PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES

Management of Post-Hemorrhagic Ventricular Dilatation (PHVD) in Preterm Infants

Implementation Date: May 7, 2021

Clinical Practice Guideline: Management of Post-Hemorrhagic Ventricular Dilatation (PHVD) in Preterm Infants

Points of emphasis/Primary changes in practice:

1. Post-hemorrhagic ventricular dilatation (PHVD) is associated with a high risk for subsequent adverse motor and cognitive neurodevelopmental outcomes.
2. Clinical features of PHVD such as apneas, vomiting, full fontanel, sunsetting, splaying sutures, rapid increase in head circumference [HC] are late findings.
3. Ventricular measurements by cranial ultrasound (cUS) allow for early detection of ventricular dilatation and close monitoring its progress.
4. Progressive ventricular dilatation is associated with worse neurodevelopmental outcome and earlier interventions have the potential to improve outcome when compared to later interventions.
5. We are introducing a risk stratification framework which depends on changes in ventricular measurements supported by clinical signs and additional measurements using Doppler US as well as Near Infra-Red Spectroscopy (NIRS) as foundation for management.

Questions? Please contact: Director of Neonatal Neurocritical Care Program- Department of Pediatric Newborn Medicine

Clinical Guideline Name	Post-Hemorrhagic Ventricular Dilatation (PHVD)
Effective Date	03/01/2021
Revised Date	
Team Leader(s)	Neonatal Neurocritical Care Program- Department of Pediatric Newborn Medicine
Approved By	Department of Pediatric Newborn Medicine Clinical Practice Council CWN SPP BWH SPP Steering Nurse Executive Board/CNO
Keywords	PHVD, IVH, Lumber Puncture, Shunt

This is a clinical practice guideline. While the guideline is useful in approaching post-hemorrhagic ventricular dilatation (PHVD) clinical judgment and / or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

I. Purpose

To provide guidance about management of post-hemorrhagic ventricular dilatation (PHVD) in preterm infants

II. All CPGs will rely on the NICU Nursing Standards of Care. All relevant nursing PPGs are listed below.

NICU/SCN L.1 Assisting with Lumbar Puncture (LP)

III. Scope

These guidelines establish an approach for evaluation, monitoring and management of neonates presenting with progressive ventricular dilatation following intraventricular hemorrhage (IVH), (post-homorganic ventricular dilatation, PHVD) in the Newborn Intensive Care Unit.

IV. Guidelines

1. Incidence:

Severe forms of intraventricular hemorrhage (IVH) continue to occur in up to 15% of extremely premature infants,(Stoll, Hansen et al. 2015) and more than half of these infants develop post-hemorrhagic ventricular dilatation (PHVD).(Murphy, Inder et al. 2002) PHVD is a term that represents the progressive ventricular dilatation resulting from the presence of IVH and encompasses other terms, such as post-hemorrhagic hydrocephalus (PHHC). PHVD is associated with a high risk for subsequent adverse motor and cognitive neurodevelopmental outcomes.

2. Pathophysiology and Neuropathology of PHVD

The relation of PHVD to brain injury and dysmaturation in the human premature infant has been supported by a variety of studies of experimental models and of human infants. It is critical to place these studies in the context of the rapid and complex developmental events occurring in the premature brain in the third trimester. The critical vulnerability of the immature cerebral white matter, particularly the actively differentiating pre-oligodendrocyte (pre-OL), to injury, combined with a propensity of the immature microglia and astrocytes to pro-inflammatory activation, renders this developmental period unique in the neuropathological consequences of PHVD.

The mechanisms of the deleterious effects on the brain of the human infant with PHVD are likely multifactorial. Cerebral white matter, thalamus, hippocampus and cerebellum appear to be particularly involved. It seems likely that in addition to cerebral ischemia, mechanical distortion and neuroinflammation, factors related to the presence of blood, leading ultimately to iron release and free radical formation, are pathogenic. The important pathogenic role of blood products, especially iron, and resulting neuroinflammation have major implications for types of therapeutic interventions. Because the hydrocephalic state would be expected to enhance the intraparenchymal movement of blood products, the early institution of interventions that involve CSF drainage seems critical (El-Dib, Limbrick et al. 2020)

3- Clinical Assessment:

The commonly cited clinical features of PHVD include:

- Local signs such as full fontanel, sunsetting, and splaying sutures
- Systemic signs such as apnea and vomiting
- Rapid increase in head circumference (HC)

