PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES

Bundle for Prevention of Intraventricular Hemorrhage in the Neonatal Intensive Care Unit



Clinical Practice Guideline: Bundle for Prevention of Intraventricular Hemorrhage in the Neonatal Intensive Care Unit

Points of emphasis/Primary changes in practice:

- Germinal Matrix /Intraventricular Hemorrhage (GM-IVH) continues to be a significant problem affecting extremely preterm infants and is associated with increased mortality and worse neurodevelopmental outcome.
- Applying bundles of care has been associated with reduction of risk of IVH in extremely preterm infants.
- A bundle of care requires consistent workflows which include the following prenatal, delivery room and postnatal measures:
    - Antenatal Steroids
    - Delayed Cord Clamping
    - Optimizing peripartum delivery management (Golden Hour)
    - NIRS monitoring
    - Handling and head positioning
    - Hemodynamic stability
    - Optimizing respiratory support
    - Avoiding hypernatremia
    - Pain control and optimizing sedation

Rationale for change:

- While most of the guidelines and recommendations in this protocol have been published elsewhere in DPNM CPGs, there is an unmet need to summarize and emphasize the bundle of care aimed at reducing GM-IVH in extremely preterm infants.
- Prophylactic indomethacin will no longer be used for prevention of GM-IVH due to controversial potential efficacy and high risk of complications.

Questions? Please contact Director of Neonatal Neurocritical Care

Clinical Guideline Name	**Bundle for Prevention of Intraventricular Hemorrhage in the Neonatal Intensive Care Unit**
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This is a clinical practice guideline. While the guideline is useful in approaching the prevention of intraventricular hemorrhage in neonates in the newborn intensive care unit, 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

The purpose of this clinical practice guideline is to address the prevention of Germinal Matrix-Intraventricular hemorrhage (GM-IVH) in the NICU. The scope of this guideline includes the following aspects of medical management:

1. Antenatal Steroids
2. Delayed Cord Clamping
3. Optimizing peripartum delivery management (Golden Hour)
4. NIRS
5. Handling and positioning
6. Hemodynamic stability
7. Optimizing respiratory support
8. Avoiding hypernatremia
9. Pain control and optimizing sedation

In each of these interventions we will provide:

- Background: which summarizes the rationale and current evidence of the intervention
- Guidelines: which summarizes current BWH guidelines supporting the intervention
- Recommendations: which summarizes consensus opinion based on current evidence in absence of definite BWH guidelines

II. All CPGs will rely on the NICU Nursing Standards of Care.

All relevant nursing PPGs are listed below:

NICU/SCN B.1 Arterial and Venous Blood Drawing

NICU N.1 Neutral Head Positioning Guidelines

WNH M.3 Administration of Magnesium Sulfate for Obstetrical Patients in the Center for Women and Newborns

WNH S.1 Skin to Skin Care
NICU S.2 Endotracheal Tube Suctioning
WNH T.5 Administration of Tocolytics for the Treatment of Preterm Labor

Relevant Ob Medical Staff Notes and DPNM CPGs:
Use of Magnesium Sulphate for Neuroprotection from Cerebral Palsy
Optimal Cord Clamping Protocol
Optimal Umbilical Cord Clamping CPG
Care of the Extremely Low Birth Weight (ELBW) Infant: The Golden Hour
Head Ultrasound (HUS) Screening in Premature Infants
Clinical NIRS in the NICU
Premedication for Nonemergent Endotracheal Intubations in the Neonate
Early Management of Respiratory Distress Among Infants Born Before 37 Weeks of Gestation
Neonatal ICU Blood Gas Guideline
Prevention and Management of Bronchopulmonary Dysplasia (BPD) (In Press)

III. Background on Incidence, Pathogenesis and Outcomes of GM-IVH Grading

GM-IVH is classified as:

- GMH (Grade I): Bleeding confined to periventricular area (germinal matrix).
- Grade II: Intraventricular bleeding (10-50% of ventricular area on sagittal view).
- Grade III: Intraventricular bleeding (> 50% of ventricular area or distends the ventricle).
- Periventricular Hemorrhagic Infarction (PVHI) AKA Grade IV: Intra-parenchymal hyerechoic echodensity represents periventricular hemorrhagic infarction.

Severe IVH is terminology used to describe Grade III IVH or PVHI.

Cerebellar hemorrhage is common in the most immature/sickest infants. They may vary in size and small lesions are difficult to identify on ultrasound. Larger hemorrhage is associated with motor, cognitive, language, autism and behavioral abnormalities.

Incidence:
The incidence of germinal matrix hemorrhage in Very Low Birth Weight Infants (VLBW) is 25%, with severe forms occurring in 5%.[1]
Risk of IVH is highest in the most premature of infants and the incidence of severe IVH is greatest at lower gestational age (GA). Data from NICHD, which focused on neonates 22-28 weeks GA, shows an overall incidence of severe IVH in 1386/ 9705 (14.3%). The incidence increases as GA decreases, as shown in **Table 1.** [2]

Table 1: Incidence of Severe IVH according to GA

GA	Incidence of severe IVH (2012-2018)
22	52/136 (38%)
23	289/819 (36%)
24	308/1251 (25%)
25	260/1500 (17%)
26	202/1752 (12%)
27	143/1905 (8%)
28	123/2342 (5%)

Pathogenesis:

The site of origin of IVH characteristically is the *subependymal germinal matrix.* This cellular region immediately ventrolateral to the lateral ventricle serves as the source of cerebral excitatory neuronal precursors between approximately 10 to 20 weeks of gestation. In the second half of gestation, it provides neuroglial precursors that become cerebral oligodendroglia and astrocytes and late migrating GABAergic neurons destined for the cerebral cortex and, especially, the thalamus.

