

## Caring for the Infant with Neonatal Brain Injury



Monica Lemmon, MD

Duke University Medical Center  
Duke-Margolis Center for Health Policy

## Disclosures

- There will be discussion of off-label and/or experimental medications in this presentation.
- I have no relevant financial disclosures.

## Learning Objectives

- Define the scope of fetal and neonatal neurology
- Review common neonatal neurologic diagnoses and their management
- Outline potential challenges faced by parents caring for infants with or at risk of neurodevelopmental impairment
- Highlight emerging interventions and models of care in neonatal neurology

*The infant does not advertise his or her neurological disorder with the drama that older children and adults exhibit, but with patience and diligence we can discover a treasure of important clinical clues when we elicit a complete history and careful physical examination.*

-JJ Volpe

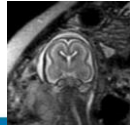


## Fetal & Neonatal Neurology



## Fetal neurology: A growing field

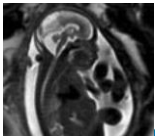
- Increasing use of fetal MRI and prenatal genetic screening
- Neurologists and neurosurgeons increasingly asked to help families understand prenatal CNS findings



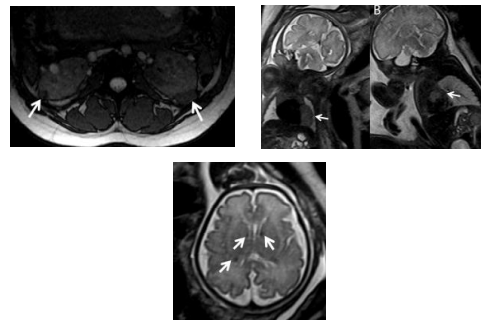
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## Relevant Conditions

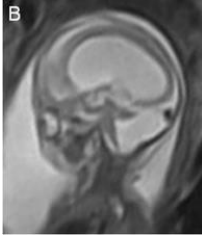
- Brain malformation
  - Lissencephaly
  - Schizencephaly
  - Holoprosencephaly
  - Heterotopias
  - “Dandy Walker”
- Destructive lesions
  - Hemorrhage
  - Stroke
  - Congenital infection
- Known genetic conditions
  - Tuberous sclerosis
  - SMA



## Tuberous Sclerosis



## Posterior Fossa Malformation



Poretti et al. Cerebellum 2016.



Limperopoulos et al. Am J OB/GYN 2006.

## Fetal Neurology: Relevance to Pediatrician

- Often have specialized post-natal care
- Coordination between many services (neonatology, neurosurgery, neurology, palliative care)
- High risk of increased parental anxiety around diagnostic and prognostic uncertainty

## Neonatal Neurology

- Hypoxic ischemic encephalopathy
- Perinatal arterial ischemic stroke
- Encephalopathy of prematurity
  - Intraventricular hemorrhage
  - Periventricular leukomalacia
  - Post-hemorrhagic hydrocephalus
- Congenital brain malformations
  - Congenital hydrocephalus
  - Schizencephaly
  - Lissencephaly
- Meningitis
- Neuromuscular disease
  - Congenital myopathy
  - SMA
  - Fetal akinesia



## Hypoxic ischemic encephalopathy

- Most common cause of brain injury in term infants
- Affects approximately 3 of 1000 live births
- Despite definitive benefit of hypothermia, up to 40% die or experience moderate to severe disability
- ~2000 studies

Shankaran et al. NEJM 2012.

## Hypoxic Ischemic Encephalopathy

- Therapeutic hypothermia started within 6 hours of birth, received for 72 hours
- Continuous EEG monitoring (gold-standard)
- Head ultrasound (at least 1)
- Brain MRI



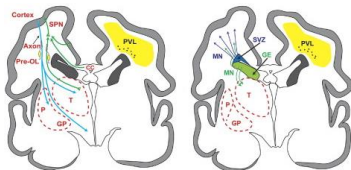
## HIE: Ongoing/upcoming studies

- Late cooling
- Premie cooling
- Neonatal seizure trials
- Cooling +
  - Erythropoetin
  - Darbeoetin
  - Xenon
  - Cell based therapy



## Encephalopathy of Prematurity

- Neonatal brain injury results not only in tissue injury, but in disruption of future brain development
- Intraventricular hemorrhage
- Periventricular leukomalacia



Volpe, Sem Ped Neurol, 2009.

