# Developing a Neuro NICU

### Courtney Wusthoff, MD MS

Assistant Professor, Neurology Neurology Director, LPCH Neuro NICU





# Acknowledgments

Frances Cowan

Miriam Martinez-Biarge

Susan Hintz

Kathi Randall

Sonia Bonifacio

## Disclosures

- I have no conflicts of interest
- I will discuss off-label use of anti-epileptic drugs (AEDs) for treatment of neonatal seizures

# Learning Objectives

At the conclusion of this activity, participants should be able to...

- 1. Summarize the benefits of a designated Neuro NICU
- 2. Debate the benefits and drawbacks of requiring specific certification for cooling centers
- 3. Evaluate opportunities to provide enhanced brain care in your NICU

### A Newborn with Seizures

- 41-week boy readmitted on day 5 with suspected seizures, lethargy
- Normal pregnancy, maternal UTI at 36 weeks
- Delivery vacuum-assisted with 3 pop-offs, "difficult"
- One day of phototherapy for jaundice, then discharged home
- Day 4- sleepier, feeds less
- Day 5- two seizures → 911

- Are these seizures?
- What is the cause?
- How can we customize treatment?

## Outline

- Why a Neuro NICU?
- Models of Neonatal Neurology Care
- The LPCH Neuro NICU
- Improving brain care at your center

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# Why a Neuro NICU?

- NICU survival is improving
- Neurodevelopmental outcomes are a priority
- Technology has improved to allow better neuromonitoring, imaging and intervention
- Converging expertise in fetal medicine, neonatology, neurology, neuroradiology, neurosurgery, developmental pediatrics

### Neonatal Neurocritical Care Service Is Associated With Decreased Administration of Seizure Medication

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(S)SAGE

Sharon O. Wietstock, MSc1, Sonia L. Bonifacio, MD2, Charles E. McCulloch, PhD3, Michael W. Kuzniewicz, MD, MPH2,4, and Hannah C. Glass, MDCM, MAS<sup>2,5</sup>

Original Article

Implementation of a Neurocritical Care Program: Improved Seizure Detection and Decreased Antiseizure Medication at Discharge in Neonates With Hypoxic-Ischemic Encephalopathy

Rani Ameena Bashir MD a, Liza Espinoza MD a, Sakeer Vayalthrikkovil MD a. Jeffrey Buchhalter MD b,c, Leigh Irvine NPa, Luis Bello-Espinosa MD b,c, Khorshid Mohammad MD a,\*

### Time to electroencephalography is independently associated with outcome in critically ill neonates and children

\*† Iván Sánchez Fernández, \* Arnold J. Sansevere, \*Rejean M. Guerriero, \*Ersida Buranigi, \*Phillip L. Pearl, †Robert C. Tasker, and \*Tobias Loddenkemper

> Epilepsia, 58(3):420-428, 2017 doi: 10.1111/epi.13653

Section of Neonatology, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada

b Section of Pediatric Neurology, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada

Department of Pediatrics, Alberta Children's Hospital Research Institute, University of Calgary, Calgary, Alberta, Canada

## Outline

- Why a Neuro NICU?
- Models of Neonatal Neurology Care
- The LPCH Neuro NICU
- Improving brain care at your center

## The first Neuro ICN



- Dedicated Neuro-Intensive Care Nursery
  - Virtual unit in 58-bed intensive care nursery
  - Cohort of trained NICN nurses
  - Co-management model with a Neonatal Neurology Service in-unit
- 150 consults/year
  - 75% transferred for specialized care
  - 2/3 term, 1/3 preterm
  - 50% have primary neurologic diagnosis

# Neuro Expertise as a NICU Resource

- Hammersmith Hospital & Imperial College NHS
  - Referral Center for West London
  - Neurologist within a NICU
  - Consulted on 1-3 babies per week
- Currently over 12 "Neuro NICUs nationwide"
  - Neonatal Neurology
  - Designated neonatal neurologist





## Tele-Neuro-NICU

- Kaiser Permanente Northern California non-profit integrated health care delivery network with >3.8 million members, ~35,000 births per year
- 13 pediatric neurologists provide phone or in-person consultation to 21 hospitals
- In-person coverage at 2 Level III NICU's (22 and 24 beds),
   phone consults at other sites
- 1-3 in-person NICU consults/week (1 in 5 call)
- Special interest in vascular neurology, High Risk Infant Follow-up Clinic 3 days/month

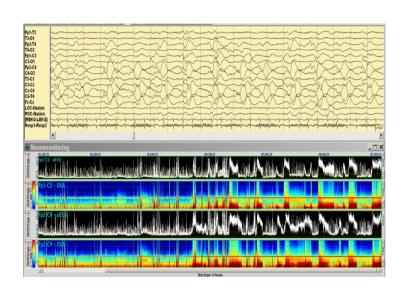
## Tele-Neuro-NICU

### ORIGINAL ARTICLE

Telemedicine for genetic and neurologic evaluation in the neonatal intensive care unit

