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# Medicolegal Pitfalls in Determining the Timing, Mechanism, and Preventability of Perinatal Hypoxic-Ischemic Brain Injury

*Barry S. Schifrin, MD; Maureen Sims, MD*

***"Understanding the timing, mechanism, and preventability of fetal neurological injury and its subsequent handicaps is vital. Statistics implicate intrauterine perinatal asphyxia (about 1-6 /1000 live births) in stillbirth and perinatal mortality (about 1 million annually) (2)."***

**An Overview:**

Understanding the timing, mechanism, and preventability of fetal neurological injury and its subsequent handicaps is vital. Statistics implicate intrauterine perinatal asphyxia (about 1-6 /1000 live births) in stillbirth and perinatal mortality (about 1 million annually) (2). About 25% showed major neurological impairments such as hypoxic-ischemic encephalopathy (HIE), neonatal encephalopathy, as well as subsequent cerebral palsy (CP), epilepsy, and developmental delay. About half of survivors suffer from neuropsychological sequelae, including immediate or delayed onset executive functioning disorders (3, 4). As the survival of these afflicted children improves, the already high economic toll continues to burgeon.

Birth asphyxia is "a condition of impaired blood gas exchange, leading, if it persists, to progressive hypoxemia and hypercapnia." WHO defines asphyxia as "the failure of the neonate to begin breathing successfully" (5). These definitions, among others, fail to provide sufficient clinical rigor to affirm the diagnosis in any individual case or research study of outcome (6, 7). Although the finding of a low pH and base excess in umbilical or neonatal blood (cut-off values vary, sometimes considerably) is considered the most objective assessment of intrapartum hypoxia, metabolic acidosis is a poor surrogate for injury (8). The clinical risk factors for adverse outcomes, however, have not changed over the past several decades despite advances in obstetrical care and the widespread recognition that many maternal and obstetrical risk factors for adverse neonatal outcomes are potentially modifiable (9). These risk factors include nulliparity, hypertension, diabetes mellitus, and such intrapartum risk factors as emergency cesarean birth, "non-reassuring fetal status," failure to progress, intrapartum hemorrhage, and an intrapartum sentinel event (shoulder dystocia, cord prolapse, uterine rupture, placental abruption). Neonatal risk factors included male sex, birth at late preterm gestation (35+0 – 36+6 weeks), Apgar score <4 at 5 minutes, respiratory distress requiring ventilatory support, and severe acidosis at birth (9). Some require a "sentinel event" to diagnose intrapartum injury (10).



Basic controversies exist regarding the definitions of neonatal encephalopathy (NE) and hypoxic-ischemic encephalopathy (HIE) (11, 12). Similarly, while there is agreement that many "sentinel events" defined above are associated with perinatal asphyxia, the vast majority of cases do not involve a sentinel event – even if one were to consider a prolonged fetal bradycardia a "sentinel event. Further, with prompt attention, most offspring from sentinel events do well (Perlman).

This lack of consistency helps to explain the varying estimates of the relationship between intrapartum events and subsequent neurological impairment in the offspring, including not only disorders of neonatal adaptation but long-term outcomes such as epilepsy, CP, and ASD, (13, 14) after major congenital malformations and chromosomal disorders are excluded (15). These issues are thrown into stark relief during medicolegal encounters alleging substandard care as the cause of preventable perinatal injury.

Invariably, in the cauldron of the courtroom, however, the desire to assign fault competes, often energetically, with the demand for exculpation. To prevail in the encounter, too often, it seems, a blind eye has been turned to evidence-based medicine, critical thinking, and equipoise. As a result, trials of similar cases come to opposite judgments, sometimes determined based on nonobjective or ignored medicolegal and forensic evaluations (1, 16).

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Given the disparate outcomes in judgments and the size of any

award, there is a widespread notion that a trial is a lottery. Obstetricians argue that judges and juries cannot sufficiently comprehend medical decisions and bristle at so-called runaway verdicts. The plaintiff's bar argues about the lack of training of judges and the availability of qualified experts, while others have argued that there is more malpractice than lawsuits and that physicians already have too much immunity.