The pathogenesis of IVH is considered best in terms of intravascular, vascular, and extravascular factors. Clearly, the pathogenesis of IVH is multifactorial, and to some extent different combinations of these factors are operative in different patients.[1].

Intravascular Factors:

Fluctuating cerebral blood flow

Ventilated preterm infant with respiratory distress syndrome

Increase in cerebral blood flow

Systemic hypertension: importance of pressure-passive circulation
Rapid volume expansion
Hypercarbia
Decreased hematocrit
Decreased blood glucose

Increase in cerebral venous pressure

Venous anatomy: U-turn in direction of venous flow
Labor and vaginal delivery
Respiratory disturbances

Decrease in cerebral blood flow (followed by reperfusion)

Systemic hypotension: importance of pressure-passive circulation

Platelet and coagulation disturbance

Vascular Factors:

Tenuous capillary integrity and vulnerability of capillaries to hypoxic-ischemic injury

Extravascular Factors:

Excessive fibrinolytic activity

Outcomes:

The incidence of major neurological sequelae (spastic hemiparesis or quadriparesis, dystonia, cognitive deficits) after minor degrees of hemorrhage is slightly higher than in infants without hemorrhage. This increases to approximately 50% in infants with severe hemorrhage and a *clearly higher* incidence occurs in infants with IVH complicated by periventricular hemorrhagic infarction or cystic periventricular leukomalacia, or both. *Prognostic estimates* can thus be refined considerably by assessment of the presence and the degree of parenchymal injury by detailed imaging. It is highly likely that such estimates could also be considerably improved by more sophisticated understanding of the full impact of GMH-IVH on subsequent cerebral development. An estimation of incidence of adverse outcome is summarized in Table 2. [1]

Table 2: Incidence of Neurological Sequela following GM-IVH as a function of severity of hemorrhage:

Severity of hemorrhage	Incidence of definite neurological sequelae
Grade I	15%
Grade II	25%
Grade III	50%
Grade III and apparent periventricular hemorrhagic infarction	75%

The first 72 hours post birth ("the critical window") is the highest risk period for acute preterm brain injury and 90% of IVH occurs within this time frame. [1] Careful perinatal management of these infants has the potential to prevent brain injury and improve outcomes.

IV- Measures taken to help with prevention of IVH

1. **Antepartum Management:**
   a) **Antenatal Steroids**

Background:

Corticosteroids accelerate organ system maturity in animal models. The timing of the last dose of corticosteroid before delivery is important, as risk of IVH is significantly reduced

when the interval since the last dose is greater than 48 hours, compared with less than 24 hours. [3]

The most recent Cochrane review concluded that antenatal corticosteroids probably reduce the risk of IVH (RR 0.58, 95% CI 0.45 to 0.75; 8475 infants) and lead to a reduction in developmental delay in childhood (RR 0.51, 95% CI 0.27 to 0.97; 600 children). [4]

Data supports the use of antenatal steroids as low as 22 weeks GA as it is associated with both improved survival and improved survival without major morbidity.[5]

Guidelines:
Antenatal steroids are administered to pregnant women at 23-34 weeks gestation with increased risk of preterm delivery within the next 7 days.

Recommendations:
If active resuscitation is planned for an infant at 22 weeks GA, antenatal betamethasone should be considered after discussion with the obstetrician and the patient.

Relevant DAG:
Betamethasone DAG

b) Tocolytics

Guidelines:
Use of tocolytics should be encouraged by obstetricians to allow for at least a 24-hour period after the second dose of Betamethasone.

Relevant CPG:
WNH T.5 Administration of Tocolytics for the Treatment of Preterm Labor

c) Antenatal Magnesium Sulphate:

Background:
Although antenatal magnesium is not associated with reduced IVH, it has been shown to improve neurodevelopmental outcomes. Magnesium has several intracellular actions, including anti-inflammatory effects and inhibition of the influx of calcium into cells. Both a Cochrane review [6] and a meta-analysis of five randomized control trials (RCTs) [7] demonstrated that magnesium sulphate effectively decreased the risk of CP (RR 0.69, 95% CI 0.55 to 0.88) and the composite outcomes of death or cerebral palsy (RR 0.86, 95% CI 0.75 to 0.99). The ACOG recommends that hospitals that elect to use magnesium sulfate should develop specific guidelines for their departments regarding inclusion criteria,

treatment regimens, concurrent tocolysis, and monitoring in accordance with one of the larger trials.[8]

Guidelines:

- IV Magnesium Sulphate is indicated for those expected to deliver between 24-32 GA, and anticipated to deliver within 4 hours, if not contraindicated.
- If delivery has not occurred within 24 hours following initiation of preventative treatment, Magnesium Sulphate infusion should be discontinued, unless delivery is now anticipated within 4 hours.
- If preterm birth is again threatened after an interval of 6 hours since discontinuing Magnesium Sulfate for neuroprotection, re-treatment is recommended.

Relevant CPG:
Use of Magnesium Sulphate for Neuroprotection from Cerebral Palsy

d) Transport:

Background
Transport of preterm infants following birth may be a risk factor for IVH, brain injury and mortality.[9, 10] This risk appears to be independent of mode of transport, distance travelled and the experience of the transporting team.[11] Possible causes for this include noise, vibration and acceleration during travel.[12]

Recommendations:
In utero transport of high-risk pregnancies to a tertiary care center with a higher level NICU is preferable over the transport of critically ill neonates, especially in the first few days after birth.

