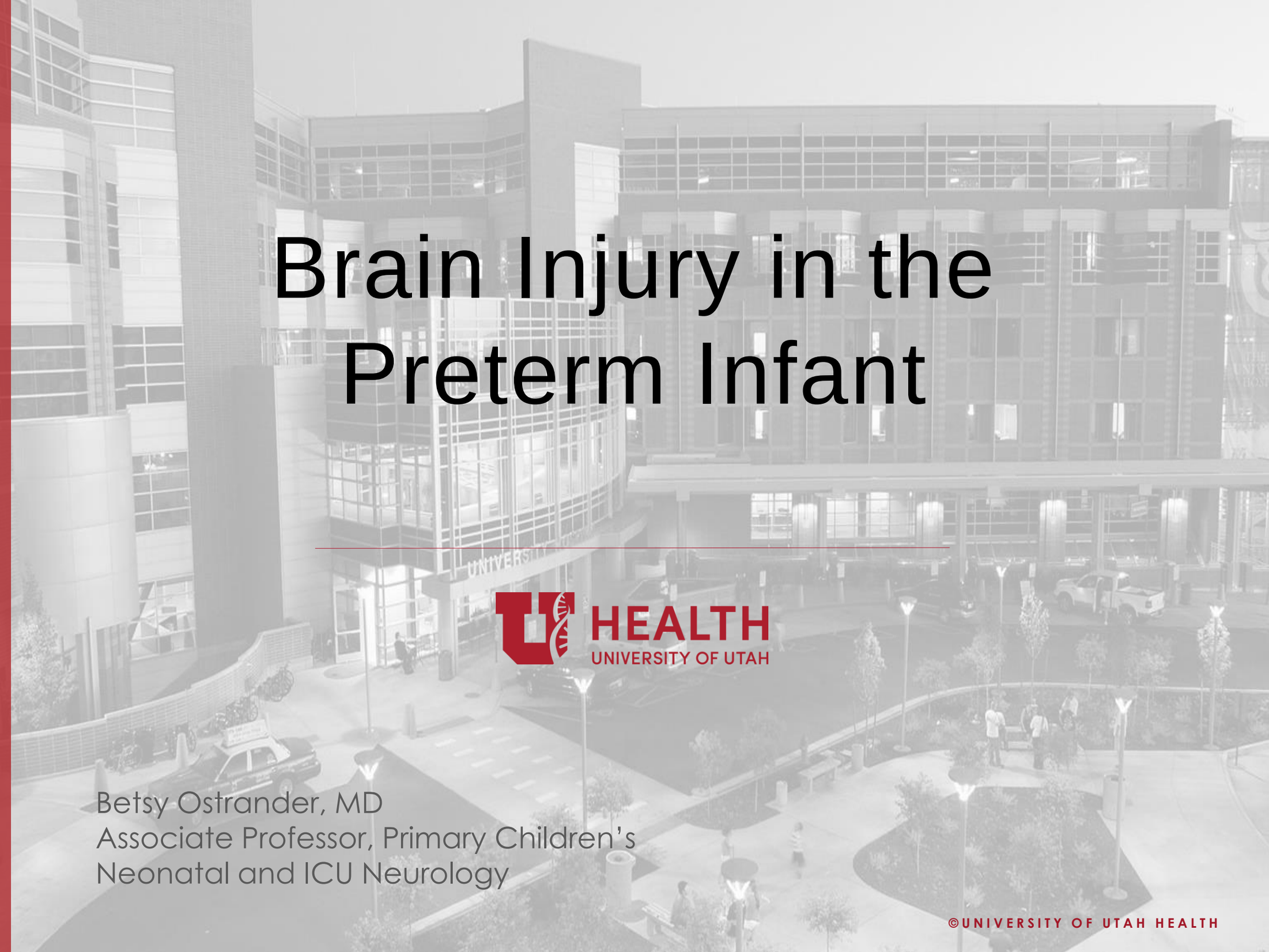
Brain Injury in the Preterm Infant



Betsy Ostrander, MD
Associate Professor, Primary Children's
Neonatal and ICU Neurology

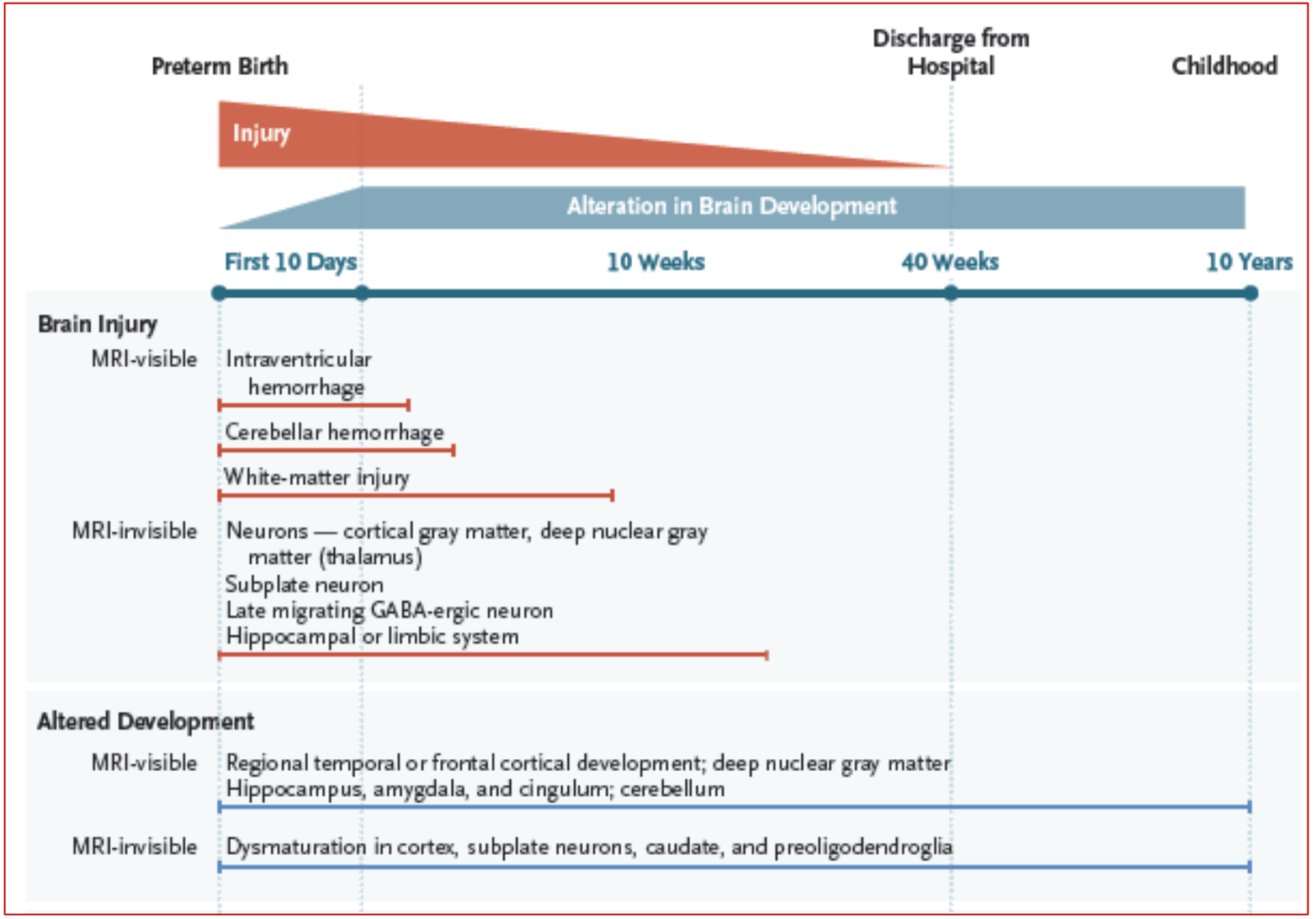
DISCLOSURES

- Nothing to disclose
- Off label use of seizure medications is discussed

LEARNING OBJECTIVES

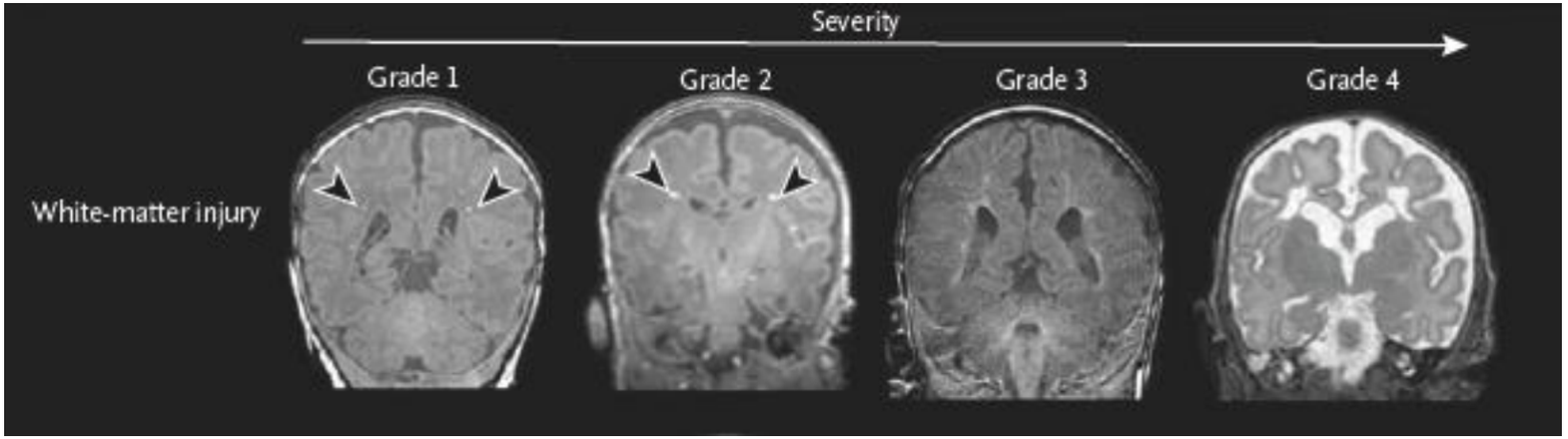
- Identify common types of brain injury patterns in preterm infants
- Review principles of IVH evaluation and management of post hemorrhagic ventricular dilation
- Discuss seizure semiology, monitoring and treatment

TIMELINE OF VULNERABILITY



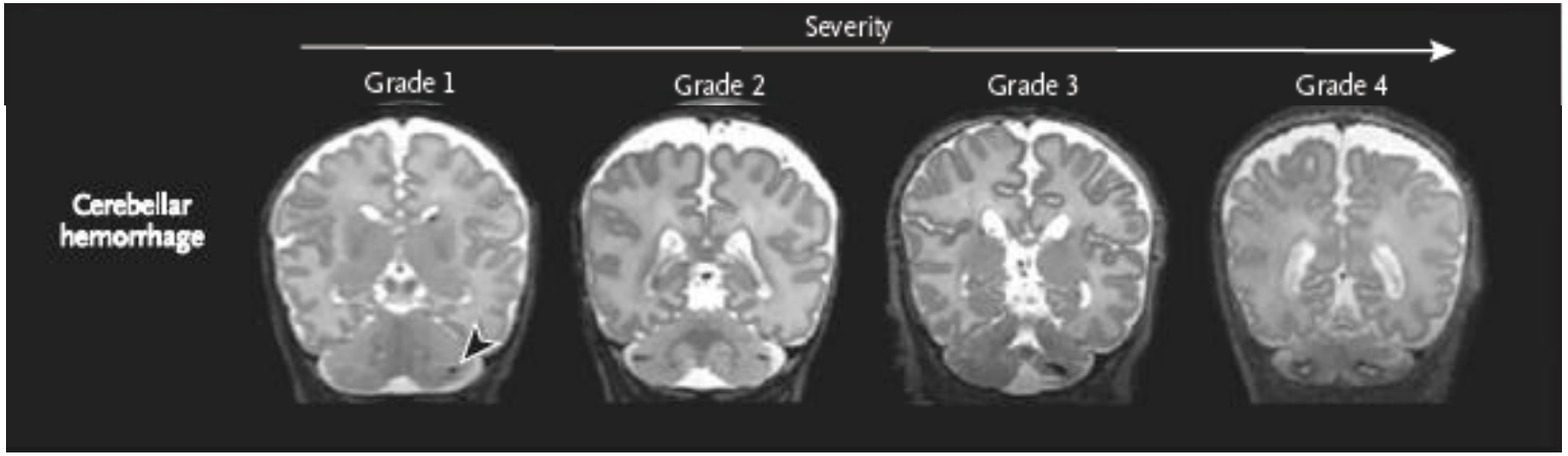
Inder et al. NEJM 2020

WHITE MATTER INJURY



- Risk factors: Hypoxia-ischemia & inflammation
- Period of highest risk 23-32 weeks
- Focal cystic necrosis (5%), focal microscopic necrosis (15-25%) and diffuse non-necrotic lesions (50%)