TL Wenger<sup>1,2</sup>, J Gerdes<sup>3</sup>, K Taub<sup>4</sup>, DT Swarr<sup>1,3</sup>, MA Deardorff<sup>1</sup> and NS Abend<sup>4</sup>

37 of 39 abnormalities on neuro exam identified (92%) in pilot study

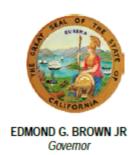


 Tele-EEG rapidly growing nationwide

# **Special Case: Cooling Centers**



# State of California—Health and Human Services Agency Department of Health Care Services



DATE: November 17, 2016 Numbered Letter: 06-1116

Index: Program Administration

TO: CALIFORNIA CHILDREN'S SERVICES (CCS) PROGRAM COUNTY

ADMINISTRATORS, MEDICAL CONSULTANTS, AND STATE SYSTEMS

OF CARE DIVISION OFFICE STAFF

SUBJECT: PROGRAM REQUIREMENTS FOR PROVIDING NEONATAL

THERAPEUTIC HYPOTHERMIA

#### I. PURPOSE

This Numbered Letter (N.L.) describes minimum requirements for CCS Programapproved Neonatal Intensive Care Units (NICUs) to provide therapeutic hypothermia services to neonates.

# California Cooling Centers

- In 2013, Bay Area Cooling Summit began to discuss voluntary standards for sites
- Workgroups targeted specific aspects
  - Training/education
  - EEG/aEEG
  - Ancillary services
- A 2014 survey by Sonia Bonifacio assessed current practices and desired practices of 54 California neonatologists
  - 65% were already cooling

Table 2. Therapeutic Hypothermia			
		n	%
Type of TH	Selective head cooling	1	2.4
	Whole body cooling	37	88.1
	Both	4	9.5
TH protocol used	Yes	42	100.0
TH protocol based on one used in			
a randomized controlled trial	Yes	39	92.9
	No	1	2.4
	Don't know	2	4.8
Neurology consulted for			
neonates who receive THb	Yes	39	92.9
	Depends	1	2.4
	No	0	0.0

Table 2. Therapeutic Hypotherm			
		<b>.</b>	0/
		n	%
Brain monitoring used	Yes	37	88.1
	No	5	11.9
Type of brain monitoring <sup>c</sup>	aEEG	13	31.0
	EEG	4	9.5
	both aEEG and EEG	21	50.0
	Don't know	1	2.4
Percent of MRIs reviewed by			
Pediatric Neuroradiologist	None	7	16.7
	< 50%	5	11.9
	50-99%	4	9.5
	100%	26	61.9
Percent of neonates treated			
with TH referred for follow-up	<50%	0	0.0
	50-99%	3	7.1
	100%	39	92.9

# Practices Important for Providing Safe & High Quality TH

- Critical essential service, should be required at all cooling centers
- Recommended important or advisable, but hospital could perform cooling without this
- Optional may be desirable, but not al all required for every cooling center
- No Opinion

Table 3. Opinions about Providing Therapeutic Hypothermia		Community/ Intermediat e Centers <sup>a</sup>		Regional Centers <sup>b</sup>		Total	
		n	%	n	%	n	%
Pediatric Neurologist							
available to consult	Critical	19	57.6	10	47.6	29	53.7
	Recommended	10	30.3	10	47.6	20	37.0
	Optional	3	9.1	0	0.0	3	5.6
Nursing Staff trained in TH	Critical	29	87.9	16	76.2	45	83.3
	Recommended	3	9.1	5	23.8	8	14.8
Access to Developmental							
Followup	Critical	32	97.0	21	100.0	53	98.1
	Recommended	0	0.0	0	0.0	0	0.0
	Optional	0	0.0	0	0.0	0	0.0
Palliative Care Team	Critical	11	33.3	3	14.3	14	25.9
	Recommended	13	39.4	14	66.7	27	50.0
	Optional	7	21.2	3	14.3	10	18.5
	No Opinion	1	3.0	1	4.8	2	3.7
OT/PT available to consult	Critical	24	72.7	15	71.4	39	72.2
	Recommended	6	18.2	6	28.6	12	22.2
	Optional	2	6.1	0	0.0	2	3.7

Table 3. Opinions about Provi Hypothermia	ding Therapeutic	Interr	nunity/ nediate		gional		
		Cer	iters <sup>a</sup>	Cer	nters <sup>b</sup>	To	tal
		n	%	n	%	n	%
aEEG monitoring throughout							
тн	Critical	22	66.7	16	76.2	38	70.4
	Recommended	5	15.2	4	19.0	9	16.7
	Optional	5	14.2	0	0.0	5	9.3
	No Opinion	0	0.0	1	4.8	1	1.9
Continuous video EEG							
monitoring	Critical	7	21.2	5	23.8	12	22.2
	Recommended	12	36.4	10	47.6	22	40.7
	Optional	13	39.4	5	23.8	18	33.3
	No Opinion	0	0.0	1	4.8	1	1.9
Continuous video EEG							
monitoring available 24/7	Critical	7	21.2	3	14.3	10	18.5
	Recommended	8	24.2	10	47.6	18	33.3
	Optional	15	45.5	7	33.3	22	40.7
	No Opinion	1	3.0	1	4.8	2	3.7
Pediatric Neuroradiologist							
review MRI	Critical	13	39.4	6	28.6	19	35.2
	Recommended	15	45.5	10	47.6	25	46.3
	Optional	3	9.1	5	23.8	8	14.8
	No Opinion	1	3.0	0	0.0	1	1.9

