BIRTH TRAUMA LITIGATION: PROVING THE CAUSE OF NEWBORN NEUROLOGIC INJURY[1]

By Richard C. Halpern

Proving the cause of newborn neurologic injury in birth trauma litigation, an essential step to a successful lawsuit, is both complex and challenging. Determining causation begins with the newborn's brain. The areas of the brain affected, the pattern of brain injury and the evolution of injury all provide vital information about the mechanism of injury and the timing of injury. Early neuroimaging can distinguish between chronic injury and acute injury, thereby establishing a window of opportunity for harm. Once that window has been defined, the timing of injury can be further refined through obstetrical and neonatal clinical data.[2] Events occurring during the narrowed window of opportunity can then be considered for causation and/or contribution to injury and, applying the differential diagnosis, the most likely cause can be determined within a reasonable degree of medical probability.

While there is still much that is not understood about the precise way acute neurologic injury occurs in newborns, modern neuroimaging techniques allow the detection of lesions occurring at or near the time of birth. The pathway to injury, in some scenarios, may be difficult to describe, but the time at which injury occurs is often far clearer. Proof of timing does not rely on a single test or clinical variable, but rather the evaluation of all the antenatal, peripartum and neonatal data. In my view, where the weight of evidence supports a particular cause and timing for neonatal neurologic injury, any outlying variables must be considered either non-essential or possibly spurious.

Neuroimaging, done at the appropriate time, can rule out antenatal causes, proving newborn neurologic injury occurred at or near the time of birth. Neuroimaging reveals patterns of injury and the involved areas of the brain - vital clues to the mechanism of injury. When used in combination with obstetrical and neonatal clinical data, the likely time of injury can be reasonably narrowed sufficiently to prove causation on a balance of probabilities. One must not be discouraged by assertions that neuroimaging is imprecise, allowing timing of injury to be determined only within days rather than hours[3], as the timing of injury

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[1] This article expands on my previous birth trauma papers. *See* Richard C. Halpern, *Intrapartum Pathways to Neonatal, Neurological Injury – A Lawyer's View of the Medicine*, Thomson Rogers (Nov. 2013) and Richard C. Halpern, *Revisiting Intrapartum Pathways to Neonatal Neurologic Injury – A Lawyer's View of the Medicine*, Thomson Rogers (Jan. 19, 2015).

[2] This is not to say that other evidence may not be relevant to causation. For example, genetic factors may be at play, there may be placental abnormalities, maternal conditions can affect fetal health, and the fetus itself may have conditions that affect morbidity and mortality. Importantly, more than one factor may be at play.

[3] Mary E. D'Alton, et al., *Neonatal Encephalopathy and Neurologic Outcome*, 209 (2nd ed. 2014) also referred to as the new green book at 209.

can be refined using the obstetrical and neonatal data. Judicious application of the differential diagnosis will often provide clear or probable evidence of cause and timing.

The pattern of brain injury provides clues regarding the mechanism of injury, and, therefore, the events that may have caused or contributed to the injury. Brain injury may be found on one or both sides of the brain in a diffuse pattern, or there may be focal lesions on one or both sides of the brain. Regardless of the topography of brain injury, in the setting of acute brain lesions of any description, the search for the likely cause is limited to a finite period of time where clinical events are closely monitored.[4] Even where antenatal or genetic factors might be contributory in some fashion, the search must be for the peripartum events occurring within the window of opportunity that triggered the injury.

Much of the medical literature on newborn neurologic injury occurring at or around the time of birth is concerned with hypoxia-ischemia (asphyxia) and describes topography of brain injury that is mostly diffuse and bilateral. This asphyxial model of injury can be due to intermittent repetitive interruptions in fetal oxygenation, called “prolonged partial hypoxia-ischemia”, or more profound interference with fetal oxygenation, called “total or near total hypoxia-ischemia”. I will use the term “asphyxia” in place of “hypoxia-ischemia”. Asphyxia has been associated in the medical literature with a metabolic acidosis in cord blood, but both ischemia and hypoxia occur without a metabolic acidosis.

Certainly, with regard to prolonged partial asphyxia, and often with near total asphyxia, the brain damaging ischemia is preceded by periods of hypoxia leading to a building fetal metabolic acidosis and, ultimately, fetal hypotension. Hypotension reduces perfusion of blood to the brain globally, explaining the diffuse and bilateral topography of brain lesions with this mechanism of injury. Recently, some medical literature has paid more attention to acute newborn neurologic injury that is focal, resulting in injury to a defined area of the brain affected by the distribution of a particular cerebral blood vessel. These injuries are strokes and may or may not be accompanied by a metabolic acidosis or fetal hypotension. For these injuries there is a reduction in perfusion (ischemia) in a particular region or regions of the brain. It is beyond controversy that asphyxial injury can be caused by the mismanagement of care during labour and delivery (“intrapartum”). This paper will explore issues concerned with asphyxial injury as well as whether stroke may be preventable, in some cases, by better management of intrapartum care. Importantly, stroke can also “occur” with asphyxia.

