Eligibility Criteria for Therapeutic Hypothermia

UCSF Neuro Intensive Care Nursery (NICN)

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Eligibility criteria *to be considered* for cooling: *Must fulfill all three criteria*

I	Infants **≥ 36 weeks** gestational age and **≤ 6 hours** of age
I	**ONE** or more of the following: **A. Low Apgar score** • ≤ 5 at 10 minutes **B. Prolonged resuscitation at birth** • chest compressions, intubation, or mask positive pressure ventilation at 10 minutes **C. Severe acidosis** • pH ≤ 6.99 from cord or patient blood gas within 60 minutes of birth **D. Abnormal Base Excess** • ≤ -12 mmol/L in cord gas or blood gas within 60 minutes of birth
III	**THREE** or more signs of encephalopathy at any time between **1-6 hours** after birth: *(see Appendix A: Encephalopathy Scoring Worksheet at end of document for more details)* A. Altered level of consciousness (decreased or hyperalert) B. Abnormal spontaneous activity C. Abnormal posture D. Abnormal tone (hypotonia or hypertonia) E. Abnormal reflexes (suck, moro, gag) F. Abnormal autonomic response (pupils, apnea or intubated for insufficient respiratory drive) *Note: In cases where no exam available, abnormal aEEG/seizures may qualify (discuss with NICN)*

Exclusion Criteria:

- < 36+0 weeks gestational age or age > 6 hours of age at time of referral/evaluation
  - Current evidence shows limited/no benefit and potential harm with therapeutic hypothermia in infants <36+0 weeks gestation (Faix et al., *JAMA Pediatr*, 2025, 179(4):396-406).
  - Take steps to prevent secondary brain injury (consult NICN, review "Non-Qualifier Guidelines")
- Coagulopathy with active bleeding not responding to interventions
- Malformations, syndromes, or metabolic disorders that carry high risk of hemodynamic instability during cooling (such as CDH, hydrops, and cardiac anomalies with single ventricle physiology)

If any questions regarding eligibility, please discuss with the NICN team and Neonatology attending

Identification of Infants:

- Staff (MD, NNP, RN) to identify patients eligible for cooling as soon as possible after birth
  - ✓ **Qualifying neurological exam** between 1-6 hours after birth should be documented or attested by the Neonatology Attending.
- Neonatal Clinical Laboratory/RN to notify provider (MD, NNP) of panic values from cord/1st blood gas
  - ✓ **pH ≤ 6.99** (cord blood gas or 1st patient blood gas)
  - ✓ **Base excess equal to or worse than -12 mmol/L** (cord blood gas or 1st patient blood gas)

TIP SHEET: Therapeutic Hypothermia (Cooling) for Neonatal Encephalopathy

UCSF Neuro Intensive Care Nursery (NICN)

UCSF Access Center (877-822-4453)

1) **Identify patients that might benefit from cooling within 6 hours of birth**
   a. After initial resuscitation and stabilization, consider if patient is appropriate candidate

MUST BE	**a. ≥ 36 weeks gestational age** and **≤ 6 hours** of age
WITH	**b. One or more of the following:** **i. Low Apgar Scores: ≤ 5 at 10min of life** **ii. Prolonged Resuscitation: e.g. chest comp, ETT/mask vent at 10 min life** **iii. Severe Acidosis: pH ≤ 6.99 from cord or 1st patient gas** **iv. Severe Base Excess: ≤ -12 mmol/L from cord or 1st patient gas**
AND	**c. Encephalopathy (*see Encephalopathy Scoring Worksheet*)**

