Management of Ischemic Neonatal Encephalopathy

Once indicated, treatment should be initiated as soon as possible.

To be eligible infant must demonstrate moderate to severe encephalopathy consisting of altered state of consciousness (as shown by lethargy, stupor, or coma) and at least one of the following: Hypotonia, abnormal reflexes, weak or absent suck, clinical seizures, EEG recording of at least 20 minutes duration that shows either moderately/severely abnormal background activity OR seizure.

And one of the following:
- At 10 minutes after birth: Apgar score < 5 / continued need for resuscitation: endotracheal or mask ventilation.
- Acidosis defined as either umbilical cord pH or any arterial pH < 7.0, or a base deficit > 16 mmol/L (or base excess < -16 mmol/L) within 60 minutes of birth (arterial or venous blood).

Contraindications:
- > 48 hours of life at the time of evaluation
- Prenatally diagnosed syndrome or metabolic disorder not compatible with survival
- Evidence of head trauma or skull fracture causing major intracranial hemorrhage

Initiate hypothermia

Initiate EPO

Do NOT do both (unless infant is part of the HEAL clinical trial)
**General Evaluation and Management:**

**Labs:**
1. ABG
2. follow Na and K
3. lactate
4. creatinine
5. troponin
6. AST, ALT
7. PT/PTT
8. CBC and platelets
9. CRP
10. Ammonia (one time)
11. Cortisol if hypotensive

**Imaging:**
1. HUS on arrival
2. MRI of brain with MRS of deep brain nuclei at day of life 10-14

**Other diagnostics:**
1. EEG on admission (following HUS, but do not delay if middle of night and HUS cannot be obtained) to stay in place minimum of 48 hours
2. Neurology consult
3. NIRS probe placed on forehead to stay in place until 24 hours following completion of rewarming

**Further management:**
- **Maintenance of adequate oxygenation:** Modest hypocarbia is usually observed in infants with mild asphyxia who breathe spontaneously; therefore, if mechanical ventilation is required, the PaCO2 should be maintained near 30-35 torr, and the PaO2 around 80 torr. Most asphyxiated infants have compliant lungs, and therefore high levels of PEEP are unnecessary and should be avoided. PaCO2’s of less than 25 torr should be avoided.
- **Restoration of an adequate circulating blood volume and hematocrit,** with subsequent moderate fluid restriction (60-80 ml/kg/day) should be maintained for 3-5 days if cardiac and renal function permit.
- **Seizures should be treated** ([see Seizure Protocol](#)).
- **Bicarbonate** has recently become more controversial as evidence of worsening intracellular pH and respiratory acidosis increase, discuss with attending before use. This dose also provides enough sodium for the first 1-2 days, and sodium is usually not required in maintenance fluids. Persistent metabolic acidosis reflects either inadequate cardiac output or inadequate distribution of cardiac output and should be treated with volume expansion, vasoactive drugs, or both.
• Corticosteroids, diuretics, and other barbiturates are unproven and possibly dangerous and should not be routinely used; their use must be discussed with the attending physician or fellow.
• If there is a concern for infection, a lumbar puncture should be performed to rule out meningitis when the infant is clinically stable.

**EPO Considerations:**
• EPO is not FDA approved for the treatment of HIE, however, there is a growing evidence for its benefit in this population. **Such information may be shared with parents** if deemed appropriate by the attending.
• **Dose:** use recombinant human erythropoietin 1000 U/Kg IV every 48 hours for a total of 6 doses or until discharge whichever is sooner.
• May feed infant once acidosis resolves, and infant is hemodynamically stable without the use of inotropic support.

**Therapeutic Hypothermia Considerations:**

**Hypothermia effects to monitor:**
• prologns the half-lives of medications
• inhibits antimicrobial activity
• creates anticoagulant effects
• increases oxygen consumption
• transient hyperglycemia
• QT prolongation
• significant overcooling (~32ºC) may result in a shutdown of the infant’s peripheral circulation. Rewarming rate should not exceed 0.5ºC per hour to prevent vasodilation, hypotension, and possible seizures (as seen in some animal studies)

**Other considerations:**
• Do not feed during cooling.

**Rewarming after Cooling:**
1) Complete 72 hours of cooling at 33.5ºC.
2) Re-warm patient slowly.
   • Warm by 0.5ºC increments every hour.
   • Use “Gradient Variable Mode” on cooling unit.
     o Set Gradient Variable to ± 5º to limit extreme fluctuations in blanket temperature.
     o Initially increase set point from 33.5ºC to 34.0ºC and monitor patient closely.
     o Adjust set point upward by 0.5º increments every one hour, as tolerated.
   • If not tolerated, re-warming can be delayed or prolonged at attending discretion.
   • Aim to re-warm infant over 6-9 hours with goal rectal temperature: 36.5º - 37.0ºC.
3) Monitor laboratory results: Results may dictate rates of re-warming.
   • *Glucose, Calcium, Potassium, Magnesium* - Send 1 hour after re-warming has begun.
   • *Arterial blood gas* - Send 3 hours after re-warming has begun.
4) Once rectal temperature of 36.5°C achieved for 60 minutes:
   • Discontinue cooling blanket and maintain under radiant warmer as per routine.
   • May also use the “Monitor Only Mode” on the cooling blanket, or monitor rectal temperature on the GE monitor for 24 hours.
   • Goal skin/axillary temperature: 36.5°C-36.7°C and core and core/rectal temperature: 36.7°C-37.0°C.
   • Note: It may take a few hours for skin to self-regulate normal skin temperatures.

**Discontinuing Hypothermia:**
- Require unanimous approval by the NICN Team. *(see Early Exit Guidelines).*
  Apparent improvement in encephalopathy or EEG readings after 6 hours is **NOT** an indication to discontinue treatment.
- Documentation: Indications for cooling and neuro exams should be included in Admission H&P and Daily Progress Notes.
- Adverse events: Patient events are monitored & documented per NICU routine, including bedside flow sheets, blood gas/lab values, and daily progress notes. Significant events are documented in the EMR.

**References:**