Therapeutic Hypothermia:
What’s Hot in Cooling

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Disclosures

William Knight
Therapeutic Hypothermia: What’s Hot in Cooling

FINANCIAL DISCLOSURE:
No relevant financial relationship exists
What is a long “down-time?”

- 10 minutes
- 20 minutes
- 30 minutes
- 40 minutes
Case Presentation

- 78 year old man collapses at the mall
- EMS activated
- No bystander CPR
- No AED
- EMS arrives 8 minutes after collapse
78 year-old man

- CPR initiated for 2 minutes
78 year-old man

- Intubated
- More CPR
- Epinephrine
- Atropine
- Rhythm check
78 year-old man

- ROSC after 20 minutes from collapse
- Transported to local ED
Past Medical History
- Hypertension
- Diabetes
- Coronary Artery Disease
  - 2 stents 6 years ago

Medications
- Atenolol
- ASA
- Lipitor
- Lisinopril
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>108/54</td>
</tr>
<tr>
<td>HR</td>
<td>92</td>
</tr>
<tr>
<td>RR</td>
<td>12 (vent)</td>
</tr>
<tr>
<td>SpO2</td>
<td>100% on 100% FiO2</td>
</tr>
<tr>
<td>GCS</td>
<td>7</td>
</tr>
<tr>
<td>E</td>
<td>2 – opens eyes to pain</td>
</tr>
<tr>
<td>V</td>
<td>1 – intubated</td>
</tr>
<tr>
<td>M</td>
<td>4 – withdraws from pain</td>
</tr>
</tbody>
</table>
Head CT
Because you don’t want to miss...
I’m not dead yet!
The Problem

- High field mortality rate
- High in-hospital mortality rate
- Survivors have high neurologic morbidity
Objectives

- History
- Pathophysiology
- Practical application
- Initial Management
- Complications
- EMS Implications
Epidemiology

- Incidence of sudden cardiac arrest
  - 62 per 100,000 people (industrial countries)
  - 350,000 cases per year (US and Europe)

- Despite nearly 40+ years of ALS
  – survival rates are still very poor
  - <½ of those with ROSC survive to hospital discharge

- Physician surveys show disappointing rates of hypothermia use
  - 91% from US
  - 74% had never used hypothermia for cardiac arrest
    - Insufficient data available
    - Technically difficult
    - Not included in ACLS guidelines
To treat cardiac arrest, doctors cool the body

By Robert Davis
USA TODAY

When his heart stopped in the middle of his workday, Dean Cowles fell clinically dead in one of the best places in the world to suffer sudden cardiac arrest.
Doctors are reinventing how they treat sudden cardiac arrest, which is fatal 95 percent of the time. A report from the border between life and death.

Media
Hypothermia therapy saves Loveland man

By Brian O'Donnell - Loveland@CommunityPress.com - November 16, 2009

When Thomas Hufford was diagnosed with prostate cancer last year, he had three treatment options, all of which would give him 10 to 15 years to live.

- More Loveland news

Hufford, a 76-year-old Loveland resident, chose to have radioactive seeds surgically implanted into his prostate to kill the cancer.

Immediately after the surgery, his life expectancy changed drastically when he suffered a massive heart attack.

Dr. Andrew Gorusch, a University Hospital physician, and his team
Focus on Technology

Controlled hypothermia is helping restore life. Details during Focus on Technology with Ann Thompson.

By Ann Thompson

Listen to the MP3 (4:36)

Focus on Technology Podcasts

Debra Siegel, the patient, in her Hyde Park home
WHAT'S WORKING: Quick thinking and new cooling technique save man's life

Posted: Jul 19, 2011 5:55 PM
Updated: Jul 19, 2011 11:12 PM

By Kimberly Holmes Wiggins - bio | email

CINCINNATI, OH (FOX19) - In a medical emergency, we all know that seconds count. East End native can certainly testify to that fact. He had a heart attack at the Cincinnati Zoo, but lived to tell the tale.

