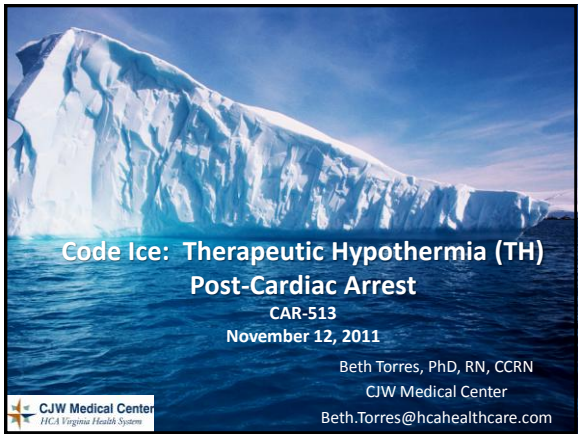

Mrs. D

- Mrs. D collapsed at church. She was removed to the foyer where CPR was performed by an EMS-trained bystander.
- Although an AED was present on-site, it was not used.
- EMS arrived within 4-5 minutes. She received a total of 2 shocks for v.fib by FD EMS. She experienced ROSC. Cardiac monitor showed SR after 2nd shock.
- Patient presents unconscious to the ED s/p resuscitation of a v.fib cardiac arrest.

Objectives

- At the completion of this session, the participant will
  - Discuss the evolution of therapeutic hypothermia and the science underlying the therapy
  - Discuss the indications for use
  - Describe the process of therapeutic cooling: When and how?

Therapeutic Hypothermia Outline

- Case presentation
- Background
- Review of the relevant literature
- Summary of current recommendations
- Overview of CJW Medical Center hypothermia protocol

Out-of-Hospital Cardiac Arrest (OHCA)

- Out-of-hospital cardiac arrest claims 236,000 – 325,000 lives each year in the United States
- Survival rates range from 2 - 9% with 3-7% of survivors returning to previous level of functioning
- Accounts for about half of all deaths due to cardiovascular disease
- Even when resuscitation efforts are successful, recovery is often limited by anoxic encephalopathy

Keonig et al (2008). *Neurologic Clinics*

Potential Mechanisms of Cerebral Injury

- Numerous deleterious biochemical reactions contribute to the death of neurons in vulnerable regions of the brain, such as the cerebral cortex, hippocampus & cerebellum
- Including:
  - Cellular membrane dysfunction→Excitotoxicity injury
  - Calcium influx intracellularly→ ↑ oxygen-free radicals
  - Lipid peroxidation; Protein oxidation
  - Inflammation
- Process begins with arrest & can continue for days

Keonig et al (2008). *Neurologic Clinics*

Seminal Studies

The New England
Journal of Medicine

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MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Enrollment from 3/96-1/01

Inclusion

- Witnessed arrest
- VF; pulseless VT; presumed cardiac origin
- Age 18-75
- CPR within 5-15 min by EMS
- Interval of no more than 60 minutes from collapse to ROSC

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Exclusion

- Tympanic temp < 30°C
- Coma prior to arrest due to drugs that depress CNS
- Pregnancy
- Responsive to verbal commands after ROSC
- MAP < 60 mmHg 30 min after ROSC
- Hypoxemia with O2 sat <85%
- Terminal illness
- Known coagulopathy

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

- Randomized Study
- Multicenter trial
- 275 patients
- Cooled to 32-34° C within 4 hours of ROSC & maintained for 24 hours
- Primary Outcome: Survival to hospital discharge with good neurologic function within 6 months

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MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

- Results:
  - 75 of 136 patients treated with hypothermia (55%) survived to discharge with good neurologic outcome as compared to 54 of 137 treated with normothermia (39%)
- Conclusion:
  - Suggests that treatment with moderate hypothermia increases rate of favorable neurologic outcome & decreases mortality

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INDUCED HYPOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

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

STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUIST, M.B., B.S., BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.Sc.

