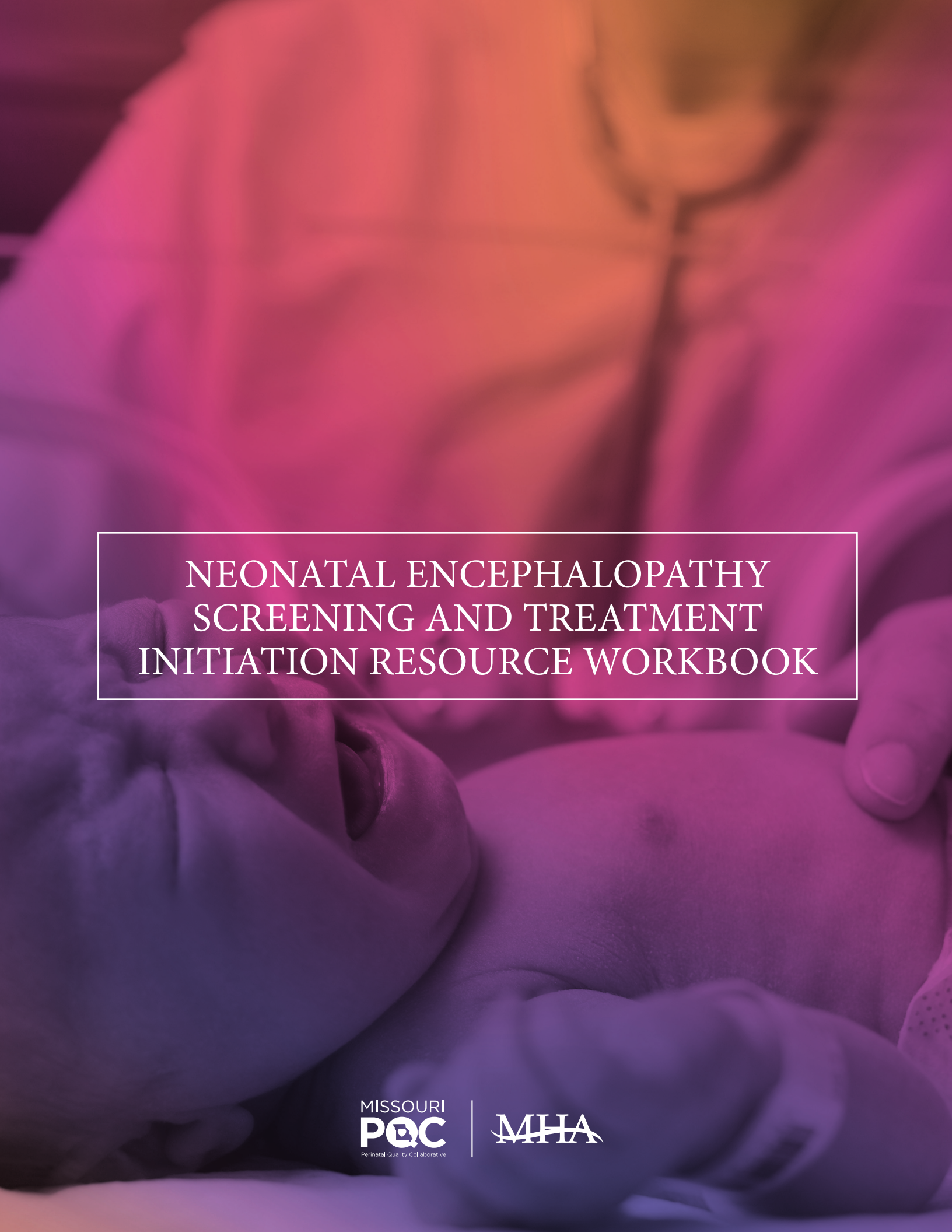




NEONATAL ENCEPHALOPATHY SCREENING AND TREATMENT INITIATION RESOURCE WORKBOOK

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These efforts would not be possible without the collective vision and collaboration of the Missouri Department of Health and Senior Services, Missouri Hospital Association, and members of the Missouri Maternal-Child Learning and Action Network. MC LAN members represent a diverse group of stakeholders from clinical backgrounds, professional associations, government agencies, community-based organizations and community representatives who have committed support to reducing maternal morbidity and mortality in Missouri, including the March of Dimes, Missouri Section of the American College of Obstetricians and Gynecologists, Missouri Chapter of the American Academy of Pediatrics, Missouri Primary Care Association, Missouri DHSS, Missouri Department of Social Services MO HealthNet Division, Missouri Foundation for Health, Missouri Chapter of the Association of Women's Health, Obstetric and Neonatal Nurses, Nurse Practitioners in Women's Health Association, Missouri Chapter of the Amniotic Fluid Embolism Foundation, Generate Health, St. Louis Integrated Health Network, Bootheel Perinatal Network, Healthy Blue MO, Home State Health, United Healthcare, Nurture KC, Promise 1000, M-Brace Birthing, SafiMoms365, the Doula Foundation and Simply Strategy. These partners successfully aligned efforts to bring Alliance for Innovation on Maternal Health initiatives to Missouri in 2019 and connect directly to the Missouri Pregnancy-Associated Mortality Review Board, which identifies leading causes of morbidity and mortality.

The MO PQC also acknowledges the contributions of AIM, the national, cross-sector commitment designed to lead in developing and implementing patient safety bundles to promote safe care for every U.S. birth. Founded in 2014 through a cooperative agreement funded by the Health Resources and Services Administration and executed by ACOG, the AIM program provides expert technical support and capacity building to multidisciplinary state-based teams, most often perinatal quality collaboratives, leading targeted rapid-cycle quality improvement via implementation of patient safety bundles. An AIM patient safety bundle is a