





Clinical Practice Guideline: Head Ultrasound (HUS) Screening in Premature Infants

# Points of emphasis/Primary changes in practice:

- 1- Clear indications for HUS screening in asymptomatic premature infants
- 2- Identification of the timing and frequency of HUS screening
- 3- Expanding the measurements performed on HUS and providing recent reference values.

# Rationale for change:

Although HUS is routinely used in NICU, there has not been an updated guideline to minimize variability in practice.

**Questions?** Please contact: The Neurocritical Care Working Group



Clinical Guideline Name	Head Ultrasound (HUS) Screening in Premature Infants
Effective Date	September 19, 2016
Revised Date	
Contact Person	Medical Director, NICU
Approved By	Department of Pediatric Newborn Medicine Clinical Practice Council <u>09/08/16</u> CWN PPG <u>08/31/16</u> BWH SPP Steering <u>09/21/16</u> Nurse Executive Board/CNO <u>9/26/16</u>
Keywords	Head ultrasound- cranial ultrasound- IVH – PVL -PHVD

This is a clinical practice guideline. While the guideline is useful in approaching the use of HUS screening in premature infants, clinical judgment and / or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

#### Introduction

The incidence of Germinal Matrix- Intraventricular Hemorrhage (GM-IVH) in very low birth weight infants (< 1500 grams at birth) is about 25% with the incidence of the severest forms of IVH (grades III and IV) being approximately 5%. About 50% of infants with GM-IVH are "clinically silent" and show no abnormal signs indicative of the lesion. <sup>1-3</sup> About 30–50% of infants with a large IVH develop post-hemorrhagic ventricular dilatation (PHVD) and around 20–40% of infants with a severe GMH–IVH will consequently need a permanent ventriculoperitoneal shunt. <sup>4,5</sup> On the other hand, periventricular leukomalacia seems to be the most important determinant of neurologic morbidity seen in preterm infants who survive the neonatal period. Although the cystic form, with focal necrotic lesions, is usually associated with the development of cerebral palsy (CP) in infancy, the more diffuse form, which is not well visualized with cranial ultrasound, may relate to cognitive and behavioral problems. <sup>6</sup> Finally, in more recent years, cerebellar hemorrhage has been recently recognized as an important complication of extreme prematurity and is associated with increased morbidity and mortality. <sup>7,8</sup>

Head ultrasound via the cranial fontanels allows for rapid bedside evaluation of the neonatal brain. The standard views for HUS are the sagittal and coronal views through the anterior fontanel. In addition, the mastoid fontanel allows better visualization of the posterior fossa and brainstem <sup>9,10</sup>, while the posterior fontanel allows for better visualization of the trigone and occipital horn of the lateral ventricles as well as the posterior fossa. <sup>11</sup> Major abnormalities on HUS (including grade III to IV IVH, or cystic PVL) are predictive of cerebral palsy and neurodevelopmental impairments. <sup>12-19</sup>



# **Role of HUS screening in Premature Infants**

# 1- Germinal Matrix- Intraventricular Hemorrhage (GM-IVH)

The classic grading system of GM- IVH was initially described by Papile et al.<sup>20</sup> Findings were graded on a scale from I to IV. Periventricular hemorrhagic infarction is the term that substituted "grade IV IVH" as it represents a distinct pathological entity caused by obstruction of blood flow in the terminal veins leading to venous infarction and hemorrhage into the surrounding tissue.<sup>21,22</sup> The onset of GM-IVH on HUS is by the first day of life in at least 50% of affected infants, with up to 90% of lesions present by 72 hours <sup>23,24</sup> and all lesions visible by 7 days.<sup>12</sup> However, further *progression of an initial IVH* occurs in approximately 20% to 40% of the affected infants, with the maximal extent generally seen by 3 to 5 days after the initial diagnosis.<sup>25,26</sup>

