Hypoxic Ischemic Encephalopathy:

Pearls for the LNC

Joan Earley, MSN, RNC-NIC, C-ELBW, CPNP, CLCP

Keywords: hypoxic-ischemic encephalopathy, Sarnat Staging, neurologic syndrome, neuroprotective, hypothermia

The legal nurse consultant (LNC) who assists attorneys with hypoxic-ischemic encephalopathy cases must have a toolbox to assist attorney clients. The LNC must know how to decipher medical records to determine risk factors, prognosis, and the timing of neurologic insults impacting the neonate with HIE. Pearls the LNC can use to understand the medicolegal aspects of this condition are provided.

Hypoxic-ischemic encephalopathy (HIE) is a devastating birth injury. HIE is a brain injury caused by asphyxia that prevents adequate blood supply from circulating to the brains of primarily term infants. Hypoxic events can occur during the prenatal, intrapartum, or postnatal period (Allen & Brandon, 2011).

The incidence of HIE is 1.5-2.5 per 1000 live births. Nearly 2-4 % of term babies are affected by HIE. Low birth weight neonates have an increased incidence of 60% (Association of Women's Health, Obstetric, and Neonatal Nurses [AWHONN] et al., 2015). According to Volpe, 20% of cases of HIE occur in the antepartum period, and 30% in the intrapartum period (Inder & Volpe, 2018). HIE causes 21% to 23% of neonatal deaths and 6-9% of neonatal deaths in term babies (Finder et al., 2020) (Zanelli et al., 2018). Worldwide, 1 million deaths per year are attributed to HIE. Even though this statement may be controversial, many experts consider HIE a

significant cause of cerebral palsy (CP) (Inder & Volpe, 2018).

HIE can negatively impact the quality of life of neonates and their families. Even children mildly affected can have long-term problems such as developmental delay. Children with severe asphyxia may be at risk for aspiration pneumonia and require feeding tubes. They may need respiratory support and frequent suctioning. Long-term follow-up may be necessary for orthopedic issues such as scoliosis, dislocated hips, and visual deficits. They may require communication devices, follow-up with speech therapists, surgery for scoliosis, physical therapy, orthotics, and baclofen pumps for spasticity if needed. They require special wheelchairs and adaptive home devices. They also require appropriate education plans. This list is not inclusive. Parents and the child's caretakers require respite care for much-needed mental and physical rest. Caretakers often must stop working to care for their affected child. The family experiences a loss of income. The family also mourns the loss of educational opportunity and future income for their affected child (Eunson, 2015).

It is estimated that the long-term financial needs of children with HIE and subsequent cerebral palsy may be over 900,000 dollars for those with comorbid cognitive difficulties (Husted, 2015). The LNC and life care planner (LCP) can assist the plaintiff or defense attorneys in determining the future needs of newborns affected by HIE. The LCP can consult with the physical medicine and rehabilitation (PM&R) physician, neurologist, physical therapist, family, and later the neuropsychologist, for example, to determine the future needs of affected children. The LNC must become familiar with the antecedents of HIE to assist attorneys with brain injury cases. A discussion of the causes of HIE follows.

This activity is designed to increase knowledge of the LNC in assisting attorneys with hypoxic-ischemic encephalopathy cases. The LNC must know how to decipher medical records to determine risk factors, prognosis, and the timing of neurologic insults impacting the neonate with hypoxic-ischemic encephalopathy.

Upon completion of the learning activity the learner will be able to:

a. Identify incidence and antepartum risk factors for hypoxemic-ischemic encephalopathy in neonates.
b. Recognize and determine prognosis and the timing of neurologic insults through medical record review.
c. Identify the medicolegal aspects of hypoxemic-ischemic encephalopathy and better assist plaintiff and defense attorneys with these cases.

The author, reviewers, and nurse planners all report no financial relationships that would pose a conflict of interest.

This activity has been awarded 1 Contact Hour of credit. The activity is valid for credit until September 1, 2025.

To receive CE credit, read the article and pass the CE test online at http://www.aalnc.org/page/the-journal-of-legal-nurse-consulting

CEs are free to members during the membership year and can be purchased as a 4-issue subscription of $65/year for non-members.