structured way of improving the process of care and patient outcomes: a small, straightforward set of evidence-based practices that, when performed collectively and reliably, have been proven to improve patient outcomes. Patient safety bundles are developed by expert multidisciplinary working groups, supported by the AIM staff at ACOG. Working groups include representatives appointed by professional member organizations, known experts and researchers specializing in the clinical topic, and patients with lived experience. The bundle development process includes design of measures and metrics for implementation and multiple levels of review from engaged stakeholders.

This publication would not be possible without the collaborative partnerships, programmatic alignment and passionate engagement from stakeholders throughout Missouri who are firmly committed to moving the health outcomes of mothers and infants from one of the worst in the nation to one of the best. A wide net was cast to contacts across the state in order to form the Neonatal Encephalopathy Steering Committee, the authors of this resource workbook.

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The Evidence

Neonatal encephalopathy is an umbrella term used to describe brain dysfunction in a newborn, manifesting as an alteration in mental status and abnormal neurologic examination.¹ NE may be caused by a variety of conditions and perinatal events that can lead to neurologic dysfunction including hypoxia-ischemia, metabolic disorders, inflammatory conditions, thromboembolic disorders and genetic factors.² While estimates vary, hypoxic-ischemia is believed to account for 30%-80% of neonatal encephalopathy cases.² Hypoxic-ischemic encephalopathy is broadly defined as neonatal encephalopathy that is caused by a disruption in oxygen or blood flow to the infant's brain shortly before, during or after delivery.³ This can be due to a variety of causes potentially occurring during the labor and delivery process, including umbilical cord prolapse or rupture, uterine rupture, maternal trauma, maternal hemorrhage, severe maternal hypotension, maternal cardiovascular collapse or shoulder dystocia, to name a few. These perinatal events decrease blood and therefore oxygen perfusion to the infant's vital organs, most notably their brain.