### 2- Ventriculomegaly

Ventriculomegaly is detected by HUS with excellent sensitivity.<sup>27</sup> Levene described a ventricular index that is defined as the distance in millimeters between the midline and lateral border of the smaller lateral ventricle in the coronal plane at the level of the foramen of Monro. <sup>28</sup> Ventricular diameter > 4 mm above the 97th percentile is considered severe and has been used as an inclusion criterion for different studies as a marker of progressive ventricular dilatation requiring intervention. <sup>29-31</sup> An updated graph with more extremely immature infants from 23 weeks GA was recently published. <sup>32</sup> Davies et al. <sup>33</sup> proposed a more detailed methodology that includes measuring different distances including anterior horn width (AHW), thalamo-occipital distance (TOD), third ventricle width and fourth ventricle width and length. A newer reference range was also published in 2012. <sup>34</sup>

# 3- White Matter Injury (Periventricular Leukomalacia)(PVL)

White matter injury appears on HUS as increased periventricular echogenicity that may or may not develop into cysts. Cyst development (c-PVL) is often not detectable by HUS until 4 to 6 weeks following injury as coagulation necrosis and cellular loss evolve over time. It is to be noted that the incidence of c-PVL has declined significantly over the years. White matter injury is better identified and evaluated using MRI. Term equivalent MRI is indicated for premature infants at highest risk for brain injury. <sup>36</sup>



# 4- Cerebellar Hemorrhage

The sensitivity and specificity of HUS to detect cerebellar hemorrhage is variable because the cerebellum is echogenic and often difficult to distinguish from infarctions and hemorrhages. With careful attention to asymmetry in echogenicity and the use of mastoid or posterior fontanelle views, these lesions are more easily visualized.<sup>37,38</sup>

# **Imaging Protocols**

There is no universally accepted protocol for HUS screening in the preterm infant. The Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society states: "Routine screening cranial ultrasonography should be performed on all infants of 30 weeks' gestation once between 7 and 14 days of age and should be optimally repeated between 36 and 40 weeks' postmenstrual age". In Europe, HUS may be done more frequently. Some centers perform HUS as soon as possible after admission, at least once a week until discharge, and again at term equivalent during the first follow up visit. This variation in frequency and timing of imaging may affect the ability of HUS to detect abnormality and subsequently predict outcome.

### **Interpretation of Normal Head Ultrasound**

While head ultrasound is useful in detecting hemorrhage, ventricular dilatation and cystic changes, a "normal head ultrasound" does not exclude brain injury and does not imply normal outcome. In a report by NICHD, about one third of Extremely Low Birth Weight Infants with normal head ultrasounds had either significant mental developmental delay or cerebral palsy at the age of 18 to 22 months' corrected age. <sup>40</sup> This limitation should be acknowledged in documentation and in parents counselling.



The following guidelines were based on the consensus on the importance of HUS screening for premature infants at highest risk of brain injury. These guidelines are aimed at those with no clinical signs or symptoms. In presence of clinical signs or symptoms, suggestive of intracranial pathology, the clinician will request HUS regardless of screening criteria.

# 1. Purpose

To provide guidelines for Head Ultrasound (HUS) Screening in premature infants admitted to BWH NICU.

# 2. Indications of HUS screening:

- 1- Gestational Age < 32 weeks, or
- 2- Birth Weight < 1500 gm

# 3. Timing of Screening HUS:

# a- Less than 28 weeks GA

- 1- At 1 day of life
- 2- At 3 days of life
- 3- At 1 week of life
- 4- At 1 month of age
- 5- At 36 weeks' Postmenstrual age (if no term equivalent MRI completed)

#### b- From 28 weeks to less than 32 weeks GA

- 1- At 3 days of life
- 2- At 1 week of life
- 3- At 1 month of age
- 4- At 36 weeks' Postmenstrual age (if no term equivalent MRI completed)

### 4. Frequency of HUS if abnormal:

HUS will be repeated twice a week until abnormality is stable or resolving then routine US screening will be continued as scheduled.

However, in case of ventricular dilatation up to 3 HUS/week in the first 3 week of life will be considered.