Events associated with HIE include cord prolapse, uterine rupture, abruption placenta, placenta previa, maternal hypotension, breech presentation, or shoulder dystocia. Abnormal fetal heart rate tracings, poor umbilical cord gases, low Apgar scores, meconium-stained fluid, and the neonate's need for respiratory support during the first few minutes of life are associated with HIE. Conditions related to impaired oxygen delivery and decreased cerebral blood flow can lead to HIE. An important caveat is that there are other causes of neonatal encephalopathies, such as infections and metabolic disorders (Reynolds & Talmage, 2011).

HIE occurs in two phases: primary energy failure and secondary energy failure. As previously discussed, the preliminary failure phase of HIE starts with a reduction in cerebral blood flow initiated by a triggering event (Allen & Brandon, 2011). Oxygen is decreased in the primary energy failure stage. Lactic acid levels increase during anaerobic metabolism (Reynolds & Talmage, 2011). Also, decreased cerebral blood flow leads to less adenosine triphosphate (ATP) energy production. Low levels of ATP disrupt mechanisms that maintain cellular integrity, such as the sodium/potassium pump (Allen & Brandon, 2011).

An excessive increase in positively charged sodium ions results in the depolarization of the baby's brain neurons. Glutamate, an excitatory neurotransmitter, is released during this process. Glutamate binds to glutamate receptors resulting in increased intracellular calcium and sodium. The increased intracellular calcium and sodium cause cellular edema, ischemia, necrosis, and cell death (apoptosis). Cellular necrosis disrupts the cell membrane.

Necrosis causes brain cells to swell and rupture, leading to cell death in the primary energy phase of HIE. When cells rupture, released contents cause inflammation. Inflammatory mediators damage white cell matter. This leads to scar formation. The brain cells may die or recover if there are fewer severe

insults. Cell death leads to cell shrinkage. Apoptosis can occur several days after the initial injury. Necrosis causes decreased brain function.

If the damage during the primary energy failure phase is severe, further injury occurs in the secondary energy phase. There is a period of recovery if blood flow is restored. This brief recovery period is called the latent period. During this period, vital signs may be normal. The severity of the ischemic damage can determine if the recovery period is brief or lasts longer. The latent period is the best time for treatment. The latent period can last 6 hours.

The secondary energy failure phase may occur 6-48 hours after the initial insult. Inflammation, excitotoxicity, and oxidative stress contribute to secondary energy failure. Free radical production causes oxidative stress with necrosis and cell death.

Neonates use high levels of oxygen while transitioning from fetal life. The fetal brain has decreased levels of antioxidants and is ill-equipped to eliminate free radicals produced during a hypoxic-ischemic event. Neuronal tissue is damaged as a result.

Increased levels of the neurotransmitter glutamate cause a cascade of events, such as the excess flow of calcium and sodium into neural cells. Glutamate in normal levels is an important neurotransmitter for hearing, vision, learning, memory, and somatosensory function. Disrupted neurotransmission impairs the development of the neonatal brain (Allen & Brandon, 2011).

Volpe states three events occur as HIE develops (Inder & Volpe, 2018, p. 512). These events comprise neurological syndrome. They include:

1. Evidence of fetal distress and fetal risk for hypoxia/ischemia, FHR abnormalities, sentinel event, fetal acidemia
2. The need for resuscitation and low Apgar scores
3. An overt neurological syndrome in the first hours or days of life

Sarnat developed a system for the classification of HIE from Stage 1 (mild), Stage 2 (moderate), to Stage 3 (severe) in the 1970s. See the table below (Casey et al., 2011):