Neonatal encephalopathy occurs in two stages: an initial insult to the brain when it is deprived of oxygen and/or blood flow and secondary injury, caused by reperfusion of the brain and subsequent dispersion of toxins from damaged brain cells. This reperfusion injury occurs between six and 48 hours of life for the infant.³ In an effort to prevent or limit this secondary injury, it is imperative that infants with moderate or severe NE receive therapeutic hypothermia treatment prior to six hours of life. By cooling the body to 33.5°C to 34.5°C for 72 hours, the brain's metabolic demands are lowered and the excitatory neurotransmitters are reduced, helping to prevent further brain injury.⁴ Therapeutic hypothermia provided within six hours of life for term infants (between 37 and 42 weeks of completed gestation) and near-term or late preterm infants (between 35 and 36 completed weeks of gestation) with moderate-to-severe HIE has been shown to decrease morbidity and mortality.⁵

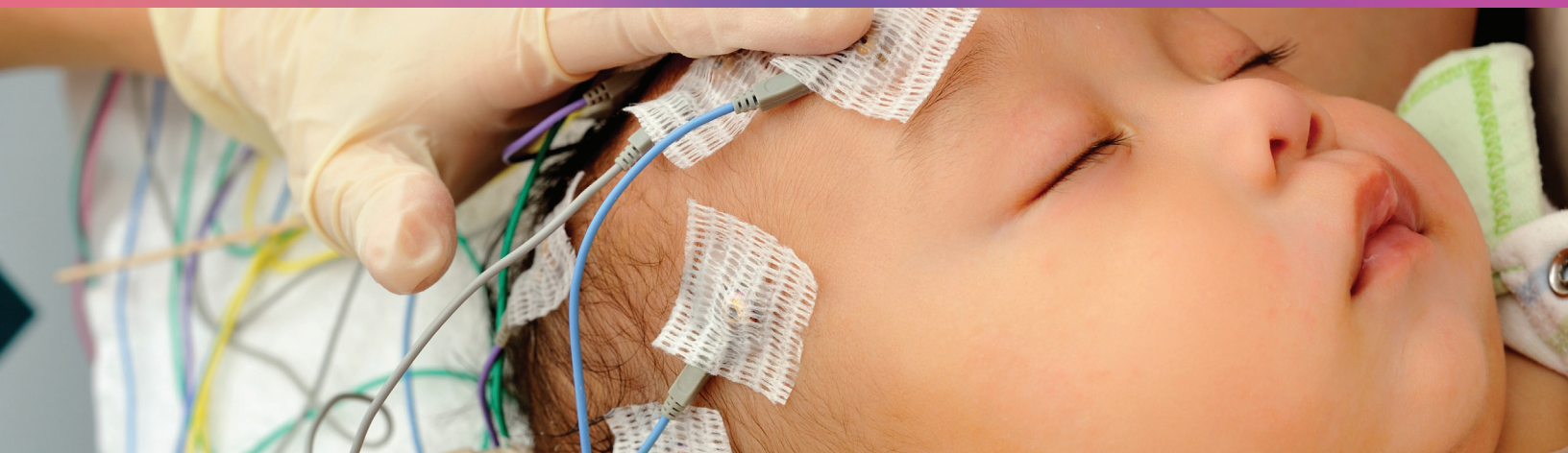
Timely determination of which infants qualify for therapeutic hypothermia is key to successful treatment. Providers must consider the patient's perinatal history, lab results (including pH and base deficit) and their neurological status (ideally, this is assessed within one hour of delivery).⁶ The Modified Sarnat Exam is the most frequently used tool to assess the degree of encephalopathy in newborns. The exam includes six categories (i.e., level of consciousness, spontaneous activity, posture, muscle tone, primitive reflexes and autonomic function), each of which can have mild, moderate or severe abnormalities.⁶ In addition to perinatal history and lab results, a term or near-term newborn must present with seizures or have three of the six categories scored in the moderate or severe range to qualify for therapeutic hypothermia.⁶ For infants who have mild neonatal encephalopathy, serial hourly neurologic exams are recommended until the infant either develops seizures or moderate/severe NE requiring TH or six hours have passed since birth (the window for TH treatment has passed). If the infant has three consecutive normal neuro exams, then continue with clinically appropriate newborn care with no further need for serial hourly neurological exams.⁵