May 16th, 2011 is a day that 55-year-old Tony Huffman will never forget, even though he can’t remember it. He was at the Cincinnati Zoo, chaperoning a field trip for his nephew and the rest of his third grade class.
**History of Hypothermia**

- First clinical reports on use of hypothermia published in the 1940s and 1950s
- Many studies on physiologic effects in humans performed in the 1950s
- Case series and experimental studies published in the 1950s and 1960s
  - No randomized controlled trials
  - Moderate or deep hypothermia
History of Hypothermia

- Described by ancient Egyptians, Greeks and Romans

Hippocrates  Celcus en Galaenus
History of Hypothermia

- 1814 - Napoleonic Wars
  - Baron Larrey - Napoleon’s surgeon-general
  - Wounded soldiers put close to a campfire died earlier than those who were not re-warmed
History of Hypothermia

- First clinical reports published in the 1940s and 1950s


EARLY EXPERIENCES WITH LOCAL AND GENERALIZED REFRIGERATION OF THE HUMAN BRAIN

TEMPLE FAY, M.D.†

Philadelphia, Pennsylvania

Fig. 5. Early method of total refrigeration with recording thermocouple (89.5°F, rectal). Patient was under Amytal Sodium, chloral hydrate and paraldehyde anesthesia. This patient (a physician) insisted upon keeping socks on.
EARLY EXPERIENCES WITH LOCAL AND GENERALIZED REFRIGERATION OF THE HUMAN BRAIN

TEMPLE FAY, M.D.†
Philadelphia, Pennsylvania

Fig. 8. With this mobile refrigeration apparatus, G.M. (April 9, 1846) was able to enjoy a fair degree of activity in the ward during the weeks of local refrigeration of the brain through an implanted capsule (Fig. 3) in the cavity of an evacuated glioma.
Nazi experiments simulated conditions soldiers (especially downed pilots) suffered during war. The purpose of these experiments was:

- To determine the cause of death from hypothermia
  - Cardiac or metabolic
- To ascertain at what temperature death occurs
- To determine the best resuscitation methods
- To determine what type of protective clothing was most effective

"SS [Schutzstaffel (protection echelon)] Sturmbannführer Dr. Sigmund Rascher (right) and Dr. Ernst Holloehner (left) observe the reactions of a Dachau prisoner who has been immersed in a tank of ice water in an attempt to simulate the extreme hypothermia suffered by pilots downed over trigid seas. The freezing experiments were designed to establish methods of treatment for persons in a state of shock as a result of prolonged exposure to the cold. The medical experiments performed on Dachau prisoners involved the placing of the victim in a tank of ice water until he lost consciousness (70-90 minutes), followed by abrupt attempts to restore his normal body temperature by various means.... This photo is taken from a film found in the Munich home of Dr. Sigmund Rascher."
World War II

Methods:
- Immersion in ice-cold water
- Exposure to outside environment
- No interest in therapeutic hypothermia
- Research purely aimed at accidental hypothermia
  - Recovery from hypothermia
THE USE OF HYPOTHERMIA AFTER CARDIAC ARREST

DONALD W. BENSON, M.D.
G. RAINNEY WILLIAMS, JR., M.D.
FRANK C. SPENCER, M.D.
ADOLPH J. YATES, M.D.

