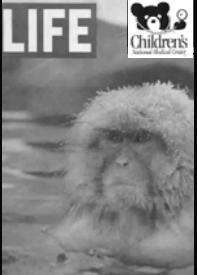

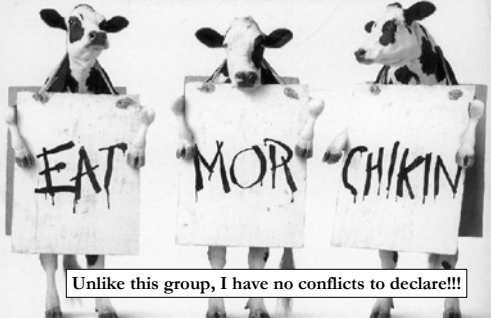



Therapeutic Hypothermia
Prevention for Neonatal Hypoxic-Ischemic Brain Injury



Steve Baumgart, MD
Tsun Chang, MD
Billa Short, MD
And the Departments
of Neonatology and
Neurology at the
Children's National
Medical Center,
Washington, DC


www.childrensnmc.com



Unlike this group, I have no conflicts to declare!!!

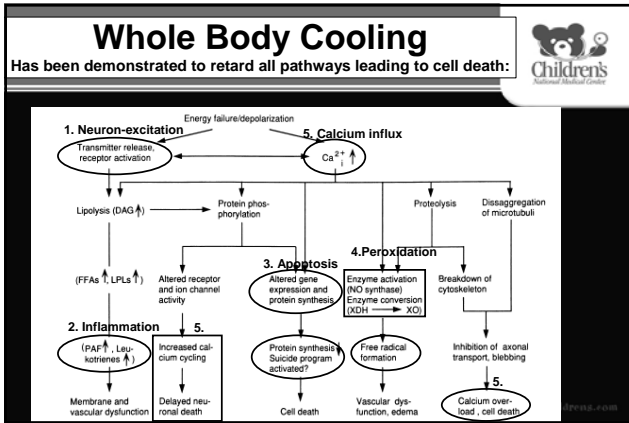
www.childrensnmc.com

Goals of This Talk

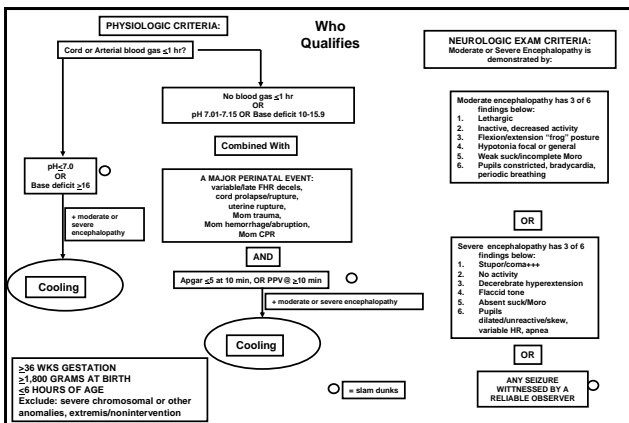


- How is hypothermia neuroprotective?
- Who is eligible for hypothermia therapy?
- How, exactly, is hypothermia implemented in NICU?
- What's happened to the patients we've cooled?


www.childrensnmc.com








Cooling Protocol Timeline



- Transport call received for candidate with slam dunk:
 - pH \leq 7.00 or base deficit \geq 15
 - Major perinatal event with Apgar at 10 min \leq 5. Je requires ET-PPV
- Transport mobilized ASAP, may use helicopter, to retrieve baby by 6 hour arrival deadline
- Blanketrol water mattresses precooled to 5°C (41°F)
- Baby quickly examined to confirm encephalopathy by Neonatologist/Neonatal Neurologist using a standard checklist
- Baby placed on cooled mattress immediately switched to autoregulate temperature to 33.5°C, mattress captures baby within 35-40 mins.
- Technician begins 72 hour videoEEG recording on 16 channels to monitor seizures/suppression/recovery

www.childrensnmc.com

Whole Body Cooling Apparatus: Cincinnati SubZero Blanketrol II™



Baby on cooling mattress (blanketrol)

Infant lies supine on infant-size cooling mattress

Blanketrol mattress with circulation - 9 L cool or ultra-warm water through the mattress