1. Stage 1 clinical presentations of HIE, according to Sarnat, include hyper-responsiveness to stimulation, increased deep tendon reflexes, few oral secretions, and usually no seizures. Seizures may also occur if there are preexisting conditions such as hypoglycemia (AWHONN et al., 2015, p. 762).
2. Stage II of Sarnat classification (moderate encephalopathy) includes an overactive doll's eye reflex, increased DTRs, (deep tendon reflexes), periodic respiration, lethargy, strong grasp, and myoclonus. Stage II is a critical phase because the infant can improve or deteriorate. EEG abnormalities, seizures, cerebral edema, and lethargy are signs of deterioration. Signs of improvement in Stage II are cessation of seizure activity, normal EEG, and an increase in the level of consciousness.
3. Stage III (severe encephalopathy) Sarnat classification clinical signs and symptoms include apnea and bradycardia, requiring ventilator support, and decreased level of consciousness. Seizures occur within the first 6-12 hours after birth. Seizure activity may be subtle or generalized in premature neonates and multifocal clonic in the term baby. Term babies may be subtle or generalized in premature neonates and multifocal clonic in the term baby. Term babies may also exhibit subtle seizure signs such as staring or twitching of the tongue. Deep tendon reflexes are decreased or absent in Stage III Sarnat classification. These infants can deteriorate in 24-72 hours. Those who survive have feeding difficulties. They are unable to suck and swallow. These hypotonic infants have poor neurologic outcomes.

The legal nurse consultant who assists attorneys with HIE cases must examine the medical records for possible risk factors contributing to brain injury; antepartum risk factors (occurring before birth) may include the following test results:

Sarnat & Sarnat Staging (1976)

	Stage 1	Stage 2	Stage 3
Consciousness	**hyperalert**	**Lethragic of obtunded**	**Stupor or coma**
Activity	**Normal**	**Decreased**	**Absent**
Neuromuscular control Muscle tone Posture Stretch reflexes	 Normal Mild distal flexion Overactive	 Mild hypotonia Strong distal flexion Overactive	 Flaccid Intermittent decerebration Decreased or absent
Primitive Reflexes Suck Moro Tonic Neck	 Weak Strong Slight	 Weak or absent Weak, incomplete Strong	 Absent Absent Absent
Autonomic function Pupils Heart rate	 Normal Tachycardia	 Miosis Bradycardia	 Mydriase or variable, unequal Variable
Seizures	**None**	**Common**	**Uncommon**

FETAL MOVEMENT

Maternal reports of decreased fetal or decreased movement noted on ultrasound may indicate "chronic uteroplacental insufficiency." The mother's self-report of fetal movement is a standard method of determining "fetal well-being" (Inder & Volpe, 2018, p. 326).

FETAL HEART RATE

The non-stress test is used to assess fetal response to movement. The fetus should demonstrate at least two heart rate accelerations (of at least 15 beats per minute) above the baseline heart rate for at least 15 seconds; as a response to movement or vibro-acoustical stimulation in 20 minutes. If this occurs, this is considered a reactive non-stress test and is predictive of fetal well-being. A caveat is that the 24–28-week-old fetus may have a non-reactive stress test and be neurologically intact (Inder & Volpe, 2018).

CONTRACTION STRESS TEST

This test consists of the fetal heart rate response to oxytocin or nipple stimulation. Oxytocin and nipple stimulation can cause contractions. Late decelerations as a response after 50% or more of contractions are indicative of an abnormal contraction stress test. Late decelerations indicate fetal distress as a response to contractions. Uterine contractions may produce variable decelerations as well. The variable deceleration fetal heart rate tracing indicates umbilical cord compressions during contractions. Sometimes the variable deceleration fetal heart rate pattern indicates oligohydramnios (decreased amniotic fluid) (Inder & Volpe, 2018).

FETAL BIOPHYSICAL PROFILE

The five components of the biophysical profile include fetal breathing, movement, tone, heart rate reactivity, and amniotic fluid volume. Each piece, if present, is given a score of 2 points. A score of 8-10 is considered normal. A score of 6 is equivocal, and a score of 4 or less is abnormal. Oligohydramnios (decreased amniotic fluid warrants further investigation of the fetal biophysical profile (Inder & Volpe, 2018).

FETAL GROWTH

Ultrasound detection of intrauterine growth retardation is an important finding. Ten to 15% of growth retarded neonates are at risk for intrapartum asphyxia caused by placental insufficiency (Inder & Volpe, 2018).

UMBILICAL ARTERY DOPPLER VELOCITY

Doppler ultrasound detects decreased umbilical artery diastolic flow velocity in intrauterine growth-restricted neonates (IUGR). The absence of diastolic flow leads can lead to fetal demise and asphyxia (Inder & Volpe, 2018).

