

Innovative Care of the Newborn Brain: Stanford University September 26-27, 2018

Krisa Van Meurs, MD and Kathi Salley Randall, MSN, RNC, CNS, NNP-BC

On a warm late-summer morning in September 170 neonatologists and neonatal nurses from around the globe joined together to learn about how to create a NeuroNICU program, to perform an in-depth neuro exam, deepen their knowledge of therapeutic hypothermia, and focus on the clinical utility of bedside brain monitoring.

“The two-day conference was held at the gorgeous Frances G. Arrillaga Alumni Center in the center of Stanford University campus... Attendees were also from NICU’s as far away from California as Montreal, Florida and Brazil, and this provided for rich conversations and networking for everyone who attended. ”



The two-day conference was held at the gorgeous Frances G. Arrillaga Alumni Center in the center of Stanford University campus and the weather provided the attendees with the warmth and sun that we all expect from Northern California summers. Attendees were also from NICU’s as far away from California as Montreal, Florida and Brazil, and this provided for rich conversations and networking for everyone who attended.

The topics presented at this year’s conference spanned a wide range. Here are just a few highlights of talks given by our team of neonatal and neurology experts:



Clinical findings in HIE

- **Abnormal neurologic exam:**

- Level of consciousness
- Tone
- Tendon reflexes
- Primitive reflexes
- Respiratory function
- Autonomic function

- **Other clinical findings:**

- Need for resuscitation
- Seizures
- EEG abnormalities
- Other organ injury



Slide 1: Clinical findings in HIE

- Dr. Courtney Wusthoff, Neonatal Neurologist gave three talks at this year's Innovative Care Conference. She presented on the complexities of diagnosis and management of neonatal seizures, pitfalls of the neonatal neurological examination, and gave an excellent review of the fetal neuro-development and sequelae of disrupted development.
- Drs. Valerie Chock (Neonatologist) and Kelly Mahaney (Pediatric Neurosurgeon) teamed up for a presentation on the pathophysiology of brain injuries in term and preterm infants and discussed the neurosurgical management of at risk infants.
- Dr. Krisa Van Meurs, Neonatologist and Medical Director of the NeuroNICU, gave a presentation that reviewed HIE and hypothermia from the pathophysiology of the insult, the current evidence on the impact that hypothermia can provide to improve outcomes, and a peek at the future of neuroprotection for this high-risk population.

- Dr. Sonia Bonifacio, Neonatologist and Co-Medical Director of our NeuroNICU, gave an excellent review of neonatal stroke and facilitated one of our small group workshops on Advanced aEEG Cases.
- Dr. Susan Hintz, Director of the Johnson Center's Maternal Fetal Medicine Program presented a comprehensive overview of both short and long-term neurodevelopmental outcomes of extremely premature infants.
- Dr. Richard Shaw and Angelica Moreyra, PhD shared with the attendees a review of the results of their intervention research to reduce anxiety and PTSD in NICU parents.
- Kathi Randall, NNP our NeuroNICU Program Consultant gave a practical presentation on how we each can provide neuro-protective care on a daily basis through simple interventions like infant massage, nutrition, pain management, parental presence, and skin-to-skin care.

"By adding these exceptional presenters to the long list of local experts who typically present at the Stanford NeuroNICU course this two-day seminar offers the best way for anyone interested in the neonatal brain to become immersed in the best science and practical bedside approaches for caring for a variety of infants with, or at-risk for, brain injury."

- For infants with neurological injury, palliative and comfort care are important topics for caregivers to consider, and one of our NNP's from the LPCH NICU, Diana Kobayashi gave a great review of the literature and perspectives on how we can continue to improve in providing comfort care when critical care is no longer indicated.

Should a baby be cooled after 6 hours?

How this happens:

- Arrival at a cooling center after 6 hrs of age
- Progress from stage I to III/III encephalopathy after 6 hrs of age
- Are not recognized to qualify until after 6hrs of age
- Cooling cannot be initiated within 6 hours of age (equipment or personnel not available)

Slide 2: Clinically relevant questions regarding patient management.





