New Developments in Cardiopulmonary Arrest: Therapeutic Hypothermia in Resuscitation

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Emergency Medicine
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Case Presentation

- **3:40 (+ 6:00 minutes) – Columbus EMS Medic 7 arrived at victim**
- **Initial rhythm: VF**
- **3:42 (+ 8:00 minutes) – Shock once**
- **In coma**
- **Intubated & given amiodarone**

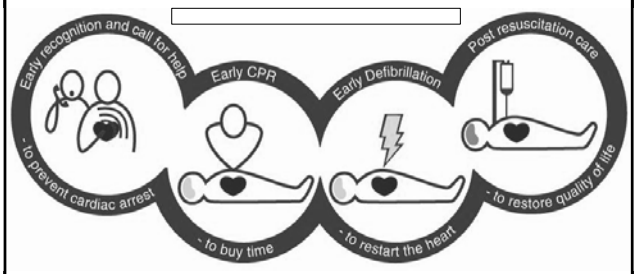
Case Presentation

- **Oct 11, 2007, 3:25 PM**
- **Ohio State student, E.H. left calculus class.**
- **3:34 – Collapsed on grass outside.**
- **Nurse walking by began aggressive chest compressions.**
- **3:35 – 9-1-1 called.**
- **3:36 – Ambulance dispatched.**

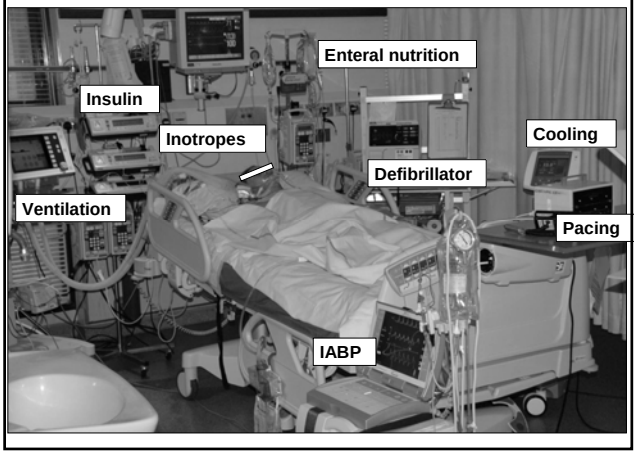
Cooling

- **Began therapeutic hypothermia**
- **Warmed 24 hours later**
- **Visited patient in hospital on post-arrest day 3…**

Chain of Survival



Nolan J. Resuscitation 2006; 71: 270-1



Objectives

- **Describe clinical efficacy for therapeutic hypothermia for comatose victims of cardiac arrest**
- **Detail the methods for inducing therapeutic hypothermia**
- **Review the political barriers to implementing a therapeutic hypothermia protocol**

Hospital Care Matters

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journal homepage: www.elsevier.com/locate/resuscitation

Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest☆,☆☆

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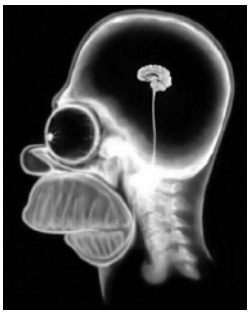
Brain Temperature Control

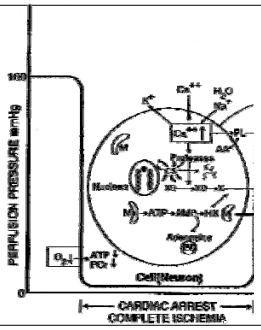
- **Prevention of hyperthermia**
  - ✓ **Hyperthermia common for 2-3 days**
    - **Takino M. Intensive Care Med 1991;17:419-20**
  - ✓ **Hyperthermia associated with poor outcome**
    - **Zeiner A. Arch Intern Med 2001;161:2007-12**
    - **Hickey RW. Crit Care Med 2003;31:531-5**
- **Therapeutic hypothermia**

Saving the Brain

- **Cerebral perfusion**
- **Sedation**
- **Control of seizures**
- **Glucose control**
- **Temperature control**



Hypothermia: Mechanism of action?