Table 3. Opinions about Prov Hypothermia	iding Therapeutic	Inter	nunity/ mediat entersª		gional nters <sup>b</sup>	To	tal
		n	%	n	%	n	%
From quality perspective, is there a minimum number of neonates to							
be treated	No	10	30.3	5	23.8	15	27.8
	Yes	22	66.7	16	76.2	38	70.4

- In practice, median number of cooled infants at each site was 12/year
- Respondents suggested a minimum volume of 10 neonates/year

# **Special Case: Cooling Centers**



State of California—Health and Human Services Agency
Department of Health Care Services



- Cooling Centers shall treat 6 patients annually
- If <12 patients per year, have a formalized relationship with a regional center of expertise
- Neonatologist working in conjunction with a pediatric neurologist and clinical nurse specialist
- Child neurologist available for consultation at all times, at minimum by phone
- cEEG available, at minimum, during regular hours
- cEEG must be interpreted within 24 hours
- All babies get eiterh cEEG or aEEG for duration of cooling and rewarming
- All infants must perform on site MRI prior to discharge, to be interpreted by a neuroradiologist with experience in neonatal brain imaging

## Outline

- Why a Neuro NICU?
- Models of Neonatal Neurology Care
- The LPCH Neuro NICU
- Improving brain care at your center

## The LPCH Neuro NICU

- Patients
  - Which patients?
  - When/for how long?
- People
- Technology
  - Neuromonitoring
  - Neuroimaging
  - Neuroprotection
- Training & Research
- Care after the NICU

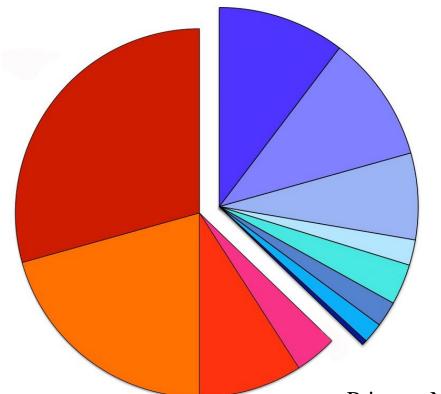
## What is the LPCH Neuro NICU?

- 6 bed virtual unit within a unit
- Opened April 2013
- Emphasis on training, communication, and high quality interdisciplinary care
- Joint daily Neuro NICU rounds
- Core team of >70 Neuro NICU trained RNs
- In our first year, 220 babies received care in the Neuro NICU

# The NNICU Top <del>10</del> 13

Diagnosis	LOS	Monitoring	Neuro consult
HIE/cooling	7-10	aEEG/cEEG & NIRS	Yes
Seizures	7	aEEG/cEEG	Yes
ECMO/pre-ECMO	7	NIRS	PRN
Critical/unstable	7	NIRS & consider aEEG	PRN
Preemie <29 weeks	7-10	NIRS	PRN
Grade III/IV or hydrocephalus	7	aEEG/cEEG	Yes
Metabolic disease	7	aEEG/cEEG	PRN
CNS anomalies/Primary neurologic disorders	7	aEEG/cEEG	Yes
Cyanotic CHD	7	NIRS	PRN
CNS infection	7	aEEG/cEEG	Yes
Symptomatic PDA	7	NIRS	PRN
Brief Resolved Unexplained Event /ALTE	3	aEEG	PRN
Indirect Hyperbilirubinemia >95 <sup>th</sup> %	3	aEEG & NIRS	PRN

### 2013-2014 NNICU Admissions



- 247 patients
- 28% of NICU volume
- 64% had a nonneurological primary diagnosis
- 42% preterm

### Primary Medical Diagnoses

- Cyanotic CHD (29.3%)
- Extreme Prematurity < 28 weeks (20.7%)
- Critical/Unstable (9.1%)
- Metabolic Disease (3.7%)

### Primary Neuro Diagnoses

- Seizure (10.3%)
- HIE/Cooling (10.3%)
- Neuro Concerns w/o firm diagnosis (7.0%)
- Meningitis (5.2%)
- ☐ Grade III/IV IVH/Hydrocephalus (3.3%)
- Neural tube defects (2.1%)
- CNS anomalies (1.7%)
- Stroke (0.4%)

# People: Interdisciplinary Care

- Designated Neuro NICU nurses
- Neonatology providers
- Neurology consult service
- Developmental care team
- Neurosurgery, Neuroradiology
- High Risk Infant Follow-Up Clinic

