own temperature and adapt to changes, thereby maintaining homeostasis (Boulant 2000).
Thermoregulation

• Core temp is tightly regulated within a narrow range at 36 - 37 degrees Celsius (C) (Sessler, 2009).

• Sensory receptors on the skin, peripheral tissues, and organs are constantly sensing differences in body temperature
  - Afferent input from these changes in local body temperature are centrally integrated within the pre-optic region of the hypothalamus
  - Alterations within this set-point temperature or thermoneutral zone or inter threshold range activates behavioral as well as physiological response to maintain homeostasis.
Thermoregulation: Set Point

• Maintaining Homeostasis
  – Behavioral responses
    • wearing heavy clothing in cold weather
    • turning on air conditioning during warm weather to keep oneself cool
    • abolished in comatose and sedated patients
  – Physiological response
    • Allows humans to live in different environments
    • Thermoregulatory defense mechanisms are upregulated to maintain homeostasis (Sessler, 2009)
Thermoregulation:
Set Point

- **Physiologic Response**
  - Pre-optic region of the hypothalamus contains temperature sensitive and temperature insensitive neurons, effector neurons
    - Activation of warm sensitive neurons results in an increase in their firing rate which signals to heat loss effector neurons to produce vasodilation of blood vessels and sweating.
    - Allows heat to escape through evaporation, which cools down the body.
    - Vasodilation of blood vessels increases blood flow which promotes heat loss via convection and conduction processes.
Thermoregulation: Set Point

- Maintaining Homeostasis: Physiologic Response
  - Pre-optic region of the hypothalamus contains temperature sensitive and temperature insensitive neurons, effector neurons
  - Decrease in the firing of warm sensitive neurons during cooling allows cold sensitive neurons to increase their firing rates which stimulate heat production effector neurons to produce heat retention mechanisms
    - Arteriovenous (AV) vasoconstriction
    - Shivering

(Boulant, 2000).
Thermoregulation: Set Point

- Temperature insensitive neurons mediates input from both the warm sensitive neurons and the cold sensitive neurons
  - Regulates temperature through synaptic stimulation or inhibition of these neurons
  - Pyrogen-induced fever from cytokine release crosses the blood brain barrier causing pertubations of set-point temperature (Boulant).
Thermoregulation: Set Point

• Maintaining Homeostasis
  
  – Vasoconstriction
    
    • Occurs to produce heat retention
    
    • Comes from AV shunts in the body located in the extremities
      
      – Primary function is to shunt blood away as the body’s temperature lowers a few tenths of a degree below the body’s set point of 37 degrees C
      
      – Creates a reduction in blood flow to the arms and legs
Thermoregulation: Set Point

• Maintaining Homeostasis
  – Vasoconstriction
  • Piloerection, or goosebumps, are seen first as the body attempts to shunt blood from the peripheral compartment in an attempt to stop heat loss and conserve heat (Landsberg L, Saville ME, and Young JB 1984).
  • Lowers the temperature in the extremities
Thermoregulation: Set Point

• Maintaining Homeostasis
  – NOTE: Heat created by deep organs located in the trunk and cranium is kept inside this area and is usually 2-4 degrees higher than the peripheral compartment (Sessler 2009).
  – Heat flows toward the lower temperature creating a thermoregulatory vasomotion phenomena allowing for the efficient transfer of heat from the core when needed (Sessler 2009).
Thermoregulation: Set Point

• Maintaining Homeostasis
  – Shivering – How?
    • If skin receives continuous sensation of cold, motor neurons are stimulated creating a shiver response in the muscles of the body
    • Motor response begins in the trunk and spreads to the extremities in an attempt to generate heat
    • Shivering mechanism occurs when the body temperature falls approximately one degree C below the vasoconstriction threshold

(Sessler 2009)
• an involuntary, rhythmic tremor of skeletal muscle groups which consists of oscillatory involuntary movement (Sessler 2009)
  