Baltimore, Maryland*
## Data from Twenty-Seven Cases of Cardiac Arrest

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age</th>
<th>Sex</th>
<th>Site of arrest and date</th>
<th>Operation or episode at arrest</th>
<th>Neurological status after arrest</th>
<th>Interval from arrest to hypothermia</th>
<th>Average temperature during hypothermia, Centigrade</th>
<th>Duration of hypothermia, hr.</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1½</td>
<td>F</td>
<td>Operating room 4/7/58</td>
<td>General anesthesia; debridement of burn</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 4 days</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>F</td>
<td>Operating room 6/23/56</td>
<td>General anesthesia; appendectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ineffictual massage</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>M</td>
<td>Operating room 12/25/57</td>
<td>General anesthesia; stab wound of the chest</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ineffictual massage</td>
</tr>
<tr>
<td>4</td>
<td>41</td>
<td>M</td>
<td>Recovery room 9/11/57</td>
<td>Postpneumonectomy, 23 hr.</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 4 hr.</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>M</td>
<td>Recovery room 12/22/57</td>
<td>Postpyelolithotomy, 15 hr.</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 2 hr.</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>M</td>
<td>Recovery room 6/13/57</td>
<td>Ruptured aortic aneurysm</td>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td>Died 35 days; never responded</td>
</tr>
<tr>
<td>7</td>
<td>70</td>
<td>M</td>
<td>Recovery room 10/31/56</td>
<td>After suturing, bleeding ulcer, 2 hr.</td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>Died 7 days; progressive deterioration</td>
</tr>
<tr>
<td>8</td>
<td>74</td>
<td>M</td>
<td>Anesthesia room 11/4/56</td>
<td>Acute cholecystitis, peritonitis</td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>Died 13 days; pneumonia and brain damage</td>
</tr>
<tr>
<td>9</td>
<td>13</td>
<td>M</td>
<td>Recovery room 5/16/58</td>
<td>Exploratory laparotomy</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>M</td>
<td>Operating room 12/16/56</td>
<td>General anesthesia; evacuation of traumatic hemothorax</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>11</td>
<td>35</td>
<td>M</td>
<td>Anesthesia room 9/15/58</td>
<td>Anesthesia induction</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>M</td>
<td>Operating room 5/22/56</td>
<td>General anesthesia; attempted pneumonectomy</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>13</td>
<td>58</td>
<td>M</td>
<td>Anesthesia room 4/1/57</td>
<td>Anesthesia induction; ruptured aortic aneurysm</td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>14</td>
<td>64</td>
<td>F</td>
<td>Recovery room 6/24/57</td>
<td>Postcholecystectomy, 4 hr.</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>15</td>
<td>84</td>
<td>E</td>
<td>Operating room 11/21/57</td>
<td>General anesthesia</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>Case No.</td>
<td>Age</td>
<td>Sex</td>
<td>Site of arrest and date</td>
<td>Operation or episode at arrest</td>
<td>Neurological status after arrest</td>
<td>Interval from arrest to hypothermia</td>
<td>Average temperature during hypothermia, Centigrade</td>
<td>Duration of hypothermia, hr.</td>
<td>Outcome</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
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<td>-------------------------</td>
<td>--------------------------------</td>
<td>---------------------------------</td>
<td>-----------------------------------</td>
<td>---------------------------------------------</td>
<td>----------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>F</td>
<td>Bronchoscopy 11/28/57</td>
<td>Bronchoscopy; local anesthesia</td>
<td>Severe</td>
<td>1 hr.</td>
<td>30°</td>
<td>3</td>
<td>Died 4 hr.</td>
</tr>
<tr>
<td>17</td>
<td>45</td>
<td>F</td>
<td>Operating room 6/10/58</td>
<td>General anesthesia; breast biopsy</td>
<td>Severe</td>
<td>1 hr.</td>
<td>32°</td>
<td>24</td>
<td>Died 24 hr.</td>
</tr>
<tr>
<td>18</td>
<td>53</td>
<td>M</td>
<td>Operating room 2/7/58</td>
<td>General anesthesia; thoracotomy</td>
<td>Severe</td>
<td>1 hr.</td>
<td>31°</td>
<td>48</td>
<td>Died 3 days</td>
</tr>
<tr>
<td>19</td>
<td>55</td>
<td>M</td>
<td>Operating room 6/16/58</td>
<td>General anesthesia; hernia repair</td>
<td>Severe</td>
<td>3 hr.</td>
<td>30°</td>
<td>8 days</td>
<td>Died 9 days; did not respond</td>
</tr>
<tr>
<td>20</td>
<td>57</td>
<td>M</td>
<td>Operating room 9/24/58</td>
<td>General anesthesia; suprapubic prostatectomy</td>
<td>Severe</td>
<td>1 hr.</td>
<td>30°</td>
<td>77</td>
<td>Died 3 days</td>
</tr>
<tr>
<td>21</td>
<td>58</td>
<td>M</td>
<td>Operating room 8/18/58</td>
<td>General anesthesia; pneumonectomy</td>
<td>Severe</td>
<td>6 hr.</td>
<td>31°</td>
<td>84</td>
<td>Died 5 days</td>
</tr>
<tr>
<td>22</td>
<td>3</td>
<td>M</td>
<td>X-ray department 1/22/57</td>
<td>General anesthesia; bronchogram</td>
<td>Severe</td>
<td>2 hr. 40 min.</td>
<td>31°</td>
<td>36</td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>23</td>
<td>6</td>
<td>F</td>
<td>Bronchoscopy 8/12/58</td>
<td>General anesthesia; bronchoscopy</td>
<td>Severe</td>
<td>1 hr.</td>
<td>32°</td>
<td>48</td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>24</td>
<td>9</td>
<td>F</td>
<td>Accident room 8/20/57</td>
<td>Asthmatic attack</td>
<td>Severe</td>
<td>1 hr. 30 min.</td>
<td>30°</td>
<td>34</td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>25</td>
<td>10</td>
<td>M</td>
<td>Operating room 4/5/58</td>
<td>General anesthesia; rectal pull-through</td>
<td>Severe</td>
<td>1 hr. 30 min.</td>
<td>32°</td>
<td>72</td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>26</td>
<td>38</td>
<td>M</td>
<td>Accident room 9/28/57</td>
<td>Pericardial tamponade</td>
<td>Severe</td>
<td>1 hr. 50 min.</td>
<td>32°</td>
<td>36</td>
<td>Lived; no residual</td>
</tr>
<tr>
<td>27</td>
<td>39</td>
<td>F</td>
<td>Accident room 11/16/57</td>
<td>Stab wound of chest</td>
<td>Severe</td>
<td>3 hr.</td>
<td>31°</td>
<td>48</td>
<td>Lived; no residual</td>
</tr>
</tbody>
</table>
THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*
HACA 2002

