100 BILLION NEURONS:
Exploring the next generation of NICUs designed to support optimal brain development

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LEARNING OBJECTIVES

1. List the three stages of brain development

2. Outline the 4 pillars of the next generation NICU

3. Give an example of how your NICU can alter the environment, a policy, or the overall culture of care to optimize neurodevelopment of babies in the NICU
THE BRAIN IS A DYNAMIC ORGAN

Changing dramatically in **structure** and **function** in the first 5 years of life
- Rapid growth
- Folding to increase surface area
- Grey matter to white matter
- Synaptic Changes

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**Figure 7**  Periods of functional development

- Experience-dependent synapse formation
- Neurogenesis in the hippocampus

Image: Courtesy C. Nelson
EMBRYONIC PHASE

Week 4 = Differentiation of Neural Tube

Week 7 = Cortex is Visible

Week 10 = Thalamus & Hypothalamus Evolve

Week 12 = Hemispheres
**PROLIFERATION**

- Occurs between 8-16 weeks gestation
- Toxins can significantly alter number of neurons
- Chemicals and environmental substances can reduce the number of neurons

**MIGRATION**

- Peaks between 3 and 5 months gestation
- Complete by 6 months gestation
- Migration is critical for development of the cerebral cortex and deeper structures. (6 layers)
  - Basal ganglia
  - Hypothalamus/thalamus
  - Brainstem
  - Cerebellum
  - Spinal Cord
ORGANIZATION

Peaks 5 months (20 weeks) gestation and continues for several years after birth
NEURONAL ORGANIZATION

• Basis for brain function, allow to function as integrated whole
• Complex circuitry
• Cell differentiation, death, synaptic development, neurotransmitters
• Stabilization of cell connections
MYELINATION

- Myelin, a fatty covering, insulates the circuitry; prevents leakage of current and enables rapid, efficient transmission of nerve impulses
- Enhances intercellular communication

MYELINATION

Starts at 16 weeks; takes off at 24 weeks; mature at 2 years

Predictable progression
- central to peripheral
- caudal to rostral
- dorsal to ventral
- sensory to motor
THREATS TO BRAIN DEVELOPMENT: PRENATAL

Toxic Exposures (Drugs, Alcohol, Chemicals)

Maternal Stressors:
- Poverty
- Malnutrition

Congenital Developmental Disruptions
- Of CNS
- Of Cardiac
THREATS TO BRAIN DEVELOPMENT: NEONATAL

Prematurity

Toxic Exposures (Drugs, Alcohol, Chemicals)

Stress & Distress

Malnutrition
THREATS TO BRAIN DEVELOPMENT: CHILDHOOD

Prematurity Complications

Poverty, Neglect, Malnutrition

Maternal Depression & Mental Illness
PILLAR #1: NEURO-ASSESSMENT
PILLAR #2 - BEDSIDE BRAIN MONITORING

What about the brain?

- Blood pressure
- End tidal CO2
- SaO2
- Temperature
- Heart rate
- Respiratory rate

BEDSIDE NEUROMONITORING DEVICES

- Continuous video EEG (cEEG)
- Amplitude integrated EEG (aEEG)
- Near infrared Spectroscopy (NIRS)

BRAIN FUNCTION

BRAIN PERFUSION
PILLAR #3: NEURO-PROTECTION

Initially the term (NP) applied to treatments and cares to prevent injury and cell death

Now, it encompasses all interventions that promote normal development and prevent disabilities

PREVENTION OF INJURY
POTENTIALLY BETTER PRACTICES TO PREVENT BRAIN INJURY IN VLBW INFANTS

1. Antenatal betamethasone
2. Optimize peripartum management and delivery at a center with a NICU
3. Direct management by Neonatologists/NNPs
4. Minimize pain and stress
   1. Avoid early LP
   2. Developmental Care
5. Optimal Positioning (Mid-line)
6. Treat hypotension (Keep MAP > 30 not GA)
7. Limit postnatal indomethacin use
8. Optimize respiratory support
9. Limit sodium bicarbonate use
10. Use post-natal dexamethasone judiciously (>42 days & too early)


MAINTAIN MIDLINE HEAD POSITION X 72 HOURS
PREVENTION OF NICU COMPLICATIONS

Mounting Evidence for infection and inflammation and it’s impact on brain development

Rethink other NICU programs as Neuro-protective

• NEC Prevention
• Sepsis Prevention
• Ventilator-Induced Brain Injury

Kolan, J of Child Neuro, 2014
Yu, JAMA, 2013

CONTAINMENT OF INJURY
THERAPEUTIC HYPOTHERMIA FOR HIE

- Both body and head cooling have been shown to reduce death and neuro-developmental impairment (RR 0.75, 95% CI 0.68-0.83) and NNT = 7
- Many studies underway to validate effectiveness in different populations & using adjunctive treatments

IDENTIFICATION AND TREATMENT OF SEIZURES

Seizures can accelerate cell death in HI injuries and adversely affect neurogenesis in animal models.