  – An emergency mechanism
  
  – Natural physiological response to an altered hypothalamic set-point

• As temperature descends to below the set-point of 36 degrees Celsius
  
  – efferent signals crossing the median forebrain bundle terminating in the hypothalamus communicates down to the reticulo spinal neurons in the lower brainstem which activates shivering
  
  – Lesions within this “efferent pathway” are associated with absence shivering (Hemingway; Gilbert and Benarroch, 2008).
Thermoregulation:

- **Downside**
  
  - \(^{\uparrow}\) BMR 5x normal (Eyolfson, Tikuisis, Xu et al 2001)
  
  - \(^{\uparrow}\) energy expenditure, oxygen consumption and carbon dioxide production (Badjatia, 2008)
  
  - May retard the cooling process as heat is transferred from core to the periphery (Sessler, 2009)
  
  - Creates cerebral metabolic stress (Polderman, 2009)
Thermoregulation:

**Downside**

- Post op: ↑ a patients post-operative pain by stressing and stretching the muscles near incisions (DeWitte and Sessler 2002)

- Post-op cardiac patients:
  - associated with a hyperdynamic response as manifested by tachycardia, elevated cardiac indices, low mixed venous oxygen consumption (Ralley, Wyands, Ramsay, Carli, Macsullivan, 1988)

- Elderly patients receiving spinal anesthesia
  - shivering response occurred at a much lower core temperature
  - places them at a greater risk for complications (Vassilief, Rosencher, Sessler, Conseiller, 1995).
Temperature Regulation
Scientific Overview
Systemic Effects of Lowering Temperature

Courtesy of Daiwai Olson
<table>
<thead>
<tr>
<th>Table</th>
<th>Induction</th>
<th>Maintenance</th>
<th>Rewarm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>2-4 hours</td>
<td>C: 16-24 hrs</td>
<td>C: 18 hrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N: 48-96 hrs</td>
<td>N: 3-4 days</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Shift into cell</td>
<td>Normalizes</td>
<td>Shifts Extracellular</td>
</tr>
<tr>
<td>UO</td>
<td>Up</td>
<td>Normalizes</td>
<td>Drops</td>
</tr>
<tr>
<td>Blood Sugar</td>
<td>Elevates</td>
<td>Insulin resistant</td>
<td>Drops</td>
</tr>
<tr>
<td>Shivering Issue</td>
<td>Yes</td>
<td>Monitoring</td>
<td>Yes</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Up</td>
<td>Stable</td>
<td>Drops</td>
</tr>
</tbody>
</table>
Systemic Complications

- **GI:**
  - Impaired motility
  - Ileus
- **Pulmonary:**
  - Increased risk of pneumonia
- **Metabolic:**
  - ↑ fat metabolism
  - √ lactic acidosis
- **Renal:**
  - Diuresis/fluid loss
  - Electrolyte changes
- **Shivering:**
  - ↑ muscle activity
- **Cardiovascular:**
  - Tachycardia (35-36)
  - Bradycardia (<35)
  - Vasoconstriction
  - Arrhythmias
- **Hematologic:**
  - ↓ platelets
  - Impaired leukocyte, neutrophil, macrophage function
Scientific Overview

Systemic Effects – Fluid & Electrolyte

• Sodium and Potassium are the key electrolytes.

• K+ shifts intracellular in the setting of hypothermia

• Sodium is exchanged extracellularly

• Where-ever go-eth the sodium, so go-eth the water

Courtesy of Daiwai Olson
Monitoring Labs

- Induction: every 1 hour
- Maintenance: every 4-6 hours
- Re-warming: every 2 hours

Cool

into cell

Warm

to plasma
Electrolyte Thresholds

- **Potassium < 3.2**
  - 40 meq over 2 hours (central line) or 4 hours (peripheral line)
- **Magnesium < 2.0**
  - 2 grams over 1 hour
- **Phosphorus < 2.0**
  - NaPhosphorus 12 mmol/L over 3 hrs
- **Ionized Calcium < 1.0 mmol/L**
  - 2 grams Calcium gluconate over 30 minutes
Induction Hypothermia
K and insulin
Scientific Overview
Systemic Effects - Cardiac

Arrhythmia

• Bradycardia
• Torsades de Pointes
• Prolonged Q-T interval
  • Measure q shift and document
    – QTc > 0.45 sec (call MD)
    – J Waves
Cardiac Effects of Hypothermia:
Bradycardia

- Be careful when using Neo and Precedex
  - Causes bradycardia
Induced hypothermia is contraindicated for patients with know coagulopathy.