Especially in the last several decades, medicolegal claims imputing negligent perinatal care (obstetrical/neonatal) in the causation of brain injury have been increasing worldwide. Perhaps the most publicity has come from England, where allegations of obstetrical/perinatal negligence threaten to bankrupt the NHS. They have been estimated to account for about half of the UK's activities of the National Health Service Litigation Authority (17). In the US, claims of negligently inflicted perinatal injury top the list of pediatric claims (from 1985 to 2008) with an average indemnity of about 500,000 dollars (18) although large "runaway" verdicts, though uncommon, become well publicized in the lay or even medical literature (19).

In this context, we here briefly review some of the obstetrical and neuroradiological issues that continue to confound medical progress and the results of allegations of substandard care in "birth-injury cases."

**Electronic Fetal Monitoring**

The problems of interpreting the CTG (Cardiotocography) during litigation are numerous, and recent articles have questioned how a technology so encumbered by a classification with its high rate of inter- and intra-observer variation and its poor correlation with adverse outcomes despite a high cesarean section rate can be offered with any authority in a court of law (19), there seems to be limited cross-fertilization between obstetrical and neonatal providers. While there is considerable emphasis in the medical literature on the value of a detailed pathological examination of the placenta (20) in these cases, there seems to be little demand or appetite for an informed interpretation of the CTG tracing itself. Indeed, in many situations where the child is transported to a higher level of care, the tracing does not accompany the child (21).

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Attempting to correlate CTG findings with outcomes, one encounters numerous "medical designations" summarizing the interpretation of the CTG tracing and the urgency of intervention. The term "emergency cesarean section" may refer to the need for urgent intervention or any unscheduled cesarean section, whatever its urgency. One can only applaud the recent attempts to define a genuinely emergent cesarean section (22). Hopefully, this will be done with the understanding that eliminating the need for urgency in the first place is a much more desirable clinical objective.

Under indications for intervention, a reviewer might find such expressions as "intolerance to labor," "non-reassuring fetal status," "fetal bradycardia," and others. The terms "fetal distress" and "perinatal asphyxia," unfortunately, have been "officially" removed from the obstetricians' lexicon by the ACOG (23). The desire to be "fair of speech" impedes understanding of the impact of pre-existing fetal conditions at the onset of labor, the evolution of patterns, or the impact of contractions and pushing in the 2nd stage of labor (24-26).

Most studies dealing with the relationship between fetal heart rate patterns and outcomes start with those known to be acidotic at delivery. This approach is also common in those attempting to use deep learning to automate the interpretation of tracings. In reality, the most "severe" patterns, thought to be pathognomonic of fetal acidemia, correlate with umbilical acidemia less than 50% of the time. More telling, however, is the understanding that even severely low pH and base deficit values are even poorer predictors of either low Apgar score or the need for specialized neonatal care (27). Vintzileos has called attention to the numerous pathophysiological processes, including cerebral ischemia, that may impact the fetal heart rate pattern that is not dependent upon systemic fetal acidemia; indeed, fetal heart rate patterns along with clinical indicators may be far better predictors of outcome than is the umbilical pH (21, 28, 29).

Nor is the immediate outcome of the newborn, including pH, dispositive of either injury or freedom from subsequent birth-related handicap. Notwithstanding, it is believed that most hypoxic-ischemic injuries occur during the peripartum period (15, 30). Adding to this belief are observed benefits of therapeutic hypothermia (TH), which must be applied within 6 hours of injury (31).

***"Despite the apparent relationship of fetal heart rate patterns to fetal behavior (21), including neurological injury, reviews in the literature tend to define all fetal heart rate decelerations as hypoxic in origin (32). The ACOG/AAP 3-tier classification is based on the presumed risk of fetal acidemia."***

Despite the apparent relationship of fetal heart rate patterns to fetal behavior (21), including neurological injury, reviews in the literature tend to define all fetal heart rate decelerations as hypoxic in origin (32). The ACOG/AAP 3-tier classification is based on the presumed risk of fetal acidemia. Category I, with its reassuring tracing, is designated as a tracing where the fetal pH is normal and hypoxia is absent (33). The classification does not assess fetal behavior or neurological integrity. Class II patterns include fetuses with diverse FHR patterns and diverse outcomes ranging from normal to hypoxic to injured (34). While Category II patterns are considered "indeterminate" and require "close observation,"

the classification offers little guidance to the care provider and less protection if the case comes to litigation. Most Class III patterns thought to represent fetal acidemia are not acidemic at birth.