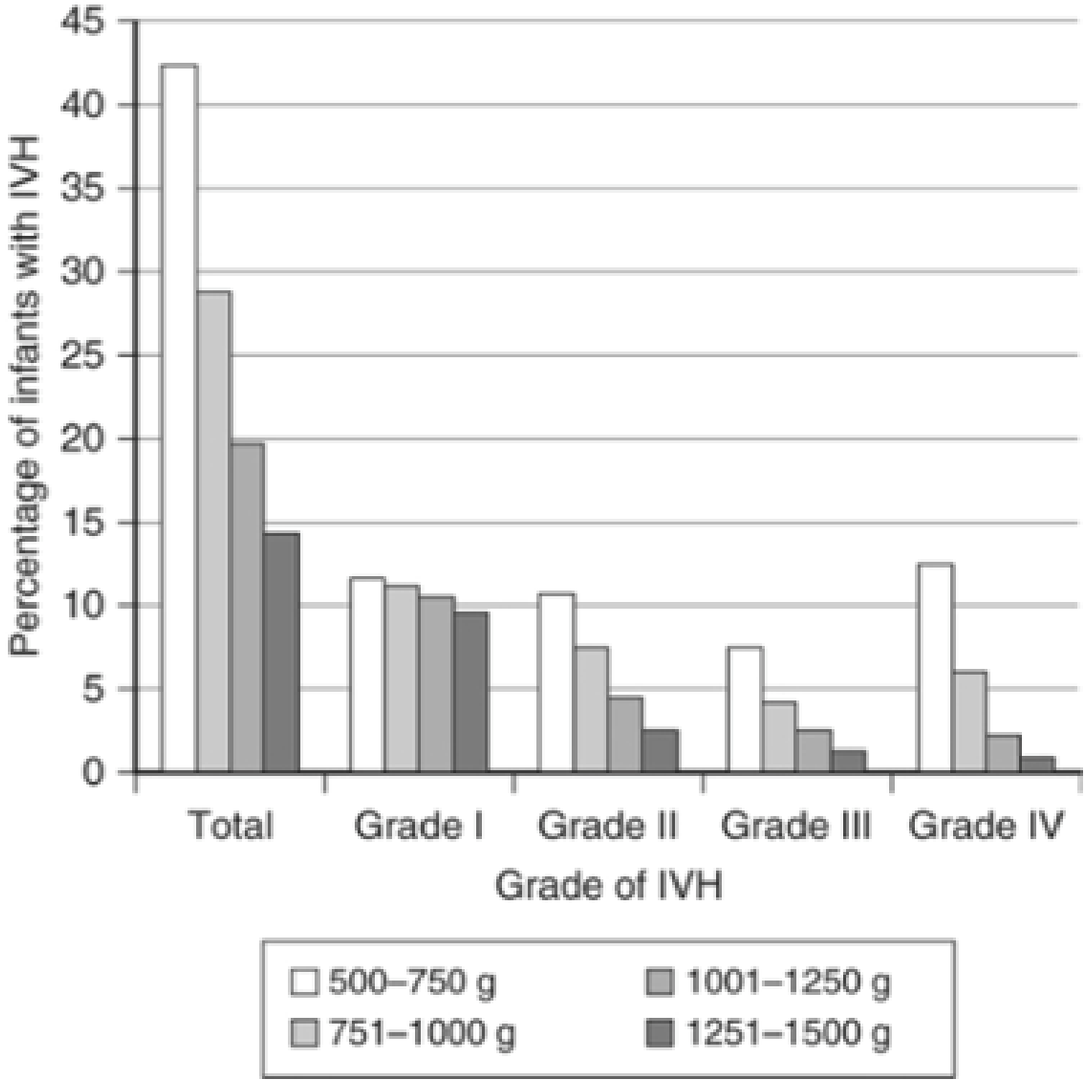
CEREBELLAR HEMORRHAGE



- Incidence in < 30 weeks: 3% (HUS) – 19 % (MRI)
- Risk factors: cardiorespiratory instability & prematurity

INTRAVENTRICULAR HEMORRHAGE

- On average, incidence around 20%
- Severe IVH 5-10%
- Decreasing incidence with increased age/weight
- Most often 24-48 hrs after birth



Volpe's Neurology of the Newborn, 6th Ed,
Shankaran S et al J Pediatric 2020

IVH GRADING & TIMING

Papile

- Grade 1: GMH limited to subependymal caudothalamic notch
- Grade 2: GMH + blood filling less than 50% of the ventricle
- Grade 3: GMH + blood filling more than 50% of a distended ventricle
- "Grade 4": Grade 3 + periventricular hemorrhagic infarct
  - *Consequence of IVH, not extension*

Volpe

- Grade 1: Germinal matrix hemorrhage (GMH)/IVH less than 10% of lateral ventricle
- Grade 2: GMH + IVH filling 10-50% of the ventricle
- Grade 3: GMH + blood filling more than 50%
- Separate notations:
  - Periventricular hemorrhagic infarct
    Ventricular dilation (>6mm AHW)