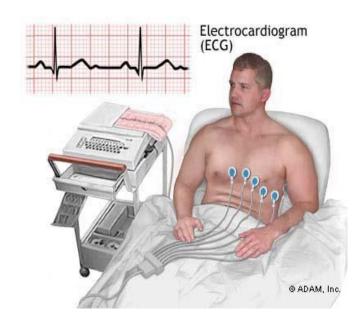
# Technology: Brain Monitoring

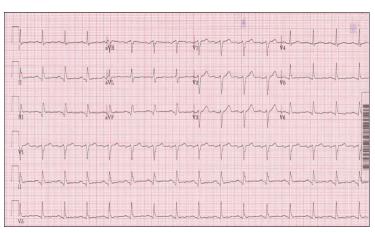
- Continuous Video-EEG monitoring
- Amplitude-integrated EEG (aEEG)
- Near Infrared Spectroscopy (NIRS)
- Complimentary, bedside tools used in conjunction with clinical assessment and other diagnostics
- Provide real-time information about brain function

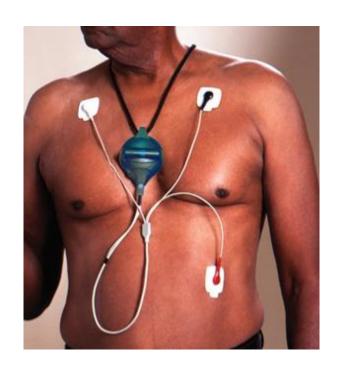
## **Brain Monitoring: EEG**

- Video EEG monitoring available 24/7
- Remote review by pediatric neurophysiologists
- Standard care for neonates with suspected seizures
- Evidence-based protocols for high risk patients

# ECG vs Screening Telemetry









# Technology: When to get (a) EEG?

- When there is an obstacle to the neuro exam, but information on brain function is needed
- To formulate prognosis
- Any baby where seizures are suspected
- In neonates at high risk for seizures
- To assess response to treatment



# Technology: Impact of Monitoring

- Implementation of cEEG in a Neuro NICU<sup>1</sup>
  - 51%
     → 48% with clinically diagnosed seizures
  - 34%→ 53% had seizures on EEG
  - 0%
     → 14% with subclinical seizures diagnosed
  - 70%→ 37% discharged on antiseizure medicine
  - 62.2 mg/kg → 46 mg/kg mean phenobarbital
- cEEG and aEEG Influences Management<sup>2</sup>
  - Spot EEG only vs aEEG vs cEEG
  - Adjust risk of antiseizure med use ↓67%
  - With aEEG ↓38%

<sup>2.</sup> Jan S. Dev Neurosci 2017

# Technology: Impact of Monitoring

- Monitoring with a standard treatment protocol<sup>2</sup>
  - Phenobarbital levels 56.8 → 41 ug/ml
  - Status epilepticus 46→36%
  - Length of stay decreased 9.7 days
- Neurocritical care service with VEEG<sup>2</sup>
  - Received 30 mg/kg less phenobarbital
  - 5 fewer days seizure medicine