In the preterm infant, there are two factors that reduce the sensitivity of fontanel pressure or HC changes for evaluating the degree of significant ventricular dilatation. The first factor is that compliance is higher in the preterm infant, such that lower pressures are sufficient to cause progressive ventricular distension resulting in major compression of the cortical mantle before any effect is apparent on sutures or on HC. The second factor relates to the larger extracerebral space in very preterm infants requiring considerable ventricular dilatation before changes in fontanel pressure and a rapid increase in HC occur. Consistent with this notion, a poor correlation was found between the Evans ratio (the ratio of bifrontal horn diameter to the biparietal bone diameter) and HC measurements.(Ingram, Huguenard et al. 2014)

4- Ventricular measurements

The "ventricular index" (VI), defined by Levene and Starte(Levene and Starte 1981), is the most commonly used measurement and is assessed in the coronal view. The VI is the distance between the midline (falx) and the lateral border of the lateral ventricle at the level of foramen of Monro. Another commonly used measurement is the "anterior horn width" (AHW), also measured in the coronal view just anterior to the thalamic notch.(Davies, Swaminathan et al. 2000) For both measurements, normal values and cut-off values for PHVD have been reported.(Levene and Starte 1981, Davies, Swaminathan et al. 2000, Brouwer, De Vries et al. 2012) The "thalamo-occipital distance" (TOD) measures the occipital horn in the parasagittal plane and is of additional value because there can be a discrepancy in size between the anterior and occipital horns of the lateral ventricle. The AHW and TOD measures can indicate the so-called 'ballooning' shape of the lateral ventricles, and these measures relate best with 3D volumetric ultrasound measurements.(Benavente-Fernandez, Lubian-Gutierrez et al. 2017) The morphology of the ventricles can assist in the differentiation between dilatation due to PHVD or ventricular dilatation due to cerebral atrophy, since ventricular dilatation is typically associated with ballooning of the

ventricles. In addition, assessing the extracellular space will assist in differentiating the two causes of dilatation. The absence of any extra-axial space would support the conclusion that the dilatation relates to CSF accumulation, while the presence of extra-axial space suggests cerebral atrophy.(De Vries, van Haastert et al. 2011) (see Head Ultrasound (HUS) Screening in Premature Infants CPG)

5- Other Measurements:

Additional use of the **Doppler US** resistive index (RI), the difference between peak systolic flow velocity and lowest diastolic flow velocity divided by the peak systolic flow velocity, provides information about cerebral hemodynamics, especially cerebrovascular resistance. With progressive PHVD, initially a rise in systolic flow is seen, followed by a decrease, absent or even inverted diastolic flow.(van Alfen-van der Velden, Hopman et al. 2007) Significant changes in RI following application of pressure to the anterior fontanel, a measure of cerebral compliance, correlated with intracranial pressure and future need for shunt placement. In one study, infants with hydrocephalus who did not need shunt placement had Δ RI 19% ± 6 (range 3%-29%), while those who ended needing shunt placement had ΔRI of 74% ± 9 (range 47%-132%). (Taylor and Madsen 1996)

In addition, **near infrared spectroscopy (NIRS)** studies have shown that regional cerebral oxygen saturation is progressively impaired with increasing dilatation, and gradual improvement following CSF drainage.(Norooz, Urlesberger et al. 2015, Kochan, McPadden et al. 2017) (See Clinical NIRS in the NICU CPG)

As these changes occur when PHVD is severe, intervention is best started prior to the presence of these changes.

6- Relationship of ventricular size to outcome

In contrast to data derived from post-natal post-inflammatory hydrocephalus in term born infants and children,(Kulkarni, Schiff et al. 2017) the association between the maximal size of ventricular measurements in PHVD in preterm infants and neurodevelopmental outcomes has been supported by more than one study.(Srinivasakumar, Limbrick et al. 2013, Leijser, Miller et al. 2018, Cizmeci, Groenendaal et al. 2020)

Two retrospective, observational studies showed a reduction in shunt requirement when LPs and reservoir insertion were performed before the 97 percentile +4 mm line was crossed.(de Vries, Liem et al. 2002, Brouwer, Groenendaal et al. 2008) In another retrospective study of 32 preterm infants, external ventricular drainage (using bedside insertion of an intravenous catheter connected to a closed drainage plastic container) performed early (defined as ≤25 days after birth) was associated with better scores for adaptive, personal social, communication, and cognitive functions at 6 years of age compared to those with later intervention.(Bassan, Eshel et al. 2012) In addition, a more recent observational study has shown results favoring earlier therapeutic intervention for PHVD using cUS measures. (Leijser, Miller et al. 2018)