2) **Contact UCSF Access Center (877-822-4453)** – Discuss if patient is appropriate for cooling
   a. Contact early, contact often
3) **Turn down/off external heat sources and avoid hyperthermia**
   a. Document time and *do not actively cool patients.* (Passive cooling ok)
4) **Monitor core (rectal) temperature** – Continuously (if equipped) or often (with thermometer)
   a. *Target rectal temperature = **33.5˚C** (92.3˚F)*
   b. Check temperature frequently *(e.g., every 15 minutes)* and record on flow sheet.
   c. Core temp may fall <33.5˚C with passive cooling. Be prepared to restart low-heat if needed
5) **Secure vascular access** – Before peripheral vasoconstriction occurs with cooling
   a. *Umbilical venous and arterial access*, if possible
   b. Peripheral IV at a minimum
6) **Maintain adequate sedation** – Keep patient comfortable. Avoid shivering and minimize cold stress.
   a. *Morphine: 0.05-0.1mg/kg IV*, then *0.05mg/kg q6* and *prn* until transport team arrives
7) **Treat only clinical seizures** – No prophylactic dosing
   a. *Lorazepam (Ativan): 0.1mg/kg IV*, repeat once as needed for suspected seizures
   b. Phenobarbital: 20mg/kg IV, repeat once as needed for confirmed seizures
8) **Expect these physiologic states in cooled infants** – Avoid over reacting and monitor trends
   a. Heart rate may appropriately fall (even <100bpm) as patient reaches <34°C
   b. Manage blood pressure and oxygenation as usual. Maintain normal values
   c. Consider volume replacement therapy with normal saline or colloid if perfusion compromised. Otherwise, consult Regional Center for management of persistent acidosis or hypotension
9) **Monitor electrolytes closely -** maintain within normal ranges
   a. Fluctuations often seen in *Ca, K, Mg* and *Glucose* levels with cooling
10) Avoid **over ventilation** and **over oxygenation.** Both may exacerbate risk of brain injury
   a. Target pCO2=45-55
   b. PaO2 should be < 100mmHg and oxygen saturation goal 92-97%
11) Send **Blood cultures** and consider starting **Ampicillin** and **Gentamicin**
   a. Send other labs if urgently indicated, but do not delay transport for routine labs

Management of Outborn Infants Eligible for Cooling

UCSF Access Center (877-822-4453)

1) UCSF Access Center RN (**877-822-4453**) to identify **babies potentially *eligible* for cooling:**
   - Screen potential candidates by the following criteria (see also *Eligibility Criteria* sheet):
     - **≥ 36 weeks** and **≤ 6 hours** of life
     - **Prolonged resuscitation at birth**. (One or more of following)
       - ✓ Low Apgar Scores: **≤ 5** at **10 minutes**
       - ✓ Severe acidosis: **pH ≤ 6.99**
       - ✓ Base excess: **≤ -12 mmol/L**
     - **THREE or more signs of encephalopathy at any time between 1-6 hours after birth:** (*see Appendix A: Encephalopathy Scoring Worksheet at end of document*)
       - ✓ Altered level of consciousness (decreased or hyperalert)
       - ✓ Abnormal spontaneous activity
       - ✓ Abnormal posture
       - ✓ Abnormal tone (hypotonia or hypertonia)
       - ✓ Abnormal reflexes (suck, moro, gag)
       - ✓ Abnormal autonomic response (pupils, apnea or intubated for insufficient respiratory drive)
   - **Discussed with UCSF ICN attending on-call (877-822-4453)** within **6 hours** of birth
   - FAX/email information to referring MD if UCSF ICN attending recommends passive cooling:
     - ***Management Guidelines for Outborn Infants Eligible for Cooling*** (this sheet)
     - ***Parent Information Sheet***

2) **Take immediate steps to minimize ongoing brain injury**
   - **Provide ABCs**
     - Resuscitate and support per NRP guidelines
       - ✓ May include intubation, mechanical ventilation and pharmacologic support
   - **Turn down/off radiant warmers or heaters. Infants should not be warmed.**
   - **Prevent secondary brain injury**
     - Avoid *hyperoxia* (goal O2 sat 92-97% with PaO2 <100mmHg)
     - Avoid *hypocarbia* (goal pCO2 45-55mmHg)
     - Avoid *hypoglycemia* (maintain serum glucose levels > 60)
     - Appropriately volume resuscitate before providing base replacement (e.g., bicarb).