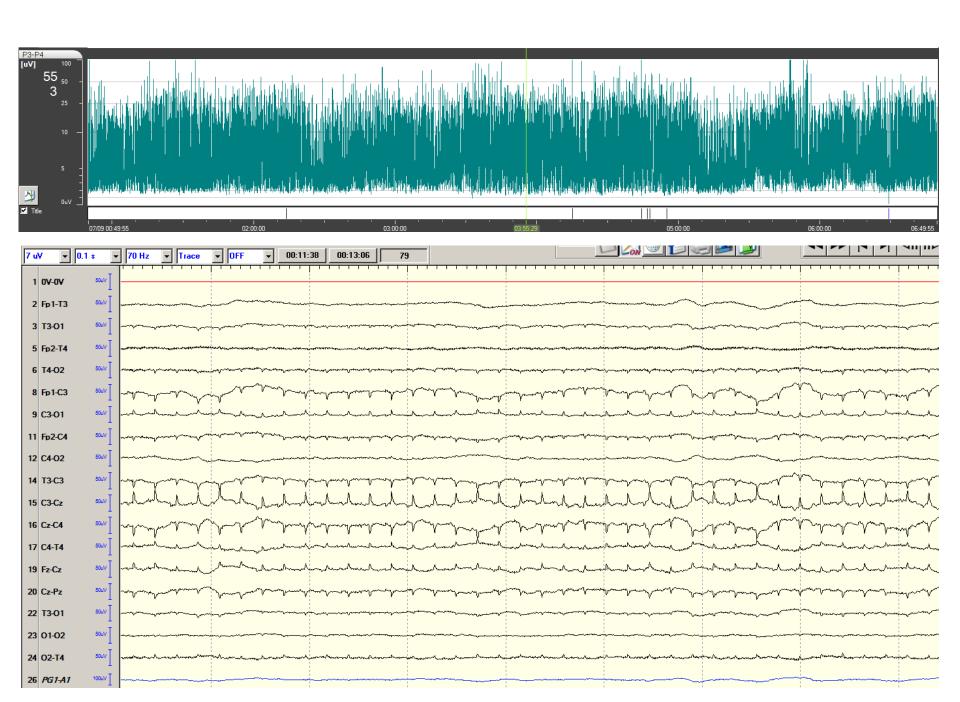
# www.acns.org/guidelines.cfm

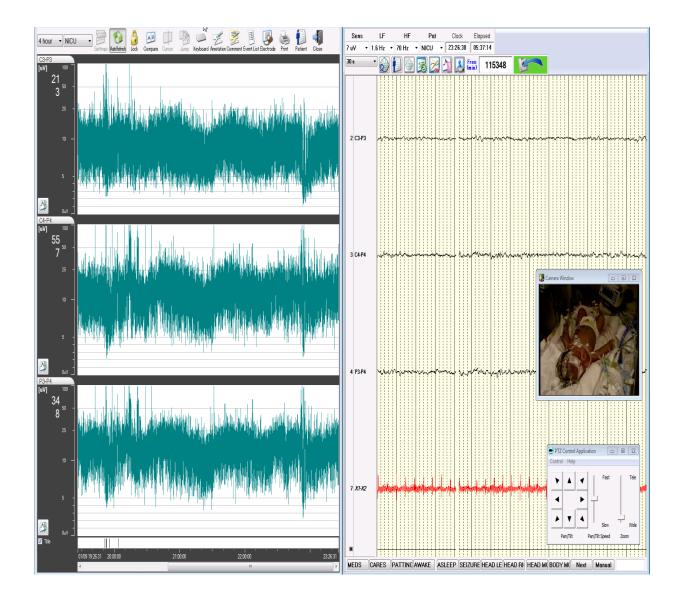
### ACNS GUIDELINE

The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates

Renée A. Shellhaas,\* Taeun Chang,† Tammy Tsuchida,† Mark S. Scher,‡ James J. Riviello,§ Nicholas S. Abend, Sylvie Nguyen,¶ Courtney J. Wusthoff,# and Robert R. Clancy

J Clin Neurophysiol 2011;28: 611-617





## Technology: NIRS

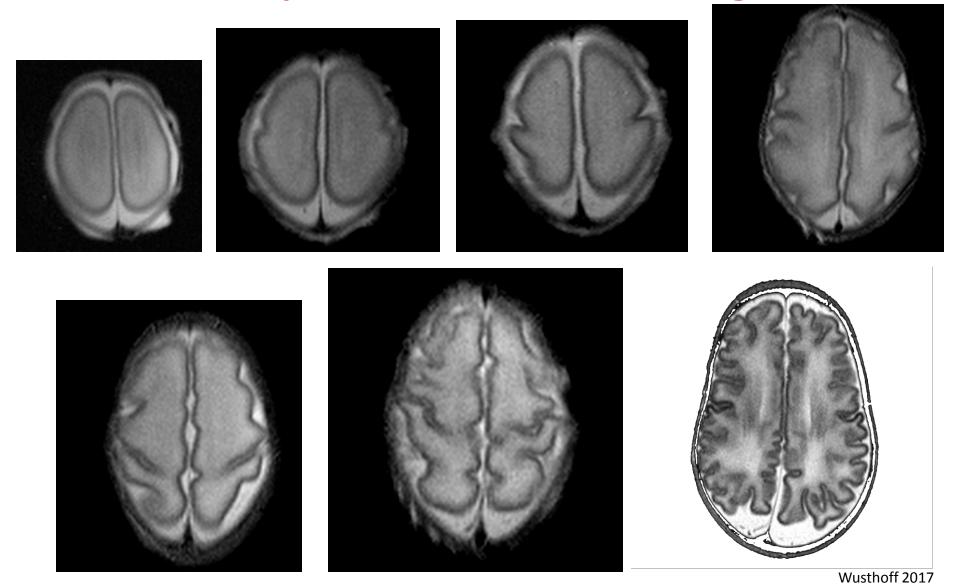
Near Infrared Spectroscopy (NIRS)





# Technology: Imaging

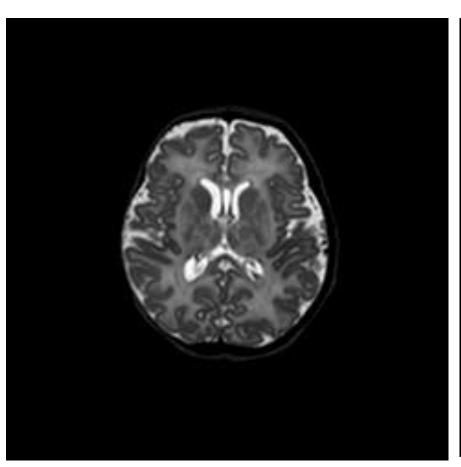
Brain development from 24 to 40 weeks gestation