2. Intrapartum Interventions:

a) Mode of delivery:

Background:

There is no evidence to suggest that routine caesarean section confers protective benefit over vaginal delivery for preterm infants at risk for mortality or IVH, including intraparenchymal lesions [13, 14] except when they are in a breech position. [15, 16] Prolonged labor, however is associated with increased rates of IVH. [17]

Recommendations:
Ideally the decision on mode of delivery would be based on a multidisciplinary discussion between the laboring mother, her obstetrical team and the neonatology team.

b) Delayed Cord Clamping

Background:
Delayed cord clamping allows blood flow between the placenta, umbilical cord and baby to continue, and may aid in transition. The most recent Cochrane review which included 25 studies, and 3100 babies and their mothers found that delayed cord clamping reduces the number of babies who die before discharge (aRR 0.73, 95% CI 0.54 to 0.98), reduces the number of babies with any grade IVH (aRR 0.83, 95% CI 0.7 to 0.99), but no difference in the number of babies with severe IVH (aRR 0.94, 95% CI 0.63 to 1.39). [18]

On the other hand, umbilical cord milking, in extreme preterm infants (<28 weeks), appears to be associated with an increased frequency of severe IVH. [19]

Guidelines:
All neonates will receive 60 seconds of delayed cord clamping following birth unless contraindicated. Contraindications include:

- Monochorionic multiple gestations
- Maternal hemoglobin <7 gms/dl (in case delay affects efficiency of treatment of post-partum hemorrhage)
- Placental abnormalities, including but not limited to vasa previa, placenta previa, accreta and abruption.
- Need for resuscitation beyond drying, warmth and stimulation

Relevant CPG:
Optimal Cord Clamping Protocol
Optimal Umbilical Cord Clamping CPG

3. Postnatal Interventions:

a) Optimizing peripartum delivery management (Golden Hour)

Background:
Stress can accelerate oxygen consumption and impair resuscitation, and hypothermia might be associated with increased risk for acute brain injury and death.[20] Measures to reduce hypothermia include using polyethylene wrapping or bag to keep babies warm, regulating the temperature in the delivery room at 25°C to 26°C, using a preheated servo-controlled radiant warmer with a temperature sensor, providing a thermal mattress, putting a hat on the infant, and providing a preheated transport incubator. [21, 22]
Although numerous measures have been proposed to reduce hypothermia, these measures have not necessarily been proven to reduce death or prevent major morbidities (except pulmonary hemorrhage).[21] Although prevention of hypothermia seems prudent [23], avoiding hyperthermia is equally important as it too may be associated with increased mortality. [24]

Guidelines:

The Golden Hour clinical practice guideline was developed to standardize the preparation for and initial care of the extremely premature and low birthweight infant (ELBW), especially those < 28 weeks or EFW < 1000g. **Please refer to the CPG for specifics**.

- Steps prior to delivery should include: Prenatal consult, Pre-delivery team huddle, and setting up a Giraffe Omnibed in the delivery room for infant to be resuscitated on.
- Delivery and NICU admission rooms should be set to 77°F, chemical warming mattress should be placed on Omnibed and hooded polyethylene bag should be available to place infant in at time of delivery and on transport. The chemical warming mattress retains heat for 2 hours and should accompany infant on transport and upon admission.
- Pulse oximeter probe and EKG limb leads will be applied while securing infant in hooded polyethylene bag.
- Provide initial respiratory care using current relevant CPG
- Weigh in DR x 2 to confirm weight□weigh in hooded polyethylene bag and account for weight of bag (hooded bag weighs 30 grams).
- Voalte message to be sent to admitting team with weight and details of respiratory support. Admitting team will notify Pharmacy and x-ray (Call radiology at 27185 rather than page) of impending ELBW admission. Goal is to be out of delivery room by 15 minutes of life.
- Admission takes precedence over rounds □admitting Fellow oversees Golden Hour. If admitting multiples, admitting Attending responsible for 2nd baby. For higher order multiples, clear plan for well-staffed team to be made prior to delivery.
- Admitting RN will prepare IVF for PIV and UVC line placement, RT will be prepared for surfactant administration if intubated.
- If infant is intubated, x-ray should be waiting in the NICU for immediate chest x-ray to confirm ETT placement prior to surfactant administration.
- PIV placement by RN while Fellow is setting up for Umbilical lines. Umbilical line placement should be initiated as soon as possible while infant remains in polyethylene bag. Draw bloodwork from line as ordered and x-ray to confirm placement. Line is to be secured and sterile fluids attached to line(s).
- Goal timeline for Omnibed closure is 60 minutes of life.