In one European schema, all variant FHR patterns are classified as hypoxic - chronic, subacute, or acute - whether or not the patterns are accompanied by fetal acidemia (35). The abnormal patterns of "chronic hypoxia" with persistently reduced / absent baseline variability seen at the onset of monitoring is found with increased frequency with placental insufficiency (fetal growth restriction, postdate pregnancy, maternal diabetes, hypertension), chorioamnionitis, genetic anomalies, and toxic exposure and may be accompanied by discreet placental pathology (36, 37). Often, however, there is no apparent clinical correlation. With "chronic hypoxia" tracing at the outset of monitoring, especially in the face of a previously normal pattern, the diagnosis of pre-existing fetal neurological injury must be entertained – fetal neurological normality may not be assumed. These patients are frequently delivered quickly with variable Apgar scores and pH and base deficit results. Notwithstanding, neurological injury in survivors is similar to those with more pronounced, acute problems appearing during labor. Again, the severity of the outcome was more dependent upon the tracing than the umbilical pH (25).

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On the other hand, it is not reasonable to presume that the growth-restricted fetus, for example, was neurologically injured prior to labor, especially if, on admission to labor and delivery, the FHR tracing was reassuring, reflective of normal fetal responsiveness and behavior. A similar question arises in a genetically challenged child: can they also suffer hypoxic-ischemic injury during the intrapartum period, and what part of the subsequent handicap is related to the time in labor?

The most important prognostic feature relative to the timing of injury appears to be the normal FHR pattern at the outset of labor. This pattern with a stable baseline rate in the normal range, moderate variability, cyclic accelerations with fetal movements, especially in association with uterine contractions, and stable heart rate in the normal range permits the inference of normal fetal responsiveness and behavior and the absence of hypoxic/ischemic/traumatic or infections assaults on the fetus. The evolution of the patterns, especially in light of the clinical correlates (*e.g.*, oligohydramnios), will provide insight into the timing, mechanism, and preventability of any neurological injury (21, 38). There appears to be no example of a previously normal fetus, subjected to any of these assaults, who fails to respond with changes in its FHR pattern. Further, though uncommon, there appear to be specific patterns that can only be explained by acute ischemic injury – not asphyxia (39, 40). This pattern, referred to as the "conversion pattern," has thus far been unerring in its prediction of neurological injury in the fetus although it does not reliably predict the specific MRI pattern of injury which might include BGT (Basal Ganglia and Thalmus), white-matter injury, stroke, or even "normal MRI". Having defined the pattern as highly predictive of injury does not, in and of itself, permit the conclusion that the injury was preventable. Indeed, though it is uncommon, the pattern may appear following a normal pattern with such speed as to preclude benefit from even the most rapid intervention (41). It must be understood that on these occasions, the deceleration represents the injury itself and not some harbinger of asphyxia.

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The confusion in obstetrical terminology is accompanied by similar issues in neonatology, pediatric neurology, and neuroradiology. Universally agreed-upon definitions of neonatal and hypoxic-ischemic encephalopathy (HIE) are still lacking (42), leading to controversy over whether the cause has been a perinatal insult (43). Complicating this picture further is the fetus's gestational age. It is well known that prematurity by itself leads to additional risks and vulnerability in the early postpartum period.

In the courtroom, it is frequently necessary to challenge the putative relationship of CP (and other disorders) to an intrapartum event (one estimate - 10–20% (44); where the presence of "severe asphyxia" is deemed a requirement for assigning the timing of the injury to the events of labor and delivery. Severe asphyxia (pH<= 7.0 was one of the "essential criteria" promulgated by the 2003 ACOG/AAP monograph (45). Absent this finding, the "defensive" guidelines require that the timing and mechanism of injury be assigned elsewhere. While this guideline has likely dissuaded attorneys from undertaking litigation in the past, there would seem to be no scientific justification for these "essential criteria" in assigning the timing of fetal neurological injury. Indeed, in a review of CP cases in which the FHR pattern on admission to labor and delivery was reassuring, over two-thirds failed to show significant

acidemia at birth. Low Apgar scores and neonatal encephalopathy were more common, but these criteria were not considered a prerequisite for fetal injury sustained intrapartum (40). Notwithstanding, one still encounters the "essential criteria" in the defense of some cases.