• Attendees at this year's conference listening to Krisa Van Meurs speaking

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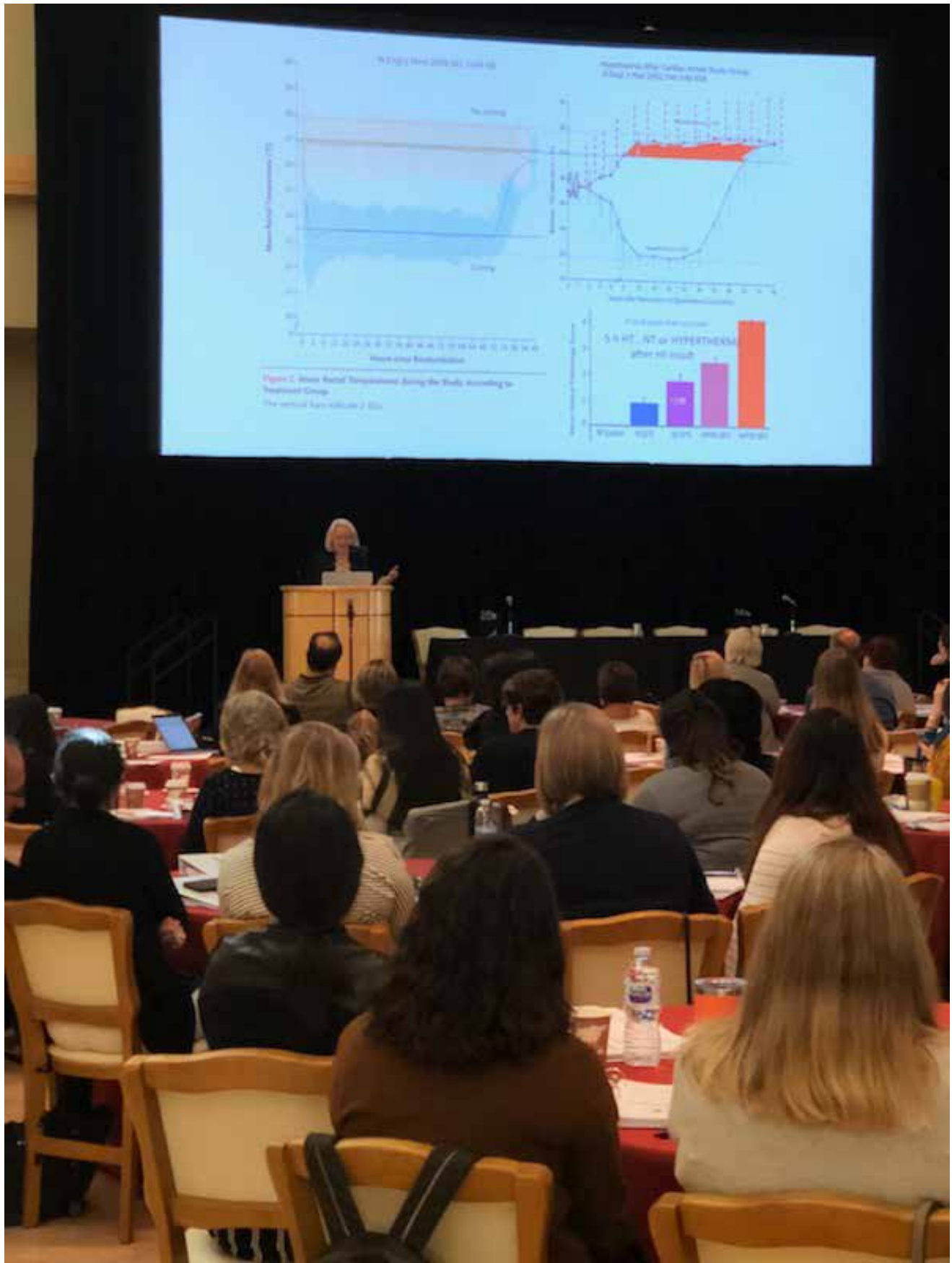
Conference organizers caught by the camera

In

We love to conclude our conference with a presentation by a parent or family and this year was no exception as we heard a passionate telling of the story of prematurity by one of our family advocates from the department of family centered care, Nina Boiadjeva.

