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SYNAPSE CARE SOLUTIONS

Intraventricular Hemorrhage and Post Hemorrhagic Ventricular Dilation: Current Approaches to Improve Outcomes

Diane Wilson

RN (EC), MN, NP-Peds, NNP-BC

Diane has over 25 years of experience in Neonatal Intensive Care at the Hospital for Sick Children in Toronto, Canada. She has been practicing as an Nurse Practitioner for 10 years in the acute care setting. She has a special interest in infants with brain injury and congenital brain malformations in her practice setting of Neonatal Neurocritical Care. She participates in international research and education focused on improving neurological outcomes for children with brain injury.

CONTACT INFORMATION:

Find Diane in the Whova Event App

- or -

Email - diane.wilson@sickkids.ca

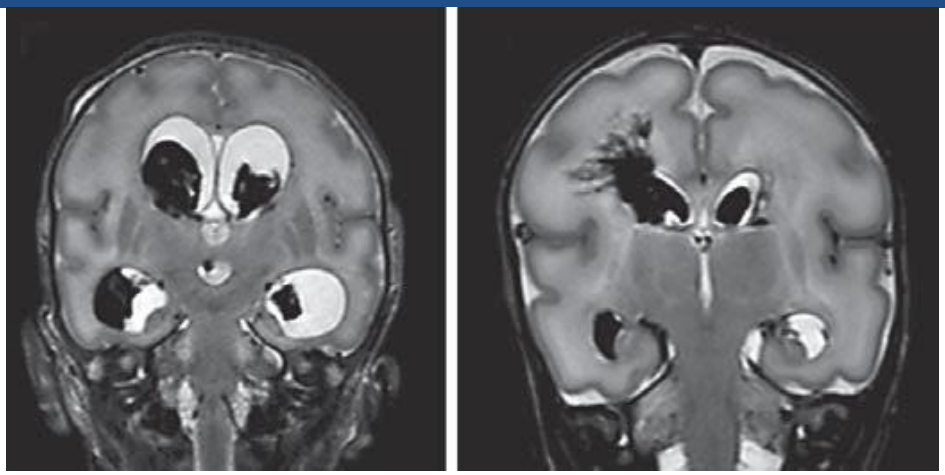
Top Takeaways

1.

2.

3.

Intraventricular Hemorrhage - Post-Hemorrhagic Ventricular Dilatation: Current approaches to improve outcomes



Diane Wilson

Neonatal Neurology, The Hospital for Sick Children, Toronto, Canada

ONE Conference: February 9th, 2020

Objectives

1. Describe two physiological risk factors for intraventricular hemorrhage (IVH)

2. Describe 2 clinical features of symptomatic PHVD

3. List 2 approaches to mitigate long term neurodevelopmental sequelae from PHVD

Disclosures

- No disclosures

Acknowledgment

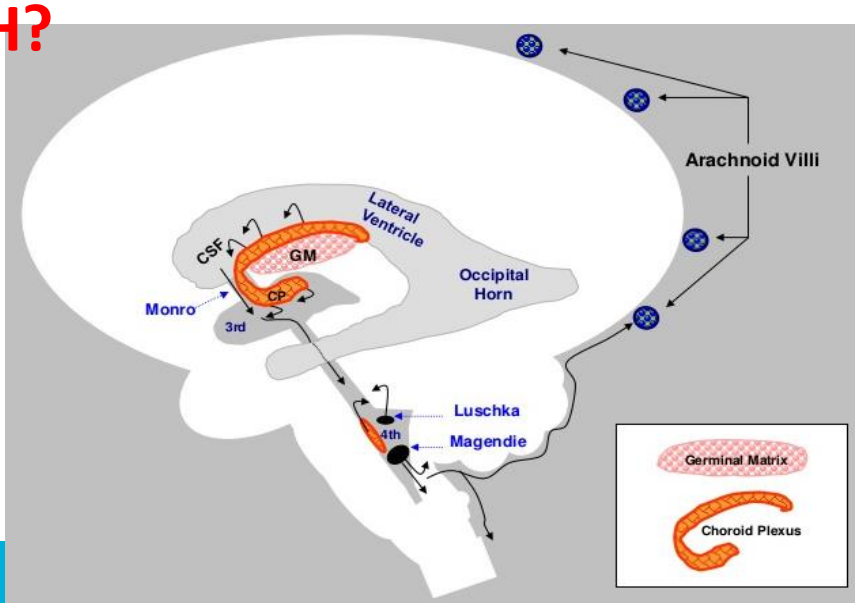
- Dr Lara M Leijser, neonatologist, for sharing her expertise and images.

IVH - Etiology

Q1: In preterm infants, what is generally the source of bleeding in IVH?

Germinal Matrix

The germinal matrix, which is the source of neural stem cells, persists until at least [redacted] weeks gestational age.



IVH - Etiology

Suggested mechanisms

- Germinal matrix: immature, fragile vasculature.
- Fluctuation in the cerebral blood flow
  - lack of autoregulation in preterm infants

Q2: Name factors implicated in CBF fluctuation that can lead to IVH

Robinson, J Neurosurg Pediatrics 2012; Volpe, 2008

IVH - Etiology

Q2: Name factors implicated in CBF fluctuation that can lead to IVH

- Abrupt elevation in systemic BP
  - Rapid volume expansion with fluid boluses
  - CPR / Difficult intubation
  - Noxious stimuli
  - Neonatal transport
- Hypo/hypercarbia
- Anemia
- Severe RDS
- Pneumothorax

IVH - Etiology

Q3: Name 3 medical interventions shown to decrease the incidence of IVH in very preterm neonates

IVH – Etiology and Protective Factors

Cochrane Library
Cochrane Database of Systematic Reviews

Antenatal Steroids

Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth (Review)

Roberts D, Brown J, Medley N, Dalziel SR

Cochrane Library
Cochrane Database of Systematic Reviews

Prophylactic Indomethacin

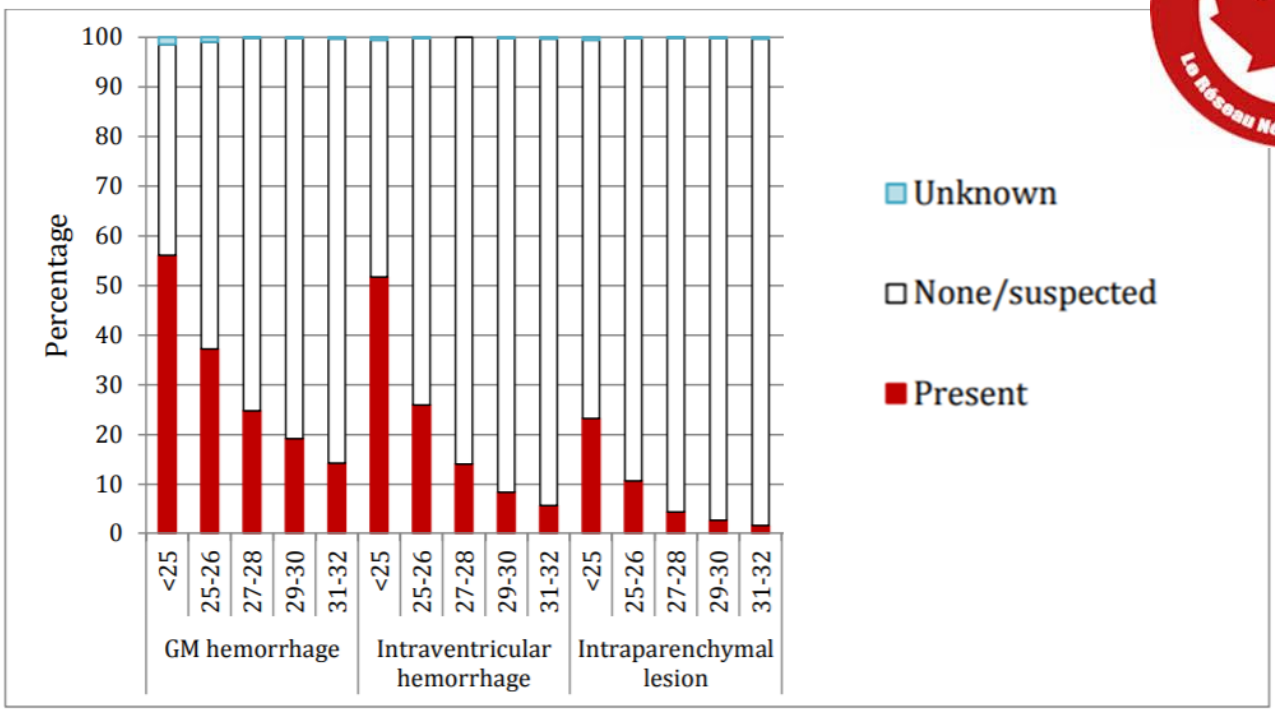
Prophylactic intravenous indomethacin for preventing mortality and morbidity in preterm infants (Review)