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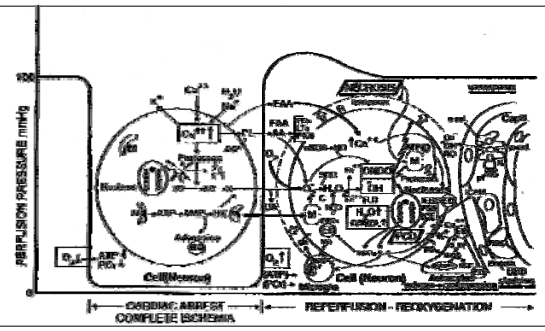
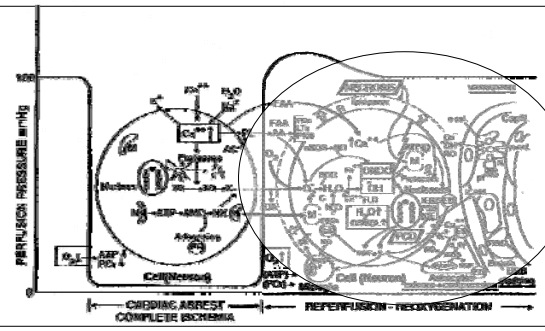


Hypothermia: Mechanism of action?

- **Suppression of free radicals**
- **Blocking pathological protease cascades**
- **Suppression of apoptosis (48 h)**
- **Suppression of pro-inflammatory cytokines (5 days)**

Polderman K. Lancet 2008;371:1955-69

Hypothermia: Mechanism of action?

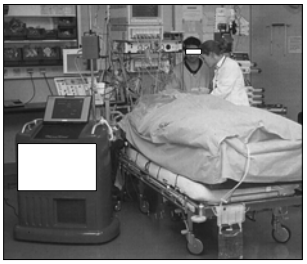


Scientific Evidence

Number Needed to Treat

- **Plavix for STEMI: NNT = 23 (composite endpoint)**
- **PCI vs tPA for STEMI: NNT = 100 (mortality)**
- **Statins for ASCVD: NNT between 163 – 639 (mortality per yr of therapy)**
- **Therapeutic hypothermia for comatose VF survivors: NNT = 6 (good neuro outcome)**

HACA Study Cooling Technique



- **External cooling (ED)**
- **32-34ºC for 24 hr**
- **Cooling tent +/- ice packs**
- **Passive rewarming over 8 hours**
- **Pancuronium**
- **Bladder temperature**

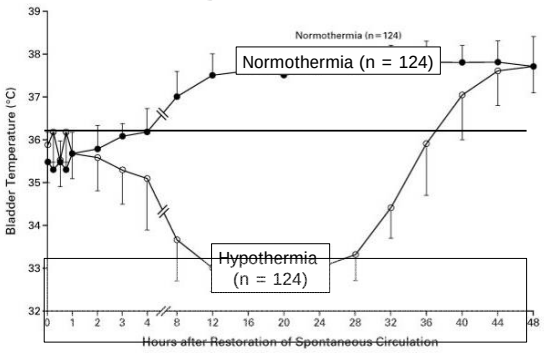
The New England Journal of Medicine

VOLUME 346 FEBRUARY 21, 2002 NUMBER 8

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

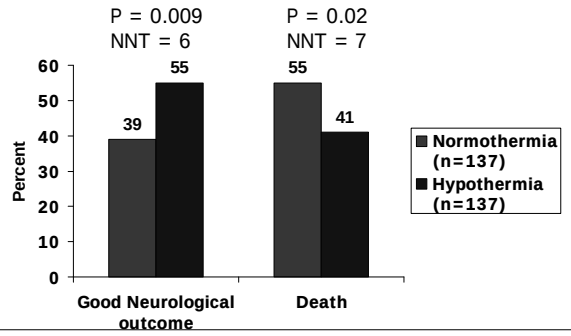
THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

