Induced Hypothermia for Cardiac Arrest
Cardiac Arrest Epidemiology

400,000 arrests / year in U.S.A

3 / 4 Out-of-hospital

1-5% survival to hospital discharge

Only 2% with Good neurological outcome

1 / 4 In-hospital

10-20%
Reality is many patients with functional organs but non-functional brains
The major reason that patients die after successful resuscitation is that their brains have been damaged by global cerebral ischemia.

- Biological cascade due to ischemia (same as neuro/stroke)

- Damaging effects of reperfusion injury – once you get the blood flowing again...its damaging to the already vulnerable brain tissue.

Need for Neuroprotective Therapy
The brain’s problem with cardiac arrest.

Sudden global ischemia →

Energy supply ends →

Cellular metabolism ceases →
The brain’s problems don’t end there.

Without metabolism,
Cells begin to deteriorate

the point of no return

is the fragmentation of
nuclear DNA (apoptosis)
Problems are just beginning!

The cerebral microcirculation is disrupted by cell breakdown products,
The return of circulation should help, right?

Sorry.

The return of circulation initially brings cytotoxic substances released from cells elsewhere in the body resulting in a further cycle of destruction.
Hypothermia Mechanisms

Ischemia → Reperfusion

- Reactive Oxygen Species (ROS)
- Inflammatory Cascades
- Mitochondrial Dysfunction

Vascular Dysfunction/Hypotension
Apoptosis-organ dysfunction
Cerebral Edema
Approaches to salvaging function
Successful Intervention:

- Hypothermia is the only therapy for neurologic resuscitation proven to be successful by randomized controlled clinical trials.
MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

**European : HACA Trial**
- 275 patients randomized to cooling or normal temps
- Cooling time: 6.5 hrs to 34°C using surface cooling

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<tr>
<th></th>
<th>Hypothermia</th>
<th>Normothermia</th>
<th>p</th>
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<tbody>
<tr>
<td>Good Outcome</td>
<td>55%</td>
<td>39%</td>
<td>0.009</td>
</tr>
<tr>
<td>Mortality</td>
<td>41%</td>
<td>55%</td>
<td>0.02</td>
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**Australian Study:**
- 77 patients randomized
- Used ice packs to cool; Cooling rate .9 C/hour

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<tr>
<td>Good Outcome</td>
<td>49%</td>
<td>26%</td>
<td>0.046</td>
</tr>
<tr>
<td>Mortality</td>
<td>51%</td>
<td>68%</td>
<td>NS</td>
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For every six patients treated, one life saved
Unconscious adult patients with return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours when the initial rhythm was ventricular fibrillation (VF). *Class IIa*

Similar therapy may be beneficial for patients with non-VF arrest out of hospital or for in-hospital arrest. *Class IIb*
2010 AHA Guidelines

- IH after CA is now a LEVEL I recommendations for all comatose survivors of V.Fib and V.Tach arrests.
- IH after CA remains a LEVEL IIb recommendation for all comatose survivors of PEA or Asystole arrests.
- Patients should be given 72 hours to declare themselves after rewarming before decisions are made re: withdrawal of support.
2015 Guidelines

• All Comatose adult patients with ROSC after cardiac arrest should have TTM (targeted temperature management) of 32C – 36C for at least 24 hours after achieving target temperature.
• It is recommended to prevent fever after TTM is achieved. (some studies suggest fever after rewarming is associated with worsened neurologic injury)
Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

Niklas Nielsen, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Tobias Cronberg, M.D., Ph.D., David Erlinge, M.D., Ph.D., Yvan Gasche, M.D., Christian Hassager, M.D., D.M.Sc., Janneke Horn, M.D., Ph.D., Jan Hovdenes, M.D., Ph.D.,

CONCLUSIONS

In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C. (Funded by the Swedish Heart–Lung Nicole P. Juffermans, M.D., Ph.D., Matty Koopmans, R.N., M.Sc., Lars Køber, M.D., D.M.Sc., Jørund Langørgen, M.D., Gisela Lilja, O.T., Jacob Eifer Møller, M.D., D.M.Sc., Malin Rundgren, M.D., Ph.D., Christian Rylander, M.D., Ph.D., Ondrej Smid, M.D., Christophe Werer, M.D., Per Winkel, M.D., D.M.Sc., and Hans Friberg, M.D., Ph.D., for the TTM Trial Investigators*)
Thoughts for Discussion