Cochrane Library
Cochrane Database of Systematic Reviews

Delayed Cord Clamping

Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes (Review)

Rabe H, Diaz-Rossello JL, Duley L, Dowswell T



IVH - Epidemiology

Term Infants can also develop IVH – pathogenesis is different and depends on the underlying cause:

- Trauma during delivery
- Coagulation anomaly
- Sinovenous thrombosis
- Gene mutation of the collagen genes (COL4A1 and COL4A2)

IVH – Epidemiology in term infants

Among term neonates with IVH, 30 % had cerebral sinovenous thrombosis

Intraventricular Hemorrhage in Term Neonates Caused By Sinovenous Thrombosis

Yvonne W. Wu, MD, MPH,[1,2]
Shannon E. G. Hamrick, MD,[2] Steven P. Miller, MD,[1,2]
Marlyse F. Haward, MD,[2] Michael C. Lai, MD,[3]
Peter W. Callen, MD,[3] A. James Barkovich, MD,[2,3]
and Donna M. Ferriero, MD[1,2]

The cause of intraventricular hemorrhage in term neonates is poorly understood. Among 29 neonates of at least 36 weeks' gestation with intraventricular hemorrhage, 9 (31%) had cerebral sinovenous thrombosis. Of the 26 neonates who underwent computed tomography or magnetic resonance studies, those with thalamic hemorrhage were more likely to have sinovenous thrombosis than those without thalamic involvement (4/5 vs 5/21, $p = 0.03$). Term neonates with intraventricular hemorrhage should undergo neuroimaging to evaluate the presence of sinovenous thrombosis.

Ann Neurol 2003;54:123–126

Clinical presentation IVH

Q4: Timing of IVH – when IVH is most likely to occur in the preterm neonate?

a) 90% by day 3 of life
b) 90% by 6 hours of life
c) 50% by the end of the first week of life
d) The risk is the same during the neonatal life until 34 weeks of life

Clinical presentation IVH

- 50 % on the first day of life, 25% on the second day of life, 15% on the third day of life (90% by day 3 of life)
- 20-40% = progression of hemorrhage over 3 to 5 days

Ahn, Korean Med Sci 2015; Radic, J Neurosurg Pediatr 2015; Robinson, J Neurosurg Pediatrics 2012; Papile, J Pediatr 1978; Volpe, 2008

Clinical presentation IVH

- Majority = clinically asymptomatic and detected by routine HUS screening
- If clinical symptoms:
  - Irritability, HBG drop, sudden clinical deterioration
  - Rarely : Increased ICP (↑ HC, full fontanel, spells, seizures, change in consciousness)

Ahn, Korean Med Sci 2015; Radic, J Neurosurg Pediatr 2015; Robinson, J Neurosurg Pediatrics 2012; Papile, J Pediatr 1978; Volpe, 2008

IVH – Imaging

Serial head ultrasound (HUS):

Reliable for detection and staging

MRI: Associated lesions

Radic, J Neurosurg Pediatr 2015; Papile, J Pediatr 1978; Volpe, 2008

IVH – Classification

- Classification by **Papile,** adapted by Volpe

Grade I:

Grade II:

Grade III:

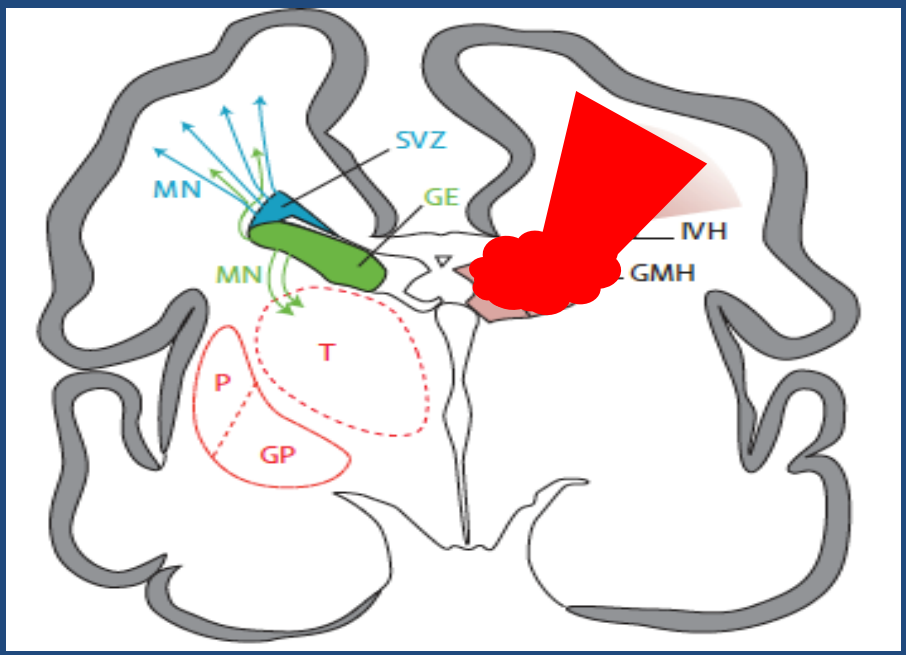
Grade IV:

Separate note: Ventricular dilatation, WM involvement

Radic, J Neurosurg Pediatr 2015; Papile, J Pediatr 1978; Volpe, 2008

Intraventricular hemorrhage

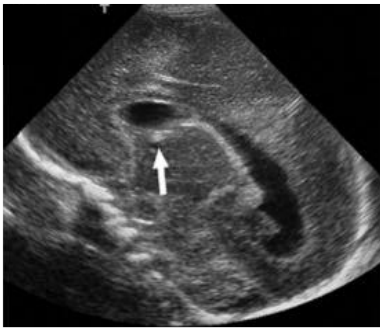
SickKids

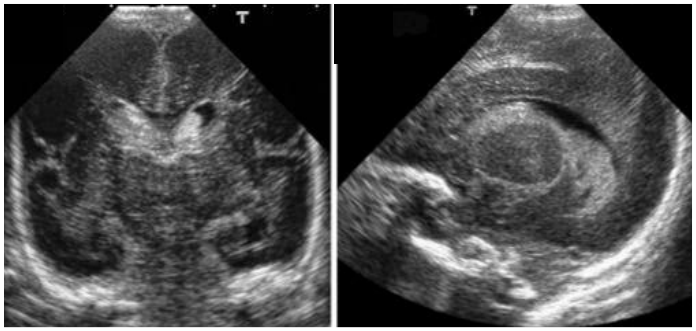


Volpe JJ. Lancet Neurol 2009;8:110-24.