Cooling was Slow



N Engl J Med 2002; 346: 557-63

The Hypothermia After Cardiac Arrest (HACA) Study Group



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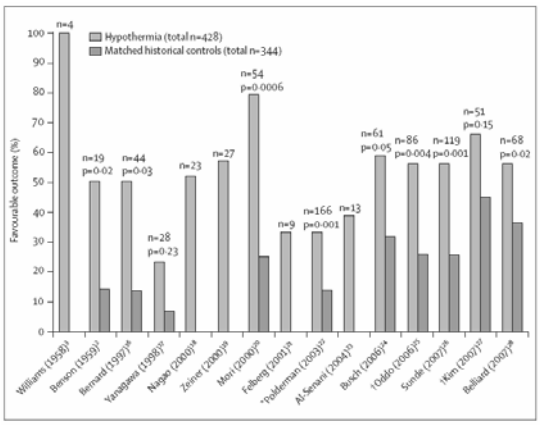

Polderman K. Lancet 2008;371:1955-69

Therapeutic hypothermia after cardiac arrest

An Advisory Statement by the ALS Task Force of the International Liaison Committee on Resuscitation (ILCOR)

- **Unconscious adult patients with spontaneous circulation after out of hospital cardiac arrest should be cooled to 32-34°C for 12-24 hours when the initial rhythm was VF**
- **For any other rhythm, or cardiac arrest in hospital, such cooling may also be beneficial**

Nolan J. Resuscitation 2003; 57:231-5

Exclusions (relative)

- **Severe systemic infection**
- **Severe cardiogenic shock (SBP< 90 mmHg despite inotropes)??**
  - ✓ **But: Skulec R. Acta Anaesthesiol Scand 2008;52:188-94**
- **Established multiple organ failure**
- **Pre-existing medical coagulopathy**

Speed of Cooling May Matter

ELSEVIER

International Journal of Cardiology 133 (2009) 223–228

International Journal of Cardiology

www.elsevier.com/locate/ijcard

Early achievement of mild therapeutic hypothermia and the neurologic outcome after cardiac arrest

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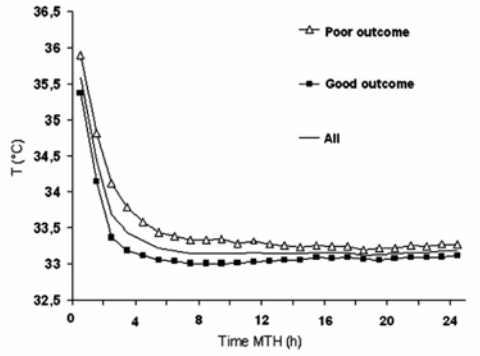


Fig. 1. Time course of MTH among patients with good and poor neurologic outcome. The curves indicate the course of mean body core T during MTH among patients with good and those with poor outcome as well as in the entire patient group.

Early Cooling and Outcome

- **49 consecutive patients cooled with invasive cooling (Alsius system)**
- **78% OHCA; 84% VF/VT**
- **28/49 (57%) good outcome = CPC 1 or 2**
- **Multivariate analysis: time to target temperature = OR 0.69 (0.51 – 0.98) for good outcome per hour**

Wolff B. Int J Cardiol 2008

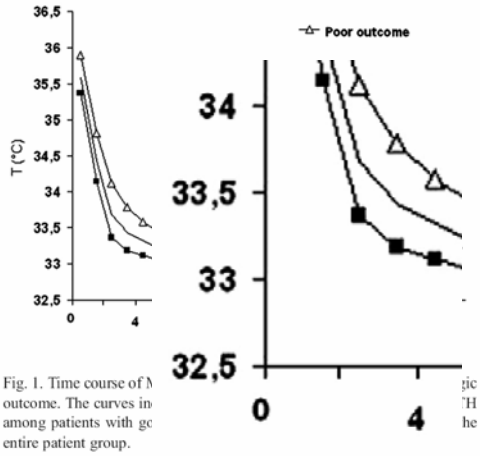
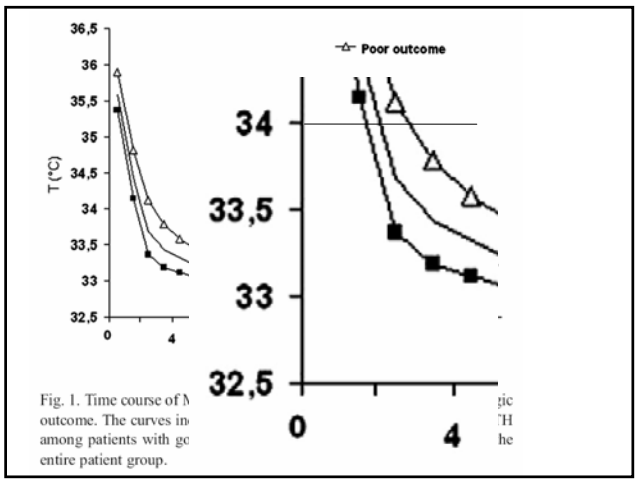