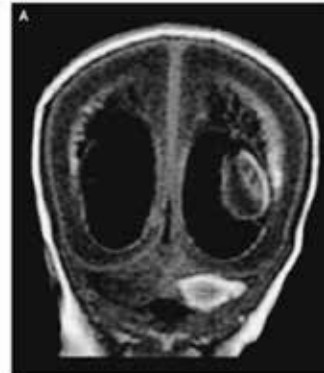
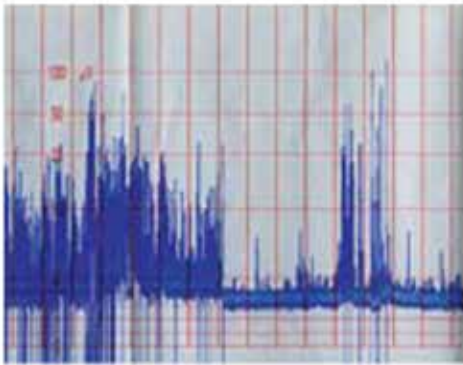
addition to the incredible local faculty who presented on a variety of NeuroNICU topics, three international experts in the neonatal neurology field were also on the agenda.

- Dr. Lena Hellstrom-Westas, from Uppsala, Sweden, presented on the history and current use of aEEG



Marianne Thoresen lecturing

Severe IVH



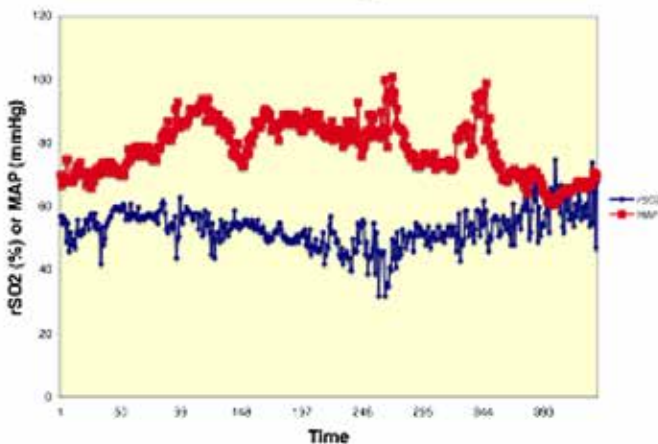
26 week infant with grade IV IVH
discontinuous -> flat/isoelectric pattern

Olischar et al, *Acta Paediatrica* 2007; 96: 1743-1750

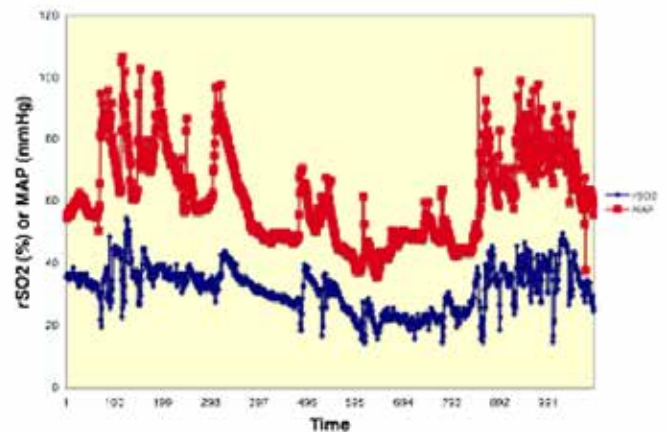
IVH

- Cerebral autoregulation

Intact Autoregulation



Impaired Autoregulation



NIRS Measures

- NIRS-measured regional oximetry measures provides a non-invasive measure of end-organ oxygenation and perfusion.
- * correlates with jugular venous saturation