Stage	Normal (N)	Mild (MI)	Moderate (Mod)	Severe (Sev)
1. Level of consciousness	Normal	Hyperalert/irritable	Lethargic/obtunded	Stupor/coma
2. Spontaneous activity	Normal	Normal/jittery	Decreased	Absent
3. Muscle tone	Normal	Normal/slightly increased	Hypotonic	Flaccid
4. Posture	Normal	Mild distal flexion	Strong distal flexion	Decerebrate
5. Primitive reflexes	Normal	Weak	Weak/uncoordinated	Absent
a. Suck				
b. Moro	Normal	Exaggerated	Weak/incomplete	Absent
6. Autonomic function	Normal	Dilated	Constricted	Unequal/fixed/ dilated
a. Pupils				
b. Heart Rate	Normal	Tachycardia	Bradycardia	Variable
c. Respirations	Normal	Normal	Periodic breathing	Apnea

Table 1 Neonatal Encephalopathy (Modified Sarnat) Staging Examination. Source: Bonifacio, S. L., & Hutson, S. (2021). The term newborn: Evaluation for hypoxic-ischemic encephalopathy. *Clinics in Perinatology*, 48(3), 681-695. <https://doi.org/10.1016/j.clp.2021.05.014>

Together with therapeutic hypothermia, an infant with moderate/severe NE will receive neuroimaging to assess for a potential cause of NE and any brain injury that may exist.⁵ While imaging can provide clues to the areas of the brain that may have experienced an injury for patients with NE, the extent of the injury may not be known for several months to years.³ Some infants who experience this brain injury may not have any negative long-term health outcomes, while others may experience developmental delays, intellectual disabilities (ranging from mild to severe), epilepsy, cerebral palsy, organ (including heart, lung, kidney and liver) dysfunction and even death.³ The negative long-term health impacts of NE not only impact the infant, but also their families and communities. Data suggests that parents of patients treated with therapeutic hypothermia (patients with NE) may experience acute and chronic feelings of loss and grief for their child.⁵ However, medical teams can help families struggling with loss and grief by offering wraparound services (including support from social workers) as well as providing trauma-informed care and open communication regarding the diagnosis, treatment and follow-up plan related to long-term developmental outcomes.⁵ Although the lifetime direct and indirect costs of neonatal encephalopathy are not yet fully understood, the economic, productivity and social costs associated with its long-term health outcomes are estimated to be substantial.

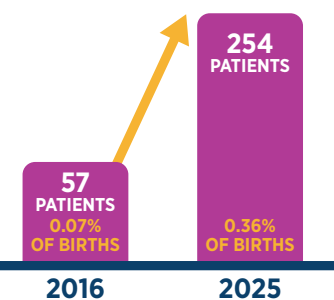
Often, the severity of health complications depends on how long the infant's brain was without oxygen or blood flow and how it was treated.³ For this reason, **it is vitally important that NE is identified as early as possible through screening, that evidence-based therapeutic hypothermia treatment is initiated without delay, and that patients and their families receive ongoing support during their care.**



Missouri's Call to Action

Unfortunately, the rate of neonatal encephalopathy is not well known. In developed countries, NE is estimated to occur in every three to four infants per 1,000 live births, with NE due to HIE occurring in one to three infants per 1,000 live births.^{2,6} In Missouri, true rates of NE are hard to determine. This is due largely to the nature of the diagnosis. For instance, not all patients who are treated for NE with therapeutic hypothermia will have an NE or HIE diagnosis in their electronic health record. Rather, some patients may have diagnosis codes related to symptoms of NE (e.g., seizures or abnormal breathing) but not be diagnosed with NE or HIE following treatment. For this reason, data are difficult to quantify. However, using diagnosis codes listed in a 2021 study by Bandoli et al. to run Missouri data, it is estimated that the number of patients with NE in Missouri has increased from **57 patients in 2016 (0.07% of births) to 254 patients in 2025 (0.36% of births)**, which would align with averages for infants born in developed countries.²