![Graph showing survival rates for Hypothermia and Normothermia over days.](image)

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Hypothermia</th>
<th>Normothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>137</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td>92</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>83</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>9</td>
</tr>
</tbody>
</table>
TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA


**Table 1. Clinical Characteristics of the 77 Patients with Anoxic Brain Injury Who Were Eligible for Randomization.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hypothermia (N=43)</th>
<th>Normothermia (N=34)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>66.8</td>
<td>65.0</td>
<td>0.55</td>
</tr>
<tr>
<td>Range</td>
<td>49–89</td>
<td>41–85</td>
<td></td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>58</td>
<td>79</td>
<td>0.05</td>
</tr>
<tr>
<td>Arrest witnessed (%)</td>
<td>95</td>
<td>94</td>
<td>0.81</td>
</tr>
<tr>
<td>Bystander performed cardiopulmonary resuscitation (%)</td>
<td>49</td>
<td>71</td>
<td>0.06</td>
</tr>
<tr>
<td>Time from collapse to emergency-medical-services call (min)</td>
<td>2.1±1.9</td>
<td>2.7±3.0</td>
<td>0.32</td>
</tr>
<tr>
<td>Time from call to emergency-medical-services arrival (min)</td>
<td>7.9±3.1</td>
<td>8.3±2.8</td>
<td>0.60</td>
</tr>
<tr>
<td>Time from arrival to first DC shock (min)</td>
<td>2.5±2.2</td>
<td>2.0±1.2</td>
<td>0.22</td>
</tr>
<tr>
<td>Time from first shock to return of spontaneous circulation (min)</td>
<td>13.6±11.2</td>
<td>12.1±7.9</td>
<td>0.48</td>
</tr>
<tr>
<td>Time from collapse to return of spontaneous circulation (min)</td>
<td>26.5±12.9</td>
<td>25.0±8.9</td>
<td>0.54</td>
</tr>
<tr>
<td>Number of DC shocks</td>
<td>4.2±3.0</td>
<td>4.1±3.2</td>
<td>0.87</td>
</tr>
<tr>
<td>Dose of epinephrine (mg)</td>
<td>2.2±2.1</td>
<td>2.2±1.9</td>
<td>0.97</td>
</tr>
</tbody>
</table>
TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA


TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

<table>
<thead>
<tr>
<th>OUTCOME*</th>
<th>HYPOTHERMIA (N=43)</th>
<th>NORMOTHERMIA (N=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or minimal disability (able to care for self, discharged directly to home)</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Moderate disability (discharged to a rehabilitation facility)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Severe disability, awake but completely dependent (discharged to a long-term nursing facility)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Severe disability, unconscious (discharged to a long-term nursing facility)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>22</td>
<td>23</td>
</tr>
</tbody>
</table>

*The difference between the rates of a good outcome (normal or with minimal or moderate disability) in the hypothermia and the normothermia groups (49 percent and 26 percent, respectively) was 23 percentage points (95 percent confidence interval, 13 to 43 percentage points; P = 0.046). The unadjusted odds ratio for a good outcome in the hypothermia group as compared with the normothermia group was 2.68 (95 percent confidence interval, 1.02 to 6.88; P = 0.046). The odds ratio for a good outcome in the hypothermia group as compared with the normothermia group, after adjustment by logistic regression for age and time from collapse to return of spontaneous circulation, was 5.28 (95 percent confidence interval, 1.47 to 18.76; P = 0.011).
Hypothermia for neuroprotection after cardiac arrest: Systematic review and individual patient data meta-analysis

Michael Holzer, MD; Stephen A. Bernard, MD; Said Hachimi-Idrissi, MD; Risto O. Roine, MD, PhD; Fritz Sterz, MD; Marcus Müllner, MD, MSc on behalf of the Collaborative Group on Induced Hypothermia for Neuroprotection After Cardiac Arrest

Table 2. Long and short-term neurologic recovery

<table>
<thead>
<tr>
<th>Trial</th>
<th>Hypothermia No. (%)</th>
<th>Normothermia No. (%)</th>
<th>Risk Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive at hospital discharge with favorable neurologic recovery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HACA (41)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>72/136 (53)</td>
<td>50/137 (36)</td>
<td>1.51 (1.14–1.89)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.006&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bernard (42)</td>
<td>21/43 (49)</td>
<td>9/34 (26)</td>
<td>1.75 (0.99–2.43)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.052&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hachimi-Idrissi (49)</td>
<td>3/16 (19)</td>
<td>0/17 (0)</td>
<td>7.41 (0.83–62)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>.15&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Summary estimate</td>
<td></td>
<td></td>
<td>1.68 (1.29–2.07)</td>
<td></td>
</tr>
<tr>
<td>Alive at 6 months with favorable neurologic recovery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HACA (41)</td>
<td>71/136 (52)</td>
<td>50/137 (36)</td>
<td>1.44 (1.11–1.76)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.009&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Hypothermia for neuroprotection after cardiac arrest: Systematic review and individual patient data meta-analysis

Michael Holzer, MD; Stephen A. Bernard, MD; Said Hachimi-Idrissi, MD; Risto O. Roine, MD, PhD; Fritz Sterz, MD; Marcus Müllner, MD, MSc on behalf of the Collaborative Group on Induced Hypothermia for Neuroprotection After Cardiac Arrest

Number Needed to Treat

6
How does it work?
3 phase model of resuscitation

- Electrical and Circulatory → reduce the duration of global ischemia (primary brain injury)

- Metabolic → attenuate post-resuscitation disease due to reperfusion injury (secondary brain injury)
Global Ischemia and Reperfusion

PHASE I

VF \rightarrow Ischemia \rightarrow ROSC

Phase I Therapies:
- Defibrillation
- CPR
- Ventilation
- Drug Therapy
- Augmented Perfusion
Simplified scheme of the mechanisms of ischemia
Effects of Mild Hypothermia
Complications of Hypothermia

- Most significant complications are related to degree of hypothermia
  - Hypothermia abandoned for 40+ years!