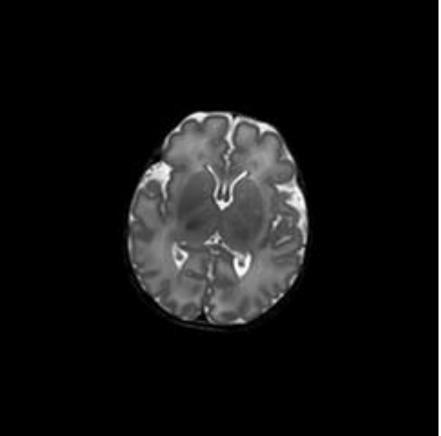


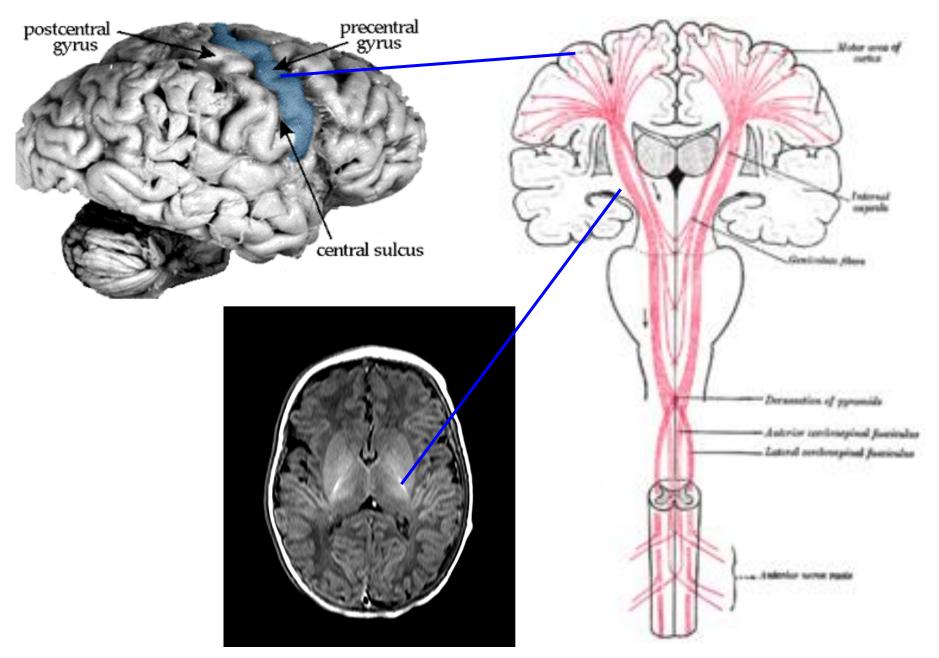


Can neurologists say anything useful about prognosis?

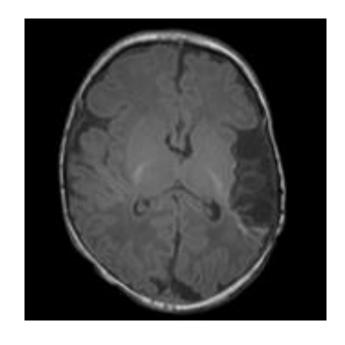
# Imaging: Two newborns with HIE



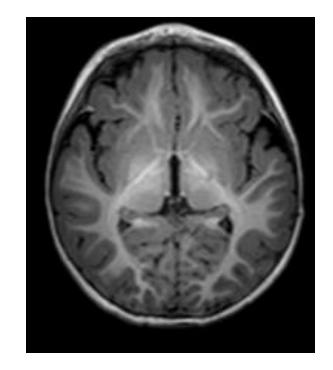




## **Imaging & Prognosis**



No hemiplegia



Hemiplegia

#### Neuroprotection: Developmental Care

"(Although) Nursing has been limited to signify little more then the administration of medicines.....It ought to signify the proper use of air, light, warmth, cleanliness, quiet, and the administration of diet."

Florence Nightingale, 1859

## Teaching: Team Training

- Med Students, Peds Residents, Neuro Residents, NICU Fellows, Visiting Trainees
- Neuro NICU Training course
  - >70 team members graduated to date
- Quarterly Skills Workshops
  - Neuro examination of the neonate
  - Use of therapeutic hypothermia
  - aEEG use and interpretation
- Weekly Perinatal Case Conference
- "5-minute Friday" team teaching
- Regional Outreach (MCCPOP)



#### Research

NNICU Database Page 1 of 10

#### **NNICU Database Admission Data**

Study ID			
NNICU Admission Data			
LPCH Admit Year and Month (YYYY-MM)	Found in H&P or Discharge Summary	(Please enter just year and month in this field)	
Date and time of birth Found in Delivery Summary or H&P		(Enter exact date and time of birth in this field.)	
Date of LPCH Admission Found in Discharge Summary		(Enter date)	
Date of NNICU admission Found in NNICU database (excel)		(Enter date)	
Date of LPCH discharge Found in Discharge Summary		(Enter date)	
Length of NNICU Admission (Calculated)		(This field will automatically calculate)	

Home

#### WebAuth Login

Log in with WebAuth

# The Neurologic Exam for Neonates with Suspected Encephalopathy

Best viewed using Firefox or Chrome. May not be compatible with all versions of Internet Explorer.