Relevant CPG
Care of the Extremely Low Birthweight (ELBW) Infant: The Golden Hour

b) Near Infra-Red Spectroscopy (NIRS)

Background:
Multiple studies have reported increased NIRS cerebral regional saturation ($crSO_2$) in the first hours of life in premature infants who later developed GM-IVH.[25-27] However, patients already identified with IVH are noted to have lower $CrSO_2$. [28-31] The SafeBoosC II feasibility trial demonstrated that it was possible to reduce the burden of cerebral hypoxia in preterm infants using a combination of NIRS monitoring with an evidence-based treatment guideline during the first three days of life. [32] Post-hoc analysis found that early cerebral hypoxia was associated with a higher incidence of severe IVH. [33] SafeBoosC III is

currently underway to determine whether NIRS monitoring in extremely preterm infants can help reducing the composite of either death or severe brain injury. [34]

Guidelines:
To allow for monitoring cerebral perfusion and saturation NIRS is used in the following indications:

1. Routine monitoring of extremely premature infants < 28 weeks GA for the first 72 hours of life
2. Neonates with significant anemia requiring transfusion (before, during and after)
3. Infants receiving inotropes or hydrocortisone for BP support (before, during and after inotropes)
4. Infants on significant respiratory support (e.g., high pressures, HFV, iNO)
5. Preterm infants with PDA to evaluate for hemodynamic significance
6. Infants with hydrocephalus (especially before, during and after therapeutic LP or surgical intervention)

- **A decrease in $crSO_2$** could be associated with decreased cerebral O_2 delivery/ perfusion or increased O_2 consumption. A patient with significantly decreased $crSO_2$ relative to baseline or absolute $crSO_2$ < 60 % needs to be evaluated for anemia, hypoxia, hypotension, chest hyperinflation, hypocarbia and treated accordingly.

- **An increase in $crSO_2$** could be associated with increased cerebral O_2 delivery/ perfusion or decreased O_2 consumption. A patient with significantly increased $crSO_2$ relative to baseline or absolute $crSO_2$ > 90% needs to be evaluated for hyperoxia, hypercarbia, hypoglycemia, over sedation or severe brain injury

Relevant CPG:
Clinical NIRS (Near Infra-red Spectroscopy) in the NICU

c) Prophylactic indomethacin

Background:

Early studies suggested that indomethacin reduced the risk of IVH however secondary analysis of the data found that this risk reduction was seen in male infants but not female infants. Subsequent RCTs found no difference in neurodevelopmental outcome. [35-37] As many PDAs often close spontaneously and the potential for side effects from cyclo-oxygenase inhibitors are significant, the use of prophylactic indomethacin has been controversial and was advised to be used only when there is a significant risk of developing

IVH using statistical models. [38] The use of prophylactic indomethacin in other centers has overall declined, and recent reports including one from our center, have shown that use of prophylactic indomethacin was not associated with reduction of severe IVH and conversely possibly associated with increased complications. [39, 40]

Guidelines:

Prophylactic indomethacin for severe IVH prevention will be no longer used. Hemodynamically significant PDA will be monitored and potentially treated as needed.

d) Handling and head positioning

Background:

Head position may affect cerebral hemodynamics and contribute to the development of GM-IVH in very preterm infants. Turning the head toward one side may occlude jugular venous drainage while increasing intracranial pressure and cerebral blood volume. It is suggested that cerebral venous pressure is reduced, and hydrostatic brain drainage improved if the infant is cared for in the supine 'head midline' position.

The most recent Cochrane Review included three RCTs, with a total of 290 infants (either < 30 weeks' gestational age or < 1000 g body weight) and showed that supine midline head position is associated with reduced neonatal mortality (RR 0.49, 95% CI 0.25 to 0.93), but did not show effect on rates of GM-IVH (RR 1.11, 95% confidence interval (CI) 0.78 to 1.56) and severe IVH (RR 0.71, 95% CI 0.37 to 1.33). The certainty of the evidence was very low for all outcomes because of limitations in study design and imprecision of estimates.[41]

However, care bundles which included midline head positioning have been associated with decreased risk of IVH. [42, 43] Another component of this bundle was to avoid lifting the legs of the extremely premature infant during cares to avoid associated hemodynamic changes. [43]

Guidelines:

1. **Neutral Head Positioning:**

- Neutral head positioning will be supported for the first 72 hours of life for all infants under 32 weeks gestation.
- Neutral/midline head positioning consists of keeping the head and trunk of the infant in midline (alignment of nose, knees, and toes in an imaginary straight line).
- Turning and positioning from side to side will be done by log rolling and keeping the head midline to the body with gentle handling during all interventions.

- Positioning devices may be used for ventilator tubing.
- Positioning supports (including but are not limited to: linens, Freddy Frogs , Bendy Bumpers , etc.) may be used to keep the head and body midline.
- Modified Skin to Skin can be provided in the side lying position.
- Head of bed elevation should remain at least at 15°. When an x-ray is done using the in-bed tray, the bed needs to be flat to pull out the x-ray tray. The bed can be readjusted once x-ray is complete. Documentation of neutral/midline positioning is to occur at least every 4 hours in electronic health record (EHR).
- Avoidance of head down position and sudden elevation of the legs
- A supporting Licensed Independent Provider (LIP) order should be written daily for the first 72 hours of life to maintain neutral head positioning.

2. Skin to Skin

- Determine whether skin to skin care is appropriate for a specific infant and document the plan in the infant's chart.
- For NICU infants under 32 wks gestation and under 72 hrs of age refer to NICU N.1 Neutral Head Positioning: Use log-roll technique for turning.
- The following should be discussed and evaluated:
  - Mechanically ventilated infants requiring labile vent support (highly variable FiO_2, manual breaths with manipulations, frequent vent changes).
  - Infants with O_2 requirements >50%.
  - Infants with chest tubes, umbilical lines or peripheral arterial line
- For infants that are <1000 grams:
  - Monitor for temperature stability at all times using the patient control probe.
  - Place incubator/warming table on air control to prevent excessive cooling of incubator.

