Therapeutic Temperature Management
Caring for the Patient & Managing Complications

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Objectives

By the end of the session the participant will be able to:

• Discuss the evidence to date related to therapeutic temperature management for the post-cardiac arrest patient.

• Identify the pros and cons of both TTM to 36 degrees vs 33 degrees.

• Review the different methodologies/devices used for TTM

• Describe potential complications of TTM and appropriate anticipatory interventions and troubleshooting to implement as they occur.
Temperature Assessment
Methods to Monitor Body Temperature

Peripheral Temperatures
- Rectal
- Oral
- Axillary
- Bladder

Core Temperature
- Brain / Bolt
- Pulmonary Artery
- Temporal Artery
- Tympanic
- Esophageal
<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>
<tr>
<td>Rectal</td>
<td>&gt; Up to 1° F (0.6° C)</td>
<td>Reading may be delayed from core temperature change</td>
<td>Fecal material Improper placement in children can perforate the rectum</td>
</tr>
<tr>
<td>Axilla</td>
<td>&lt;2.2° F (1.2° C)</td>
<td>Variable</td>
<td>Dwell time important for accurate reading</td>
</tr>
<tr>
<td>Groin</td>
<td>&lt;2.2° F (1.2° C)</td>
<td>Variable</td>
<td>Dwell time important for accurate reading</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td>Placement is key</td>
<td>Needs to be in lower 1/3 of esophagus</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td></td>
<td>Affected by urine volume or bladder irrigations</td>
</tr>
<tr>
<td>Tympanic</td>
<td></td>
<td>Technique is key</td>
<td>Affected by cerumen or fluid behind tympanic membrane</td>
</tr>
</tbody>
</table>

http://enw.org/Research-Thermometry.htm
How Should Temperature be Measured

Clinicians should continuously monitor the patient’s core temperature

- Esophageal thermometer
- Bladder catheter in non-anuric patients
- Pulmonary artery catheter – if placed
- Axillary and oral temperatures
  - inadequate for measurement of core temperature changes, especially during active manipulation of temperature for therapeutic hypothermia
  - true tympanic temperature probes are rarely available and often unreliable

*Peberdy 2010 Circulation*
Methods During Hypothermia

Bladder

• Studies have shown a strong correlation between bladder and other core temperatures, because the urine is a filtrate of the blood and the kidney’s receive 20% of cardiac output.

• Minimally invasive, as it requires a urinary catheter with a thermistor tip to be inserted into the bladder

• It is explained that bladder temperatures track core temperature changes better than rectal, but the readings may be altered due to urinary volume or if the patient is receiving bladder irrigations

• Lags behind other temperature measurements

Monitoring Methods During Hypothermia

Esophageal

- Due to the length of the esophagus, the placement of the sensor is critical. If it is too high in the esophagus the reading will be affected by tracheal air.
- Proper placement is in the lower third of the esophagus which will allow the sensor to be closer to the heart and aorta, and that it will accurately reflect the core temperature. It also indicates changes in core temperature significantly faster than peripheral sites.

Pathophysiology of Post-Cardiac Arrest Syndrome

- Brain injury
- Myocardial dysfunction
- Systemic ischemia-Reperfusion Response
- Persistent Precipitating Pathology

Circulation 2008; ILCOR Consensus Statement: Post Cardiac Arrest Syndrome
Brain Injury

Pathophysiology

• Disrupted calcium homeostasis
• Free radical formation
• Cell death signaling pathways
• Reperfusion injury
• No reflow
• Additional insults:
  • Pyrexia
  • Hyperglycemia
  • Hyperoxygenation

Potential Treatments

• Therapeutic hypothermia
• Early hemodynamic optimization
• Airway protection and mechanical ventilation
• Seizure control

Bernard, Duffy Kaye, 2011
Myocardial Dysfunction

Pathophysiology

• Stunning phenomenon: global hypokinesis (myocardial stunning)
• Elevated LVEDP
• Preserved coronary blood flow (exclude patients with Acute Coronary Syndrome)

Potential Treatments

• Early revascularization of Acute MI
• Early hemodynamic optimization
• Intravascular fluids
• Inotropes
• IABP
• LVAD
• ECMO

Bernard, Duffy Kaye, 2011
Systemic Ischemia-Reperfusion Response

Pathophysiology

- Impaired tissue oxygen delivery and utilization
- Reperfusion injury
- Endothelial activation
- Systemic Inflammatory Response (SIRs)
- Impaired vasoregulation
- Activation of clotting cascades
- Intravascular volume depletion
- Adrenal suppression
- Impaired resistance to infection