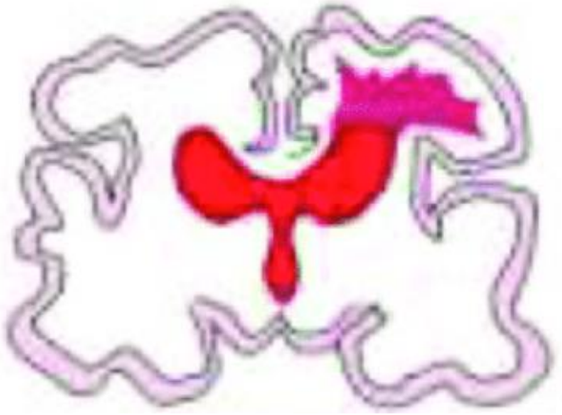
All grades of IVH can lead to PVHI

IVH GRADING

Grade 1 - GMH

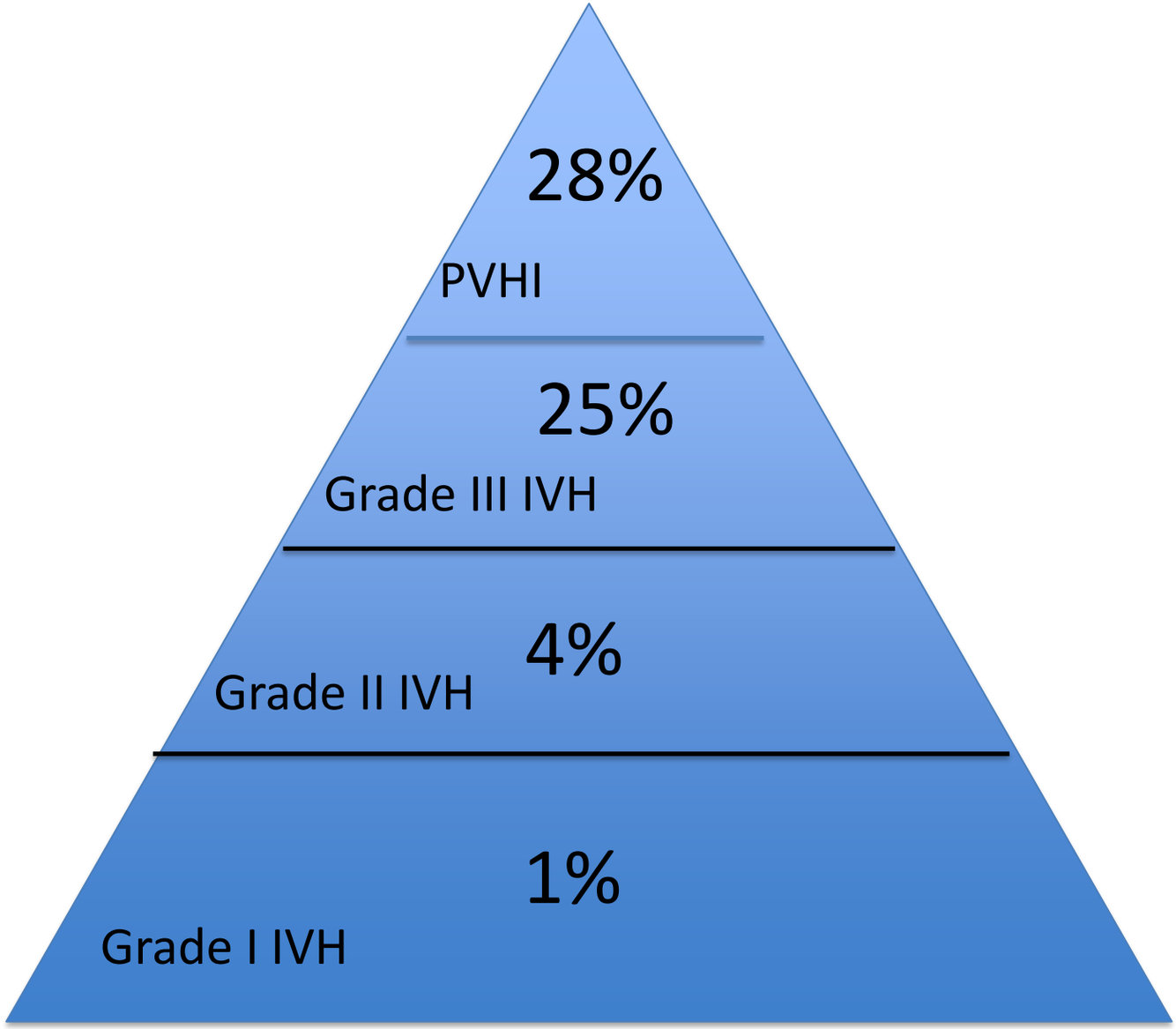
Grade 2 – IVH without dilatation

Grade 3 – IVH with dilatation



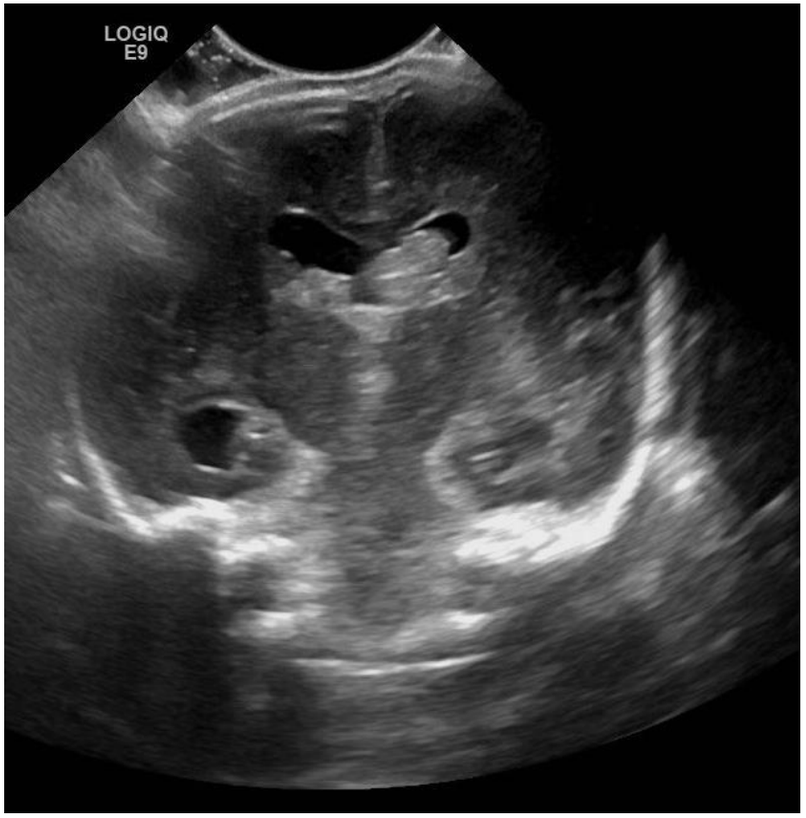
Grade 3 IVH with L PVHI

INCIDENCE OF PHVD

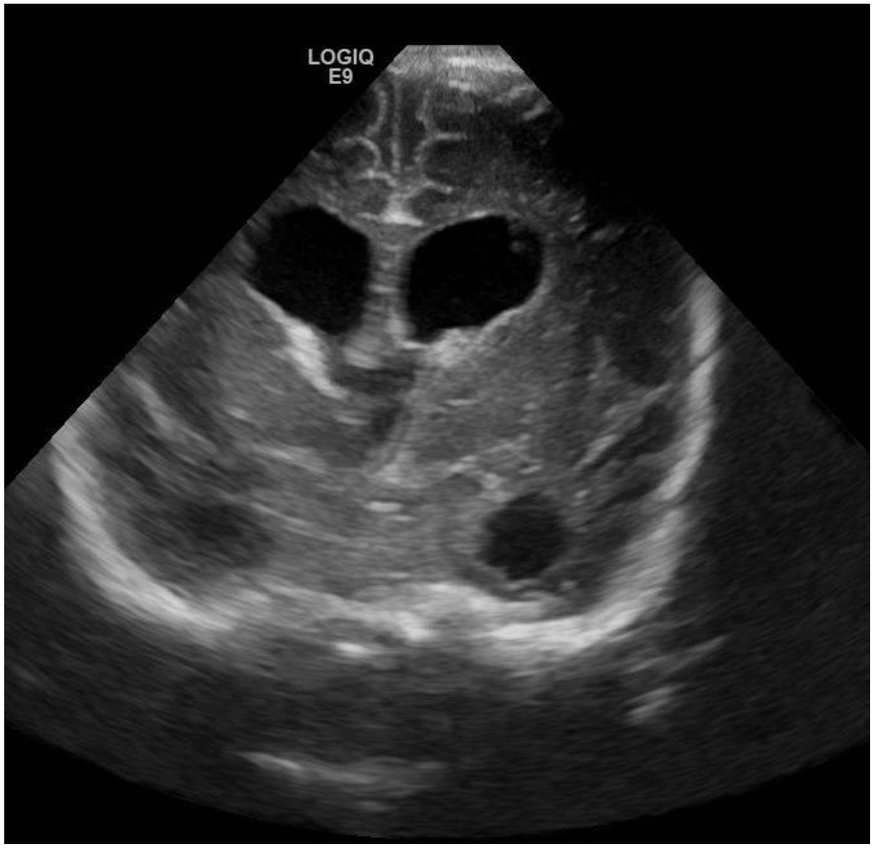


Christa EA et al. J Neurosurg Pediatr, 2016
Shankaran S et al. J Pediatr 2020

PHVD – PROGRESSIVE

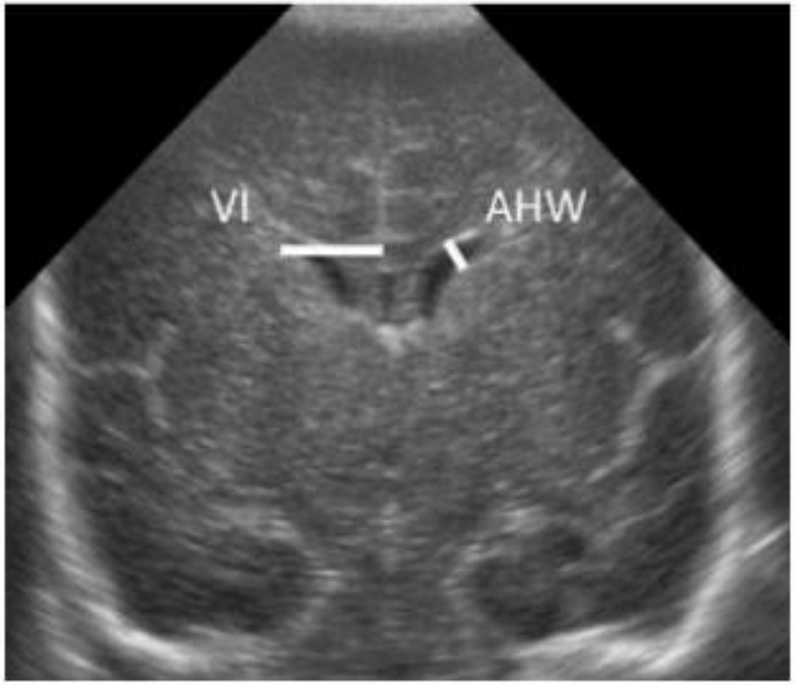


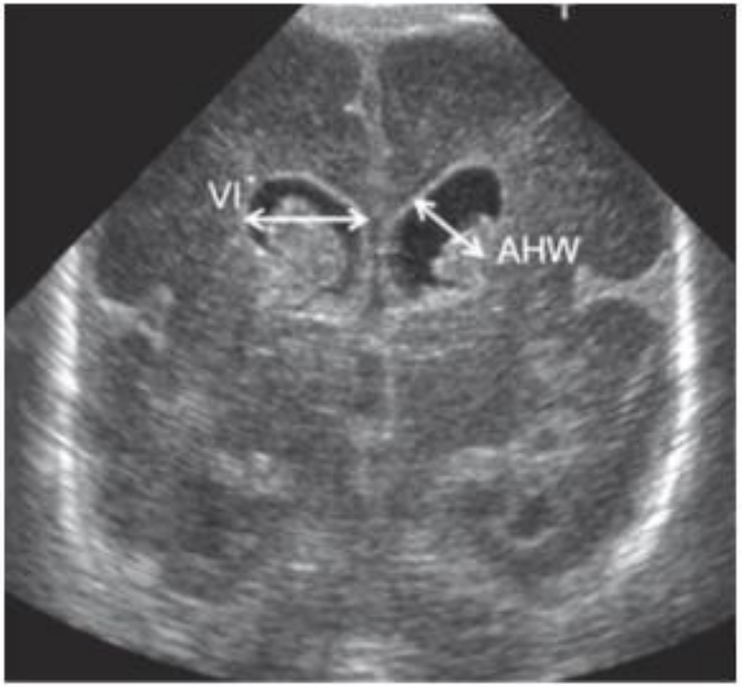
DOL 7



DOL 60

HOW DO WE MEASURE?

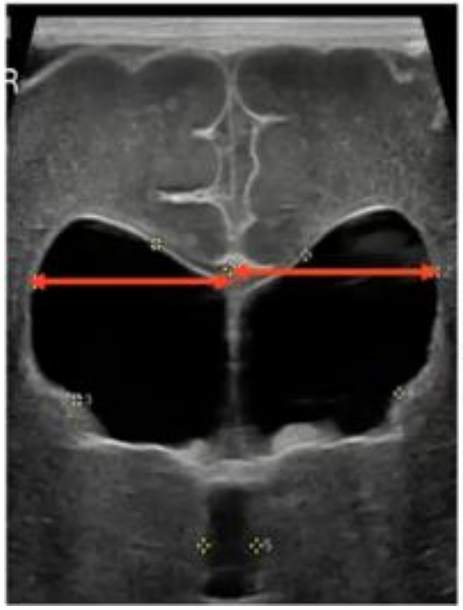




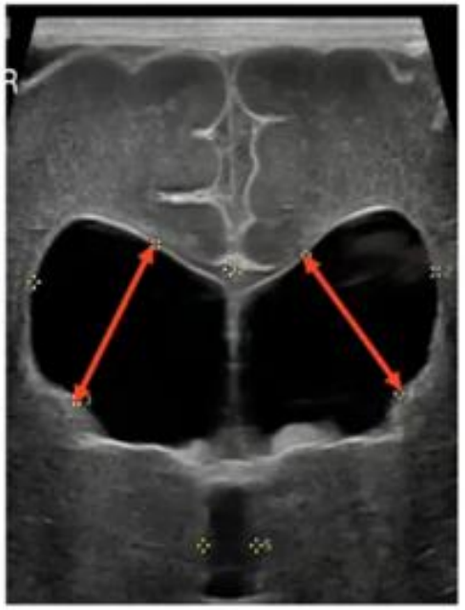
- VI = Ventricular Index
- AHW = Anterior Horn Width