N Engl J Med, Vol. 346, No. 8 · February 21, 2002

- Randomized Study
- 77 patients
- Cooled to 33° C within 2 hours of ROSC & maintained for 12 hours
- Primary Outcome: Survival to hospital discharge with good neurologic function

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

STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUIST, M.B., B.S., BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.SC.

Enrolled in Australia 9/96-6/99

- **Inclusion**: VF upon arrival of EMS; successful ROSC; persistent coma after ROSC; transfer to one of 4 participating centers
- **Exclusion**: age less than 18; women less than 50; cardiogenic shock with SBP <90; other possible causes of coma; unavailable ICU bed

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

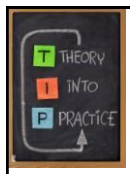
STEPHEN A. BERNARD, M.B., B.S., TIMOTHY W. GRAY, M.B., B.S., MICHAEL D. BUIST, M.B., B.S., BRUCE M. JONES, M.B., B.S., WILLIAM SILVESTER, M.B., B.S., GEOFF GUTTERIDGE, M.B., B.S., AND KAREN SMITH, B.SC.

- Results
  - 21 of 43 patients treated with hypothermia (49%) survived to discharge with good neurologic outcome as compared to 9 of 34 treated with normothermia (26%)
- Conclusion
  - Suggests that treatment with moderate hypothermia appears to improve outcomes in patients with coma after resuscitation from OHCA

Therapeutic Hypothermia

Potential Mechanisms of benefit:

- Reduced cerebral metabolic rate & oxygen demand→ ↓ cerebral edema & ICP
- Stabilization of cell membranes
- Suppression of reactions associated with reperfusion injury including:
  - Free radical production
  - Inflammatory response & cytokine release
  - Excitatory amino acid release
  - Calcium shifts



ILCOR Advisory Statement

Recommendations made in October 2002

- Unconscious adult patients with ROSC after OHCA should be cooled to 32 – 34 °C for 12 to 24 hours when the initial rhythm is VF
- Such cooling may also be beneficial for other rhythms or in-hospital cardiac arrest

Nolan, et al. (2003). *Circulation.*

Inclusion/Exclusion Criteria

- Early studies conducted with VF & Pulseless VT patients only
- Oddo et al (2008) concluded that time from collapse to ROSC strongly associated with outcomes.

"Only 3.1% of patients with time to ROSC > 25 minutes survived, as compared to 65.7% with time to ROSC ≤ 25 minutes" (p. 2296)

2010 AHA Recommendations

- "Systematic post–cardiac arrest care after ROSC should continue in a critical care unit with expert multidisciplinary management and assessment of the neurologic and physiologic status of the patient. This often includes the use of therapeutic hypothermia" (p.13).
- "Therapeutic hypothermia and percutaneous coronary interventions (PCIs) should be provided when indicated" (p. 15).

American Heart Association (2010)

2010 AHA Recommendations

"Therapeutic hypothermia (to 32°C to 34°C) may be beneficial for adolescents who remain comatose after resuscitation from sudden witnessed out-of-hospital VF cardiac arrest. Therapeutic hypothermia (to 32°C to 34°C) may also be considered for infants and children who remain comatose after resuscitation from cardiac arrest" (p.22).

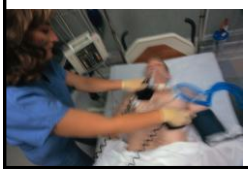
American Heart Association (2010)

Important Information to Determine Inclusion

- Witnessed or unwitnessed?
- How long down before CPR initiated?
- Initial rhythm?
- Defibrillated? How many times?
- Time of ROSC?
- Total time from collapse to ROSC?

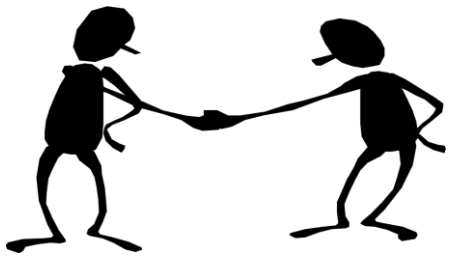
More Important Information

- Advanced Directive?
- Allow natural death? DNR?
- Dementia?
- Emesis during intubation?



