East of England Neonatal ODN
(Hosted by Cambridge University Hospitals)

EAST OF ENGLAND NEONATAL NEUROPROTECTION GUIDELINE
MANAGEMENT OF POST HAEMORRHAGIC VENTRICULAR DILATATION

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Guidance specific to the care of neonatal patients

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Key Words: PHVD (Post-Haemorrhagic Ventricular Dilatation), VAD (ventricular access device) SGVS (sub-galeal ventricular shunt), VI (ventricular index), AHW (Anterior Horn width), TOD (Thalamic occipital distance)

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MANAGEMENT OF POST HAEMORRHAGIC VENTRICULAR DILATATION

CONTENTS

Refer: i. Policy on Management of ventricular access devices in PHVD

1. INTRODUCTION

The major complication associated with intra-ventricular haemorrhage (IVH) in preterm infants is the development of post-haemorrhagic ventricular dilatation (PHVD), which is associated with poor neurodevelopmental outcome particularly in those requiring intervention[1].

- There is wide variation in diagnosis and management of PHVD among the units in UK[2].
- Measurement commonly used is Levene's ventricular index was established in 1981[3].
- Newer technology and resolution of Ultrasound, increased survival of premature infants and newer evidence on PHVD necessitates the need for revisiting the management of PHVD.

Thus appropriate management of PHVD based on evidence-based guidelines is important in order to prevent its progression and decrease its impact on neurodevelopmental outcome.

2. DEFINITION

i. Levene's Criteria for PHVD:

- PHVD is defined as ventricular index (VI) above 97th percentile on the Levene's chart. Ventricular index is defined as "the horizontal measurement from the midline falx to the lateral aspect of the anterior horn of the lateral ventricle in the coronal plane obtained at the level of the third ventricle/foramen of Monro"[3].

ii. New criteria use to define PHVD[4 -5] are:

- Anterior horn width (AHW)- diagonal width of anterior horn measured at its widest point in the coronal plane (Normal ≤ 6 mm).
- Thalamo-occipital distance (TOD) – distance between the outermost part of thalamus at its junction with choroid plexus and outer most part of the occipital horn in parasagittal plane (Normal ≤ 25 mm).

  (see flow chart for AHW and TOD measurement for intervention and Appendix 1 ventricular measurement risk zones)

3. MAGNITUDE OF PROBLEM

- The incidence of IVH reported in the literature varies from 15-30% in preterm infant <32 weeks.[6,7]
- The risk of developing PHVD is up to 12% in neonates with Grade 2 IVH and 80% in Grade 3 IVH based on Papile classification.[8-10]
- The incidence of high grade IVH[1] increases up to 50% with birth weight <750 grams[11].
- The incidence of PHVD requiring intervention is reported to be 25-50% in infants with Grade 3 IVH[12].
- Progressive PHVD is shown to be associated with a three to four-fold increase in neurodevelopmental delay [13- 15].
- 53% of neonates with Post-haemorrhagic parenchymal infarction will develop PHVD[16].

4. AETIOLOGY

Several mechanisms are thought to result in PHVD.

- Acute obstructive ventricular dilatation results from blockage of CSF drainage pathway by blood clot in the cerebral aqueduct or the 4th ventricle outlet (foramen of Luschka and Magendie)[17.]
- Literature suggests prolonged period of raised intra-ventricular pressure with periventricular oedema and persistent dilatation of the ventricle, results in mechanical compression of white and grey matter damaging neuronal pathways [18 19]. Also, an animal study has demonstrated early drainage of CSF in rats with induced hydrocephalus results in compensatory myelination before axonal injury and better cerebral perfusion and oxidative metabolism [20].
- One of the established mechanisms disproved by recent evidence includes the theory of arachnoid villi. Communicating ventricular dilatation after IVH is usually a gradual process and thought to occur due to blockage of arachnoid villi and arachnoid granulation by micro thrombi. It is also thought to result from inflammation and the commonest site of arachnoiditis is in posterior fossa[21]. This theory is not supported with robust data, as arachnoid granulation are not present in preterm infants, granulations are seen at term gestational [17].