Fig. 1. Time course of M
outcome. The curves in
among patients with go
entire patient group.



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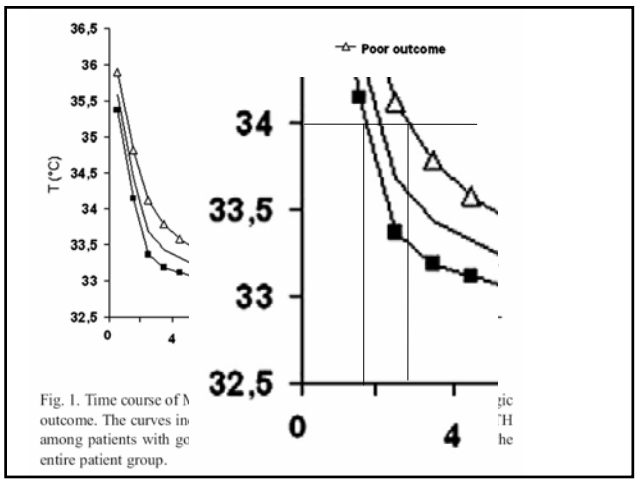
Prehospital cooling versus emergency department cooling

- **VF cardiac arrest (n = 234)**
- **2 L cold saline prehospital vs. ED**
- **Temperature**
  - ✓ **Before saline = 35.8ºC**
  - ✓ **On ED arrival = 34.4ºC versus 35.9ºC**
- **Survival to discharge 48% (EMS) versus 51% (ED)**

Bernard S. Presented at ReSS 2008 New Orleans



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The Hard Part

Inducing Hypothermia

Phases of Hypothermia

- **Induction – get to < 34°C rapidly**
- **Maintenance phase – tight control (maximum fluctuation 0.2 – 0.5°C)**
- **Rewarming phase – slow 0.25°C h^{-1}**
  - ✓ **Deranged cerebrovascular reactivity if > 37°C – Lavinio A. BJA 2007;99:237-44.**

Polderman KH. Crit Care Med 2009;37:1101-20

Induction of Cooling

- **2 liters of ice cold saline kept in refrigerator**

Cooling Techniques

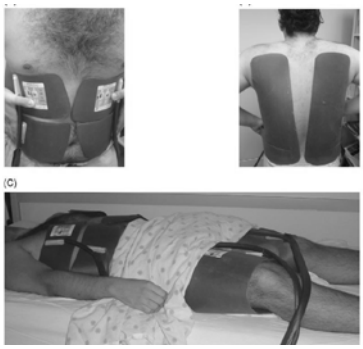
External	Internal
✓ Ice packs, wet linen, fans	✓ Cold IV saline
✓ Cooling blankets • Air, e.g. Polar Air • Water, e.g. Blanketrol	✓ Intravascular catheters • Intravascular balloons • Metal catheter • Helix system
✓ Pre-refrigerated cooling pads	
✓ Hydrogel-coated pads	
✓ Cold water immersion	

Polderman KH. Crit Care Med 2009;37:1101-20

External Cooling

Laerdal MediCool

Water-circulating Surface Cooling Device (Arctic Sun□)



Circulating cold water blankets

Arctic Sun vs Standard Cooling blankets & ice bags

- **Multicenter, randomized trial with cooling blankets and ice (n=30) or the Arctic Sun (n=34)**
- **Subjects cooled <34°C target at 4 hours = 71% (Arctic Sun) vs 50% (standard cooling group, p=0.12).**
- **Median time to target was 54 minutes faster in the Arctic Sun group than the standard cooling group (p<0.01).**
- **Survival rates with good neurological outcome were similar; 46% of Arctic Sun patients and 38% of standard patients had a cerebral performance category of 1 or 2 at 30 days (P=0.6).**