- LOC after ROSC?
- Pre-hospital 12-Lead ECG?
  - ST segment ↑
  - QT prolongation?
- Medications given in the field?
  - Sedation?
  - Paralytic?
  - Amiodarone?
  - Chilled NS started?
  - Ice packs in place?

EMS→ ED Communication



Cooling the Patient

- Cooling Adjunct Therapies
- Surface Cooling
- Endovascular Cooling

Time to Target Temperature

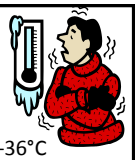
- Inclusion: all cardiac rhythms; in-hospital & pre-hospital CA; ROSC ≤ 60 minutes; CPR within 20 minutes of collapse
- **Results:** Showed time to target temperature to be an independent predictor for good outcome.
- Patients with good outcomes demonstrated a greater drop in T after 1 hour & reached target temp faster

Wolff et al (2008)

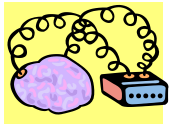
Induction of TH

- Initial temperature & temperature monitoring
- Chilled Normal Saline (NS)
  - Supported by many studies: Bernard (2008); Kim et al (2007); Larsson & Rubertsson (2010)
  - 30-40ml/kg, up to 2 liters, of 4°C NS
  - Infuse over 30-60 minutes
  - Decreases core temperature by 1.6-2°C
- Ice Packs

Induction Phase



- Controlling shivering
  - Most likely to occur when core Temp. 34-36°C
  - Wrap hands/feet in warm blanket; Bair hugger
  - Propofol
  - Neuromuscular Blocking Agents (NMBA)
    - Before cooling
    - During cooling
    - During rewarming
    - EEG monitoring



Induction Phase

- Sedation

  - Initiate prior to giving a paralytic
  - Fentanyl infusion (usual dose range 25-200 mcg/hour)
  - Midazolam infusion (usual dose range 1-7 mg/hour)

Case Study

- 30 yo female, 2 weeks post-partum
- 12/22/10 Went to Patient First with chest pains
- Had a seizure at Patient First; MD administered 2 mg Ativan
- Patient went into cardiac arrest 1 min. later
- CPR; EMS called 2144; EMS arrived 2154
- Polymorphic VT initial rhythm
- Defibrillated 200 joules

Case Study, cont

- 2220 Patient unresponsive post-ROSC; GCS 3
- 2220 On the way to the hospital, RSI performed to protect the patient's airway
- Medications administered
  - 2220 Magnesium 2 mg
  - 2230 RSI: Vecuronium 7 mg; Versed 3 mg

Case Study, cont

- 2237 In ED, patient unresponsive
- CT done
- Code Ice called
- Ice packs applied
- Total of 2 L chilled NS administered
- K+ 2.5 on admission
- Initial T 97.7 ®
- Endovenous catheter inserted
- Consults
  - Cardiology
  - Pulmonology
  - Neurology

Case Study, cont.

- 12/23, 0017 to CCU
  - 0200 95.9 ®
  - 0300 93®
- Cooled for 24 hours
- Re-warmed
- Extubated 12/24
- Transferred to floor 12/26
- Discharged to home 12/30
- Returned in January for Cardiac Cath & EP studies
  - EF 40%
  - EP study negative

Maintenance Phase

- Monitoring for complications
- "Cold" diuresis
- Electrolyte shifts
  - Potassium
  - Magnesium
  - Ionized calcium
  - Phosphorous
- Cardiac Dysrhythmias

Maintenance Phase

- Insulin Resistance & Hyperglycemia
  - Hyperglycemia common in diabetic & non-diabetic patients following CA
  - ↓ insulin sensitivity; ↓ insulin secretion; ↑ fat metabolism
  - Survival to discharge higher in non-diabetic patients
  - Target moderate glycemic control: 144 to 180 mg/dL
  - Avoid hypoglycemia