Potential Treatments

- Early goal-directed therapy/hemodynamic optimization
- Intravenous fluid
- Vasopressors
- High-volume hemofiltration
- Temperature control
- Glucose control
- Antimicrobials

Bernard, Duffy Kaye, 2011
Persistent Precipitating Pathology

Pathophysiology

- CV disease:
  - AMI/ACS
  - Cardiomyopathy
  - Chronic ischemic myocardial scars
- Pulmonary disease (COPD, asthma)
- CNS disease (CVA)
- Thromboembolic (PE)
- Toxicological (overdose, poisoning)
- Infection (sepsis, pneumonia)
- Hypovolemia hemorrhage, dehydration

Potential Treatments

- Disease-specific interventions guided by patient condition and concomitant Post-Coronary Arrest Syndrome

Bernard, Duffy Kaye, 2011
Study: 2007

- Formal protocol for post-cardiac arrest care
- Increased survival to hospital discharge with a **favorable neurological outcome from 26% to 56%**

Protocol included:

- Therapeutic hypothermia
- Early coronary reperfusion after cardiac arrest
- Hemodynamic support of post-arrest stunned myocardium
- Rapid weaning from positive pressure ventilation
- Glycemic control
Patient Inclusion Criteria

• Cardiac arrest with ROSC (may include non-cardiac causes such as pulmonary embolism)
• Unresponsive or not following commands following cardiac arrest
• Core temperature ≥35° C following ROSC
• Witnessed arrest with down time < 60 minutes
• Stable hemodynamics with or without external means (i.e. pressors or IABP)
Patient Exclusion Criteria

- Existing DNR/End stage terminal illness
- Sustained refractory ventricular arrhythmias
- Comatose state or severe neuro dysfunction prior to arrest
- Pregnancy
- Awake and responsive to verbal commands following cardiac arrest
- Active bleeding/GI bleeding
- Relative exclusion
  - Septic shock
  - Chronic renal failure
  - Extreme age
Part 9: Post–Cardiac Arrest Care

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Mary Ann Peberdy, Co-Chair*; Clifton W. Callaway, Co-Chair*; Robert W. Neumar; Romeryko G. Geocadin; Janice L. Zimmerman; Michael Donnino; Andrea Gabrielli; Scott M. Silvers; Arno L. Zaritsky; Raina Merchant; Terry L. Vanden Hoek; Steven L. Kronick
Pre-Induction (Initiation)

• ED Physician will assess patients for appropriateness of treatment (OHCA)
• Pulmonary/Critical Care Intensivist consultation for admission to critical care
• Cardiologist – consider cath lab for STEMI
• Neurology – neuro evaluation
Phases of TTM

1. Initiation
   - Start cooling immediately
   - Analgesia/Sedation
   - Recognize/treat shivering

2. Maintenance
   - Close attention to BP, O₂ sat, volume, glucose, K⁺, seizures

3. Rewarming
   - Begin 24h after induction
   - 0.25°/hr
   - Watch BP, glucose, K⁺

4. Normothermia
   - Avoid fevers
Induction (Initiation)

- Ventilation Management
- Noninvasive/invasive BP monitoring
- Hemodynamic catheter to assess fluid volume & hemodynamic status: PA catheter, Precept, FloTrac
- Sedation Assessment
  - RASS score every 30 minutes
  - Bispectral index monitor (BIS) –continuous
  - Continuous EEG
- Temperature Monitoring Foley/esophageal catheter with a temperature probe
- External or Internal cooling device
Induction

• Sedation and Analgesia
  • Morphine/Fentanyl
  • Propofol/Versed

• Paralytic
  • Prior to induction of hypothermia: Administer paralytic agent IV
  • Vecuronium.
  • Cisatracurium (Nimbex): Renal impairment exists

• Seizure control
  • Loading dose: Fosphenytoin (Cerebyx) 1000 mg IV then 100 mg IV every 8 hours

• Induction of hypothermia
  • 30 cc/kg IV bolus iced saline (4° degrees C) over 30 minutes
  • When available begin device cooling
  • Note time when patient achieved goal core temperature
Induction

Monitor BP/MAP
- Invasive/noninvasive
- Goal for MAP is >80 and <100 mm Hg (cerebral perfusion)

Monitor Temperature
- Patient temp & Device water temp q 1 hour

Shivering Assessment
- Bedside Shivering assessment Scale (BSAS)
  - Shivering protocol- control