Notwithstanding the attention to hypoxia and acidemia, it appears that cerebral ischemia is the obligatory prerequisite of injury. Claiming that every ischemic lesion is preceded by (systemic) fetal hypoxia can no longer be maintained (1). This is supported by numerous lines of experimental and clinical evidence – reviewed elsewhere (46), as is the discussion of the molecular pathways leading to neuronal death (47). Also considered elsewhere are discussions of the impact of therapeutic hypothermia, the first therapy that has shown promise in improving the outcomes for neonates with moderate to severe NE following a presumed intrapartum insult. Fanaroff et al. discuss TH's obstetric and medicolegal implications and suggest a five-step approach to analyzing neonatal cases for causation, etiology, timing of occurrence, responsibility, and liability (48). Notwithstanding, the timing of the insult is often unknown, and the severity of encephalopathy may change under observation. Also evolving is the understanding that patients with "mild" encephalopathy" previously considered "benign", may have a significant risk of adverse long-term outcomes (49-51).

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Ultimately, the clinical presentation of HIE appears to offer no specific link to the timing of injury. The latency for first observable seizures following a prominent asphyxial event can range from minutes to a few days, and in the case of stroke, weeks to months, and executive function problems, years to decades later (52, 53).

MRI findings in newborns with HIE are often produced and discussed in medio-legal cases. MRI interpretations are divided into those injuries of the watershed areas (the areas least perfused) multicystic encephalomalacia, ulegyria in watershed injury referred to as partial, prolonged (usually over 1 hour) hypoxic-ischemic injury to the term fetus (54, 55). This distribution pattern develops in part because the heavy sympathetic innervation of the neocortex facilitates reduced flow to this area in order to preserve the vital function assigned to the basal ganglia, thalamus, and hippocampus, which receive blood supply from the vertebral/basilar system which has little sympathetic innervation (56). The BGT pattern involving bilateral hypoxic-ischemic insults of the posterior putamina and ventrolateral thalami and involvement of the peri-Rolandic region and the inferior limb of the internal capsule are often referred to as an 'acute, profound pattern' that has been clinically linked to sentinel events (57, 58).

The problem arises, especially in medicolegal cases, when BGT injury is made a synonym for an acute, profound hypoxic-ischemic injury and, following along the syllogistic cascade, when the injury is unpredictable and unpreventable (59). Equipoise, however, demands the understanding that many, if not most, cases of GBT injury cannot reasonably be connected to any sentinel event, and issues of foreseeability and preventability cannot be derived from these findings. In each case presented by Smith et al., a prolonged, abnormal tracing was associated with BGT findings without any obvious sentinel event. Various authors report similar associations (60, 61). Martinez-Biarge et al. reported that almost 60% *of the 393 cases with* 'acute hypoxia ischemia' on MRI had no sentinel event. An abnormal cardiotocograph (CTG) was present in at least 276 of the total cohort, permitting the strong inference that the provenance of the acute hypoxic injury was "fetal distress" (62). Of equal interest, Martinz-Biarge et al. and Hartmann et al. reported overlapping risk factors for both HIE and "stroke" (63, 64).

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Similarly, the documentation of periventricular leukomalacia (PVL) is often deemed pathognomonic of an insult occurring between the 24th and the 34th gestational week despite the absence of any clinical correlation. It has been shown, however, that the radiographic finding of PVL may occur in the term fetus (65). Even in the preterm newborn, the appearance of PVL is associated with obstetrical risk factors that may have benefitted from the early use of cesarean section (66).

