Systemic Hypothermia in Neonates With Hypoxemic-Ischemic Encephalopathy (HIE)

1. **Patients with a presumptive diagnosis of hypoxic-ischemic encephalopathy who meet ALL of the following five criteria are eligible for this order set.**

   Check off each positive finding:

   1. Gestational Age greater than or equal to 35 weeks gestation
   2. Birth weight greater than or equal to 1.8 kg
   3. less than or equal to 6 hours since insult occurred
   4. **ONE OR MORE** of the following predictors of severe HIE:

      a) pH less than or equal to 7.0 with base deficit of greater than or equal to16 on arterial blood gas determination (base excess more negative than -16)

      b) pH7.01--7.15 , base deficit 10-15.9 or no blood gas available and acute perinatal event (cord prolapse, heart rate decelerations, uterine rupture) and either

      APGAR less than or equal to 5 at 10 minutes or assisted ventilation at birth required for greater than or equal to 10 min

      Note: If an arterial blood chord or patient blood gas is not available may use a venous gas from the patient for screening criteria.

5. **Seizures or 3 of 6 of the following:**

Clinical Criteria	**Signs of Encephalopathy**	
	Moderate Encephalopathy	**Severe Encephalopathy**
1. Level of consciousness	Lethargic	Stupor/coma
2. Spontaneous activity	Decreased activity	No activity
3. Posture	Distal flexion, complete extension, frog leg posture	Decerebrate
4. Tone	Hypotonia (focal or general), hypertonia (focal or truncal).	Flaccid
5. Primitive reflexes		
Suck	Weak or bite	Absent
Moro	Incomplete	Absent
6. Autonomic system		
Pupils	Constricted	Skew deviation /dilated/non-reactive to light
Heart rate*	Bradycardia	Variable
Respirations	Periodic	Apnea or intubated

***HR** *should only be used as an entry criteria if the patient in normothermic at the time of staging.*

Exclusion Criteria

- Presence of lethal chromosomal abnormalities
- Severe IUGR
- Significant intracranial hemorrhage with a large intracranial hemorrhage (Grade III or intraparenchymal echodensity (Grade IV))(Note: may start hypothermia without obtaining HUS if not immediately available. Should be obtained as soon as possible after the start of hypothermia.)

2. Initiation of Hypothermia Guidelines – First 24 hours

1. Consult HIE team.
2. NPO or consider low volume feeds (trophic) depending on the clinical condition of the neonate
3. VS Q15 X4, then Q30 X2 then Q1^0
4. Record strict I&O
5. Place Foley catheter if urinary output is low, may remove if urine output is deemed adequate
6. Place neonate on servo-controlled cooling device (Blanketrol® III or Criticool®)
7. Place indwelling rectal or esophageal temperature probe.
8. Adjust set temperature to maintain rectal or esophageal temperature in the range of 33.0 to 34.0°C with a target of 33.5°C using servo-controlled cooling blanket. Notify MD or NNP if temperature falls outside this range.
9. Record rectal or esophageal and axillary temperatures q hour
10. Move infant's position on the blanket q 30 minutes to avoid skin injury
11. Set lower heart rate limit at 70.

    Educational Guideline: Cooled babies at temperatures of 33-34°C have mild bradycardia of around 100 bpm. A heart rate consistently above 120 bpm in cooled infants with temperatures of 33-34°C suggests that the infant is distressed or may have volume loss. The bedside clinician may consider increasing the sedation if appropriate. If the sedation if increased and the HR continues to remain, it is recommended to evaluate for potential sources of bleeding such as intracranial or intra-abdominal. Conversely, a heart rate below 70 may lead to decreased cardiac output. The clinician may consider increasing the temperature set point by 0.3°C increments to a maximum of 35°C.
12. Start a continuous opiate infusion at a low dose or intermittent dosing.
13. Laboratory and other studies
    a. Obtain Cranial ultrasound with Doppler flow to measure resistive index as soon as possible

       Educational Guideline: Ordered to rule out other causes of encephalopathy and as an indicator of severity of hypoxic-ischemic injury. If the patient does have a Grade I-II IVH, daily head ultrasounds should be performed to assure that the hemorrhage is not expanding. If the bleeds are extending in spite of optimal replacement of coagulation factors and platelets, rewarming should be considered to control bleeding.

    b. Place cerebral function monitor (aEEG) on patient or obtain continuous video EEG monitoring. Monitor for 72 hours and during rewarming.

    c. Consider echocardiogram due to neonates with HIE having cardiac dysfunction often with the need pressor support and the association of HIE with pulmonary hypertension

    d. Consider renal ultrasound with Doppler flow if the patient has anuria or severe oliguria

    e. Arterial blood gases with lactate q 6 hours

    f. Electrolyte panel with ionized calcium, magnesium, and phosphorus now and q 12 hours while undergoing hypothermia therapy

    g. CBC with differential and platelets now and q 12 hours

    h. PT, INR, PTT, Fibrogen, D-Dimer now and q 12 hours while undergoing hypothermia therapy

       Educational Guideline: consider therapy to maintain PT less than 19, Fibrinogen greater than 100, platelets greater than 50,000 as HIE is associated with increased risk of coagulopathy or bleeding

Educational Guideline: If coagulation profile is abnormal requiring correction, follow-up in 6 hours after treatment. If normal x 2 without replacement, discontinue coagulation profile monitoring

i. Urine dipstick for blood, q 24 hours while undergoing hypothermia therapy

14. Liver function test (LFTs) now and at 24 hours.
15. Accu checks- Q1^0 until 3 consecutive results that are appropriate, then Q2^0 for 4h then Q4^0 for 24h then Q8^0 for 24h.
16. Perform serial Sarnat exams and document results every 24 hours.
17. Place neonate on cerebral oximetry.