This paper will be concerned primarily with ischemic newborn brain injury, both diffuse and focal, that might be attributed to mismanagement of labour and delivery. I contend that the conventional thinking of how and why newborn

[4] The last few weeks of pregnancy usually have increased antenatal visits and during labour there is close monitoring of both fetus and mother.

neurologic injury occurs is evolving, but too slowly. The prominence of intrapartum events as a cause for newborn neurologic injury must be acknowledged if morbidity is to be reduced. Safe obstetrical care demands an appreciation for the intrapartum antecedents to newborn neurologic injury.

Incidentally, the search for the cause of newborn neurologic injury is not important exclusively, or even primarily, for the purposes of accountability or litigation. Indeed, the main purpose of identifying the cause of these injuries should be the improvement of obstetrical care and the prevention of future injuries. Reducing harm should undoubtedly be the priority, although I am not convinced that there is sufficient attention paid to this objective in some corners of the medical community, with some members of that community overly preoccupied with resisting litigation. At times I wonder if there is not a conspiracy of silence or willful ignorance. Preventable injuries should reasonably result in both compensation for those wronged and lessons learned for care providers. The fact that some birth trauma lawsuits are successful against physicians and hospitals is not an argument for tort reform, but rather an argument for improving care and reducing morbidity. Only negligent care results in the imposition of liability. A better understanding of causation can reduce substandard care through recognition of potentially harmful fetal stress. Reduce substandard care and fewer lawsuits will inevitably follow.

CAUSATION IN BROAD TERMS

Neuroimaging, particularly with MRI, can be used to approximate the timing of the occurrence of lesions on the newborn brain.[5] Where injury occurs at or around the time of birth, it is best to establish timing with a scan done within the first week of life.[6] Usually lesions will become apparent on the second day of life, although severe lesions or stroke may be seen on day one.[7] The time at which abnormalities become apparent on imaging allows one to distinguish between chronic antenatal injury and acute peripartum injury.

Where MRI identifies lesions with recent onset, and clinical features consistent with hypoxia are present such as abnormal fetal heart (FHR) tracings and metabolic acidosis in cord blood, one can reasonably be assured that the newborn has hypoxic-ischemic encephalopathy (HIE).[8] More will be said below about the importance of intrapartum clinical data, but a normal tracing upon admission that becomes abnormal in the setting of acute neonatal brain lesions more likely than not may point to an intrapartum timing of injury.

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[5] Joseph J. Volpe, *Neonatal Encephalopathy: An Inadequate Term For Hypoxic Ischemic Encephalopathy*, 72 Annals of Neurology 156 (2012).
[6] *Id at* 161.
[7] *Id.*
[8] *Id.* at 162.

The topography of brain injury characteristically associated with intrapartum asphyxia is well established in the medical literature.[9] Where neuroimaging demonstrates acute lesions that are known to arise from intrapartum asphyxial events, the pathway to proving causation should be clear. Evidence of developing hypoxia on the intrapartum FHR tracing together with other factors discussed in this paper and my previous papers will establish the cause.[10]

A study by Martinez-Biarge (2013) describes that the vast majority of encephalopathic infants have neuroimaging data consistent with an acute hypoxic-ischemic event and that seldom is there evidence for longstanding antenatal injury.[11] The study concludes by saying that intrapartum developments are necessary for the development of HIE. In other words, most neurologically injured babies incur their injury in the intrapartum period, though antenatal factors may potentiate some injuries. This supports my contention that the search for a cause, in most cases, must be for events occurring during labour and delivery.

There are a great number of variables to be considered and evaluated in the analysis of causation. Gestational age, maternal medical conditions, antenatal factors, infection, poor fetal growth, and genetic factors are but a few. Where none of these other factors are present, however, the causation analysis is substantially simplified. In my view there is ample medical (and common sense) support for the following proposition:

If:

1. Pregnancy was uneventful;
2. There is no obvious fetal abnormality that must have preceded labour;
3. Labour begins with a normal (category I) reassuring fetal heart tracing;
4. During labour the fetal heart tracing becomes atypical or abnormal (category II or III);
5. The newborn develops a neonatal encephalopathy; and
6. Neuroimaging demonstrates evidence of an acute brain injury;

Then it is likely that ischemic brain injury occurred during labour.[12]

There are some important observations to add to this proposition. First, umbilical cord gases are important clues to both cause and timing, but a systemic