Monitor Labs
- Electrolytes: q 2 hours
- PT/PTT/INR, lactate, cardiac enzymes: q4 hours
- Blood sugars: 120mg/dl - 180mg/dl start insulin therapy when patient reached 33° degree X 6 hours
- BMP, mag, ionized calcium, phosp q 6 hours
# Induction

<table>
<thead>
<tr>
<th>HACA Induction</th>
<th>Q 15 minutes</th>
<th>Q 2 Hours</th>
<th>Q 4 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital Signs</td>
<td>Electrolytes</td>
<td>PT/PTT/INR</td>
<td></td>
</tr>
<tr>
<td>SpO2</td>
<td>Lactate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>Cardiac enzymes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETCO2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RASS/Bispectral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pupillometry</td>
<td></td>
<td></td>
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<tr>
<td>BSAS</td>
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   - 0.25°/hr
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   - Avoid fevers
Maintenance

- Discontinue paralytics once goal temperature
- If unable to control shivering with protocol – restart paralytic
- Maintain goal temperature for 24 hours

<table>
<thead>
<tr>
<th>HACA Maintenance</th>
<th>Q 1 hour</th>
<th>Q 6 hours</th>
<th>Q 8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital Signs</td>
<td>Blood Sugar</td>
<td>12 Lead EKG</td>
<td></td>
</tr>
<tr>
<td>SpO2</td>
<td>BMP</td>
<td>Document QTc</td>
<td></td>
</tr>
<tr>
<td>ECG</td>
<td>Magnesium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETCO2</td>
<td>Ionized Calcium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RASS/Bispectral</td>
<td>Phosphorus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient/Device Temperature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pupilometry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSAS</td>
<td></td>
<td></td>
<td></td>
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   - Avoid fevers
Rewarming

- Controlled re-warming to 37° C at 0.25° C per hour
- Restart shivering management
- Once target temperature is achieved, continue to monitor core temperature hourly for 72 hours

<table>
<thead>
<tr>
<th>HACA Re-Warming</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Q 30 minutes</strong></td>
</tr>
<tr>
<td>Vital Signs</td>
</tr>
<tr>
<td>SpO2</td>
</tr>
<tr>
<td>ECG</td>
</tr>
<tr>
<td>ETCO2</td>
</tr>
</tbody>
</table>
Re-Warming

Vasodilation causes hypotension
  • May require several liters IVF
More shivering during this phase
Inflammation increase at higher temperature
  • “post resuscitation syndrome”
  • Increased ICP

If hyperkalemia develops during rewarming, decrease Device set temperature by 0.5°C (no lower than 33°C), then
  • Contact physician for a renal consult: dialysis or CRRT
  • Use potassium lowering strategies:
    • D50/Insulin
    • Kayexalate
Rewarming

• Experimental data have demonstrated that body temperature regulation during rewarming is critical and may have important implications.

• Fast re-warming (>0.5° C/hour) after hypothermic post cardiopulmonary arrest or traumatic brain injury may aggravate brain damage.

• Literature supports 0.2° C to 0.5° C per hour

Gordon, ML et al. Perfusion 2010; 25
Suehiro E, Povishock JT. J Neurosurg 2001; 94
Povilshock JT, Wei EP. J Neurotrauma 2009; 26
Thermoregulation

- Temperature is regulated by neural feedback mechanisms which operate primarily through the hypothalamus.
- Thermoregulation consists of a complicated network:
  - Temperature sensitive neurons
  - Temperature insensitive neurons
  - Effector neurons
    - Heat loss
    - Heat production
  - Responsible for the ability of the body to regulate one’s own temperature and adapt to changes, thereby maintaining homeostasis.

(Boulant 2000)
Hypothalamus: Set Point

Core Temp of 98.8°F or 37.1°C

Thermoreceptors in hypothalamus

Warm sensitive neuron ↑ firing rate

Signal heat loss effector neurons
- Vasodilatation
- ↑ Sweating (Evaporation)
- ↑ Blood flow

Increase in body temperature

Decrease in body temperature

Normal body temperature (37°C)

No Change in body temperature
Temperature remains at set point

Thermoreceptors in hypothalamus

Cold sensitive neuron ↑ firing rate

Signal heat production effector neurons
- Vasoconstriction
- ↓ Sweating
- Shivering

Increase in body temperature

Decrease in body temperature

Normal body temperature 37°C)

Boulant, JA. Clin. Infect Dis. 2003;31 Suppl 5
Hypothalamic Set Point

- Compression or injury to this area of the brain may cause abnormal thermoregulation
- Thermoregulatory Set Points can become elevated after an injury to the hypothalamus