Coagulopathy is more common with DEEP hypothermia.

“No increase risk of coagulopathy at 33 C” Dr. Tokutomi (2004)

“hypothermia is an independent predictor of bleeding in swine” Dr. Martini (2005)

The “Triangle of Death” (hypothermia, coagulopathy, and acidosis) may be covariates
Scientific Overview
Systemic Effects – Skin Integrity

Frostbite

Hypothermia reduces blood flow and tissue metabolism and may result in breakdown of the cell membrane.

Check your pts skin

Unfortunately, the solution to this is nursing research and largely neglected.

Courtesy of Daiwai Olson
Scientific Overview
Systemic Effects - Infection

• Hypothermia decreases macrophage migration
  – This may increase the risk of infection
  – This may worsen outcomes when an infection is present

• Accidental hypothermia is a predictor of sepsis
Risk: Increased ICP in Neuro Patients

- ICP increases with attempted rewarm
Management of Temperature

• HACA and Neuro Population
  – Protocols with specific temp management directives post HACA and for Neuro disorders
    • Maintenance of temperature 36-37°C
    • Automated interventions
      – Pre printed physician orders
      – Meds/cooling strategies
SHIVERING
Assessment of Shivering

• Assess every hour

• Use Bedside Shivering Assessment Scale (BSAS)
  • Palpate pectoralis muscle & neck/mandible region
  • Humming or vibration is an early indication of shivering

• Goal: BSAS ≤ 1

• ***Treat shivering as early as possible
  to prevent rigorous shivering!!
Bedside Shivering Assessment Scale (BSAS)

- Palpate masseter, pectoralis, deltoids and quadriceps muscles
- 0 = No shivering
  1 = Mild shivering localized to neck and/or chest
  2 = Shivering involving neck and/or chest & arms
  3 = Intermittent generalized shivering involving all 4 extremities
Temp Control: Assessing Shivering

- Objective: BIS EMG Tracing
  - Picks up microshivering
Shivering

To CT scan:
Machine unplugged

Patient Temperature
Patient Temperature Set Point
Water Temperature (Right Axis)
Shivering
Non-Pharmacological Management of Shivering

- Insulation of cutaneous thermoreceptors on hands, feet and head
  - Hot Packs to palms of hands and soles of feet
  - Socks
  - Head wrap (towel)
  - Bair Hugger
Step-Wise Management of Shivering

- **Step 1: Institute when cooling:**
  - Acetaminophen 650 mg Q4h PR or feeding tube
  - Buspirone 20 mg Q8h per feeding tube
  - Bair-Hugger at 43°C

- **Step 2: If shivering**
  - Non-sedating
    - Magnesium sulfate 0.5-1g/hr IV (goal 3-4 mg/dL)
  - Sedating: choose one of the following:
    - Meperidine 25 mg IV every 1 hour prn
    - Dexmedetomidine 0.2-1.5 mcg/kg/hour IV
    - Fentanyl 50-200 mcg/hour IV

- **Step 3: For refractory shivering**
  - Propofol 20-100 mcg/kg/min IV
  - Paralytics

Source: Columbia Mayer and Badjatia
# Normothermia Protocol

**Mission Hospital**

**ST JOSEPH HEALTH SYSTEM**

**HOSPITAL CLINICAL GUIDELINE**

**Collaborative Practice Council**

**Title:** Normothermia in Critical Neuro and Post-Hypothermia Patients, Maintenance of

## Objective:

<table>
<thead>
<tr>
<th></th>
<th>Maintain normothermia (36.5°C to 37.5°C) in patients during the acute phase of</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TBI – Admit to 7 days</td>
</tr>
<tr>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td>Ischemic stroke and intracerebral hemorrhage – Admit to 7 days</td>
</tr>
<tr>
<td>1.3</td>
<td>Aneurysmal SAH with vasospasm – Admit to 14 days</td>
</tr>
<tr>
<td>1.4</td>
<td>Post hypothermia after cardiac arrest for 3 days</td>
</tr>
</tbody>
</table>
Normothermia Order Set
Methods to Induce Hypothermia
Older Methods

- Ice baths and open windows in Philadelphia
- Cooling helmets
- Ice bags
- Iced lavage via OG/NG
- Cooling blankets
- Iced NS IV
- Frozen french fries...What?
Temperature Management Devices

• Many systems available
  – Choose the system that works best for your institution
  – Make sure the system has a feedback loop
Methods to Monitor Body Temperature
Variable Methods

Core Temperature
- Brain / Bolt
- Pulmonary Artery
- Temporal Artery
- Tympanic
- Esophageal

Peripheral Temperatures
- Rectal
- Oral
- Axillary
- Bladder
<table>
<thead>
<tr>
<th>Site</th>
<th>Variance from Core Temperature</th>
<th>Reliability</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>&lt; 0.8° F (0.5° C)</td>
<td>Affected by placement</td>
<td>Recent foods or fluids adversely affect the reading</td>
</tr>
</tbody>
</table>
| Rectal   | > up to 1° F (0.6° C)          | Reading may be delayed from core temperature change | -Fecal material  
-Improper placement in children can perforate the rectum |
| Axilla   | <2.2° F (1.2° C)               | Variable                         | Dwell time important for accurate reading                                    |
| Groin    | <2.2° F (1.2° C)               | Variable                         | Dwell time important for accurate reading                                    |
| Esophagus| Placement is key               |                                  | Needs to be in lower 1/3 of esophagus                                        |
| Bladder  |                                |                                  | Affected by urine volume or bladder irrigations                              |
| Tympanic | Technique is key               |                                  | Affected by cerumen or fluid behind tympanic membrane                         |

http://enw.org/Research-Thermometry.htm
Hypothermia In Neurologic Disorders
Hypothermia:
Who? When? What Temp?

• **Who are we going to cool?**
  – Refractory Increased ICP
  – Stroke
  – Vasospasm refractory to therapy

• **What temperature?**
  – 33 degrees C

• **When?**
  – Neurosurgeon decision
  – *Neuro CNS consult*
  – *Mandatory Intensivist consult*
Inclusion Criteria

- Refractory increased ICP
- Stroke: malignant cerebral edema
- Aneurysmal SAH refractory to traditional therapies

Exclusion Criteria

- Pregnancy
- Age <15 or > 75
- Existing DNR status
- Brain death
- End stage terminal illness
- Chronic renal failure
- Active bleeding/GI bleeding
- Shock
- Platelet count < 50,000
- Known coagulopathy (INR > 3.0)
- Patients on: Barbiturates/Vasopressin
Baseline Monitoring

- Endotracheal intubation and mechanical ventilator
- ECG monitoring, pulse oximeter, CO2 monitor
- Non-invasive/Arterial catheter for BP monitoring
- CVP and/or PA catheter to assess fluid volume status
  - Goal:
    - Refractory increased ICP and TBI:
      - Must volume resuscitate first!!
      - CVP 6-10 mm Hg/PCWP 8-12 mm Hg
- Bispectral index monitor (BIS)
- ICP/LICOX
- Foley catheter with a temperature probe (preferred) or esophageal temperature probe
Baseline Assessment

- Assess the patient’s clinical status, prior to initiating hypothermia protocol
- Obtain vital signs
  - Assess cardiac rhythm and document QTc (QT/square root of the previous R-R)
  - Assess pulmonary status
- Assess baseline level of consciousness and neurologic status
- Assess baseline laboratory values
- Obtain hemodynamic monitoring lines
  - Insert central lines
- Insert cooling device (central access) or apply pads
Initiating Hypothermia