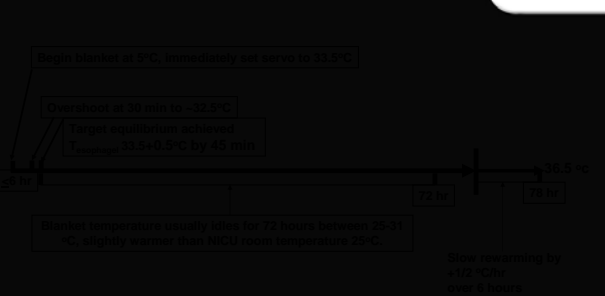



Fig 2. The infant lies supine on the infant-size blanket. The adult-size blanket is suspended vertically alongside the cooling unit. Both blankets are attached to the cooling unit with water circulation through them.

Cooling Protocol Timeline



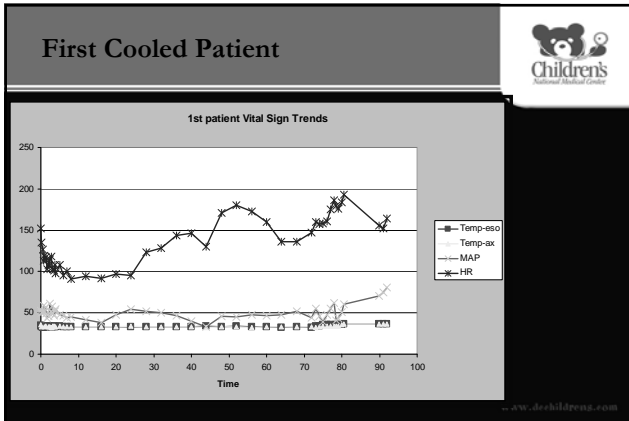
Blanket mattress at 5°C immediately but warms to 33.5°C

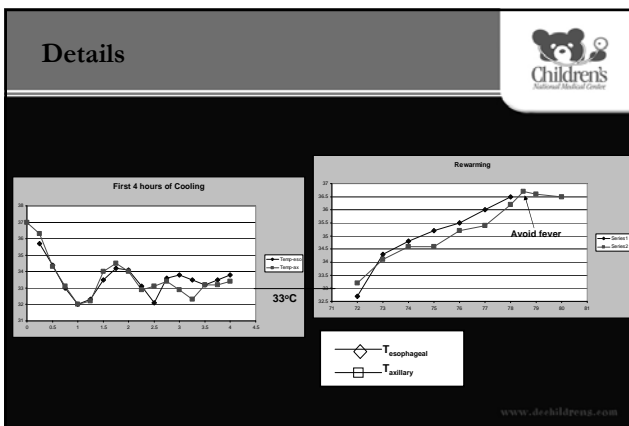
Temperature drops to 33.5°C by 40 min

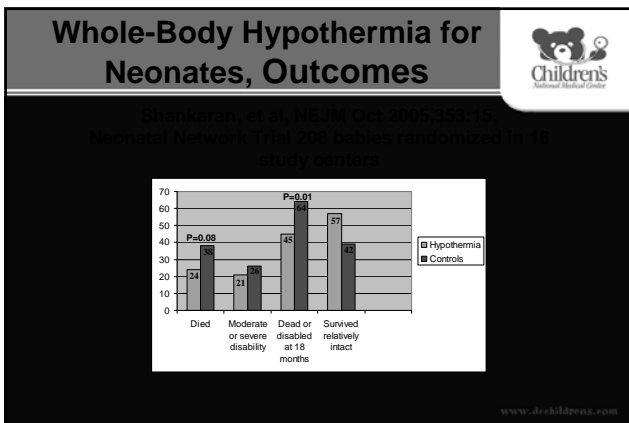
Temperature stabilizes at 33.5°C by 45 min

Blanket temperature quickly returns to 72 hours to 33.5°C


www.childrensnmc.com









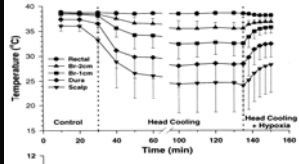
Head Cooling RCT Outcomes



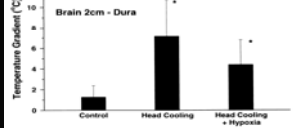
• Children's Cool Cap Study Group, 2010
 • PALS, 2015, New Zealand and World-wide
 • Recently FDA approved 2016
 • RCT: 2016-2018
 • 100% of 1000 children
 • Average of 10 mins AND PPT in 2018
 • Temperature level H-H, AND
 • Abnormal of ED (depression, seizure)
 • No head cooling (depression, seizure)
 • Worst head cooling (PPT, seizure AND
 • Radiation warmer second 1000 (aged 1-14)



Why Not Head Cooling?