The most recent RCT conducted was the ELVIS trial (Early versus Late Ventricular Intervention Study) which enrolled 126 preterm infants ≤ 34 weeks' gestation with progressive PHVD following a severe IVH. Treatment was either started at a low threshold (LT) (VI > 97th percentile and AHW > 6 mm and/or TOD > 25 mm), or at a higher threshold (HT) (VI > 97th percentile +4 mm and AHW > 10 mm). There was no significant difference between the two groups for the primary outcome, i.e. death and /or VP-shunt placement (30% LT and 37% for HT infants). A VP-shunt was inserted in 12/64 (19%) infants in the LT and in 14/62 (23%) infants in the HT group, the lowest rates reported so far in the literature. (de Vries, Groenendaal et al. 2019) In a nested study, on TE MRI, those in the LT group has better Brain Injury Kidokoro score and had smaller ventricles. (Cizmeci, Khalili et al. 2019). At 2 years of age the risk of developmental impairment was low among both study groups, with 75% of all infants tested achieving a cognitive composite score of ≥ 85. On multivariable analysis, being in the LT group was associated with a decreased risk of composite adverse outcome (death/cerebral palsy/BSID score <70), after correcting for gestational age and hemorrhage severity (adjusted odds ratio [aOR]: 0.24, 95% confidence interval [CI], 0.07 to 0.87, p=0.03). Furthermore, a significant relationship was established between ventricular size (using the maximal Frontal and Occipital Horn Ratio, FOHR) and cognitive and motor outcome for all infants combined. (Cizmeci, Groenendaal et al. 2020)

These findings support the conclusion that timely intervention with reduction of the extent of ventricular dilatation may mitigate brain injury associated with ventricular dilatation and lead to improved neurodevelopmental outcomes.

7- Lumbar Puncture

Intervention typically starts with lumbar punctures (LPs) for two key reasons. The first is related to the need to decompress the ventricle on an urgent basis, often leading LPs to be temporizing while neurosurgical evaluation and surgical planning occur. The second is that 2-3 LPs may prevent the need for further neurosurgical intervention, as was demonstrated in the ELVIS study, in which 2-3 LPs reduced the need for surgery in up to one quarter of all cases.(de Vries, Groenendaal et al. 2019)

Earlier data related to LPs in PHVD therapy are summarized in a Cochrane review that reports that there is no evidence that LPs alone are effective in avoiding shunt surgery or improving neurological development.(Whitelaw and Lee-Kelland 2017) However, it is important to note that this review included only four trials performed 1980-1990 with significant variation in indication, timing, number and effectiveness of LPs. The majority of these studies included infants with severely dilated ventricles, with LPs starting relatively late, and high variation in number of LPs (1-40) and volume drained. Of note, in the largest study included in this Cochrane review, more than 50% of the early intervention group eventually received invasive ventricular taps. (Group 1990)

8- Neurosurgical Interventions:

Recent evidence-based guidelines under the auspices of the Joint American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) Pediatric Section identified ventricular reservoir (VR) or ventricular subgaleal shunt (VSGS) as treatment 'options'.(Mazzola, Choudhri et al. 2014) Complications reported with temporizing measures include obstruction, infection, need for revision and other rare complications like CSF leak, porencephalic cysts and intracranial hemorrhage (Tubbs, Banks et al. 2005, Wang, Amin et al. 2014, Badhiwala, Hong et al. 2015) **.** The HCRN (Hydrocephalus Clinical Research Network), study titled "Shunting Outcomes in Post-hemorrhagic Hydrocephalus (SOPHH)", compared VR versus VSGS as temporizing measures and found no difference between VR and VSGS in rates of infection, CSF leak, death or VP-shunt rate. (Wellons, Shannon et al. 2017) While the VR by default needs more frequent skin breaks than VSGC, it is worthy of note that minimizing complications from reservoir drainage can be obtained by systematic care, including strict sterile

precautions, using a trained provider for removal of the CSF, removing the fluid slowly at not greater than 1ml/minute and carefully considering skin care over the site of the reservoir.(Brouwer, Groenendaal et al. 2015)

A more definite surgical intervention could be considered and includes Ventricuo-peritoneal shunt (VP shunt). The decision for VP- shunt, is based on such factors as infant's age, weight or clinical condition, and CSF protein and red cell count.