$$rScO_2 = \frac{HbO_2}{HbO_2 + HHb}$$

$$FTOE = \frac{SaO_2 - rScO_2}{SaO_2}$$

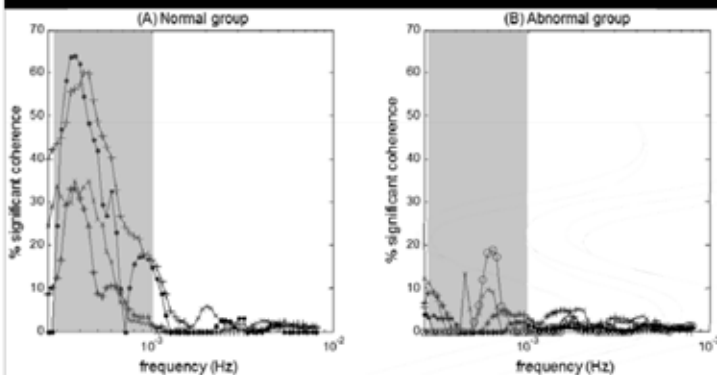
Understanding NIRS physiology is essential in evaluation of local cooling effects



The National Perinatal Association (NPA) is an interdisciplinary organization that gives voice to the needs of parents, babies and families and all those interested in their health and wellbeing. Within NPA, parents and professionals work together to create positive change in perinatal care through education, parent programs, professional guidelines and events.

www.nationalperinatal.org

Abnormal outcomes at 2 y are associated with decreased NVC



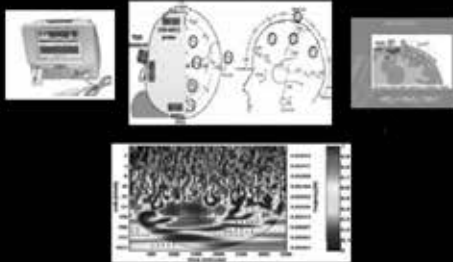
Chalak, L. Nature Scientific reports 2017

Summary of Findings

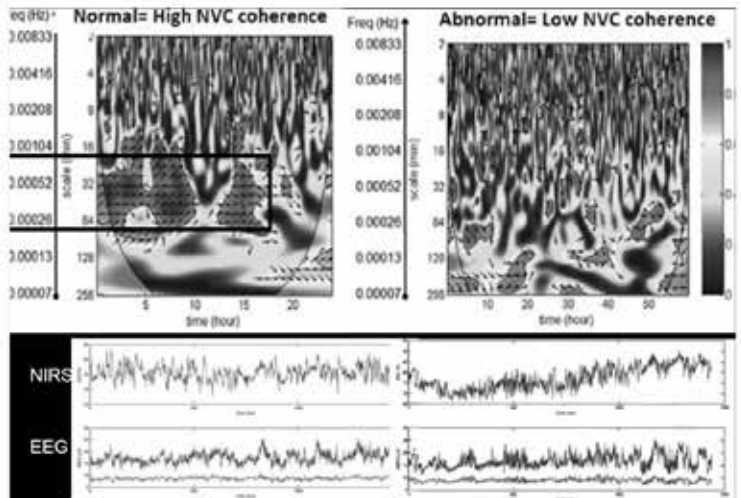
- The *Wavelet Neurovascular Bundle* can provide dynamic measures of the cerebral autoregulation and neurovascular coupling (CA and NVC)
- These hemodynamic parameters have the potential to impact risk stratification strategies, therapeutic decision making and prediction of outcomes after birth