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[9] *Id.* at 157.
[10] *See* Footnote 1.
[11] Miriam Martinez-Biarge, et al., *Antepartum and Intrapartum Factors Preceding Neonatal Hypoxic-Ischemic Encephalopathy*, 132 Pediatrics e952 (2013).
[12] Frances Cowan, et al., *Origin and Timing of Brain Lesions in Term Infants With Neonatal Encephalopathy*, 351 Lancet (2003).

metabolic acidosis is not required to prove causation.[13] As will be seen below, in the case of neonatal arterial ischemic stroke, there is often no metabolic acidosis. Second, the neuroimaging findings require only acute injury, and not a particular topography of injury (injury need not be diffuse and need not be bilateral). Third, even where there are some abnormalities during pregnancy, later newborn neurologic injury may still be causally connected to intrapartum mismanagement.

At the same time, I do not assert that liability is proven when all the elements of this proposition are present. A breach of the standard of care must still be proven. Further, even where the pregnancy was complicated, or where there are antenatal conditions that might impact on fetal well-being, one may still be able to establish that injury was caused or contributed to by intrapartum events and that care may have been substandard. My assertion in the proposition set out above is simply that proving newborn brain injury is due to intrapartum events, absent complicating variables, is more straightforward than some of the literature would have parents, lawyers and physicians believe. Proof can still be established when some of these complicating variables are present.

The importance of the proposition offered above cannot be exaggerated. In pursuing these cases, lawyers and parents must not be discouraged by arguments in some medical literature that most newborn injury occurs in the antenatal period. To the contrary, intrapartum injury is much more common than many medical investigators would have us believe.[14] In 2012 Volpe stated that HIE is by far the most common cause of neonatal encephalopathy (NE).[15]

It is worth repeating that establishing the likelihood that newborn brain injury occurred intrapartum involves two crucially important steps: first, early assessments of the brain using scanning techniques[16] that can determine if the injury is of recent onset[17] (proving "acute brain injury"); and, second, identifying the labour and delivery events that might be on the causal pathway leading to the pattern of brain injury observed (the "mechanism of injury"). In every case, other potential causative factors must be considered and either ruled out or evaluated for any contribution to the outcome.

The mechanism of injury has to do with the intrapartum events that may be on the causal pathway leading to the final topography of brain injury. This is a subject of considerable controversy, not only in any lawsuit that might ensue, but also in the scientific community as reflected in the medical literature on the subject. No matter what the antecedent events to brain injury are, ultimately the

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[13] Schifrin, Barry S. & Ater, Stewart, *Fetal Hypoxic and Ischemic Injuries*,18 Obstet-Gynecol 112. Volpe, *supra* at 161, where bad cord gases may not be seen with rapid changes associated with sentinel events like abruption or uterine rupture.
[14] Cowan, *supra* note 12, at 740.
[15] Volpe, *supra* note 5, at 157.
[16] MRI, CT, US.
[17] Perhaps only narrowing the window of opportunity to 5 to 7 days.

damage to brain tissue is caused by ischemia – a decrease in perfusion of blood to an area of the brain. The ischemia may be due to reduced blood supply to the brain globally (as occurs with hypotension and asphyxia) or from focal interruptions directly to cerebral blood vessels (that could occur through compression or blockage of the cerebral vessel).

Impaired oxygenation to the fetal brain can arise from issues with the placenta or umbilical cord, systemic issues of perfusion often associated with a metabolic acidosis, or from disruptions to cerebral blood flow (CBF) that may be systemic but can also be local to a particular area of the brain.[18] The latter are generally not associated with a systemic fetal metabolic acidosis and therefore may occur without asphyxia, although hypoxia is often a factor and asphyxia may be present.

NEWBORN BRAIN SICKNESS (NEONATAL ENCEPHALOPATHY) IN TERM BABIES

A precise definition of some medical terms is needed to better understand this discussion. The term "neonatal encephalopathy"[19] refers to newborn brain sickness, but does not attribute a cause for that brain sickness.[20] NE refers to a newborn with below normal consciousness, often manifested by problems with respiration and tone.[21] Importantly, NE may be due to antenatal causes, birth asphyxia, or other acute events occurring peripartum. Where asphyxia is the cause of NE, the newborn is said to be suffering from HIE.[22] Asphyxia is associated generally with a persistent impairment of gas exchange that leads to decreased oxygen in the blood (hypoxemia) and increased carbon dioxide (hypercapnia) causing a metabolic acidosis. Having said that, impaired gas exchange may not become severe enough to cause a metabolic acidosis that leads to hypotension, yet there is an association between hypoxia and all patterns of ischemic brain damage.

NE is broadly divided into three categories: mild, moderate and severe. Asphyxial injury causing moderate and severe NE is more likely to result in

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[18] Schifrin, *supra* note 13, at 115.