Thus, neuroradiological images are not dispositive of the timing, the foreseeability, or the preventability of injury. As recommended by several authors, the finding of a 'BGT pattern of injury' should contain the added comment, "awaiting clinical (neonatal) and obstetrical correlation," and avoid any term related to the injury's duration, severity, or preventability. Further, sentinel events should not be deduced or imputed (67). MRI neuroimaging exams obtained in the first weeks of life appear reliable for excluding an earlier antepartum injury or malformation (1). The findings of brain swelling, cortical highlighting, loss of gray-white matter differentiation, abnormalities in basal ganglia, and thalami are generally accepted as consistent with perinatal insult but of insufficient specificity. Each has been associated with no obvious asphyxial birth event (12). Finally, it is essential to remember that even in the most accurate and advanced application, obvious neurological defects sustained around the time of birth may not be observable on MRI (68). This fact significantly limits its overall negative predictive value (1). Neuroimaging does not represent the only surrogate of a pathological assessment in these cases.

To remove the limitations of some of the conventional wisdom about the timing, mechanisms, and indicators of injury, we need to take better advantage of the evidence already available to enhance labor and delivery outcomes for both mother and child. Better outcomes beget fewer allegations of malpractice.

**References**


1. Fineschi V, Viola RV, La Russa R, Santurro A, Frati P. A Controversial Medicolegal Issue: Timing the Onset of Perinatal Hypoxic-Ischemic Brain Injury. Mediators of Inflammation. 2017;2017:11.
2. Moshiro R, Mdoe P, Perlman JM. A Global View of Neonatal Asphyxia and Resuscitation. Frontiers in pediatrics. 2019;7:489.
3. Marlow N, Rose AS, Rands CE, Draper ES. Neuropsychological and educational problems at school age associated with neonatal encephalopathy. Arch Dis Child Fetal Neonatal Ed. 2005;90(5):F380-7.
4. Anderson V, Spencer-Smith M, Coleman L, Anderson P, Williams J, Greenham M, et al. Children's executive functions: are they poorer after very early brain insult. Neuropsychologia. 2010;48(7):2041-50.
5. WHO. Guideline on basic newborn resuscitation. 2012.
6. Ellenberg JH, Nelson KB. The association of cerebral palsy with birth asphyxia: a definitional quagmire. Dev Med Child Neurol. 2013;55(3):210-6.
7. Laptook AR. Birth Asphyxia and Hypoxic-Ischemic Brain Injury in the Preterm Infant. Clin Perinatol. 2016;43(3):529-45.
8. Graham EM, Ruis KA, Hartman AL, Northington FJ, Fox HE. A systematic review of the role of intrapartum hypoxia-ischemia in the causation of neonatal encephalopathy. Am J Obstet Gynecol. 2008;199(6):587-95.
9. Stoke RS, V, Hocking, K,Jardine, L Kumar, S. Perinatal antecedents of moderate and severe neonatal hypoxic eschemic encephalopathy: an Australian birth cohort study. 2022.
10. Perlman JM. Intrapartum asphyxia and cerebral palsy: is there a link? Clin Perinatol. 2006;33(2):335-53.