HOW DO WE MEASURE

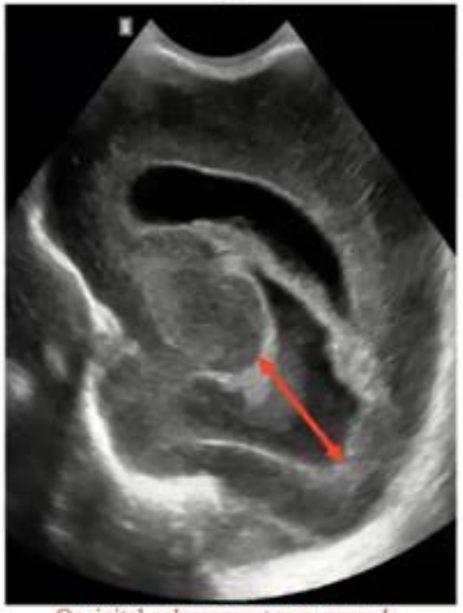
Ventricular Index



Anterior Horn Width

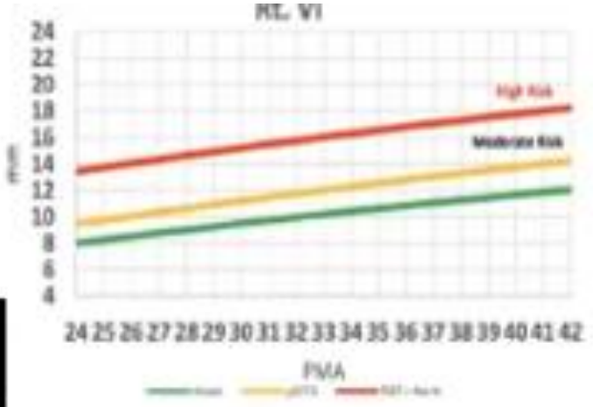


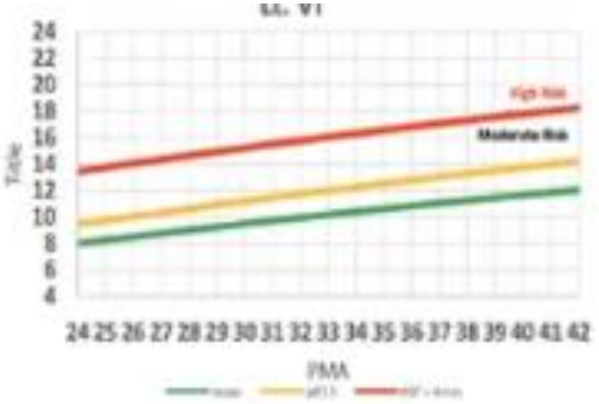
Thalamo-occipital Distance

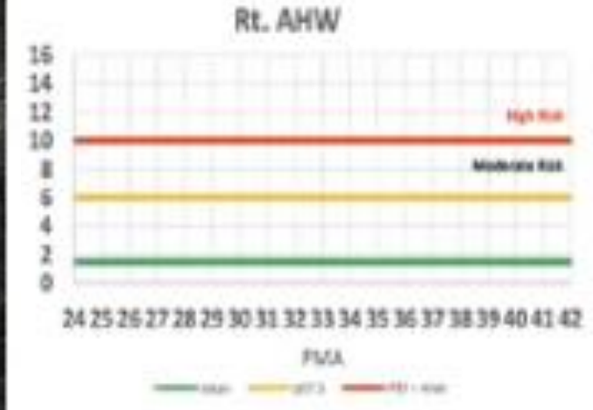


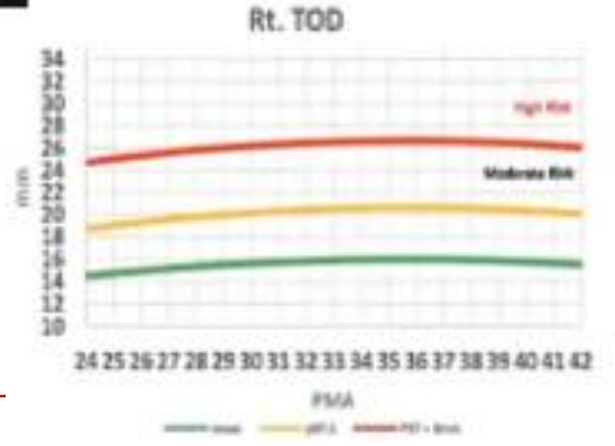
Occipital enlargement may precede frontal enlargement

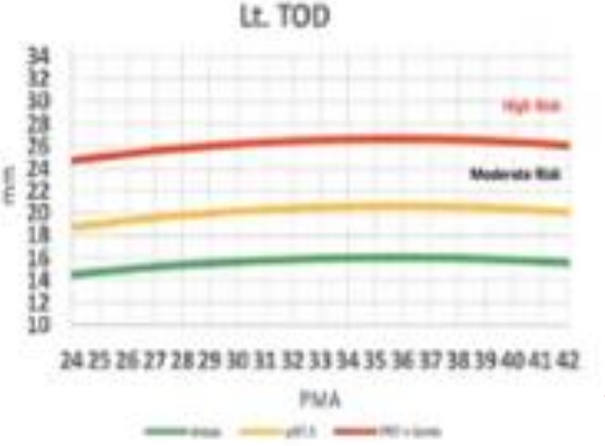
Levene MI and start Arch Dis Child 1981
El-Dib et al J Pediatr 2020