Encephalopathy is defined by the presence of one or more signs in at least three of the following six categories:

- level of consciousness
- spontaneous activity
- nosture
- tone
- primitive reflexes
- autonomic nervous system

When findings are mixed, the extent of encephalopathy is determined by which category describes the majority of signs. If signs were equally distributed, categorize based on the level of consciousness.

#### Diagnostic Table

Normal	Mild Encephalopathy	Moderate Encephalopathy	Severe Encephalopathy







#### Diagnostic Table

	Normal	Mild Encephalopathy	Moderate Encephalopathy	Severe Encephalopathy
Level of consciousness	When awake, alert, fixes on visual stimuli (see example)	Irritable, hyperalert, poor feeding, excess crying alternating with sleeping	Lethargic (see example)	Stupor or coma
Spontaneous activity	Frequent spontaneous movements (see example)	Increased, jittery (see example)	Decreased activity	No activity (see example)
Posture	Extremities flexed in toward the trunk (see example)	Slight flexion, slight extension (see example)	Distal flexion, complete extension (see example)	Decerebrate
Tone	Normal (see example)	Normal or slightly increased (see example)	Hypotonia (focal or general) (see example)	Flaccid (see example)
Primitive	Strong	Uncoordinated	Weak or	Absent

#### Care After the Neuro NICU

- High Risk Infant Follow Up
  - Standard for all Neuro NICU grads
  - In-depth developmental evaluations
- Neurology Follow Up
  - Offered to all Neuro NICU grads
  - With Neonatal Neurologist or the inpatient consulting physicians
- Outpatient Neonatal Neurology Clinic
  - Referrals accepted from outside NICUs
  - Outpatient referrals for neonates and young infants

## Back to Our Case...

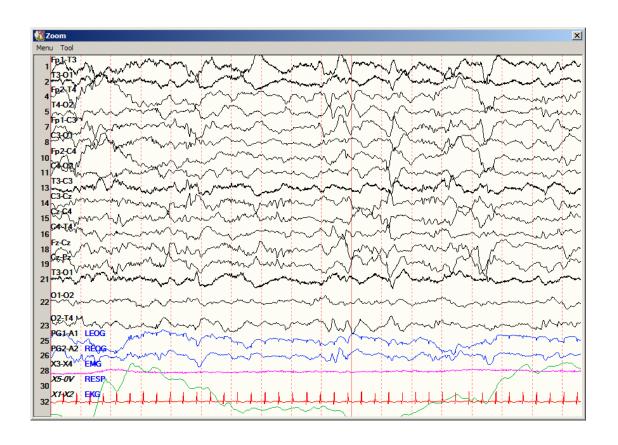
#### A Newborn with Seizures

- 41-week boy readmitted on day 5 with suspected seizures, lethargy
- Normal pregnancy, maternal UTI at 36 weeks
- Delivery vacuum-assisted with 3 pop-offs → "difficult" delivery
- One day of phototherapy for jaundice, then discharged home
- Day 4- sleepier, feeding less
- Day 5- two shaking episodes → parents called 911

- Are these seizures?
- What is the cause?
  - How can we customize treatment?

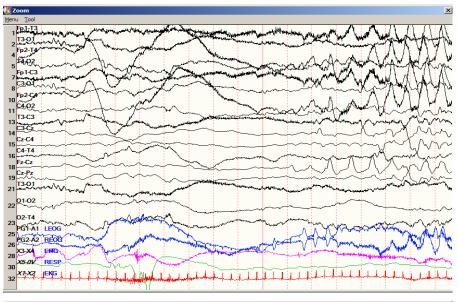
#### **EEG Monitoring**

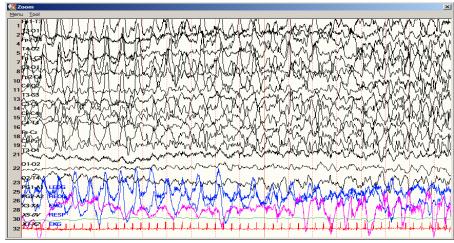
- First hour: Abnormally slow background with sharps
- Next hour: More of the same



#### **EEG Clues**

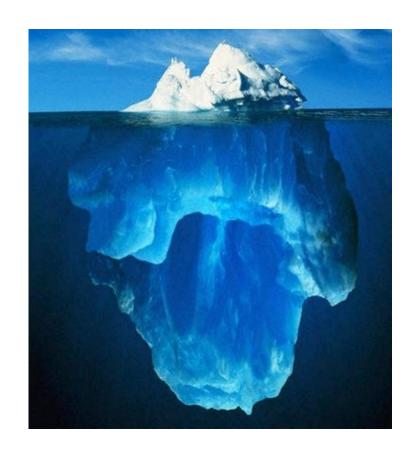
- Seizures confirmed on EEG
- 5 seizures over the next 24 hours; 3 are identified at the bedside, 2 are recognized only on video EEG.
- Multiple medications given, with seizure frequency gradually improving
- Still encephalopathic
- Why?