Relevant CPG:
NICU N.1 Neutral Head Positioning Guidelines
WNH S.1 Skin to Skin Care

e) Hemodynamic stability

Background

Rapid blood draw from central lines and rapid infusions should be avoided as they may be associated with fluctuations in cerebral blood flow and thus increased risk of IVH. The use of hummingbird system for lab draws reduces the total movement of blood and fluid during the draw procedure by 70% for every blood draw vs our previous methods and has the potential to reduce IVH .Historically, hypotension was considered a risk factor for IVH due to concerns regarding reduced cerebral perfusion, however BP is a poor marker of

cerebral blood flow.[44] Recent studies have demonstrated no difference in IVH rates between infants with isolated hypotension and normotension.[45, 46] Multiple studies have associated the use of vasopressors to treat hypotension in preterm infants with the development of IVH and brain injury due to rapid changes in systemic blood pressure [47, 48]

Guidelines:
Blood withdrawn from a UA line MUST be done slowly, drawn over at least 40 seconds and returned at the same rate over 40 seconds.
The Hummingbird system for lab draw should be used in all central lines lab draws.

Recommendations:
As the use of inotropes is a significant risk factor for acute brain injury, the care provider should be cautious when treating hypotension in premature infants. Indications to consider inotropes use and type should include, along with low blood pressure, a combination of prolonged capillary refill, decreased urine output, elevated lactate, decreased cerebral oxygen saturation by NIRS and preferably echocardiography findings.

Relevant CPG:
NICU/SCN B.1 Arterial and Venous Blood Drawing

f) Optimizing respiratory support

Background

1. Intubation

The process of intubation may cause hypoxemia, bradycardia, intracranial hypertension, increased cerebral blood flow, systemic hypertension and pulmonary hypertension and repeated attempts of intubation may carry an increased risk of IVH. [49]

2. ETT Suction:

Routine care of preterm infants in the NICU including ETT suction, carries a risk of causing significant fluctuations in cerebral blood flow, a known risk for IVH. [50]

3. Mode of Ventilation

Mode of ventilation could have significant effect of outcomes of extremely preterm infants. Volume-targeted ventilation has been associated with lower odds of severe IVH (OR 0.53, 95% CI 0.37 to 0.77) compared with pressure-limited ventilation. [51] On the other hand, the use of high frequency ventilation has been associated with improved survival and overall outcomes in the extremely preterm infants.[52]

4. CO_2 Management

Hypercapnia, defined as PCO_2 blood levels >60 mmHg, is a risk factor for acute brain injury in ELBW infants, [53] and increasing PCO_2 levels appear to have a dose-dependent relationship with IVH risk.[54] In fact, both extreme hypercapnia (PCO_2 >60 mmHg) and hypocapnia (PCO_2 <35 mmHg) may cause brain injury and should be avoided. [55]

Guidelines:

1. **Intubation:**
   Optimize the intubation procedure following current respiratory CPG

2. **Pre-medication for non-emergent intubation**
   Premedication should be used for all non-emergent endotracheal intubations.
   Recommended approach:
   - Nonpharmacologic interventions (swaddling and positioning)
   - Analgesia medications should be used for all non-emergent intubations e.g. fentanyl. (Versed should not be used in this population)
   - Vagolytic agent should be considered
   - Muscle relaxant should be considered

   Intubation without premedication may be acceptable during the following situations: resuscitation in the delivery room, an intubation that is required following an acute deterioration or critical illness that is defined as emergent by the physician, and/or infants with upper airway anomalies**.**

3. **ETT Suctioning:**
   - RT will follow guidelines regarding ETT suction in the newborn
   - HR and O_2 SAT are monitored continuously.
   - Applied suction will not exceed 5 seconds with each attempt
   - Increase FiO_2 in smallest increments when necessary to maintain oxygen saturations within target oxygen saturations parameters.
   - When necessary, pre-oxygenation, generally by increasing O_2 10%, and manual breaths help with recovery time. Caution is needed to avoid hyperoxygenation in extremely preterm infants.
   - Anticipate the need to notify RT prior to suctioning HFJV, oscillator, or any unstable infant.

4. **Proper respiratory management per current respiratory CPGs:**

- Preterm infants born at < 30 weeks gestation who need mechanical ventilation because of severe RDS should be given surfactant immediately after initial stabilization, and preferably within 1 hour after birth.
- Mode of ventilation and respiratory management need to adhere to current respiratory CPGs according to gestation age and respiratory status.
- Caffeine treatment is recommended within the first 12 postnatal hours in all babies <30 weeks

5. CO_2 Management:

- Both hypercapnia and hypocapnia should be avoided and should be treated as critical values.
- Any critical blood gas result requires a plan and/or a ventilator change made to move towards normalization of the blood gas value
- Transcutaneous monitoring should be initiated and maintained on all patients 34 weeks or less requiring ventilator support and any patient who receives surfactant and is actively weaning. Special attention is needed to observe for skin integrity and for contraindications to use transcutaneous monitoring in the extremely premature infants.

Relevant CPG:

Premedication for Nonemergent Endotracheal Intubations in the Neonate
NICU S.2 Endotracheal Tube Suctioning
Early Management of Respiratory Distress Among Infants Born Before 37 Weeks of Gestation
Caffeine DAG (NICU)
Neonatal ICU Blood Gas Guideline
Prevention and Management of Bronchopulmonary Dysplasia (BPD) (In Press)

g) Hypernatremia

Background

Preterm infants are at increased risk of hypernatraemia due to excessive transdermal water loss particularly in the first days of life. Studies have also shown that preterm infants inadvertently receive 2-3 times the recommended sodium intake over the first 2 weeks of life.[56] Increase sodium intake over the first week of life is associated with increased risk of IVH, with one study demonstrating a 31% increase in rates of severe IVH with increasing sodium intake.[56] Potential sodium sources include TPN, medications, IV flushes and umbilical catheter infusions.