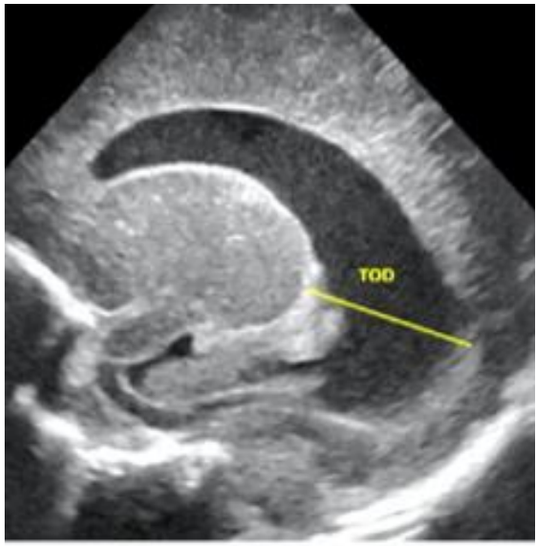


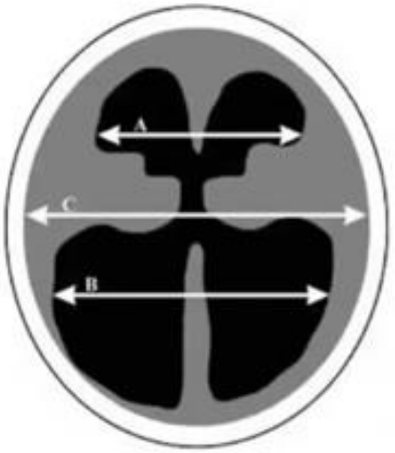




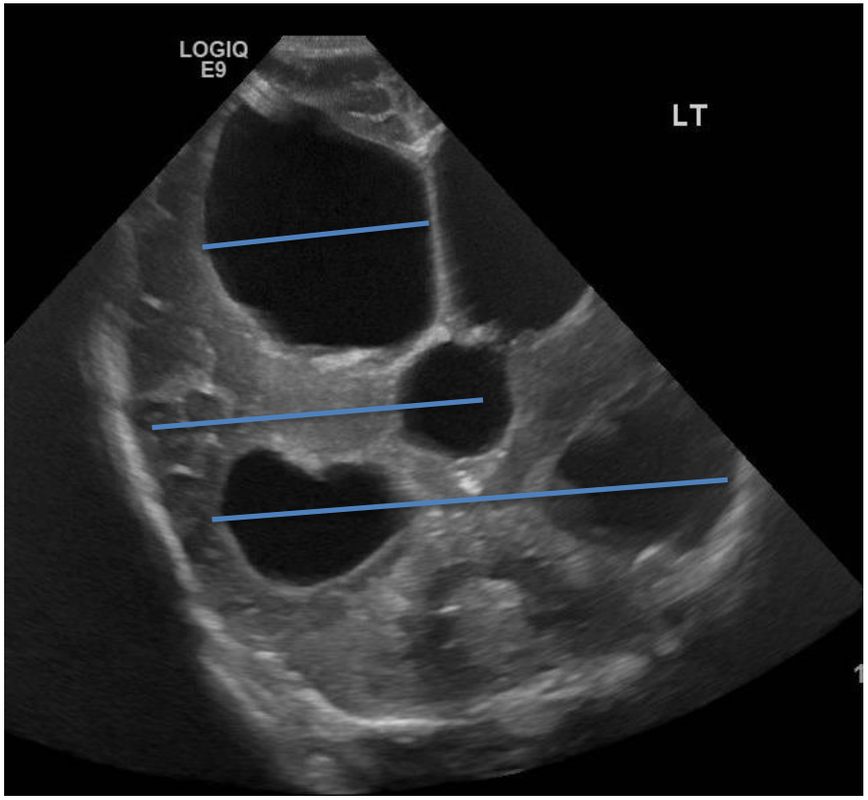


VENTRICULAR MEASUREMENTS



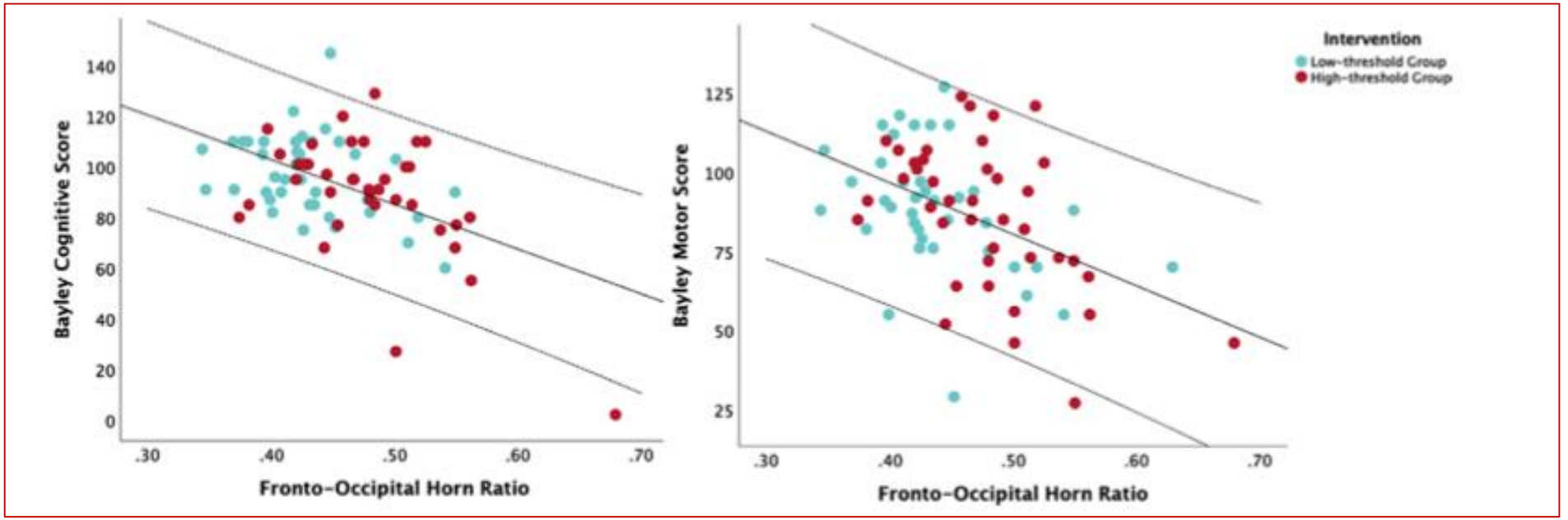


Frontal and Occipital Horn Ratio
A+B/2C



- TOD: thalamo-occipital distance
- FOR: Fronto-occipital horn ratio

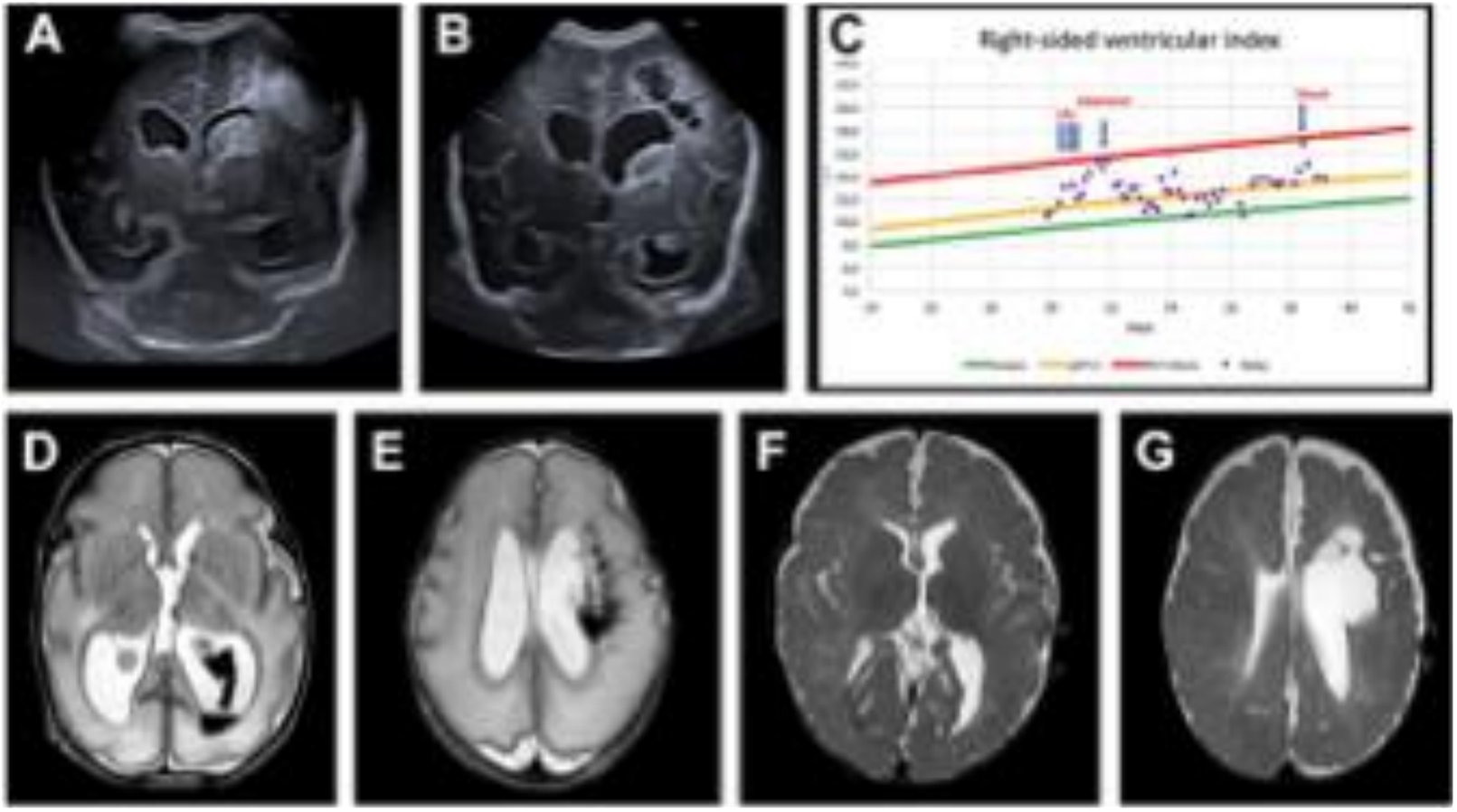
VENTRICULAR SIZE AND OUTCOMES



Larger ventricles negatively associated with cognitive and motor outcomes

Cizmeci, MN et al. J Pediatr, 2020

PROGRESSION AND INTERVENTION



Christensen et al. Clin Perinatol 2025

PHVD CLINICAL PATHWAY

Post-Hemorrhagic Ventricular Dilatation (PHVD) Clinical Pathway - 2025 update

University of Utah and IHC Canyons Region

For questions contact Betsy Ostrander 773 844-4462 or Jen Keene 801 803-9399

All infants <32 weeks PMA or >32 weeks if medical issues concerning for IVH receive cranial US between DOL 5-10

IVH Grade III/PVHI

- HUS (weekly on Monday)
- VI > +2 SD and AHW > 6 mm? [A]
  - YES
  - NO[B]

IVH Grade I/II

- HUS on day 30 of life
- IVH Grade III/PVHI or increased ventricular size
  - YES → HUS (weekly on Monday)
  - NO → No further US unless clinically indicated

Normal

- No further US unless clinically indicated

Consult PCH Neurology - ICU team who will coordinate with Neurosurgery Team

- If at OSH NICU, prepare to transport to PCH for evaluation for CSF diversion.
- If worsening dilation, consider reservoir placement when VI > 2 SD +4mm and AHW >10mm.
- If reservoir delayed due to infection/illness or ventricular dilation is slowly progressive, will consider high volume LP or direct ventricular tap with goal of 10 ml/kg CSF extraction.

[A] *VI = Ventricular Index*
AHW = Anterior Horn Width

[B] *Continue HUS weekly on Monday until 3 stable US*

- *NO intervention within first week of birth in case of fresh IVH as chance of re-bleed.*
- *NO LPs in case of aqueduct stenosis (enlargement of 3rd ventricle with small 4th ventricle); in case of suspicion of aqueduct stenosis*
- *Multi-specialty discussion required if concern for ex vacuo dilation contributing to ventricular size*

Approved Neurology, Neurosurgery, NICU DT - xx 2025

Intermountain Health

HEALTH UNIVERSITY OF UTAH

Post-Hemorrhagic Ventricular Dilatation (PHVD) Clinical Pathway

AFTER RESERVOIR PLACEMENT

Daily CSF tap via reservoir up to 10mL/kg/tap with aim of VI <2 SD + 4 mm and AHW < 10 mm. HUS after 2 taps, then continue weekly HUS on Monday.[C]

Improving

Gradually decrease frequency and amount of CSF taps as tolerated

- Weaning of taps tolerated → Monitor until ventricle size stable for at least 3 weekly HUS
- Weaning of taps not tolerated → If no stabilization by term, consider VP shunt placement

Not Improving

Ongoing daily or twice daily if needed CSF tap via reservoir up to 10mL/kg/tap with U/S to monitor dilatation → If no stabilization by term, consider VP shunt placement

[C] Reservoir Tapping Tips:

- Hold tap if fontanelle sunken prior to tap and notify neurology who will evaluate prior to recommending next tap
- If taps poorly tolerated (bradycardia that persists after tap), obtain HUS and notify neurology

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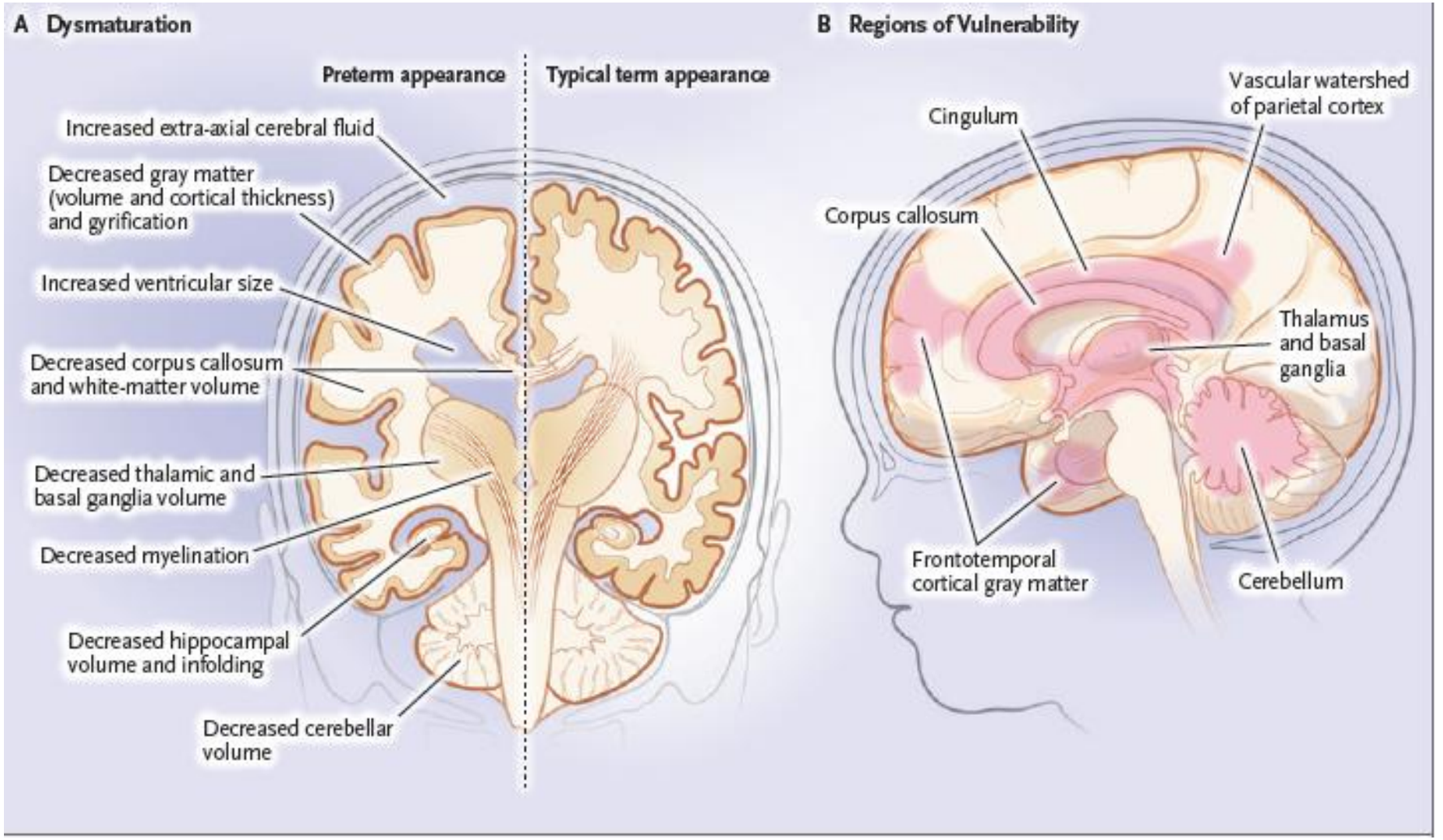
BRAIN DYSMATURATION



BRAIN INJURY AND FUNCTIONAL IMPAIRMENT

6x CP
11x CVI
4x hearing loss

CP 75%

Table 1. Evidence of Association of Brain Injury and Dysmaturation with Functional Impairment in Preterm Infants and Potential Interventions to Improve Outcomes.*

Functional Impairment	Brain Injury				MRI-Defined Brain Dysmaturation		
	High-Grade Intraventricular Hemorrhage	Cystic White-Matter Injury	Diffuse White-Matter Injury	Cerebellar Hemorrhage	Frontal or Temporal Region	Basal Ganglia or Thalamus	Cerebellum
Early development	Strong	Strong	Strong	Moderate	Moderate	NC	Moderate
Motor function	Strong	Strong	Moderate	Strong	ND	Moderate	Moderate
IQ	Strong	Strong	Moderate	Strong	Moderate	Moderate	Moderate
Language	Moderate	Strong	Moderate	Moderate	Moderate	NC	Moderate
Visuospatial function	Moderate	Strong	Moderate	Weak	NC	NC	Weak
Memory	Moderate	Moderate	Moderate	NC	Moderate	Moderate	Weak
Attention and executive function	Moderate	Moderate	Moderate	NC	Moderate	Weak	Weak
Academic performance	Moderate	Strong	Moderate	NC	NC	Moderate	NC
Behavior	Moderate	Moderate	Moderate	Moderate	NC	Moderate	Moderate
Interventions	Antenatal glucocorticoids, magnesium sulfate, delayed cord clamping NICU: physiological stability — prevent fluctuations in carbon dioxide, glucose, blood pressure Cerebrovascular monitoring to ensure stable cerebral perfusion Neurorehabilitation with parent–infant interaction and infant developmental therapy				Provide appropriate nutrition: macronutrients and micronutrients, maternal breast milk Minimize distress and stressful or painful experiences Enhance nurturing: skin-to-skin care, parental presence and engagement, exposure to human voices Home-based developmental programs		

Inder et al. NEJM 2020

NEONATAL SEIZURES

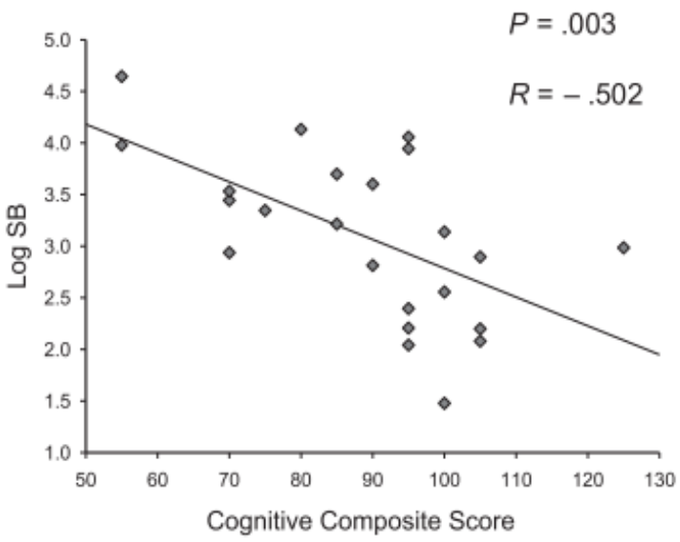
DO SEIZURES MATTER?