Variation in temperature may reflect shivering
# Systemic Effects with Phases of Hypothermia

<table>
<thead>
<tr>
<th></th>
<th>Induction</th>
<th>Maintenance</th>
<th>Rewarm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time</strong></td>
<td>2-4 hours</td>
<td>C: 18-24 hours</td>
<td>C: 18 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N: 48-96 hours</td>
<td>N: 3-4 days</td>
</tr>
<tr>
<td><strong>Electrolytes</strong></td>
<td>Shift into cell</td>
<td>Normalizes</td>
<td>Shift extracellular</td>
</tr>
<tr>
<td><strong>UO</strong></td>
<td>Up</td>
<td>Normalizes</td>
<td>Drops</td>
</tr>
<tr>
<td><strong>Blood Sugar</strong></td>
<td>Elevates</td>
<td>Insulin Resistant</td>
<td>Drops</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>BP↑ HR↓</td>
<td>HR↓</td>
<td>BP ↓ HR ↑</td>
</tr>
<tr>
<td><strong>Shivering Issue</strong></td>
<td>Yes</td>
<td>Monitoring</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Pharmacologic Route</strong></td>
<td></td>
<td>Altered Metabolism Avoid SQ</td>
<td></td>
</tr>
</tbody>
</table>
Systemic Complications

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

• Shivering is identified as one of the most frequent consequence of TTM

Who experienced more shivering?

- Surface cooling: 24% (n = 92)
- Core cooling: 27% (n = 75)
Shivering

Assess it!

Prevent it!

Manage it!
Effect of Shivering on Brain Tissue Oxygenation During Induced Normothermia in Patients With Severe Brain Injury

Mauro Oddo · Suzanne Frangos · Eileen Maloney-Wilensky · W. Andrew Kofke · Peter D. Le Roux · Joshua M. Levine

Fig. 1 Individual PbO₂ data points values at baseline and during shivering for each patient with SAH (dotted lines; n = 5) and TBI (full lines; n = 10); black squares represent mean ± SD PbO₂ at the two different conditions (baseline versus shivering). **P < 0.001 for comparisons between baseline and shivering within the patient cohort (paired t test)
Shivering Assessment Methods

• Subjective:
  • Observe for piloerection (goosebumps)
  • Bedside Shivering Assessment Scale (BSAS)

• Objective
  • Bispectral Index Monitoring
Subjective Assessment

• Prevent rigorous shivering
  • Assess every hour
    • Look for goosebumps (piloejerction)
    • Palpate pectoralis muscle and neck/mandible region
    • Humming or vibration is an early indication of shivering

Olson, DM et al. Am J Cri Care 2013; 22
Bedside Shivering Assessment Scale (BSAS)

0 = No shivering
detected on palpate of masseter, pectoralis, deltoids and quadriceps muscles

1 = Mild shivering
localized to neck and/or chest

2 = Moderate Shivering
involving neck and/or chest & arms

3 = Severe Shivering
Intermittent generalized shivering involving all 4 extremities
Assessment of Shivering

- BIS EMG Tracing &/OR Continuous EEG
- Picks up microshivering
Objective: BIS Shivering Assessment

• Patient sedation with midazolam & fentanyl
  • Hypothermia at 33 C
  • BIS = 75
  • EMG = Max
  • BASA = 0
Objective: BIS Shivering Assessment

• Patient dosed with paralytic
  • BIS = 33
  • EMG = 0
  • BSAS = 0
Objective: Water Temperature Post Intervention

- Water temp 30.4°C
- With patient temp stable on slope –
- Rewarming to 37°C
Control of Shivering

Monitor!

- Water and patient temperature and trend indicator
  - Watch for drop in water temperature to $< 12^\circ$ C
  - $>1$ arrow = overexertion and machine is working hard to reduce patient temperature
Control of Shivering

• Foley Temperature probe position
  • Make sure Foley is positioned toward end of the bed and there is no back flow

• Esophageal temperature probe correct placement

• Micro-shivering
  • Check BIS and watch the EMG line for activity
  • Look for elevated goose bumps or feel for raised bumps
Prevention of Shivering During TTM
The Columbia Anti-Shivering Protocol