- Strict adherence to MILD (32-34°C) hypothermia
  - Do not overcool

- Complications most prominent with deep hypothermia
  - (>30°C)
# HACA Study

## Table 4. Complications during the first seven days after cardiac arrest.*

<table>
<thead>
<tr>
<th>Complication</th>
<th>Normothermia</th>
<th>Hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no./total no. (%)</td>
<td>no./total no. (%)</td>
</tr>
<tr>
<td>Bleeding of any severity†</td>
<td>26/138 (19)</td>
<td>35/135 (26)</td>
</tr>
<tr>
<td>Need for platelet transfusion</td>
<td>0/138</td>
<td>2/135 (1)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>40/137 (29)</td>
<td>50/135 (37)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>9/138 (7)</td>
<td>17/135 (13)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2/138 (1)</td>
<td>1/135 (1)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>14/138 (10)</td>
<td>13/135 (10)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>6/138 (4)</td>
<td>6/135 (4)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>5/133 (4)</td>
<td>9/136 (7)</td>
</tr>
<tr>
<td>Seizures</td>
<td>11/133 (8)</td>
<td>10/136 (7)</td>
</tr>
<tr>
<td>Lethal or long-lasting arrhythmia</td>
<td>44/138 (32)</td>
<td>49/135 (36)</td>
</tr>
<tr>
<td>Pressure sores</td>
<td>0/133</td>
<td>0/136</td>
</tr>
</tbody>
</table>
Hypotension not a cause to cease therapy
- Vasopressors
- Dobutamine
- Fluids
Inclusion criteria:

- Primary cardiac arrest with return of spontaneous circulation (ROSC) in or out of the hospital
  - Initial rhythm is not an inclusion or exclusion criteria. Victims of ventricular fibrillation, ventricular tachycardia, PEA, and asystole are included in this protocol.
- Age ≥ 16
- Unresponsive after ROSC
  - Patient does not follow commands
- Requires mechanical ventilation
- Mean arterial pressure can be maintained ≥ 70 mmHg with stability (including with pressors and fluids)
Exclusion criteria:

- Pulseless greater than 60 minutes
- Patient is greater than 12 hours from return of spontaneous circulation
- Pregnancy. All women of age ≤ 55 need a negative urine or serum β-HCG
  - May consider maternal-fetal medicine consult prior to inclusion
- Another reason to be comatose:
  - Comatose at baseline
  - Drug overdose
  - Head trauma
  - Stroke, ICH, SAH
  - Status epilepticus
- Post cardiovascular surgery this admission
- Hypothermia (temperature <30 ºC) before cooling efforts begin

- Known coagulopathy or bleeding problem
  - Active bleeding
  - INR > 1.7
  - PTT > 1.5x normal
  - Platelets < 50,000

- IVC filter
  - excluded from long cooling catheter (Icy) must use shorter cooling catheter (Cool-Line) via IJ or subclavian approach

- Surgical incision greater than 5cm within the previous 72 hours
- Existing DNR or DNI orders.
Institute concurrently with reperfusion

Do not delay one therapy for the other
Practical Applications

Solutions Outflow
Back to
CoolGuard
System

15 Ga Infusion Lumen

Temperature
Controlled Saline
Infusion

Serpentine Cooling Coils

CSZ
Cincinnati Sub-Zero

UC Neuro

ICL
CRYSTAL
ICE

Machine

Human Figure

Machine

Machine
New Technology

Actual patient temperature
System cooling/warming intensity level
User-determined patient target temperature
User-determined rate of temperature change
Optimal cooling devices