Another approach, which could potentially reduce the long-term shunt-related morbidity in these infants, is endoscopic third ventriculostomy (ETV) without or with choroid plexus cauterization (ETV/CPC). This intervention could serve as an alternative to CSF shunting in PHVD, though reported success rates are variable, at least early in infancy in this population.(Stone and Warf 2014, Kulkarni, Riva-Cambrin et al. 2018, Riva-Cambrin, Kestle et al. 2019). Success rates for ETV/CPC, performed following temporizing measures, are enhanced by selecting infants who are close to or preferably well beyond term equivalent age and who have no obstruction of the prepontine cistern on preoperative MRI.(Warf, Campbell et al. 2011)

9- Framework for management of PHVD:

Combining the evidence from preclinical data supporting the ability of early interventions to reverse brain injury and from clinical data indicating that the best neurodevelopmental outcomes have been reported in centers and trials using ventricular measurements as criteria for interventions now makes it prudent to adopt this evidence to clinical practice.

Recognition of increased ICP using such clinical signs as rapid head growth, separated sutures or bulging fontanelles is very important. However, waiting for any of these late signs to develop can lead to late interventions and the potential for worsening brain injury. Nonetheless, the development of such signs should be concerning enough to initiate interventions even with modest increases in ventricular measurements. Doppler US and NIRS are also adjunct tools which can aid with decision making.

Based on these principles, the following algorithm relies on standardized ventricular measurements, clinical signs and supplementary tests to assign risk categories for infants with PHVD. Based on such risk assessment, providers can determine the frequency and types of

assessments, and the timing of temporizing measures, neurosurgical referral as well as neurosurgical interventions.

To recognize the risk category effectively and timely, we encourage plotting all ventricular measurements (VI, AHW and TOD) using a simple tool which was developed from data from the study by Brouwer et al.(Brouwer, De Vries et al. 2012) to help the clinician better assess and risk progress. **(Appendix 1)** An electronic spreadsheet is also available online to be downloaded, stored in secure servers and used for individual patients in two formats: First format is for postmenstrual age (PMA) 24-42 weeks (https://tinyurl.com/PHVD-Measures) and another one is for PMA 24-29 weeks (https://tinyurl.com/PHVD-Measures-2).

Patients with PHVD will be categorized into 3 risk groups (Appendix 2)

A- **The low-risk group (Green zone)**

Identification: infants with IVH with VI ≤ 97th percentile, AHW ≤ 6 mm and TOD ≤ 25 mm. To fulfill this category, there should be neither clinical signs of increased ICP nor alteration in Doppler US and NIRS.

Plan:

- Monitor closely and evaluate by cUS at least twice weekly until the ventricles are stable for 2 weeks and then every 1-2 weeks until 34 weeks' PMA.
- A term equivalent MRI is recommended in these infants to delineate the degree of brain injury as well as any alterations in brain maturation.

B- The moderate-risk group (yellow zone)

Identification: infants with IVH with VI >97th percentile, AHW > 6 mm and /or TOD > 25 mm. To fulfill this category, there should still be no clinical signs of increased ICP as well as no alteration in Doppler US and NIRS.

Plan:

- Neurology and Neurosurgery consultation.
- LPs 2-3 times, aiming for removing 10 ml/kg of CSF. LP should not be performed more often than once a day.
- cUS before and preferably also following the LP to assess its effect

- cUS at least 2-3 times per week until ventricles are stable for 2 weeks and then every 1-2 weeks.
- A term equivalent MRI is also recommended.

C. The High-risk group (Red zone)

Identification:

- infants with VI >97th percentile+ 4mm, and AHW > 10 mm. Such infants include some of those in the yellow zone whose ventricles fail to stabilize on sequential cUS scans.
- Infants with clinical criteria (rapid increased in HC > 2 cm per week, separated sutures or bulging fontanelles) and evidence of progressive ventricular dilatation will also fulfill the red zone criteria, irrespective of their cUS measurements
- Alterations in Doppler US and NIRS, if available, can assist with risk stratification.

Plan:

- Could benefit from 2-3 LPs done acutely, while planning neurosurgical interventions.
- Neurosurgical interventions including VR or VSCG, and might include a VP- shunt or ETV/ CPC

APPENDICES:

Appendix 1- A practical clinical tool to monitor commonly used ventricular measures.