<table>
<thead>
<tr>
<th>Step</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td>• Acetaminophen</td>
</tr>
<tr>
<td></td>
<td>• Buspirone</td>
</tr>
<tr>
<td></td>
<td>• Magnesium Sulfate</td>
</tr>
<tr>
<td></td>
<td>• Skin Counter Warming</td>
</tr>
<tr>
<td>1</td>
<td>Mild Sedation</td>
</tr>
<tr>
<td></td>
<td>• Dexmedetomidine or opioid</td>
</tr>
<tr>
<td>2</td>
<td>Moderate Sedation</td>
</tr>
<tr>
<td></td>
<td>• Dexmedetomidine and opioid</td>
</tr>
<tr>
<td>3</td>
<td>Deep Sedation</td>
</tr>
<tr>
<td></td>
<td>• Propofol</td>
</tr>
<tr>
<td>4</td>
<td>Neuromuscular Blockade</td>
</tr>
<tr>
<td></td>
<td>• Paralytic Vecuronium (Norcuron)</td>
</tr>
</tbody>
</table>

Choi HA, et al. Neurocrit Care. 2011;14(3)
Columbia Group Experience

18% had shivering controlled with
- Counterwarming
- Buspirone
- Acetaminophen
- Magnesium

50% of the time added dexmedetomide infusion then
- Opiates
- Propofol (<10% of time)

Choi HA, et al. Neurocrit Care. 2011;14(3)
Non-Pharmacological Management of Shivering

- **Counter-warming**
  - Skin threshold can be manipulated by skin counter-warming
- **Insulation of cutaneous thermoreceptors on hands, feet and head**
  - Hot Packs to palms of hands and soles of feet
  - Socks
  - Head wrap (towel)
- **Forced Air Convection Warming Blanket (Bair Hugger)**
  - Temperature receptors on the skin's surface send impulses to the brain. Perceiving warmth, sometimes fools the brain and temporarily suppress shivering
## Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>• Acts by inhibiting cyclooxygenase-mediated prostaglandin synthesis to lower the hypothalamic set point</td>
</tr>
<tr>
<td>Buspirone</td>
<td>• Acts on 5-HTLA receptor to lower the shivering threshold</td>
</tr>
<tr>
<td></td>
<td>• Has a synergistic effect when added to other anti-shivering interventions</td>
</tr>
<tr>
<td>Magnesium</td>
<td>• Effective in increasing comfort</td>
</tr>
<tr>
<td></td>
<td>• Decrease time to goal temperature</td>
</tr>
<tr>
<td></td>
<td>• Peripheral vasodilation</td>
</tr>
</tbody>
</table>
## Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Why</th>
</tr>
</thead>
</table>
| Meriperidine | Lower shivering threshold  
By its effect on the alpha-2B adrenoceptor subtype  
By working synergistically with both buspirone and dexmedetomidine  
Side Effect: Lowers the seizure threshold |
| Fentanyl     | Less selective anti-shivering properties  
Primary mechanisms of shiver control is related to selective impact on brain-injured patients |
## Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Why</th>
<th>Main Side Effect</th>
</tr>
</thead>
</table>
| Dexmedetomidine | • Central alpha-2 receptor agonist  
                     • Effective anti-shivering properties on both vasoconstriction and shivering thresholds | Bradycardia and hypotension  
Less respiratory depression  
Use of dexmedetomidine to counter shivering is considered off label |
| Propofol     | Frequently use for sedation  
Mildly reduces vasoconstriction and shivering thresholds | Hypotension  
Negative cardiac inotropy  
Sedation  
Propofol infusion syndrome |
| Paralytic    | Last choice  
• Quickest method  
• Commonly used during induction of hypothermia to achieve target temperature | Elimination neuro exam and requires more aggressive sedation |
Management Of Shivering

**Step 1: Induction:**
- Acetaminophen 650 mg Q4hours PR/OG/NG fever greater than 37° C or 1000 mg IV over 15 minutes every 6 hours
- Buspirone 30 mg Q8hours per OG/NG times 3 doses

**BSAS 1:**
- Forced Air Convection Warming Blanket (Bair-Hugger) at 43°C
- Non-sedating:
  - Magnesium sulfate: start at 0.5gm/hr IV, titrate up 0.5 gm/hr q 6 hrs (goal Mg level at 3-4 mg/dL)
- Sedating- choose one of the following:
  - Meperidine: 25 mg IV every 30 mins PRN; do not exceed 500 mg/24 hours
  - Dexmedetomidine : 0.3-1.5 mcg/kg/hour IV and titrate up to 0.7 mcg/kg/min to a RASS of -3
  - Fentanyl: 50-200 mcg/hour IV