11. Volpe JJ. Neonatal encephalopathy: an inadequate term for hypoxic-ischemic encephalopathy. Ann Neurol. 2012;72(2):156-66.
12. Schendel D, Nelson KB, Blair E. Neonatal encephalopathy or hypoxic-ischemic encephalopathy? Annals of Neurology. 2012;72(6):984-5.
13. Miller SP, Ramaswamy V, Michelson D, Barkovich AJ, Holshouser B, Wycliffe N, et al. Patterns of brain injury in term neonatal encephalopathy. J Pediatr. 2005;146(4):453-60.
14. Draper ES, Kurinczuk JJ, Lamming CR, Clarke M, James D, Field D. A confidential enquiry into cases of neonatal encephalopathy. Arch Dis Child Fetal Neonatal Ed. 2002;87(3):F176-80.
15. Cowan F, Rutherford M, Groenendaal F, Eken P, Mercuri E, Bydder GM, et al. Origin and timing of brain lesions in term infants with neonatal encephalopathy. Lancet. 2003;361(9359):736-42.
16. Elder DE, Zuccollo JM, Stanley TV. Neonatal death after hypoxic ischaemic encephalopathy: does a postmortem add to the final diagnoses? Bjog. 2005;112(7):935-40.
17. Yau CWH, Leigh B, Liberati E, Punch D, Dixon-Woods M, Draycott T. Clinical negligence costs: taking action to safeguard NHS sustainability. Bmj. 2020;368:m552.
18. Donn SM, Chiswick ML, Fanaroff JM. Medicolegal implications of hypoxic-ischemic birth injury. Semin Fetal Neonatal Med. 2014;19(5):317-21.
19. Hirsch E. Electronic Fetal Monitoring to Prevent Fetal Brain Injury: A Ubiquitous Yet Flawed Tool. JAMA. 2019;322(7):611-12.
20. Redline RW, Roberts DJ, Parast MM, Ernst LM, Morgan TK, Greene MF, et al. Placental pathology is necessary to understand common pregnancy complications and achieve an improved taxonomy of obstetric disease. Am J Obstet Gynecol. 2022.
21. Schifrin BS. Electronic Fetal Monitoring-Prevention or Rescue? Frontiers in pediatrics. 2020;8:503.
22. Paily Paily V, Girijadevi R, George S, Tawab A, Sidhik A, Sudhamma A, et al. Crash Caesarean Delivery: How to Optimise Decision-to-Delivery Interval by Initiating a Novel Code? A Clinical Audit. The Journal of Obstetrics and Gynecology of India. 2022.
23. ACOG. ACOG Committee Opinion #303: Inappropriate use of the terms fetal distress and birth asphyxia. Obstet Gynecol. 2004;104(4):903.
24. Takita H, Hasegawa J, Arakaki T, Nakamura M, Tokunaka M, Oba T, et al. Antenatal ultrasound screening using check list before delivery for predicting a non-reassuring fetal status during labor. J Matern Fetal Neonatal Med. 2017:1-6.
25. Jonsson M, Agren J, Norden-Lindeberg S, Ohlin A, Hanson U. Neonatal encephalopathy and the association to asphyxia in labor. Am J Obstet Gynecol. 2014;211(6):667.e1-8.
26. Schifrin BS C, WR, Deymier, P. Cranial Compression Encephalopathy: Fetal Neurological Injury and the Mechanical Forces of Labor and Delivery. In: . LZaLDL, editor. Stress and Developmental Programming of Health and Disease: Beyond Phenomenology. New York: Nova Science Publishers, Inc.; 2014. p. 188-220.
27. Clark SL, Hamilton EF, Garite TJ, Timmins A, Warrick PA, Smith S. The limits of electronic fetal heart rate monitoring in the prevention of neonatal metabolic acidemia. Am J Obstet Gynecol. 2017;216(2):163 e1- e6.
28. Vintzileos AMS, JC Abnormal fetal heart rate patterns caused by pathophysiologic processes other than fetal acidemia. AJOG. 2023.