- Did not test the same hypothesis as HACA trial and Bernard-TTM actively controlled temp for the entire time.
- Bystander CPR rate was high (73%).
- Collapse to time of CPR was 0-2 min.
- Time to Target Temp In 33C was approx 8 hours vs approx 6h – longer than recommendation.
- Was the 33C group sicker?
- Did the normothermia group in HACA and Bernard trials become hyperthermic?
Comparison of Patient Selection

<table>
<thead>
<tr>
<th></th>
<th>33C</th>
<th>36C</th>
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<tbody>
<tr>
<td>Time to ROSC</td>
<td>29 minutes</td>
<td>24 minutes</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>67%</td>
<td>79%</td>
</tr>
<tr>
<td>Shockable Rhythms</td>
<td>76%</td>
<td>85%</td>
</tr>
<tr>
<td>Age</td>
<td>66 y/o</td>
<td>62 y/o</td>
</tr>
<tr>
<td>Temp on Admit</td>
<td>35.1C</td>
<td>35.5C</td>
</tr>
<tr>
<td>Lactate post ROSC</td>
<td>6.7</td>
<td>5.1</td>
</tr>
</tbody>
</table>
**How Low Do We Cool?**

- Neurological and cardiovascular benefits are evident with mild hypothermia (32°C)
- Complications increase with moderate (30°C) and deep (15°C) hypothermia
Cooling Methods

Crash Cool Phase
Maximum Cooling Rate

Rewarm Phase
Slow, controlled Rewarm to avoid ICP rebound

Maintenance Phase
Tight control within 32-34°C range

Must be able to Control All 3 Phases
Hyperthermia Following Cardiac Arrest

- 83% of cardiac arrest patients develop fever\(^1\).
- After the initial 48 hours after resuscitation, most patients showed a rapid rise in body temperature\(^2\).
- For each Celsius degree higher than 37°C, the risk of an unfavorable neurologic recovery increases.

Hyperthermia is a potential factor for an unfavorable functional neurologic recovery after successful cardiopulmonary resuscitation\(^3\).

CoolGard stopped after rewarming, Patient spiked fever post CA

Target temp. 33°C
Target temp. 36.5°C
Target temp. 37°C
How “Ice” helps the brain
Hypothermia - Neuroprotective?

- The thinking is that it is like the mammalian diving reflex: When the body experiences a rapid exposure to submersion in cold water, this causes peripheral vasoconstriction, directing blood to major organs including the brain.
- Triggers Bradycardia, reducing myocardial oxygen demand.
How “Ice” Helps the Brain

- Stabilizes excitotoxin and free radical reactions
- Stabilizes cell membranes (including BBB)
- Reduces intracellular acidosis
- Reduces ICP
- Reduces cerebral edema
- Reduces cerebral metabolism (5-7% for every degree reduction)
- Exerts an anti-inflammatory effect on the biochemical cascade of “reperfusion injury”
Who to Cool: Indications

- ROSC after cardiac arrest
  - Rhythm – only studied in V-Fib and pulseless V-tach, but why not other rhythms?
  - Down-time no more than 30 to 60 minutes
- > 18 years old
  - Why not children
- Females
  - If less than 50 years old, need a negative pregnancy test
- Comatose or not following verbal commands
- Core temperature not already hypothermic
Who to Cool: Relative Contraindications

- Persistent hypotension
  - MAP <60 despite IVF and stable doses of vasopressors
- Active bleeding
- Known coagulopathy or thrombocytopenia
- Positive pregnancy
- Refractory ventricular arrhythmias
- Severe bradycardia without a temporary pacemaker
- Existing DNR status
- Known end-stage terminal illness pre-arrest
- Severe neurological dysfunction pre-arrest
How do we “Ice”??
Current Methods:

- External Cooling
  - Ice packs
  - Cooling blankets
  - Surface cooling with conductive surface pads

- Internal Cooling
  - Iced lavage
  - Cooled IV saline
  - Intravascular
Intravascular Cooling

Closed-loop system
How The Heat-Exchange Works

Closed-loop system – no fluid infusion
Why Intravascular Is Superior:

Makes NURSES life easier!!!
Okay, Really why is IVTM Best??