There may be as much as an 8°C gradient between a cooler brain surface and warmer deep brain structures receiving blood flow at core temperature 34-35°C.


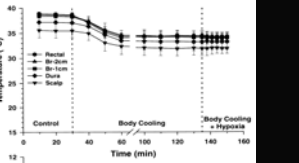


Legend: * p < 0.05, ** p < 0.01, *** p < 0.001

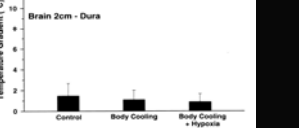
Legend: * p < 0.05, ** p < 0.01, *** p < 0.001

PEDIATRICS

Why Not Head Cooling?


There's ~2°C gradient between a cooler brain surface and deep brain structures receiving whole body cooling.




Legend: * p < 0.05, ** p < 0.01, *** p < 0.001

Legend: * p < 0.05, ** p < 0.01, *** p < 0.001

PEDIATRICS





Bottom Line for Cooling in fewer words



- In randomized studies, bad outcomes (death or severe disability) were reduced from about two-thirds, to less than half of the infants treated with cooling versus conventional supportive therapy.
- In these studies, nearly intact survival approached or exceeded 50% in an illness where normal outcomes are unusual.

www.childrens.com



Whole Body Cooling: Children's Hospital's 1st Patient



A patient undergoing whole body cooling in the ICU.

www.childrens.com

Whole Body Cooling: Children's Hospital's 9th Patient

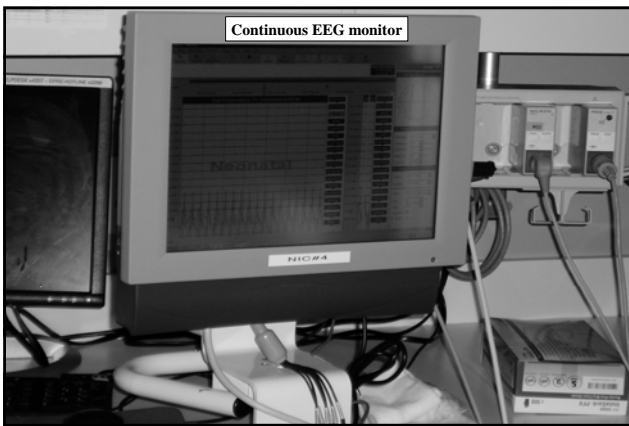


A patient undergoing whole body cooling in the ICU.

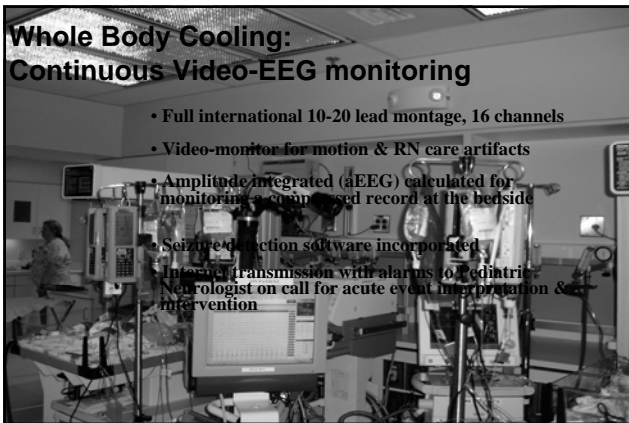
www.childrens.com



**Whole Body Cooling:
Neuro-intensive care corridor
May, 2006**





Continuous EEG monitor



**Whole Body Cooling:
Continuous Video-EEG monitoring**

- Full international 10-20 lead montage, 16 channels
- Video-monitor for motion & RN care artifacts
- Amplitude integrated (aEEG) calculated for monitoring & compressed record at the bedside
- Seizure detection software incorporated
- Intra-hospital transmission with alarms for pediatric Neurologist on call for acute event interpretation & intervention