Appendix 2- Proposed algorithm for risk stratification and management of infants with PHVD

Appendix 3- Notes on Interventions for PHVD

Appendix 4- Management of Post- Hemorrhagic Ventricular Dilatation (PHVD) Information for Parents

REFERENCES:

1) Badhiwala, J. H., C. J. Hong, F. Nassiri, B. Y. Hong, J. Riva-Cambrin and A. V. Kulkarni (2015). "Treatment of posthemorrhagic ventricular dilation in preterm infants: a systematic review and meta-analysis of outcomes and complications." J Neurosurg Pediatr **16**(5): 545-555.

2) Bassan, H., R. Eshel, I. Golan, D. Kohelet, L. Ben Sira, D. Mandel, L. Levi, S. Constantini, L. Beni-Adani and I. External Ventricular Drainage Study (2012). "Timing of external ventricular drainage and neurodevelopmental outcome in preterm infants with posthemorrhagic hydrocephalus." Eur J Paediatr Neurol **16**(6): 662-670.

3) Benavente-Fernandez, I., M. Lubian-Gutierrez, G. Jimenez-Gomez, A. M. Lechuga-Sancho, S. P. Lubian-Lopez and F. Neonatal Neurology (2017). "Ultrasound lineal measurements predict ventricular volume in posthaemorrhagic ventricular dilatation in preterm infants." Acta Paediatr **106**(2): 211-217.

4) Brouwer, A., F. Groenendaal, I. L. van Haastert, K. Rademaker, P. Hanlo and L. de Vries (2008). "Neurodevelopmental outcome of preterm infants with severe intraventricular hemorrhage and therapy for post-hemorrhagic ventricular dilatation." J Pediatr **152**(5): 648-654.

5) Brouwer, A. J., F. Groenendaal, K. S. Han and L. S. de Vries (2015). "Treatment of neonatal progressive ventricular dilatation: a single-centre experience." J Matern Fetal Neonatal Med **28 Suppl 1**: 2273-2279.

6) Brouwer, M. J., L. S. De Vries, F. Groenendaal, C. Koopman, L. R. Pistorius, E. J. H. Mulder and M. J. N. L. Benders (2012). "New reference values for the neonatal cerebral ventricles." Radiology **262**(1): 224-233.

7) Cizmeci, M. N., F. Groenendaal, K. D. Liem, I. C. van Haastert, I. Benavente-Fernández, H. L. M. van Straaten, S. Steggerda, B. J. Smit, A. Whitelaw, P. Woerdeman, A. Heep and L. S. de Vries (2020). "Randomized Controlled Early versus Late Ventricular Intervention Study in Posthemorrhagic Ventricular Dilatation: Outcome at 2 Years." J Pediatr.

8) Cizmeci, M. N., F. Groenendaal, K. D. Liem, I. C. van Haastert, I. Benavente-Fernandez, H. L. M. van Straaten, S. J. Steggerda, S. B. J., A. Whitelaw, P. Woerdeman, A. Heep and L. S. de Vries (2020). "Randomized Controlled Early versus Late Ventricular Intervention Study (ELVIS) in Posthemorrhagic Ventricular Dilatation: Outcome at 2 Years." Submitted.

9) Cizmeci, M. N., N. Khalili, N. H. P. Claessens, F. Groenendaal, K. D. Liem, A. Heep, I. Benavente-Fernandez, H. L. M. van Straaten, G. van Wezel-Meijler, S. J. Steggerda, J. Dudink, I. Isgum, A. Whitelaw, M. Benders, L. S. de Vries and E. s. group (2019). "Assessment of Brain Injury and Brain Volumes after Posthemorrhagic Ventricular Dilatation: A Nested Substudy of the Randomized Controlled ELVIS Trial." J Pediatr **208**: 191-197 e192.

10) Davies, M. W., M. Swaminathan, S. L. Chuang and F. R. Betheras (2000). "Reference ranges for the linear dimensions of the intracranial ventricles in preterm neonates." Arch Dis Child Fetal Neonatal Ed **82**(3): F218-223.

11) de Vries, L. S., F. Groenendaal, K. D. Liem, A. Heep, A. J. Brouwer, E. van 't Verlaat, I. Benavente-Fernandez, H. L. van Straaten, G. van Wezel-Meijler, B. J. Smit, P. Govaert, P. A. Woerdeman and A. Whitelaw (2019). "Treatment thresholds for intervention in posthaemorrhagic ventricular dilation: a randomised controlled trial." Arch Dis Child Fetal Neonatal Ed **104**(1): F70-f75.

