<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Description of Revision</th>
<th>Completed By / Revised By</th>
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<tbody>
<tr>
<td>1.0</td>
<td>December 2018</td>
<td>Version 1 of topic completed</td>
<td>see Acknowledgments</td>
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</table>
Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient/guardian, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

This knowledge topic is based on the following guidelines available on AHS Insite:
1. Alberta Health Services. Neuroprotection Package for HIE Bundle Clinical Guideline Calgary Critical Care Program 2017
2. Alberta Health Services. Therapeutic Hypothermia (Cooling) Therapy on Transport Practice Guideline; Calgary 2017
3. Therapeutic hypothermia Guidelines; Edmonton; March 1, 2016
4. Canadian Pediatric Society Position Statement: Hypothermia for newborns with hypoxic-ischemic encephalopathy 2018
Rationale

Moderate to severe perinatal hypoxic ischemic encephalopathy (HIE) remains an important cause of mortality and acute neurological injury with subsequent long term neurodevelopmental disabilities.¹ Perinatal events leading to HIE frequently result in multi-system organ damage with significant abnormality in hemostasis, and renal, gastrointestinal, and cardiac functions. The risk of disability and impaired cognitive development is related to the severity of HIE. A large systematic review and meta-analysis of 11 randomized controlled trials including 1505 term and late preterm infants (gestational age equal to or more than 35 weeks) with moderate/severe HIE showed that therapeutic hypothermia resulted in statistically significant and clinically important reduction in the combined outcome of mortality or neurodevelopmental disability at 18 months of age, mortality, and neurodevelopmental disability in survivors.² The incidence of HIE is approximately 1/1000 to 8/1000 live births.³ Therapeutic Hypothermia is considered standard neuroprotective treatment for moderate to severe HIE and has been shown to be a safe procedure.⁴

HIE is often unanticipated and many neonates are initially cared for in community centres, or in regional and rural hospitals. There is a limited window to begin therapeutic hypothermia for neonates with HIE. Thus, early recognition and transport of these neonates is critical. Primary care physicians, community pediatricians and clinicians play an essential role in this process.
Goals of Management

Definitions

Hypoxic Ischemic Encephalopathy (HIE) – This term describes abnormal neurologic behavior in the neonatal period arising as a result of a hypoxic-ischemic event. The severity of hypoxic-ischemic encephalopathy (HIE) can be defined as mild, moderate, or severe depending on symptoms and signs.

Therapeutic Hypothermia – Therapeutic hypothermia or whole-body cooling includes systemic hypothermia to achieve and maintain a rectal temperature between 33°C and 34°C.5

Passive Cooling – Removal of all external heat sources to the neonate including radiant warmer, blanket, shirt, or hat to achieve a temperature of 33°C – 34°C.6,7

Active Cooling – Active cooling is whole body cooling with cooled gel packs or a cooling device to achieve a temperature of 33°C – 34°C.5

Principles

1. When a neonate is suspected to have HIE, a referral to a neonatologist or pediatrician on site, if available, should be initiated as soon as possible. In centres without a capacity for therapeutic hypothermia, a referral to a Level III NICU should be initiated immediately by calling Referral, Access, Advice, Placement, Information, and Destination Center (RAAPID) to connect with the on call neonatologist at a cooling centre.

2. It is recommended that moderate or severe HIE should be identified and therapeutic hypothermia initiated within 6 hours of birth based on inclusion criteria.

3. In equivocal cases, sufficient time should be allowed for stabilization and transition (at least 1 hour) before making the final encephalopathy staging.

4. Consideration for the underlying etiology of encephalopathy (e.g. perinatal opioids) should always be given as not all diagnosed encephalopathy is due to HIE.

5. Therapeutic hypothermia is administered in designated cooling centres with capacity for administration of active cooling, intensive physiological monitoring, EEG monitoring, and management of complications associated with HIE, its underlying case, and therapeutic hypothermia. In consultation with a neonatologist or pediatrician, non-cooling centres may initiate passive cooling in preparation for transport to a cooling centre.

6. The decision of therapeutic hypothermia, as well as the risks and benefits should be communicated with parents and the discussion documented in the patient’s chart.

7. It is recommended that all neonates eligible for therapeutic hypothermia regardless of treatment are referred for neonatal follow up clinic following discharge from the NICU.
Inclusion Criteria
Neonates must meet the following criteria (Appendix A and B):

- Gestational age of 35 weeks or greater
- Birth weight more than 1800 grams
- Less than 6 hours of age and who meet criteria A and B

Criteria A
The neonate meets any one of the following:

- pH less than or equal to 7 in an arterial or venous cord blood gas or any blood gas obtained within 1 hour of birth (if no cord gas available).
- Base excess (BE) of less than or equal to -16 mmol/L in an arterial or venous cord blood gas or any blood gas obtained within 60 minutes of birth (if no cord gas available).
- An Apgar score of less than or equal to 5 at 10 minutes of age
- Ongoing need for positive pressure ventilation at 10 minutes of age

Criteria B
The neonate meets the following:

- **Seizures OR**
- Clinical finding suggestive of moderate or severe HIE in at least 3 of the following six categories:
  - Level of consciousness
  - Spontaneous activity
  - Posture
  - Tone
  - Primitive reflexes
  - Autonomic system

The presence or absence and level of encephalopathy should be determined after the initial stabilization and preferably around 1 hour of age. Careful clinical reassessment of mild encephalopathy in the context of fetal acidosis and/or perinatal depression is extremely important as there are neonates who deteriorate clinically after 60 minutes of age.

Therapeutic Hypothermia Calculator App is available to assist with determining eligibility for therapeutic hypothermia:

- For desktops and laptops: [http://thcalculator.appspot.com/Main.html](http://thcalculator.appspot.com/Main.html)

Relative Exclusion Criteria
The following is a general list of exclusion criteria to help guide decision-making:

- Severe intrauterine growth restriction (IUGR) defined as birth weight below 3rd percentile
- Major congenital anomalies*
- Major chromosomal abnormalities other than Trisomy 21 (e.g. Trisomy 13, 18)
- Severe uncontrolled bleeding including disseminated Intravascular Coagulation (DIC)

* Some infants with HIE and congenital anomalies such as congenital diaphragmatic hernia and certain congenital heart diseases may benefit from therapeutic hypothermia. In those unique situations, careful consideration and discussion with parents is important to determine eligibility for therapeutic hypothermia.
Early Recognition

There is a therapeutic ‘window of opportunity’ that exists in the interval following resuscitation of an asphyxiated neonate before a secondary phase of impaired energy, metabolism and injury may occur.

Despite the importance of early recognition and initiation of Therapeutic Hypothermia, resuscitation and stabilization remains a priority. Sufficient time should be allowed for stabilization and transition (at least 1 hour) before making the final encephalopathy staging.

Indications for increased clinical assessment of neonates who may meet criteria for therapeutic hypothermia include (but are not limited to):

1. A Perinatal Event
   Neonates frequently have a perinatal event that is indicative of fetal distress such as:
   - Fetal heart rate abnormalities including but not limited to late decelerations, severe variable decelerations, decrease or loss of variability or terminal bradycardia
   - Evidence of placental bleeding and/or fetal blood loss (e.g. uterine rupture, placental abruption, fetal exsanguination from a vasa previa or massive feto-maternal haemorrhage)
   - Cord occlusion or prolapse
   - Prolonged extraction of the neonate

2. Neonatal Resuscitation
   - Depressed neonate at birth requiring sustained resuscitation for greater than 10 minutes.
   - Time to spontaneous sustained respirations of greater than 5 minutes
   - Abnormal level of consciousness

If the infant is born in non-cooling centre, early consultation with a neonatologist at a Level III facility is recommended to ensure accurate diagnosis, early management, and timely mobilization of the transport team. When neonatal HIE is suspected, consultation with a neonatologist should be initiated by calling RAAPID. These consultations may be facilitated by telehealth when available.

Initial Assessment

When a perinatal event is recognized, it is optimal for the most responsible practitioner (MRP) to be available at birth or as soon as possible after delivery. It is essential that a thorough examination of the neonate is performed and documented to determine if signs of encephalopathy are present.