- CSF absorption occurs mainly via deep venous drainage system, and lymphatic channels[21]. Therefore, ependymal and sub-ependymal damage results in destruction of ependymal cilia thereby affecting CSF flow and production[23].
- Alternation of blood brain and CSF barriers results in increased CSF proteins (i.e. Plasminogen activator inhibitor1, TGFβ1, TGFβ2, VEGF, cytokines), which results in osmotic gradient leading to ventricular inflammation and dilatation [24].
- Iron induced ependymal damage and up-regulation of aquaporin water channels have been thought to be responsible for post haemorrhagic ventricular dilatation[25].

5. SYMPTOMS AND SIGNS

The symptoms and signs of raised intracranial pressure develop several weeks following the onset of PHVD due to immature white matter and the large extradural space in pre-term brain. As the ventricular size increases considerably before affecting the anterior fontanelle pressure or the head circumference [26], it is therefore recommended to monitor PHVD with regular ventricular measurements (VI/AHW/TOD).

i. Recognition of raised intracranial pressure

- Bulging fontanelle
- Splaying of the cranial sutures
- Presence of apnoea/vomiting
- Decreased alertness/lethargy
- Hypotonia
- Hypertonia
- Poor feeding
- RI >0.85
- Increased discontinuity on EEG

ii. Guide on Monitoring of signs of raised intracranial pressure

- Twice weekly head circumference
  - Head circumference enlarges by approximately 1mm/day between 26-32 weeks of gestation, 0.7mm/day between 32 -40 weeks.
  - A measurement of >4mm over 2 days or 14mm over 7 days is excessive[27].
- Twice weekly head scans with RI and ventricular measurements.

- Weekly neurological assessment.
- Daily neuro-observations including HR, BP, level of alertness, vomiting, apnoeas.

6. PROGRESSION OF PHVD

- The natural progression of post haemorrhagic ventricular dilatation is determined by severity of intra-ventricular haemorrhage and the evolution of PHVD.
- With IVH grade 2 (Volpe's classification), slow progressive dilatation of ventricles usually occurs after 14 days whereas with grade 3 IVH ventricles will dilate more rapidly, within days[13]. (See Figure 1).