## Considerations for pediatrician

- Risk of neurodevelopmental impairment & spasticity
- Risk of seizure, including infantile spasms
- Feeding difficulties
- Complex medical therapies

## Neonatal Seizures

- Rarely have well-organized generalized tonic-clonic events
- 'Subtle' seizures: Ocular phenomena, oral-buccal-lingual movements, chewing, apnea, tachycardia
- Hard to diagnose—50% accuracy among health care providers
- 80-90% of electrographic seizures do not have a clinical correlate

Malone 2009, Scher 2003, Clancy 2006, van Rooij 2007



## Post-natal epilepsy

- Those with brain injury on MRI and neonatal seizures likely highest risk
- Varied appearance of seizures in first year of life
- When in doubt, call your local neurologist!

## Infantile Spasms

[The child] continued to thrive until he was **four months old**. It was at this time that I first observed slight bobbing of the head forward, which I then regarded as a trick, but were, in fact, the first indications of disease; for these bobbing increased in frequency, and at length became so frequent and powerful, as to cause a **complete heaving of the head forward toward his knees, and then immediately relaxing into the upright position**: these bowings and relax things would be repeated alternately at intervals of a few seconds, and repeated from 10 to 20 or more times in each attack...; which attack would not continue for more than two or 3 minutes; he sometimes has two, three, or more attacks in the day; they come on whether sitting or lying; just before they come on, he is all alive and in motion, making a strange noise, and then all of a sudden down goes his head and upwards his knees; he then appears frightened and screams out...

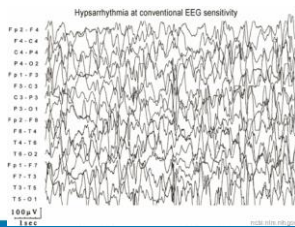
Dr. West, 1841

## Infantile Spasms



## Infantile Spasms

- Neurologic emergency
- Associated with developmental regression
- Earlier treatment = improved outcome
- Treatments:
  - ACTH
  - Prednisolone
  - Vigabatrin
  - Ketogenic diet

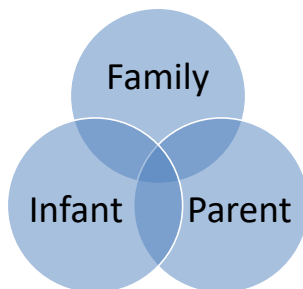


## Spasticity

- Velocity dependent increase in tone
- Non-pharmacologic treatments
  - Therapy
  - Bracing
- Pharmacologic treatments
  - Baclofen
  - Gabapentin
  - Diazepam
  - Botulinum toxin injections



## Outcomes



## Communication Challenges

- Qualitative study of parents of infants with neonatal encephalopathy
- Identified three primary communication challenges
  - Fragmented communication
  - Difficulty understanding complex medical information
  - Prognostic uncertainty

Lemmon et al. *Pediatrics* 2016.

## Representative quotes

*It was just day by day; we're just going to have to see how she does for the next 6 months. And I don't think you understand what that means to a parent. **It can really mess up the mom when she doesn't know how her kid's going to be.***

*It [prognosis] could be anything from slower developmental functioning, to difficulty learning that seemed very mild, to an inability to see, to talk, or physical disability. **It just seemed like the range was massive. The full range of brain function was on the table.***

## *Parent Experience of Neonatal Encephalopathy: The need for family-centered outcomes*

- Cooling other longitudinal interventions offer promise for infants with hypoxic ischemic encephalopathy
- Early therapies & developmental follow-up are cornerstones of care
- These interventions only work if families meaningfully participate
- Family resiliency & engagement are critical for long-term infant outcome

## Results

### Theme 1: Families experience **cumulative loss & grief**

- Perinatal crisis—"robbed" of birth experience
- Neonatal course—disrupted bonding, breast feeding
- Subsequent missed developmental milestones—loss of "normal" child

*It's so much more than just having a traumatic birth. It's the death of the dream of imagining yourself giving birth and holding your baby with your husband there. It's this magical moment that you think about forever. Whereas...it soon becomes a trauma situation.*

-Mother of infant with brain injury

## Representative Quote

I never really thought about how the physician would probably be, sort of, “a check in,” who is constantly saying, well here are the milestones, here’s where we should be, we’re concerned if we’re not... So when you hit a milestones benchmark, that’s the point at which you find out there’s something that you should be looking at. Given the history, you really want to make sure there isn’t anything you’re missing.

