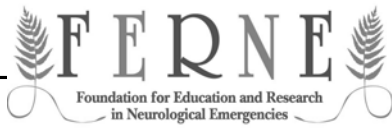


**FERNE / MEMC IV Brain Illness and Injury Course:  
Hypothermic Resuscitation in Patients with CNS Injury Due to Cardiac Arrest  
Brian O'Neil, MD, FACEP**

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**Hypothermic  
Resuscitation in  
Patients with CNS  
Injury Due to Cardiac  
Arrest**

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**FERNE**  
Foundation for Education and Research  
in Neurological Emergencies

***FERNE Brain Illness  
and Injury Course***

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**4<sup>th</sup> Mediterranean  
Emergency Medicine  
Congress  
Sorrento, Italy  
September 17, 2007**

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**Brian J. O'Neil, MD**  
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**Disclosures**

- Advisory Boards: Heartscape, BMS
- Speakers' Bureau: GSK, Sanofi-Aventis, BMS, Schering Plough
- Site PI: Artic Sun-RESCUE trial
- ACEP Research Committee
- Co-Chair ACEP Research Forum
- Board Member: FERNE

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***Learning Objectives  
and Key Clinical  
Questions***

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## Session Objectives


- **Discuss Hypothermia and Ischemia:**
  - Physiology, mechanisms
- **Review:**
  - Current evidence, clinical trials
- **Examine:**
  - Future Therapies
- **Practical Recommendations:**
  - You can use today

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## Post-Ischemic Cerebral Reperfusion

- CPR restores ROSC in about 100,000 patients a year in the US
- 60% of these die from neurologic complications
- Only 3-20% of resuscitated patients are able to resume their former lifestyles

Krause GS, Kumar K, White BC, Aust SD, Wiegenstein JG. Ischemia, resuscitation, and reperfusion: Mechanisms of tissue injury and prospects for protection. Am Heart J 1986; 111:768-80.


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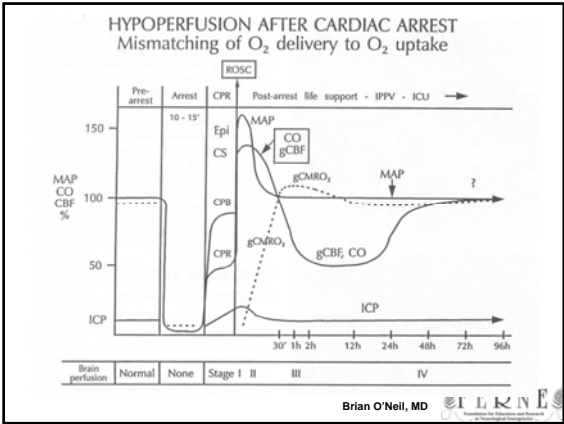
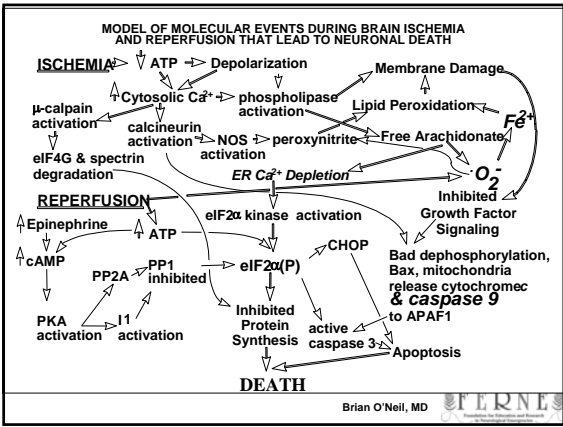
## Neuroprotection 1955-2000

### Trials of Neuroprotection Agents in Stroke:

Neuroprotective Agents Tested	49
RCTs Performed	114
Patients Enrolled	21,445
Trials with Positive Results	0


Kidwell CS et al. Stroke 32(6):1349-59.

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## Historical Observations


- **Not Dead till Warm and Dead**
  - Cold patients would awaken in the Morgue
- **Kids / Hockey Players-** fall through ice, long rescue times, but good recovery
- **Hibernation:** state of low oxygen, acidosis, low energy supply
- **Basic science animal research** showed promising results

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### Hypothermia: Potential Mechanisms

- 6% ↓ in metabolic rate per 1° C reduction in brain temperature
- CMR declined to 50% after brain cooling to 32 degrees C (CBF & CMR coupled)
- blocks release of excitatory amino acid
- reduces early calcium rise
- reduces calpain specific and cytoskeletal damage

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### Clinical Hypothermia

- Bernard et al (77 pts)
  - external cooling, ice bags, initiated by EMS at ROSC
  - 33.5 C within two hours ROSC cooled for 12 hours
  - Good outcome = 49% v 26%

