Cooling the Cardiac Arrest Patient

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Disclosures

- None

Outline

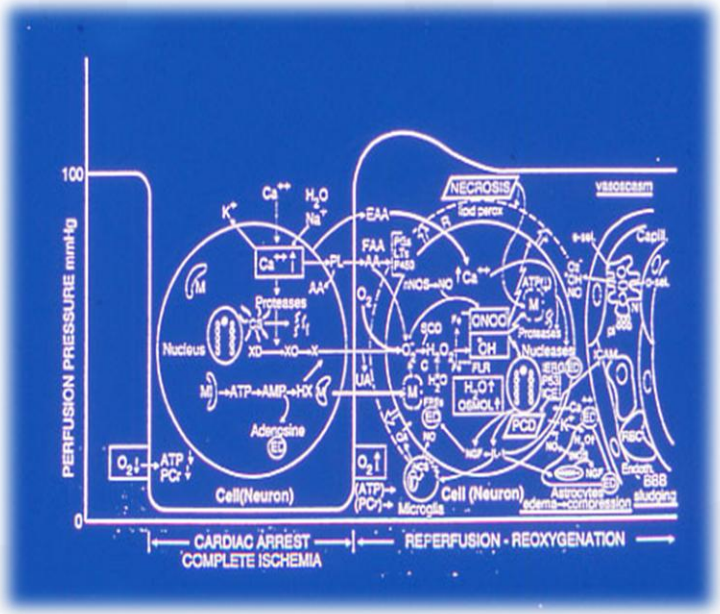
- ***Rationale for Therapeutic Hypothermia***
- ***Supportive Evidence***
- ***Patient Selection***
  - VT/VF Arrests
  - Non-VT/VF Populations
  - Witnessed vs. Un-witnessed Arrests
- ***Timing of Therapy***

RATIONALE AND EVIDENCE

Anoxic Brain Injury

- **NO FLOW STATE**→ minimal injury in 1st hour following cardiac arrest
- Majority of brain injury occurs during ***REPERFUSION***

- Reperfusion
  - » Free radical production
  - » Anti-oxidant depletion
  - » Enzyme dysfunction
  - » Apoptosis



Failure of Single-Target Drugs

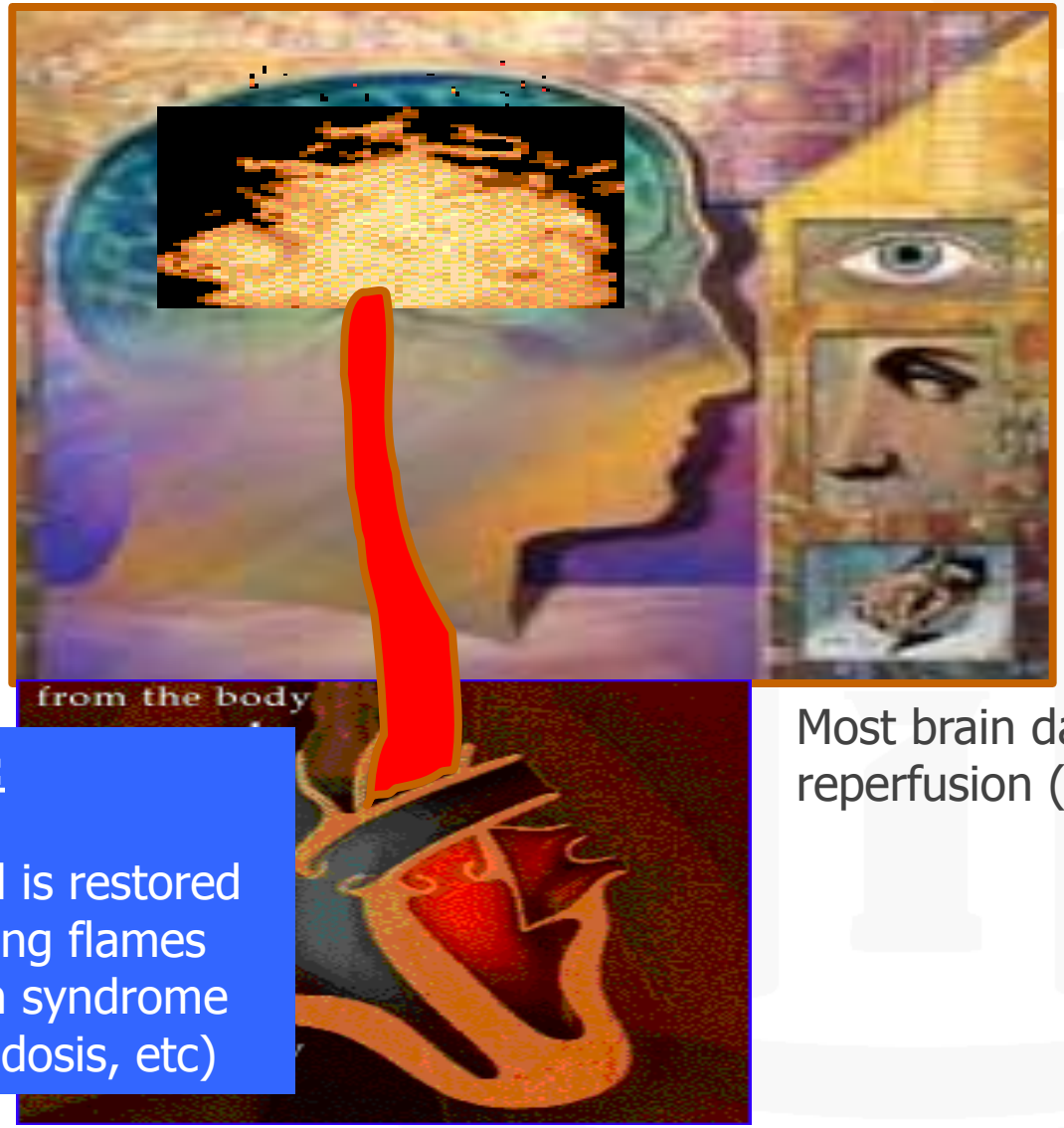
American Stroke Association®
A Division of American Heart Association

Ginsberg, M. D. Stroke 2009;40:S111-S114

Normal brain
Normal blood flow

Ischemia Occurs

Brain is injured and ***NEEDS HELP!***



REPERFUSION:

Warm toxic blood is restored
Triggers smoldering flames
Post resuscitation syndrome (free radicals, acidosis, etc)

Most brain damage during reperfusion (window of Rx)

Courtesy of Laurence Katz, MD, FACEP

THERAPEUTIC HYPOTHERMIA

PUTS THE FIRE OUT!

Courtesy of Laurence Katz, MD, FACEP

HOW DOES IT REALLY WORK

- Decreases metabolic demands in **ALL** organs → Brain, heart, kidneys, gut,…
- Decreases all reperfusion pathways (especially free radical production)
- Activates adaptive protective mechanisms (e.g. pre-conditioning) – similar to *hibernation*
- Decreases intracranial pressure