GMH-IVH – Imaging and Classification

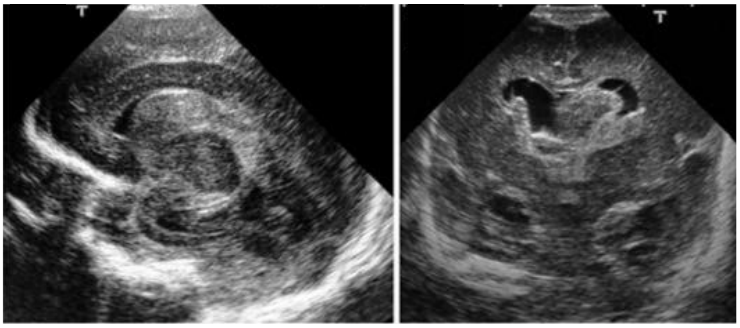
Grade I

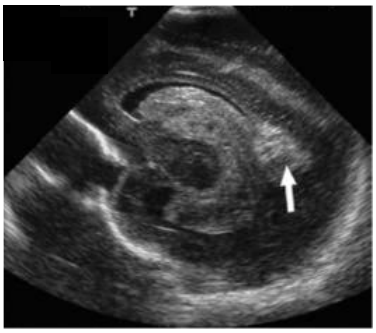




Grade II

Grade III



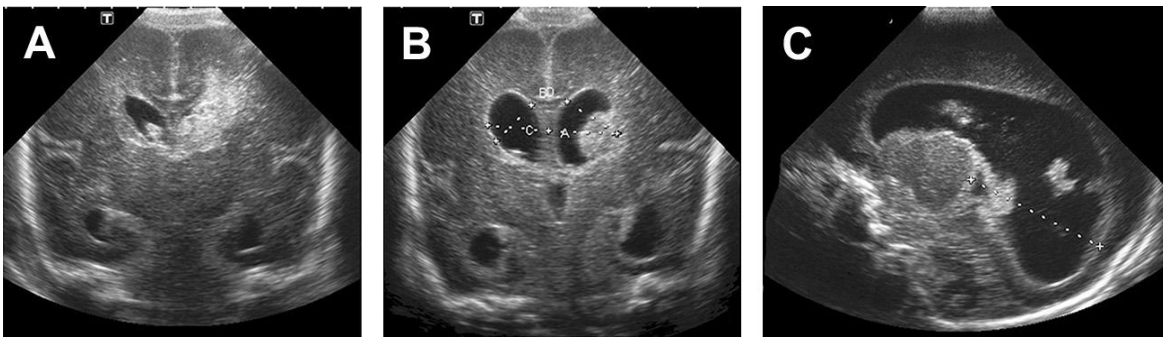


PVHI / Grade IV

GMH-IVH - Complications

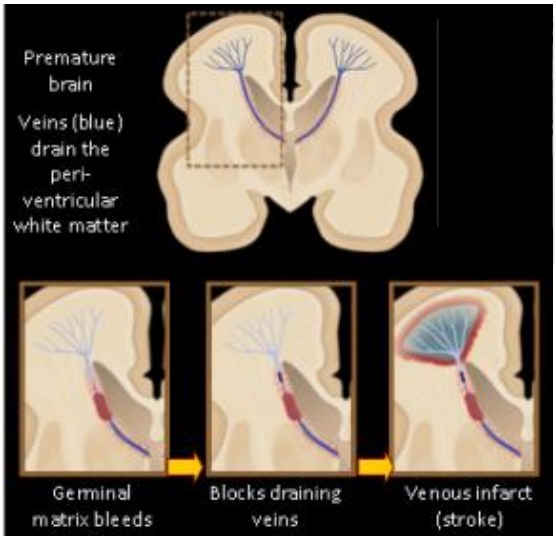
Complications:

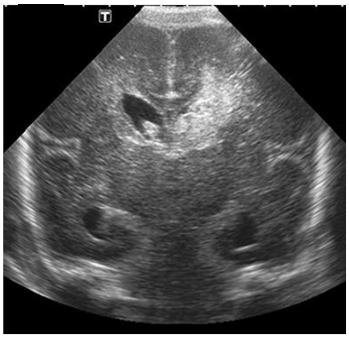
- **Periventricular Hemorrhagic Infarction** (PVHI / PHI / IVH grade IV) [A]
- **Post-Hemorrhagic Ventricular Dilatation** (PHVD) [B-C]
- Associated changes: Widespread WM injury, **cerebellar changes**, smaller tissue volumes

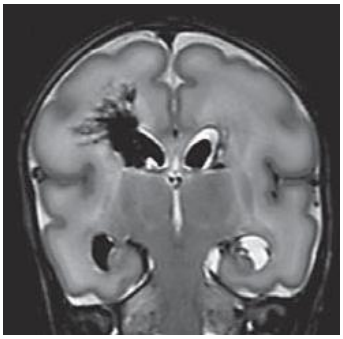


PVHI

- <6% of preterm infants
- Venous congestion (pressure)
- Unilateral / bilateral
- Imaging
  - Serial HUS
  - MRI details



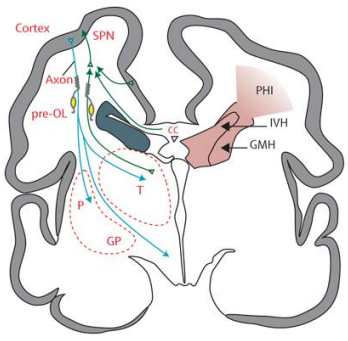


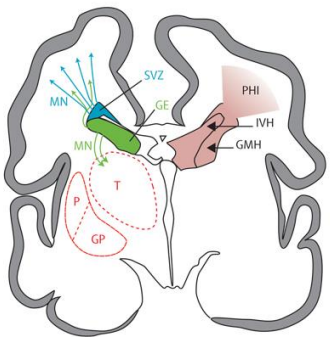


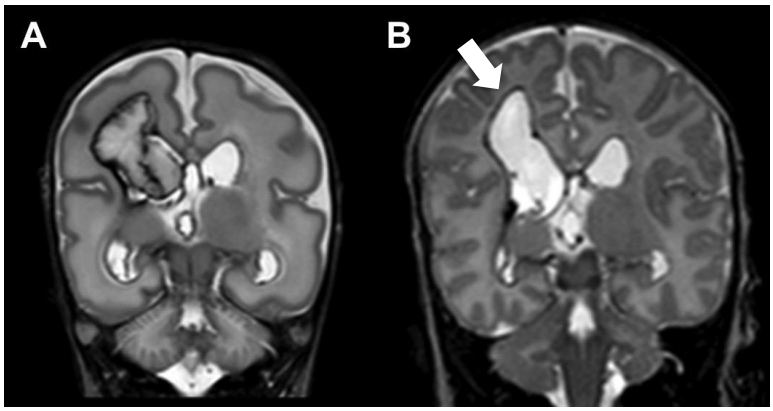
Volpe, Lancet Neurology 2009; Benders Clin Perinatol 2014

PVHI

- Porencephalic cyst (necrosis) **A → B**
- Impairs brain growth and maturation
- Implications for outcome







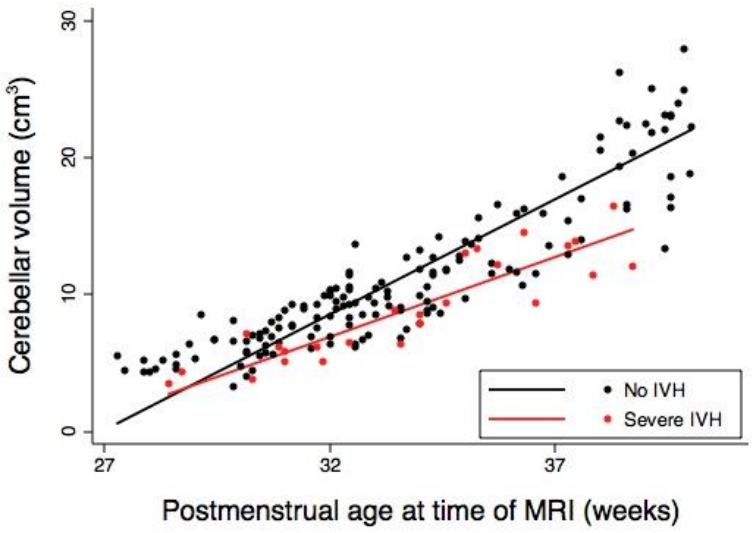
Volpe, Lancet Neurology 2009; Benders Clin Perinatol 2014

IVH & Neurodevelopmental Outcome

Outcome of IVH depends on:

1. Toxic effects of free blood products on brain development
   - Blood products = neurotoxic, direct injury to progenitor cells in germinal matrix
2. Size of IVH
3. Location of parenchymal brain injury
4. Hydrocephalus and VP shunting

IVH & Neurodevelopmental Outcome
Toxic effects of blood products



Long term effects to other structures such as the cerebellum

IVH & Neurodevelopmental Outcome
Size of IVH

Mild IVH (grade 1-2):

- Outcome comparable to those without IVH
- Outcome influenced by presence WM and cerebellar injury
- 50% born <32 weeks GA show learning difficulties at school age