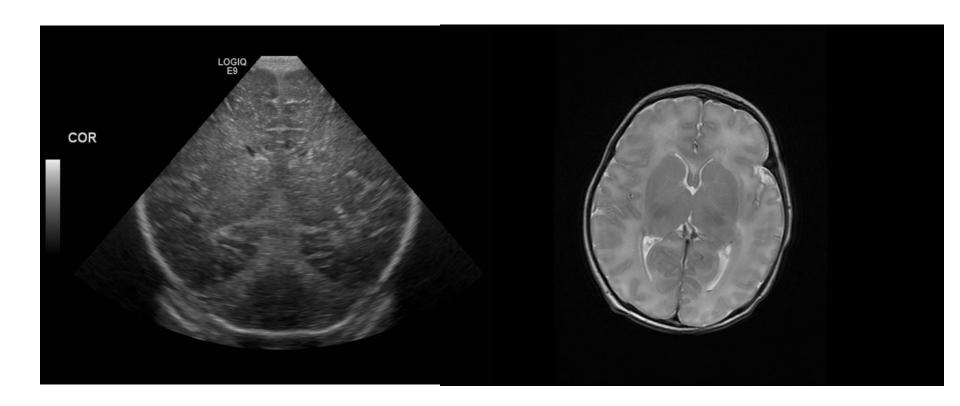


# Most Neonatal Seizures are Symptomatic

- ~80% of neonatal seizures are symptomatic of acute brain injury
- Common causes:
  - Cerebral hypoxia-ischemia (~50% in US)
  - Stroke/hemorrhage (15-30%)
  - Infection
  - Malformations
  - Electrolytes/hypoglycemia
- ~20% due to early-onset epilepsy
  - KCNQ2 mutations most common
  - Brain malformations/other syndromes



## Neuroimaging



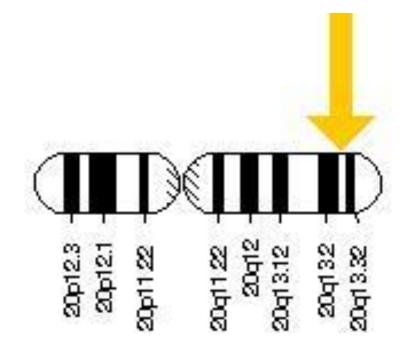
- Brain imaging normal
- Lab studies normal
- Evaluation for infection negative

### Talking with Parents

- Parents very concerned that vacuum assisted delivery related to seizures
- Mother had been offered C-section, but wanted to try for vaginal delivery, which led to VAVD
- Parents worry that their decision had caused baby harm
- Father's nephew (patient's cousin) has ADHD and mild developmental delays
- Father learns his own brother (patient's uncle) had "mild seizures" as a young child, which he outgrew before adulthood

## **Genetic Testing Performed**

- Based on this history, a provisional diagnosis of Benign Familial Neonatal Seizures (BFNS) is made
- Genetic testing confirms a heterozygous mutation in the KCNQ2 gene
- Known cause of BFNS



#### KCNQ2 and Neonatal Seizures

- BFNS occurs in <2/10,000
- Frequent, brief seizures start day 2-3
- Typically tonic or clonic seizures (not myoclonic)
- Often difficult to control
- Otherwise healthy baby
- Normal MRI, variable EEG findings
- Seizures spontaneously resolve ~4 months
- Most commonly caused by KCNQ2 mutations, less commonly KCNQ3 mutations

Ronen GM et al, Neurology 1993 Ronen GM et al, J Pediatr 1999 Wusthoff CJ, J Ped Epilepsy 2012

#### Outline

- Why a Neuro NICU?
- Models of Neonatal Neurology Care
- The LPCH Neuro NICU
- Improving brain care at your center

## Improving Brain Care at Your Center

- Gather stakeholders
- Inventory strengths and assets
- Identify 1-3 targets for first round
- Start by building on strengths:
  - Cooling
  - Seizures
  - IVH
  - Nursing
  - Developmental care
  - Fetal Medicine
  - Genetics
  - Neurosurgery
  - Neuroradiology
  - HRIF/DB Peds

- EEG
- aEEG
- NIRS
- Ultrasound

#### Brain Care at Your Center

- Patients
  - Which patients?
  - When/for how long?
- People
- Technology
  - Neuroprotection
  - Neuromonitoring
  - Neuroimaging
- Training & Research
- Care after the NICU

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#### More Information

http://neonatology.stanford.edu/ClinicalCare/NeuroNICU.html