#### 5. Technical Guidelines:

The following imaging protocol will be followed:

- Still and Video Clips Views:
  - Anterior fontanelle
    - Coronal
    - Sagittal
    - Parasagittal R and L
  - o Posterior fontanelle view
  - Mastoid view

#### 6. Measurements:

In case of presence of intraventricular hemorrhage (IVH) the following measurements will be completed and reported as measurement in mm:

- 1- Ventricular Index (VI) (R and L)
- 2- Anterior Horn Width (AHW) (R and L)
- 3- Thalamo-occipital Distance (TOD) (R and L)

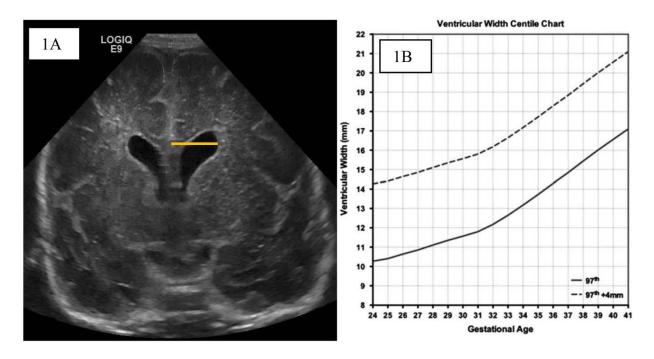
# 7. Appendix:

Summary of the Significance of Lateral Ventricles Measurement on Head Ultrasound



# Appendix 1: Ventricular Index (VI)

**Definition:** The distance in millimeters between the midline and the lateral border of the anterior horn of lateral ventricles. It is measured in the coronal view at the level of foramen of Monro. (Figure 1A)



#### Significance:

**Normative Values:** Normative values has been established in 1981 using cross-sectional data from infants from 27-42 weeks GA. An updated graph with more extremely immature infants from 23 weeks GA was recently published <sup>32</sup> (Figure 1B)

**Abnormal VI: VI > 4 mm above 97<sup>th</sup> percentile** was reported to be associated with about 50–60% being shunt dependent, over 60% disabled, and around 20% mortality. <sup>41</sup> For that reason, VI > 4 mm above 97<sup>th</sup> percentile was used as intervention criteria for many trials  $^{29,31,42}$ 

However, in a retrospective study, early intervention ( $VI > 97^{th}$  percentile) was associated with 16% need for VP shunt compared to 62% if late intervention (VI > 4 mm above  $97^{th}$  percentile) criteria was used <sup>43</sup>

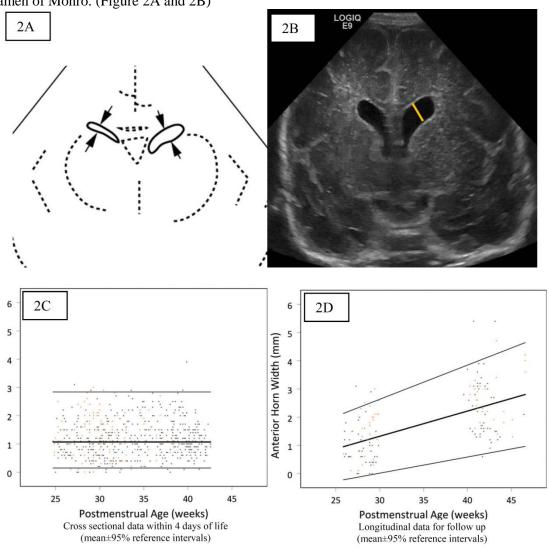
In the ongoing ELVIS (early versus late ventricular intervention study) study:

- Criteria for early intervention are: VI > p97 +AHW >6 mm and/or TOD >24mm
- Criteria for late intervention are: VI > p97 + 4mm and AHW > 10 mm



# Appendix 2: Anterior Horn Width (AHW)

**Definition:** The distance in millimeters between the medial wall and floor of the lateral ventricle. It is measured at the widest point of the anterior horn of the lateral ventricles, in the coronal view at the level of foramen of Monro. (Figure 2A and 2B) <sup>44</sup>



#### **Significance:**

Rounding "ballooning" of the frontal horns and an increase in AHW could be an early sign of increased ICP. While several authors reported no or just minimal change in AHW with GA, an evident increase in AHW was noted by others <sup>45</sup>