Severe IVH (grade 3-4): associated with worse outcomes

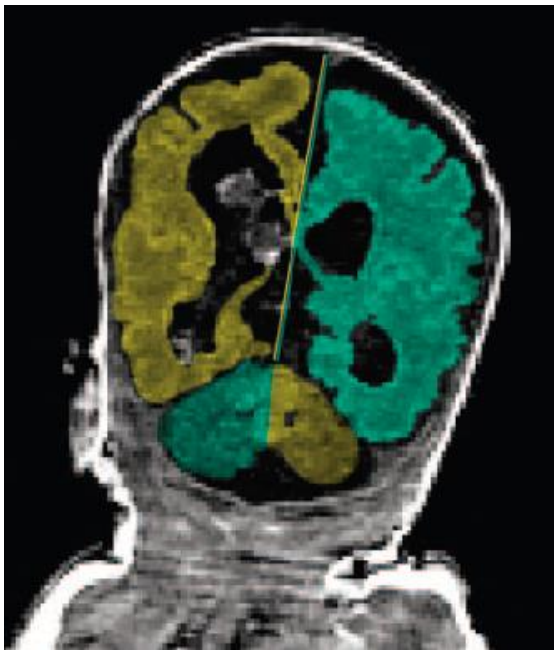
- Higher incidence of motor and cognitive difficulties
- Motor difficulties correlate with location of injury

IVH & Neurodevelopmental Outcome
Size of IVH

Size of IVH	% IVH	Neurological Sequelae	Death
Grade 1	40%	15%	3%
Grade 2	25%	25%	9%
Grade 3	20%	50%	18%
PVHI	15%	75%	29%

Volpe, Neurology of the Newborn, 5th ed. 2008

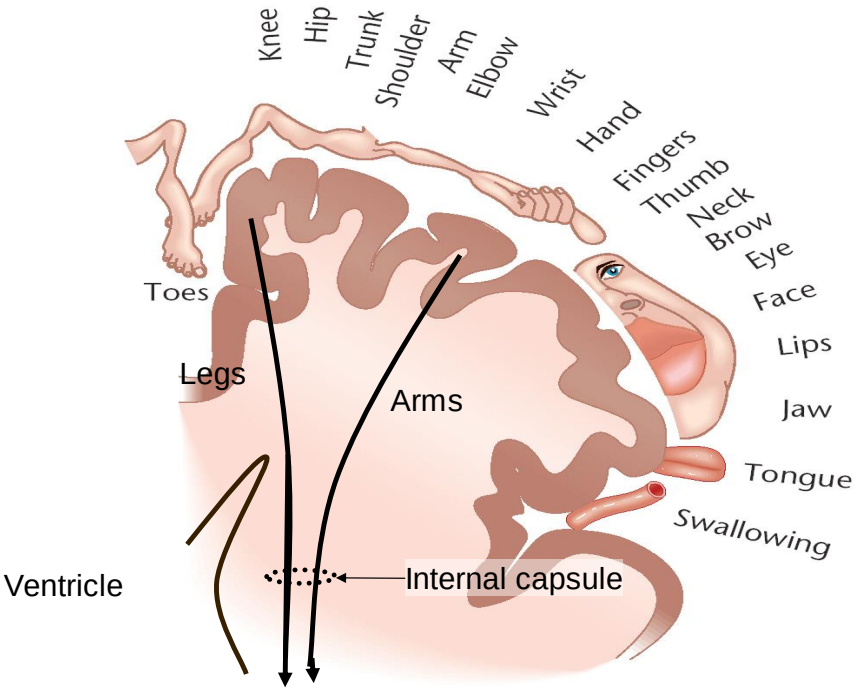
IVH & Neurodevelopmental Outcome
Size of IVH



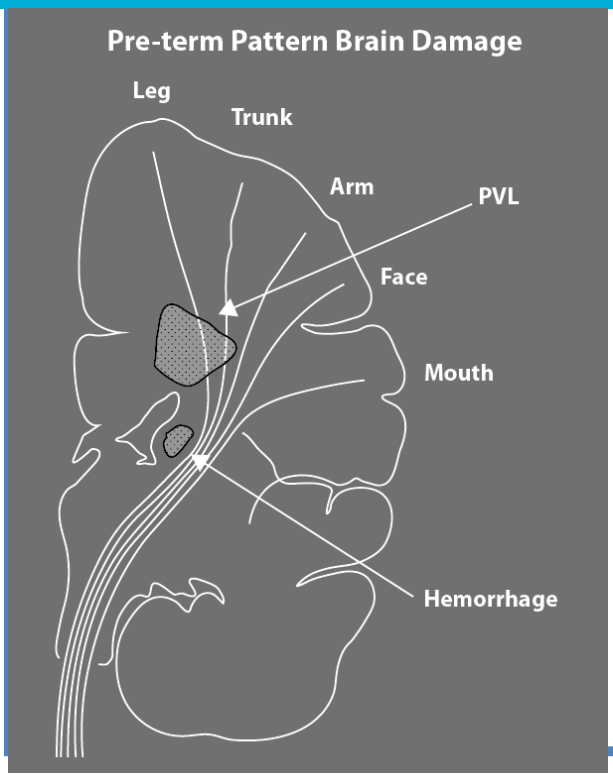
- Large IVH associated with ipsilateral cerebral and contralateral cerebellar volume loss

Limperopoulos C, *et al.* Pediatrics. 2005;

IVH & Neurodevelopmental Outcome
Location



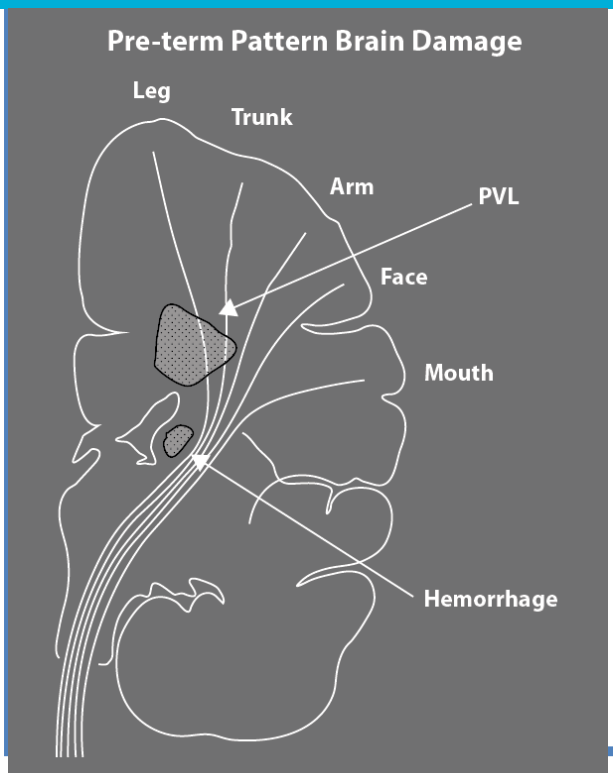
IVH & Neurodevelopmental Outcome Location



What is the classic motor impairment in bilateral grade 3 IVH?