- Accurate
- Quick
- Easy set up and Management
- Controlled (All Phases)
- Safe (No Wet Floors)
- Does not interfere with patient care
- Non-Labor Intensive – Saves Nursing Time
- Can be Proactive not only Reactive
Intravascular = Nursing Time Saved

**Objective:** To study the effectiveness of catheter based heat exchange systems in the reduction of fever in patients in the Neuro ICU and measure the impact on nursing time devoted to managing patient temperature.

**Materials and Methods:** This study was a prospective randomized, non-blinded trial in which conventional treatment of fever with acetaminophen and water cooling blankets (conventional group) was compared to conventional treatment plus a Cool Line™ catheter based heat exchange system (Abiomed Corporation, Irvine, CA). Four patient populations were included in the trial: subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), ischemic infarction (CI) and traumatic brain injury (TBI). Temperature was recorded hourly for a minimum of 3 and up to 7 days following randomization. The temperatures were graphed and the area under the fever curve which exceeded 37.9 °C was used as an index of fever burden. The efficacy of the Cool Line catheter system was determined by its ability to reduce fever burden in an intention to treat analysis. The nursing staff was asked to estimate the hourly work required to ensure appropriate fever management for both the Cool Line and Control patients. The nursing staff filled out a form at the end of each shift estimating time devoted to managing fever. The time intensity forms were organized according to patient ID and calculated.

**Results:** A total of 294 patients were enrolled over 20 months half of which were randomized to receive conventional fever management and half conventional management and the catheter based heat exchange system. Of the patients 41% had SAH, 24% TBI, 23% ICH and 13% ischemic stroke. The two fever control groups were matched in terms of age, body mass index, gender and overall neurological severity score distribution. The Cool Line catheter group demonstrated a 64% reduction in fever burden for the first 72 hours (2.67 degree hours in the catheter group versus 7.92 degree hours in the conventional group). The use of the Cool Line catheter system was also associated with a 43% reduction in the amount of nursing time (6.2 hours in the Cool Line group versus 10.6 hours in the control group) devoted to the management of a patient’s fever.

**Conclusions:** The Abiomed Cool Line catheter based system is more effective in reducing fever than conventional management in Neuro ICU patients and has a significant impact on associated nursing time.

Abstract Presentation for AACN Region 6 Mgr., September 27, 2004

NEURO-85

- 43% Reduction in Nursing Time towards patient Management
Sarasota Experience

RESUSCITATIVE HYPOTHERMIA AFTER CARDIAC ARREST: PERFORMANCE IN A COMMUNITY HOSPITAL

Cindy Grimes, RN, Rhonda Anderson, MSN, Todd Horituchi, MD, Mauricio Concha, MD, Bruce Fleegler, MD and Kenneth Hurwitz, MD*

Sarasota Memorial Hospital, Sarasota, FL

PURPOSE: Induced hypothermia improves outcome after cardiac arrest due to ventricular fibrillation. We studied induced hypothermia in a community hospital setting after cardiac arrest due to any cause.

METHODS: A case-control study was conducted in a publicly owned, non-academic, acute care hospital. Thirty-eight patients who underwent induced hypothermia were compared to 103 patients who did not undergo hypothermia. After resuscitation from cardiac arrest, patients underwent hypothermia using an established protocol at the discretion of the treating clinicians. Hypothermia was achieved with either external devices or an intravascular cooling catheter system. Outcome measures included mortality, neurologic recovery, and length of stay (LOS).

RESULTS: The groups were similar in age, sex, APACHE III score, and Glasgow Coma Score (GCS). Hospital mortality in the hypothermia group was 53% versus 71% in the control group (p=0.07). Hospital mortality in 10 patients treated with intravascular cooling was 40%. Compared to Apache III predicted mortality, the hypothermia group mortality ratio was 0.76, versus 1.4 for the control group. Among survivors, the change in GCS from admission to ICU discharge was 7.2 +/- 4.0 (baseline 4.4, discharge 11.7) in the hypothermia group and 6.6 +/- 4.3 (baseline 4.0, discharge 10.6) in the control group (p=0.32). Also among survivors, the ICU LOS was 2.6 +/- 3.5 days less than Apache III predicted in the hypothermia group versus 0.5 +/- 6.8 days less in the control group (p=0.08).