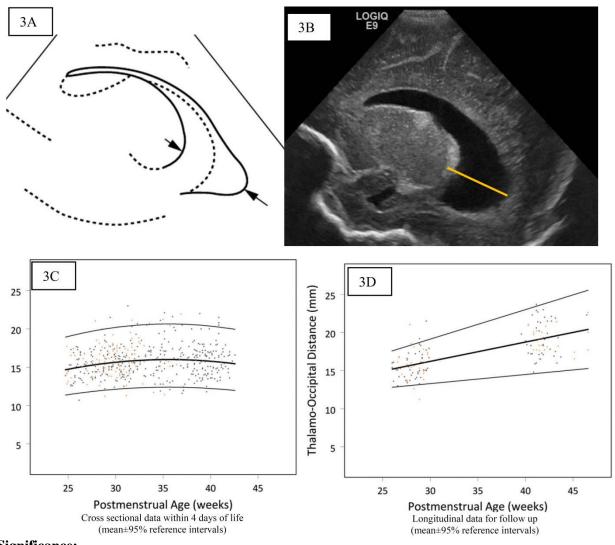
**Normative Values:** Figure 2C can be used in first HUS while figure 2D can be used for follow up.<sup>34</sup> **AWH of 5 or less is acceptable**. In the majority of neonates, the AHW is less than 3 mm. An AHW between 3 and 5 mm was not associated with neurodevelopmental impairment at a single follow up visit in a small group of 13 infants within the first year of life. <sup>46</sup>

**Abnormal AHW:** Values **exceeding 6 mm**, however, are associated with ventricular ballooning and might suggest the need for treatment.



# **Appendix 3: Thalamo-occipital Distance (TOD)**

**Definition:** is the distance in mm from the outermost point of the thalamus, at its junction with the choroid plexus, to the outermost part of the occipital horn posteriorly in the oblique parasagittal view. (Figure 3A and 3B) 44



# Significance:

Enlargement of Occipital horn is usually could be detected before is usually more significant than anterior horn dilatation. Sometimes, it may represent the only site of ventricular dilatation. Whether it is stable across GA has been controversial <sup>45</sup>

**Normative Values:** Figure 3C can be used in first HUS while figure 3D can be used for follow up.<sup>34</sup> According to Davies et al., the mean is  $16.7 \pm 4$  mm (Range 8.7-24.7) <sup>44</sup>