Spastic Diplegia

IVH & Neurodevelopmental Outcome 3. Location



A large unilateral PVHI could lead to hemiplegia

IVH & Neurodevelopmental Outcome
Location of PVHI

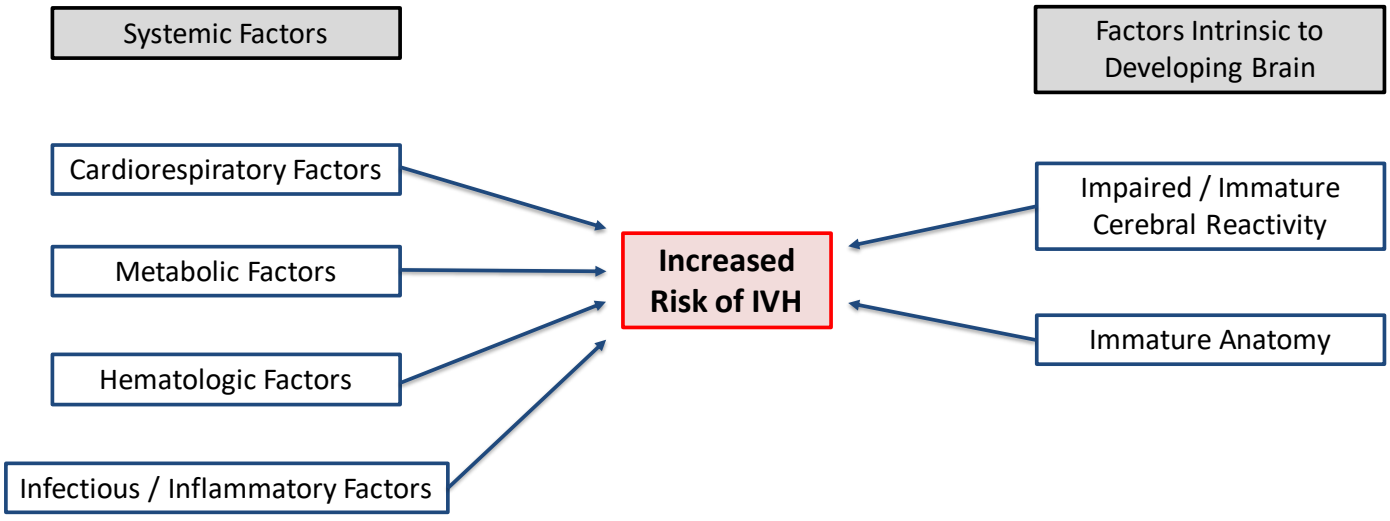
TABLE 2 Association of PVHI With Neurodevelopmental Outcomes

Parameter	*n*	Unilateral PVHI (*n* = 52)	Bilateral PVHI (*n* = 17)	*P*
CP, % (*n*)	69	67 (35)	88 (15)	.090[a]
CP severity, % (*n*)	69			<.001[a]
None or mild		63 (33)	12 (2)	
Moderate or severe		37 (19)	88 (15)	
MDI, median (IQR)	62	82 (49–90)	49 (49–50)	<.001[b]
MDI >70, % (*n*)	62	64 (30)	7 (1)	<.001[a]
PDI, median (IQR)	61	53 (49–80)	49 (49–50)	.020[b]
PDI >70, % (*n*)	61	43 (20)	7 (1)	.009[a]
Vision impairment, % (*n*)	68	17 (9)	31 (5)	.200[a]
Seizure disorder, % (*n*)	69	13 (7)	29 (5)	.100[a]

[a] Pearson test.
[b] Wilcoxon test.

Maitre NL *et al*. Pediatrics 2009;124(6):e1153-60

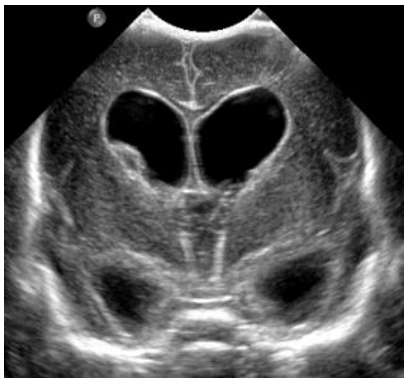
Management of GMH-IVH / PVHI



No single measure preventing GMH-IVH → Combination of measures

Robinson, J Neurosurg Pediatrics 2012

PHVD



- ~30-50% infants with large IVH
- <2nd week of GMH-IVH
- Ventricular size >97th percentile
- Etiology
  - Acute: Impaired CSF outflow (clot)
  - Intermediate: Impaired CSF reabsorption (clots, proteins, fibrosis)
- Initially 'silent'; signs increased ICP late

Levene, ADC 1981; Davies, ADC 2000; Brouwer, Radiology 2012; Ahn 2015; Ellenbogen 2016

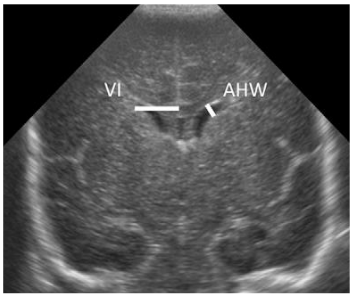
Adverse Effects of PHVD

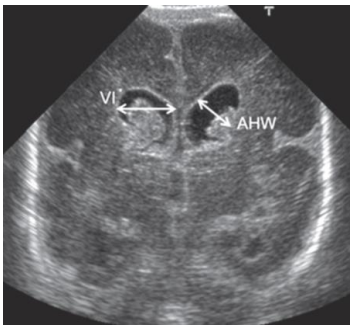
Cerebral hemodynamics	Doppler / PET / NIRS
Neurophysiology	CFM / SEP / VEP Increase in latency
Biochemistry	CSF: Cytokines VEGF Hypoxanthine NPBI TGFß-1 sFAS ↑

de Vries 1990; Kempley 1993; Du Plessis 1995; Soul 2004; Olischar 2004; van Alfen 2007; Olischar 2009; Klebermass 2012; Norooz 2015

PHVD - Imaging

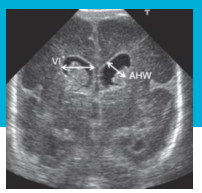
- Serial HUS:
  - Follow onset and progress PHVD
  - DOL 3 and 7, weekly → Intensify if PHVD
  - Ventricular size: Visual ↔ Measurements
- MRI:
  - Limited for PHVD
  - Important for additional brain injury

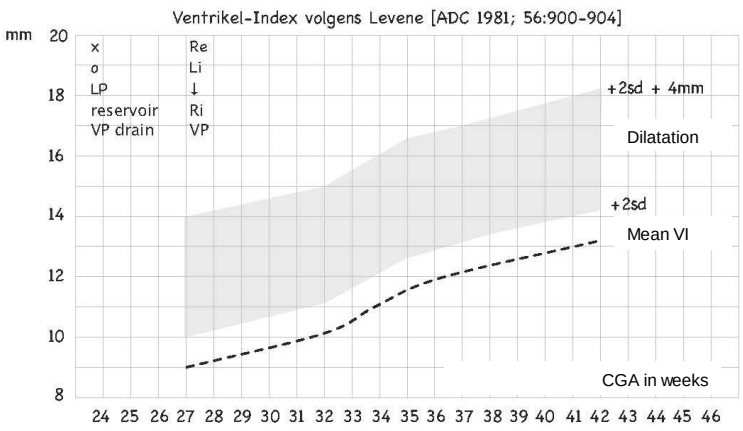




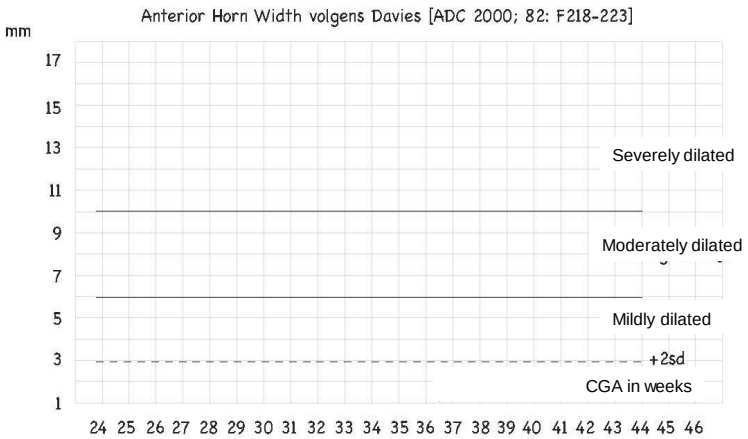
Levene, ADC 1981; Davies, ADC 2000; Brouwer, Radiology 2012; Ahn 2015; Ellenbogen 2016

Measurements Ventricular Size





VI, Ventricular Index



AHW, Anterior Horn Width

Levene, ADC 1981; Davies, ADC 2000; Brouwer, Radiology 2012

Management of PHVD

- Prevention of prolonged pressure on immature, vulnerable WM and neurodevelopmental deficits
- ~35-40% infants need intervention
- Complicated by:
  - Blood and high protein level
  - Weight and instability infant
- Complications: Infection, overdrainage, revision, skin lesion, anesthetics, additional brain injury