Non Invasive Neurovascular Coupling

EEG + NIRS



Chalak, L. Dev Neuroscience 2017

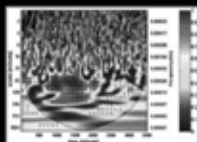


Chalak, L. Dev Neuroscience 2017

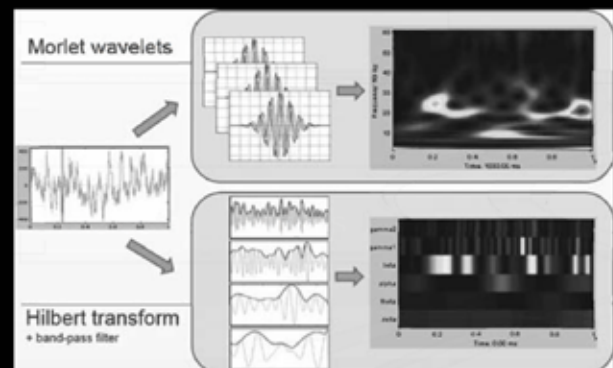
Weather-Forecast Tool to Evaluate Neonatal Brain Health



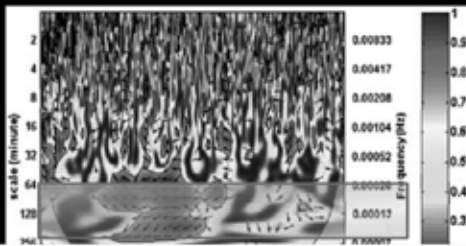
Wavelet mathematical tool provides optimal representation of BOTH time and frequency



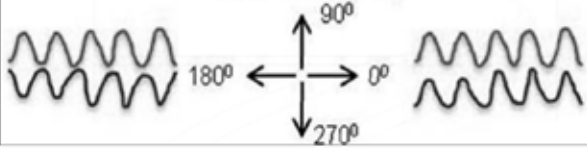
Wavelet Paradigm Shift Prior Analyses either Frequency OR Duration



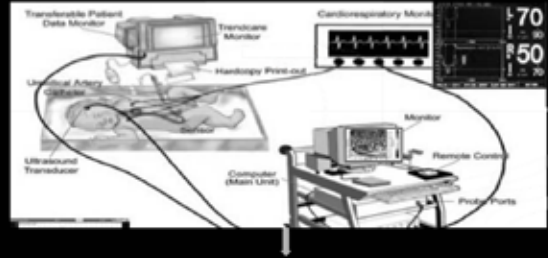
The Wavelet Quantifies Correlation with time, frequency, gain



Phase relationship



Neuromonitoring at Bedside: The Wavelet NV Bundle



Cerebral autoregulation (CA):

- BP • CBF

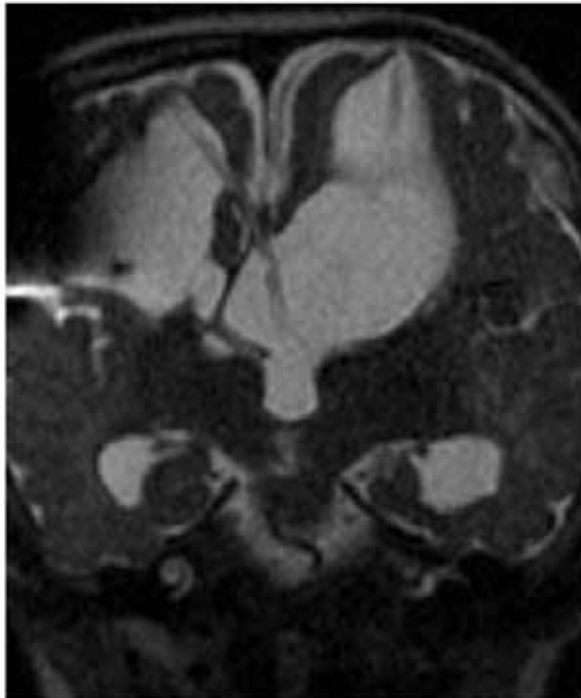
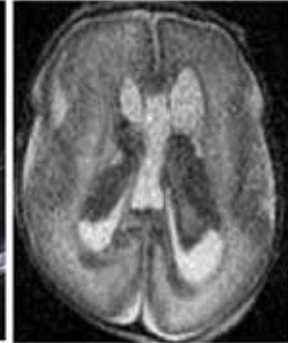
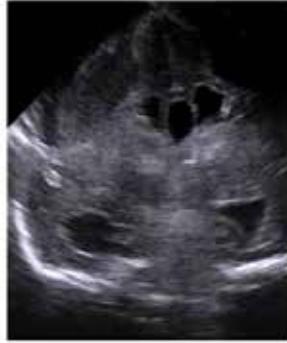
Neurovascular coupling (NVC):