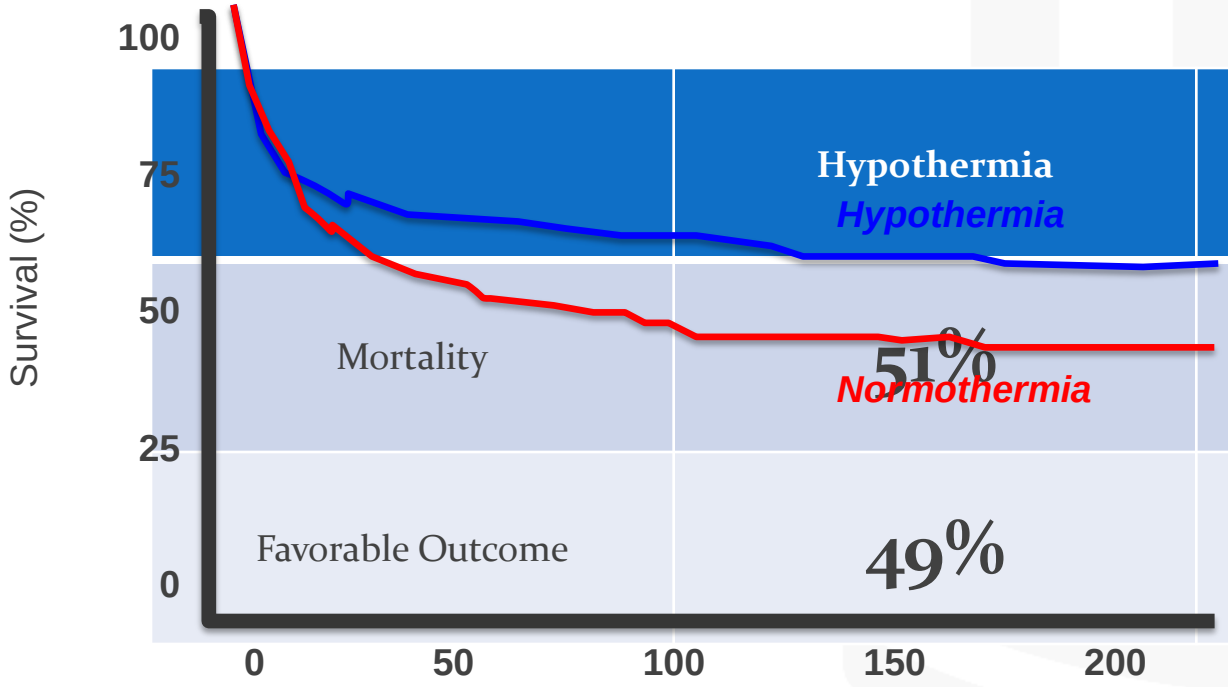
IMPACT OF HYPOTHERMIA ON THE REST OF THE BODY?

Decreased heart rate
Increased systemic vascular resistance (SVR)
Decreased cardiac output (but stroke volume is usually preserved)
Increased renal blood flow → *diuresis*
Increased K+ uptake into cells → *hypokalemia*
Decreased phosphate concentrations
Impacts acid/base status → *decreased CO_2 production*
Decreased plasma insulin → *hyperglycemia*
Platelet activation, enhanced aggregation
Coagulopathy - prolonged PT, PTT
Arrhythmia
Infection

THE EVIDENCE

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.



	Hypothermia	No Hypothermia
Mortality	41%	55% (p = 0.009)
Favorable Neurologic Outcome	55%	39% (p=0.02)

(p=0.046)

NEJM 2002; 346.

THE EVIDENCE

- *Number Needed to Treat* →

Aspirin in Acute MI = 42

ICD Implantation after VT/VF Arrest = 13

Lung-Protective Ventilation in ARDS = 12

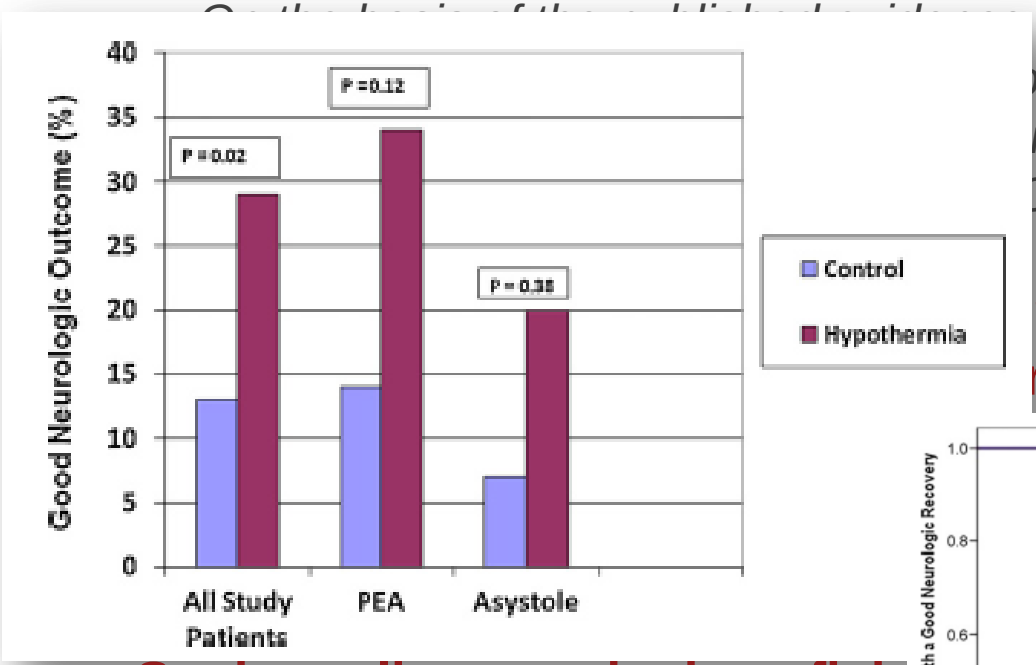
Revascularization in MI Complicated by Shock = 8

Therapeutic Hypothermia in Cardiac Arrest = 6 (95% CI 4-13)

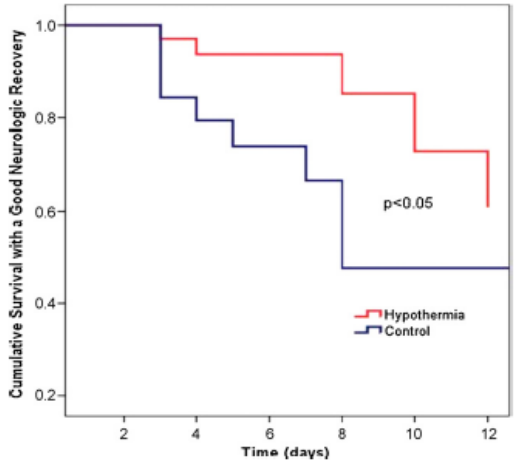
PATIENT SELECTION

ILCOR Recommendations

...to date, the ...orce of the ...itation (ILCOR) ...October 2002:



...pontaneous ...rdiac arrest



- **Such cooling may be beneficia...**
  or in-hospital cardiac arre...

Lundby JB et al. Resuscitation 2012;83:202-7.