**BSAS 2:**
- Propofol at 10 mcg/kg/min; titrate up by 5-10 mcg/kg/min every 10 mins to a RASS of -3

**BSAS 3:**
- Paralytics of choice, if shivering continues titrate up to suppression of shivering and maintain at 1-2 twitches out of four on peripheral nerve stimulator

Based on Columbia Mayer and Badjatia
Phases of TTM

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Preventing Hyperthermia
Physiological Effects of Hyperthermia

- Increased metabolic rate
- Increased blood velocity
- Increased cerebral blood volume
- Increased oxygen consumption
Elevated Temperature Causes

In the ischemic/post anoxic brain

Cellular Derangements

Cell Damage

Cell Death
Pyrexia and neurologic outcomes after therapeutic hypothermia for cardiac arrest

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Methods: Retrospective multicenter US clinical registry study of post-cardiac arrest patients treated with TTM at 11 hospitals between 5/2005 and 10/2011. We assessed the incidence of rebound pyrexia (defined as temperature >38°C) in post-arrest patients treated with TTM and subsequent clinical outcomes of survival to discharge and “good” neurologic outcomes at discharge, defined as cerebral performance category (CPC) 1-2.

Results: In this cohort of 236 post-arrest patients treated with TTM, mean age was 58.1 ± 15.7 y and 106/236 (45%) were female. Of patients who survived at least 24 h after TTM discontinuation (n = 167), post-re-warming pyrexia occurred in 69/167 (41%), with a median maximum temperature of 38.7 (IQR 38.3-38.9). There were no significant differences between patients experiencing any pyrexia and those without pyrexia regarding either survival to discharge (37/69 (54%) v 51/98 (52%), p = 0.88) or good neurologic outcomes (26/37 (70%) v 42/51 (82%), p = 0.21). We compared patients with marked pyrexia (greater than the median pyrexia of 38.7°C) versus those who experienced no pyrexia or milder pyrexia (below the median) and found that survival to discharge was not statistically significant (40% v 56% p = 0.16). However, marked pyrexia was associated with a significantly lower proportion of CPC 1-2 survivors (58% v 80% p = 0.04).
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Conclusions: Rebound pyrexia occurred in 41% of TTM-treated post-arrest patients, and was not associated with lower survival to discharge or worsened neurologic outcomes. However, among patients with pyrexia, higher maximum temperature (>38.7°C) was associated with worse neurologic outcomes among survivors to hospital discharge.

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Pyrexia Post Cardiac Arrest
Rebound Hypothermia Post HACA

Prevalence and effect of fever on outcome following resuscitation from cardiac arrest*

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Objective: Evaluate the prevalence of fever in the first 48 h after cardiac arrest and its effect on outcomes.

Methods: Review of patients treated between 1/1/2005 and 6/30/2010. Fever was defined as \(T \geq 38.0^\circ C\). We classified categories of post-cardiac arrest illness severity as (1) awake, (II) coma + mild cardiopulmonary dysfunction (SOFA cardiac + respiratory score < 4), (III) coma + moderate-severe cardiopulmonary dysfunction, and (IV) deep coma. Associations between fever and survival or good neurologic outcome were examined between hypothermia (TH) and non-TH groups.

Results: In 336 patients, mean age was 60 years (SD 16), 63% experienced out-of-hospital cardiac arrest and 65% received TH. A shockable rhythm was present in 40%. Post arrest illness severity was category II in 38%, category III in 20%, and category IV in 42%. Fever was present in 42% of subjects, with a post-arrest median onset of 15 h in the non-TH cohort and 36 h in TH cohort. Fever was not associated with survival within the whole cohort (OR 0.32, CI 0.15, 0.68) or TH cohort (OR 1.21, CI 0.69, 2.14), but was associated with survival in non-TH cohort (OR 0.47, CI 0.20, 1.10). Fever was not associated with good outcomes in the whole cohort (OR 0.83, CI 0.49, 1.40), TH cohort (OR 1.09, CI 0.56, 2.12) or non-TH cohort (OR 0.34, CI 0.11, 1.05).

Conclusions: The development of fever within the first 48 h after ROSC is common. Fever is associated with death in non-TH patients. TH treatment appears to mitigate this effect, perhaps by delaying fever onset.
Clinical paper
Assessment of risk factors for postrewarming “rebound hyperthermia” in cardiac arrest patients undergoing therapeutic hypothermia

3.3. Association of rebound hyperthermia with morbidity and mortality

The presence of rebound hyperthermia is associated with an increased risk of in-hospital mortality. 40 of the 99 (40.4%) patients without rebound hyperthermia experienced any cause in-hospital death. This is compared to 27 of the 42 (64.3%) patients who experienced rebound hyperthermia (OR: 2.66; 95% CI: 1.26–5.61; p = 0.011).