- EEG • CBF



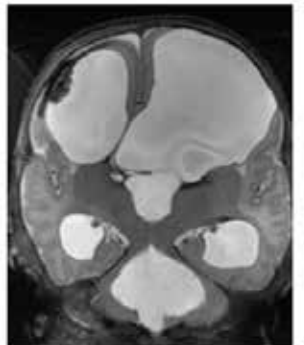
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Case 2

- 25 weeks 6 days GA
- E. Coli sepsis
- Bilateral grade IV IVH, bilateral subdural hemorrhages





The LPCH NeuroNICU Journey

Program Stats:

- 1 year anniversary – 226 patients
- 2 year anniversary – 260 patients
- 3 year anniversary – 370 patients
- 4 year anniversary – 494 patients
- Total 1,350 infants



The Neuro NICU is Multi-Disciplinary

Neonatology & Nursing



Pediatric Neurosurgery



Child Neurology



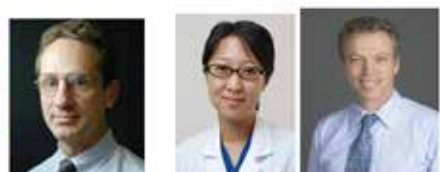
Developmental Behavioral Pediatrics/ High Risk Infant follow-up Clinic



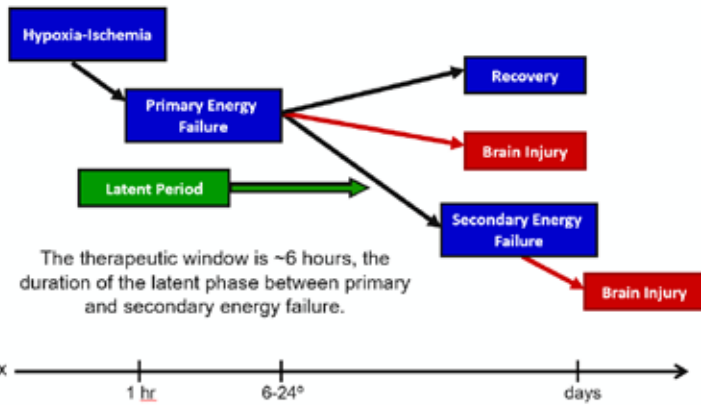
Developmental Team



Neuroradiology Child Psychiatry



Mechanism of brain injury during HIE



Slide 3: Brain Injury during HIE

Need for cooling plus therapies

	Controls	Cooled
Death or moderate to severe disability	62-83%	44-55%
Death	27-57%	24-38%
Cerebral palsy	30-48%	19-33%

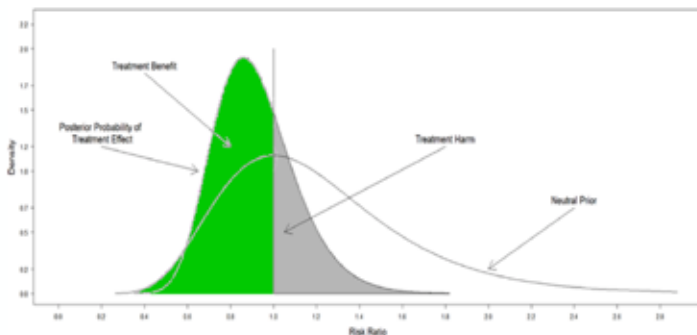
Conclusion: Additional neuroprotective strategies are needed to further reduce mortality and morbidity.