Initial assessment should include:

- Cardiorespiratory status
  - Assess and address the neonate’s respiratory and hemodynamic status. Neonates with HIE may have respiratory depression and require respiratory support.

- Neurological status
  - Assess the level of encephalopathy, mild, moderate or severe (Appendix B)
  - Perform focused neurological exam after stabilization in consultation with the Neonatologist (Appendix B), and repeat the exam at the following intervals:
    - Between 2 to 3 hours of age and;
    - Between 4 to 6 hours of age of life to determine if there has been any significant change in the neonate’s neurological status
Table 1. Clinical Criteria for Hypoxic Ischemic Encephalopathy

<table>
<thead>
<tr>
<th>Category</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
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<tbody>
<tr>
<td><strong>Level of Consciousness</strong></td>
<td>Hyper alert</td>
<td>Lethargic</td>
<td>Stupor or Coma</td>
</tr>
<tr>
<td><strong>Spontaneous Activity</strong></td>
<td>Normal</td>
<td>Decreased</td>
<td>No Activity</td>
</tr>
<tr>
<td>Neuromuscular Control</td>
<td>Tone</td>
<td>Normal</td>
<td>Mild hypotonia</td>
</tr>
<tr>
<td></td>
<td>Posture</td>
<td>Mild distal flexion</td>
<td>Strong distal flexion</td>
</tr>
<tr>
<td></td>
<td>Stretch Reflexes</td>
<td>Overactive</td>
<td>Overactive</td>
</tr>
<tr>
<td></td>
<td>Segmental myoclonus</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Primary Reflexes</td>
<td>Suck</td>
<td>Weak</td>
<td>Weak or Absent</td>
</tr>
<tr>
<td></td>
<td>Moro</td>
<td>Strong</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td>Oculovestibular</td>
<td>Normal</td>
<td>Overactive</td>
</tr>
<tr>
<td>Autonomic System</td>
<td>Sympathetic</td>
<td>Parasympathetic</td>
<td>Absent</td>
</tr>
<tr>
<td></td>
<td>Pupils</td>
<td>Dilation</td>
<td>Constriction</td>
</tr>
<tr>
<td></td>
<td>Heart Rate</td>
<td>Tachycardia</td>
<td>Bradycardia</td>
</tr>
<tr>
<td></td>
<td>Respiration</td>
<td>Normal</td>
<td>Periodic</td>
</tr>
<tr>
<td></td>
<td>Secretions</td>
<td>Sparse</td>
<td>Profuse</td>
</tr>
<tr>
<td>Seizures</td>
<td>None</td>
<td>Common</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Pain status</td>
<td>Neonatal Pain, Agitation and Sedation Scale (N-PASS) score or Preterm Infant Pain Profile (PIPP) score should be completed on initial assessment and then every 4 hours following admission to the NICU</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calgary AHS internal website: Pain: assessment and management guidelines</td>
<td></td>
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<tr>
<td></td>
<td>Edmonton AHS internal website: Management of pain and non-painful stress guideline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Integrity</td>
<td>Perform an initial skin integrity assessment.</td>
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**Special Considerations**

Neonates not meeting the criteria for Therapeutic Hypothermia

Neonates who do not meet the criteria for therapeutic hypothermia still require frequent assessment, particularly during the first 6 hours of life to ensure that any degree of encephalopathy has not progressed. A repeat neurological exam should be carried out between:

- 2 to 3 hours of life for neonates who meet criteria A but not criteria B
- 4 to 6 hours of life to assess for any significant neurological changes

Any significant changes should be immediately discussed with the neonatologist in the tertiary centre as this may affect management and disposition.

**Note:** If the MRP believes that an infant will benefit from Therapeutic Hypothermia despite not meeting the cooling criteria (e.g. borderline GA or BW, beyond 6 hours of age, or borderline moderate encephalopathy), the options should be discussed with the family and verbal consent taken and documented before proceeding with Therapeutic Hypothermia.
What is the optimal timing for initiation of Therapeutic Hypothermia?
Within the first 6 hours of life. There is limited evidence that starting Therapeutic Hypothermia within the first 3 hours compared to 6 hours after birth is associated with improved motor outcomes in surviving neonates with HIE.11 However, larger trials did not show similar results12. On confirmation an infant meets Criteria A and B timely initiation of active or passive therapeutic hypothermia within 6 hours of birth is recommended.

Can therapeutic hypothermia be initiated after 6 hours of age?
A multicenter randomized controlled trial of infants with moderate or severe HIE born at 36 weeks or later gestation compared Therapeutic Hypothermia initiated between 6 to 24 hours after birth to standard management (normothermia). The results indicated that Therapeutic Hypothermia initiated at 6 to 24 hours after birth may have benefit but with uncertain effectiveness.13

Recommendation: In infants with moderate or severe HIE presenting after 6 hours of age, Therapeutic Hypothermia cannot be recommended due to lack of evidence. Such intervention should not be offered as standard of care, and could be offered in the context of research studies.

Can Therapeutic Hypothermia be administered to preterm infants < 35 weeks’ gestation with HIE?
Therapeutic Hypothermia is associated with increased mortality in preterm infants based on small pilot and retrospective studies.14,15
Procedures
Therapeutic Hypothermia should be provided in a designated cooling centre where resources are available to treat possible complications. Early passive cooling prior to transfer is recommended for moderate to severe HIE.

Cardiorespiratory Support
- Assess airway, breathing and circulation.
- Initiate oxygen therapy to maintain O₂ saturations at 90% to 95%.
- Determine need for supported ventilation (CPAP or PPV).
- Assess heart rate, blood pressure, and perfusion status.

Therapeutic Hypothermia

Non-cooling centres
For neonates who meet the criteria for Therapeutic Hypothermia, begin passive cooling after initial stabilization and in preparation for the Neonatal Transport Team. Parents should be informed about the procedure and plan. Passive cooling aims for a target temperature of 33 – 34°C and is achieved by:
- Removing all external heat sources,
- Turning off the radiant heat warmer,
- Unbundling the neonate (a diaper may be left on).

Continuous rectal temperature monitoring could be used if available. Otherwise rectal temperatures should be measured every 15 minutes. In absence of a rectal probe, axillary temperature should be measured every 15 minutes to avoid overcooling. (A core temperature less than 33°C is dangerous). Ensure that an appropriate thermometer that can read temperatures as low as 32°C is used. This type of thermometer is available through AHS (Internal Item Number 304735). It is important to avoid fluctuations in temperature during the cooling process.

If the neonate’s temperature falls to 33°C a blanket can be placed over the neonate or the radiant heater output can be set to 5 to 10% and the temperature continued to be monitored. Notify the MRP of any fluctuations in temperature.

Active cooling is initiated by the Neonatal Transport Team using their local protocols.

- Calgary: Refer to Calgary’s Internal AHS Document: Neuroprotection Package for Neonatal HIE: Procedure for High-Risk Transport
- Edmonton: Refer to Edmonton’s Internal AHS Document: Therapeutic Hypothermia Transport Protocol

Designated cooling centres
For neonates who meet the criteria for Therapeutic Hypothermia, active cooling should be initiated using a servo-controlled cooling device to achieve target temperature 33.5 ± 0.5°C. Cooling devices may vary between centres. Please refer to the local guidelines and manufacturer recommendation for initiation and maintenance of Therapeutic Hypothermia.

- Calgary: Refer to Calgary’s Internal AHS Document: Neuroprotection Package for Neonatal HIE: Procedure
- Edmonton: Refer to Edmonton’s Internal AHS Document: Therapeutic Hypothermia Guidelines
**Possible Adverse Events Associated with Therapeutic Hypothermia**

Serious adverse events are rare and likely reflect the severity of the illness rather than the treatment itself. Complications relating to perinatal asphyxia that may worsen with Therapeutic Hypothermia include:

- Cardiac arrhythmia
- Hypotension
- Respiratory distress
- Clinical bleeding or abnormal clotting (coagulopathy)
- Electrolyte imbalance – hypernatremia, hypokalemia
- Metabolic acidosis (pH less than 7.25)
- Abnormal renal function
- Elevated liver enzymes
- Bone marrow depression
- Subcutaneous fat necrosis

**Electroencephalography (EEG) Monitoring**

Assessment with amplitude-integrated electroencephalogram (aEEG) for at least 20 minutes, when available, may provide a useful tool to document the background and/or seizure activity. However, decision to initiate Therapeutic Hypothermia should be based on the eligibility criteria described above. aEEG should be interpreted in discussion with a neonatologist. Appendix F provides a simple guide for aEEG interpretation.