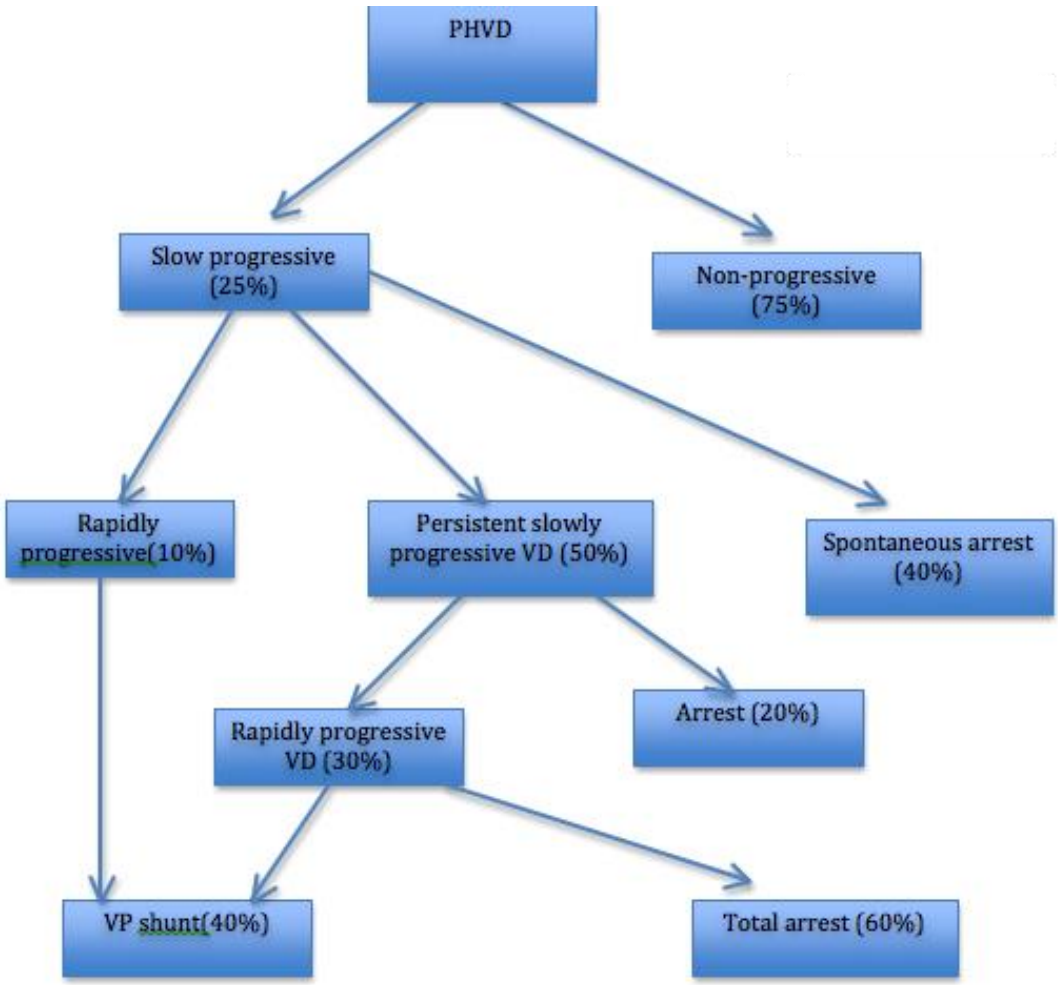


Figure 1: Outcome of infant with PHVD
Source: Adapted from Newborn Neurology (Volpe, 2008)

7. DIAGNOSIS AND MONITORING OF PHVD

7.1 Diagnosis using Levene's Ventricular Index

- To diagnose PHVD and evaluate the need for intervention, measurement of ventricular size by means of cranial ultrasonography (cuss) has been shown to be superior to measurement of head circumference or assessment of clinical symptoms of raised intracranial pressure[28 29].
- The ventricular measurement helps in diagnosis, timing of therapeutic intervention and predicting neurodevelopmental outcome [30]
- PHVD is defined as ventricular index above the 97th percentile for GA on Levene's chart[3].
- Currently, across the units in our network and in majority of centres in UK and Europe, VI is the established criterion for diagnosis of PHVD[2].
- Limitations of Levene's Index:
    a. VI increases only in severe hydrocephalus and may fail to identify PHVD with mild dilatation.
    b. In Levene's study preterm infants younger than 26 weeks gestational age were not included[3,4].

7.2 Newer ventricular measurements for PHVD (Appendix 1)

The newer ventricular measurements are AHW, TOD and others. The new references for AHW and TOD ventricular measurement have been reported for 25 to 42 weeks gestational age by Brouwer et al, 2012[4 5].

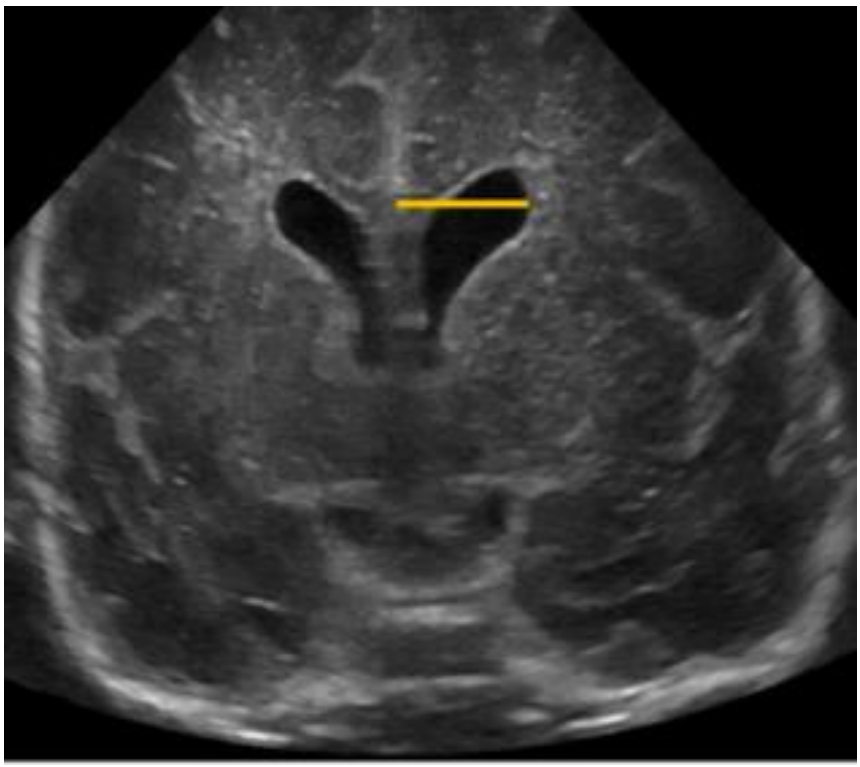


Figure 2: Ventricular index (yellow horizontal line)
Source: Brower et al 2012

7.2.1 AHW:

- Anterior horn width is defined as diagonal width of anterior horn measured at its widest point in the coronal plane.

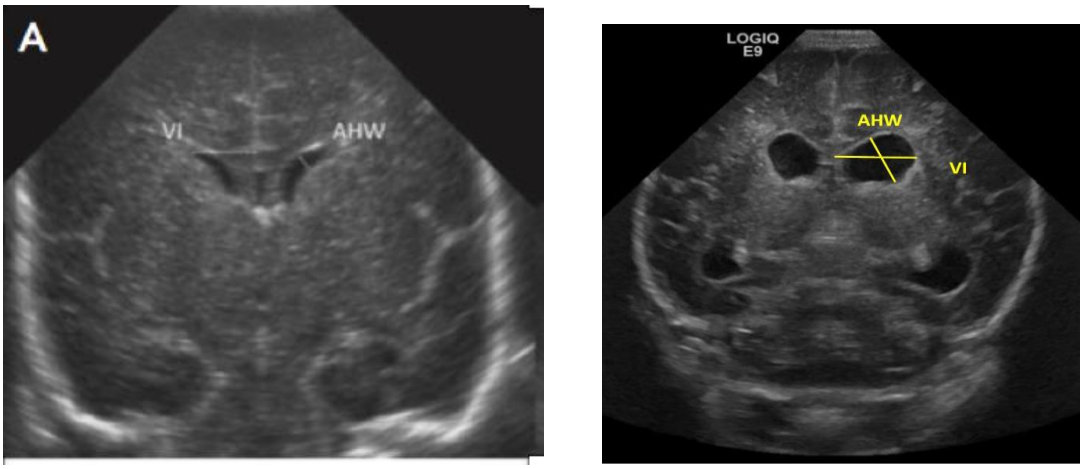


Figure 3: A) Anterior horn width (AHW)

Source: Brower et al, 2012, El-Dib M,2020

- The early sign of increase intracranial pressure is rounding of anterior horn width and hence AHW has been suggested as sensitive ventricular measurement for early ventricular enlargement than VI [30 31].
- Majority of studies have shown AHW remains constant with GA[4], except Sondhi et al[31].

7.2.2 Thalamo-occipital distance (TOD)

- TOD is defined as distance between the outermost part of thalamus at its junction with choroid plexus and outer most part of the occipital horn in parasagittal plane[4].
- Thalamo-Occipital Distance varies with gestational age and measurement of TOD can be challenging but evaluation of TOD is of clinical value.
- TOD may show earliest and fastest increase in size in PHVD. Brouwer et al. study (2012) reported 97th percentile TOD measurement of 19 mm for preterm and 21mm for term infants[4 5] suggests PHVD. El-Dib M et al, (2020)in their study has define ventricular measure risk zone for individual gestational age (see Appendix 1).

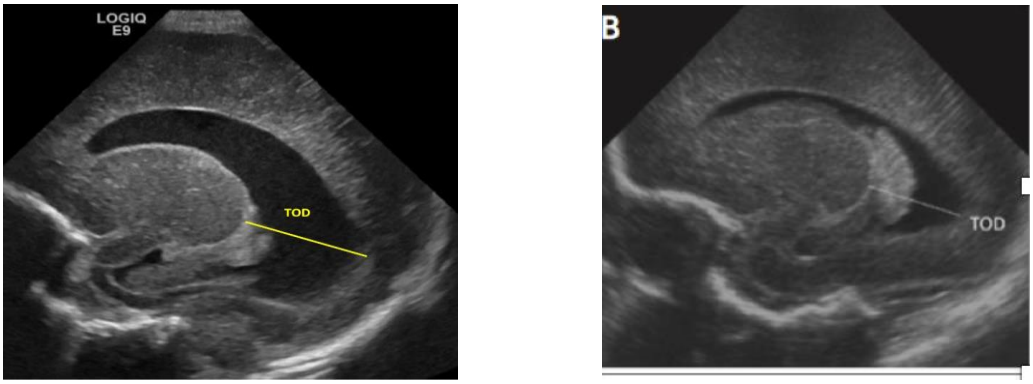


Fig 4: B) Thalamo-occipital distance (TOD)