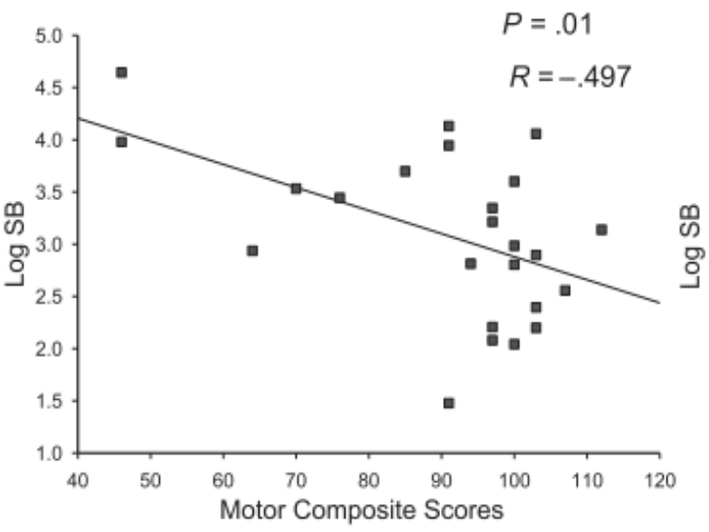
Seizures are common: 1-5 per 1000 term neonates[1,2] and between 5%[3] and 48%[4] in preterm neonates <34 weeks

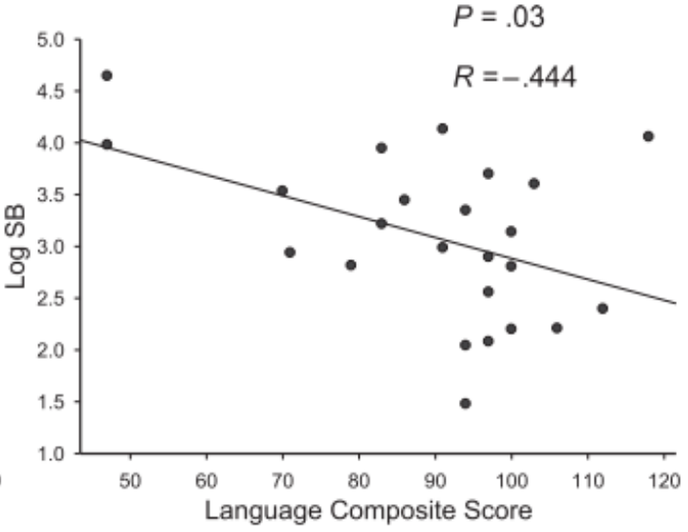
Seizures can cause injury to the neonatal brain

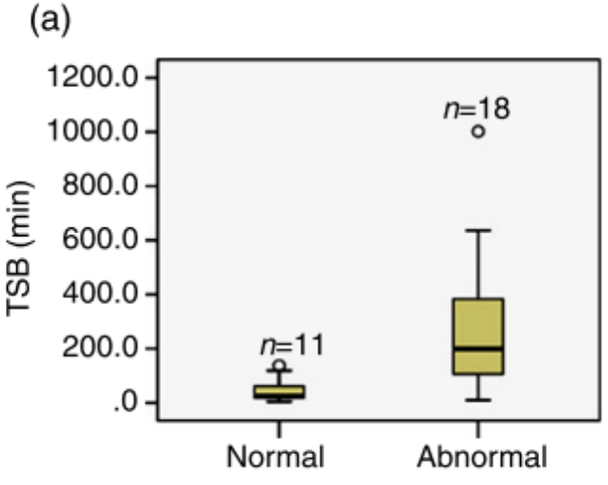
1- Lanska et al 1995
2 – Glass 2009
3 – Lloyd RO J pediatr 2017
4 – Vesoulis ZA Pediatr Res 2013

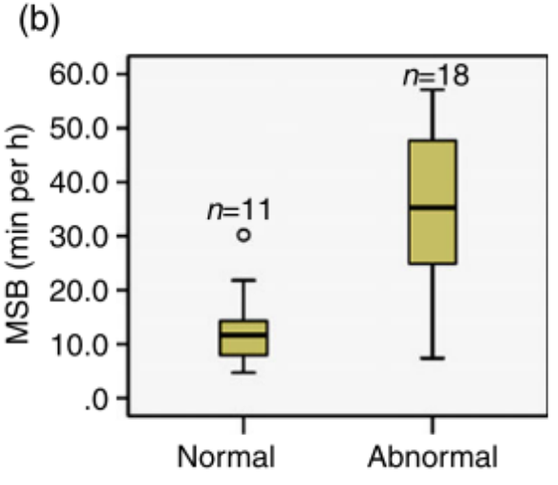
Neurodevelopmental outcomes worsen with increased seizure burden





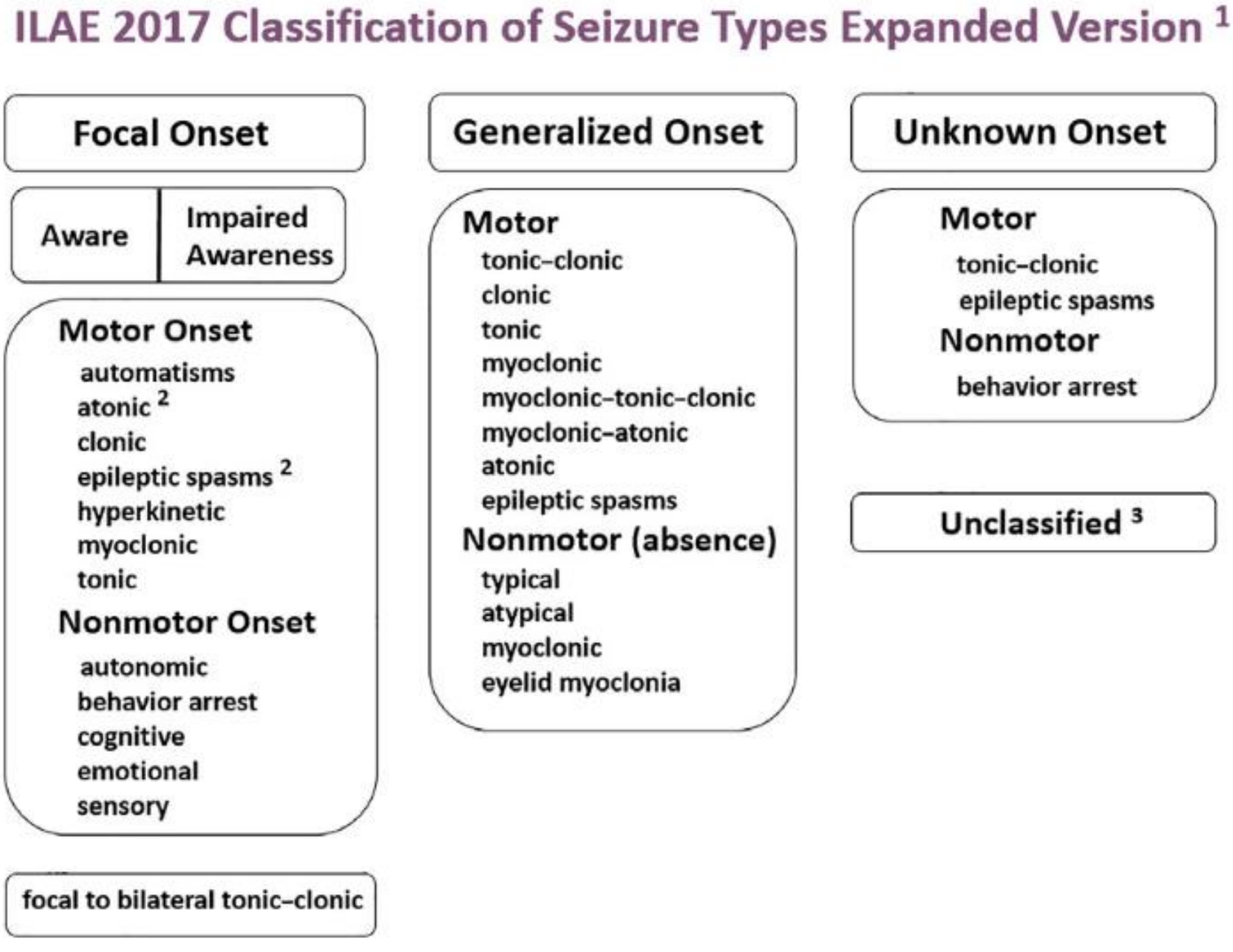






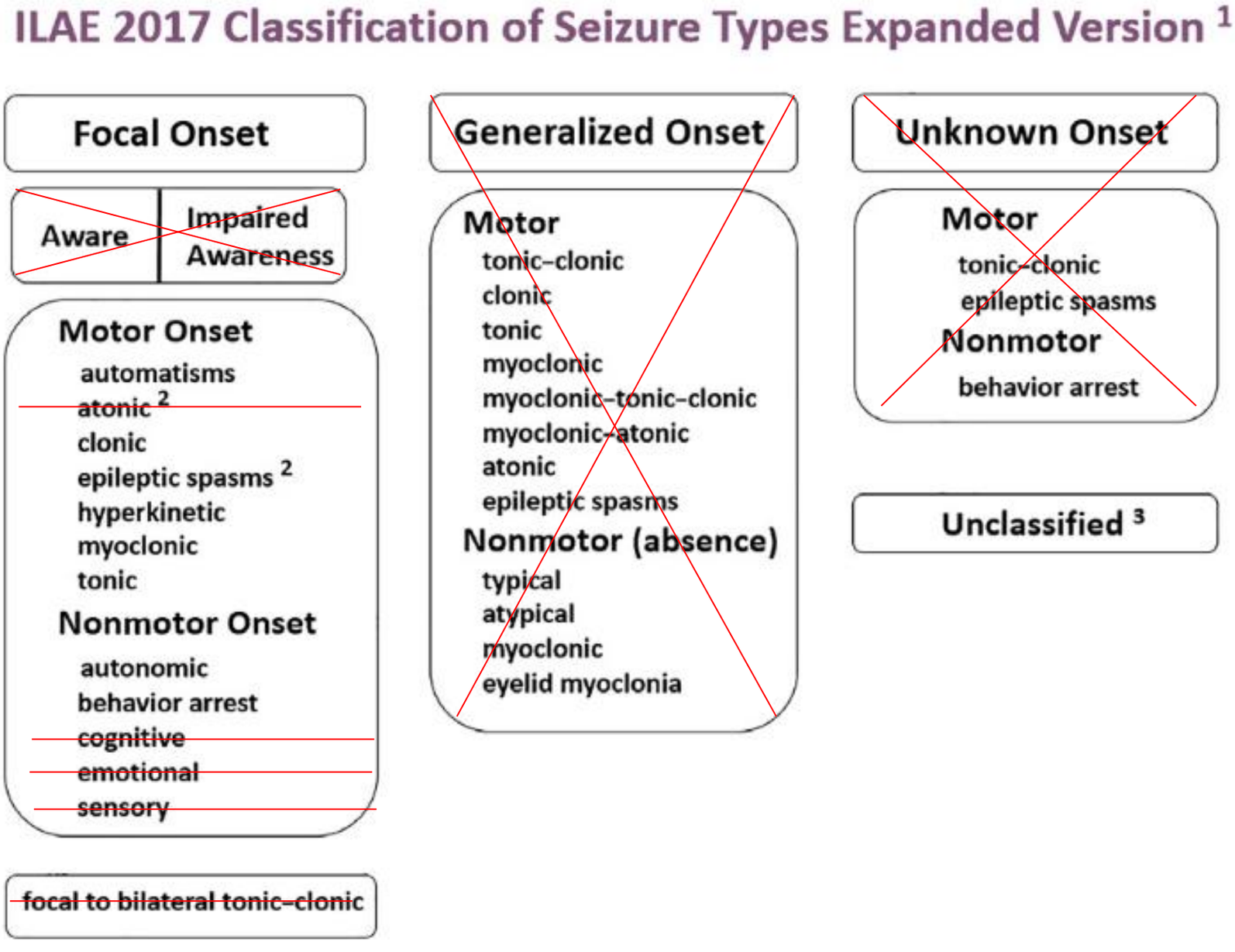
1- Srinivasakumar et al. (2015)
2 - Kharoshankaya 2016
3 – Payne et al 2014

