Chapter 17: Central Nervous System

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A. Neonatal Seizures

- Neonatal seizures more often present with subtle symptoms
  - Apnea, lip smacking, tongue thrusting, tonic eye deviation, leg pedaling, cyanotic spells, autonomic dysfunction
  - Focal rhythmic flexion of extremity or distal joint (wrist/hand, ankle/foot)
  - Generalized tonic-clonic seizures are rare
  - Electroclinical dissociation (subclinical seizures) is common

Differential Diagnosis

- Hypoxic-ischemic encephalopathy
  - Most common etiology of neonatal seizures
- Cerebral vascular
  - Intracranial hemorrhage
    - Intracerebral/parenchymal, intraventricular, subarachnoid, subdural
  - Arterio-venous malformation (AVM)
  - Stroke: arterial or venous
- Congenital CNS malformations
  - Agenesis of corpus callosum
  - Polymicrogyria
  - Lissencephaly
  - Schizencephaly
  - Hemimegancephaly
  - Focal cortical dysplasia
  - Holoprosencephaly
  - Subcortical band heterotopia (gray matter heterotopia)
- Metabolic
  - Hypoglycemia
  - Hypocalcemia/ Hypomagnesemia
  - Hypo/Hypernatremia
  - Pyridoxine dependency
  - Inborn errors of metabolism – amino acidopathies, organic acidopathies
- Infection
  - Meningitis

- TORCH
- Drug Toxicity
  - Withdrawal-barbiturates, benzodiazepines, opioids (heroin, methadone)
  - Maternal anesthetics-accidentally injected into fetal scalp during delivery
- Neurocutaneous Disorders
  - Tuberous Sclerosis (gene: TSC1, TSC2)
  - Incontinenta Pigmenti (gene: IBKKG)
  - Sturge-Weber (gene: GNAQ)
- Neonatal Onset Epilepsy Syndromes
  - Benign familial neonatal epilepsy (days 2-3, remission in 1 to 12 mo)
    - Autosomal dominant: KCNQ2, KCNQ3, SCN2A
  - Benign nonfamilial neonatal epilepsy ("fifth day fits")
  - Early myoclonic encephalopathy
  - Early infantile epileptic encephalopathy (Ohtahara's syndrome)
  - Malignant migrating partial seizures of infancy (rare)

Work up for Seizures

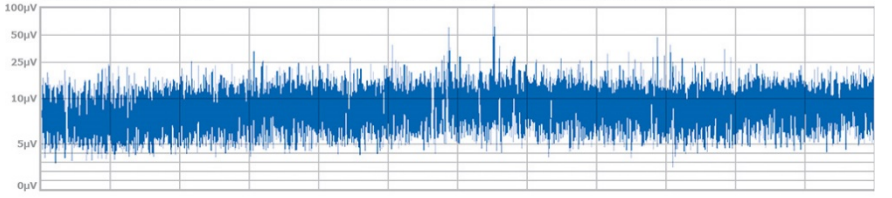
- History
  - Maternal history – drug use, IDM, infection
  - Delivery history – birth trauma, hypoxic events
- PE
  - Signs of trauma – bruising, petechiae
  - Dysmorphic features/congenital anomalies
  - Neurologic status
- Labs
  - Blood sugar
  - Electrolytes, calcium, magnesium
  - CBC with differential, blood culture
  - Blood gas, ammonia-if concerns for inborn error of metabolism
  - Consider UA/Urine Culture and CSF studies
- Continuous video EEG, aEEG*
- Imaging
  - Ultrasound – best for IVH in preemie, may miss intracranial bleed in term infants (subdural or subarachnoid hemorrhage)
  - CT scan – good for concerns of intracranial bleeding in term infants

– MRI – best for structural anomalies and hypoxic-ischemic injury

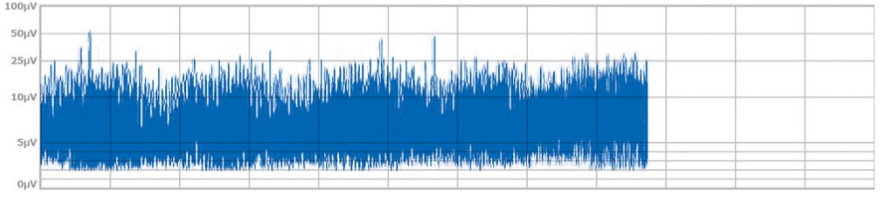
***Monitoring with Amplitude-Integrated EEG (aEEG)**