Institutional sandbox

Busy ED

Consultant buy-in

Reimbursement - no specific billing code to justify cooling devices
Prognosis

- No reliable markers of prognosis available

- Certainly not in the first 24 hours!
### TABLE 1: Frequency of Occurrence of Clinical and Electrophysiological Characteristics of Survivors and Nonsurvivors of CA at Hospital Discharge

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>( p )</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No. (%)</td>
<td>45 (41)</td>
<td>66 (59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean yr ± SD (range)</td>
<td>60.2 ± 14.9 (17–85)</td>
<td>58.8 ± 14.7 (22–84)</td>
<td>0.630</td>
<td>( t )</td>
</tr>
<tr>
<td>Female gender, No. (%)</td>
<td>7/45 (16)</td>
<td>15/66 (22)</td>
<td>0.468</td>
<td>Fisher</td>
</tr>
<tr>
<td>Noncardiac etiology, No. (%)</td>
<td>3/45 (7)</td>
<td>13/66 (20)</td>
<td>0.166</td>
<td>Fisher</td>
</tr>
<tr>
<td>Non-VF CA (asystolic or PEA), No. (%)</td>
<td>7/45 (16)</td>
<td>38/66 (58)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>ROSC &gt;25 minutes, No. (%)</td>
<td>11/45 (24)</td>
<td>43/66 (65)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>≥1 brainstem reflexes absent, No. (%)</td>
<td>2/45 (4)</td>
<td>45/66 (68)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Motor response worse than flexion, No. (%)</td>
<td>11/45 (24)</td>
<td>58/66 (88)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Early anoxia, No. (%)</td>
<td>2/45 (4)</td>
<td>35/66 (53)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Epileptiform activity on the first EEG, No. (%)</td>
<td>4/45 (9)</td>
<td>35/66 (54)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Unreactive EEG background, No. (%)</td>
<td>3/45 (8)</td>
<td>53/65 (81)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Bilaterally absent N20 on the SSEP, No. (%)</td>
<td>0/44 (0)</td>
<td>33/56 (59)</td>
<td>&lt;0.001</td>
<td>Fisher</td>
</tr>
<tr>
<td>Time to first EEG, median days, range (No. of subjects)</td>
<td>2, 1–4 (45)</td>
<td>2, 1–5 (65)</td>
<td>0.319</td>
<td>( U )</td>
</tr>
<tr>
<td>Time to SSEP, median days, range (No. of subjects)</td>
<td>2.5, 1–5 (44)</td>
<td>2, 1–8 (56)</td>
<td>0.341</td>
<td>( U )</td>
</tr>
</tbody>
</table>

*Papillary, ocipitofrontal, conical. CA = cardiac arrest; SD = standard deviation; VF = ventricular fibrillation; PEA = pulseless electrical activity; ROSC = return of spontaneous circulation; EEG = electroencephalography; SSEP = somatosensory evoked potentials.*
BACKGROUND: For more than 25 years, the prognosis for recovery post cardiac arrest and the decision making for withdrawal of care has been based on the neurological exam at 72 hours. Whether this paradigm also applies to patients receiving hypothermia therapy (HT) post-arrest has not been thoroughly investigated.

PURPOSE: To determine the time course of neurological recovery following HT post Out-of-Hospital Cardiac Arrest (OHCA).

Primary Endpoints: Time to awakening post OHCA, cerebral performance category (CPC), survival to discharge (SDC)

Secondary Endpoints: peri arrest and post CA care

Results: A total of 47 OHCA pts, 15 received HT, with 7 (46.6%) SDC. Of the 32 pts who received conventional care (no hypothermia), 13 (40.6%) SDC. Among survivors, those receiving hypothermia as compared to conventional care, were more likely to have a witnessed arrest, 86% vs 69%; bystander CPR, 43% vs 8%; and ventricular fibrillation as their initial rhythm, 57% vs 46%. In those treated with conventional care, 38.5% were alert shortly following resuscitation, and 80% of these patients had a CPC score of 1 or 2 on day 3. The figure presented here depicts the time course of change in CPC score in patients receiving HT with

Primary Outcome: Of the 15 OHCA pts with HT, 7 (46.6%) SDC with 83% discharged with a CPC of 1 or 2

Conclusion: Contrary to the established paradigm, patients with hypothermia achieve substantial neurological awakening that may start at day 3 but is not apparent until day 7 and possibly longer.