The legal nurse consultant who assists with HIE cases should examine the medical record (history)for antepartum risk factors that can lead to decreased placental blood flow and HIE in the newborn. These risk factors include (Inder & Volpe, 2018, p. 449):

- Preeclampsia
- Maternal diabetes
- Intrauterine growth restriction
- Twin gestation
- Maternal trauma/hemorrhage
- Post dates
- Maternal thyroid disease
- Maternal age

TORCH infections: (congenital infections passed to the baby during pregnancy, delivery, or after birth) TORCH is an acronym for toxoplasmosis, other (syphilis, varicella, mumps, parvovirus, and HIV; rubella, cytomegalovirus, and herpes simplex.

Intrapartum risk factors for HIE that may be noted in the labor and delivery medical records include:

- Chorioamnionitis
- Uterine rupture
- Abruption placenta
- Cord prolapse
- Placenta previa
- Placental vasculopathy
- Thick meconium
- Fetal heart rate abnormalities
- Fetal acidemia
- Resuscitation needed by the neonate and Apgar scores less than 7
- Inadequately trained personnel providing NRP (neonatal resuscitation)
- Shoulder dystocia
- Failed vacuum extraction
- Sentinel events (Torbenson et al., 2017)

As noted earlier, inborn metabolism errors are often mistaken for HIE. The LNC should identify significant factors in the family medical history in the medical records. Inborn errors of metabolism often present after a period of wellness in the neonate. There are usually no initial signs of asphyxia at birth. Mitochondrial disorders cause symptoms similar to neonatal encephalopathy (Aslam et al., 2019).

Inborn errors of metabolism that cause symptoms similar to HIE include sulfite oxidase deficiency, nonketotic hyperglycinemia, cytochrome C, Clara transaminase, 3-phosphoglycerate dehydrogenase, urea cycle defects, peroxisomal disorders, mitochondrial defects, disorders of pyruvate metabolism, and urea cycle defects (Aslam et al., 2019).

Genetic causes of neonatal encephalopathies include congenital myoclonic dystrophy type I and factor V Leiden. Neonatal neuromuscular myopathies also cause neonatal encephalopathy (NE) (Aslam et al., 2019).

Clotting disorders such as V Leiden and prothrombin mutations cause strokes in neonates. Infections also cause NE.

The legal nurse consultant should review the medical records to determine if hypothermia treatment for a neonate with HIE was started within 6 hours of injury.

Thus, there are multifactorial causes of neonatal encephalopathies (Zanelli et al., 2018).

The LNC should note lab results in conjunction with the physical and history may indicate the extent of brain injury. Some laboratory test results to consider are:

Serum electrolytes: Low serum sodium, potassium, and chloride levels along with reduced urine output and increased edema (excessive weight gain) may indicate SIADH (syndrome of inappropriate antidiuretic hormone, acute renal tubular damage, especially in the first 2-3 days of life.

Cardiac enzyme results may indicate heart damage from asphyxia.

Renal function lab results such as serum creatinine, creatinine clearance, and blood urea nitrogen levels (BUN) may indicate renal damage from HIE.

HIE damage affecting liver function can be assessed by following platelet counts, partial thromboplastin time, and fibrinogen labs.

Labs such as fetal cord gases, arterial blood gases, and lactate results should be reviewed to gain information about the extent of neurological insult (Zanelli et al., 2018).

The LNC should also look for imaging study reports in the medical records when assisting with HIE cases. Magnetic Resonance Imaging (MRI) is the preferred imaging study, especially for following infants with moderate to severe HIE. Patterns of injury and prognosis can be identified on MRI (Zanelli et al., 2018).

Plaintiff and defense attorneys will find MRI studies helpful in determining pre-existing brain defects. For example, defects such as inflammatory processes, hydrocephalus, trauma, and congenital malformations can be detected on MRI.

EEG results, hearing screens, and retinal exam reports also provide valuable clues regarding the severity of HIE. Echocardiography results are important to examine because HIE can cause decreased cardiac contractility and ejection fraction. Supportive care was the only treatment available for HIE 10-15 years ago. The supportive care consisted of blood pressure maintenance, prevention of hypoglycemia, seizure medication, and ventilator support (Zanelli et al., 2018).