29. Jindal S, Steer PJ, Savvidou M, Draycott T, Dixon-Woods M, Wood A, et al. Risk factors for a serious adverse outcome in neonates: a retrospective cohort study of vaginal births. BJOG. 2023.

30. Ghei SK, Zan E, Nathan JE, Choudhri A, Tekes A, Huisman TA, et al. MR imaging of hypoxic-ischemic injury in term neonates: pearls and pitfalls. Radiographics. 2014;34(4):1047-61.

31. Chalak LF, DuPont TL, Sánchez PJ, Lucke A, Heyne RJ, Morriss MC, et al. Neurodevelopmental outcomes after hypothermia therapy in the era of Bayley-III. J Perinatol. 2014;34(8):629-33.

32. Lear CA, Galinsky R, Wassink G, Yamaguchi K, Davidson JO, Westgate JA, et al. The myths and physiology surrounding intrapartum decelerations: the critical role of the peripheral chemoreflex. J Physiol. 2016;594(17):4711-25.

33. Macones GA, Hankins GDV, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development Workshop Report on Electronic Fetal Monitoring: Update on Definitions, Interpretation, and Research Guidelines. Obstetrics & Gynecology. 2008;112(3):661-6.

34. Frey HA, Liu X, Lynch CD, Musindi W, Samuels P, Rood KM, et al. An evaluation of fetal heart rate characteristics associated with neonatal encephalopathy: a case-control study. Bjog. 2018.

35. Pinas A, Chandraharan E. Continuous cardiotocography during labour: Analysis, classification and management. Best Pract Res Clin Obstet Gynaecol. 2016;30:33-47.

36. Ernst LM, Bit-Ivan EN, Miller ES, Minturn L, Bigio EH, Weese-Mayer DE. Stillbirth: Correlations Between Brain Injury and Placental Pathology. Pediatr Dev Pathol. 2016;19(3):237-43.

37. Wong DS, Poskitt KJ, Chau V, Miller SP, Roland E, Hill A, et al. Brain injury patterns in hypoglycemia in neonatal encephalopathy. AJNR Am J Neuroradiol. 2013;34(7):1456-61.

38. Vintzileos AM, Smulian JC. Decelerations, tachycardia, and decreased variability: have we overlooked the significance of longitudinal fetal heart rate changes for detecting intrapartum fetal hypoxia? Am J Obstet Gynecol. 2016;215(3):261-4.

39. Schifrin BS, Ater S. Fetal hypoxic and ischemic injuries. Curr Opin Obstet Gynecol. 2006;18(2):112-22.

40. Evans MI, Eden RD, Britt DW, Evans SM, Schifrin BS. Re-engineering the interpretation of electronic fetal monitoring to identify reversible risk for cerebral palsy: a case control series. J Matern Fetal Neonatal Med. 2019;32(15):2561-9.

41. Schifrin BS. The CTG and the timing and mechanism of fetal neurological injuries. Best Pract Res Clin Obstet Gynaecol. 2004;18(3):437-56.

42. Kurinczuk JJ, White-Koning M, Badawi N. Epidemiology of neonatal encephalopathy and hypoxic-ischaemic encephalopathy. Early Hum Dev. 2010;86(6):329-38.

43. ACOG. Neonatal Encephalopathy and Neurologic Outcome. D'Alton M, editor: ACOG; 2014.

44. Colver A, Fairhurst C, Pharoah PO. Cerebral palsy. Lancet. 2014;383(9924):1240-9.

45. ACOG. Neonatal Encephalopathy and Cerebral Palsy: Defining the pathogenesis and Pathophysiology. Washington, DC: ACOG; 2003 January, 2003. 94 p.

46. Schifrin BS, Deymier P, Cohen WR. Cranial compression ischemic encephalopathy: fetal neurological injury related to the mechanical forces of labor and delivery. Stress and Developmental Programming of Health and Disease: Beyond Phenomenology: Nova Science Publishers, Inc.; 2014.

47. Turner JM, Mitchell MD, Kumar SS. The physiology of intrapartum fetal compromise at term. Am J Obstet Gynecol. 2020;222(1):17-26.

48. Fanaroff JM, Ross MG, Donn SM. Medicolegal considerations in the context of neonatal encephalopathy and therapeutic hypothermia. Semin Fetal Neonatal Med. 2021;26(5):101266.

49. Chalak L, Ferriero DM, Gressens P, Molloy E, Bearer C. A 20 years conundrum of neonatal encephalopathy and hypoxic ischemic encephalopathy: are we closer to a consensus guideline? Pediatr Res. 2019;86(5):548-9.

50. Chalak L, Latremouille S, Mir I, Sánchez PJ, Sant'Anna G. A review of the conundrum of mild hypoxic-ischemic encephalopathy: Current challenges and moving forward. Early Hum Dev. 2018;120:88-94.

51. Chalak LF. Best practice guidelines on management of mild neonatal encephalopathy: Is it really mild? Early Hum Dev. 2018;120:74.

52. Lindstrom K, Lagerroos P, Gillberg C, Fernell E. Teenage outcome after being born at term with moderate neonatal encephalopathy. Pediatr Neurol. 2006;35(4):268-74.

53. Gacio S, Munoz Giacomelli F, Klein F. Presumed perinatal ischemic stroke: A review. Arch Argent Pediatr. 2015;113(5):449-55.