Source: Brower et al, 2012, El-Dib M,2020

7.3 Others

- The clinical value of third and fourth ventricle is unclear, but the measurement of 3rd & 4th ventricles when combined with lateral ventricular diameters can provide underlying etiology of ventricular dilatation[30].

- Blood and CSF biomarkers are being investigated with respect to diagnosis, efficacy of treatment and prediction of neurodevelopmental outcomes.
- CSF levels of biomarkers, amyloid precursor protein (APP), soluble APPα and L1 adhesion molecule (L1CAM), are significantly and specifically increased with untreated PHVD and return to normal after intervention[33].
- In future CSF biomarker may have significant role in monitoring PHVD progression and it's treatment.
- Other investigations i.e. Resistance Index (RI), visual evoked potentials, amplitude integrated EEG, and near-infrared spectroscopy (NIRS) may help in optimising timing of intervention in PHVD [18].
- RI of 0.85 suggests increased intracranial pressure and indicates impaired perfusion[2]. RI returns to normal after adequate CSF drainage.

8. TREATMENT

Infants with PHVD who requires permanent shunt are at significant risk of developing cerebral palsy and cognitive impairment [7,34]. Large multicentre observational study showed in late intervention group who required shunt had lower cognitive (p=0.002) and motor scores (p=0.03)[35]. The hypothesis for the abnormal neurodevelopmental outcome in these infants, is due to permanent white matter injury resulting from severe and prolonged dilatation of ventricles. [35]

8.1. Treatment Modalities

8.1.1. Non- surgical management (refer flow chart management of PHVD)

- If the infant is showing excessive head growth and VI is above the 97+4th centile or is symptomatic it is recommended to perform therapeutic LP. Serial tapping of CSF by lumbar puncture is commonly used as a temporary measure to reduce intracranial pressure. (2-3times/week)
- Minimum of 10ml/kg of CSF is needed to be removed in order to have a significant effect on ventricular size. It is however wise to limit the volume of CSF removed to a maximum of 20ml/kg as larger volumes removed faster than 1ml/kg/min may be followed by apnoeas, bradycardia and desaturation.

- Ventricular tapping has been associated with increased development of CSF infection and loculated hydrocephalus[36].
- In those cases where repeated lumbar puncture is necessary to control excessive head enlargement and raised intracranial pressure is suspected, referral should be made to the Neurosurgical team for insertion of a temporising shunt.
- Cochrane review concluded that lumbar puncture treatment failed to reduce disability or need for the VP shunt surgery[38].
- Pharmacological treatment with diuretics in PHVD has shown no difference in mortality or need of VP shunt but has been associated with poor neurodevelopmental outcome[36].
- Short-term outcome of randomised trial of Drainage, Irrigation and Fibrinolytic Therapy (DRIFT) for Premature Infants with Post-haemorrhagic Ventricular Dilatation was associated with secondary haemorrhage and high mortality/ severe disability [36].
- Long-term outcome of DRIFT study showed decrease in severe cognitive disability from 59% to 33%. Overall 48% were not able to walk and 20% were unable to communicate[39].
- Sensorimotor disabilities were noted to be less in DRIFT group but were not statistically significant [39].

8.1.2. Surgical Management

8.1.2 a. Temporary interventions

1. **External ventricular drainage (EVD)**

   A Catheter is introduced into frontal horn of lateral ventricle and distal end is connected to externalised closed drainage system, which is at height to control CSF drainage (10-20ml/kg/day). This drainage system is able to resolve PHVD in 30-40% of cases[41]. A recent study has concluded that placement of an EVD within the first 25 days may improve cognitive function in infants with PHVD [42]

2. **Ventricular access devices (reservoir)**

   A ventricular catheter is connected to an access device (reservoir) in the subcutaneous area, which can be used to aspirate 10-20 ml/kg /day of CSF to decrease intracranial

pressure. This device can resolve PHVD in 30% of cases, which is marginally less than EVD. It is also associated with infections, skin defect and CSF leaks[42 44].