In term newborns with HIE, seizures on EEG are associated with higher mortality and disability at 19 months. Wyatt JS, et al. Pediatrics (2007)

PILLAR #4 - NEURO-DEVELOPMENT

Interventions That Aim To:
- **Grow New Neurons (neurogenesis)**
- **Investigational:**
  - EPO
  - Stem Cell
  - IGF-1
- **Practical:**
  - Massage
  - Kangaroo Care
**GROW & NURTURE NEURONS**

Interventions That Aim To:
- *Nurture the neurons we have*

**NEONATAL NUTRITION**

The Phenomenon Extra Uterine Growth Restriction

Growth is Brain

Optimal Nutrition is Neuroprotective
- Protein
- Essential Fatty Acids
WHAT IS NEURO-PROTECTION??
Interventions That Aim To:
• Nurture the neurons we have
• Minimize Stress and Pain

Appendix A

NICU Infant Stressor Record Sheet (~28 weeks).

INSTRUCTIONS: Enter the time that the procedure was performed (eg: 9:15 am)  

<table>
<thead>
<tr>
<th>Acute Items</th>
<th>(score 5)</th>
<th>7am-8am</th>
<th>8am-11am</th>
<th>11am-1pm</th>
<th>1pm-3pm</th>
</tr>
</thead>
<tbody>
<tr>
<td>extremely stressful</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple attempts inserting IV, IA, UAC/IVC</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Intubation</td>
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<tr>
<td>Insertion pneumothorax chest drain</td>
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<td></td>
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<tr>
<td>Eye examination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>very stressful</td>
<td>(score 4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sectioning of ETT tube</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sectioning of nose and mouth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Removing infant from incubator/bed (unwrapped)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insertion of IV, IA, UAC/IVC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insertion of percutaneous long line</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chronic Items</th>
<th>(score 5)</th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>extremely stressful</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>very stressful</td>
<td>(score 4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>having systemic infection</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>HFU/Jet vent without sedation</td>
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</tr>
</tbody>
</table>
WHAT IS NEURO-PROTECTION??

Interventions That Aim To:

- Offer Positive Sensory Experiences
MINIMIZE EFFECTS ON SENSORY DEVELOPMENT

Tactile
* 8-12 weeks

Vestibular
* 10-14 weeks

Gustatory
* 12-16 weeks

Olfactory
* 14 weeks

Auditory
* 19-25 weeks

Visual
* 5th month through 1st year of life

WHAT IS NEURO-PROTECTION??

Interventions That Aim To:
* Nurture the neurons we have
* Minimize Stress and Pain
* Offer Positive Sensory Experiences
* Minimize Parent-Child Separation
WHAT IS NEURO-PROTECTION??

Interventions That Aim To:

* Protect Sleep
NOISE IN THE NICU

Chronic Stress Exposure
- Can cause physiologic instability

Areas of Research:
- Linked to attention disorders
- Linked to increased ototoxicity of some meds
- Alarm Fatigue

REM SLEEP DEPRIVATION

Results in:
- Disordered sensory system development in infants
- Disordered or disrupted learning and memory creation
- Loss of cortical plasticity into adulthood
- Smaller adult brain size
WHAT IS NEURO-PROTECTION??

Interventions That Aim To:
  * Promote Strong Bonds between Baby and Family

CREATE BONDS THAT WILL LAST A LIFE-TIME
INTEGRATIVE MODEL OF DEVELOPMENTAL CARE

- Safeguarding sleep
- Optimizing nutrition
- Minimizing stress and pain
- Protecting skin
- Positioning and handling
- Partnering with families
- Healing Environment
  - Smell, sound, touch, temperature, light

FINAL THOUGHTS

Brain injury is a reality of many infants in the NICU.

The brain is the organ that has the greatest impact on long term quality of life and function.

We have the opportunity to improve the quality of life of high-risk infants, and the quality of care provided through the expansion of new technologies, therapies, and practices.
**THE 4 PILLARS OF NEURO-CONSCIOUS NICU**

<table>
<thead>
<tr>
<th>Neuro-Assessment</th>
<th>Neuro-Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinical /pain assessment</td>
<td>• EEG</td>
</tr>
<tr>
<td>• Metabolic</td>
<td>• aEEG</td>
</tr>
<tr>
<td>• MRI/MRS</td>
<td>• NIRS</td>
</tr>
<tr>
<td>• Ultrasound</td>
<td>• Hearing Screen</td>
</tr>
<tr>
<td>• Follow up care</td>
<td>• HeRO</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neuro-Protection</th>
<th>Neuro-Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cooling</td>
<td>• Environment</td>
</tr>
<tr>
<td>• Medications</td>
<td>• Sleep</td>
</tr>
<tr>
<td>• Nutrition</td>
<td>• Stress/Separation</td>
</tr>
<tr>
<td>• IVH Bundles (Head position, etc..)</td>
<td>• Positioning</td>
</tr>
<tr>
<td></td>
<td>• Support during procedures</td>
</tr>
</tbody>
</table>

**WHERE ARE YOU NOW? WHERE ARE YOU GOING?**

**Neuro-NICU’s can be a:**

- QI project
- Expanded Program
- New unit design/environment
- Change in culture
Free Online Training

"How To" Series
Videos, Lectures, Q&A's

WWW.SYNAPSECARE.COM
REFERENCES

Theories of Neuroprotection:

Outcomes:

In-Utero Exposures:
- Environmental Working Group 2004 — 10 Americans Study


REFERENCES


Infections and Brain Injury - Kolan, J of Child Neuro, 2014; Yu, JAMA, 2013


Pain, and Parents:
- NICU Parents and PTSD - Shaw, Clements, Poehlmann, Pediatrics 2011