Neonatal Encephalopathy in Missouri



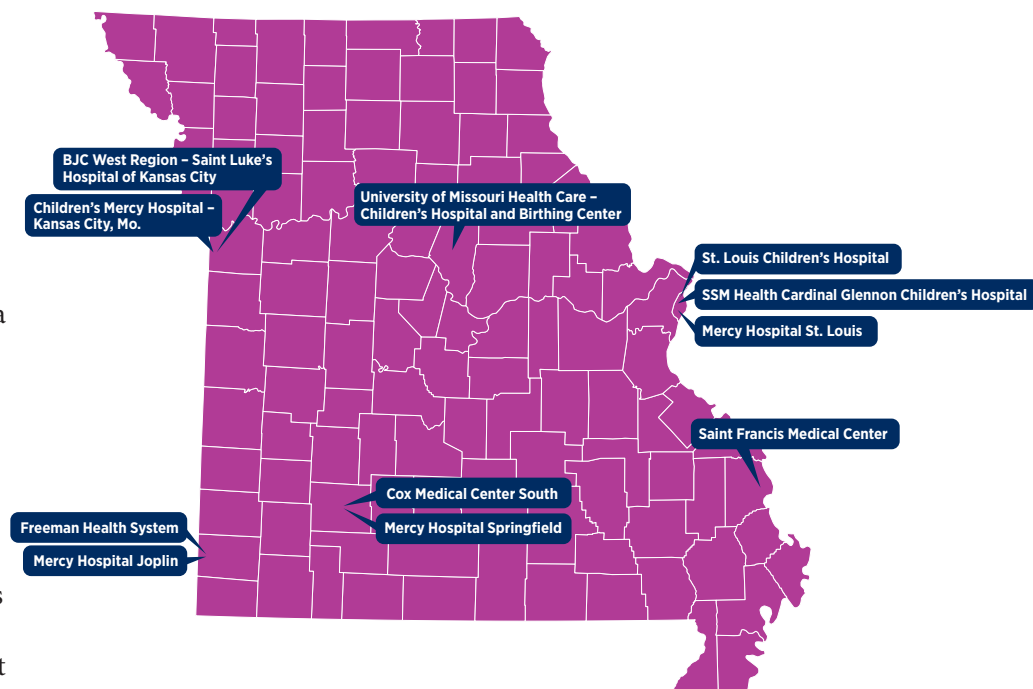
Missouri Therapeutic Hypothermia Cooling Centers

- » BJC West Region – Saint Luke's Hospital of Kansas City
- » Children's Mercy Hospital – Kansas City, Mo.
- » Cox Medical Center South
- » Freeman Health System
- » Mercy Hospital Joplin
- » Mercy Hospital Springfield
- » Mercy Hospital St. Louis
- » Saint Francis Medical Center
- » SSM Health Cardinal Glennon Children's Hospital
- » St. Louis Children's Hospital
- » University of Missouri Health Care – Children's Hospital and Birthing Center

With this steady increase in patients diagnosed with NE in mind, as well as the long-term health implications and their associated costs for the patient, their family and communities, it is important for medical teams across the state to take steps to reduce long-term morbidity and mortality from NE. This can be done by ensuring all eligible patients with neonatal encephalopathy are consistently recognized and treated with therapeutic hypothermia, as appropriate, within six hours of life to help prevent further brain injury.