3. **Ventriculo-subgaleal shunts (VSGS)**

   VSGS is a continuous CSF drainage system, which drains CSF into the subgaleal space. It can include a subgaleal reservoir that can be used to tap in case of VSGS failure. Infection rate with VSGS reported varies with the centres and ranges between 5-15%[41].

   Recent studies have shown no significant difference in neurodevelopmental outcome and infection rate, shunt implantation or revision between VAD and VSGS [12 44].

4. **Endoscopic third ventriculostomy**

   This procedure has been used in cases with VAD failure[40].

8.1.2 b. Permanent Intervention

The permanent surgical procedure includes ventriculo-peritoneal shunt.

Referral for a permanent VP shunt

- VP shunting should not be carried our as the primary treatment when progressive PHVD is diagnosed.
- Approximately 50% of infants diagnosed with PHVD do not need a permanent shunt.
- Permanent shunt surgery is usually done around term in an infant who has had a reservoir and is needing repeated taps to maintain head growth or if there is persistent excessive head enlargement.

8.2. Recent evidence on Early vs. Late intervention

- Studies with NIRS and Doppler ultrasound techniques have shown improved cerebral perfusion, and oxygenation following early intervention with CSF drainage [45].
- Retrospective and multicentre observational studies have shown early intervention (VI >97mm) of PHVD results in better neurodevelopmental outcome compare to late intervention (VI>97+4mm or symptomatic infants) [14,44,45]
  - For example, in de Vries study [46], CP was observed in 15% of infants with early intervention whereas it was 26% in infants treated with late intervention.

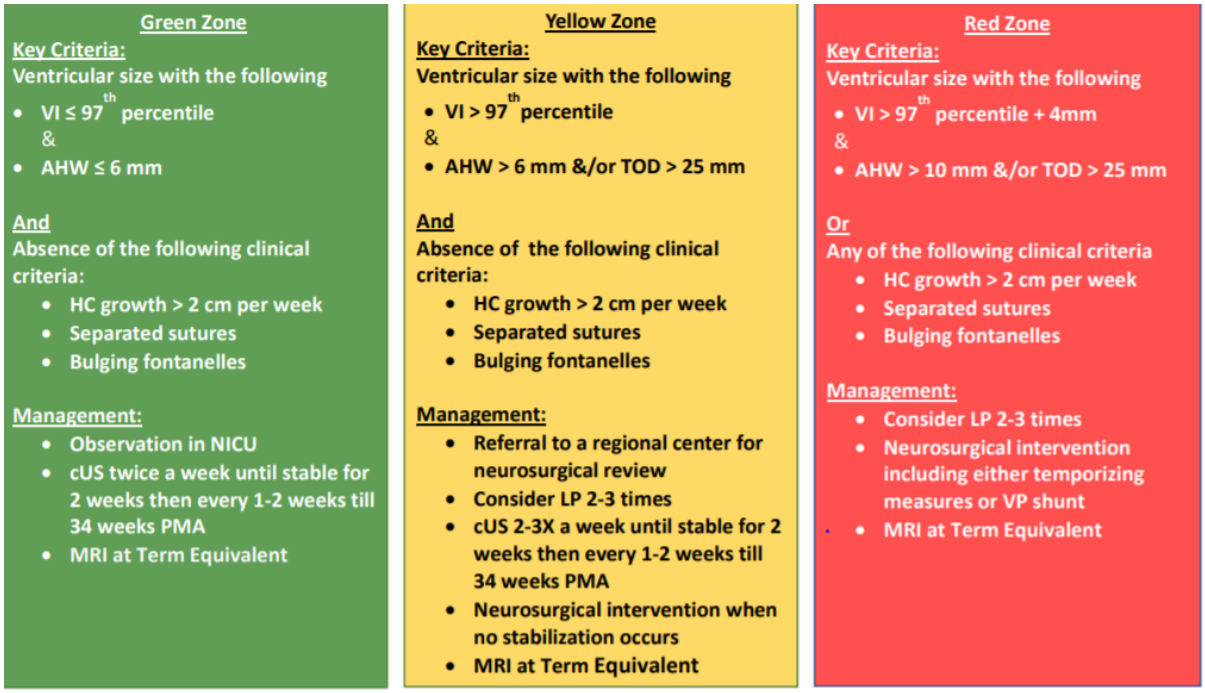
- Brouwer study[18] showed delayed cognitive outcome was only 5.4% in early intervention, and was as high as 30% in late intervention (P=0.02).