- aEEG is a bedside tool used to monitor brain function and identify seizure activity. Most common electrode placement includes biparietal (P3 and P4) and central leads (C3 and C4). Hydrogel, cups or needles can be applied to the scalp for monitoring.
- Classification
    - Continuous (lower margin >5μV and upper margin 10-25μV)
    - Discontinuous (lower margin<5μV and upper margin >10μV)
    - Burst Suppression (lower margin <5μV and upper margin >25μV)
    - Low Voltage (lower margin<5μV and upper margin <5μV, variability)
    - Flat (lower margin<5μV and upper margin <5μV, isoelectric)
- Seizures present as a sudden onset of rhythmic activity lasting >10sec
    - Lower and upper margins appear like continuous “humps”
    - Artifacts such as patting, oscillator use, hiccups, EKG can mimic seizure appearance on aEEG

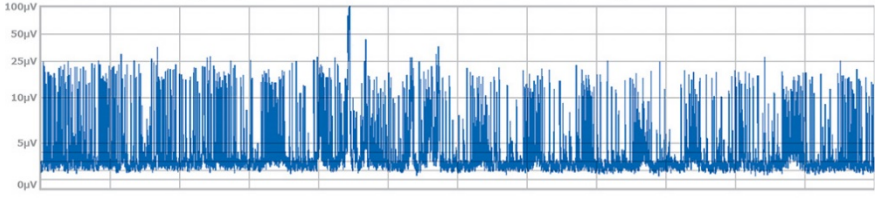
Pattern: **Continuous** Lower Margin: **>5μV** Upper Margin: **10-25μV**



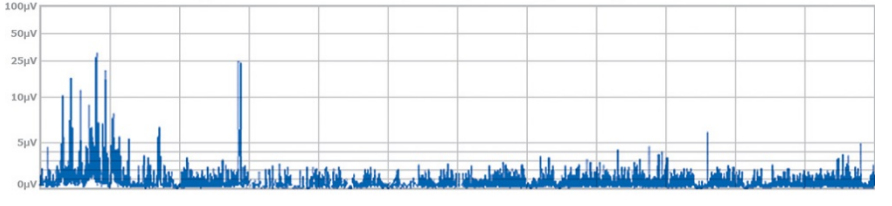
Pattern: **Discontinuous** Lower Margin: **<5μV** Upper Margin: **>10μV**



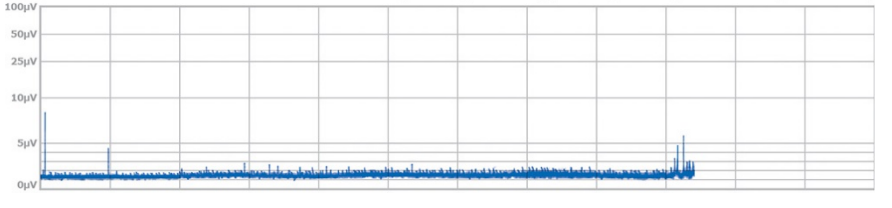
Pattern: **Burst Suppression** Lower Margin: **<5μV** Burst: **>25μV**



Pattern: **Low Voltage** Lower Margin: **<5μV** Upper Margin: **<5μV** with some variability



Pattern: **Flat** Lower Margin: **<5μV** Upper Margin: **<5μV** (Isoelectric)



Seizure Treatment

- Correct electrolyte disturbances
- Anticonvulsants

Levetiracetam (Keppra)

1st Loading dose: 50 mg/kg

2nd Loading dose if ongoing seizures: 50 mg/kg

Maintenance dose: 25 mg/kg BID

Desired blood levels: not established

Adverse effects: none known in neonates (reports of irritability, behavioral dysregulation in older children receiving high doses)

Phenobarbital

1st Loading dose: 20 mg/kg

2nd Loading dose if ongoing seizures: 10 mg/kg

Maintenance dose: 2.5 mg/kg BID

Desired blood levels: 20-40 mcg/ml

Adverse effects: Can cause respiratory depression, hypotension

Vimpat (Lacosamide)

1st Loading dose: 10 mg/kg

2nd Loading dose if ongoing seizures: 5-10 mg/kg

Maintenance dose: 5 mg/kg BID, then increase to 10mg/kg BID

Desired blood levels: not established

Adverse effects: asymptomatic bradycardia and/or prolonged PR interval, can consider 12 lead EKG