Shankaran S, *NEJM* (2005)
 Gluckman P, et al. *Lancet* (2005)
 Azzopardi D, et al. *NEJM* (2009)
 Simbruner G, et al. *Pediatrics* (2010)
 Jacobs S, et al. *Arch Pediatr Adolesc Med* (2011)

Stanford University

Slide 4: Additional therapies are needed.

Probability of treatment benefit



Conclusion: 76% of newborns cooled between 6-24 hours will have some benefit.

Laptook A, et al. *JAMA* (2017) Stanford University

Slide 5: Analysis favors treatment.

in the NICU, as well as a comprehensive review on neonatal pain and the controversies on best practices and management from her international perspective.

- Dr. Lina Chalak from UT Southwestern in Dallas, TX enchanted the audience with her elegant presentation

Potential therapies to augment hypothermia for HIE

- **Anticonvulsant or antiexcitatory**
Phenobarbital, topiramate, levetiracetam, **xenon**, magnesium sulfate, bumetanide
- **Anti-inflammatory or antioxidant**
Sodium cromoglicate, minocycline, indomethacin, melatonin, N-acetylcysteine, allopurinol, pomegranate polyphenols, 7-nitroindazole, 2-iminobiotin, **necrostatin 1**
- **Multiple mechanisms**
Erythropoietin
- **Growth factors and cell-based therapies**
Nerve growth factor, insulin-like growth factor 1, brain derived neurotrophic factor, **autologous cord-blood transplantation**

Modified from Johnston MV et al. *Lancet Neurology* 2011

Stanford University

Slide 6: Potential for Augmentation Exists.

on the neuro-vascular bundle and its delicate balance especially for those with brain injury. Both she and Dr. Hellstrom-Westas led afternoon workshops on the advanced use of aEEG and NIRS which were both extremely popular break-out sessions this year.

- And finally, Dr. Marianne Thoresen, one of the world's leading experts in neonatal physiology and hypothermia provided the attendees with an overview of the history and future of neonatal neuro-protection, including cooling, Xenon, Melatonin, mother's milk and more. And then she concluded the morning session on the 2nd day with a deep review of the pathophysiology of HIE, the mechanism by which cooling works, and bedside pearls for care that may influence these infants' outcomes.

By adding these exceptional presenters to the long list of local experts who typically present at the Stanford NeuroNICU course this two-day seminar offers the best way for anyone interested in the neonatal brain to become immersed in the best science and practical bedside approaches for caring for a variety of infants with, or at-risk for, brain injury.

If you and your team are interested in attending a future conference, the dates for 2019 are in the planning stages and we will certainly share those with you as soon as we can. To join their mailing list, click here (<https://goo.gl/forms/jN49Vy0VM0Su3XaH3>) or email Dr. Krisa Van Meurs, the Medical Director of the LPCH/Stanford NeuroNICU at: vanmeurs@stanford.edu

The authors have indicated no relevant disclosures.

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4 Pillars of Neuro-NICU Care



Corresponding Author



Krisa Van Meurs, MD
Rosemarie Hess Endowed Chair,
Division of Neonatal and Developmental Medicine
Professor-Med Ctr Line
Department: Pediatrics - Neonatology
Stanford University
750 Welch Rd. #315
Stanford, California 94305-5731
(650) 723-5711 (office)
vanmeurs@stanford.edu



Kathi Salley Randall, MSN, RNC, CNS, NNP-BC
NeuroNICU Program Consultant, Lucile Packard
Children's Hospital at Stanford
President/Owner of Synapse Care Solutions
kathi@synapsecare.com