- The neurodevelopmental outcome results of ELVIS study are awaited, though this study showed no difference in primary outcome of VP shunt placement in infants with PHVD in early or late intervention group [35].

8.3 Referral to Neurosurgical Team at Addenbrooke's Hospital

The ventricular indices persistently remains >97+4 mm and AHW >5 mm, TOD>26 mm (see flow chart), infant should be referred to Neurosurgical Team at Addenbrooke's Hospital. All the referral should be made on the link, http://www.orioncloud.org. The Neurosurgical team would contact the referral unit on the same day with the advice on further management plan.

9. FLOW CHART: Management of PHVD[5]



(adapted from El-Dib M, Limbrick Jr. DD, Inder T, Whitelaw A, Kulkarni AV, Warf B, Volpe JJ, de Vries LS, Management of Post-hemorrhagic Ventricular Dilatation in the Preterm Infant The Journal of Pediatrics (2020), doi: https://doi.org/10.1016/j.jpeds.2020.07.079)

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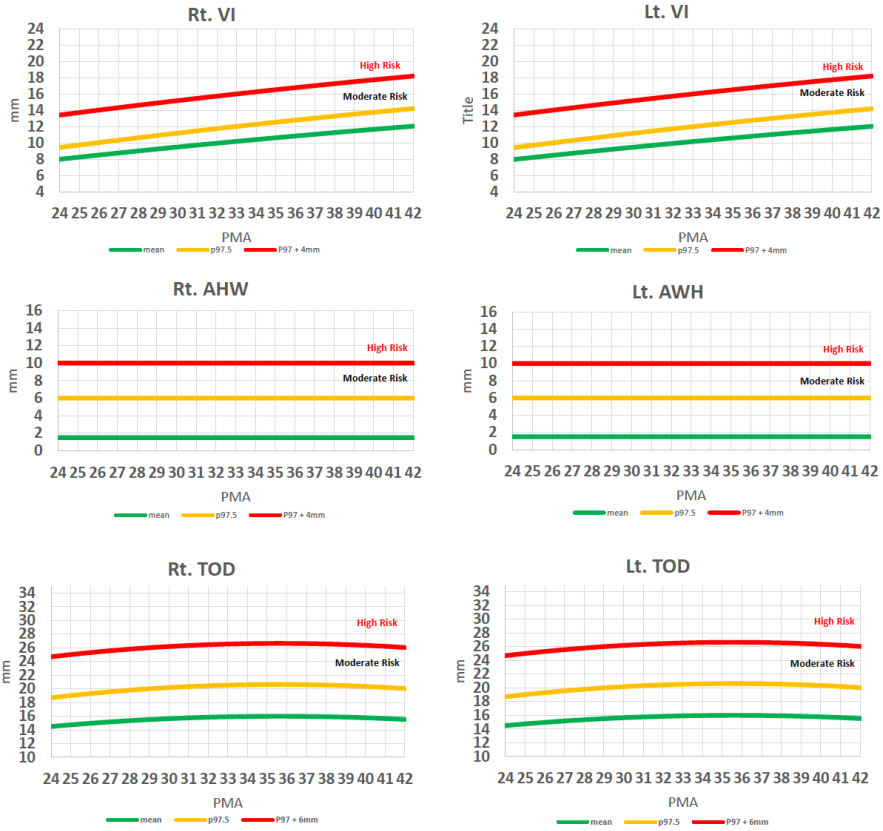
APPENDIX 1[5]

Name:
DOB:

Ventricular Measurement Risk Zones



Date	PMA	Rt. TOD	Rt. VI	Rt. AHW	Lt. TOD	Lt. VI	Lt. AHW

(ref: El-Dib M, Limbrick Jr. et al,Management of Post-hemorrhagic Ventricular Dilatation in the Preterm Infant The Journal of Pediatrics (2020), doi: https://doi.org/10.1016/j.jpeds.2020.07.079)