## Theme 2: Families experienced **entangled infant & family interests**

- Maternal choices re: delivery
- Maternal post-partum care vs. presence for infant
- No prenatal planning for job/family disruption
- Complex home care, quit job vs trust others
- Guilt—a bad outcome will be my fault

## Theme 3: Parents evolved into & found meaning in **role as advocate**

- May start with blame (self, clinicians)
- My baby needs individualized hospital care
- I know best what services my child needs
- I am extra vigilant
- My child is perfect

## Areas for targeted interventions

1. **Additional layers of parent support** for all TH families:
  1. Palliative care consults, social work, pastoral care, local and online resources
  2. Routinely assess whole family well-being at follow-up
2. Anticipate real or perceived **trade-offs between infant & family well-being**:
  1. Explore parent guilt
  2. Troubleshoot barriers: transportation, housing, competing family obligations
  3. Shared decision-making should disentangle family & infant interests
3. **Advocacy roles** help families cope:
  1. Offer “advocacy training” to focus parents’ efforts
  2. Incorporate families as key stakeholders in study design, data interpretation & dissemination
4. Better **define and measure family outcomes** related to NE/ TH
  1. Psychological outcomes: anxiety, guilt
  2. Social outcomes: financial strain, work lost, relationships
  3. Parenting outcomes: hypervigilance, “vulnerable child”



## Models of Care



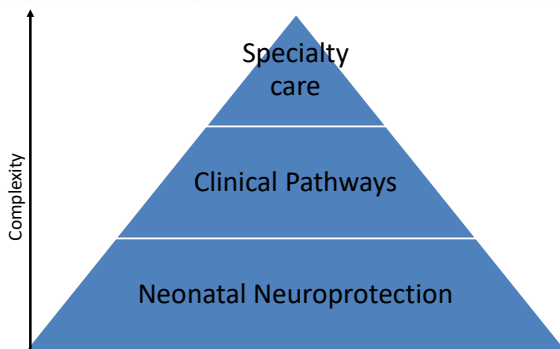
Sue Peloquin, RN  
<https://pediatrics.ucsf.edu/pediatric-specialties/neonatology/nicn>

## Neonatal Neurocritical Care

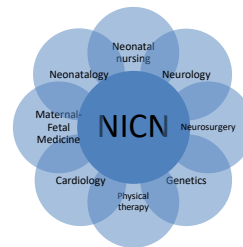
- Goal: To improve neurodevelopmental outcomes for infants at risk of brain injury.
- Components:
  - Dedicated neonatal neurocritical care team
  - Specialized nursing expertise
  - Expertise in neonatal monitoring, electrophysiology, neuroimaging, neurodevelopmental care and intervention
  - High risk infant follow-up



Glass et al., Neurocritical Care 2010.



## An interdisciplinary approach



## Impact of NICN teams

- Improved seizure detection
- Decreased phenobarbital burden
- Decreased AED use at discharge

Weitstock JCN 2015.

Bashir et al, Pediatric Neurology 2016.

## Opportunities for Collaboration

- PQCNC: Perinatal quality collaborative of NC
  - Quality improvement initiatives
  - Best practices
- NICHD: Neonatal network
  - Ancillary studies
  - Ongoing: Premie cooling



## Volpe: Lessons Learned



1. Examination of the infant requires patience, a careful eye, and minimal intrusion.
2. We attribute the most importance to what we see by neuroimaging, although what we see often is not of most importance.
3. We forget that neonatal brain is vigorously developing and that neonatal brain injury results not only in tissue loss but also disturbances in subsequent brain development.
4. We think we know it all.

## Summary

- Fetal and neonatal neurology are growing in scope.
- Emerging interventions offer hope for families and clinicians.
- Parents of children with or at risk of neurodevelopmental impairment likely have unique needs.
- New interventions and models of care in neonatal neurology may improve infant and family outcomes.

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## Questions?



References available on request