Fosphenytoin

1st Loading dose: 20 PE/kg
(PE: phenytoin equivalents)

2nd Loading dose if ongoing seizures: 10 PE/kg

Maintenance dose: 4-8 PE/kg/day

Desired blood levels: 6-15 mcg/ml

Adverse effects: arrhythmias, bradycardia, hypotension

B. Intraventricular Hemorrhage

- Periventricular bleeding from the subependymal germinal matrix in preemie
  - Bleeds in term infants are from choroid plexus
- Germinal matrix involutes around 36 weeks gestation
- 90% of IVH occurs in the first 3 days of life
  - 50% in first 24 hours
  - May progress in the first 5-7 days

Papile's classification:

- Grade 1: Isolated germinal matrix hemorrhage
- Grade 2: Intraventricular hemorrhage without dilatation of the ventricle
- Grade 3: Intraventricular hemorrhage with ventricular dilatation
- PVHI: periventricular hemorrhagic infarction represented by intra-parenchymal echodensity (formerly known as Grade IV)

Risk Factors:

- Prematurity < 30 wks gestation
- Perinatal asphyxia, Birth Trauma
- Rapid fluctuations in blood pressure
- Shock
- PDA

- Antenatal steroids are protective

Diagnosis:

- Head Ultrasound (HUS)
  - Guidelines from American Academy of Neurology
- Screen all infants less than 30 weeks gestation
- First ultrasound at 7-14 days of age
- Repeat ultrasound at 36-40 weeks PMA or discharge
- Consider term equivalent age MRI for infants with history of abnormal HUS

C. Periventricular Leukomalacia

- Cystic lesions in corticospinal white matter adjacent to the lateral ventricles
  - Due to repeated hypoxic-ischemic events from cerebral hypoperfusion in the neonatal period
  - Hypoxic injury causes necrotic cell death
- Seen most commonly in premature infants
- Leads to long-term neurodevelopmental disability
  - Spastic diplegic cerebral palsy

D. Apnea

Apnea: Absence of breathing for >20 seconds or short pause (>10 sec) associated with oxygen desaturation or bradycardia

Periodic Breathing: Cyclic pauses in breathing for ≤ 10 secs followed by a series of rapid, shallow breaths

Bradycardia:

- For infants < 30 wk: HR <100/min for >10 sec
- For infants ≥ 30 wk: HR <80/min for >10 sec

ractical tips:

- Apnea of prematurity: Typical onset is 2-3 days in preemies <34 weeks' gestation
- Apnea in a full-term infant is never physiologic
- Apnea on first day of life is abnormal, search for causes other than prematurity

auses of Apnea and Bradycardia by Gestational Age

All ages	Premature Infant	Full term infant
Sepsis	Apnea of prematurity	Cerebral infarction
Meningitis	PDA	Polycythemia
Hypoxia	HMD	Drug Withdrawal
Aspiration	NEC	
GER	PV-IVH	
Pneumonia	Anemia of prematurity	
Cardiac disorder	Posthemorrhagic Hydrocephalus	
Post-extubation atelectasis	Polycythemia	
Seizures		
Cold Stress		
Metabolic imbalance		
Airway malformations		
CNS malformations		

pproach to Apnea & Suspicion of Reflux

- Most spells are <u>not</u> temporally linked to reflux
- Usually apnea precedes the reflux when temporally linked
    - Only 3% of spells preceded by reflux

nterventions for Apnea:

1. Positioning: Optimize left side down and prone.
2. Continue bolus feeds (every 3 hours). No strong evidence that continuous drip feeds will decrease apnea/bradycardia/desaturation spells.
3. Consider thickening feeds using commercial reflux formula (see Reflux Guideline)
4. No evidence to support changing/decreasing maintenance caffeine dose (no evidence to support caffeine worsening reflux)
5. Anti-reflux medications should be used with caution, and if no difference is observed in frequency or severity of spells after 5-7 days of therapy, consider discontinuation.

eferences:

1. Olson DM. Neonatal Seizures. *Neoreviews* 2012;13;e213 DOI: 10.1542/neo. 13-4-e213.
2. Donna M. Ferriero MD. Neonatal Brain Injury. *N Engl J Med* 2004;351:1985-95.
3. Volpe JJ, Inder TE, Darras BT, de Vries LS, du Plessis AJ, Neil JJ, Perlman JM. (2018) *Volpe's Neurology of the Newborn, 6th edition*. Elsevier.

lypoxic Ischemic Encephalopathy

- Incidence = 3-5/1000 live births
- Mortality up to 60%
- Generally occurs after event of perinatal asphyxia
    - Event is not always easily recognized

erinatal Asphyxia

- ACOG and AAP "Neonatal Encephalopathy and Neurologic Outcome, 2nd Edition" 2019
    - Asphyxia
        - Marked impairment of gas exchange leading, if prolonged, to progressive hypoxemia, hypercapnia, and significant metabolic

acidosis.

- Describes a process of varying severity and duration rather than an end point.
- Should not be applied to birth events unless specific evidence of markedly impaired intrapartum or immediate postnatal gas exchange can be linked to neurologic illness in the neonate.

- Perinatal Asphyxia
  - Profound metabolic or mixed acidemia (pH <7.0 on umbilical arterial blood gas)
  - Persistence of an Apgar score of 0-3 for >5 minutes
  - Neurologic manifestation in the immediate neonatal period (seizures, encephalopathy)
  - Evidence of multi-organ dysfunction in the immediate neonatal period

Neonatal Encephalopathy Exam (Modified Sarnat Score)

	Level of Encephalopathy			
	Normal/None	**Mild**	**Moderate**	**Severe**
1. Level of Consciousness	0 – Normal/ Alert	1 – Hyperalert or irritable (responsive to minimal stimuli)	2 – Lethargic	3 – Stupor or coma
2. Spontaneous Activity	0 – Normal	-----	2 – Decreased activity	3 – No activity
3. Posture	0 – Predominantly flexed	1 – Mild flexion of distal joints (fingers, wrist)	2 – Flexion of distal joints or complete extension	3 – Decerebrate
4. Tone	0 – Strong flexor tone in all extremities	1 – Slightly increased tone in extremities	2a – Hypotonia (focal or general) 2b – Hypertonia (focal or general)	3a – Flaccid 3b – Rigid
5. Primitive Reflexes[1]: **Suck**	0 – Strong, coordinated, easy to elicit	1 – Weak, coordinated	2 – Weak and uncoordinated, and/or bite	3 – Absent
Moro	0 – Complete	1 – Exaggerated	2 – Incomplete	3 – Absent
6. Autonomic System[1]: **Pupils**	0 – Normal	1 – Mydriasis (dilated), reactive	2 – Myosis (constricted), reactive	3 Deviated/unequal, dilated, or fixed/ nonreactive to light
Heart Rate	0 – Normal: 100 – 160 bpm	1 – Tachycardia: >160 bpm	2 – Bradycardia: <100 bpm	3 – Variable
Respiration	0 – Normal: regular respirations	1 – Tachypnea, Hyperventilation	2 – Periodic breathing	3a – Apnea, requires on-going PPV or intubation, and has spontaneous breaths 3b – Apnea, requires on-going PPV or intubation, and does not have spontaneous breaths

Documenting the Neonatal Encephalopathy Exam (.HIEEXAM)

Contribution: Megan Berube, MD

1. **Level of consciousness:** 0- Normal/Alert; 1- Hyperalert or irritable, responsive to minimal stimuli; 2-Lethargic; 3-Stupor or coma
2. **Spontaneous activity:** 0-Normal; 2-Decreased activity; 3-No activity
3. **Posture:** 0- Predominantly flexed; 1- Mild flexion of distal joints (fingers, wrist); 2- Flexion of distal joints or complete extension; 3-Decerebrate
4. **Tone:** 0- Strong flexor tone in all extremities; 1 – Slightly increased tone in extremities 2a- Hypotonia (focal or general); 2b- Hypertonia (focal or general); 3a- Flaccid; 3b- Rigid
5. **Primitive reflexes:***

   Suck: 0- Strong, coordinated, easy to elicit; 1- Weak, coordinated; 2- Weak and uncoordinated, and/or bite; 3- Absent

   Moro: 0- Complete; 1- Exaggerated; 2- Incomplete; 3- Absent
6. **Autonomic system:***

   Pupils: 0- Normal; 1 – Mydriasis (dilated), reactive; 2 – Myosis (constricted), reactive; 3- Deviated/unequal, dilated, or fixed/nonreactive to light

   Heart rate: 0- Normal (100-160 bpm); 1- Tachycardia (>160 bpm); 2- Bradycardia (<100 bpm); 3- Variable

   Respiration: 0- Normal; 1 – Tachypnea, hyperventilation; 2- Periodic breathing; 3a – Apnea, requires on-going PPV or intubation, and has spontaneous breaths; 3b – Apnea, requires on-going PPV or intubation, and does not have spontaneous breaths

For Primitive Reflexes (Suck, Moro) and Autonomic System (Pupils, Heart Rate, Respirations), the em with the highest score determines the level of encephalopathy.

otal categories with score of 0 = ____
otal categories with score of 1 = ____
otal categories with score of 2 = ____
otal categories with score of 3 = ____

- Neonate has a normal encephalopathy exam if he/she has scores of 0 in all six categories.
- Neonate has mild encephalopathy if he/she has < three categories with a score of 2 or 3, but has a score of 1, 2, or 3 in at least one category.
- Neonate has moderate encephalopathy if he/she has a score of 2 in three or more categories.
- Neonate has severe encephalopathy if he/she has a score of 3 in three or more categories

leonatal Encephalopathy Exam Definitions

1. **Level of consciousness:**
   a. **Hyperalert -** Full wakefulness with eyes open/staring but decreased frequency of blinking/tracking. Spontaneous motor activity normal or decreased with lowered threshold to all stimulus types.
   b. **Irritability -** Lowered threshold with excessive response to all stimulus types. Can be seen with varied states including hyperalert, lethargy, and obtundation.
   c. **Lethargy -** Slightly delayed but complete response to stimuli with slightly increased threshold for eliciting responses and decreased spontaneous movement
   d. **Obtundation -** Delayed and incomplete responses with markedly increased threshold to all sensory stimuli and little or no motor activity
   e. **Stupor -** No spontaneous eye opening and tactile stimulation elicits poorly sustained eye opening. Responds only to strong, noxious stimuli. Absent gag, corneal reflex.
   f. **Coma -** No eye opening with vigorous tactile stimulation.
2. **Spontaneous activity:**
   a. **Decreased spontaneous activity -** Decreased frequency or amplitude of spontaneous facial and extremity movements.
   b. **Absent spontaneous activity -** Movements absent.
3. **Posture:**
   a. **Distal flexion -** Fingers, toes in strong flexion; incomplete extension of fingers when stroked on dorsal surfaces. Thumbs flexed, adducted, opposed across palms (i.e. "cortical thumbs").
   b. **Decerebrate posturing -** Head, neck, and back are arched in extension (opisthotonos), elbows are extended, wrists are pronated, and hips are adducted.
4. **Tone (remove positioning barriers for accurate examination of tone):**
   a. **Hypotonia -** Focal or generalized decreased resistance to passive movement. Associated with greater extension of the extremities than normal.
   b. **Hypertonia -** Focal or generalized increased resistance to passive movement. Associated with greater flexion of the extremities than normal.
   c. **Flaccid -** "Flat on the mat" appearance. May be associated with frog-leg posturing with arms and hips/legs lying in abduction.
   d. **Rigidity -** "Lead pipe" feel of extremities, severe hypertonia with extreme resistance to passive movement. Does not depend on imposed speed or threshold of movement. Unilateral contraction of antagonist or agonist muscle groups can occur with rigidity, but the limb does not tend to return to a fixed posture or extreme joint angle. May be associated with exaggerated deep tendon and tactile reflexes.

5. **Primitive Reflexes:**
   a. **Weak suck -** Some sucking noted, but it is not as vigorous or sustained as it should be. A pacifier or gloved finger can be easily pulled from the mouth.
   b. **Absent suck -** No sucking or root reflex elicited.
   c. **Bite -** Insertion of pacifier or gloved finger into mouth elicits neonate to "clamp down" or bite object. No sucking motion elicited.
   d. **Moro -** The Moro reflex is elicited by holding the baby's head and shoulders off the mat with arms held in flexion on chest. While supporting the head and neck, the examiner suddenly lets the head and shoulder drop while releasing the arms. The arms should fully abduct and extend, then return towards midline with the hand open and the thumb and index finger forming a "C" shape. An incomplete Moro is marked by absence of any component or any asymmetry in movements. Incomplete Moro reflex often extends irregularly but typically does not return to midline.
   e. **Absent Moro -** Absence of any reflexive activity (see above for method of eliciting Moro reflex).
6. **Autonomic System:**
   a. **Dilated pupils (mydriasis) -** Normal pupil size for term newborns is 3.9 mm +/- 0.8 mm. Dilated pupils are larger than this even in bright light.
   b. **Constricted pupils (miosis) -** Normal pupil size for term newborns is 3.9 mm +/- 0.8 mm. Constricted or pinpoint pupils are smaller than this even in dim light.
   c. **Unequal; Fixed; Dilated; Poor light reflex pupils -** Pupils that are not normally symmetrically aligned or symmetrically dilated, are fixed in position, or that do not accommodate (constrict) in the presence of light.
   d. **Tachycardia -** Resting heart rate > 160 beats per minute.
   e. **Bradycardia -** Resting heart rate of < 100 beats per minute, typically 80-90 beats per minute. Only occasional increases to 120+ beats per minute are noted.
   f. **Variable heart rate -** Resting heart rate varies considerably without a consistent baseline.
   g. **Periodic breathing -** Three or more respiratory pauses of three seconds or longer separated by normal breathing for less than 20 seconds. Often associated with shallow breathing pattern.
   h. **Apnea -** Absence of airflow and respiratory effort lasting 20 seconds or longer. Apnea may also be present if a respiratory pause is shorter than 20 seconds but is associated with heart rate change or oxygen desaturation.

Therapeutic Hypothermia Protocol

UWHealth

Hypoxic Ischemic Encephalopathy (HIE) – Neonatal – Inpatient Guideline Summary

Target Population: Neonatal infants with suspected or diagnosed HIE

Link to Full Guideline: Hypoxic Ischemic Encephalopathy - Neonatal - Inpatient

Therapeutic Hypothermia Assessment Tool

Infant must meet the following criteria to be considered for treatment:

- Gestational age ≥ 35 and 0/7 weeks
- Birth weight ≥ 1800 grams
- ≤ 6 hours of life at time of initial evaluation

AND

I. Clinical and/or biochemical criteria
II. Demonstrate moderate or severe encephalopathy
III. Does not meet ANY listed exclusion criteria

Step I: Clinical and biochemical criteria

- History of acute perinatal event (e.g., uterine rupture, placental abruption, umbilical cord prolapse or avulsion, or severe fetal heart rate abnormality)
- APGAR score < 6 at 10 minutes of life
- Prolonged resuscitation, defined as positive pressure ventilation (via bag-mask or advanced airway) initiated at birth and continued for at least 10 minutes
- pH ≤ 7.0 on arterial cord blood gas or first postnatal hour blood gas
- Base deficit ≥ 12 mEq/L on arterial cord blood gas or first postnatal hour blood gas

Infant meets clinical and biochemical inclusion criteria if A or B are met:

A. pH ≤ 7.0 **or** base deficit ≥ 12 mEq/L
B. pH between 7.0 and 7.15 with history of an acute perinatal event **and** at least one of the following:
   i. Apgar score < 6 at 10 minutes
   ii. Prolonged resuscitation

Step II: Neurologic evaluation using neonatal encephalopathy exam

- Inborn evaluation should occur after 15 minutes of life using .HIEEXAM
- Outborn evaluation should be done with referring site under guidance of medical control, use of telemedicine (if able) is strongly encouraged

Infant meets neonatal encephalopathy inclusion criteria if A or B are met:

A. Seizures
B. Moderate or severe encephalopathy using neonatal encephalopathy exam (See Appendix1: Neonatal Encephalopathy Exam or EPIC smartphrase .HIEEXAM)

Exclusion criteria:

- Presence of major congenital anomalies
- GA < 35 and 0/7 wks
- Severe IUGR; BW < 1800 g
- Moribund infants for whom no additional intensive therapy will be offered, as determined by attending neonatologist

Relative contraindications:

- Infant > 6 hours old at time of initial evaluation
- Severe hemodynamic compromise
- Severe coagulopathy with active bleeding
- Confirmed venous sinus thrombosis

Additional considerations:

- Consult PICU for infants with critical congenital heart disease who require cooling
- If there is a question whether to initiate cooling, place aEEG, obtain STAT Pediatric Neurology consult, and begin passive cooling for up to 6 hours while decision is being made
- If infant is outborn, eligibility will be determined in conjunction with the referring clinician. An infant with a qualifying exam prior to transfer, will still be cooled per the guideline regardless of admission exam

Therapeutic Hypothermia Strategy: Cooling and Re-Warming

Cooling – Targeted esophageal temperature of 33.5-34.5°C

- Therapeutic hypothermia (i.e., active or passive cooling) should be initiated within 6 hours of life
- Once targeted temperature is reached (i.e., first esophageal temperature), maintain for 72 hours

Re-warming

- Re-warm after 72 hours from first esophageal temperature
- Slow re-warming of patient preferred at rate of 0.5°C per hour to core body temperature of 36.5°C
- Maintain normothermia with the cooling blanket for 24 hours s/p rewarming to avoid rebound hyperthermia

For additional information on conducting cooling on transport, passive cooling and cooling in NICU, refer to Neonatal Whole Body Cooling Procedure

Therapeutic Hypothermia – Patient Labs for Monitoring	
Lab (Normal Range)	**Suggested Frequency**
Temperature corrected blood gas, lactate, ionized calcium (iCa) (4.5-5.3 mg/dL which equals: 1.12-1.32 mmol/L; 2.25-2.65 mEq/L)	Every 6 hours for first 24 hours then every 12-24 hours (minimum during cooling) **Note:** Temperature corrected blood gases are available on the NICU ABL 90 and the main lab. To get temperature corrected readings, do the following: • On workstation order, clearly write patient's temperature at time of draw • If processed in the NICU, notify respiratory therapy of the patient's current temperature and desire for temperature corrected blood gases. The temperature corrected values that will appear in Health Link include: • PH, TEMP CORRECTED • PCO2, TEMP CORRECTED • PO2, TEMP CORRECTED
Glucose	Every hour during initiation of cooling until temp 33.5-34.5°C is reached; thereafter, check every 6 hours during cooling. During rewarming, check at start of rewarming, every 2 hours x 2, then PRN and with lab draws
Chemistries (Ca 8.7-10.1 mg/dL) (Mg 1.8-2.3 mg/dL) (K 4.0-6.0 mEq/L)	Check Electrolytes, Ca, Mg, Phos every 12-24 hours during cooling Consider monitoring during rewarming
CBC	Check every 12-24 hours
Cultures	Obtain blood culture; consider sputum and cerebral spinal fluid culture
PT/PTT/INR	Check every 24 hours
BUN/CR	Check every 12-24 hours
AST/ALT	Check every 24 hours

Therapeutic Hypothermia – Medical Management by System	
System	**Considerations**
Monitoring (including radiographic studies)	• Babygram STAT on admission; confirm esophageal probe placement • aEEG/cEEG on admission • Cranial ultrasound on admission with Doppler* • NIRS (i.e., cerebral and renal) • Echocardiogram if hemodynamically unstable or concern for pulmonary hypertension • Brain MRI* - If severely encephalopathic and family is considering withdrawal of support, discuss early MRI with neuroradiologist and consider obtaining at 24-48 hours of life - Routine MRI and MRS on DOL #4-5 - Consider follow-up MRI and MRS on DOL #10-14 ***When ordering, must note "HIE Protocol" in comment section to ensure appropriate study***
Fluids, Electrolytes, Nutrition (FEN)	• NPO through rewarming • Initial total fluid goal of 50-60 mL/kg/day (D10W) • Treat hypovolemia with volume (normal saline, PRBCs) • If acidosis worsens base deficit > 10 mEq/L, consider: - Normal Saline (NS) (10 mL/kg IV) - Sodium bicarbonate (1-2 mEq/kg IV over 30 mins) - Add sodium acetate to maintenance fluids
Respiratory	• Avoid hypocapnia (goal PCO_2 45-50 mmHg) • Avoid hyperoxia (goal PaO_2 80-100 mmHg, SpO_2 < 98%) • Persistent pulmonary hypertension (PPHN) may worsen in some cases, consider pre- and post-ductal monitoring
Cardiovascular	• Continuous BP monitoring with arterial line preferred • Monitoring with 3-lead EKG • Maintain BP in normal range (SBP 60-70 mmHg / DBP 40-50 mmHg and MAP 40-50 mmHg) • If needed, support BP: 1st choice dopamine 2-5 mcg/kg/minute • Heart Rate: Expect bradycardia < 100 bpm • For deep bradycardia (< 80 bpm): - May be tolerated if BP is stable within target range and perfusion is appropriate on physical exam - If not tolerated, raising core temp to 34°C may be adequate; if symptomatic bradycardia persists, consider dopamine