ILAE 2017



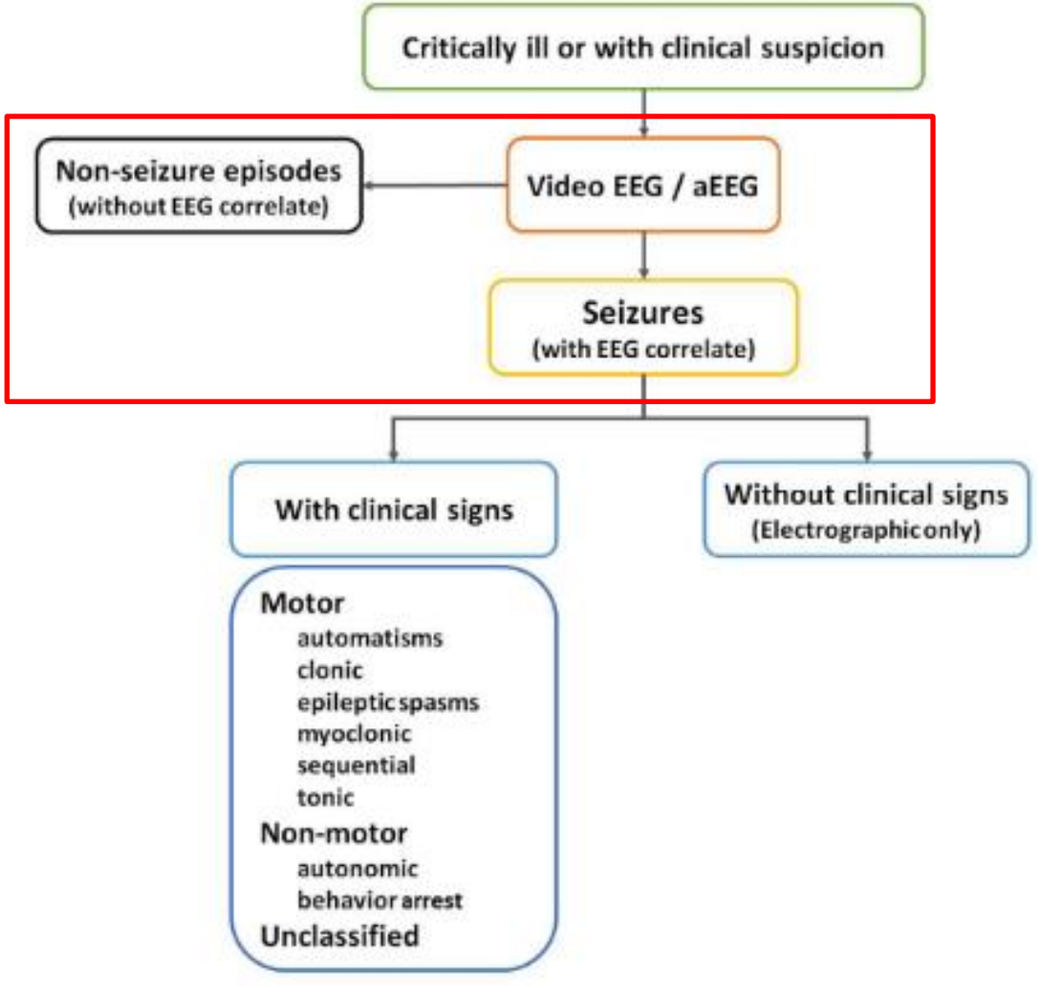
Fisher et al, Epilepsia 2017

ILAE – not great for neonates



Fisher et al, Epilepsia 2017

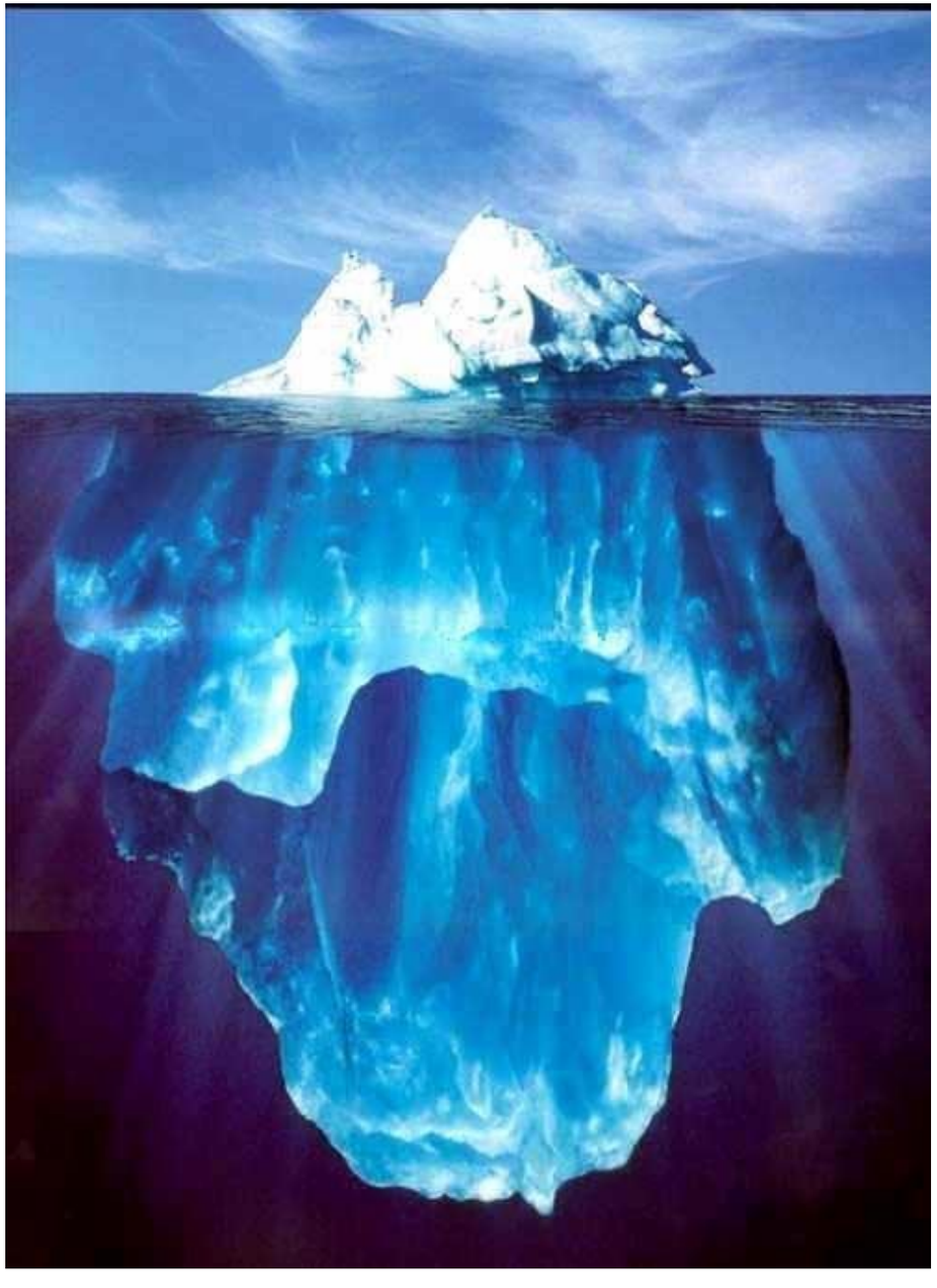
EEG is necessary for accurate seizure diagnosis

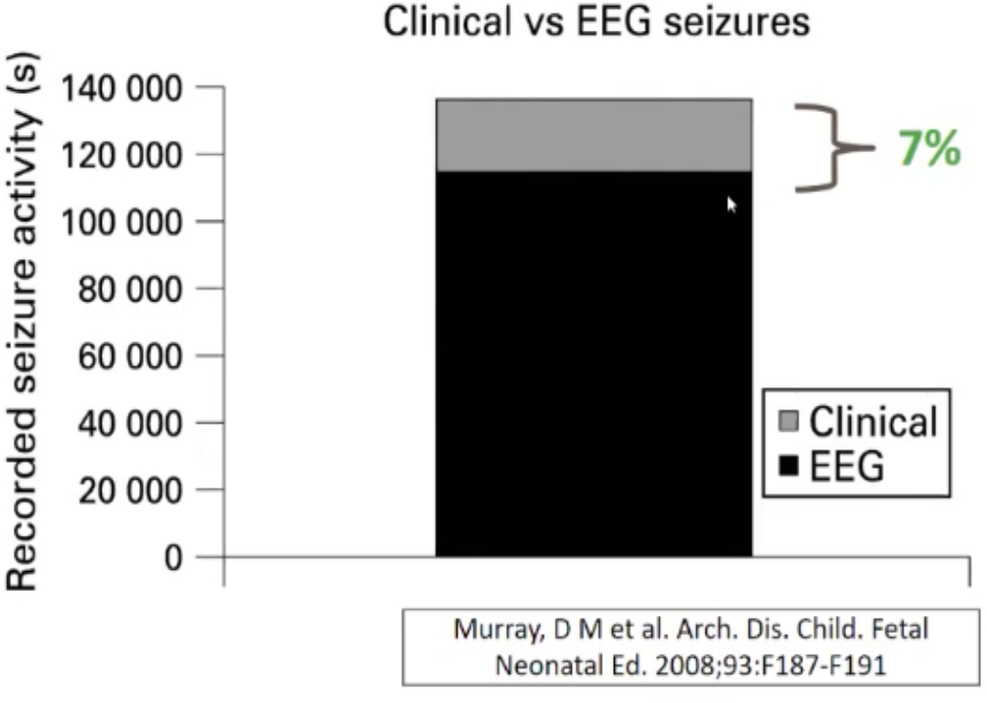


- 137 experienced NICU personnel viewed videos of neonatal seizures and seizure mimics and indicated which was which
- 50% was the average score
- Jitteriness, sleep myoclonus, abnormal movements, vital sign fluctuations are all commonly mistaken
- One series found 73% of clinical seizures from nursing notes had no EEG correlate

Malone et al, Epilepsia 2009
Murrey et al 2008

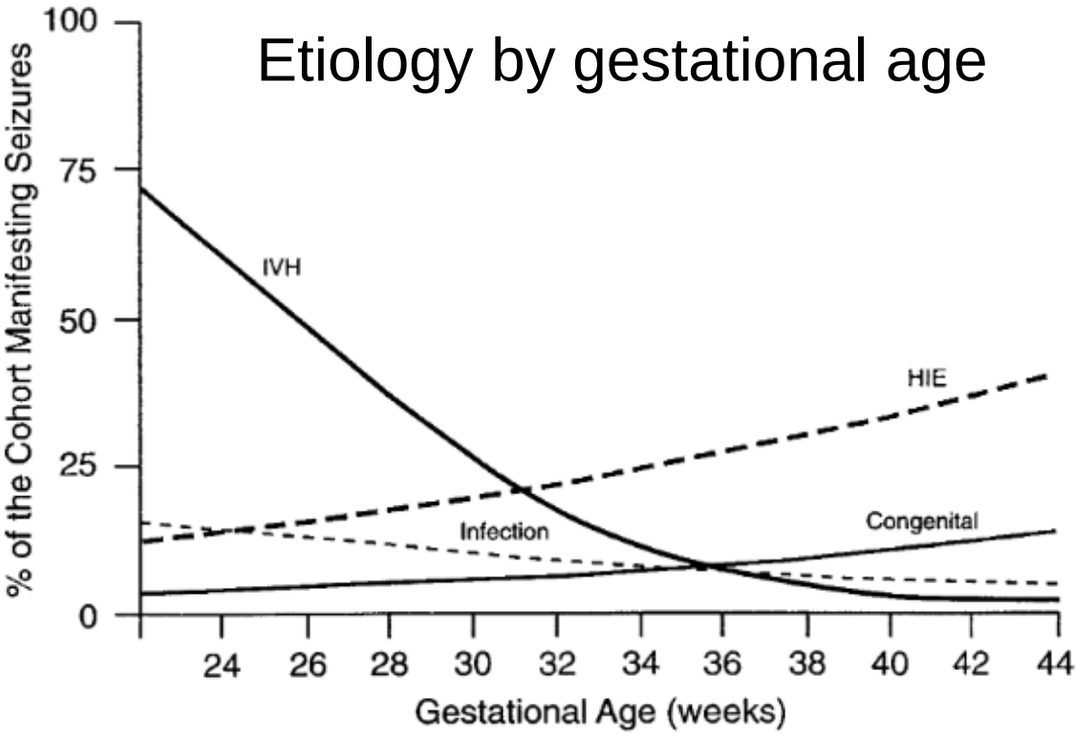
EEG is necessary for complete seizure diagnosis



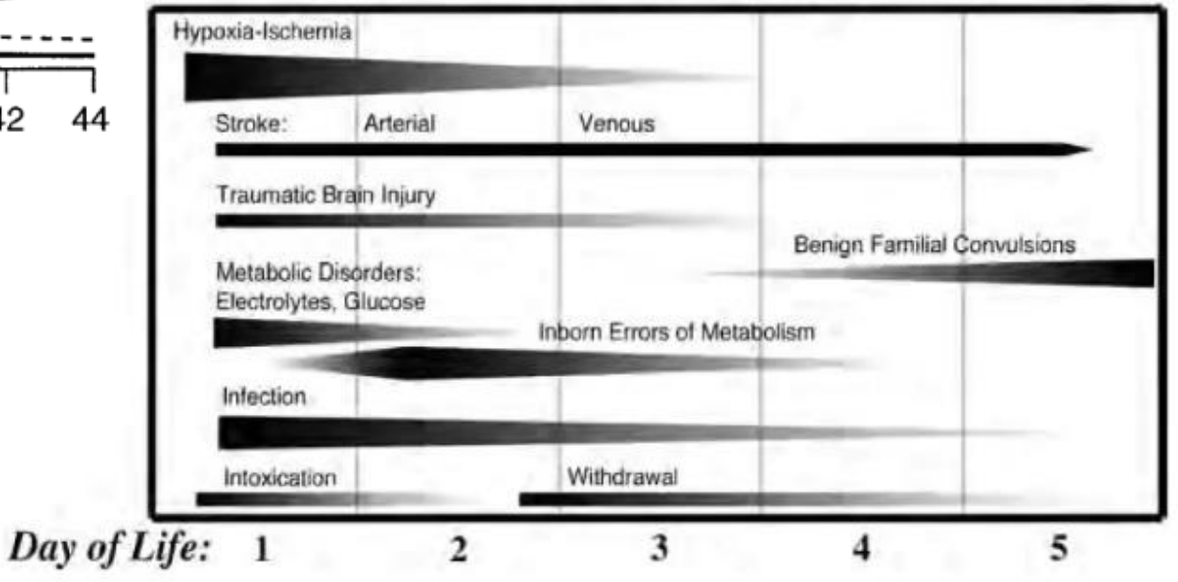


Age as a clue to seizure etiology

Etiology by gestational age

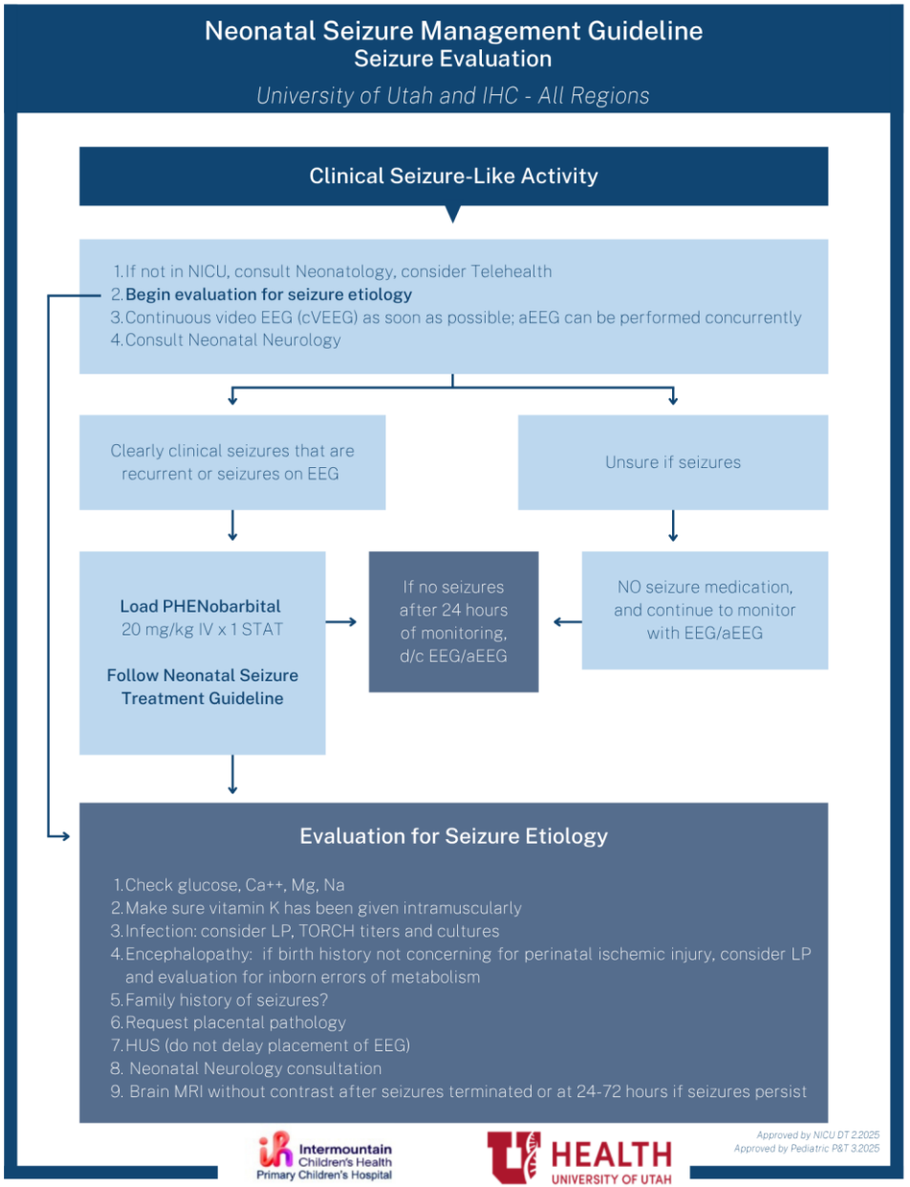


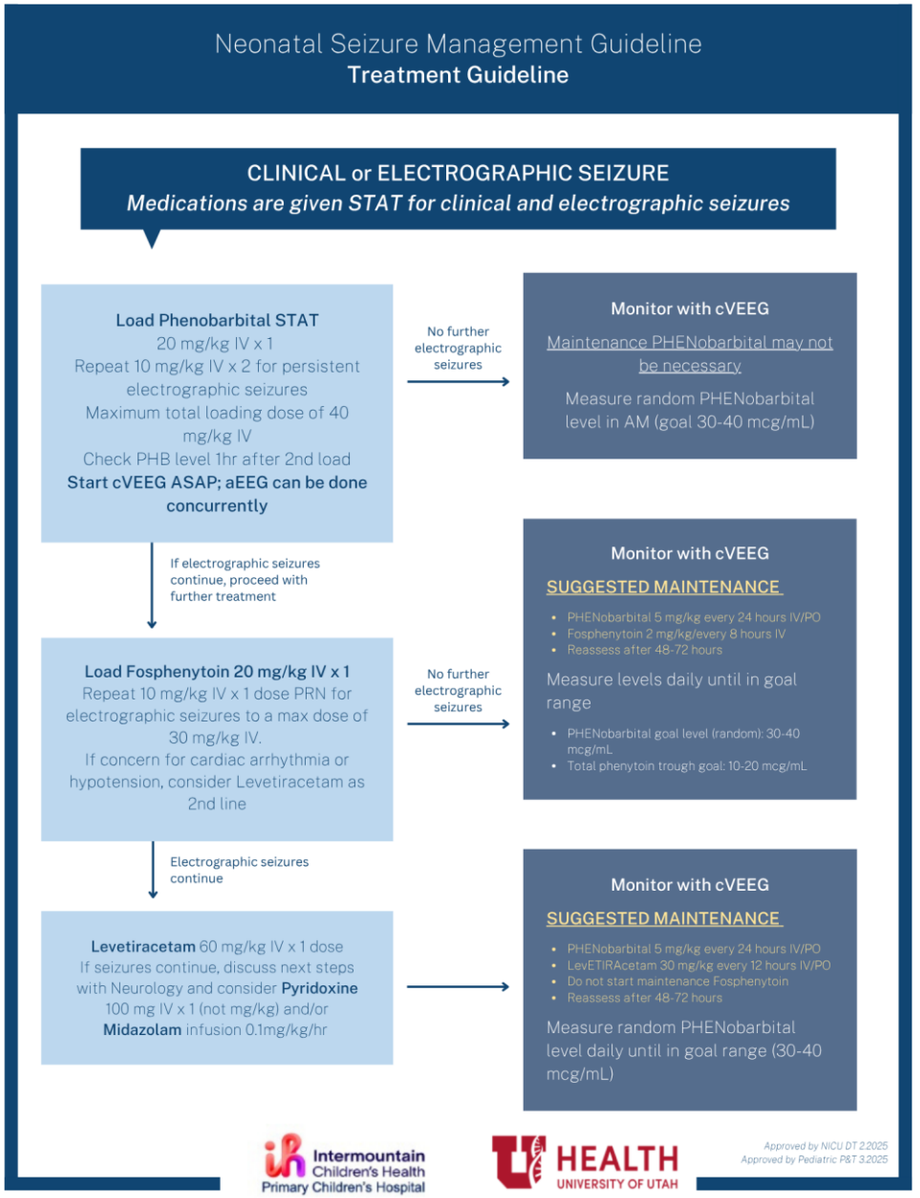
Etiology by Day of Life



Sheth et al. J perinatology 1999
Miller et al , new York academic press 2006

NEONATAL SEIZURE TREATMENT





SUMMARY

- Neonatal seizure diagnosis is tricky and requires an EEG to confirm
- Most seizures are acute, symptomatic seizures… but not all
- Treatment options are slim – phenobarbital, fosphenytoin and levetiracetam in most

Questions?

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HEALTH
UNIVERSITY OF UTAH

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