Due to the medical complexity of moderate or severe NE, treatment for this diagnosis is not offered at every hospital. Rather, within the state of Missouri, neonates can receive therapeutic hypothermia at a limited number of Level III and IV NICUs across the state. For this reason, it is critically important for every birthing facility to have a referral and transport plan in place for patients requiring time-critical TH treatment. Transport teams who care for these patients should

be trained on infant neurological exams, passive or active cooling (depending on what resources are available) and medical treatment of these infants. Once the patient reaches the cooling center, they should either continue or begin active cooling in an effort to reach therapeutic temperature within six hours of life. In addition to therapeutic hypothermia, these higher level of care facilities should be able to provide advanced medical care that this patient population requires, including mechanical ventilation, continual monitoring of vital signs, frequent lab work, neuroimaging (including EEGs and MRIs), neurological support and consultation at all times, and family support resources.⁵



MO PQC Patient Safety Bundle for Neonatal Encephalopathy

The Missouri Perinatal Quality Collaborative encourages all stakeholders in infant health to take action to reduce morbidity and mortality from NE by implementing the Neonatal Encephalopathy patient safety bundle. Guided by the expertise and input of the Neonatal Encephalopathy Steering Committee, this bundle was developed to provide a practical framework for multidisciplinary teams to address shared challenges in the screening and timely treatment of neonatal encephalopathy. These challenges include early screening and recognition of NE at the birthing center, thorough neonatal neurological examinations, timely transfer of the patient to a cooling center, and achievement of therapeutic hypothermic temperature within six hours of life.

The patient safety bundle provides a structured framework for delivering evidence-based care and improving patient outcomes. This bundle is structured similarly to the national AIM safety bundles using the five Rs of readiness, recognition and prevention, response, reporting and systems learning, and respectful, equitable and supportive care.⁷ The bundle has been further broken down into three components centered on the medical team members responsible for care.



Readiness – Every Care Setting

☐ Birthing Facility

- ☐ Develop a standard process for screening, monitoring and early treatment of NE.
- ☐ Provide interprofessional education on screening, monitoring and treatment protocols, including conducting yearly interprofessional team-based drills with timely debriefs.
- ☐ Develop and maintain a timely and reliable care escalation plan (including appropriate consultation and transport to a higher level of care if medically indicated).

☐ Transport Team

- ☐ Partner with the cooling center to develop and adhere to standardized protocols for the monitoring and treatment of NE.
- ☐ Provide education regarding how to perform and document infant neurological examinations.
- ☐ Ensure transport teams are aware of NE treatment centers in Missouri.
- ☐ Provide education on screening, monitoring and treatment protocols, including conducting yearly team-based drills with timely debriefs.
- ☐ Adopt a standardized, reliable process for priority transfer of patients with NE.

☐ Cooling Center

- ☐ Develop a standardized process for the initiation/continuation of active cooling to achieve therapeutic temperature within six hours of life.
- ☐ Develop a guideline for the roles and responsibilities of interdisciplinary team members pertaining to the infant neurological examinations.
- ☐ Develop a highly reliable, standardized treatment protocol/bundle for patients receiving therapeutic hypothermia (including neuro assessments, feeding plan, medication protocols and imaging).
- ☐ Provide interprofessional education on monitoring and treatment protocols for NE, including conducting yearly interprofessional team-based drills with timely debriefs.
- ☐ Develop and maintain a timely and reliable care escalation plan if deemed medically necessary.

Recognition and Prevention – Every Patient

- ☐ Birthing Facility
 - ☐ Implement a protocol for screening, monitoring and communicating concerns (using standardized language) related to possible HIE-associated events.
 - ☐ Assess and document infant neurological status using the Modified Sarnat Exam for patients with concern for NE.
 - ☐ A provider trained in performing the Modified Sarnat Exam should be consulted if not present.
 - ☐ Assess and document blood gas results for patients with concern for NE.
 - ☐ Adhere to a standard screening process for NE.
- ☐ Transport Team
 - ☐ Adhere to a standard screening process for NE for all outborn patients.
 - ☐ Assess and document infant neurological status using the Modified Sarnat Exam for patients with concern for NE.
 - ☐ A provider trained in administering the Modified Sarnat Exam should be consulted if not present.
- ☐ Cooling Center
 - ☐ Implement a protocol for screening, monitoring and communicating concerns (using standardized language) related to worsening neurologic status.
 - ☐ Assess, monitor and document infant neurological status.
 - ☐ Assess, monitor and document serial lab results as appropriate.