Rebound hyperthermia is associated with increased neurologic morbidity as measured by the modified Rankin scale. The two-sided Mann–Whitney U test between the two groups of patients gives p = 0.011, suggesting that there is a statistically significant difference in neurologic morbidity as measured by a modified Rankin scale between patients that experience rebound hyperthermia and those that do not.
Post-hypothermia fever is associated with increased mortality after out-of-hospital cardiac arrest.  


Methods: In the period 2004–2010, a total of 270 patients resuscitated after OHCA and surviving a 24-h protocol of TH with a target temperature of 32–34°C were included. The population was stratified in two groups by median peak temperature (≥38.5°C) within 36 h after rewarming: PHF and no-PHF. Primary endpoint was 30-days mortality and secondary endpoint was neurological outcome assessed by Cerebral Performance Category (CPC) at hospital discharge.

Results: PHF (≥38.5°C) was associated with a 36% 30-days mortality rate compared to 22% in patients without PHF, \( p_{\text{log-rank}} = 0.02 \), corresponding to an adjusted hazard rate (HR) of 1.8 (95% CI: 1.1–2.7), \( p = 0.02 \). The maximum temperature (HR = 2.0 per °C above 36.5°C (95% CI: 1.4–3.0), \( p = 0.0005 \)) and the duration of PHF (HR = 1.6 per 8 h (95% CI: 1.3–2.0), \( p < 0.0001 \)) were also independent predictors of 30-days mortality in multivariable models. Good neurological outcome (CPC1-2) versus unfavourable outcome (CPC3-5) at hospital discharge was found in 61% vs. 39% in the PHF group compared to 75% vs. 25% in the No PHF group, \( p = 0.02 \).
Pyrexia Post Cardiac Arrest
Rebound Hypothermia Post HACA

Post-hypothermia fever is associated with increased mortality after out-of-hospital cardiac arrest.


Conclusions: Post-hypothermia fever ≥38.5 °C is associated with increased 30-days mortality, even after controlling for potential confounding factors. Avoidance of PHF as a therapeutic target should be evaluated in prospective randomized trials.

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Elevated Temperature in HACA Increases

- Length of Stay
- Morbidity
- Mortality
“The good news is that you’re no longer running a fever.”
Normothermia Implementation

- Acetaminophen IV or per rectum
- Cool room, wet towels, alcohol baths, ice bags
- Iced saline 30 mL/kg bolus over 30 mins X 1
- Surface external adhesive pads
- Surface blanket device
- Intravascular device
Normothermia Success

• Dependent on adequate:
  - Temperature gradient (actual at 37°C)
  - Sedation / Anagelsia
  - Associated conditions (i.e. elevated ICP)
Normothermia

• Post Cardiac Arrest
  • Once the patient returns to 37 C following hypothermia treatment
  • Keep it Normal for 72 hours duration
Fluid & Electrolytes
Systemic Effects – Fluid & Electrolyte

- Sodium and Potassium are the key electrolytes.
- K+ shifts intracellular in the setting of hypothermia.
- Sodium is exchanged extracellularly.
- Water follows Sodium → the extracellular space.

Courtesy of Daiwai Olson
Induction of Hypothermia

As Temp < 35° C
- Cold diuresis
- CVP ↓
Electrolyte Thresholds

Monitor and be careful with replacement, anticipate changes with rewarming:

- **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
  - Na Phosphorus 12 mmol/L over 3 hrs
- **Ionized Calcium** < 1.0 mmol/L or Calcium Level < 4 mg/dL
  - 2 grams Calcium gluconate over 30 minutes
Effects of Hypothermia: Electrolyte Changes

- K + Rider
- Ca ++ Given
- Mg Rider
Patient Warming - Electrolytes

- Sodium will drop
- Potassium will rise
Systemic Effects – Cardiac (Arrhythmia)

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

$$QTc = \frac{QT}{\sqrt{RR}}$$

For illustration only.
Cardiac Vascular Management

- Goal for MAP is >80 and <100 mm Hg (cerebral perfusion)
- AHA post arrest management = MAP of ≥ 65 and ScvO2 ≥ 70%
  - Volume bolus up to 30 mL/kg
  - Inotropes and Dilators are titrated to cardiac output/index
- Metabolic Acidosis
  - Restoration of perfusion should correct acidosis, resist urge to hyperventilate patient
  - Give fluid bolus
  - May need NaHCO3 if continues