Note: if the neonate is clinically improving, the bedside clinician may consider decreasing the lab frequency. If the frequency is decreased, please make sure the frequency is a multiple of the written frequency (ex. Q8 labs changed to Q16 or Q24).

Re-Warming Guidelines (To be performed at 72 hours of cooling)

1. Electrolyte panel with ionized calcium, magnesium, and phosphorus prior to rewarming
Call with results before re-warming and do not re-warm until electrolyte abnormalities are resolved
2. Check vital signs, make sure HR < 120 and BP mean > or = 40. Call if abnormal
3. Re-warm infant by increasing the set temperature on the servo controlled cooling blanket by 0.1-0.5 ˚C every hour until patient temperature is 36.5 degrees C, then discontinue cooling blanket
4. During re-warming, VS q 1 hour
5. If infant begins to have seizures during the re-warming process, stop re-warming and maintain infant at current temperature until seizures are under control
6. After re-warming is completed, manage radiant warmer per nursery routine
7. Diffusion Weighted MRI with spectroscopy at 4-5 days of life and again at 7-12 days of life.
If only 1 MRI can be obtained, it should occur at 7-12 days of life.
Educational Guideline: Diffusion Weighted MRI (performed with all studies) and Spectroscopy (needs to be ordered separately) are adjuncts in determining prognosis.

Twenty-four (24) Hours after re-warming
1. PT, Fibrinogen, D-Dimer
2. Urine dipstick for blood
3. CBC with differential and platelets
4. Electrolyte panel with ionized calcium, magnesium, and phosphorus

Follow-up Studies
Refer to Early Steps Program

Management of Outborn Neonates Eligible for Systemic Hypothermia

Instructions for outside facility

Monitoring Instructions:

1. Monitor core (rectal) temperature closely (continuous or intermittent)
2. Continuous rectal temperature monitoring (preferred method, if available)
   a. Gently insert lubricated rectal probe to approx 6cm, tape to thigh
   b. Document temperature and vital signs every 5-15 minutes (on flow sheet)
3. Intermittent rectal temperature checks (until transport team arrives)
   a. Gently insert lubricated thermometer rectally ~2cm
   b. Document temperature and vital signs every 5-15 minutes (on flow sheet).

Educational Guideline: **Temperature Conversion Chart (˚C =>˚F)**

- ^{o}C to ^{o}F Conversion formula: $^{o}C = 5/9 \times (^{o}F-32)$
  - 30.0˚C = 86.0˚F
  - 33.0 ˚C = 91.4˚F
  - 33.5˚C = 92.3˚F ←Target Temperature
  - 34.0˚C = 93.2˚F
  - 37.0˚C = 98.6˚F

Passive Hypothermia Instructions:

1. Turn off radiant warmers.
2. A target core (rectal) temperature of 33.5˚C.
   Educational guideline: Cooled babies have depressed metabolism, so generate less heat
   If baby has never been warmed: they are easily overcooled, even passively.
3. If the temperature drops below 33.0˚C, turn the radiant warmer on with a temperature set at 0.5˚C above the current temperature. May increase by 0.5˚C every 30 minutes until the temperature is at the target of 33.5˚C. At this point, the radiant warmer can be discontinued. If the temperature drops below the target temperature of 33.5˚C, this procedure may be repeated.

Mild HIE

If a neonate who has a:

1. Gestational Age greater than or equal to 35 weeks' gestation
2. Birth weight greater than or equal to 1.8 kg
3. less than or equal to 6 hours since insult occurred

And has biochemical evidence of a possible hypoxic-ischemic insult as evidenced by:
a) pH less than or equal to 7.0 with base deficit of greater than or equal to16 on arterial blood gas determination (base excess more negative than -16)
b) pH7.01--7.15, base deficit 10-15.9 or no blood gas available and acute perinatal event (cord prolapse, heart rate decelerations, uterine rupture) and either:
APGAR less than or equal to 5 at 10 minutes or assisted ventilation at birth required for greater than or equal to 10 min
c) or a difficult birth or resuscitation

However, the baby does not have seizures, meet 3 of the 6 of the neurologic exam criteria for entry into the therapeutic hypothermia. The bedside clinician should consider:

1. Serial neurologic exams for the first 6 hours of life. Consider admission to the NICU for close monitoring.
2. Monitor temperature closely and prevent from becoming warmer than 37^0C.
3. If the bedside clinician is very concerned about possible injury, ie. There was a sentinel event such as an abruption, the pH was less than 7.0 on a cord gas, the clinician may consider:

a. LFTs (abnormal with an AST or ALT above 100) [1]
b. Cardiac enzymes (Tropinin T (greater than 0.1) or I and CK total and CK-MB (greater than 25 IU/l) [1]
c. Lactic acid (greater than 7.5) [1]
d. Coagulation studies
e. NICHD hypothermia score
f. May consider aEEG monitoring for 30 minutes to determine background pattern.

Labs should be drawn at 1 hour of age [1].

1. Shah, S., M. Tracy, and J. Smyth, Postnatal lactate as an early predictor of short-term outcome after intrapartum asphyxia. J Perinatol, 2004. 24(1): p. 16-20.