Response – Every Event

- ☐ Birthing Facility
 - ☐ Demonstrate high reliability in utilizing a standardized treatment protocol (including maintaining normothermia or initiating passive or active cooling to achieve therapeutic temperature by six HOL).
 - ☐ Deploy a timely and reliable care escalation plan (including obtaining appropriate consultation and transport to a higher level of care if medically indicated).
- ☐ Transport Team
 - ☐ Demonstrate high reliability in utilizing a standardized treatment protocol (including maintaining normothermia or initiating passive or active cooling to achieve therapeutic temperature by six HOL).
- ☐ Cooling Center
 - ☐ Achieve therapeutic hypothermia temperature within six HOL or ASAP within 24 HOL.
 - ☐ Demonstrate high reliability in utilizing a standardized treatment protocol/bundle for patients receiving therapeutic hypothermia (including neuro assessments, feeding plan, medication protocols and imaging).
 - ☐ Deploy a timely and reliable care escalation plan as medically necessary.



Reporting and Systems Learning – Every Unit

- ☐ Birthing Facility
 - ☐ Monitor outcome, process and structure measure data related to NE screening and treatment.
 - ☐ Establish a culture of utilizing huddles and post-event debriefs for every case of NE to identify successes and opportunities.
 - ☐ Develop a standardized approach for communicating with the cooling center and transport team as needed.
 - ☐ Perform multidisciplinary reviews of all NE cases to identify possible systems issues.
- ☐ Transport Team
 - ☐ Develop a standardized approach to communicate with the cooling center.
 - ☐ Monitor outcome, process and structure measure data related to NE screening and treatment.
- ☐ Cooling Center
 - ☐ Develop a standardized approach for communicating with the birthing facility and transport team.
 - ☐ Monitor outcome, process and structure measure data related to NE monitoring and treatment.

Respectful, Equitable and Supportive Care – Every Unit/Provider/Team Member

- ☐ Birthing Facility, Transport Team, Cooling Center
 - ☐ Engage in open, transparent and empathetic communication with the patient's family.
 - ☐ Include the patient's family as part of the multidisciplinary care team to establish trust and ensure informed, shared decision-making that incorporates the family's values and goals.
 - ☐ Provide trauma-informed support and education to the patient's family.
 - ☐ Plan for reunification of mother and infant as soon as medically appropriate (Birthing Facility).

Resources

Tools

[Therapeutic Hypothermia for Neonatal Encephalopathy Criteria Algorithm](#)

[Indications of Possible Neonatal Encephalopathy](#)

Exam

[Serial Neurologic Exams](#)

[Blood Gases](#)

Passive Cooling Initiation and Patient Transfer

[Assessing Eligibility for Therapeutic Hypothermia](#)

[Passive Cooling for Patients with Neonatal Encephalopathy](#)

[Transportation of Patient with Neonatal Encephalopathy](#)

[Missouri Therapeutic Hypothermia Cooling Centers and Referral Hospitals](#)

Active Cooling Initiation

[Initiation of Active Cooling for Patients with Neonatal Encephalopathy](#)

Family Educational Resources

[FAQ About Neonatal Encephalopathy and Cooling Therapy](#)

[Therapeutic Hypothermia for Parents](#)

[Hope for HIE Website - Hypoxic Ischemic Encephalopathy](#)

[CDC's Developmental Milestones | Learn the Signs. Act Early.](#)

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- ⁸ Alliance for Innovation on Maternal Health. (n.d.). *Patient safety bundles*. AIM. <https://saferbirth.org/patient-safety-bundles/>