- Apply cooling device
- Obtain physician order for initiation of sedation and analgesia for cooling.
  - Administer Analgesia
  - Start Propofol infusion at 10 mcg/kg/min and increase 10 mcg/kg/min every 10 minutes to achieve BIS 40-60.
  - When patient in cooled state, the dose needed to maintain sedation may be less due to decrease metabolism
Using Paralytics

• Prior to induction of hypothermia:
  – Administer paralytic agent IV push,
    • Vecuronium 0.1 mg/kg IV bolus, with a goal of a train of four (TOF) 1 of 4. The paralytic will reduce the incidence of shivering as hypothermia is induced.
    • Note: if renal impairment exists, Cisatracurium (Nimbex) should be considered.
  
• Discontinue paralytics once temperature is 33 degrees C unless piloerection occurs then restart
Instituting Cooling

• Induction of hypothermia
  – 30 cc/kg IV bolus iced saline (4 degrees C) over 30 minutes
  – Usually drops temperature 2 degrees C
  – Once complete, begin device cooling

• Helpful to counter the cold diuresis
BP Control in Hypothermia

- **Cooling:**
  - Diuresis: maintain euvolemia
  - Vasoconstriction and less pressors

- **Warming:**
  - Vasodilation
  - Need more fluids and pressors

- **Anticipate need for BP support.**

- **Monitor BP/MAP/CPP/ICP/PbtO2.**
  - Use fluids to maintain euvolemia. Target CVP 6-10 mm Hg or PCWP 8-12 mm Hg.
  - Use vasopressors or vasoactive medications to increase MAP once euvolemic.
Monitoring Hypothermia

- Document water temp and patient bladder temp q 1 hour
- Assess VS, Temp, ECG, SpO2, ET CO2 and presence of shivering q 15 minutes during induction of hypothermia, then q 30 minutes x 2 hours, then every hour.
  - If you notice the temperature increasing, the patient may have microshivering (look for piloerection/shaking)
- Assess Labs
  - Blood glucose every 1 hour
  - Initiate Insulin therapy to keep BG 110 -180 mg/dl
  - Measure BMP, CA, Mg, Phosphorus, Lactic acid q2h during induction, q6h maintenance, and q2h rewarm
  - Measure CBC/Coags every 12 hours
Goal Core Temperature
33 °C: ICP/Ischemia

Do not go below the target!!!
Goal Temperature

- Note time when patient achieved goal core temperature and document.
- Maintain goal temperature for 48-96 hours or a total of 96 hour since initiation of hypothermia.
- If patient demonstrates hemodynamic instability at 33 degrees Celsius, notify physician, stop cooling and initiate rewarming... but only at
  - 0.05 degrees per hour (Refractory Increased ICP)
  - 0.15 degrees per hour (stroke/cerebral vasospasm)
Rewarm: Return to normothermia

- Once patient’s core temperature reaches 36.0°C, titrate propofol off, and turn off neuromuscular blocker.
  - Watch for piloerection and drops in PbtO2
  - Try Demerol
  - May need to restart paralytic
- Assess for rebound hyperthermia
- Continue to utilize the Artic Sun Cooling Machine to maintain normothermia (37.0°C) for 7 days
Don’t forget...

- Obtain order for stress ulcer prophylaxis: pantoprazole (Protonix) 40mg IV daily
- Place knee high sequential compression device on legs or consider Lovenox for DVT prophylaxis
- Turning and aggressive pulmonary toilet
- No Subcutaneous injections
Management of Temperature in Vulnerable Populations

Case Studies

ICP refractory to

1° and 2° Interventions

Vascular Insult: I.S. vs Vasospasm

Cooling to 33 degrees Celsius
Management of Temperature in Vulnerable Populations
Case Studies

ICP refractory to 1\degree and 2\degree Interventions

Vascular Insult

Cooling to 33 degrees Celsius
Event: 5/14 8:45pm

- 39 year old female experiences onset of right arm/leg hemiplegia, aphasia, right facial droop while grocery shopping @8pm
  - History: 2 days of headaches
  - Marathon runner, rides horses
- Code Stroke Alert
- To CT scan 20 minutes after arrival