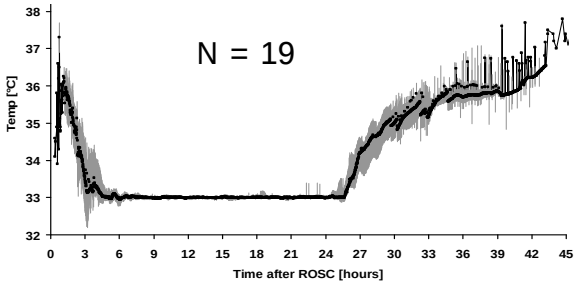
Heard K, et al., AHA Scientific Sessions 2007

External techniques: Overcooling is frequent

- **Retrospective review of 32 cases**
- **Surface cooled to target of 32-34ºC**
  - ✓ **20/32 (63%) < 32ºC**
  - ✓ **9/32 (28%) < 31ºC**
  - ✓ **4/32 (13%) < 30ºC**
- **Rebound hyperthermia (>38ºC) at 12-18 h after rewarm in 7/32 (22%)**

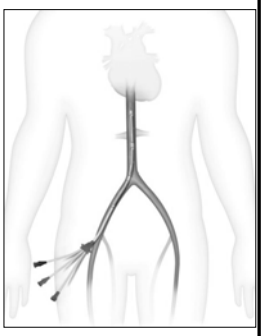
Merchant RM. Crit Care Med 2006; 34: S490-4

Endovascular cooling after cardiac arrest



Sterz F. Curr Opin Crit Care 2003; 9: 205-10

Endovascular Cooling



Therapeutic Hypothermia: Physiological effects / complications

- **Shivering**
- **Vasoconstriction**
- **Bradycardia**
- **Infection, coagulopathy**
- **Diuresis - hypovolemia**
- **☐ K^+, ☐ Mg^+, ☐ Ca^{2+}**
- **☐ Insulin sensitivity**
- **Impaired GI absorption**

Polderman KH. Crit Care Med 2009;37:1101-20

Prevent Shivering:

- NMBA may be used
  - Eliminates thermoregulatory defense mechanisms
  - If used:
    - Paralytic infusion may be discontinued when temp is 34 °C (93.2 °F)
    - If shivering occurs, then neuromuscular blockade should be resumed
    - No need to do Train of Four, it's not accurate in the hypothermic patient
- Sedation
  - Typically used, with or without NMBA
  - Given continuously

Monitor Temperature

- Continuously Monitor Temperature with Core temp probes
  - Esophageal
  - Pulmonary artery
  - Bladder probe
- Also use a secondary temperature to monitor
- Frequency
  - Every 30 minutes during cooling and rewarming
  - Every hour during maintenance

Prevent Shivering:

- Caution with maintenance dosing of sedatives and NMBA's, as clearance decreases with hypothermia
- Lower doses needed in elderly due to blunted counter-regulatory response

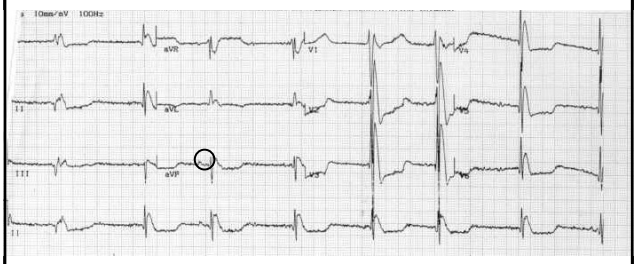
Cardiovascular Effects

- Mild bradycardia and increase in BP
  - ✓ No treatment typically required
- CO decreased by 25-40%
  - ✓ Largely due to decreases in heart rate
  - ✓ Contractility typically increases
  - ✓ Supply-demand balance for O2 usually maintained or improved
- Peripheral vasoconstriction
  - ✓ Obtain good vascular access prior to cooling