54. Reid SM, Dagia CD, Ditchfield MR, Reddihough DS. Grey matter injury patterns in cerebral palsy: associations between structural involvement on MRI and clinical outcomes. Dev Med Child Neurol. 2015;57(12):1159-67.

55. Robertson CM, Perlman M. Follow-up of the term infant after hypoxic-ischemic encephalopathy. Paediatr Child Health. 2006;11(5):278-82.

56. Sheth RD, Bodensteiner JB, Riggs JE, Schochet SS, Jr. Differential involvement of the brain in neonatal asphyxia: a pathogenic explanation. J Child Neurol. 1995;10(6):464-6.

57. Misser SK, Barkovich AJ, Lotz JW, Archary M. A pictorial review of the pathophysiology and classification of the magnetic resonance imaging patterns of perinatal term hypoxic

ischemic brain injury - What the radiologist needs to know…. SA J Radiol. 2020;24(1):1915.

58. de Vries LS, Groenendaal F. Patterns of neonatal hypoxic-ischaemic brain injury. Neuroradiology. 2010;52(6):555-66.

59. Bhorat IE, Buchmann E, Soma-Pillay P, Nicolaou E. Cerebral palsy and its mediolegal implications in low resource settings - the need to establish causality and revise criteria to implicate intrapartum hypoxia. A narrative review. S Afr Med J. 2023;113(6):E229.

60. Harteman JC, Nikkels PG, Benders MJ, Kwee A, Groenendaal F, de Vries LS. Placental pathology in full-term infants with hypoxic-ischemic neonatal encephalopathy and association with magnetic resonance imaging pattern of brain injury. J Pediatr. 2013;163(4):968-95 e2.

61. Barnette AR, Horbar JD, Soll RF, Pfister RH, Nelson KB, Kenny MJ, et al. Neuroimaging in the evaluation of neonatal encephalopathy. Pediatrics. 2014;133(6):e1508-17.

62. Martinez-Biarge M, Diez-Sebastian J, Wusthoff CJ, Mercuri E, Cowan FM. Antepartum and Intrapartum Factors Preceding Neonatal Hypoxic-Ischemic Encephalopathy. Pediatrics. 2013;132(4):e952-e9.

63. Harteman JC, Groenendaal F, Kwee A, Welsing PM, Benders MJ, de Vries LS. Risk factors for perinatal arterial ischaemic stroke in full-term infants: a case-control study. Arch Dis Child Fetal Neonatal Ed. 2012;97(6):F411-6.

64. Martinez-Biarge M, Cheong JL, Diez-Sebastian J, Mercuri E, Dubowitz LM, Cowan FM. Risk Factors for Neonatal Arterial Ischemic Stroke: The Importance of the Intrapartum Period. J Pediatr. 2016.

65. Lasry O, Shevell MI, Dagenais L. Cross-sectional comparison of periventricular leukomalacia in preterm and term children. Neurology. 2010;74(17):1386-91.

66. Bauer M, Fast C, Haas J, Resch B, Lang U, Pertl B. Cystic periventricular leukomalacia in preterm infants: an analysis of obstetric risk factors. Early Hum Dev. 2009;85(3):163-9.

67. Hayakawa K, Tanda K, Koshino S, Nishimura A, Kizaki Z, Ohno K. Pontine and cerebellar injury in neonatal hypoxic-ischemic encephalopathy: MRI features and clinical outcomes. Acta Radiol. 2020;61(10):1398-405.

68. Chau V, Poskitt KJ, Dunham CP, Hendson G, Miller SP. Magnetic resonance imaging in the encephalopathic term newborn. Curr Pediatr Rev. 2014;10(1):28-36.

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*Barry Schifrin, M.D,*
*Western University of Health Sciences, Pomona, California*
*Formerly, Professor of Obstetrics & Gynecology*
*Keck School of Medicine, University of Southern California*
*Los Angeles, California*

*Corresponding Author:*

*Maureen E. Sims, M.D.*
*Professor of Pediatrics*
*Geffen School of Medicine,*
*University of California, Los Angeles*
*Los Angeles, California*
*email:* mes@g.ucla.edu