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Fluid administration as well as vasoactive (eg, norepinephrine), inotropic (eg, dobutamine), and inodilator (eg, milrinone) agents should be titrated as needed to optimize blood pressure, cardiac output, and systemic perfusion (Class I, LOE B). Although human studies have not established ideal targets for blood pressure or blood oxygenation, a mean arterial pressure ≥65 mm Hg and an ScvO2 ≥70% are generally considered reasonable goals.
Hypothermia Research - MI

- Animal Studies (variety of mechanism to cool)
  - Improve myocardial salvage
  - Reduced myocardial infarct size
  - Reduced the no-reflow phenomenon
  - Reduced left ventricular remodeling
  - Better long-term left ventricular function

- Humans studies (surface cooling & endovascular heat-exchange catheters)
  - Appears to have no detrimental effects on left ventricular function or regional myocardial blood flow
  - May improve microvascular reflow to previously ischemic heart tissue
  - **Must be initiated early before reperfusion.**


Hypothermia Research - MI

- Two studies have already demonstrated that it is feasible to cool awake patients
- Cool – MI study: 357 pt (180 pts control, 177 pt cooled)
  - Results
  - No significant difference in final infarct size
  - Anterior MI Subset
    - Significant ST-segment resolution
    - Pts cooled to < 35°C at the time of reperfusion had significantly smaller infarct size compared with the control group (9.3% vs 18.2%; p=0.05)
    - Trend toward higher left ventricular ejection fraction values
    - Lower peak CK-MB values

Hypothermia Research - MI

- Two studies to watch
  - COOL MI II: Cooling as an Adjunctive Therapy to Percutaneous Intervention in Patients With Acute Myocardial Infarction: comparing induced mild hypothermia and normothermia in awake patients with anterior AMI who are undergoing primary PCI. Study closed, data not presented yet
  - Can Hypothermia be Incorporated Into Primary Angioplasty for Heart Attack? (CHIPAHA): Cooling 20 awake patients with acute ST elevation AMI before primary PCI using surface cooling device - Assessed infarct size at 30 days. Target completion May 2015
Pulmonary Management

- Post Arrest patients with ROSC, AHA Recommends:
  - Titration of FiO2 to a O2 saturation of ≥ 94%
    - Prevent complications of hyperoxia
  - Consider low Vt and High rate ventilation for patients at risk of ARDS
  - DVT/PE Prophylaxis
    - Patients have impaired platelets due to hypothermia but are still at risk of DVT/PE from immobility
  - Prevent Pneumonia → Sepsis
    - Possible aspiration with OHCA or IHCA
    - Hypothermia masks fever
    - Impaired neutrophil, leukocyte and macrophage function
GI/Nutrition Management

• PUD/GI Bleeding Prophylaxis
  • Protect with appropriate PPI or other agent to reduce risk
• Hold Nutrition/Tube feeding
  • Impaired GI Motility
  • Potential for ileus
  • Paralytic medications
Drug Clearance During Hypothermia

Increases drug levels and/or enhance the effect of the drug

- Reduction in the activity of many liver enzymes during hypothermia
- Reduced perfusion of the liver
- Reduced excretion of bile which decreases excretion of drugs
- Changes in distribution volume and hypothermia-induced tubular dysfunction

Drug Clearance During Hypothermia

Drug Clearance

• **Vasoactives**
  - Adrenalin and noradrenalin are slightly blunted by hypothermia
  - Half life of vasopressin is increased

• **Increase drugs levels or enhanced effects**
  - Fentanyl, remifentanil, morphine,
  - Phenytoin, nitrates, propanolol.
  - Propofol, barbitutates, midazolam,
  - Neuromuscular blockers (vecuronium, rocuronium, atracurium)
  - Volatile gas anesthesia agents

Assessment & Monitoring

• Skin Integrity
  • Increased risk of pressure ulcers
    • Decreased perfusion
    • Delayed wound healing
    • Increased risk of infection due to decrease leukocyte production

• Obese patients may take longer
  • Fat is insulating
  • More surface area to cool
  • If surface cooling – additional pads may be needed
Educational Resource for Families

http://www.med.upenn.edu/resuscitation/docs/TH_Family_Brochure_FINAL.pdf
I'm telling you, dude! They said we're not getting blindly randomised in case of cardiac arrest!

But...but what about rewarming us?

Huh, global warming will sort that out, I guess!
For more information and resources on TTM, visit our hypothermia resource pages:

https://www.med.upenn.edu/resuscitation/hypothermia/index.shtml