CONCLUSION: Induced hypothermia following cardiac arrest performs well in a community hospital setting. The intravascular cooling catheter was a safe, effective means of inducing hypothermia with a trend towards improved outcomes. Induced hypothermia may be applicable to all cardiac arrest patients regardless of cause.

CLINICAL IMPLICATIONS: Induced hypothermia is safe, simple, and inexpensive. Hospital protocols may help to ensure timely application of this important intervention. Intravascular cooling techniques show promise in terms of ease of use, effectiveness of cooling, and maintaining accessibility to the patient. Further study is needed to determine the optimal patients and techniques for therapeutic hypothermia.

DISCLOSURE: Kenneth Hurwitz, None.

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- Using hypothermia in all cardiac arrest patients
- Intravascular Cooling catheter was safe and effective
- Intravascular cooling simple, safe and effective in maintaining temperature and accessibility to the patient.
"Safety and Efficiency of Intravascular Temperature Management (IVTM) for Therapeutic Hypothermia"

Meta-analysis of all publications using intravascular catheters taking a look at efficiency and safety

• Conclusion of studies in over 1,000 reported patients:
  • IVTM is associated with less than 0.2% incidence of clinically significant thromboembolic disease.
Induction & Maintenance Considerations:

Patient Comfort:
- Fentanyl
- Morphine

Sedation:
- Midazolam
  Loading dose 2-6mg IVP
  Continuous 1-2mg/hr
- Propofol
  Start at 5mcg/kg/min titrate to comfort
Induction Considerations: Neuromuscular Blockade

Cisatricurium (Nimbex)

Monitor Paralysis using train of four (TOF)

“DO NOT PARALYZE A PATIENT WHO IS NOT ADEQUATELY SEDATED”
HOW MANY MUSCLES??
Shivering is Counterproductive

- Causes $\uparrow$ ICP
- $\uparrow$ Metabolic Rate
- Heat Producing
- $\downarrow$ SVO2
- $\uparrow$ Oxygen Consumption
Shivering Secrets…

- A lot of temp sensors are in our skin…
- Baer hugger (surface counter warming)
- Place blankets on the patient.
- Put socks on.
- Warm packs in the hands.
- Insulate the tubing with a towel as to not touch the patient.
Less Shivering = Less Medication

Shivering occurs through a narrow band of temperature

The faster you cool, the less paralytic needed.

What Happens When We Are Cold?

- Electrolyte Shifts
  - Potassium Shifts into cell
- At Start, may become hypertensive, tachycardic
- Arrhythmias
  - Bradycardia
  - Widened QRS
  - ST Elevation or Depression
  - T-Wave Inversion
  - Osborne Wave (notch on down on QRS)
Osbourne wave
When Cold Continued....

- Increased Risk of Infection.
- Possible Increase in Bleeding Time.
- Hypothermia may act as an anticonvulsant.
- For Every 1°C decline, HCT increases 2%
When Cold...

- Insulin Resistance- May require more, use IV Insulin
- Shifts the OXY-HGB dissociation curve to the left-- ↓ O2 availability and ↓ CO2 production
- Cold-Induced Diuresis (inhibition of ADH)
  - Hypophosphatemia
  - Hypomagnesium
Nursing Care for the IH Patient

- Minimal Stimulation
- No “Road Trips”
- No Bathing
- Humidifier on Vent off
- Minimal Turning
- Reduce Environmental Heat
Rewarming…Go Slow

- Electrolytes shift out of cell
- May see some hypotension
- Controlled re-warm is key
  - Helps avoid rebound ICP issues
  - Usually no faster than 0.5 °C/hr
- May see some hypoglycemia
FOOTNOTE: the "Listening to children cry in the middle of the night" gland is not shown due to it's small and underdeveloped nature. Best viewed under a microscope.
THE FEMALE BRAIN

Shoe/handbag coordination

Jealousy

Telephone skills

Need for commitment hemisphere

InDecision nucleas

Chocolate centre

Listening

Shopping

Sense of direction neuron

SEX (see note)

Footnote: Note how closely connected the small sex cell is to the listening gland.
Thank you.

Questions???