3) **PASSIVE COOLING: Eligible infants should NOT be actively cooled** at outside hospital
   - **TURN OFF RADIANT WARMERS *or* ISOLETTE HEATERS**
   - **CRITICAL IMPORTANCE: Monitor core (rectal) temperature and document with vital signs every 10-15 minutes**
     - **Continuous rectal temperature monitoring** (preferred method, if available)
       - ✓ Gently insert lubricated rectal probe to approx 6cm, tape to thigh
     - **Intermittent rectal temperature checks** (until UCSF transport team arrives).
       - ✓ Gently insert lubricated thermometer rectally ~2cm
   - **CAUTION:** Encephalopathic babies have depressed metabolism (especially if never warmed) and generate little heat. They are easily overcooled so watch for precipitous falls in core temperature below 34ºC. Always have back-up external heat sources available (e.g., radiant warmer, warm packs).

4) **Goal rectal temperature = 33.5 ºC (+/- 0.5 ºC)**
   - ºC to ºF Conversion formula: **ºC = 5/9 x (ºF-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**
   - If baby has never been warmed, they are easily overcooled, even passively
     - Once rectal temp falls to **34˚C**, have external heat sources available
     - If core temp falls **<33˚C**, turn on heat source to lowest settings
     - Slowly adjust heat sources as needed to achieve target temperature
       - ✓ Continue close monitoring to prevent rapid rewarming. If core temp rises **>34˚C**, try opening isolette ports/door or undraping
   - Expected vital sign changes: Heart rate may fall <100 bpm when approaching target temperature.
     - Maintain other vital signs (e.g., BP, pre/post ductal O2 sats) in normal range

5) **Secure vascular access ASAP** – cooling causes peripheral vasoconstriction and makes access difficult.
   - **Umbilical catheters (UAC and UVC)** – if possible
     - Double lumen UVC (first choice, if available)
     - Alternatively, UCSF Transport Team may place lines upon arrival
   - **Peripheral Access** – if unable to secure umbilical access
     - **Peripheral IV** (at minimum) – No scalp IVs (EEG leads to be placed)
     - **Consider arterial line** (e.g., radial arterial line) – for continuous monitoring and sampling

6) **Maintain adequate sedation. DO NOT LET PATIENTS SHIVER**
   - Use sedation to reduce agitation and prevent shivering as the beneficial effects of therapeutic hypothermia may be negated by shivering.
   - **Morphine: 0.05-0.1 mg/kg IV** (repeat 0.05mg/kg/dose prn discomfort or shivering)
     - Consider lower dose if neurological exam is depressed or if not agitated/shivering.
     - If transfer is delayed, consider **0.05 mg/kg IV q 6hrs** scheduled dosing
       - ✓ Continuous infusion of dexmedetomidine or morphine will be started on admission to UCSF. Please see Inborn Hypothermia guideline for more details.

7) **Laboratory/blood work**
   - **Blood gases**
     - Ensure ***cord blood gases*** are sent (**UA** and **UV**)
     - Check ***serum lactate with ABG*** on **admission** and prn
       - ✓ Avoid hypocapnea (goal Pco_2: 45-55mmHg)
       - ✓ Avoid hyperoxia (goal O2 sat 92-97% with PaO2 <100mmHg)
   - **Electrolytes and Chemistries**
     - Monitor ***calcium*** levels closely. Levels may fall with cooling.
       - ✓ Monitor ***ionized calcium*** levels with blood gases
         - ➢ Ionized calcium normal range: *1.00 - 1.50 mmol/L*
       - ✓ Check ***total calcium***
         - ➢ Total calcium normal range: *8.5 - 11 mg/dL*
     - Monitor ***magnesium*** levels closely. Levels may fall with cooling.
       - ✓ Maintain within upper normal limits
         - ➢ Target level ≥ *2.0 mg/dL*
         - ➢ Normal range: *1.5 - 2.2 mg/dL*