Beiser, et al. (2009). *Resuscitation*

Maintenance Phase

- Other complications to monitor for during TH
  - Bleeding: impaired platelet aggregation; ↑ clotting times
  - Infection: Pneumonia
  - Skin breakdown if surface cooling
  - ↓ metabolism
  - CV: VT/VF; atrial fibrillation; Prolonged PR, QRS, QTc; sinus bradycardia

Re-Warming Phase

- Passive versus active re-warming
- If active, slow process to avoid rebound hyperthermia
  - 0.25-0.5 C per hour recommended
  - Risk of poor neurologic outcome ↑'s for each degree of body temperature over 37 C
- Risk of hyperkalemia
- Shivering

Prognostication in TH Patients

- TH has improved outcomes in 1 of 6 patients
- No studies exist that detail the prognostic accuracy of the neurological examination in TH patients
- Early withdrawal of life support may not be in the best interests of TH patients & families.

Neumar, et al. (2008). *Circulation*
Peberdy et al. (2010). Circulation

Outcomes: Cerebral Performance Categories (CPC)

- **CPC 1: Full Recovery**
  - conscious and alert; able to work and to lead a normal life
- **CPC 2: Moderate disability**
  - Conscious; able to work at least part time, and independent for their ADL, with or without neurologic manifestations such as hemiplegia, seizures, ataxia, dysarthria, dysphagia, or permanent memory or mental changes

Wolfrum et al. (2008). *Critical Care Medicine, 36*(6), p. 1783

Outcomes: Cerebral Performance Categories (CPC)

- **CPC 3: Severe disability**
  - conscious, but fully dependent on others for daily support because of severely impaired cognitive function; these patients are discharged to institutions or long-term rehabilitation facilities
- **CPC 4: Persistent vegetative state**
- **CPC 5: Death**

Wolfrum et al. (2008). *Critical Care Medicine, 36*(6), p. 1783

CJW Medical Center Hypothermia Protocol

Inclusion Criteria

- VT/VF cardiopulmonary resuscitation, PEA or asystole post-cardiac arrest with ROSC & persistent coma as evidenced by no eye opening
- Estimated interval of **10 minutes** or less from patient collapse to first resuscitation attempt
- An interval of ≤ equal to 25 minutes (PEA/Asystole) or 60 minutes (VF/pulseless VT) from collapse to ROSC
- Age 18 years or older
- Time of initiation of hypothermia < 6 hours ROSC
- MAP >60 mmHg either spontaneously or with fluids & vasopressor

Exclusion Criteria

- Comatose state prior to arrest
- Pre-existing DNR status
- Metastatic cancer or other terminal illness
- Active sepsis
- Active severe bleeding
- Platelet count < 50 K
- Non-intubated patient
- Pregnancy

Mrs. D.

- In the ED:
  - "Code Ice" called
  - VS: T 96.2®
  - Ice packs placed
  - Chilled NS infusion initiated
  - King LT replaced with ETT
  - Central line placed
  - OG & foley placed
  - Labs sent
  - AMI work up done: ECG (QTc 503ms); enzymes
  - Consults to neurology & pulmonology
  - Propofol initiated
  - Repeat T after NS: 93.1®

Mrs. D

- Transferred to CCU
- Surface cooling with sleeves initiated
- Frequent VS monitoring
- SB, no ectopy
- Re-warmed without complications
- EF 55-60% the day after CA
- Cardiac cath: no significant disease
  - 2/3 of SCA deaths occur in people without any prior indications of heart disease
- ICD placed to prevent recurrence of sudden death
- Discharged 13 days after CA with CPC 1

Life-saving treatments for SCA

- **Automatic External Defibrillators (AEDs)** can increase the survival rate for SCA up to 90% by delivering a life-saving shock within the first few minutes of an attack, but they are still not widely available and people often do not know how to use them.
- **Implantable Cardioverter Defibrillators (ICDs)** are 98% effective at protecting those at risk for SCA, but only 35% of patients who could be helped by one, have them.

Source: http://www.stopcardiacarrest.org/about-sudden-cardiac-arrest/general-information.aspx

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Questions?

Beth Torres, PhD, RN, CCRN

CJW Medical Center

Beth.Torres@hcahealthcare.com