Since 2010, hypothermia has been recognized as the primary neuroprotective treatment for HIE. A cooling cap or a total body cooling blanket is utilized. The rectal or nasopharyngeal temperature must be maintained at 34-35 degrees centigrade for 72 hours. Hypothermia prevents further inflammation and cell death and must be initiated within 6 hours of birth (Mosalli, 2012).

The legal nurse consultant should review the medical records to determine if hypothermia treatment for a neonate with HIE was started within 6 hours of injury. The legal nurse consultant should also note if transfer to a level III or IV facility offering hypothermia treatment for HIE were done promptly.

Inclusion criteria for therapeutic hypothermia include:

- Infants greater than or equal to 36 weeks gestational age
- Evidence of moderate or severe encephalopathy or seizures
- Evidence of hypoxia contains two of the following
- Apgar score less than or equal to 5 at 10 minutes of age
- The continued need for mechanical ventilation or resuscitation at 10 minutes of age
- Metabolic acidosis with pH less than seven or a base deficit greater than or equal to 12mmol in cord blood or arterial blood gas within 1 hour of birth

Infants not eligible for Cooling include:

- Infants with a birth weight of fewer than 2000 grams
- Infants with gestational age less than 36 weeks
- Infants with life-threatening congenital heart disease
- Infants whose death appears inevitable.

The following case study provides an example of a neonate suffering from HIE.

- The infant may qualify for hypothermia treatment.

Case Study

Baby boy Johnson is a 39-week gestational age infant. His mother is 25 years old. This is her first baby. A stat C-section delivers Mrs. Johnson's baby by the obstetrician for decreased heart tones. He appears limp and blue with poor respiratory effort. The neonatologist is present at delivery and immediately provides positive pressure ventilation. Baby boy Johnson is intubated. His heart rate at one minute of age is 50. Chest compressions are begun. His oxygen saturation by pulse oximeter placed on his right wrist is 40%. He is given 100% oxygen. Resuscitation continues, and baby boy Johnson receives one dose of epineph-

rine per umbilical venous catheter. His heart rate increases after 5 minutes to 120. The baby's Apgar scores are one at 1 minute of age, three at 5 minutes of age, and three at 7 minutes of age. The cord blood gas pH is 6.78. The baby is prepared for transfer to the neonatal intensive care unit, where he is placed on a ventilator. Baby boy Johnson remains limp and unresponsive. His initial arterial blood gas is pH 7.0, PO2 55 HC03 of 10, and base excess of -16 mmol. The baby is loaded with phenobarbital after seizing at 30 minutes of age. Neurology is consulted and baby boy Johnson's mother is informed of his condition by the neonatologist and neurologist, as well as the plan of care. Mrs. Johnson and her husband sign the consent forms for hypothermia treatment and NICU care. An MRI is ordered by neurology. Baby boy Johnson is prepared for head cooling.

Baby boy Johnson meets the criteria for hypothermia treatment. There was a sentinel event at delivery (loss of fetal heart rate tones). There was a need for resuscitation, evidence of fetal acidemia, and low Apgar scores. Baby Johnson had evidence of asphyxia.

Summary

Neonates affected by HIE have long-term health problems, including blindness, seizures, cerebral palsy, and neurodevelopmental deficits. The LNC must be prepared to assist attorneys by knowing what to look for in the medical records. The LNC must examine the mother's history for antepartum and intrapartum risk factors that may impact the baby. MRI and lab results are tools that determine prognosis and identify preexisting conditions. Also, the LNC must be aware of signs of asphyxia and the three elements of the neurologic syndrome of HIE as noted in the case study:

1. Evidence of fetal distress and fetal risk for hypoxia/ischemia, FHR abnormalities, sentinel event, fetal acidemia
2. The need for resuscitation and low Apgar scores
3. An overt neurological syndrome in the first hours or days of life (Inder & Volpe, 2018)

The LNC can assist defense and plaintiff attorneys by creating life care plans for the future healthcare needs of neonates with HIE and examining neurology consult notes and MRI reports to determine when hypoxic events occurred. The legal nurse consultant with obstetric experience can assist the attorney by reading FHR reports to determine if signs of fetal distress were present in labor and delivery. The pearls previously discussed can assist attorney clients in identifying the timing of HIE neurologic injury (Husted, 2015).