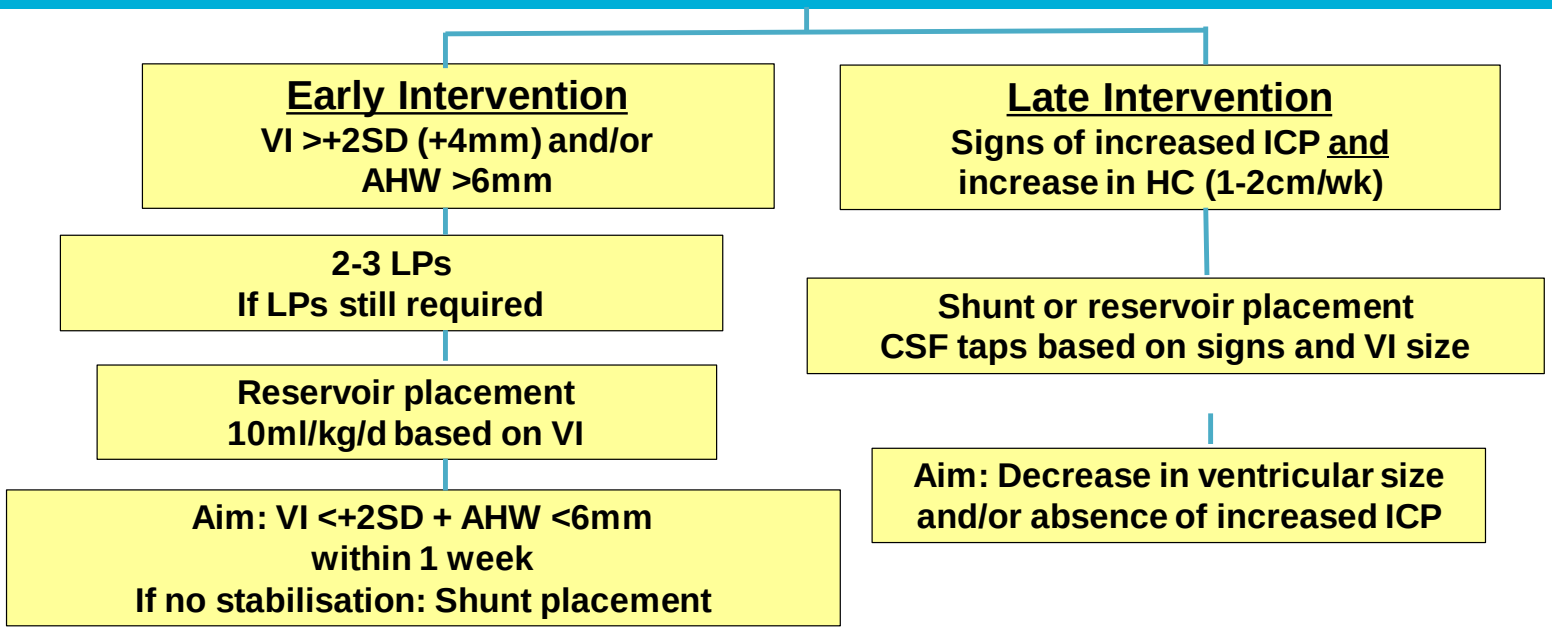
Ellenbogen, J Clin Neurosci 2016

Management of PHVD

- Different strategies studied
  - 3rd Ventriculostomy
  - Choroid plexus coagulation
  - Fibrinolytic agents
  - Diuretics / other agents
- Current practice: CSF taps (LP / reservoir) ↔ VP shunt
- No consensus on when, based on, how ??

  → No RCTs on whether or not to treat (early); benefits outcome > risks?

Approaches: Best for Outcome?



Early intervention beneficial for outcome ??

De Vries, Acta Paediatr 2002; De Vries, ELVIS trial, ISRCTN43171322

Posthemorrhagic ventricular dilatation in preterm infants

When best to intervene?

Lara M. Leijser, PhD, Steven P. Miller, MDCM, Gerda van Wezel-Meijler, PhD, Annemieke J. Brouwer, PhD, Jeffrey Traubici, MD, Ingrid C. van Haastert, PhD, Hilary E. Whyte, FRCPC, Floris Groenendaal, PhD, Abhaya V. Kulkarni, PhD, Kuo S. Han, PhD, Peter A. Woerdeman, PhD, Paige T. Church, MD, Edmond N. Kelly, FRCPC, Henrica L.M. van Straaten, PhD, Linh G. Ly, MD,* and Linda S. de Vries, PhD*

Correspondence
Dr. de Vries
l.s.devries@umcutrecht.nl

Neurology® 2018;90:e1-e9. doi:10.1212/WNL.0000000000004984

Abstract

Objective

To compare neurodevelopmental outcomes of preterm infants with and without intervention for posthemorrhagic ventricular dilatation (PHVD) managed with an "early approach" (EA), based on ventricular measurements exceeding normal (ventricular index [VI] <+2 SD/anterior horn width <6 mm) with initial temporizing procedures, followed, if needed, by permanent shunt placement, and a "late approach" (LA), based on signs of increased intracranial pressure with mostly immediate permanent intervention.

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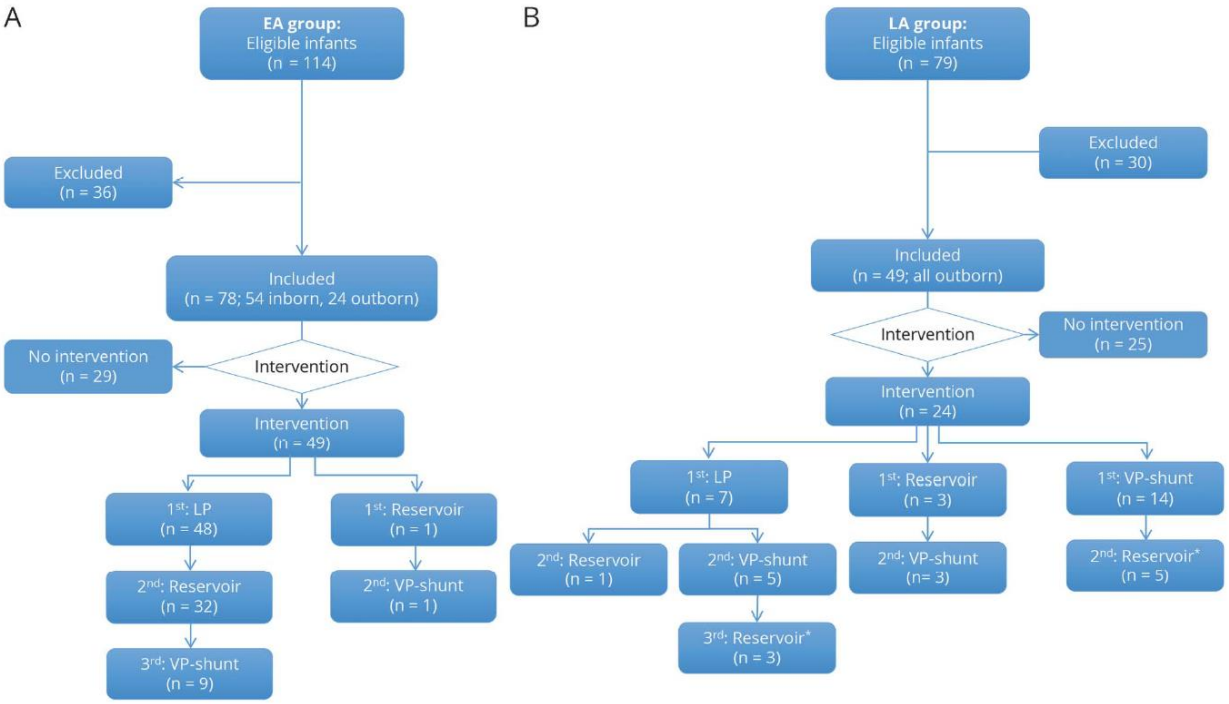
→ Class of Evidence

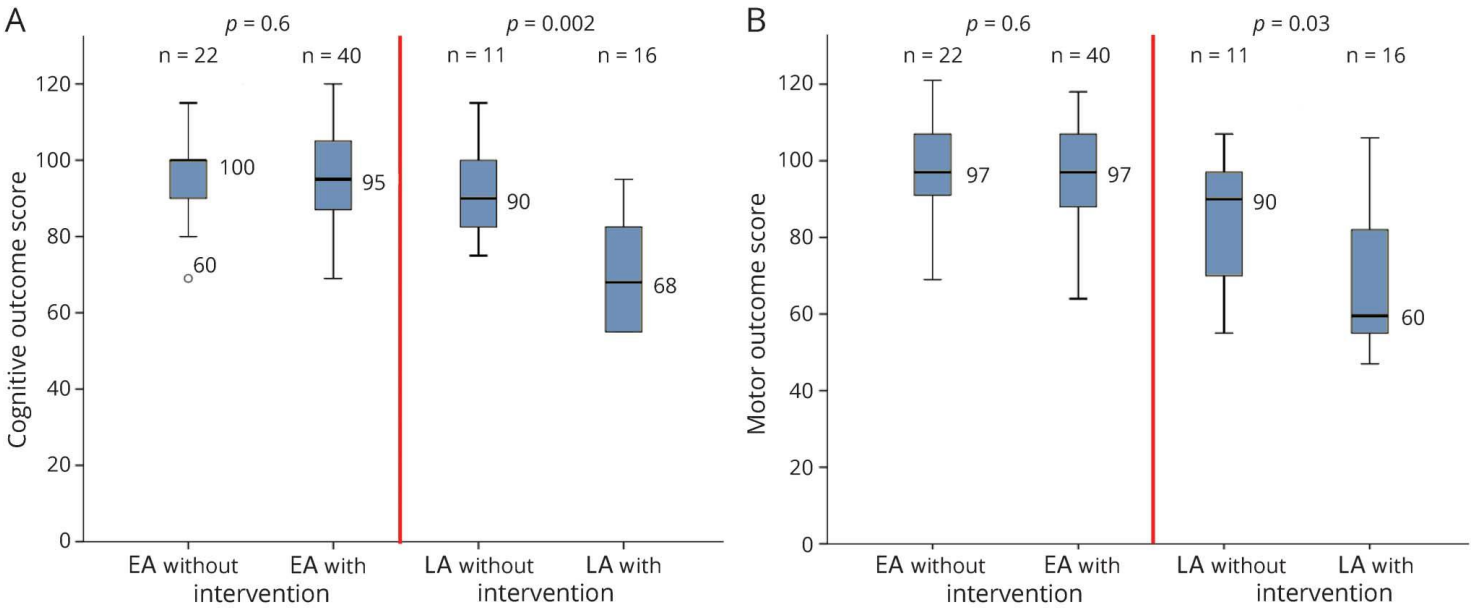


Flow diagram of eligible (total 193), excluded (total 66), and included (total 127) infants in the EA (A) and the LA (B) groups, and subsequent division of infants within the EA and LA groups based on intervention requirement. Type of first and subsequent interventions is also shown. *A ventricular reservoir was placed after VP shunt as temporary measure in case of shunt dysfunction. EA = early approach; LA = late approach; LP = lumbar puncture; VP = ventriculoperitoneal.

Table 1 Details on intervention for infants in the EA and LA groups

Intervention details (n = 73)	EA group (n = 49)	LA group (n = 24)	*p* Value
Type of first intervention, n (%)			
LP	48 (98)	7 (29)	—
Reservoir	1 (2)	3 (13)	—
VP shunt	0	14 (58)	—
Ventricular size before first intervention, median (IQR)			
VI left/right (in mm above +2 SD for age)	2.5 (1–3.5)/2.0 (0.6–3)	13.0 (10–15.9)/11.0 (11–16.4)	—
AHW left/right (in mm above 6 mm)	3 (1–4)/2.0 (1–4)	16.0 (10.3–18.8)/14.5 (10.3–20)	—
Overall type of intervention, n (%)			
LP	48 (98)	7 (29)	—
Reservoir	33 (67)	12 (50)	—
VP shunt	10 (20)	22 (92)	—
Timing, mean (range)			
First intervention			
Age, d	13 (4–45)	47 (15–147)	—
PMA, wk	29.4 (25.4–35.3)	33.1 (27–45)	—

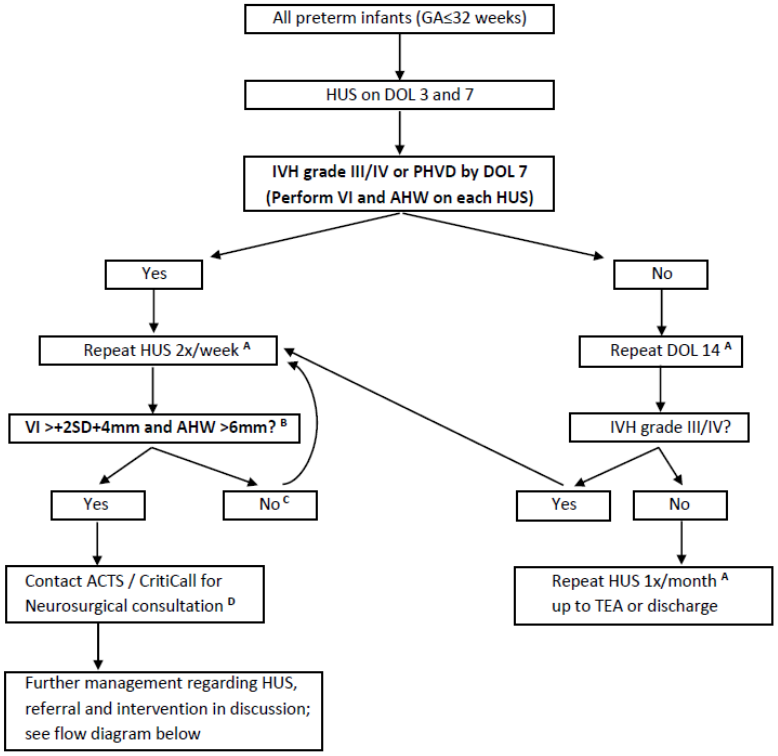
Outcome Scores Between Groups



What Next?

- Buy in from neurosurgery!
- Development of early intervention protocol
- Implementation
- Evaluation-outcome data

Surveillance Protocol



Intervention Protocol

All steps and interventions are guided by measurements of VI and AHW on HUS. HUS needs to be repeated on a **daily** basis after detection of PHVD and after each intervention. If stabilization and/or decrease of ventricular size is obtained, the frequency of HUS can be gradually reduced.

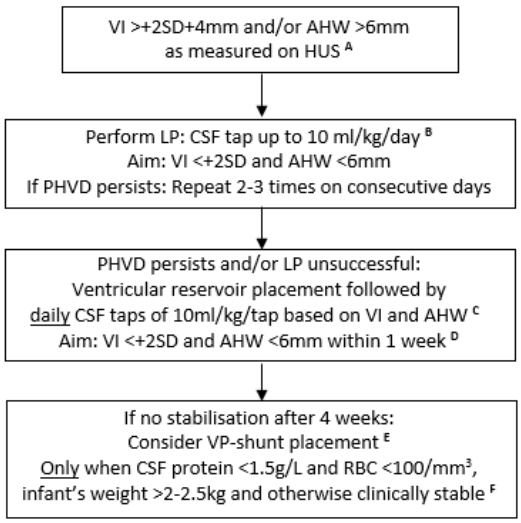
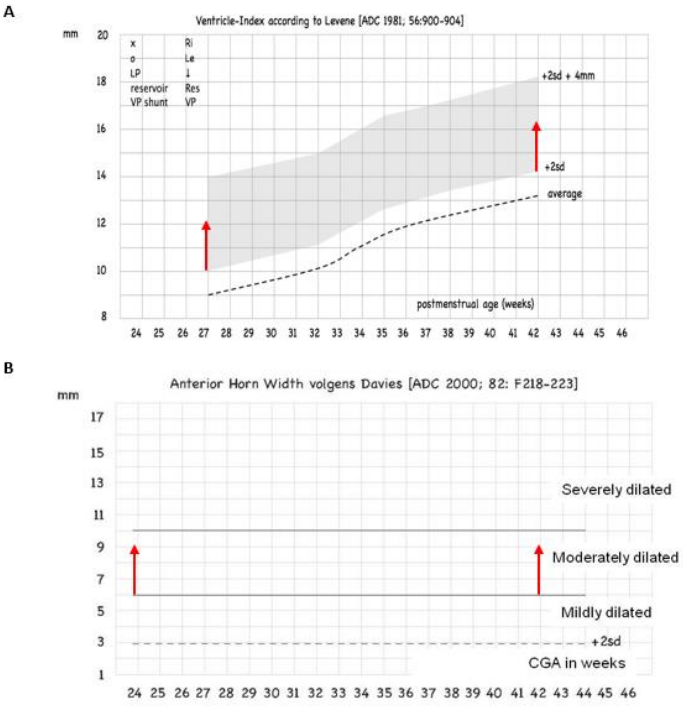


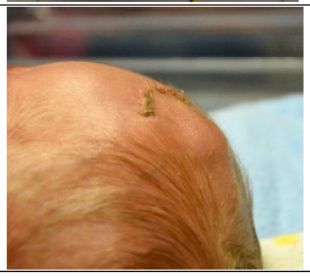
Figure 2. Normal values for ventricular size and cut-off values for ventricular dilatation for the VI (panel A) and AHW (panel B). For the VI, ventricular dilatation is regarded as a VI >+2SD line for postmenstrual age; for the AHW this is regarded as a AHW >6mm line regardless of age.