Guidelines:

- 0.45% NaCl flushes should be used as an alternative in preterm infants and potential sources of sodium should be documented and minimized where possible.
- On admission. Provider will order ½ NS flushes x 10 for PIV PRN (order to state: line maintenance & flush after medication). This is in addition to ½ NS = 0.5 Unit/mL heparin for umbilical line placement.
- RN to scan all ½ NS flushes, scan line fluid and record how much the provider gave.

h) Role of Sedation:

Background

The role of sedation or analgesia delivered by continuous infusion has not been clarified for infants who require invasive mechanical ventilation, despite extensive investigation. While it should be avoided when the duration of mechanical ventilation is expected to be short, it has been recommended when the infant□s physiology demands strict ventilator synchrony and minimization of oxygen consumption.[57] The clinician should balance the need to prevent pain and the potential risk of adverse outcome on the brain. [58] for these reasons:

- Use of Midazolam infusion in preterm infants should be avoided due to potential risk of severe IVH, PVL and death [59] likely related to associated hypotension.[60] While clinical long-term outcome data is lacking, animal studies have demonstrated worse outcomes.[61]
- Fentanyl can accumulate easily in preterm infants.[62] It has been associated with adverse neurodevelopmental effects at 24 months corrected age [63, 64] and increased cumulative dose in the first week of life was associated with reduced cerebellar growth at term equivalent age.[65]
- Morphine use in preterm infants showed mixed results.[59, 66-73] Although morphine has a potential negative effect on brain development, this seems to be dose dependent. Studies which used low doses (0.1 mg kg bolus followed by 0.01 mg/kg infusion or cumulative less than 1 mg/kg) did not demonstrate adverse brain development or neurodevelopmental outcome.[74, 75] However, when cumulative doses close to 2 mg/kg were used, they were associated with reduced cerebellar volume, poorer cognitive and motor outcomes, and behavioral problems in infancy.[76, 77]
- Dexmedetomidine: In contrast to benzodiazepines and opioids, preclinical data suggests possible neuroprotection of the immature brain.[78]. Although clinical data in preterm infants is limited, it has the potential to be beneficial given the lack of associated respiratory depression and impact on gastrointestinal motility.[79, 80]

Recommendations:

The best available combination to be used is low dose morphine (infusion ≤ 0.01 mg/kg/hour and boluses ≤ 0.05 mg/kg/dose) and possible use of dexmedetomidine

Relevant CPG:

Morphine Intravenous

Dexmedetomidine (Precedex)

Appendices

Appendix I- Summary of recommendations are summarized in Appendix1

Appendix II- Visual infographics for prevention of IVH in preterm infants

Appendix III- Parent information leaflet: intraventricular hemorrhage

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Appendix 1- Summary of Recommendations for Prevention of Intraventricular Hemorrhage in the Neonatal Intensive Care Unit

Antepartum Management:

1. **Antenatal Steroids**
   Should be administered to pregnant women at 23-34 weeks gestation with increased risk of preterm delivery within the next 7 days.
2. **Tocolytics:**
   Should be considered in to allow for at least a 24hr period after the second dose of Betamethasone
3. **Magnesium Sulphate**
   Should be administered when birth is anticipated <32 weeks to reduce severity and risk of CP
4. **In utero transport where possible**