 **CNMC/NICU Preliminary Experience**
May, 2006-May 2007




Quality Review

- 48 infants cooled on protocol
- Mean birth weight 3.37 ± 0.67 SD kg
- Gestation 38.5 ± 1.7 wks
- Admitted at ages $4:40 \pm 1:01$ hrs

www.childrensnational.com


 **CNMC/NICU Preliminary Experience**




Quality Review

- Cord pH in 45 infants
- Median 6.86
- Range 6.43-7.36
- Base deficits ranged -9 to -35

www.childrensnational.com


 **CNMC/NICU Preliminary Experience**




Quality Review

- Perinatal events recorded:
 - 16 complete abruptions
 - 4 uterine ruptures
 - 12 nuchal, vementous, or prolapsed cords
 - 17 fetal monitoring distress
- And 1 each: Maternal death/CPR, loss of fetal movement for 24 hours, traumatic home midwife delivery of 5.9 kg 1-GA infant vaginally

www.childrensnational.com




CNMC/NICU Preliminary Experience




Quality Review

- Two babies had unanticipated distress at birth:
 - One with complex coronary artery defects required CPR at birth.
 - One with congenital diaphragmatic hernia required ECMO in first 2 hours of life.

www.childrensnmc.com




CNMC/NICU Preliminary experience




Quality Review

- 11/48 infants (23%) had observed seizures to meet cooling criteria; 2 additional had EEG seizures.
- 41/48 (85%) are now surviving, all are seizure free with EEG improvement during hypothermia.
- 11/41 (28%) had a normal brain MRI at 2 wks.
- 27/41 (66%) had evidence of ischemic white matter injury or spectroscopic ischemia.

www.childrensnmc.com





CNMC/NICU Preliminary Experience



Quality Review

- 33/41 (93%) are home.
- 27/41 (68%) are feeding orally without assistance and passed hearing screening.
- 10/41 (26%) required rehabilitation or tube feeding.



www.childrensnmc.com

 **CNMC/NICU Preliminary experience** 

Quality Review

- Adverse events included 7/48 deaths (15%, $\leq 24\%$ Network):
 - Two occurred after recovery from hypothermia and before hospital discharge when EEG monitoring suddenly became nonreactive, and an MRI or CT revealed brain herniation, with an unresponsive neurologic exam.
 - One death occurred after withdrawal of ECMO with complex coronary artery defects.
 - Two infants were not resuscitated to ECMO support at the parents' request.
 - One infant with CDH had severe pulmonary hemorrhage on ECMO and parents requested stopping ECMO.
 - One infant was not resuscitated at a Rehabilitation Hospital



www.childrensnational.com

 **CNMC/NICU Preliminary experience** 

Quality Review

- The only other remarkable event occurred in one survivor who developed sinus bradycardia (HR 40's for ~8 hours) 60 hours into cooling while on VA-bypass. Bradycardia resolved with rewarming before weaning off ECMO. This infant's pH and SvO₂ remained normal without any base deficit throughout this event. MRI showed no infarct, the EEG was normal, baby is now home, PO feeding with a normal exam.


www.childrensnational.com

 **CNMC/NICU Future experience? from May, 2007** 

- We've now cooled about 3 babies/month
- We will conduct a quality review with Dr. Shankaran, consulting from the NIH
- We will participate in a hypothermia multi-center randomized trial before cannulation for ECMO [i.e. infants at risk for HIE]
- We will perform hypothermia on dialysis for hyperammonemia encephalopathy (inborn errors of metabolism, Dr. Lichter, PI, Genetics/metabolism)

www.childrensnational.com

CNMC/NICU Web



- <http://www.dccchildrens.com/dccchildrens/about/subclinical/subspecialties/nicuhome.aspx> from there click on Therapeutic Whole Body Hypothermia Program to see:
 - Parent information sheet
 - Information sheet in Spanish
 - Protocol criteria
 - Descriptive article

www.dccchildrens.com


Therapeutic Cooling/THE END




Keep cool!

www.dccchildrens.com

Temperatures from this talk, *et al.*



Mild hyperthermia	38°C	100°F
Moderate hyperthermia	40.5°C	105°F
Head coil water	10°C	50°F
Infant mattress water	20°C	68°F
Standard room in NICU	22°C	72°F
My home refrigerator	4°C	39°F
My home freezer	-18°C	0°F

www.dccchildrens.com

Neonatal Follow-up in 24 babies



- Almost 50% of patients have been followed neuro-developmentally through at least 9 months of age
- 60% had age appropriate developmental exams

www.childrensnmc.com