REFERENCES

Allen, K. A., & Brandon, D. H. (2011). Hypoxic ischemic encephalopathy: Pathophysiology and experimental treatments. *Newborn and Infant Nursing Reviews, 11*(3), 125–133. Retrieved June 26, 2022, from https://doi.org/10.1053/j.nainr.2011.07.004

Aslam, S., Strickland, T., & Molloy, E. J. (2019). Neonatal encephalopathy: Need for recognition of multiple etiologies for optimal management. *Frontiers in Pediatrics, 7*(142), 1–7. Retrieved June 25, 2022, from https://doi.org/10.3389/fped.2019.00142

Association of Women's Health, Obstetric, and Neonatal Nurses, National Association of Neonatal Nurses, American Association of Critical-Care Nurses, Verklan, M. T., & Walden, M. (2015). In *Core curriculum for neonatal intensive care nursing* (5th ed., p. 762). Elsevier.

Casey, D. M., Tella, N., Turesky, R., & Labrecque, M. (2011). Therapeutic hypothermia: Treatment for hypoxic-ischemic encephalopathy in the NICU. *Neonatal Network, 30*(6), 370–380. Retrieved June 25, 2022, from https://doi.org/10.1891/0730-0832.30.6.370

Eunson, P. (2015). The long-term health, social, and financial burden of hypoxic-ischaemic encephalopathy. *Developmental Medicine & Child Neurology, 57*, 48–50. Retrieved June 25, 2022, from https://doi.org/10.1111/dmcn.12727

Finder, M., Boylan, G. B., Twomey, D., Ahearne, C., Murray, D. M., & Hallberg, B. (2020). Two-year neurodevelopmental outcomes after mild hypoxic ischemic encephalopathy in the era of therapeutic hypothermia. *Journal of the American Medical Association Pediatrics, 174*(1), 48. Retrieved June 25, 2022, from https://doi.org/10.1001/jamapediatrics.2019.4011

Husted, L. (2015). Life care planning after neonatal encephalopathy. *Journal of Nurse Life Care Planning, XV*(4), 944–955. Retrieved June 25, 2022, from

Inder, T. E., & Volpe, J. J. (2018). Hypoxic-ischemic injury in the term infant: Clinical-neurological features, diagnosis, imaging, prognosis, therapy. In *Volpe's neurology of the newborn* (6th ed., pp. 510–563). Elsevier.

Mosalli, R. (2012). Whole body cooling for infants with hypoxic-ischemic encephalopathy. *Journal of Clinical Neonatology, 1*(2), 101. Retrieved June 25, 2022, from https://doi.org/10.4103/2249-4847.96777

Reynolds, R., & Talmage, S. (2011). "Caution! Contents should be cold": Developing a whole-body hypothermia program. *Neonatal Network, 30*(4), 225–230. Retrieved June 25, 2022, from https://doi.org/10.1891/0730-0832.30.4.225

Torbenson, V. E., Tolcher, M., Nesbitt, K. M., Colby, C. E., EL-Nashar, S. A., Gostout, B. S., Weaver, A. L., Mc Gree, M. E., & Famuyide, A. O. (2017). Intrapartum factors associated with neonatal hypoxic ischemic encephalopathy: A case-controlled study. *BMC Pregnancy and Childbirth, 17*(1), 1–7. Retrieved May 21, 2022, from https://doi.org/10.1186/s12884-017-1610-3

Zanelli, S. A., Stanley, D. P., & Kaufman, D. A. (2018, July 18). *Hypoxic-ischemic encephalopathy clinical presentation: History, physical examination* (M. L. Windle, B. S. Carter, & D. J. Nimavat, Eds.). Medscape. Retrieved June 25, 2022, from https://emedicine.medscape.com/article/973501-clinical

Joan Earley, MSN, RNC-NIC, CPNP, CLCP, LNC, is a neonatal intensive care expert witness with over 25 years-experience in neonatal nursing. In addition, Joan has over 40 years of experience in pediatric nursing. Ms. Earley graduated from Spaulding University School of Nursing and received her MSN from IUPUI School of Nursing. She is clinically active in the NICU. Joan can be reached at Joanie050@yahoo.com.