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### Clinical Hypothermia


- The European group, 136 pts,
  - VF arrest, comatose, stable hemodynamics
  - external cooling device,
  - 8 hrs = median time to target Temp (33 C)
    - 14.4% did not reach target T°
    - Cooling for a mean of 24 hours
    - Good outcome = 55% v 39%

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### Hypothermia: The Beaumont Experience


**INCLUSION**

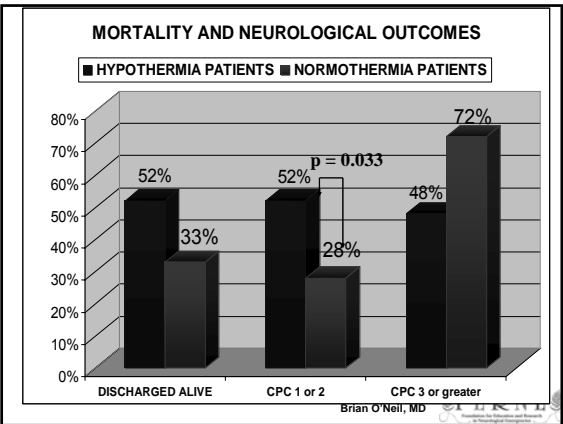
- Patients with witnessed out of hospital cardiac arrest of presumed cardiac origin
- any initial rhythm that had ACLS within 15 minutes
- restoration of spontaneous circulation, (ROSC) within 60 mins of collapse
- able to obtain informed consent by representative/family member were enrolled

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**Table 1: Baseline Characteristics**

	HYPOTHERMIA PATIENTS	NORMOTHERMIA PATIENTS
DATES	5/05-9/06	1/97-2/06
TOTAL PTS	23	80
AGE AVG	65.8	67.9
Bystand CPR	13 (56%)	45 (56%)
INITIAL RHYTHM		
vfib	14 (61%)	62 (78%)
pea	4 (17%)	5 (6%)
asystole	5 (22%)	13 (16%)
Mean time till ROSC	21	14

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## Practical Hypothermia

- First thing you need are Champions
- Next get Buy In:
  - ED, CCU, ICU, Nursing and Administration
- Sit down and hammer out a protocol
- Educate Staff
- Facilitate the first few patients

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## Practical Hypothermia

- Initiation: Sooner the Better: Pre-hospital or in-hospital
  - Ice bags in Groin, Axilla and Neck
  - Cold IV fluids
  - Regular cooling blanket
  - Intravenous catheters / Gel Pads
    - More consistent temperature regulation
- Target 33.5 °C:
  - Esophageal > bladder > rectal probes
    - Bladder probes need urine output
  - Watch for rapid drop, cooling is non-linear

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## Practical Hypothermia

- Paralyze / Sedate
  - Ativan drip: added seizure control
- Watch for:
  - Low K<sup>+</sup> and Mg <sup>++</sup>
  - High Glucose
    - Stress dose insulin with boluses
  - Bradycardia
  - Prolonged QT
  - Bleeding
  - Pneumonia/ sepsis

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## Practical Hypothermia

### Re-warming:

- Not truly active
  - Decreased rate of cooling
- Beware of temperature overshoot
  - Stop re-warming around 35° C
- Watch for:
  - Seizures
  - Arrhythmias
  - Fevers

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## What the Future Holds

- NMDA/ AMPA receptor antagonist and
  - phase II trials have recently shown some efficacy in CHI
- Estradiols and Progesterone
- Hypothermia during resuscitation
- Cannabinoids:
  - most potent antioxidants known, (dexamabinol)
  - Many receptor similarities to opioids
    - Also induces hypothermia
- Insulin and other growth factors

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## What the Future Holds

### Opioid receptor antagonists:

- $\delta$ -, DADLE,  $\kappa$  opioid receptor, BRL-52537
- proteins trigger hibernation
  - opiate antagonists reverse hibernation
- pre-conditioning protein
  - myocytes and neurons
- mechanisms: ATP-K<sup>+</sup> channels, PKC, free radicals
  - increases ERK and bcl-2

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## **Conclusions**

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- **Post-ROSC Neurologic resuscitation:**
  - needs to improve
- **Injury Mechanisms:**
  - Complex, Multi-factoral
  - Silver Bullet Trials have Failed
- **The Future Looks Bright**
- **Therapeutic Hypothermia:**
  - Currently only proven therapy
  - Cheap, Easy, risk / benefit ratio is huge

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## **Recommendations**

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### **Therapeutic Hypothermia:**

✓ **JUST DO IT** ✨

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## **Questions?**

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**[www.FERNE.org](http://www.FERNE.org)**

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