12) de Vries, L. S., K. D. Liem, K. van Dijk, B. J. Smit, L. Sie, K. J. Rademaker, A. W.

Gavilanes and N. Dutch Working Group of Neonatal (2002). "Early versus late treatment of posthaemorrhagic ventricular dilatation: results of a retrospective study from five neonatal intensive care units in The Netherlands." Acta Paediatr **91**(2): 212-217.
13) De Vries, L. S., I. C. van Haastert, M. J. N. L. Benders and F. Groenendaal (2011). "Myth: Cerebral palsy cannot be predicted by neonatal brain imaging." Seminars in Fetal and Neonatal Medicine **16**(5): 279-287.
14) El-Dib, M., D. D. Limbrick, Jr., T. Inder, A. Whitelaw, A. V. Kulkarni, B. Warf, J. J. Volpe and L. S. de Vries (2020). "Management of Post-hemorrhagic Ventricular Dilatation in the Infant Born Preterm." J Pediatr.
15) Group, V. T. (1990). "Randomised trial of early tapping in neonatal posthaemorrhagic ventricular dilatation. Ventriculomegaly Trial Group." Arch Dis Child **65**(1 Spec No): 3-10.
16) Ingram, M. C., A. L. Huguenard, B. A. Miller and J. J. Chern (2014). "Poor correlation between head circumference and cranial ultrasound findings in premature infants with intraventricular hemorrhage." J Neurosurg Pediatr **14**(2): 184-189.
17) Kochan, M., J. McPadden, W. T. Bass, T. Shah, W. T. Brown, G. W. Tye and T. Vazifedan (2017). "Changes in Cerebral Oxygenation in Preterm Infants With Progressive Posthemorrhagic Ventricular Dilatation." Pediatr Neurol **73**: 57-63.
18) Kulkarni, A. V., J. Riva-Cambrin, C. J. Rozzelle, R. P. Naftel, J. S. Alvey, R. W. Reeder, R. Holubkov, S. R. Browd, D. D. Cochrane, D. D. Limbrick, T. D. Simon, M. Tamber, J. C. Wellons, W. E. Whitehead and J. R. W. Kestle (2018). "Endoscopic third ventriculostomy and choroid plexus cauterization in infant hydrocephalus: a prospective study by the Hydrocephalus Clinical Research Network." J Neurosurg Pediatr **21**(3): 214-223.
19) Kulkarni, A. V., S. J. Schiff, E. Mbabazi-Kabachelor, J. Mugamba, P. Ssenyonga, R. Donnelly, J. Levenbach, V. Monga, M. Peterson, M. MacDonald, V. Cherukuri and B. C. Warf (2017). "Endoscopic Treatment versus Shunting for Infant Hydrocephalus in Uganda." N Engl J Med **377**(25): 2456-2464.
20) Leijser, L. M., S. P. Miller, G. van Wezel-Meijler, A. J. Brouwer, J. Traubici, I. C. van Haastert, H. E. Whyte, F. Groenendaal, A. V. Kulkarni, K. S. Han, P. A. Woerdeman, P. T. Church, E. N. Kelly, H. L. M. van Straaten, L. G. Ly and L. S. de Vries (2018). "Posthemorrhagic ventricular dilatation in preterm infants: When best to intervene?" Neurology **90**(8): e698-e706.
21) Levene, M. I. and D. R. Starte (1981). "A longitudinal study of post-haemorrhagic ventricular dilatation in the newborn." Arch Dis Child **56**(12): 905-910.
22) Mazzola, C. A., A. F. Choudhri, K. I. Auguste, D. D. Limbrick, Jr., M. Rogido, L. Mitchell and A. M. Flannery (2014). "Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 2: Management of posthemorrhagic hydrocephalus in premature infants." J Neurosurg Pediatr **14 Suppl 1**: 8-23.
23) Murphy, B. P., T. E. Inder, V. Rooks, G. A. Taylor, N. J. Anderson, N. Mogridge, L. J. Horwood and J. J. Volpe (2002). "Posthaemorrhagic ventricular dilatation in the premature infant: Natural history and predictors of outcome." Archives of Disease in Childhood: Fetal and Neonatal Edition **87**(1): F37-F41.
24) Norooz, F., B. Urlesberger, V. Giordano, K. Klebermasz-Schrehof, M. Weninger, A. Berger and M. Olischar (2015). "Decompressing posthaemorrhagic ventricular dilatation significantly improves regional cerebral oxygen saturation in preterm infants." Acta Paediatr **104**(7): 663-669.