**Seizure Management**

Seizures are common in neonates with HIE and are difficult to diagnose by clinical observation alone. Seizures are a major predictor of adverse outcome in the neonate. Discussion with the neonatologist and/or physician designate should occur immediately if the neonate displays any signs of seizures.

First line drug of choice after the establishment of ABCs and correct any electrolytes or glucose abnormalities is IV phenobarbital 20 mg/kg/dose which can be repeated up to 40 mg/kg/dose. Consultation with neurology is recommended for infants with recurrent seizures. Local protocol can be followed and/or discussion with the consultant neonatologist for the second and third line anti-seizure medications options.

**Neuroprotective Care**

- Provide gentle handling during direct care, avoid startling or rapid awakening
- Keep noise levels to a minimum
- Lighting should be kept to a low level

**Serial Neurological Assessment**

For those neonates where cooling is initiated, repeat the neurological exams are recommended at the following interval (Appendix D):

- At 24 hours after cooling initiated and;
- After rewarming and;
- At 7 days of life or before discharge (whichever comes earlier)
- More frequent assessments could be performed as clinically indicated.
Principles for Hemodynamic Support

- Cardiovascular instability is commonly seen in HIE. Hypotension can cause a secondary ischemic injury. It is important to identify the cause of hypotension, which may include hypovolemia, myocardial dysfunction, sepsis, or decreased systemic venous return due to excessive ventilation pressures.
- Hypovolemia and volume replacement should be given careful consideration. This is especially important in presence of history or physical examination findings suggestive of blood loss such as antepartum hemorrhage, placental abruption, severe pallor, and subgaleal hemorrhage.
- A target mean blood pressure should be based on gestational age plus clinical indicators rather than single value (Appendix E). However, blood pressure alone is a poor predictor of low cardiac output. Assessment of hemodynamic instability peripheral perfusion include:
  - Urine output (beyond 24 hours of age)
  - Heart rate trends
  - Oxygen saturation
  - Metabolic and lactic acidosis
An ECG and/or echocardiogram may be useful in the assessment of myocardial dysfunction.

- Therapeutic Hypothermia slightly prolongs the QT interval and commonly causes bradycardia (HR less than 100 bpm). The neonate’s temperature should be maintained above 33°C as the risk of ventricular fibrillation increases as body temperature decreases. If a neonate with moderate to severe HIE undergoing Therapeutic Hypothermia presents with tachycardia this may indicate distress, pain or other concerns such as infection. Loss of heart rate variability during Therapeutic Hypothermia has been linked with poor neurological outcomes.16

Principles for Respiratory Support

- Neonates with HIE may have respiratory depression and require mechanical ventilation. Seizures and antiepileptic drugs may lead to apnea and respiratory depression.
- Over-oxygenation should be avoided as hyperoxia increases oxidative stress and free radical production and is associated with poor long-term outcomes for neonates with HIE. In mechanically ventilated infants, iatrogenic hyperventilation should be avoided.
- Temperature correction by the blood gas machine may underestimate the PCO₂ by 10 to 15 mmHg. The pH may also be falsely low when drawn from a capillary sample due to poor perfusion.
- Newborn infants receiving Therapeutic Hypothermia should be monitored for persistent pulmonary hypertension (PPHN).

Fluid and Nutrition Management

Current recommendations for fluids and nutrition are based on the intention to avoid fluid overload, prevent cerebral edema and to avoid the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Initially during Therapeutic Hypothermia, the neonate should be NPO and parenteral nutrition or D10W should be initiated. Excessive fluid restriction can increase the risk of dehydration and hypotension resulting in decreased cerebral perfusion and further increase the risk of adverse neurological outcomes.

- Initiate emergency umbilical venous catheter (UVC) or peripheral IV access with maintenance solution of D10W
- Maintain a total fluid intake (TFI) of 40 to 50 mL/kg/day
• Neonates should remain NPO initially
• Avoid hypoglycemia and maintain blood glucose level >= 2.6 mmol/L (tested by point of care glucometer)\(^20\)
• Observe for urine output and consider weighing diapers if possible.
• Once in the cooling centre:
  o Provide parenteral nutrition with lipids to give balanced energy sources and to support neonates energy expenditure (40 to 60 kcal/kg; max protein of 1.5 g/kg/day for the first 72 hours)
  o Place on strict intake and output fluid balance with a fluid balance goal of -50 mL to +50 mL per 24 hours
  o Monitor for electrolyte disturbances paying close attention to avoid hypomagnesemia and hypocalcaemia
  o Consider adding electrolytes to PN after 24 to 48 hours once electrolytes and renal function have stabilized
  o Add phosphate to the PN as soon as possible to optimize access to intracellular glucose for fuel and to decrease secondary energy failure
  o Do not provide nutrients in excess of estimated energy requirements as overfeeding increases CO\(_2\) production which may then increase ventilator requirements
  o Enteral feeding: The current standard is to provide nothing by mouth (NPO) during Therapeutic Hypothermia. However, a small retrospective study showed that initiation of minimal enteral feeding during Therapeutic Hypothermia is safe.\(^{21, 22}\) Hemodynamic stability and normalization of blood lactate levels should be confirmed prior to initiation of minimal enteral feeding. If the most responsible neonatologist elects to start feeding, fresh expressed breast milk or donor human milk could be initiated at 1 to 2 mL/kg/feed every 3 to 4 hours. Close monitoring after initiation of feeds is advised.

**Sepsis Management**

• The maternal history should be carefully assessed for risks for early neonatal sepsis.
• If early onset neonatal sepsis is considered, a blood culture should be obtained and empiric antibiotics started.
• In infants with moderate or severe HIE, for infants who are at high risk of acute kidney injury, cefotaxime is preferred over gentamicin or tobramycin.

**Laboratory Monitoring**

• Cord blood gases: arterial and venous
• Point of care blood glucose: as soon as possible and follow local hypoglycemia protocols
• Complete blood count with differential.
• Blood culture if indicated
• Blood gas within 60 minutes of birth including lactate, if available
• INR, PTT, and fibrinogen; if available (usually done in designated cooling centres and other urban centres)
• ALT and AST; if possible
• Other baseline blood work may be recommended after consultation with the neonatologist. Generally:
  o Blood gas could be repeated as clinically indicated to ensure acceptable parameters and normalization of lactate.
  o Electrolytes and creatinine at 24 hours of age.
  o Additional tests as clinically indicated.
Documentation

- Document the events prior to resuscitation (antenatal and intrapartum),
  - The extent of the resuscitation,
  - The initial, and subsequent neurological examinations
    - Documentation on Appendix B and C
- Document procedures, consultations and conversations.

Parental Involvement

- Discuss suggested treatment with parents, document the discussion
- Provide information and resources for the parents
- Access Information for Parents on AHS Internal Website
  - Calgary: http://insite.albertahealthservices.ca/nicuc/total_body_cooling_.pdf
Order Set Components

Therapeutic Hypothermia Order Set – Non-Cooling Centres

Order Set Restrictions: For neonates greater than or equal to 35 weeks gestation with hypoxic ischemic encephalopathy and meet the criteria for Therapeutic Hypothermia

Order Set Keywords: therapeutic, hypothermia, hypoxic, encephalopathy, HIE

Order Set Requirements: Weight, Gestational Age, Time of Birth

Admit
- Admit to ________ (unit)
- Admitting physician: Dr. ____________ (accepting physician)

Transfer
- Transfer to ________ (unit) under care of ____________ (accepting physician)

Goals of Care Designation
Conversations leading to the ordering of a Goals of Care Designation (GCD), should take place as early as possible in a patient's course of care. The Goals of Care Designation is created, or the previous GCD is affirmed or changed resulting from this conversation with the patient or, where appropriate, the Alternate Decision-Maker.

Complete the Goals of Care Designation (GCD) Order Set within your electronic system, or if using paper process, complete the Provincial Goals of Care Designation (GCD) paper form.
https://www.albertahealthservices.ca/frm-103547.pdf

Safety and Precautions
- Neuroprotective care: minimal handling of the neonate, maintain noise and light levels to a minimum.