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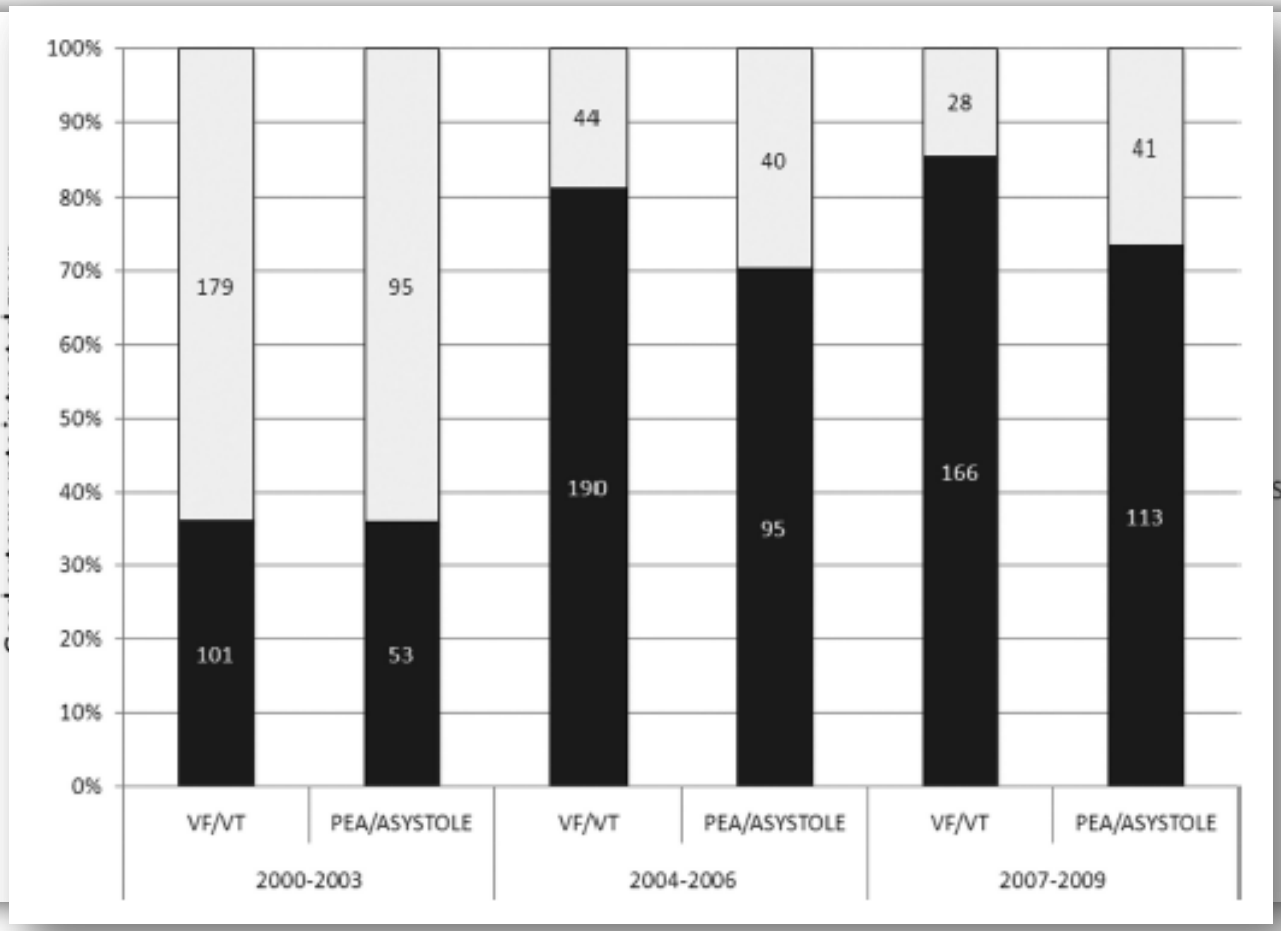
- **Such cooling may be beneficial for other rhythms or in-hospital cardiac arrest (Class IIB)**



Adjusted OR for Hypothermia in PEA/Asystole = 0.71 (95% CI 0.37-1.36)

Dumas F et al. Circulation 2011;123:877-86.

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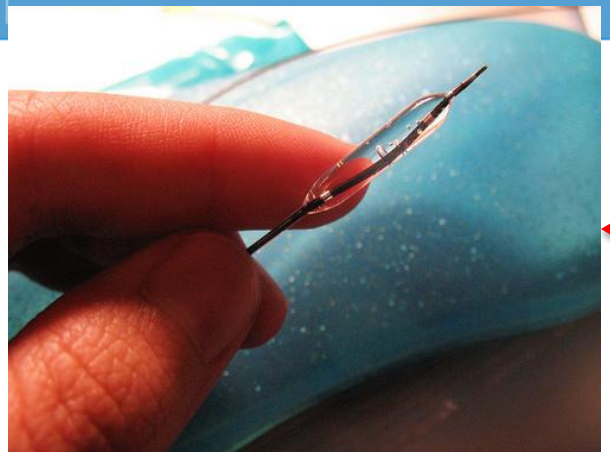
WITNESSED VS. UN-WITNESSED

- Majority of observational studies [illegible]se outcomes for un-witnessed arrests

[illegible]R OWN INSTITUTIONAL EXPERIENCE…..

NO UN-WITNESSED ARRESTS HAVE SURVIVED TO HOSPITAL DISCHARGE

TIMING IS EVERYTHING! *RIGHT?*

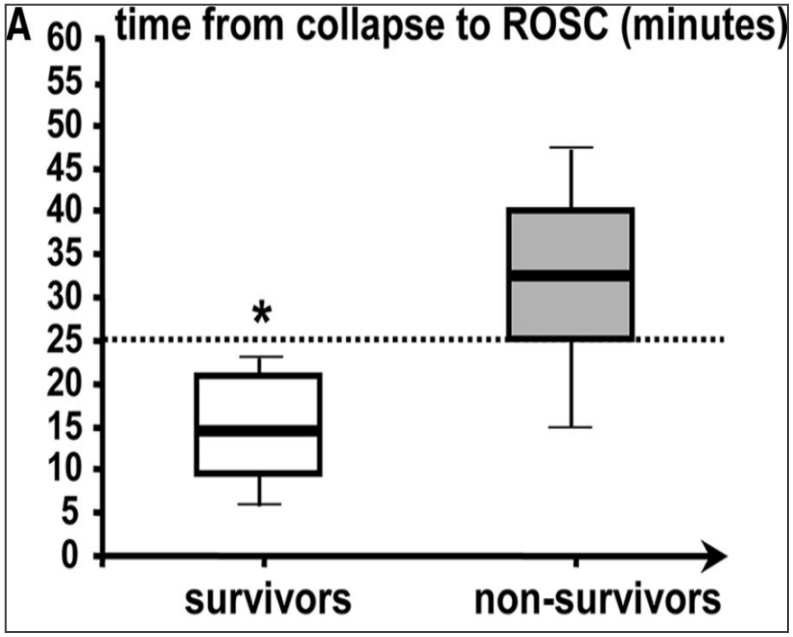


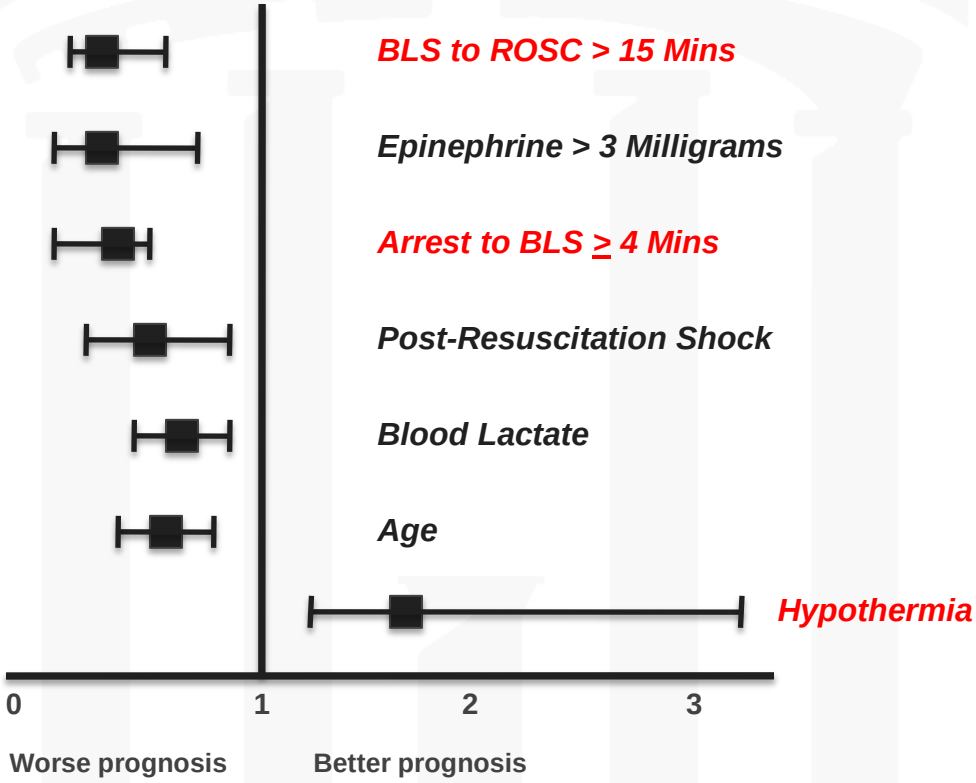
Door-to-Balloon

Prompt Intervention Is Imperative

Door-to-Ice??