Implications: The timing of decision making for care withdrawal in such critical patients should be validated in larger cohorts.

© 2010, American Heart Association. All rights reserved.
Awakening After Cardiac Arrest and Post-Resuscitation Hypothermia: Are We Pulling the Plug too Early?

BACKGROUND: For more than 25 years, the prognosis for recovery post cardiac arrest and the decision making for withdrawal of care has been based on the neurological exam at 72 hours. Time to awakening after out-of-hospital cardiac arrest (OHCA) and post-resuscitation therapeutic hypothermia (TH) varies widely. The amount of time clinicians should wait before withdrawing supportive care for comatose pts after TH is unknown.

PURPOSE: To determine the time interval from when OHCA TH pts had been fully re-warmed to 37°C to when they showed definitive signs of awakening.

Primary Endpoint: Time to awakening for OHCA TH pts.
Secondary Endpoints: 1) Time from 911 to ALS care; 2) Time pt treated with TH; 3) time re-warming to awakening measured with use of Cerebral Performance Category (CPC) score.

RESULTS: A total of 66 pts (mean age 59.5 ± 5.6 years, 62% male) were included. The time from 911 to start of advanced life support care was 9.1 ± 8.0 minutes. Time to awakening is shown in the figure. All six pts with delayed awakening (> 72 hours) had good neurological function based upon a CPC score of ≤ 2 within 30 days of OHCA. Five of 6 of these pts were intubated, comatose, and apneic 72 hours after re-warming.

Primary Outcome: Of the 66 OHCA TH pts; 6 awakened 72 hrs beyond OHCA.

CONCLUSION: Withdrawal of life support 72 hrs after arrest including re-warming may prematurely terminate life in at least 10% of potentially neurologically intact TH survivors.

IMPLICATIONS: The time clinicians should wait before withdrawing supportive care for comatose pts after TH may need to be extended beyond 72 hrs.

Keith Lurie, MD, American Heart Association ReSS

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Cath lab activated...

- 2 liters normal saline IV (4°C) infused
- Icepacks to neck, axillae, trunk and groin

- BP drops to 80/40
- HR 90s
- Levophed gtt initiated 5μg/min

- Transported to Cath Lab
100% RCA occlusion
- Successfully stented
- TIMI 3 flow
Cardiovascular ICU

- Zoll Alsius Thermoguard Catheter placed
  - Neurocritical Care consult
Core Body Temperature (°C)

Time (2 hour increments)

 Cooling: ~4 hours

 Maintenance: 24 hours

 Warming: ~5 hours

Vital signs recorded every hour
IV sedation throughout
IV paralytics until temperature ≥36 °C
Labs drawn at asterisks
ICU Course

- Maintained intubated, sedated and paralyzed for 24 hours
- Required levophed for 30 hours
- No seizures were noted
- Rewarmed at 0.3°C/hr
ICU Course

- Followed commands on HD 2
- Extubated on HD 3
- Discharged to home on HD 6
Take Home

- Cooling should be concurrent with all other therapies
  - Ice packs
  - Cooling blanket
  - 2 L ice cold saline/LR/whatever...

- Prognosis very difficult in first 72 hours
  - May need to be extended

- Early initiation can lead to continuation of therapy

- Appropriate treating centers
Questions?
References

- Jones, AE. Hypothermia after Cardiac Arrest: We Can Do This. Acad Emer Med. 2008; 15(6): 558-559


References

- Selected slides from
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- Kees Polderman, MD

- Mauro Oddo, MD