**Abnormal TOD:** Based on multiple references a value  $\geq$  25 mm is considered abnormal



#### **References:**

- 1. Dubowitz LM, Levene MI, Morante A, Palmer P, Dubowitz V. Neurologic signs in neonatal intraventricular hemorrhage: a correlation with real-time ultrasound. J Pediatr 1981;99(1):127-133
- 2. Lazzara A, Ahmann P, Dykes F, Brann AW, Jr., Schwartz J. Clinical predictability of intraventricular hemorrhage in preterm infants. Pediatrics 1980;65(1):30-34
- 3. Kadri H, Mawla AA, Kazah J. The incidence, timing, and predisposing factors of germinal matrix and intraventricular hemorrhage (GMH/IVH) in preterm neonates. Childs Nerv Syst 2006;22(9):1086-1090
- 4. de Vries LS, Brouwer AJ, Groenendaal F. Posthaemorrhagic ventricular dilatation: when should we intervene? Arch Dis Child Fetal Neonatal Ed 2013;98(4):F284-285
- 5. Adams-Chapman I, Hansen NI, Stoll BJ, Higgins R. Neurodevelopmental outcome of extremely low birth weight infants with posthemorrhagic hydrocephalus requiring shunt insertion. Pediatrics 2008;121(5):e1167-e1177
- 6. Volpe JJ. Neurobiology of periventricular leukomalacia in the premature infant. Pediatr Res 2001;50(5):553-562
- 7. Limperopoulos C, Benson CB, Bassan H, et al. Cerebellar hemorrhage in the preterm infant: Ultrasonographic findings and risk factors. Pediatrics 2005;116(3):717-724
- 8. Limperopoulos C, Bassan H, Gauvreau K, et al. Does cerebellar injury in premature infants contribute to the high prevalence of long-term cognitive, learning, and behavioral disability in survivors? Pediatrics 2007;120(3):584-593
- 9. Buckley KM, Taylor GA, Estroff JA, et al. Use of the mastoid fontanelle for improved sonographic visualization of the neonatal midbrain and posterior fossa. Am J Roentgenol 1997;168(4):1021-1025
- 10. Luna JA, Goldstein RB. Sonographic visualization of neonatal posterior fossa abnormalities through the posterolateral fontanelle. Am J Roentgenol 2000;174(2):561-567
- 11. Correa F, Enriquez G, Rossello J, et al. Posterior fontanelle sonography: an acoustic window into the neonatal brain. AJNR Am J Neuroradiol 2004;25(7):1274-1282
- 12. De Vries LS, Van Haastert ILC, Rademaker KJ, Koopman C, Groenendaal F. Ultrasound abnormalities preceding cerebral palsy in high-risk preterm infants. J Pediatr 2004;144(6):815-820
- 13. Vohr BR, Msall ME, Wilson D, et al. Spectrum of gross motor function in extremely low birth weight children with cerebral palsy at 18 months of age. Pediatrics 2005;116(1):123-129
- 14. Ancel PY, Livinec F, Larroque B, et al. Cerebral palsy among very preterm children in relation to gestational age and neonatal ultrasound abnormalities: the EPIPAGE cohort study. Pediatrics 2006;117(3):828-835
- 15. Wood NS, Costeloe K, Gibson AT, et al. The EPICure study: associations and antecedents of neurological and developmental disability at 30 months of age following extremely preterm birth. Arch Dis Child Fetal Neonatal Ed 2005;90(2):F134-140
- 16. Vohr BR, Wright LL, Poole WK, McDonald SA. Neurodevelopmental outcomes of extremely low birth weight infants <32 weeks' gestation between 1993 and 1998. Pediatrics 2005;116(3):635-643



- 17. Pinto-Martin JA, Whitaker AH, Feldman JF, Van Rossem R, Paneth N. Relation of cranial ultrasound abnormalities in low-birthweight infants to motor or cognitive performance at ages 2, 6, and 9 years. Dev Med Child Neurol 1999;41(12):826-833
- 18. Stewart A, Kirkbride V. Very preterm infants at fourteen years: relationship with neonatal ultrasound brain scans and neurodevelopmental status at one year. Acta Paediatr Suppl 1996;416:44-47
- 19. Taylor HG, Klein N, Drotar D, Schluchter M, Hack M. Consequences and risks of <1000-g birth weight for neuropsychological skills, achievement, and adaptive functioning. J Dev Behav Pediatr 2006;27(6):459-469
- 20. Papile L-A, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birth weights less than 1,500 gm. The Journal of Pediatrics 1978;92(4):529-534
- 21. Whitelaw A. Intraventricular haemorrhage and posthaemorrhagic hydrocephalus: pathogenesis, prevention and future interventions. Semin Neonatol 2001;6(2):135-146
- 22. Volpe JJ. Neurology of the newborn. 5th ed. Philadelphia: Saunders/Elsevier; 2008:xiv, 1094 p.
- 23. Paneth N, Pinto-Martin J, Gardiner J, et al. Incidence and timing of germinal matrix/intraventricular hemorrhage in low birth weight infants. Am J Epidemiol 1993;137(11):1167-1176
- 24. Perlman JM, Volpe JJ. Intraventricular hemorrhage in extremely small premature infants. Am J Dis Child 1986;140(11):1122-1124
- 25. Perlman JM, Volpe JJ. Cerebral blood flow velocity in relation to intraventricular hemorrhage in the premature newborn infant. J Pediatr 1982;100(6):956-959
- 26. Levene MI, de Vries L. Extension of neonatal intraventricular haemorrhage. Arch Dis Child 1984;59(7):631-636
- 27. Leijser LM, Srinivasan L, Rutherford MA, et al. Structural linear measurements in the newborn brain: accuracy of cranial ultrasound compared to MRI. Pediatr Radiol 2007;37(7):640-648
- 28. Levene MI. Measurement of the growth of the lateral ventricles in preterm infants with real-time ultrasound. Arch Dis Child 1981;56(12):900-904
- 29. Kennedy CR, Ayers S, Campbell MJ, et al. Randomized, controlled trial of acetazolamide and furosemide in posthemorrhagic ventricular dilation in infancy: follow-up at 1 year. Pediatrics 2001;108(3):597-607
- 30. Maertzdorf WJ, Vles JS, Beuls E, Mulder AL, Blanco CE. Intracranial pressure and cerebral blood flow velocity in preterm infants with posthaemorrhagic ventricular dilatation. Arch Dis Child Fetal Neonatal Ed 2002;87(3):F185-188
- 31. Whitelaw A, Pople I, Cherian S, Evans D, Thoresen M. Phase 1 trial of prevention of hydrocephalus after intraventricular hemorrhage in newborn infants by drainage, irrigation, and fibrinolytic therapy. Pediatrics 2003;111(4 Pt 1):759-765
- 32. Boyle M, Shim R, Gnanasekaran R, et al. Inclusion of extremes of prematurity in ventricular index centile charts. J Perinatol 2015;35(6):439-443
- 33. Davies MW, Swaminathan M, Chuang SL, Betheras FR. Reference ranges for the linear dimensions of the intracranial ventricles in preterm neonates. Arch Dis Child Fetal Neonatal Ed 2000;82(3):F218-223
- 34. Brouwer MJ, De Vries LS, Groenendaal F, et al. New reference values for the neonatal cerebral ventricles. Radiology 2012;262(1):224-233