Cardiovascular Effects

- **"Cold diuresis"**
  - ✓ **Due to vasoconstriction-induced shift of intravascular volume into central circulation**
  - ✓ **Can result in hypovolemia, particularly during induction phase**
- **Significant risk for severe arrhythmias occurs at temps below 28-30°C**
  - ✓ **Arrhythmias low risk until temp drops below 30°C**
    - **A-fib, then V-fib**
    - **Myocardium less responsive to treatment of defibrillation**

EKG Changes



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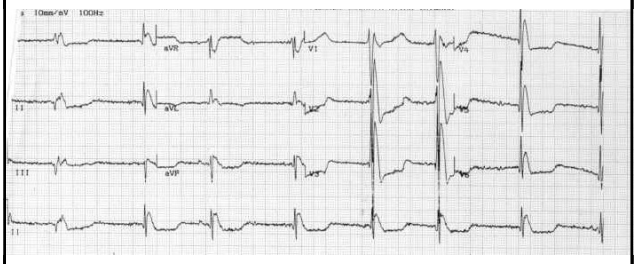

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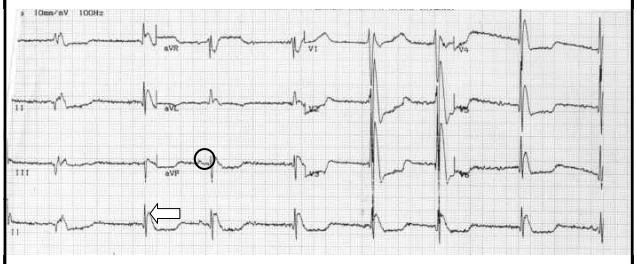

Electrolyte Disorders

- Changes to cellular homeostasis
  - Related to dysfunction of electrolyte pumps causing intracellular shifts
  - Risk greatest in induction phase
- ↓ K^+, ↓ Mg^+, ↓ Ca^{2+}
- ↓ Insulin sensitivity and production
- Careful monitoring

Other Issues

- Bedsores
  - ✓ Prolonged exposure to ice packs and peripheral vasoconstriction increases risk
- Nutrition
  - ✓ Enteral feeding should be decreased or stopped

Ventilatory Derangements

- Hypothermia affects ABG analysis
  - ✓ ABG machines warm sample to 37°C
  - ✓ Overestimates PaO2 and PaCO2
  - ✓ Underestimates pH
- Important to examine temperature-corrected values to avoid hypoxemia or significant alkalosis

Rewarming

- Rewarming phase – slow 0.25°C h^{-1}
  - ✓ Deranged cerebrovascular reactivity if > 37°C
    - Lavinio A. BJA 2007;99:237-44.
- Concerns
  - ✓ Vasodilation
  - ✓ Rebound electrolytes
  - ✓ Cardiac arrhythmias

Inducing Hospitals to Give Hypothermia

Therapeutic Hypothermia Web Resources

www.med.upenn.edu/resuscitation/hypothermia/

Protocol is Essential

Medical Center

Induced Hypothermia After Cardiac Arrest

Algorithm 1: Criteria, Cautions, and Preparation

Rationale: Use of hypothermia treatment in patients following cardiac arrest lessens the chance of ischemic brain damage and leads to improved neurological outcomes at 6 months.

GOALS / TIMELINE

- Initiate hypothermia within 6 hours of cardiac arrest.
- Sustain hypothermia for 24 hours from time of initiation of cooling to a body temperature of 32-34° C (89.6-93.2° F)
- After 24 hours of cooling, begin rewarming at a rate of 0.3–0.5° C (0.5–0.9° F) every hour up to a target of 36° C (96.8° F)

Criteria for Induced Hypothermia

Local Expertise Helpful

- **Physician who can provide phone or in person consultation to teach.**
- **Nurse with similar expertise is also desirable.**
- **After treating 2 patients, staff uniformly is impressed.**

Therapeutic Hypothermia: Summary

- **Mild hypothermia for VF OHCA supported by 2 RCTs**
- **Lower level evidence for other groups**
- **Target temp, cooling rate, duration??**
- **Surface versus internal**
- **Implementation has been slow**