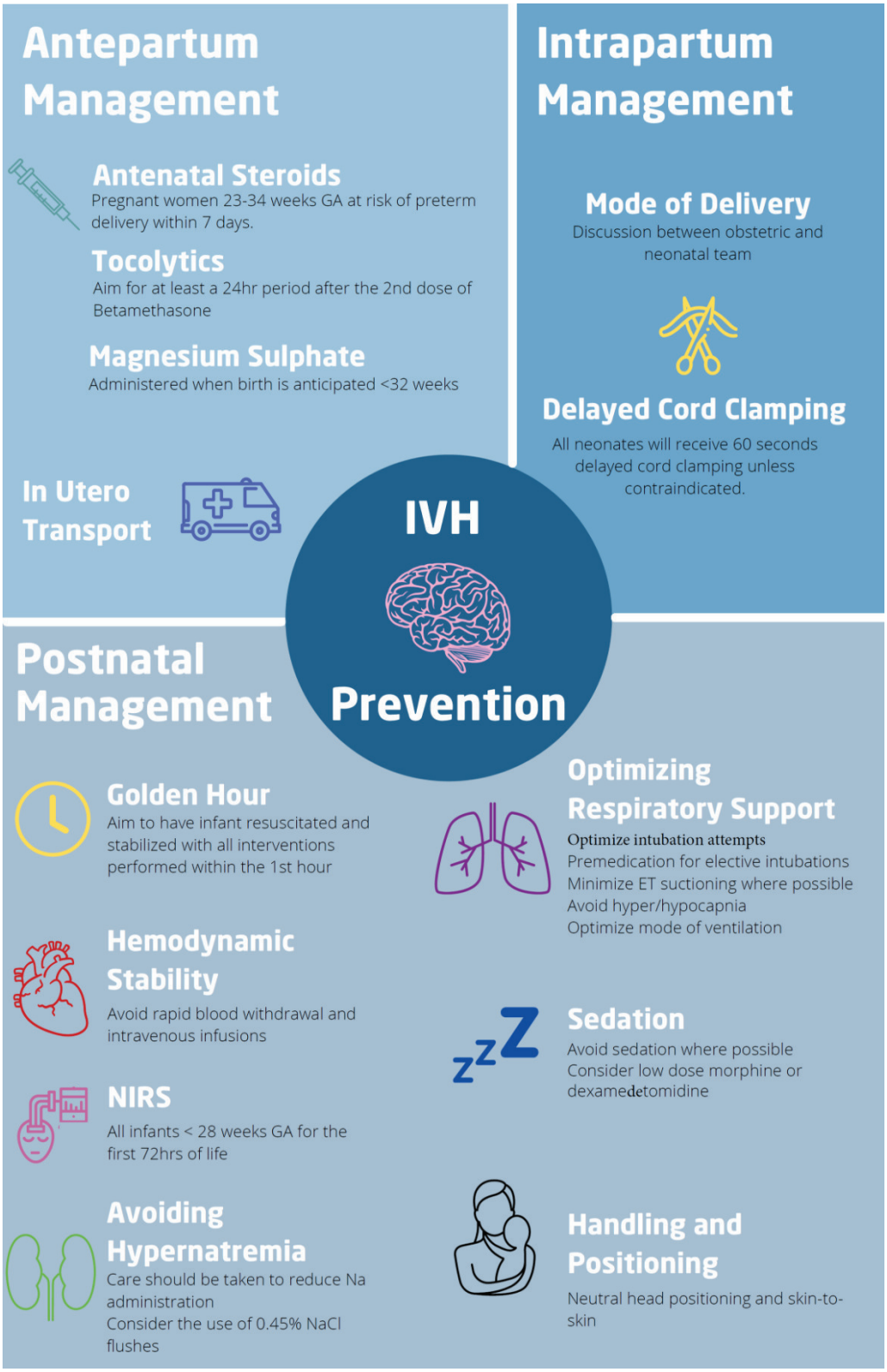
Intrapartum Management:

1. **Mode of delivery**
   Discussion between obstetric and neonatal team
2. **Delayed cord clamping**
   All neonates will receive 60 seconds delayed cord clamping unless contraindicated.

Postnatal Management:

1. **Golden Hour**
   Aim to have infant resuscitated and stabilized with all interventions performed withing the 1st hour
2. **NIRS**
   Routine NIRS monitoring is recommended for all infants < 28 weeks GA for the first 72hrs of life
3. **Handling and head positioning**
   Neutral head positioning and skin-to-skin
4. **Hemodynamic stability**
   Avoid rapid blood withdrawal and intravenous infusions
5. **Optimizing Respiratory Support**
   Careful attention to the intubation procedure
   Premedication for elective intubations
   Minimize ET suctioning where possible
   Avoid hyper/hypocapnia
   Optimize mode of ventilation
6. **Avoiding hypernatremia**
   Care should be taken where possible to reduce sodium administration.
   Consider the use of 0.45% NaCl flushes
7. **Sedation**
   Avoid sedation where possible. If necessary, consider low dose morphine or dexametomidine

Appendix II- Visual Infographics for Prevention of IVH in Preterm Infants



Appendix III:

Parent Information Leaflet: Intraventricular Hemorrhage

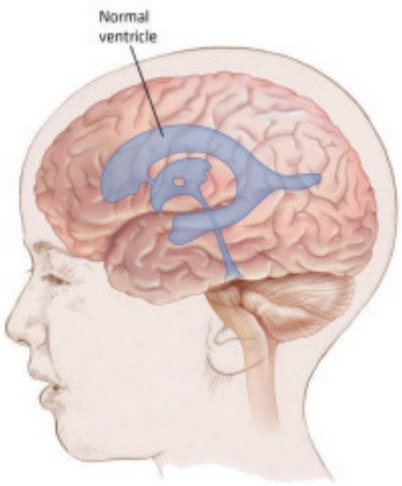
Having a baby born prematurely is a stressful and worrying time for parents. We want this information leaflet to make a difference to families by providing clear information on what IVH means, how we look after babies with IVH and what families can expect. Every baby and family are different but there are simple measures that parents may be able to do to help and support their baby during this time such as being involved in daily cares such as changing diapers, expressing milk, and holding your baby (also known as skin-to-skin) which we will support you through when the time is right for both you and your baby.

If you have any questions your healthcare team will be happy to discuss these further with you.



What is intraventricular haemorrhage (IVH)?

Our brain and spinal cord are surrounded by fluid called cerebrospinal fluid (CSF). CSF is continuously produced within small chambers or spaces inside the brain called ventricles. In preterm babies, the blood vessels that surround these ventricles, also known as the germinal matrix, are immature and fragile.



Intraventricular hemorrhage (IVH) in newborns is a condition that happens when these blood vessels bleed.

- Intraventricular means inside the ventricles
- Hemorrhage means bleeding

Who is at risk of IVH?

It is most common in newborns who are born very premature. The germinal matrix matures and disappears by around 34 weeks of gestation so bleeding after this time is rare. IVH usually starts in the first 3 days after birth, but its effects may develop over the following days and weeks. It is rare for IVH to start beyond a month of age regardless of how premature your baby is at birth.

What causes IVH?

The germinal matrix blood vessels are fragile and can easily bleed in premature babies. Changes in the volume of blood flow in the brain during the birth process or after birth may cause the blood vessels to rupture and bleed into the surrounding tissues. It is not exactly clear why IVH occurs in some babies but is more common in infants who need help with their breathing or blood pressure in the first few days after birth.