- 35. Hamrick SE, Miller SP, Leonard C, et al. Trends in severe brain injury and neurodevelopmental outcome in premature newborn infants: the role of cystic periventricular leukomalacia. J Pediatr 2004;145(5):593-599
- 36. de Vries LS, Benders MJ, Groenendaal F. Progress in Neonatal Neurology with a Focus on Neuroimaging in the Preterm Infant. Neuropediatrics 2015;46(4):234-241
- 37. Limperopoulos C, Bassan H, Gauvreau K, et al. Does cerebellar injury in premature infants contribute to the high prevalence of long-term cognitive, learning, and behavioral disability in survivors? Pediatrics 2007;120(3):584-593
- 38. Merrill JD, Piecuch RE, Fell SC, Barkovich AJ, Goldstein RB. A new pattern of cerebellar hemorrhages in preterm infants. Pediatrics 1998;102(6):E62
- 39. Ment LR, Bada HS, Barnes P, et al. Practice parameter: neuroimaging of the neonate: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2002;58(12):1726-1738
- 40. Laptook AR, O'Shea TM, Shankaran S, Bhaskar B. Adverse neurodevelopmental outcomes among extremely low birth weight infants with a normal head ultrasound: prevalence and antecedents. Pediatrics 2005;115(3):673-680
- 41. Whitelaw A, Thoresen M, Pople I. Posthaemorrhagic ventricular dilatation. Arch Dis Child Fetal Neonatal Ed 2002;86(2):F72-74
- 42. International randomised controlled trial of acetazolamide and furosemide in posthaemorrhagic ventricular dilatation in infancy. International PHVD Drug Trial Group. Lancet 1998;352(9126):433-440
- 43. De Vries LS, Liem KD, Van Dijk K, et al. Early versus late treatment of posthaemorrhagic ventricular dilatation: Results of a retrospective study from five neonatal intensive care units in The Netherlands. Acta Paediatrica, International Journal of Paediatrics 2002;91(2):212-217
- 44. Davies MW, Swaminathan M, Chuang SL, Betheras FR. Reference ranges for the linear dimensions of the intracranial ventricles in preterm neonates. Archives of Disease in Childhood: Fetal and Neonatal Edition 2000;82(3):F218-F223
- 45. Brouwer MJ, De Vries LS, Pistorius L, et al. Ultrasound measurements of the lateral ventricles in neonates: Why, how and when? A systematic review. Acta Paediatrica, International Journal of Paediatrics 2010;99(9):1298-1306
- 46. Perry RN, Bowman ED, Murton LJ, Roy RN, de Crespigny LC. Ventricular size in newborn infants. J Ultrasound Med 1985;4(9):475-477