- Monitor ***potassium*** levels closely, and correct per UCSF guidelines
  - ✓ Serum potassium normal range: *3.2 – 6.0 mmol/L*
    - *Serum K < 3.2 but > 2.5: replacement dose 0.5 mEq/kg ordered ROUTINE*
    - *Serum K ≤ 2.5: replacement dose 1 mEq/kg, ordered STAT*
- Monitor ***glucose*** levels closely
  - **Actively manage to maintain serum levels > 60 mg/dL**
- Consider ***serum ammonia*** level

o **CBC with platelets**
- Watch for thrombocytopenia
  - ✓ Follow ICN transfusion guidelines

o **Cultures**
- ***Blood cultures***
- Other sources as clinically indicated

o **Coagulation studies**
- ***PT/PTT/INR/Fibrinogen***

8) **Medical Management by Systems:**

o **<u>FEN</u>:**
- **Make baby NPO.**
- **Start D10W** (or **D5W** if hyperglycemic) at **80 ml/kg/day.**
- **Maintain normal glucose and electrolytes –** {*see 7) **Laboratory/blood work***}**.**
- **Management of acidosis –** Try to avoid base administration if circulation is re-established, as most patients self-correct over time and there is the potential for exacerbating injury with base administration or overcorrection.
  - ✓ Treat hypovolemia with volume administration as needed {see ***Blood pressure management*** below}

o **<u>Respiratory</u>:**
- **Ventilator Support** - Provide respiratory support as indicated. Intubation is not mandatory for cooling but may be needed in order to achieve adequate sedation.
  - ✓ **AVOID HYPOCAPNEA**
    - Cooling can ↓ Pco_2.
    - Maintain blood gas **Pco_2** goal: **45-55mmHg**
  - ✓ **AVOID HYPEROXIA**
    - Maintain **oxygen saturations > 92% but < 97% if in supplemental oxygen**
    - **PaO2** should be **<100mmHg**
  - ✓ Maintain air humidifier in normothermic range (37ºC)

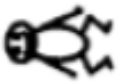
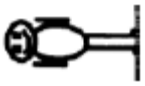
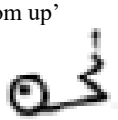
o **<u>Cardiovascular</u>:**
- **Blood pressure management -** Continuous arterial line monitoring preferred
  - ✓ Maintain blood pressure in **normal range**
  - ✓ Treat hypovolemia with volume administration as needed
    - **Normal Saline –** 10 mL/kg IV
    - **Packed Red Blood Cells** (**+/- FFP**) – if blood loss is etiology
    - Continuous IV pressors as indicated:
      - **Dopamine** (1st choice agent)
- **Heart rate**
  - ✓ Expect bradycardia (< 100 bpm) when temperature < 34º C
  - ✓ Monitor with **3-lead EKG** per routine
  - ✓ For deep bradycardia (<80bpm)

- This is often tolerated if blood pressure is maintained adequately
- If sustained profound bradycardia (< 60 bpm) or concern for inadequate perfusion:
  - Raising rectal temperature to 34° C alone may be adequate
  - Consider **atropine** instead of epinephrine
- ➢ Monitor for arrhythmias
  - Obtain rhythm strip if unusual pattern develops

- **Persistent pulmonary hypertension of the newborn (PPHN)**
  - ✓ Cooling may exacerbate PPHN
    - Assess patient history and respiratory status (*e.g.*, possible meconium aspiration syndrome, infection, RDS)
    - Assess ability to increase respiratory support if patient status dictates (*e.g.*, ability to intubate easily or provide mechanical ventilation). Maximal level of support will differ depending on the referring center.
  - ✓ **Recommendations for patients with risks for PPHN:**
    - If a child has a pre-/post-ductal SpO_2 difference ≥10% or requiring ≥40% FiO_2 to maintain sat >90%
      - UC Transport Team will bring iNO
      - Counsel family for possible need for ECMO
      - Referring hospital should *avoid hyperthermia* (over heating) by turning radiant warmer to low setting and maintain patient temperature near **36±0.5°C**
      - Patient temperature should be monitored as a *core* temperature (via indwelling rectal temp probe @ 6cm depth) if possible, or as *rectal* thermometer checks every 15 minutes (if probe not available) until the UC transport team has arrived
    - Referring center and UCSF should maintain close contact with frequent updates (e.g. hourly basis) until transport team arrives

