


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

Hypothermic Resuscitation in Patients with CNS Injury Due to Cardiac Arrest

Brian O'Neil, MD



FERNE Brain Illness and Injury Course

Brian O'Neil, MD



The Fourth Mediterranean Brain and Neurological Congress (MEMC IV)
Sorrento, Italy
TE-19 November 2007



4th Mediterranean Emergency Medicine Congress
Sorrento, Italy
September 17, 2007

Brian O'Neil, MD



Brian J. O'Neil, MD
Professor

Department of Emergency Medicine
Wayne State University,
Research Director,
William Beaumont Hospital
Royal Oak, MI

Brian O'Neil, MD



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

Brian O'Neil, MD



Learning Objectives and Key Clinical Questions


Brian O'Neil, MD



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

Session Objectives


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

Brian O'Neil, MD 

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, Wiegstein JG. Ischemia, resuscitation, and reperfusion: Mechanisms of tissue injury and prospects for protection. Am Heart J 1986; 111:768-80.


Brian O'Neil, MD 

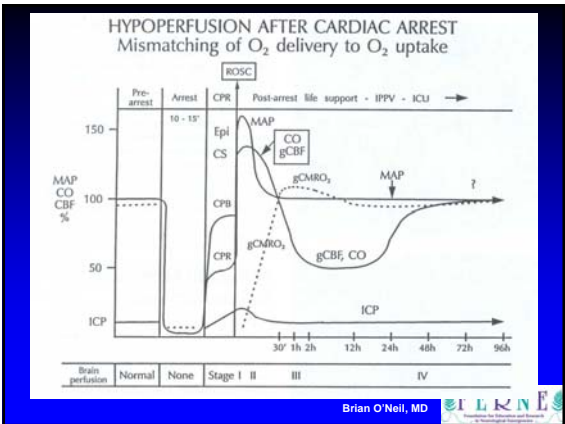
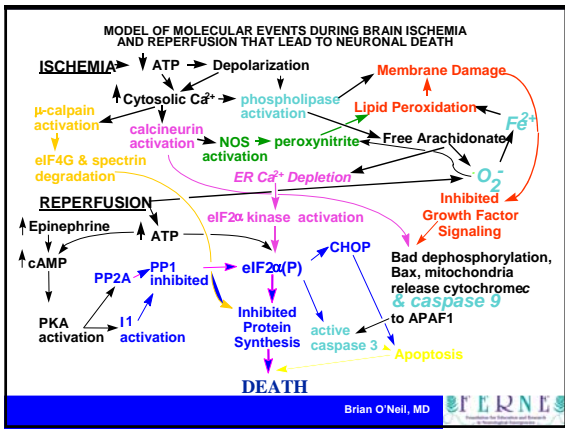
Neuroprotection 1955-2000

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.

Brian O'Neil, MD 




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

Brian O'Neil, MD 


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

Brian O'Neil, MD 


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%

Brian O'Neil, MD 

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%

Brian O'Neil, MD 

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



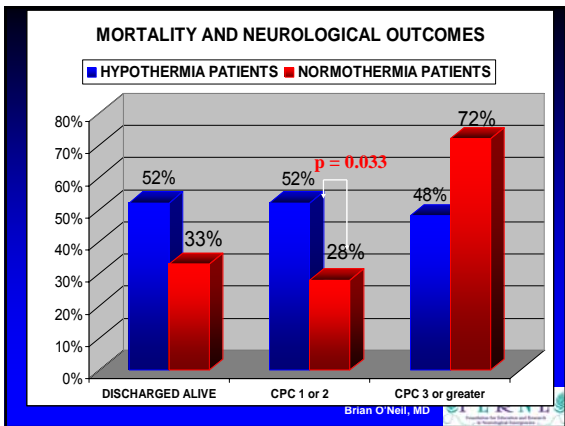
Brian O'Neil, MD 

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


Brian O'Neil, MD 



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


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

Brian O'Neil, MD 


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

Brian O'Neil, MD 

Practical Hypothermia


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

Brian O'Neil, MD 

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

Brian O'Neil, MD 

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

Brian O'Neil, MD 

What the Future Holds

Opioid receptor antagonists:

- δ-, DADLE, κ opioid receptor, BRL-52537
- proteins trigger hibernation
 - opiate antagonists reverse hibernation
- pre-conditioning protein
 - myocytes and neurons
- mechanisms: ATP-K⁺ channels, PKC, free radicals
 - increases ERK and bcl-2

Brian O'Neil, MD 

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

Conclusions

- **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

Brian O'Neil, MD



Recommendations

Therapeutic Hypothermia:

✓ **JUST DO IT** ✨

Brian O'Neil, MD



Questions?

www.FERNE.org

bo'neil@beaumont.edu

ferne_memc_2007_braincourse_oneil_hypothermic_091707_finalcd
9/27/2007 11:23 AM

Brian O'Neil, MD