Monitoring and Patient Care
Vital Signs: to include temperature (T), pulse (P), respirations (R), Blood pressure (BP) and Oxygen saturations (O₂ sat):
- Bedside cardiac monitoring – continuous
- Oxygen saturation monitoring: pulse oximetry - continuous
  - Pulse (P), Respirations (R), and Oxygen Saturation (SpO₂) every hour during passive cooling
- Blood Pressure
  - On admission
  - Without arterial line: Hourly during passive cooling
  - With arterial line: Monitor continuously

Therapeutic Hypothermia
- Initiate passive Therapeutic Hypothermia
- Temperature – Passive Cooling – maintain temperature between 33°C and 34°C (use of a rectal probe if available or appropriate axillary probe). Turn off radiant heat warmer (if in use) and any other heat sources.
  - Monitor temperature every 15 minutes. Notify the most responsible practitioner if the temperature is less than 33.5°C or greater than 35°C
- Neonatal Neurological Vitals
  - Prior to initiation of passive cooling
  - At 1 hour following initiation of passive cooling
  - At 12 hours following initiation of passive cooling
  - Notify the most responsible practitioner of any change in neurological status
Neonatal Pain Score
- On admission
- Every 4 hours for neonate who are expected to experience pain
- Before and after painful procedure

Neonatal Sedation Score
- Once per shift
- Every 4 hours for neonates receiving analgesics or sedatives

Intake and Output
- Diaper weight (Level II centres)
- Diaper count (Level I centres)

Point of Care Testing
- Blood Glucose Monitoring as per protocol

Vascular Access
- Insert Peripheral Intravenous Cannula
- Insert Umbilical Arterial Catheter (UAC)
- Insert Umbilical Venous Catheter (UVC)
  - CDS for umbilical catheters: If neonate less than 1500 grams, use 3.5 French. If neonate greater 1500 grams, use 5 French

Fluid Management
- Total Fluid Intake (TFI) – Neonate ___ mL/kg/day = ______ mL/hour
  - (Recommended TFI 40 – 50 mL/kg/day)

Maintenance Solutions
- D10W infusion _____ mL/hour
- 0.45% NaCl infusion _____ mL/hour for arterial line

Other IV
- __________________________ infusion _____ mL/hour via __________
- __________________________ infusion _____ mL/hour via __________

Additives
- Heparin 0.25 unit/mL

IV Bolus or Rapid Infusion
- D10W bolus infusion by _____ mL give over _____ minutes (2 mL/kg)
- 0.9% NaCl bolus infusion by _____ mL give over _____ minutes (10 mL/kg)

Enteral Nutrition
- NPO

Diagnostic Imaging

General Radiology
- Chest 1 Projection (AP only)
  - Stat  □ Date _______ Time _______
- Chest 2 Projections (AP and Lateral)
  - Stat  □ Date _______ Time _______
- Chest 1 Projection Decubitus (RT or LT or dorsal)
  - Stat  □ Date _______ Time _______
- Abdomen 1 Projection (AP only)
  - Stat  □ Date _______ Time _______
- Abdomen 2 Projections (AP and decubitus (RT or LT or dorsal decub or upright)
  - Stat  □ Date _______ Time _______
Chest and Abdomen Pediatric 1 Projection
☐ Stat   ☐ Date ______   Time ______
☐ Chest and Abdomen Pediatric 2 Projections
☐ Stat   ☐ Date ______   Time ______

Laboratory Investigations

Blood Gases (include lactate if available)
☐ Blood Gas:
  ☐ Arterial   ☐ Capillary   ☐ Venous
  ☐ Stat   ☐ Date ______   Time ______

Hematology
☐ Complete Blood Count (CBC) with differential
☐ PTT
☐ INR
☐ Fibrinogen

Chemistry
☐ Aspartate Aminotransferase (AST)
☐ Alanine Aminotransferase (ALT)

Microbiology
☐ Blood Culture Stat
☐ Other culture _________

Transfusion Medicine
☐ Type and Screen   Date ______   Time ______

Respiratory Care
☐ Oxygen therapy  to maintain target O₂ saturation between 90 and 95%
☐ Low flow cannula at _____ liter per minute
☐ Heated humidified high flow nasal cannula at _____ litre(s) per minute
☐ CPAP
  • Pressure _____cmH₂O
☐ BIPAP:
  • High Pressure_____cmH₂O
  • Low pressure_____cmH₂O
  • Rate _____bpm
  • Inspiratory Time__________
☐ Endotracheal Intubation
☐ Conventional Ventilation:
  • Mode _________
  • Settings: ______________________________________

Medications

Antibiotics
Recommended dose 50 mg/kg/dose
☐ ampicillin ______ mg IV once
AND
Recommended dose 50 mg/kg/dose
☐ cefoTAXime ______ mg IV once
Transitions and Referrals

- Consult Transport Neonatologist (*follow the local process for consultation*)
- Consult Social Work
- Consult ________
Therapeutic Hypothermia Order Set – Designated Cooling Centres

Order Set Restrictions: For neonates’ greater than or equal to 35 weeks gestation with hypoxic ischemic encephalopathy and meet the criteria for therapeutic hypothermia.

Order Set Keywords: therapeutic, hypothermia, hypoxic, encephalopathy, HIE

Order Set Requirements: Weight, Gestational Age, Time of Birth

Risk Assessment/Scoring Tools/Screening: N-PASS/PIPP

Admit
☐ Admit to _______ (unit)
☐ Admitting physician: Dr. ________________ (accepting physician)

Goals of Care Designation

Conversations leading to the ordering of a Goals of Care Designation (GCD), should take place as early as possible in a patient’s course of care. The Goals of Care Designation is created, or the previous GCD is affirmed or changed resulting from this conversation with the patient or, where appropriate, the Alternate Decision-Maker.

Complete the Goals of Care Designation (GCD) Order Set within your electronic system, or if using paper process, complete the Provincial Goals of Care Designation (GCD) paper form (http://www.albertahealthservices.ca/frm-103547.pdf).

Safety and Precautions
☐ Assess skin integrity every 2 to 3 hours.
☐ Change the neonate’s position every 2 to 3 hours.
☐ Neuroprotective care: Minimal handling of the neonate, maintain noised and light levels to a minimum.

Monitoring and Patient Care

Vital Signs: to include temperature (T), pulse (P), respirations (R), Blood pressure (BP) and Oxygen saturations (O₂ sat):
☐ Bedside cardiac monitoring – continuous
☐ Oxygen saturation monitoring: pulse oximetry – continuous
☐ Pulse (P), Respirations (R), and Oxygen Saturation (SpO₂) every hour during active cooling
☐ Blood Pressure
  • On admission
  • Without arterial line: Hourly during active cooling
  • With arterial line: Monitor continuously
    o Alarm limits – mean arterial pressure – Low limit ____ mmHg, High Limit ____ mmHg
☐ Notify Neonatologist/designate of any arrhythmias, BP mean less than gestational age (Appendix E), and hypoxemia (SpO2 less than 90)

Therapeutic Hypothermia
☐ Initiate Active Therapeutic Hypothermia using the cooling device to maintain temperature 33°C to 34°C.
☐ Set up cooling device according to protocol.
☐ Temperature – Insert rectal probe – continuous.
☐ Record temperature every 15 minutes for the first 4 hours of cooling and then every hour for the remainder of the Therapeutic Hypothermia.
☐ Notify Neonatologist/designate if the rectal temperature is less than 33°C or greater than 34°C despite trouble shooting the equipment
Neurological Vital Signs – Neonatal
- On admission
- At 1 hour following initiation of active cooling
- Every ☐ 12 hours ☐ ________ hours

Neonatal Pain/Sedation Score
- On admission
- Every 4 hours for neonate who are expected to experience pain
- Before and after painful procedure

Neonatal Sedation Score
- Once per shift
- Every 4 hours for neonates receiving analgesics or sedatives

Intake and Output
- Weigh: ☐ Every 12 hours ☐ Daily
- Diaper weight
- Diaper count
- Foley catheter – Insert and connect to straight drainage
- Fluid Balance every 6 hours

Point of Care Testing
- Blood Glucose Monitoring as per protocol

Neurological Assessment
- Call MD/Designate to compete neurological assessment (Appendix D) at 24 hours after initiation of hypothermia, reaching rewarming temperature and discharge (or 7 days).