- **Infectious Disease**
  - **Rule out Sepsis –** consider starting antibiotics after blood cultures obtained
    - ✓ **Ampicillin:** 50 mg/kg/dose IV q8hrs
    - ✓ **Gentamicin:** 4 mg/kg/dose IV q36hrs (note longer dosing interval)
- **Neurological**
  - **DOCUMENT COMPLETE NEURO EXAM – see Appendix A**
  - **Maintain adequate sedation** {see Section 6}
  - **Seizure control** {see ***NICN Seizure Management Guidelines***}
    - ✓ No prophylactic treatment
    - ✓ Treat seizures (suspected clinical or confirmed sub-clinical)
    - ✓ 1st choice agent for suspected seizures:
      - **STAT Lorazepam (Ativan):** 0.1 mg/kg/dose IV, repeat x 1 as needed
    - ✓ 1st choice agent for confirmed seizures:
      - **STAT Phenobarbital**: Load: 20 mg/kg IV x 1, repeat x 1 as needed
    - ✓ If 2nd agent required, discuss with UCSF
- **Skin**
  - Reposition infant every **2 hours and prn**
  - Monitor and document skin breakdown (including scalp), pressure ulcers, or subcutaneous fat necrosis

APPENDIX A: ENCEPHALOPATHY SCORING WORKSHEET

CATEGORY	NORMAL	MILD	MODERATE	SEVERE	SCORE
A. Level of consciousness	0 = Normal	1 = Hyperalert or Irritable	2 = Decreased responsiveness (delayed or incomplete response to stimuli)	3 = Minimally responsive (to deep pain/stimuli) or Unresponsive	___
B. Spontaneous activity	0 = Normal	N/A	2 = Decreased	3 = No activity	
C. Posture	0 = Normal (flexed posture of upper/lower extremities at rest) 	1 = Mild distal flexion 	2 = Distal flexion with complete extension (arm posturing with elbow extension and wrist flexion) 	3 = Decerebrate (rigid posturing with wrist flexion, arm/leg extension, pointed toes) 	___
D. Tone *Test arm traction:* Hold wrist and pull arm upwards. Note flexion at elbow and resistance while shoulder lifts off table. Test each side. *Test leg traction:* Grasp ankle and slowly pull leg upwards. Note flexion at knees and resistance as buttocks lift. Test each side. *Test axial tone:* Hold both wrists and pull arm upwards.	0 = Normal Arms flex at ~ 100° & maintained as shoulder lifts  Knee flexes and remains flexed when bottom up  Head lifts with shoulders briefly, then falls back	1 = Hypertonic Arms and legs difficult to extend, snap back forcefully; Flexion of arms < 100° when lifted  Flexion stays when back & bottom up'  Decreased head lag, arching	2 = Hypotonic Arms flex slightly or some resistance felt  Legs flex slightly or some resistance felt  Excess head lag	3 = Flaccid Arms remain straight; no resistance felt  Legs straight- no resistance left  Pronounced head lag	___
E. Reflexes Suck: **Moro:**	0 = Normal 0 = Normal	1= Uncoordinated, not sustained 1 = Low threshold to elicit	2 = Weak or bite 2 = Weak, incomplete, or high threshold	3 = Absent 3 = Absent	___ (code highest)
F. Autonomic system **Pupils:** **Respiration:**	 0 = Normal 0 = Normal	 N/A N/A	 2 = Constricted 2 = Apnea/periodic breathing	 3 = Fixed/dilated or asymmetric 3 = Intubated for apnea	___ (code highest)

*Stick figures from: Dubowitz LM, et at. Clinics in Developmental Medicine No. 148, The Neurological Assessment of the Preterm & Full-term Newborn Infant, 2nd Edition, 1999. *Does not count toward cooling criteria if child has received opiates*

Has the baby received analgesia, sedation, anti-convulsants, or paralytics prior to the exam (circle 1): **Y N**

CNS acting medications prior to exam (circle all that apply): **opiates benzodiazepines barbiturates other**

Age of baby at time of qualifying exam (circle 1): **1-2 hours 2-3 3-4 4-5 5-6 other**

Name of person performing exam: