Guidelines for Acute Care of the Neonate

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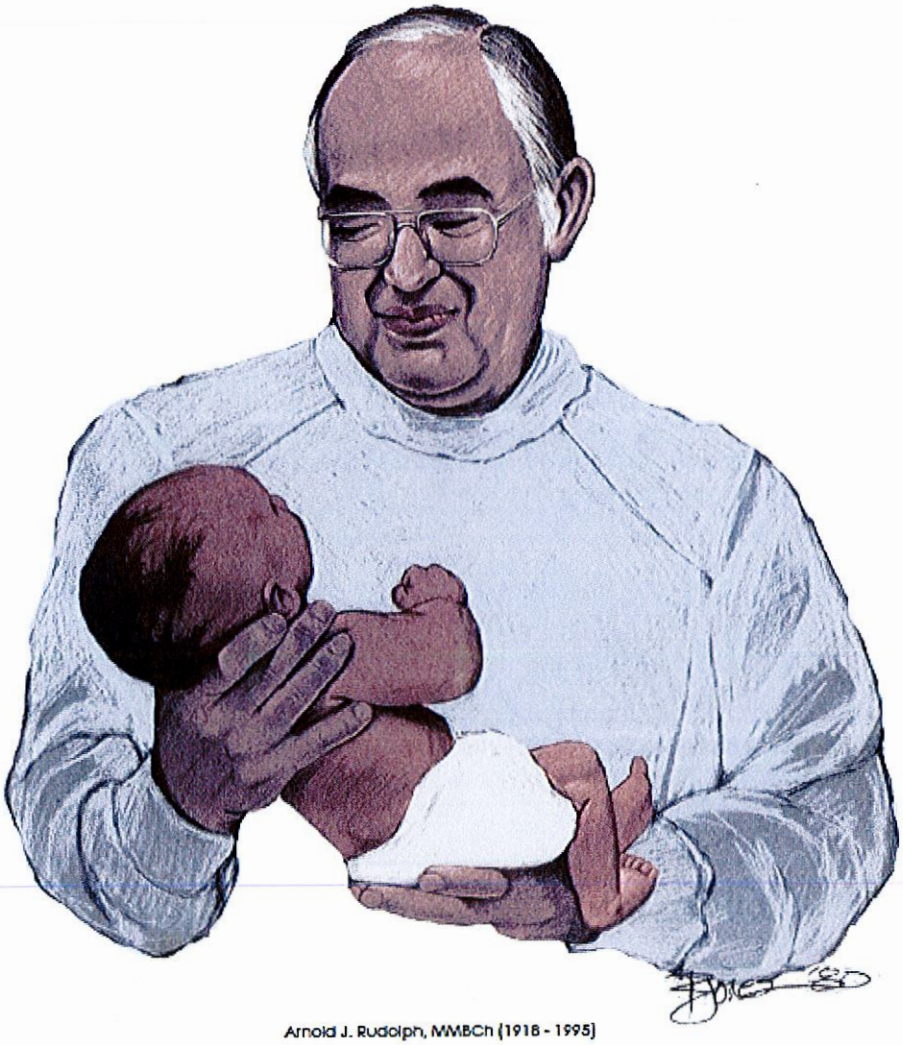

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Encephalopathy

A diagnosis of neonatal encephalopathy may be considered when an infant has both a change in mental status and an abnormal neurological examination. Alterations in mental status include hyperalertness, drowsiness, stupor, or even coma. Common neurological findings include abnormal tone (increased or decreased), seizures, non-habituating primitive reflexes, tremors, apnea, weak suck, and sometimes a bulging fontanel. The modified Sarnat classification (see Table 11–1) is the tool most frequently used to describe the severity of encephalopathy and is most appropriate for infants with hypoxic-ischemic encephalopathy (HIE).

Table 11–1. Modified Sarnat Criteria for Defining Encephalopathy

Category	Mild	Moderate	Severe
Level of Consciousness	Hyperalert	Lethargic	Stupor or coma
Spontaneous Activity	Normal	Decreased	No activity
Posture	Mild distal flexion	Strong distal flexion	Decerebrate/ extension
Tone	Normal	Hypotonia	Flaccid
Primitive Reflexes:			
Suck	Weak	Weak/absent	Absent
Moro	Strong	Incomplete	Absent
Autonomic System:			
Pupils	Dilated	Constricted	Deviated, Non-reactive
Heart Rate	Tachycardia	Bradycardia	Variable
Respiration	Normal	Periodic Breathing	Apnea

Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress: A clinical and electroencephalographic study. *Arch Neurol* 1976;33(10):696-705. Only newborns with moderate-to-severe encephalopathy should receive therapeutic hypothermia.

Neonatal encephalopathy may be seen in infants with:

- Metabolic abnormalities (hypocalcemia, hypoglycemia),
- Toxins (hyperammonemia, kernicterus),
- Inborn errors of metabolism,
- Intracranial hemorrhage,
- Cerebral infarction,
- CNS developmental anomalies (holoprosencephaly),
- Infections (sepsis, meningitis, CNS TORCH infection), or
- HIE.

The cause of the encephalopathy is not always immediately known, and automatically ascribing it to hypoxia-ischemia is not appropriate. However, certain peripartum scenarios (placental abruption, severe feto-maternal hemorrhage, maternal hypotension/shock, prolonged labor, multiple births, chorioamnionitis, placental insufficiency, IUGR) may place a newborn at increased risk for hypoxia-ischemia. Infants with hypoxic-ischemic injury severe enough to cause neurologic sequelae usually are severely depressed at birth (Apgar score ≤ 3 at 5 minutes of life), exhibit a significant acidosis (pH < 7 in cord arterial blood), and have evidence of injury to other organs (pulmonary, renal, hepatic, cardiac, bowel, bone marrow) along with the encephalopathy. Up to 10% of infants with HIE may not exhibit obvious multi-organ injury, even though encephalopathy may be severe.

Evaluation

Evaluation of an infant presenting with encephalopathy includes an in depth history and a complete neurologic examination; sequential neurologic examinations should be performed to assess what often is an evolving encephalopathic picture. The maximum Sarnat stage reached by an infant can provide prognostic information. The initial neurologic evaluation also includes initiation of continuous video EEG at admission (continues through rewarming) and MRI at 4–5 days of life. A head ultrasound (HUS) should also be performed to rule out severe intracranial hemorrhage and should be performed 8–12 hours after initiation of cooling. Additional evaluation includes CBC with differential and platelets, lumbar puncture, blood culture, blood glucose, calcium, magnesium and electrolytes. Depending upon the history and presentation, additional indicated studies may include blood ammonia level, serum and CSF lactate levels, serum and CSF amino acids, urine organic acids, and troponin I level. Evaluation of the placenta may indicate that infectious or clotting issues are involved in the etiology of the encephalopathy. If a hypoxic-ischemic etiology is strongly suspected, baseline hepatic and renal assessment, as well as an echocardiogram can be useful. If the infant's primary problems are hypotonia, respiratory depression, or both, spinal cord injury and neuromuscular diseases need to be considered.

Intervention/Therapies

Usual care for neonatal HIE is supportive intensive care which includes correcting metabolic and electrolyte disturbances, stabilizing pulmonary and hemodynamic instability, treating seizures, and monitoring other organ systems for dysfunction. Eleven international multicenter randomized clinical trials including 1,505 infants have addressed the safety and efficacy of therapeutic hypothermia as a therapy for HIE in newborns ≥35 weeks' gestation. According to the Cochrane review, therapeutic hypothermia if begun within 6 hours of birth, resulted in reduction in the mortality and/or major neurodevelopmental disability. The first trial, the CoolCap Study, which employed selected head cooling and used amplitude-integrated EEG (aEEG) abnormalities as entrance criteria, showed improved survival without severe disability (once newborns with severe aEEG abnormalities were excluded). The NICHD trial, using whole body hypothermia,

also found improved survival without severe disability in treated infants at 18 months of age. Importantly, benefits observed at 18–22 months of age persist to early school age, as shown in the CoolCap and NICHD follow-up trials. An expert panel convened by NICHD concluded that therapeutic hypothermia, if offered, needs to be performed using a rigorous set of criteria and a published protocol.

Therapeutic hypothermia is available in the TCH NICU.

Treatment Criteria for Whole Body Cooling

1. ≥35 weeks' gestation, AND
2. Biochemical evidence of a hypoxic-ischemic event:
   a) pH ≤7.00 or base deficit ≥16 mmole/L on cord gas or within first hour of life (in any blood sample),

   OR

   b) if no blood gas, or pH 7.01–7.15, or base deficit between 10 and 15.9 mmole/L: presence of an acute perinatal event and an Apgar score <5 at 10 minutes of age or need for resuscitation for ≥10 minutes,

   AND
3. Evidence of moderate-to-severe encephalopathy – seizures or abnormalities in 3 of 6 Sarnat criteria for moderate or severe encephalopathy (level of consciousness, spontaneous activity, posture, tone, primitive reflexes [suck or Moro], and autonomic nervous system [pupils, heart rate, or respiration]). Mark "severe" encephalopathy if there are more signs and symptoms in the severe vs the moderate column. If the signs and symptoms are equally distributed between severe and moderate columns, the severity is based on the level of consciousness (see Table 11-1).

Cooling should be initiated within 6 hours of birth (including passive cooling). Passive cooling should be initiated at the referral hospital after the infant has been determined to be a candidate for therapeutic hypothermia, by having all heat sources removed from the infant. It is critical to tell the referring care providers to monitor temperature every 15 minutes, and if the temperature goes <33.5°C, to turn on the radiant warmer until the transport team arrives to prevent overcooling. Active servo-controlled therapeutic hypothermia (with continuous rectal temperature) will be used during transport from the referral hospital to the TCH NICU unless infants are transferred from hospitals within the Texas Medical Center (since infants from nearby hospitals may be better served by getting to TCH as soon as possible to receive the definitive therapy instead of taking the time to initiate active cooling). For inborn infants, if the determination is made that a newborn is a candidate for therapeutic hypothermia, then passive cooling should be initiated and the infant transported to the TCH NICU.

In the TCH NICU cooling and rewarming is done according to specific protocols (Refer to nursing bedside manual for complete details of process). Infants are cooled to 33.5°C esophageal core body temperature for 72 hours using a servo-controlled cooling blanket system. The incubator or radiant warmer heat source is turned off throughout the procedure. Pediatric Neurology Service should be contacted for initiation of continuous bedside EEG. It is desirable to have arterial and central venous access during cooling, if possible. Low-dose morphine should be used to prevent agitation or shivering that occurs during therapeutic hypothermia.

During rewarming esophageal and skin temperature is monitored continuously. Rewarming is done slowly with 0.5°C increases in servo "set temp" every hour until set point reaches 36.5°C for 1 hour. Then the radiant warmer is turned on with servo set point 0.4°C above the infant's skin temperature. When the skin temperature reaches 36.5-37°C, the infant is returned to standard NICU temperature control care. Infants receiving whole body cooling will receive a Developmental Pediatrics consult and evaluation prior to discharge. Follow-up post hospitalization will include Neurology clinic visit with a brain MRI at 1 year of age, and TCH Meyer Developmental Center clinic visits at 6 months, 1 year, and 18 months of age. At 18 months, a full Bayley examination will be performed.

TCH Total Body Cooling Protocol

All supplies needed for therapeutic hypothermia are located in the TCH Swing Unit. Please refer to bedside manual for complete details of cooling process.

- Have cooling blanket ready on the radiant warmer (or use cooling blanket from transport)
- Core body temperature measured by esophageal temperature probe with placement confirmed by CXR to be located at 2/3 the distance of the esophagus
- Therapeutic hypothermia for 72 hours
- All external heat sources turned off
- Desired patient temperature is set at 33.5°C with goal temperature 33.5 ± 0.1°C
- Vital signs and urine output recorded every hour
- Total fluid goal on day 1 of 40–45 ml/kg/day (do not give fluid boluses simply for low urine output)
- NPO during cooling and rewarming
- Record initial and daily Sarnat stage (dot phrase: ".Sarnat") in the History and Physical (EPIC) and daily progress notes
- Neurologic assessment every hour until goal patient temperature achieved, then every 4 hours
- Continuous video EEG initiated immediately on admission
- Morphine drip (load with 0.1 mg/kg and then begin at 0.01 mg/ kg/hr and adjust dose to limit shivering (>0.03 mg/kg/hr is rarely needed) for the whole 72 hours of cooling
- Cranial ultrasound (with resistive index) at 8–12 hours after initiation of cooling
- Reposition infant every 2 hours while cooled
- Recommended labs to be drawn during cooling (or more often as needed):
  - » Glucose: on admission, then every hour x 6 hours, then every 12 hours x 2, then daily x 4 days

- » CBC with differential and PLT: on admission, then daily x 3 days
- » Obtain blood culture on admission
- » PT, PTT, fibrinogen: on admission, then daily x 3 days
- » Chem10, ionized calcium: on admission, then daily x 3 days
- » Arterial blood gases: on admission, then every 6 hours x 4, then every 12 hours x 2, and then daily x 3 days (or more frequently as needed)
- » LFTs: on admission and then daily for 3 days
- » Use order set: IP NEO THERAPEUTIC HYPOTHERMIA ADMISSION (EPIC)
- » Strongly consider infection as a cause of encephalopathy and obtain a blood culture on admission and begin antibiotics
- » Use NEO IP HIE H&P for Admission History and Physical (EPIC)
- » Rewarming begins after 72 hours to increase temperature 0.5°C every hour until goal temperature of 36.5°C
- » Schedule neonatal head MRI (including spectroscopy) for day 4–5 (NO CONTRAST)

Outcomes

The outcome of neonatal encephalopathy depends upon the etiology. In infants with encephalopathy due to a metabolic disorder, outcome will be related to the specific disorder. Similarly, outcome of encephalopathy related to an infectious etiology will depend upon the specific infection. If encephalopathy is due to hypoxic-ischemic injury, outcome is good if the infant has an EEG and a neurologic exam that are normal by 7 days of age. Outcomes also can be related to maximum Sarnat stage reached which is an indication of the severity of the neonatal encephalopathy. Long-term developmental and neurologic follow-up is indicated in all cases of neonatal encephalopathy. Outcome studies from the major cooling trials have indicated that whole body hypothermia is safe, is associated with improved survival and reduced severe neurodevelopmental disability at 18 months, and the benefits noted at 18 months persist to early school age.

Infants receiving whole body cooling should be referred to the TCH Meyer Developmental Center for long-term follow up.

Seizures

Definition

An epileptic seizure is defined as abnormal electrical activity in the brain that may or may not produce physical signs and symptoms which may include convulsive activity, small jerks or twitches, thought disturbances or a combination of such symptoms. The type of observed during seizures depends on the location and extent of the abnormal activity in the brain, its cause, the patient's age and general state of health.

Incidence

Seizures are frequent during the neonatal period. The incidence varies between 1–5/1000 neonates. It has been noted that premature infants are at increased risk compared to term infants.

Background and Pathogenesis

Acute symptomatic seizures are due to a specific provoking condition and are one of the commonest types of neonatal seizures. Therefore, a key factor in treating neonatal seizures is the accurate diagnosis and treatment of the underlying etiology.

Seizures may potentially exacerbate pre-existing brain injury through the following mechanisms:

Hypoventilation/apnea – resultant hypoxia and ischemia or a combination of both may cause brain injury by precipitating cardio- pulmonary collapse and hypercapnia may increase intracranial pressure by increasing cerebral blood flow.

Signs and Symptoms

Increased blood pressure – increase in the intracranial pressure.

Hypoglycemia – increased consumption secondary to anaerobic metabolism.

Increased neurotransmitter release (Excitatory amino acids) – may damage neurons.

At least some of the adverse outcomes above may be prevented by appropriate management implemented in a timely fashion and by controlling seizures.

Diagnosis

Neonatal seizures are classified as epileptic and non-epileptic. Epileptic seizures occur when there is an abnormal electrical discharge and can include tonic, clonic, and myoclonic seizures. Non-epileptic seizures may be subtle and are often associated with pedaling and posturing movements related to brainstem release phenomena. It may be difficult to differentiate epileptic from non-epileptic seizures at the bedside, particularly among premature infants. Eye deviation, blinking, fixed stare, repetitive mouth and/or tongue movements, apnea, pedaling, tonic posturing of limbs can be manifestations of seizures, immature reflexes or simply the sequelae of other illnesses.

The most common etiologies of neonatal seizures are listed in **Table 11-2.** The initial evaluation includes a sepsis work up including a lumbar puncture, metabolic studies (blood glucose, ionized calcium, magnesium, phosphorus, electrolytes, ammonia and lactate) and screening for maternal drug exposure. Ideally, an EEG should be obtained to document the presence/absence of epileptiform activity prior to the initiation of any anticonvulsant therapy; however, there may be occurrences where the clinical events are obviously epileptic in nature that warrant immediate treatment and may not require an EEG. The content and extent of additional laboratory tests (serum amino acids, urine organic acids) will depend upon the results of the initial evaluation, findings on physical examination, perinatal history and response to treatment. Imaging studies are important if intracranial processes are suspected. Head ultrasound can detect major intracranial hemorrhages and structural abnormalities, but may

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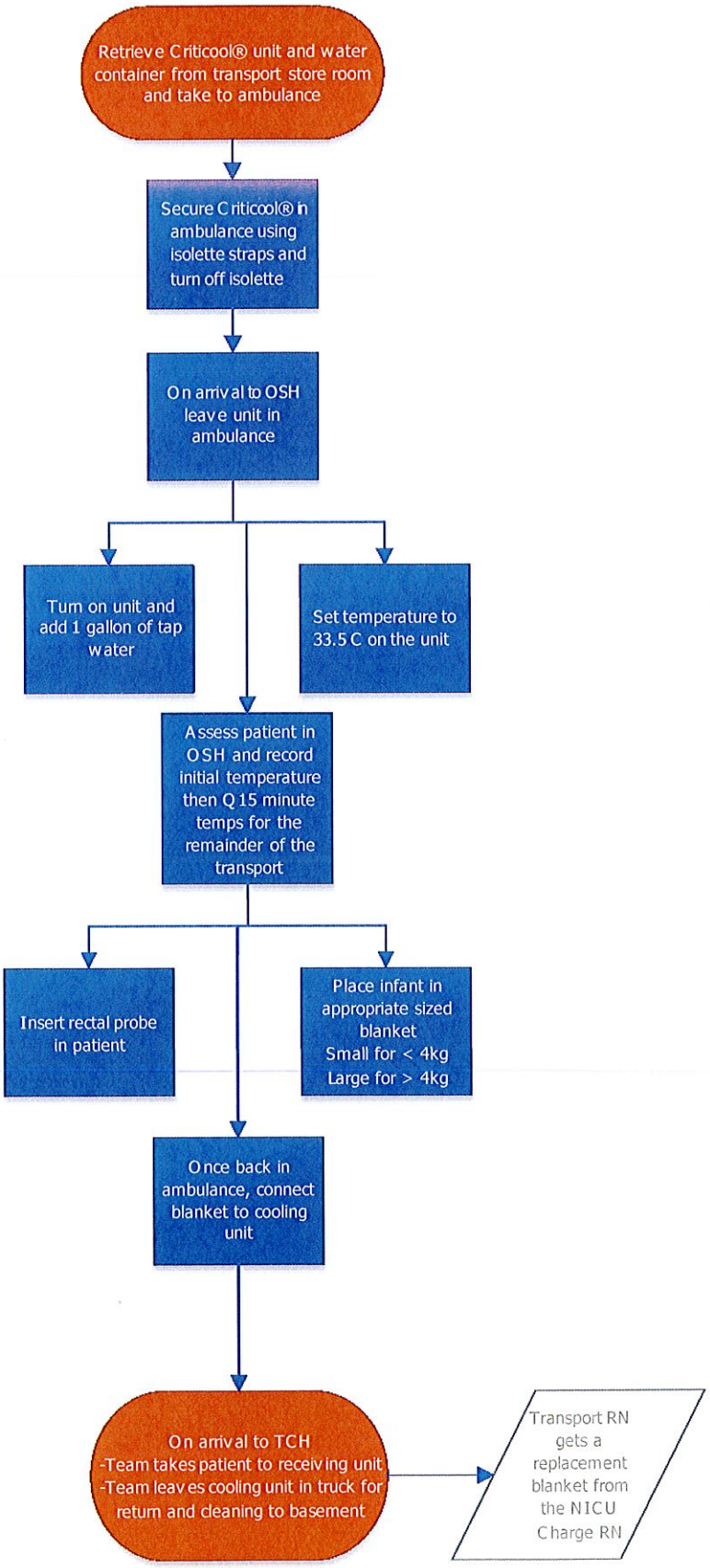
Transport Cooling Process



Cooling Admission Checklist

	Radiant Warmer • Giraffe warmer is preferred-no Delta foam needed • If using the older Ohio Warmer, use Delta foam • (Order→Epic→Pad Overlay Crib Pedi) • Place Delta Foam with champagne flutes up
	CritiCool Machine-Have it already filled up with tap water and ready to go • Proper Wrap-If the infant is coming with Kangaroo Crew they will already be on a wrap, transport will want another wrap at the bedside so they can replace their stock • Esophageal Probe (Grey cable)-once this is placed the 72 hours of cooling starts • **Surface Temp Probe (Green cable)**
	Line Cart and **Procedure Cart** if lines are needed at bedside
	Lab tubes • Gas and iCa • Glucose • CBC-Lavender Bullet • Type and Screen-Lavender Tube • LFTs-Green Bullet • PT/PTT/Fibrinogen-Blue Bullet • Chem 10-Green Bullet • Blood Culture if not already done
	EEG tech will need to be paged and a Neurology Consult