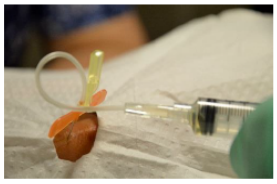
VENTRICULAR RESERVOIR (VR) TAPPING TECHNIQUE

		Major Steps	Details (if applicable)	Rationale
PREP	1	Prepare the patient	• Note the most recent head circumference and perform subjective fontanelle assessment • Monitor vital signs	• To monitor patient response to the procedure
	2	Prepare the environment	• Turn on the clock feature on the patient monitor	• To track time during the procedure in order not to exceed the recommended rate
	3	Gather equipment required for procedure	• Sterile dressing tray (includes gauze, cotton balls, and sterile drape) OR Lumbar puncture tray • Small gauge butterfly needle (25-27) • 10-20 mL syringes • Betadine solution • Sample collection containers if needed • Appropriate size sterile gloves • Procedural gown and mask	 

VENTRICULAR RESERVOIR (VR) TAPPING TECHNIQUE

		Major Steps	Key Point(s)	Rationale for Key Point(s) & Other Details
CLEAN STEPS	4	Perform hand hygiene	• As per hospital policy: HAND HYGIENE AND HAND CARE	
	5	Don personal protective equipment (PPE)	• Yellow gown, mask, and hat should be worn in preparation for sterile procedure involving bodily fluids *As per hospital policy (please insert)	
	6	Prepare the site	• Palpate the skull to identify the exact location of the reservoir • May cut any hair that interferes with the area if necessary but do not shave skin • Position baby in a comfortable position (anticipating 10-20 minute procedure) with adequate access to the reservoir	
	7	Perform initial skin preparation	• Cleanse the skin using sterile water or saline • Wait 1-2 minutes to allow skin to dry	

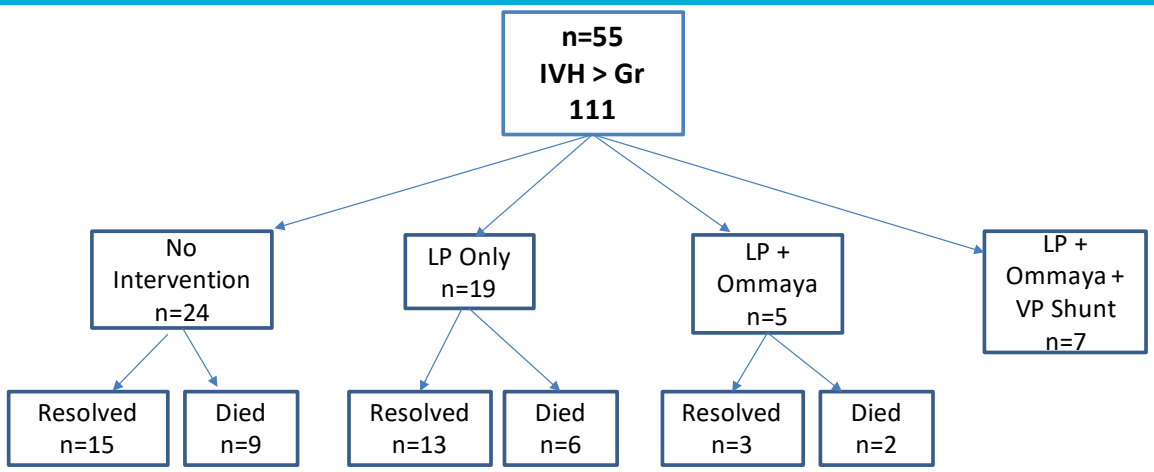
VENTRICULAR RESERVOIR (VR) TAPPING TECHNIQUE

		Major Steps	Key Point(s)	Rationale for Key Point(s) & Other Details
ASEPTIC STEPS	8	Preparation of reservoir site	• Perform Hand Hygiene: HAND HYGIENE AND HAND CARE policy • Don sterile gloves • Repeat skin preparation: Prepare skin using antiseptic solution over the reservoir site in at least a 5 cm radius around the reservoir (use chlorhexidine 0.5% with 70% isopropyl alcohol or Betadine). • Wait for 1-2 minutes for prep solution to dry • Position sterile drape to maintain sterile field	• Refer to: Clean, Disinfection, and Sterilization policy 
	9	Preparation of equipment	▪ Prepare CSF collection tubes if needed ▪ Sterilely drop all required equipment into the sterile field	
	10	Tap technique	• Insert the butterfly needle through the skin into the reservoir • Avoid any areas of skin breakdown or recent insertion site when possible • Angle needle at 30-45 degrees from the skin • Attach syringe to the end of the butterfly catheter and begin CSF aspiration • Aspirate approximately 10 mL/kg/tap at a slow rate of preferably 1 ml/min, NOT to exceed 2 mL/min	* Insert video of tapping procedure here* 
	11	CSF Samples	• CSF sample should be sent to the lab for analysis routinely at least **every 3 days for glucose, protein, cell count, and culture.**	• Consider sending more frequently if there are any relevant clinical changes such as signs or symptoms of infection. *Microbiologist approval may be required for CSF culture sent sooner than 3 days from the previous sample.*

VENTRICULAR RESERVOIR (VR) TAPPING TECHNIQUE

WRAP-UP	12	Monitoring Post Procedure	• During and after procedure patient should be monitored for: ▪ Vital signs and cardiorespiratory status ▪ Pain ▪ Changes in the fontanelle and ICP ▪ CSF leak from the tap site	
	13	Post Procedure	• On completion of VR tap procedure enter note in patient's chart including: patient tolerance of procedure, color and quality of CSF, and amount CSF aspirated.	

PHVD Tri Hospital Data 2018



Mortality Rate: 30%
Complication Rate: 7%

- Complications
  - •One CONS 48 hrs post ommaya insertion
  - •One CSF leak 6 weeks post ommaya insertion – CONS
  - •One resistant Enterobacter fecalis (VAP/UTI-meningitis)- died

39% Resolved spontaneously
35% Resolved LP only
8% Resolved to discharge home with ommaya only
18% Required VP shunt

Ryleigh's Story

Sudbury

Sudbury mom planning fundraiser for Sick Kids Hospital

Ryleigh was born at 29 weeks, and endured 2 surgeries at 2 months old

CBC News · Posted: May 21, 2019 11:39 AM ET | Last Updated: May 21, 2019

Ryleigh Valcourt was born at 29 weeks and spent the first few months of her life at Sick Kids Hospital. She is shown here with mom Kerri Chevrier and dad Johnny Valcourt. (Supplied by Kerri Chevrier)

After 2 surgeries at 2 months old, Ryleigh is hitting all of the milestones at her corrected age. She is pictured here with father Johnny Valcourt. (Kerri Chevrier)

In Conclusion

IVH and PHVD:

- Still important complications of prematurity
- Implications for outcome, particularly when associated brain lesions
- Close monitoring and early detection (and intervention) most important

Further Reading

- Meijler: Neonatal Cranial Ultrasonography (2010)
- Govaert & De Vries: An Atlas of Neonatal Brain Sonography (2010)
- Books on Neonatal Neurology and Imaging by Barkovich & Raybaud (2012),Volpe (2008), Levene (2001), Shevell & Miller (2012)
- Term infants:
  - Afsharkhas L, et al. Iran J Child Neurol. Summer 2015
  - Tavil B, et al. Blood Coagul Fibrinolysis 2016