25) Riva-Cambrin, J., J. R. W. Kestle, C. J. Rozzelle, R. P. Naftel, J. S. Alvey, R. W. Reeder, R. Holubkov, S. R. Browd, D. D. Cochrane, D. D. Limbrick, C. N. Shannon, T. D. Simon, M. S. Tamber, J. C. Wellons, W. E. Whitehead and A. V. Kulkarni (2019). "Predictors of success for combined endoscopic third ventriculostomy and choroid plexus cauterization in a North American setting: a Hydrocephalus Clinical Research Network study." J Neurosurg Pediatr: 1-11.
26) Srinivasakumar, P., D. Limbrick, R. Munro, D. Mercer, R. Rao, T. Inder and A. Mathur (2013). "Posthemorrhagic ventricular dilatation-impact on early neurodevelopmental outcome." Am J Perinatol **30**(3): 207-214.
27) Stoll, B. J., N. I. Hansen, E. F. Bell, M. C. Walsh, W. A. Carlo, S. Shankaran, A. R. Laptook, P. J. Sanchez, K. P. Van Meurs, M. Wyckoff, A. Das, E. C. Hale, M. B. Ball, N. S. Newman, K. Schibler, B. B. Poindexter, K. A. Kennedy, C. M. Cotten, K. L. Watterberg, C. T. D'Angio, S. B. DeMauro, W. E. Truog, U. Devaskar and R. D. Higgins (2015). "Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993-2012." Jama **314**(10): 1039-1051.
28) Stone, S. S. and B. C. Warf (2014). "Combined endoscopic third ventriculostomy and choroid plexus cauterization as primary treatment for infant hydrocephalus: a prospective North American series." J Neurosurg Pediatr **14**(5): 439-446.
29) Taylor, G. A. and J. R. Madsen (1996). "Neonatal hydrocephalus: hemodynamic response to fontanelle compression-- correlation with intracranial pressure and need for shunt placement." Radiology **201**(3): 685-689.
30) Tubbs, R. S., J. T. Banks, S. Soleau, M. D. Smyth, J. C. Wellons, 3rd, J. P. Blount, P. A. Grabb and W. J. Oakes (2005). "Complications of ventriculosubgaleal shunts in infants and children." Childs Nerv Syst **21**(1): 48-51.
31) van Alfen-van der Velden, A. A., J. C. Hopman, J. H. Klaessens, T. Feuth, R. C. Sengers and K. D. Liem (2007). "Cerebral hemodynamics and oxygenation after serial CSF drainage in infants with PHVD." Brain Dev **29**(10): 623-629.
32) Wang, J. Y., A. G. Amin, G. I. Jallo and E. S. Ahn (2014). "Ventricular reservoir versus ventriculosubgaleal shunt for posthemorrhagic hydrocephalus in preterm infants: infection risks and ventriculoperitoneal shunt rate." J Neurosurg Pediatr **14**(5): 447-454.
33) Warf, B. C., J. W. Campbell and E. Riddle (2011). "Initial experience with combined endoscopic third ventriculostomy and choroid plexus cauterization for post-hemorrhagic hydrocephalus of prematurity: the importance of prepontine cistern status and the predictive value of FIESTA MRI imaging." Childs Nerv Syst **27**(7): 1063-1071.
34) Wellons, J. C., 3rd, C. N. Shannon, R. Holubkov, J. Riva-Cambrin, A. V. Kulkarni, D. D. Limbrick, Jr., W. Whitehead, S. Browd, C. Rozzelle, T. D. Simon, M. S. Tamber, W. J. Oakes, J. Drake, T. G. Luerssen and J. Kestle (2017). "Shunting outcomes in posthemorrhagic hydrocephalus: results of a Hydrocephalus Clinical Research Network prospective cohort study." J Neurosurg Pediatr **20**(1): 19-29.
35) Whitelaw, A. and R. Lee-Kelland (2017). "Repeated lumbar or ventricular punctures in newborns with intraventricular haemorrhage." Cochrane Database Syst Rev **4**: Cd000216.