Infectious Disease (ID)	• Initiate rule out sepsis evaluation with empiric antibiotics for all infants being treated with therapeutic hypothermia • Start ampicillin 100 mg/kg/dose IV q12 hours and gentamicin 4 mg/kg/dose q24 hours (for patients with renal concerns, consider ceftazidime 50 mg/kg/dose IV q12 hr) • Consider lumbar puncture to rule out meningitis
Neurologic	• Obtain Pediatric Neurology consult • Document complete neuro exam and neonatal encephalopathy exam using .HIEEXAM Epic SmartPhrase • Maintain adequate sedation; *NPASS score goal -1 – Do not allow patients to shiver!* - Morphine is drug of choice - **Day 1:** Morphine loading dose 0.05 mg/kg IV - Start maintenance continuous infusion at 0.01 mg/kg/hr - Escalate infusion rate by 0.005 mg/kg/hr as needed - Provide bolus doses of morphine 0.02 mg/kg IV every 3-4 hours PRN - If continuous infusion not available, schedule morphine 0.05 mg/kg every 6 hours - **Day 2:** Wean continuous morphine infusion by half to avoid toxic accumulation; goal rate of 0.005 mg/kg/hr - **2nd Line**: Consider starting dexmedetomidine 0.2 mcg/kg/hr if morphine infusion > 0.015 mg/kg/hr - Do not administer dexmedetomidine as a loading dose or bolus due to the risk of bradycardia and hypotension - When administering dexmedetomidine, wean morphine infusion to lowest rate tolerated (may discontinue) - If on-going concerns for pain and normal liver function, consider acetaminophen 7.5-10 mg/kg IV every 6 hours PRN • Treat seizures; load with levetiracetam 50mg/kg/dose (refer to Neonatal Seizures – Neonatal – Inpatient/Emergency Department Clinical Practice Guideline for ongoing management) • Continue aEEG/EEG monitoring through re-warming process or until patient is seizure free for 24-72 hours based on Pediatric Neurology's recommendation
Skin	• Maintain pressure relieving device • Reposition every 2 hours • Monitor for fat necrosis, pressure ulcers

Patient Follow-Up

- Patients should follow up at 3 months of age after discharge with Waisman Center Newborn clinic or accessible neurodevelopment clinic
- May consider consult with Waisman Center prior to discharge for transition of care consultation
- Patients should follow up with Pediatric Neurology per service's recommendation

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12. aEEG graphic provided by NCC – National Certification Corporation

Initial Management of Newborns with Myelomeningocele

Bermans Iskandar, MD Lisa McLennan, RN

Pre-Operative Care

1. The attending neurosurgeon should be notified as soon as the ob/gyn has selected a delivery date/time. UW/AFCH Pediatric Neurosurgery: 608-263-9585.
2. On day of admission and once baby is delivered, the neurosurgery resident (AFCH or Meriter) or attending who performed prenatal visit should be notified.

Immediately after birth:

3. Initial care should be taken in keeping the myelomeningocele (MMC) defect clean and moist. Immediately after birth cover defect with sterile Telfa and then layer with wet 4x4 gauzes. Telfa should be left in place until surgery but wet sterile gauzes can be changed as needed to keep area moist. This non adherent dressing can be kept in place by covering with a steri-drape or loosely wrapping Kerlix around abdomen.
4. Care should be taken to prevent contamination or exposure of MMC area, protect from soiling with a plastic flap (steri drape).
5. Perform initial measurement of head circumference.
6. Prophylactic antibiotic coverage should be started with broad spectrum coverage (Ampicillin + Gentamicin recommended) which should be continued for 48 hr. post op.
7. Infant must be nursed and kept prone to prevent injury to the exposed neural tissue.
8. If infant has not voided within first hours of birth, bladder ultrasound/straight catheterization must be performed. Notify Urology
9. **Arrange for transfer to AFCH NICU in consultation with Neurosurgery and Neonatologist.**

For more information, go to:
https://workspaces.uconnect.wisc.edu/display/nicuunitres/Policies+and+Clinical+Practice+Guideline/MyelomeningoceleNeonatalProtocol