TIMING OF RESUSCITATION





Time from collapse to ROSC ≤25 mins
OR for survival = 45.1, p<0.001

Oddo M et al. Crit Care Med 2008;36:2296-301.

Dumas F et al. Circulation 2011;123:877-86.

What about timing of hypothermia??

TIMING OF *HYPOTHERMIA*

	Unadjusted				Adjusted[a]			
	OR	SE	95% CI		OR	SE	95% CI	
Time from arrest to TH (5 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.02	0.02	0.99	1.06	1.04		99	1.08
CPC 3–5: Poor	1.03	0.13	1.01	1.06	1.06		02	1.11
Time to target temperature (30 min increments)								
CPC 1: Good	1.00							
CPC 2: Moderate	1.05	0.06	0.95					1.21
CPC 3–5: Poor	1.04	0.04						1.27
Duration target temperature maintained (h)								
CPC 1: Good	1.00							
CPC 2: Moderate								1.32
CPC 3–5: Poor								1.15

For every 5 min delay in hypothermia initiation, there was a 6% greater odds of poor vs. good outcome at hospital discharge

ternational Cardiac Arrest Registry

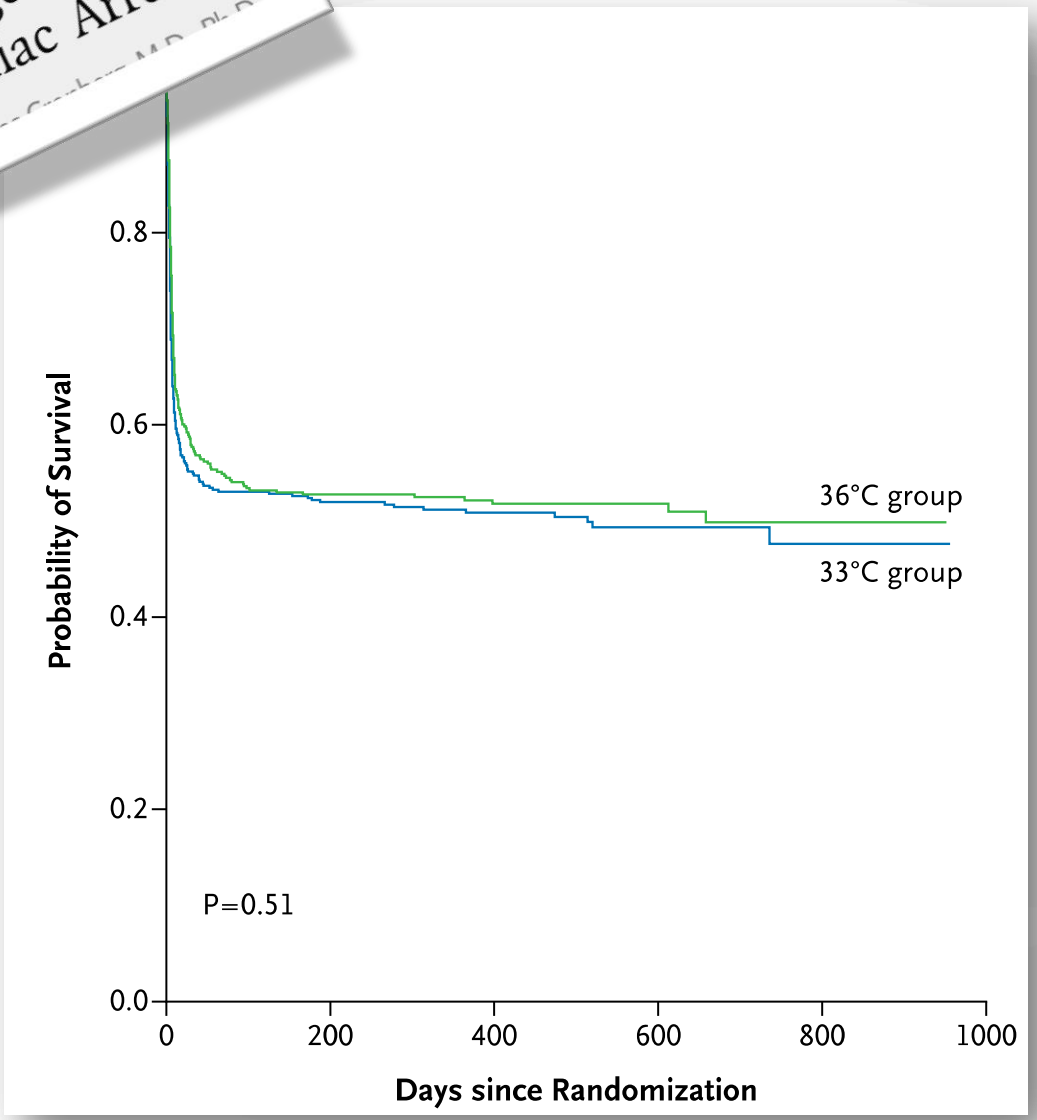
Sendelbach S et al. Resuscitation 2012. In press.

Recent Controversy?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest



Nielsen N, et al. NEJM 2013; 369.

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Processes of Care are Important!!

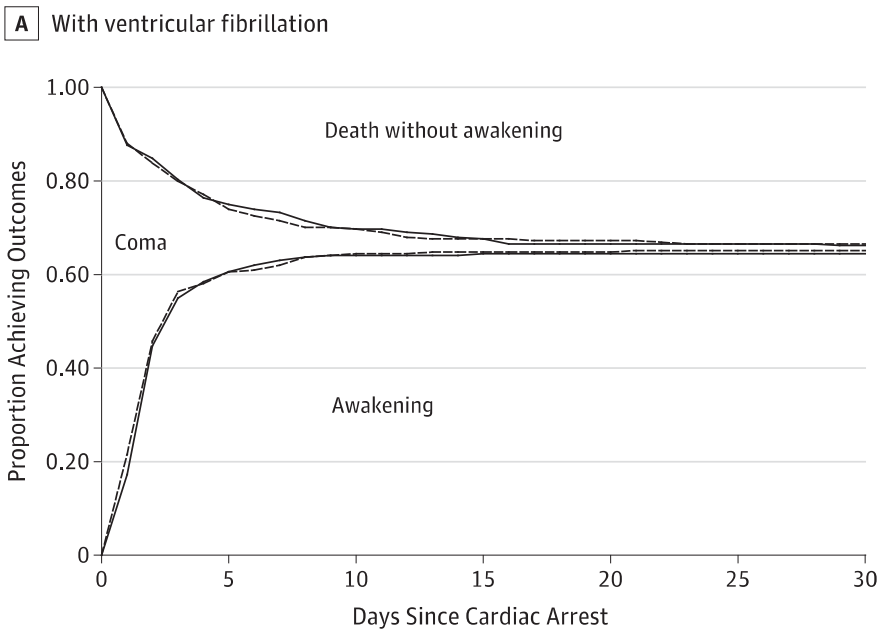
Does this Minimize the Impact of Hypothermia??

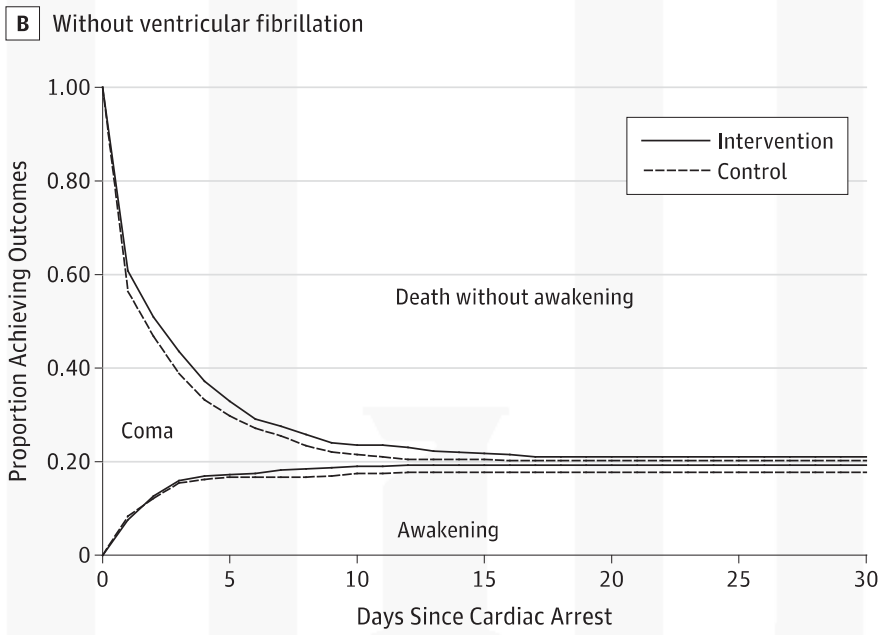
Bystander witnessed ca	420 (89)	418 (90)
Bystander perf	344 (73)	339 (73)
First		
	375 (79)	377 (81)
	349 (74)	356 (77)
sing ventricular tachycardia	12 (3)	12 (3)
Unknown rhythm but responsive to shock	5 (1)	5 (1)
Perfusing rhythm after bystander-initiated defibrillation	9 (2)	4 (1)
Asystole	59 (12)	54 (12)
Pulseless electrical activity	37 (8)	28 (6)
Unknown first rhythm, not responsive to shock or not shocked	2 (<0.5)	6 (1)
Time from cardiac arrest to event — min‡		
Start of basic life support		
Median	1	1
Interquartile range	0–2	0–2
Start of advanced life support		
Median	10	9
Interquartile range	6–13	5–13
Return of spontaneous circulation		
Median	25	25
Interquartile range	18–40	16–40

Original Investigation

Effect of Prehospital Induction of Mild Hypothermia on Survival and Neurological Status Among Adults With Cardiac Arrest

A Randomized Clinical Trial





Kim F, et al. JAMA 2014; 311.

Targeted Temperature Management is Still Important! Goal Temp Unclear!

Who Do We *Cool* at UNC?

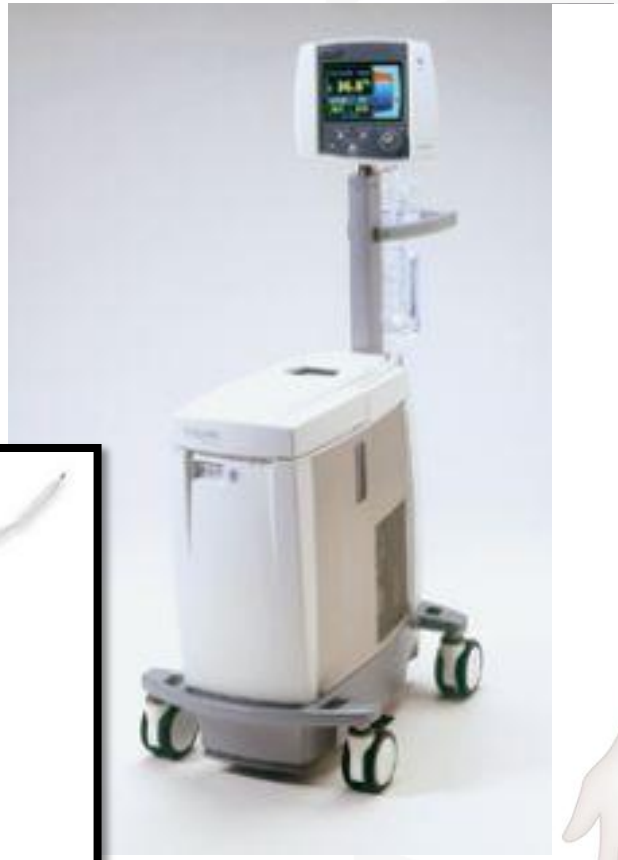
- Out-of-hospital (OOH) Cardiac Arrest
- All Rhythm Types
  - VT/VF
  - PEA
  - Asystole
- Witnessed AND Un-witnessed Arrests
- Initiated within 6hrs of ROSC

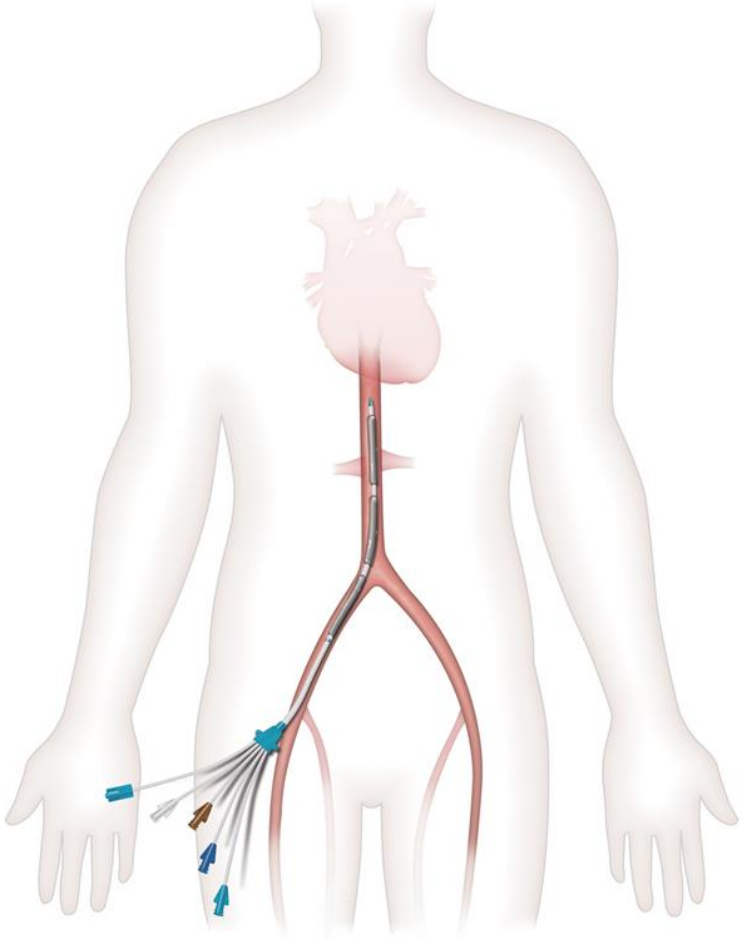
How to cool…

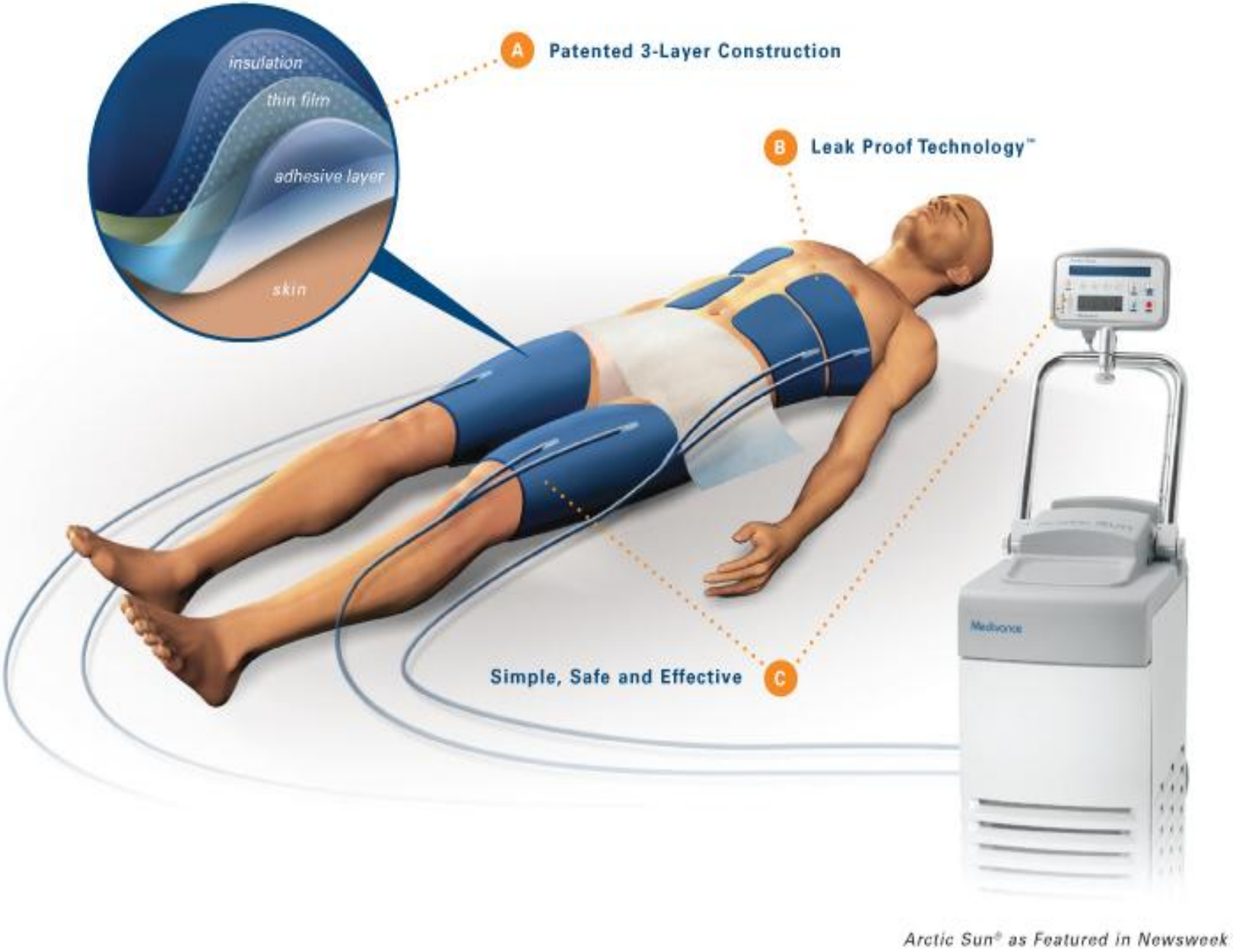
- **Low technology**
  - Intravascular cooled fluids
  - Surface application of ice
- **Intermediate technology**
  - Water-based cooling blankets
  - Air cooling methods
  - Water immersion
- **High technology**
  - Intravascular cooling catheters
  - Thermostat-controlled surface cooling systems
  - Trans-nasal aerosolized fluorocarbon

Low Technology Methods

Advanced Technology Methods







Arctic Sun® as Featured in Newsweek

UNC HEALTH CARE

Adult ICED (Induced Cooling to Eliminate Deficits) Protocol

Inclusion Criteria

- Out-of-hospital Cardiac Arrest
- CPR or Defibrillation within 15 Mins of Arrest
- Arrest to ROSC <60 Mins
- GCS <9
- Intubated/Mechanically Ventilated
- SBP >90 mmHg (with or without vasopressors)
- Age >16 yrs
- Hypothermia Initiated within 6 Hrs of ROSC

Exclusion Criteria

- Trauma, Head Injury, Drug OD, CVA, Sepsis
- DNR/DNI
- Initial Core Temperature <34 °C
- Life Expectancy <6 Months at Baseline
- Known Coagulopathy
- Uncontrolled Cardiac Dysrrhythmia
- Refractory Hypotension
- Pregnancy (Unless Consultation with OB/Gyn)

ECG, CXR, Head CT

Labs – Electrolytes, CBC, Coags, Cardiac Markers, Others

Activate STEMI Pager or Call Cath Team if Evidence of ST Elevation or Concern for Ischemic Substrate

Analgesia, Sedation, Paralysis

Fentanyl 1-2 mcg/kg IV q30 min or 2 mcg/kg/hr infusion
Midazolam 1-2 mg/hr IV q30 min or 0.125 mg/kg/hr infusion
Vecuronium 0.1 mg/kg IV bolus q30 min and prn (if needed)
ASA 325mg via NGT or PR

Initiate Hypothermia

Infuse 2L of Iced LR or NS IV (if not done by EMS or in ED)
Place Arctic Sun and Set Target Temp (33°C)
Place Central Line, Arterial Line

Maintenance of Therapy

Maintain MAP ≥80 mmHg with Fluids or Vasopressors
Blood/Urine Cultures
Electrolytes q4 hrs, Cardiac Markers
Obtain Temperature-Corrected ABGs
Continuous EEG if Concern for Seizures
DVT Prophylaxis, GI Prophylaxis

Re-Warming Protocol

Set Arctic Sun at 0.3 °C/hr
Ensure Adequate Hydration, Monitor for Vasodilatation
Monitor for Hyperkalemia
D/C Analgesia, Sedation, & Paralysis at 35-36 °C
Neurology Consultation for Prognosis (if necessary)

Quick Reference Guide 2011

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UNC Hypothermia Protocol

- **Induction:**
  - Cool to 33 C as rapidly as possible
- **Maintain** 33-33.5 C for 24 hours
- **Rewarm:**
  - Slowly (over 24 hours) to 35.5-36 C
  - Avoid complications (i.e. volume depletion, hypotension, hyperthermia, hyperglycemia)

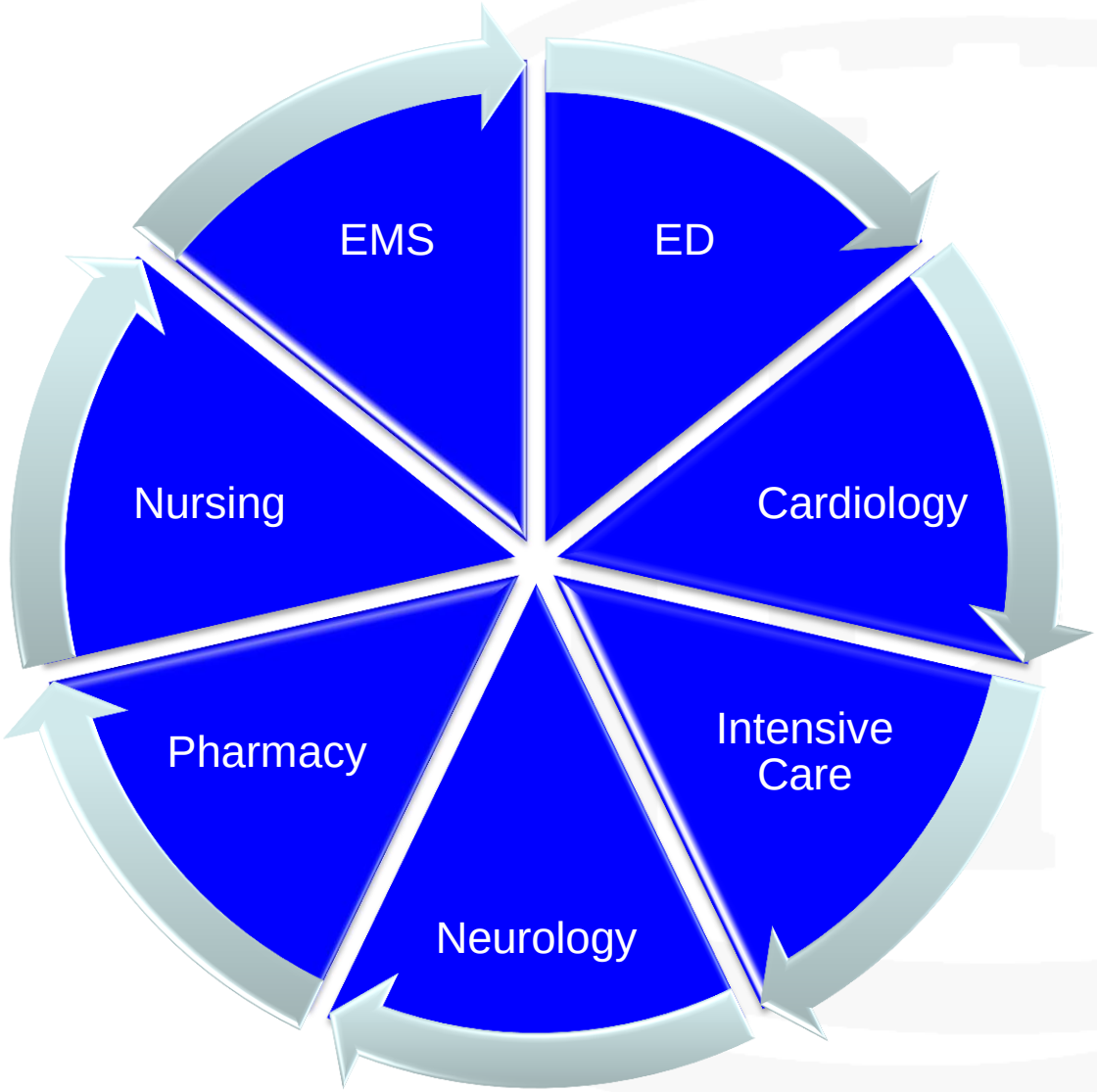
UNC Emergency Department

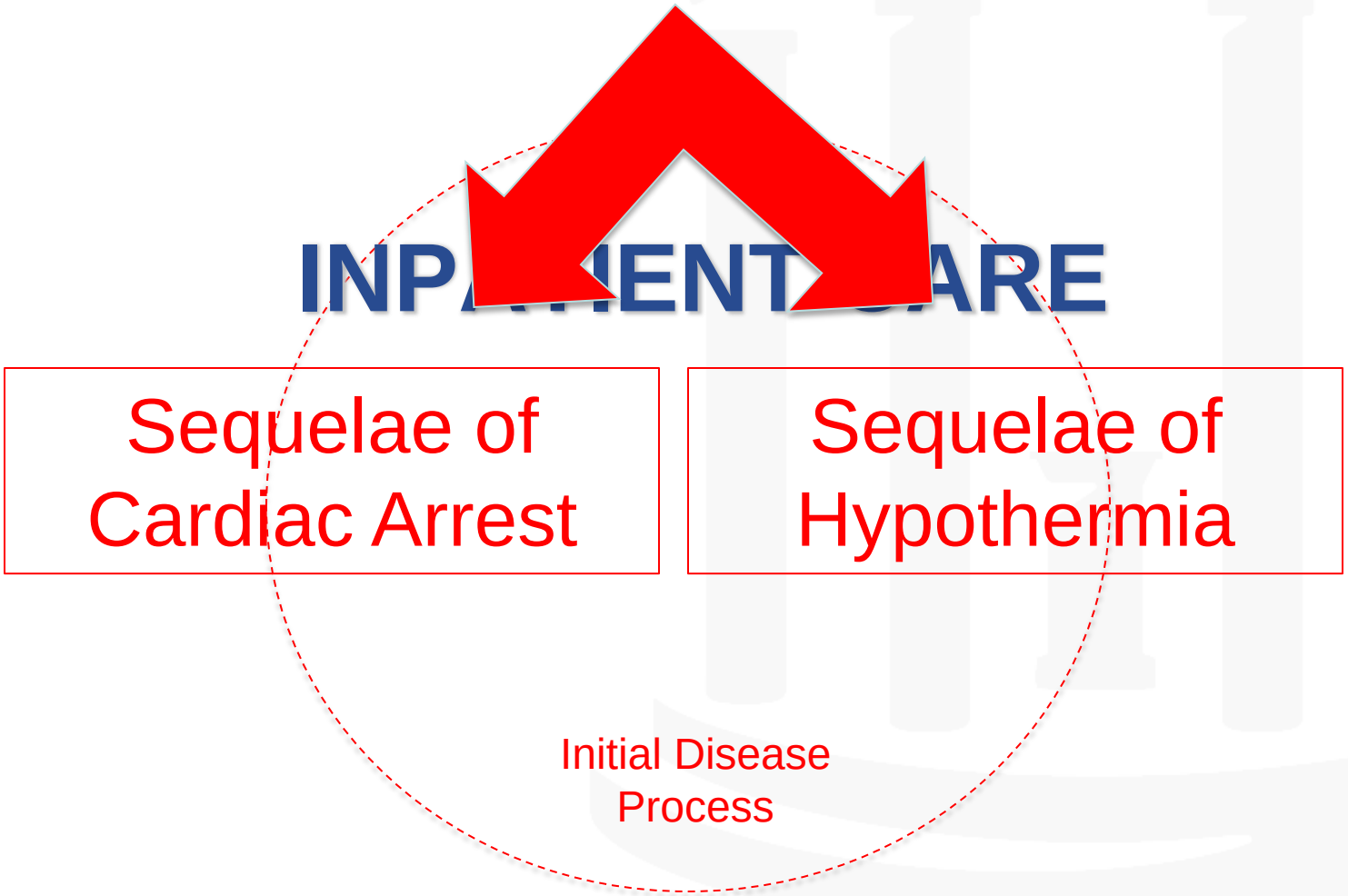
ROSC is paramount….but does not represent the end of resuscitation!!

Pre-Hospital Care

Emergency Dept
CICU/ICU
Rehabilitation
LTAC
Nursing Facility

Inpatient Care is a *TEAM EFFORT*




INPATIENT CARE
Sequelae of Cardiac Arrest
Sequelae of Hypothermia
Initial Disease Process

Post-Cardiac Arrest Syndrome

- *Sepsis-like syndrome* – release of cytokines, adhesion molecults, endotoxins → multi-organ failure

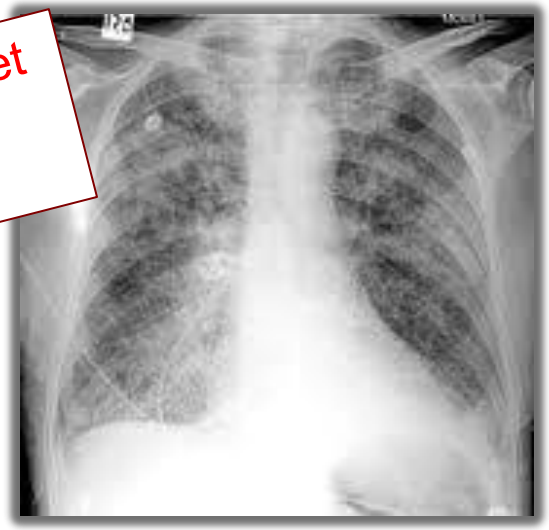
- Causes:

  - Anoxic brain injury
  - Myocardial depression/dysfunction
  - Systemic ischemia/reperfusion response
  - Capillary leak syndrome
  - Vasodilatation

Oxygenation/Ventilation

- Both cardiogenic and noncardiogenic pulmonary edema is common
- Can impact both oxygenation AND ventilation
- Data to support avoiding BOTH hypoxia AND hyperoxia
- Aim for normocapnia
- ***1st 24h are often the most challenging***

Remember ARDSNet low tidal-volume ventilation



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Circulatory Support

- Invasive hemodynamic monitoring
  - Arterial line
  - Central venous catheter
  - Swan-Ganz catheter
- Goal-directed therapy?
  - Take into account loss of cerebrovascular pressure autoregulation and the need to perfuse the post-ischemic brain (⇧ICP)
  - Hemodynamic targets remain unclear
  - NO DATA to support particular goals of care from an outcomes standpoint
  - MAP target? 60-100 mmHg

CPP = MAP - ICP

Circulatory Support

- Vasopressors to support blood pressure
- Consider inotropic agents if there is concomitant cardiac contractile dysfunction
- Mechanical circulatory support as needed:
  - Intra-aortic balloon counterpulsation (“Balloon Pump”)
  - Other percutaneous ventricular support devices (e.g. TandemHeart, Impella)
  - Extracorporeal Life Support (e.g. VV-ECMO, VA-ECMO)

Glycemic Control

- Hyperglycemia is common after cardiac arrest and the application of therapeutic hypothermia
- Need to monitor blood glucose concentrations frequently
- In critical care populations, glycemic control is directly associated with markers of ICU morbidity and mortality, infection/sepsis risk, and cost-of-care
- Target glucose levels of ≤180 mg/dL (higher mortality seen with tighter control protocols)

IMPACT OF HYPOTHERMIA

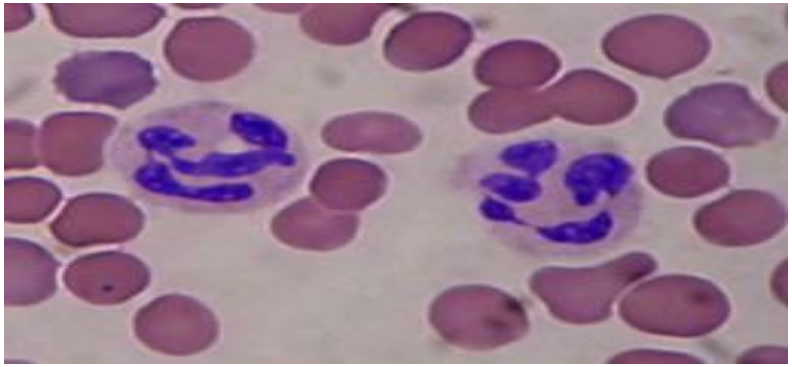
Decreased heart rate
Increased systemic vascular resistance
Decreased cardiac output; but stroke volume is usually preserved
Increased renal blood flow → *increased diuresis*
Increased K+ uptake into cells → *hypokalemia*
Decreased phosphate concentrations
Impacts acid/base status → *decreased CO_2 production*
Decreased plasma insulin → *hyperglycemia*
Platelet activation, enhanced aggregation?
Prolonged PT, PTT
Arrhythmia (greater risk with temps <30 degrees Celsius)
Infection

Shivering

- Makes it challenging to regulate/control body temperature
- Results in increased oxygen consumption
- Greatest problem often occurs during the induction phase of hypothermia
- Treat with increased sedation, neuromuscular blockade, analgesia

Fever and Infection

- Impaired immunity occurs as a result of both cardiac arrest and the application of therapeutic hypothermia
- Impaired neutrophil function seen, but conflicting outcome data
- Must be vigilant about monitoring for signs and symptoms of infection
- Fever should be avoided → associated with worse neurological outcomes

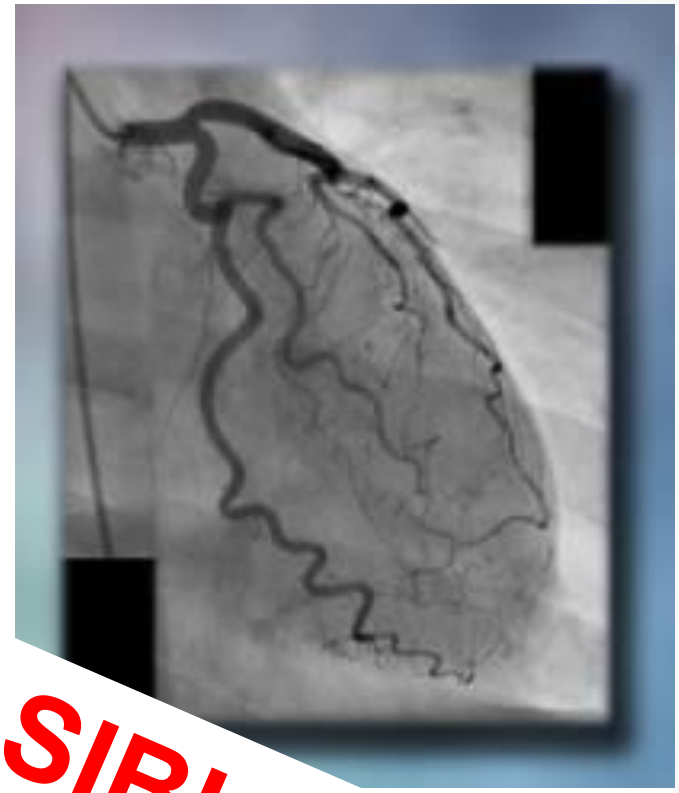


Re-warming…

Re-Warming

- ***Critical phase***
- Constricted peripheral vascular beds start to dilate → can lead to hypotension if not adequately volume resuscitated
- Hyperkalemia can develop
- Shivering can again become a problem
- Rewarm slowly --- usually at a rate no faster than 1 degree Celsius every 4 hrs
- Avoid rebound hyperthermia – associated with BAD outcomes
- Maintain sedation +/- paralysis until temperature reaches about 35 degrees Celsius

Cardiac Catheterization



FEASIBLE

- ECG can be unreliable
- Role of cath outside of STEMI is uncertain
- Many of these patients have an ischemic substrate
- Controversial – selective vs. broad application?

Other Thoughts

- How best to monitor the patient?
  - Continuous ECG, pulse oximetry
  - CVP monitoring to guide volume resuscitation
  - Arterial line for invasive BP monitoring
  - Spot vs. Continuous EEG → 20-40% will have seizure activity
  - Foley catheter with temperature probe vs. esophageal monitor
- Consider adrenal insufficiency in the vasopressor-refractory patient
- Monitor drug levels – both hypothermia AND rewarming alter drug metabolism and clearance
- Did I mention that FEVER is bad?!!

Neurologic Prognostication

- ***An evolving practice!***
- Hypothermia alters properties of sedatives, analgesics, neuromuscular blockade
- Neuro exam and electrophysiologic tests (e.g. EEG, SSEPS) can be altered
- Current American Academy of Neurology (AAN) guidelines don't take hypothermia into consideration – still use 72h mark

Neurologic Prognostication

3 small retrospective studies presented at 2010 AHA Scientific Sessions/Resuscitation Science Symposium…

Late awaking patients "slipping through the survival cracks?"

"To withdraw support, or the idea of making a pronouncement about the degree of neurologic recovery on day three, needs to be revisited"

"By day seven, if the patient is still intubated and on a ventilator, that means they're probably not going to do well"

"Even myoclonus – generally considered an ominous sign – does not necessarily predict poor outcome in the patient treated with therapeutic hypothermia

Neurologic Prognostication

- **General thoughts:**
  - Involve neurology – *particularly neuro-critical care* – early in the patient's course
  - Consider early EEG as baseline
  - Treat seizures aggressively
  - Consider supplemental imaging after normothermia achieved (e.g. CT, MRI)
  - Features that suggest poor prognosis – absence of pupillary light response or corneal reflexes, incomplete brainstem reflex recovery at normothermia, absence of EEG activity, elevated neuron-specific enolase

Easier to predict good prognosis than poor!

"For crying out loud, I was *hibernating!* ... Don't you guys ever take a pulse?"