Why is IVH a concern?

Bleeding in the brain can cause injury to the nerve cells in that area. Once injury has occurred to brain tissue, it cannot be reversed. However, a physical injury to the brain does not always mean problems with brain function and development in the future. It depends on what part of the brain is injured and how big the injury or bleed is.

Professionals usually group IVH into 4 grades depending on the amount of bleeding.

- Grade one—bleeding occurs just in a small area outside of the ventricles

- Grade two—bleeding also occurs inside the ventricles
- Grade three—ventricles are enlarged by the blood
- Grade four—bleeding also occurs in the brain tissues around the ventricles.

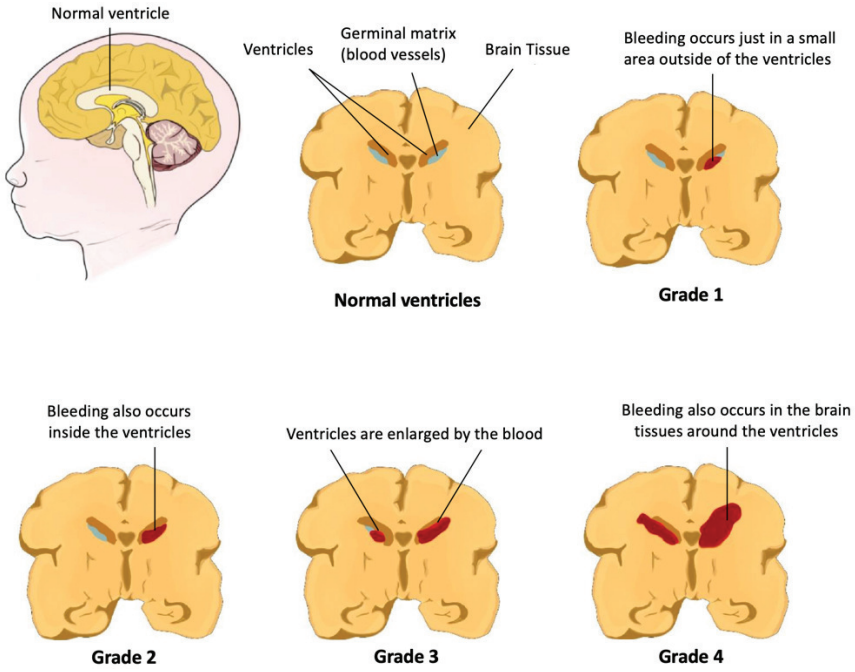


Image adapted from Egesa et al. Int J Pediatr. 2021

Grades one and two are most common and occur in about three-quarters of babies with IVH. Most often these types of bleeds do not cause future problems.

Grades three and four are less common but more serious and may result in long-term problems. If there is a lot of blood in the ventricles, the blood may clot and block the flow of CSF around the brain and spinal cord. This may lead to a build-up of fluid in the brain (also called hydrocephalus). The effect of grade four depends on how large the injury is and what areas of the brain are involved.

How is it diagnosed?

Most babies do not show any outward sign that an IVH has occurred. For this reason, babies born premature have routine screening using ultrasound especially during the first month after birth. Ultrasound is the same as the ultrasound tests performed to monitor baby's growth during pregnancy. After the baby is born, these scans can be performed at the baby's cot side, through the soft spot on their head (where the bones haven't fused together yet) called the fontanelle.



Image: radiologyinfo.org

Other ways of imaging the body (such as Magnetic Resonance Imaging or MRI) are sometimes recommended when the baby's condition is stable.

What are the symptoms:

With more severe grades of IVH, signs and symptoms may sometimes be seen. Where flow of CSF is blocked, as the ventricles enlarge, swelling of fontanelle may be noticeable. Other symptoms can also include abnormally low blood pressure and heart rate, seizures, low blood count or problems with the baby's breathing.

How is it managed?

In general, the bleeding stops fairly quickly and the clots resolve as the body responds to them. Therefore, immediate treatment is not needed. The healthcare team keeps the baby stable and treats any symptoms.

If the flow of cerebrospinal fluid is interrupted due to the bleeding, and pressure increases within the ventricles, several treatments are available including a spinal tap or surgery for the placement of a "shunt", which is a small tube that drains the fluid from the brain to another part of the body including the space beneath the scalp or the abdomen and relieves the pressure.

Can IVH be prevented?

Although we cannot completely prevent IVH from occurring, there are things that we can do to reduce the risk.

If there is a risk that a baby will be born prematurely, and there is time, we can give medications to the mother that reduce the risk of IVH and brain injury such as steroids and magnesium sulphate.

During the delivery, we try to perform delayed cord clamping if it safe for both the mother and baby to do so. This means that after the baby is born, we do not cut the umbilical cord for up to 1 minute if we can. This allows extra blood from the placenta to pulse through the umbilical cord to the baby.

After the baby is born, we try to be as gentle as possible and perform all necessary procedures quickly and safely to make sure the baby is positioned comfortably and can rest in their incubator. In the first 3 days after birth, we try to keep the head aligned with the body and not turned to either side except with the whole body.

We monitor babies brain oxygen levels, methods of breathing support and blood pressure very closely. If sedation medications are needed, we limit them to the least needed dose. We also try to limit the use of fluids that contain a lot of salt. If the baby is well enough, we will try to encourage skin-to-skin contact with parents.