Vascular Access
- Insert Peripheral Intravenous Cannula
- Insert Umbilical Arterial Catheter (UAC)
- Insert Umbilical Venous Catheter (UVC)
  - CDS for umbilical catheters: If neonate less than 1500 grams, use 3.5 French. If neonate greater than 1500 grams, use 5 French
- Insert Peripheral Arterial Line (PAL)
- Insert Peripheral Inserted Central Catheter (PICC)

Fluid Management
- Total Fluid Intake (TFI) – Neonate ___ mL/kg/day = ______ mL/hour
  - (Recommended TFI 40 – 50 mL/kg/day)

Maintenance Solutions
- D10W infusion _____ mL/hour
- 0.45% NaCl infusion _____ mL/hour
- Sodium acetate 34 mmol/L in sterile water for injection _____ mL/hour via UAC

Other IV
- ____________________________ infusion _____ mL/hour via _________
- ____________________________ infusion _____ mL/hour via _________

Additives
- Heparin 0.25 unit/mL

IV Bolus or Rapid Infusion
- D10W bolus infusion by _____ mL give over _____ minutes (2 mL/kg)
- 0.9% NaCl bolus infusion by _____ mL give over _____ minutes (10mL/kg)
Parenteral Nutrition
- Follow orders for Parenteral Nutrition. Refer to local institutional practices until provincial orders available.

Enteral Nutrition
- NPO
- Oral Immune Therapy _____ mL BUCALLY every ____ hours (when expressed breast milk available)
- Minimal enteral feeding _____ mL/kg/day divided every ___ hours (equal to ____ mL per feed) via nasogastric / orogastric tube
  - Neonates hemodynamically stable and normalized lactate levels
    - Expressed breast milk (EBM)
    - Donor human milk (DHM – Parental consent required)

Laboratory Investigations
On initiation of Therapeutic Hypothermia or if not drawn by the Transport

Blood Gases
- Blood Gas Cord Blood: arterial and venous
- Blood Gas:
  - Arterial
  - Capillary
  - Venous
  - Stat
  - Date ______ Time ______

- Blood Gas:
  - Arterial
  - Capillary
  - Venous
  - Stat
  - Date ______ Time ______

Hematology
- Complete Blood Count (CBC) with differential Date ______ Time_______

Microbiology
- Blood Culture Stat
- Other culture ___________

Transfusion Medicine
- Type and Screen Date _____ Time ______

Chemistry
Date ______ Time_____
- Aspartate Aminotransferase (AST)
- Alanine Aminotransferase (ALT)
- Alkaline Phosphatase (ALP)
- Gamma Glutamine Transferase (GGT)
- Creatinine
- Magnesium
- Lactate
- Sodium
- Potassium
- Chloride
- Bicarbonate (HCO₃)
Newborn Metabolic Screen
- Newborn Metabolic Screen  Date _________  Time _________  (Parental consent required)
  Alert: A second metabolic screen should be completed for neonates less than 2000 gm and should be drawn between 21 and 28 days (whether in hospital or not)
- Newborn Metabolic Screen  Date _________  Time _________  (Parental consent required)

Cerebrospinal Fluids
- Cerebral Spinal Fluid Culture and Gram Stain
- CSF Cell Count
- CSF Glucose
- CSF Protein
- CSF Infection Panel (Viral)

Diagnostic Imaging
- General Radiology
  - Chest 1 Projection (AP only)
    - Stat  Date _________  Time _________
  - Chest 2 Projections (AP and Lateral)
    - Stat  Date _________  Time _________
  - Chest 1 Projection Decubitus (RT or LT or dorsal)
    - Stat  Date _________  Time _________
  - Abdomen 1 Projection (AP only)
    - Stat  Date _________  Time _________
  - Abdomen 2 Projections (AP and decubitus (RT or LT or dorsal decub or upright)
    - Stat  Date _________  Time _________
  - Chest and Abdomen Pediatric 1 Projection
    - Stat  Date _________  Time _________
  - Chest and Abdomen Pediatric 2 Projections
    - Stat  Date _________  Time _________
- MR
  - MR - Brain  Date _________
  - Clinical Indication: □ Hypoxic ischemic encephalopathy

Cardiovascular
- Electrocardiograph (ECG) 12 Lead at initiation of cooling therapy

Clinical Neurophysiology
- Electroencephalograph – Complete EEG:
  - at initiation of cooling therapy within the first 24 hours
  - At rewarming Date _________
- Amplitude-Integrated EEG - Continuous
- Electroencephalograph – NICU continuous video EEG – throughout Therapeutic Hypothermia.

Respiratory Care
- Oxygen therapy  to maintain target O$_2$ saturation between ____and ____
- Low flow nasal cannula at _____liter per minute
- Heated humidified high flow nasal cannula at _____ litre per minute
- CPAP
  - Pressure _____cmH$_2$O
BIPAP:
- High Pressure______cmH₂O
- Low pressure______cmH₂O
- Rate______bpm
- Inspiratory Time__________

Endotracheal Intubation

Conventional Ventilation:
- Mode________
- Settings:________________________________________

High Frequency Oscillatory Ventilation:
- Settings:________________________________________

High Frequency Jet Ventilation:
- Settings:________________________________________

Target PCO₂ of _______

CO₂ Monitoring
- End tidal CO₂
- Transcutaneous CO₂

Medications

Analgesics
Recommended dosage 50 mcg/kg/dose to 100 mcg/kg/dose
- morphine _____ microgram IV every 4 hours for pain management

Recommended dosage 5 mcg/kg/hour to 40 mcg/kg/hour
- morphine continuous infusion _____ microgram/kg/hour IV

Recommended dosage 1 mcg/kg/dosage to 2 mcg/kg/dosage
- fentaNYL _____ microgram IV PRN for pain management

Recommended dosage 0.5 mcg/kg/hour to 3 mcg/kg/hour
- fentaNYL continuous infusion _____ microgram/kg/hour IV

Anti-Seizure
Recommended initial loading dose 20 mg/kg then 10-20 mg/kg up to 40 mg/kg
- pHENobarbital _____ mg IV once

Recommended dosage 3 mg/kg/day to 5 mg/kg/day
- pHENobarbital _____ mg IV daily

Recommended loading dose 20 mg/kg up to 30 mg/kg
- levetiracetam _____ mg IV once

Recommended dosage 10 mg/kg/day to 30 mg/kg/day; additional increases up to 45-60 mg/kg/day have been used with persistent seizure activity or clinical EEG findings.
- levetiracetam _____ mg IV daily

Recommended loading dose 10-15 mg/kg/day to 20 mg/kg/day
- fosphenytoin _____ mg Phenytoin Equivalent IV once

Recommended dosage 5 mg PE/kg/day to 8 mg PE/kg/day
- fosphenytoin _____mg Phenytoin Equivalent IV every 12 hours

Recommended loading dose 10-15 mg/kg/day to 20 mg/kg/day
- phenyTOIN _____ mg IV once
Recommended dosage 5 mg/kg/day to 8 mg PE/kg/day
☐ phenyTOIN _____mg IV every 12 hours

Recommended dosage 0.1 mg/kg
☐ LORazepam _____ mg IV once. May give up to 2 doses

Recommended dosage 10 mcg/kg/hour to 60 mcg/kg/hour
☐ midazolam infusion ______ mcg/kg/hour IV continuous

Antibiotics
Recommended dose 50 mg/kg/dose
☐ ampicillin ______ mg IV once ASAP
AND
Recommended dose 50 mg/kg/dose
☐ cefoTAXime ______ mg IV every ______ hours

Referrals
☐ Refer to Newborn Hearing Screening Program
   Important:
   • Do not screen infants with meningitis (proven or suspected) or aural atresia. Refer
directly to diagnostic hearing assessment.
   • Babies greater than or equal to 48 hours in NICU, will follow the NICU protocol for
newborn hearing screening.
   • Babies need to be greater than or equal to 34 weeks post menstrual age at the time
of screening.
   • Babies need to be medically stable (off CPAP, off HFNC, on room air or LFNC) at
the time of screening.

Other Referrals
☐ Consult Pediatric Neurology
☐ Consult Pediatric Neuro-Critical care Neurologist
☐ Lactation Consultant
☐ Social Work
☐ Psychology
☐ Spiritual Care
☐ Dietitian
☐ Other
Therapeutic Hypothermia Re-Warming (Designated Cooling Centres)

Order Set Restrictions: For neonates’ greater than or equal to 35 weeks gestation with hypoxic ischemic encephalopathy and who have undergone therapeutic hypothermia

Order Set Keywords: therapeutic, hypothermia, hypoxic, encephalopathy, HIE, re-warming

Order Set Requirements: Weight, Gestational Age, Time of Birth

Risk Assessment/Scoring Tools/Screening: N-PASS/PIPP

Safety and Precautions
- Ensure radiant heat warmer probe is attached to the neonate

Parenteral Nutrition
- Follow orders for Neonatal Parenteral Nutrition. Refer to local institutional practices until provincial orders available.

Enteral feeding
- Enteral Feeds ______ mL/kg/day divided every _____ hours (equal to _____ mL per feed) orally/ via nasogastric / orogastric tube
- Increase enteral feeds by ____ mL/kg/day
- Expressed Breast Milk
- Donor Human Milk (DHM – parental consent required)
- Infant formula____________
- Trophic Feeds ______ mL/kg/day (Include in total fluid intake TFI)

Monitoring and Patient Care
- Initiate re-warming protocol: Increase the temperature 0.5°C every hour. (It should take 6 hours to obtain normal skin core temperature)
- Vital Signs
  - Temperature
    - Every 30 minutes during the re-warming phase until stable for 2 hours
    - Then every hour for another 2 hours
    - Then every 4 hours
  - Clinical Communication: when the temperature reaches 36.5°C
    - Remove cooling blanket
    - Remove rectal probe.
    - Reactivate the radiant warmer at 0.5°C higher than the neonate’s current temperature (per servo control)
  - Pulse (P), Respirations (R) and Blood pressure (BP), Oxygen Saturation (SpO2) every hour during the re-warming phase
  - Notify: Neonatologist of any signs of hypotension, (Appendix E) and any signs of arrhythmia
- Call MD/Designate to compete neurological assessment (Appendix D) at reaching rewarming temperature and discharge or 7 days of age, which is earlier.
Clinical Decision Support

CDS Requirements:

- Assist – Calculator to determine if neonate meets the criteria for Therapeutic Hypothermia

- Available Therapeutic Hypothermia cooling calculator app to assist with determining eligibility for therapeutic hypothermia:
  - [http://thcalculator.appspot.com/Main.html](http://thcalculator.appspot.com/Main.html)
References


Relevant Guidelines and Protocols

Available on AHS Insite

- AHS Edmonton Zone
  - [https://insite.albertahealthservices.ca/tools/policy/Page12025.aspx](https://insite.albertahealthservices.ca/tools/policy/Page12025.aspx)
    - See Neurological section:
      - **Body Cooling**
        - Therapeutic Hypothermia HCS-G-1 guideline
        - Information Sheets
          - Parent Information Sheet
          - Cooling Inclusion Criteria
          - Cooling Exclusion Criteria
          - Hypothermia Blood Work
          - Tips for Blanketrol III
          - Cooling Complications

- AHS Calgary Zone
  - [https://insite.albertahealthservices.ca/tools/policy/Page11035.aspx](https://insite.albertahealthservices.ca/tools/policy/Page11035.aspx)
    - See section H:
      - **Hypothermia** - Neuroprotection Package for Hypoxic Ischemic Encephalopathy (HIE)
        - HIE Bundle: Background
        - HIE Bundle: Procedure
        - HIE Bundle: Procedure for Transport
        - Resource: Parent Information
    - See section S:
      - **Seizure**
        - Investigation and Management 2-S-5

Protocols Available on External AHS site

- AHS Provincial – Environmental Lighting Control:

- AHS Provincial – Environmental Noise Control:

Additional Guidelines

- [Canadian Pediatric Society Position Statement: Hypothermia for newborns with hypoxic-ischemic encephalopathy](https://www.nice.org.uk/ipg347)
Appendix A – Suspected HIE Eligibility Pathway

Infant with Encephalopathy and suspected HIE

Ensure stabilization: Airway, Breathing, Circulation
Allow for 1 hour of transition

GA ≥ 35 weeks?
AND
Age < 6 hours

NO

Not eligible for Therapeutic Hypothermia

YES

Apgar ≤ 5 at 10 min
OR
PPV at 10 min

NO

Assess cord gas OR postnatal blood gas within 1 hour of age

pH ≤ 7
OR
BE ≤ -16

NO

Assess for moderate or severe encephalopathy using Encephalopathy Tool

Moderate or severe encephalopathy?

NO

Not eligible for Therapeutic Hypothermia

YES

Eligible for Therapeutic Hypothermia:
Turn off radiant warmer
Remove heat sources
Insert rectal thermometer
Check temp every 15 min

NO

Go to HIE Management Algorithm

Call RAAPID
North: 1-800-282-9911
South: 1-800-661-1700
Use Telehealth if available
### Appendix B – Therapeutic Hypothermia Eligibility Tool

**PART 1: Hypoxic Ischemic Encephalopathy Serial Assessment and Therapeutic Hypothermia Eligibility Tool**

<table>
<thead>
<tr>
<th>Date of Birth:</th>
<th>Time of Birth:</th>
<th>Gestational Age:</th>
</tr>
</thead>
</table>

#### Criteria A (any of):
- □ Cord or first pH ≤ 7;
- □ Base Excess ≤ -16;
- □ Apgar ≤ 5 at 10 minutes;
- □ IPPV 10 min or greater

**Apgar score:**
- 1
- 5
- 10
- 20

**Birth weight (g):**

<table>
<thead>
<tr>
<th>Arterial Gas:</th>
<th>Venous Gas:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Cord</td>
<td>□ Postnatal, Age ___ min</td>
</tr>
<tr>
<td>□ Cord</td>
<td>□ Postnatal, Age ___ min</td>
</tr>
</tbody>
</table>

**pH:**
- Base Excess:

#### Complete a full assessment at ALL three times points below

<table>
<thead>
<tr>
<th>After Stabilization /1 Hour</th>
<th>Location:</th>
<th>Date/Time:</th>
<th>Provider:</th>
</tr>
</thead>
</table>

#### Encephalopathy Staging:
- Normal
- Mild
- Moderate
- Severe

1. Level of consciousness
2. Spontaneous activity
3. Posture
4. Tone
5. Primitive reflexes:
6. Autonomic system:

#### Seizure (clinical or electrographic)

---

**Eligible for TH:** any Criteria A AND (seizure OR at least 3 moderate/severe of the 6 major assessment categories)?

---

**At 2-3 hours of age:**

<table>
<thead>
<tr>
<th>Location:</th>
<th>Date/Time:</th>
<th>Provider:</th>
</tr>
</thead>
</table>

#### Encephalopathy Staging:
- Normal
- Mild
- Moderate
- Severe

1. Level of consciousness
2. Spontaneous activity
3. Posture
4. Tone
5. Primitive reflexes:
6. Autonomic system:

#### Seizure (clinical or electrographic)

---

**Eligible for TH:** any Criteria A AND (seizure OR at least 3 moderate/severe of the 6 major assessment categories)?

---

**At 4-6 hours of age:**

<table>
<thead>
<tr>
<th>Location:</th>
<th>Date/Time:</th>
<th>Provider:</th>
</tr>
</thead>
</table>

#### Encephalopathy Staging:
- Normal
- Mild
- Moderate
- Severe

1. Level of consciousness
2. Spontaneous activity
3. Posture
4. Tone
5. Primitive reflexes:
6. Autonomic system:

#### Seizure (clinical or electrographic)

---

**Eligible for TH:** any Criteria A AND (seizure OR at least 3 moderate/severe of the 6 major assessment categories)?

---

**aEEG Interpretation:**
- □ Not applied
- □ Continuous
- □ Discontinuous
- □ Burst suppression
- □ Isoelectric

**Document most severe tracing in 6 hours after birth. Do not interpret aEEG within 30 minutes of anticonvulsant administration.**

**Therapeutic Hypothermia:**
- □ None
- □ Passive - start time:
- □ Active - start time:

---

* Decorticate: strong distal flexion, full extension; Decerebrate: arms extended and internally rotated, legs extended with feet in forced plantar flexion
** Includes focal or generalized hypotonia

---

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---

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### Hypoxic Ischemic Encephalopathy (HIE) – All Level Nurseries

**Management Pathway**

**RESPIRATORY**
- Apnea, Cyanosis, Tachypnea, Distress
- Monitor SpO2
  - Send blood gas
- Consider respiratory support (invasive / noninvasive)
- Avoid:
  - Hypocapnea (<35)
  - Hypercapnea (>60)
  - Hypoxia
- SpO2 90-95%
- pH 7.3 - 7.4

**HEMO DYNAMIC**
- HR > 180 bpm, CRT > 3 sec, Pailor, Lactic acidosis, Hypotensive (MAP < GA)
- Evidence of hypovolemia?
  - (abruption, subgaleal hemorrhage)
  - Consider Volume expanders (NS or O Rh negative blood)
  - HR 80 - 160
  - MAP ≥ GA

**GLUCOSE AND FLUIDS**
- Is glucose < 2.6?
  - YES: Start IV D10W at 60 mL/kg/d
  - NO: Start IV D10W at 50 mL/kg/d
  - Monitor glucose every 30 min
  - Is glucose stabilizing?
    - YES: Monitor glucose as appropriate
    - NO: Give IV D10W bolus of 2 mL/kg
  - Glucose ≥ 2.6

**THERAPEUTIC HYPOThERMIA**
- Decision made for cooling
  - Turn off radiant warmer and umbilicate infant
  - Auxiliary temp (with appropriate probe)
  - Is temp < 33°C?
    - YES: Put hat & light blanket on infant. Recheck temp; if remains low, turn on warmer to 0.5°C above infant’s temp
    - NO: Monitor Temp every 30 min
  - Ambient temp 25 - 26°C
  - Core temp 33 - 34°C

**SEIZURE**
- Abnormal, rhythmic movements not suppressed by holding; Eye deviation /staring /flickering; Sudden, abrupt movements (myoclonus) + vital sign changes (desat, apnea, tachycardia, or hypertension)
- 1. Maintain ABC
- 2. Give phenobarbital IV 20 mg/kg/d
- 3. Consult Neonatologist
- If seizures persist:
  - Give another dose phenobarbital IV 20 mg/kg/d after discussion with Neonatologist
- Seizure control

**INFECTION**
- Is sepsis suspected?
  - YES:
    - Draw: blood culture and CSF culture (if meningitis suspected and baby is stable)
    - Start: Ampicillin IV 50 mg/kg/dose (increase to 100 mg/kg if meningitis suspected) and Gentamicin IV 50 mg/kg/dose
    - Consult local monographs if repeated doses required before Transport Team arrives
  - Early antibiotics administration
## Appendix D – Neurological Assessment during and after Therapeutic Hypothermia

### PART 2: Hypoxic Ischemic Encephalopathy:

Serial Neurological Assessment for Infants Receiving Therapeutic Hypothermia

<table>
<thead>
<tr>
<th>Date of Birth:</th>
<th>Time of Birth:</th>
<th>Gestational Age:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Initiation of Active Cooling (Date/Time):**

- Highest lactate: □ Yes □ No
- Inotropes: □ Yes □ No
- Renal Failure: □ Yes □ No
- DIC: □ Yes □ No

**Complete a full assessment at ALL three time points below**

#### Hour 24 of Cooling:

**Location:**

- Date/Time:
- Provider:

**Encephalopathy Staging:**

<table>
<thead>
<tr>
<th>Level of consciousness</th>
<th>Spontaneous activity</th>
<th>Posture</th>
<th>Tone</th>
<th>Primitive reflexes:</th>
<th>Autonomic system:</th>
<th>Seizure (clinical or electrographic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>No</td>
</tr>
<tr>
<td>Mild</td>
<td>Mild distal flexion</td>
<td>Hypertonia</td>
<td>Hypertonia</td>
<td>Weak</td>
<td>Dilated</td>
<td>No reaction</td>
</tr>
<tr>
<td>Moderate</td>
<td>Decorticate</td>
<td>Constricted</td>
<td>Constricted</td>
<td>Decreased</td>
<td>Incomplete</td>
<td>No activity</td>
</tr>
<tr>
<td>Severe</td>
<td>Decerebrate</td>
<td>Variable/no reaction</td>
<td>Variable/no reaction</td>
<td>No activity</td>
<td>Absent</td>
<td>Yes</td>
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</table>

**Normothermia:**

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<th>Level of consciousness</th>
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</tr>
<tr>
<td>Severe</td>
<td>Decerebrate</td>
<td>Variable/no reaction</td>
<td>Variable/no reaction</td>
<td>No activity</td>
<td>Absent</td>
<td>Yes</td>
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</table>

**7 days of age OR at Discharge:**

<table>
<thead>
<tr>
<th>Level of consciousness</th>
<th>Spontaneous activity</th>
<th>Posture</th>
<th>Tone</th>
<th>Primitive reflexes:</th>
<th>Autonomic system:</th>
<th>Seizure (clinical or electrographic)</th>
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<td>Constricted</td>
<td>Decreased</td>
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<td>No activity</td>
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<tr>
<td>Severe</td>
<td>Decerebrate</td>
<td>Variable/no reaction</td>
<td>Variable/no reaction</td>
<td>No activity</td>
<td>Absent</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Seizure (clinical or electrographic):**

- No □ Yes □ Yes

**Date of Birth:**

- Date/Time:
- Provider:

**Initiation of Rewarming (Date/Time):**

- Highest lactate: □ Yes □ No
- Inotropes: □ Yes □ No
- Renal Failure: □ Yes □ No
- DIC: □ Yes □ No

**Complete at 7 days of age or discharge (whichever comes first):**

* Decorticate: strong distal flexion, full extension; Decerebrate: arms extended and internally rotated, legs extended with feet in forced plantar flexion

**Includes focal or generalized hypotonia

### Morbidities/Adverse events (check any that apply):**

- Subcutaneous fat necrosis
- Multiple anticonvulsants for seizure control
- Anticonvulsants(s) at discharge
- Cardiac arrhythmia
- Thrombocytopenia (<20 *10^9/L)
- Coagulopathy
- Tube feeds at discharge
- Intracranial hemorrhage: ______________________
- Death
- Other: ______________________

### MRI findings:

- Normal
- Mild
- Moderate
- Severe

### EEG findings (after rewarming):

**Patient Label**

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## Appendix E – Normal Blood Pressure Values by Gestational Age

Normal blood pressure values by gestational age for day one (Mean±95% C.I. for the highest and lowest values)\(^{23}\)

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Adapted from Zubrow, Hulman, Kushner, & Falkner, 1995\(^{23}\)
Appendix F – Electroencephalography (EEG) Patterns

Background assessment is the most important value of amplitude integrated EEG:

1. The lower border of the band should be above 5 μV most of the time regardless of the pattern
2. Isoelectric and burst suppression patterns are always abnormal
3. Discontinuous pattern with normal background is normal in late preterm infants but abnormal in term infants
4. Seizure is always abnormal

Isoelectric trace (always abnormal): note the raw EEG (upper green screen) is flat, the lower screen (aEEG) lower border is almost at 0 μV with few spikes below 10 μV
Burst suppression trace (always abnormal): the raw EEG (upper green screen) is mostly suppressed with a burst (arrows) in between. The lower screen (aEEG) lower border is almost at 0 µV with spikes above 10 µV

Discontinuous trace (normal in prematurity): the raw EEG shows two distinct patterns, low frequency high amplitude (1) and high frequency low amplitude (2) in between. The aEEG background can be abnormal (lower border below 5 µV) or normal (lower border above 5 µV). The aEEG shows (wide) band
Continuous trace: the raw EEG shows mixt frequencies and amplitudes. The aEEG (lower screen) band is narrow and lower border is above 5 µV (normal)

Sleep-Wake Cycle (normal): aEEG shows normal background (lower border above 5 µV) with a combination of two patterns: continuous (1) during wakefulness and REM and discontinuous during deep sleep (2)
Seizure (always abnormal, arrows): raw EEG shows regular rhythmic spikes (arrows). aEEG shows abrupt elevation in the lower and upper border (arrows)
### Appendix G – NPASS - Neonatal Pain, Agitation, & Sedation Scale

**NPASS - Neonatal Pain, Agitation, & Sedation Scale**

<table>
<thead>
<tr>
<th>Assessment Criteria</th>
<th>Sedation</th>
<th>Normal</th>
<th>Pain / Agitation</th>
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<tr>
<td></td>
<td>-2</td>
<td>-1</td>
<td>0</td>
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<td>1</td>
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<td>2</td>
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<tr>
<td>Crying Irritability</td>
<td>No cry with painful stimuli</td>
<td>Moans or cries minimally with painful stimuli</td>
<td>No Sedation No Pain Signs</td>
</tr>
<tr>
<td>Behaviour State</td>
<td>No arousal to any stimuli No spontaneous movement</td>
<td>Aroused minimally to stimuli Little spontaneous movement</td>
<td>No Sedation No Pain Signs</td>
</tr>
<tr>
<td>Facial Expression</td>
<td>No expression</td>
<td>Mouth is lax</td>
<td>No grasp reflex Flaccid tone</td>
</tr>
<tr>
<td>Extremities Tone</td>
<td>No variability with stimuli Hypoventilation or apnea</td>
<td>No Sedation No Pain Signs</td>
<td>No Sedation No Pain Signs</td>
</tr>
<tr>
<td>Vital signs HR, RR BP, SaO2</td>
<td>No Sedation No Pain Signs</td>
<td>No Sedation No Pain Signs</td>
<td>No Sedation No Pain Signs</td>
</tr>
</tbody>
</table>

**Assessment of Sedation**
- Sedation is scored in addition to pain for each behavioural and physiological criterion to assess the infant’s response to stimuli.
- Sedation does not need to be assessed/scored with every pain assessment score.
- Sedation is scored 0 to 2 for each behavioural and physiological criterion, then summed and noted as a negative (0 to -10).
- A score of 0 is given if the infant’s response to stimuli is normal for their gestational age.
- Desired levels of sedation vary according to the situation:
  - “Deep sedation” score of -10 to -5 as goal
  - “Light sedation” score of -5 to -2 as goal
  - Deep sedation is recommended only if the infant is receiving ventilatory support, related to the high potential for apnea and hypoventilation.
- A negative score without the administration of opioids/sedatives may indicate:
  - The premature infant’s response to prolonged or persistent pain/stress
  - Neurologic depression, sepsis, or other pathology

**Chemical Paralysis**
- It is impossible to behaviorally evaluate a paralyzed infant for pain. Increases in HR and BP may be the only indicator of a need for more analgesia. Analgesics should be administered continuously by infusion or around-the-clock dosing.
- Higher, more frequent doses may be required if the infant is post-op, has a chest tube, or other pathology that would normally cause pain. Opioid doses should be increased by 10% every 3 to 5 days as tolerance will occur without symptoms of inadequate pain relief.

**Assessment of Pain / Agitation**
- Pain assessment is the fifth vital sign and should be included with every vital sign assessment (minimum once per shift).
- Pain is scored from 0 to 2 for each behavioural and physiological criterion, then summed.
- Points are added to the premature infant’s pain score based on their gestational age to compensate for their limited ability to express pain.
- Total pain score is documented as a positive number (0 to +10).
- Treatment/interventions are indicated for scores greater than 3.
- Assessments are performed before and after potentially painful procedures and following pain-relieving interventions.
- The goal of pain intervention is a score less than or equal to 3.
- More frequent pain assessment indications:
  - Indwelling tubes or lines which may cause pain, especially with movement (e.g. chest tubes) → at least every 2 to 4 hours
  - 30 minutes after a non-pharmacological intervention and/or analgesic is given for pain behaviors to assess response.
  - Receiving analgesics and/or sedatives → min 2 to 4 hrs.
  - Post-operative – at least every 2 hours for 24 to 48 hours, then every 4 hours until off medications.

**NPASS - Neonatal Pain, Agitation, & Sedation Scale**

Pat Hummel, MA, RNC, NNP, PNP & Mary Puchalski, MS, RNC

Loyola University Health System, Loyola University Chicago, 2005 (rev. 2/1/09) Pat Hummel, MA, APN, NNP, PNP

+1 for pain/agitation score if less than 30 weeks gestation/corrected age
NPASS - Neonatal Pain, Agitation, & Sedation Scale

Scoring Criteria

Crying / Irritability
-2 No response to painful stimuli; e.g., No cry with needle sticks; No reaction to ETT or nurse suctioning; No response to care giving
-1 Moans, sighs, or cries (audible or silent) minimally to painful stimuli such as needle sticks, suctioning or care giving.
0 Not Irritable – appropriate crying
+1 Infants is irritable/crying at intervals – but can be consoled. If intubated – intermittent silent cry
+2 Any of the following: Cry is high-pitched; infant cries incoherently; If intubated, silent continuous cry.

Behaviour / State
-2 Does not arouse or react to any stimuli; Eyes continually shut or open. No spontaneous movement
-1 Little spontaneous movement arouses briefly and/or minimally to any stimuli. Opens eyes briefly, reacts to suctioning; withdraws to pain
0 Behaviour and state are gestational age appropriate
+1 Any of the following: Restless, squirming, awakens frequently / easily with minimal or no stimuli
+2 Any of the following: Kicking, arching, constantly awake, no movement or minimal arousal with stimulation (inappropriate for gestational age or clinical situation i.e. post-operative)

Facial Expression
-2 Any of the following: Mouth is lax, drooling, no facial expression at rest or with stimuli
-1 Minimal facial expression with stimuli
0 Face is relaxed at rest but not lax – normal expression with stimuli
+1 Any pain face expression observed intermittently
+2 Any pain face expression is continual

Extremities / Tone
-2 Any of the following: No palmar or planter grasp or faceted tone
-1 Any of the following: Weak palmar or planter grasp, or decreased tone
0 Relaxed hands and feet – normal palmar or sole grasp with appropriate tone for gestational age

Extremities / Tone - continued
+1 Intermittent (less than 30 seconds duration) observation of toes and/or hands as clenched or fingers splayed; body is NOT tense
+2 Any of the following: frequent (greater than or equal to 30 second duration) observation of toes and/or hands as clenched, or fingers splayed; body is tense/ stiff

Vital Signs: HR, BP, RR & O₂ Saturations
-2 Any of the following: No variability in vital signs with stimuli, hyperventilation, apnea, No spontaneous respiratory effort for a ventilated infant
-1 Vital signs show little variability with stimuli – less than 10% from baseline
0 Vital signs and/or oxygen saturations are within normal limits with normal variability or normal for gestational age
+1 Any of the following: HR, BP, RR and/or O₂ are 10 to 20% above baseline; with care stimuli infant desaturates minimally to moderately (SaO₂ 76 to 85%) and recovers quickly (within 2 minutes)
+2 Any of the following: HR, BP, RR and/or O₂ are greater than 20% above baseline; with care stimuli infant desaturates severely (SaO₂ less than 75%) and recovers slowly (greater than 2 minutes); infants is out of synchrony with the ventilator – fighting the ventilator
Acknowledgements

We would like to acknowledge the contributions of the clinicians who participated in the development of this topic. Your expertise and time spent are appreciated.

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<td>Knowledge Lead</td>
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<td>Dr. Ayman Abou Mehrem</td>
<td>Provincial Clinical Knowledge Lead</td>
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<tr>
<td>Dr. Elsa Fiedrich</td>
<td>Provincial Clinical Co-Topic Lead</td>
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<td>Dr. Khorshid Mohammad</td>
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<td>Working Group Members</td>
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<td>Dr. Matthew Hicks</td>
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<tr>
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Additional Contributors

Thank you to all provincial stakeholders who participated in the review process for this topic. Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated.

For questions or feedback related to this knowledge topic please contact Clinical Knowledge Topics by emailing ClinicalKnowledgeTopics@albertahealthservices.ca