[19] *See* Sarnat, HB & Sarnat, MS, Neon*atal Encephalopathy Following Fetal Distress: A Clinical and Electroencephalographic Study*, 33 Arch Neurol 696 (1976).

[20] Volpe, *supra* note 5, Volpe note 5,. Volpe describes NE as a "non-specific" term that should not be used to describe infants with actual HIE.

[21] Supra, note 3, ACOG 2014 green book.

[22] Volpe, *supra* note 5, at 157. NE occurring in the setting of cord blood showing a metabolic acidosis, low Apgar scores, and imaging showing the topography of injury associated with acute hypoxia-ischemia should be called HIE.

permanent neurologic deficits. Injuries that are not necessarily asphyxial[23], such as neonatal stroke, are not generally associated with severe NE.[24]

EVOLUTION OF BRAIN INJURY

Another important factor for proving causation is the evolution of injury and the role it plays in timing injury. Ischemia causes brain lesions, with the neurons in the affected regions experiencing cellular change that results in edema, or swelling, within 24 to 36 hours of injury.[25] The injury peaks at between 3 and 5 days, thereafter resolving to a permanent injury. If this pattern is seen on imaging in the first 7 days of life, there is undoubtedly a peripartum injury. The evolution of these injuries will be described in more detail in the sections that follow.

Brain imaging techniques allow the recognition of both older (antenatal insults) and newer or acute insults (occurring at or around the time of birth). Searching for the cause of neurological injury in the newborn is first concerned, therefore, with determining if the problem is old or new.

NEONATAL BRAIN INJURY ASSOCIATED WITH INTRAPARTUM EVENTS

HIE can manifest in different patterns of brain injury. These patterns depend on the nature of the insult, the duration of the insult, the age of the fetus, and other variables. The areas of the brain affected often helps to understand the pathway to injury and, for the most part, the peripartum risk factors that can lead to injury.

The major varieties of newborn HIE are described by Volpe as follows:

1. Selective neuronal necrosis;
2. Parasagittal cerebral injury;
3. Periventricular leukomalacia;
4. Focal (and multifocal) ischemic brain necrosis, or stroke.[26]

The first variety, selective neuronal necrosis, is the most common injury in term babies and describes a characteristically widespread distribution of brain damage often broken down into three categories: diffuse; deep gray matter injury to the basal ganglia and thalamus (BN); or, both. It is thought that diffuse injury is most often associated with repetitive, intermittent and prolonged episodes of hypoxia. The BN pattern is generally thought to be associated with rather severe and abrupt insults. The two patterns can occur together where the intermittent

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[23] Even with stroke, there is usually an element hypoxia that exposes the fetus to the risk of focal lesions, but often it does not result in a severe metabolic acidosis that leads to fetal hypotension.
[24] Schifrin, *supra* note 13, at 113.
[25] Volpe, supra note 5, at page 159.
[26] Joseph Volpe, *Hypoxic-Ischemic Encephalopathy: Neuropathology and Pathogenesis,* Neurology of the Newborn 347-399, 348 (5th ed. 2008).

hypoxic insults are particularly severe and prolonged.[27] Within 24 to 36 hours of these injuries, there is often swelling of brain tissue, peaking at around 3 to 5 days after injury and then resolving within about a week.[28] This classic evolution of injury allows one to be confident that the injury is acute. Neuroimaging detecting this evolution can establish the "window of opportunity" for injury as being near to the time of birth. As pointed out elsewhere in this article, further refinement of the timing of injury will depend on obstetrical and neonatal clinical data. The cause of injury is ischemia to the brain thought to be associated with diminished cerebral blood flow (CBF) resulting from systemic hypotension[29], although there is no suggestion that this type of injury must be bilateral. Indeed, this type of injury has a variety of patterns that distinguish it from the watershed injury discussed below.[30]

The parasagittal injury involves lesions in the cerebral cortex and subcortical white matter.[31] This is the injury that primarily affects the asphyxiated term baby and the injury is bilateral and often symmetrical. This injury is described as a "watershed infarct" (WI).[32] This injury is attributed to decreased cerebral perfusion often due to systemic fetal hypotension.[33] While beyond the scope of this paper, the outcomes for children affected by this topography of injury can involve motor dysfunction. However, these children can have cognitive impairments in the absence of motor dysfunction.[34]

Periventricular leukomalacia (PVL) involves focal loss of brain tissue around the lateral ventricles and more diffuse damage to the surrounding white matter.[35] Like the other brain lesions, this injury is caused by hypoxia-ischemia.[36] This may involve haemorrhage into the area of lesion.[37] This is an injury primarily affecting the premature infant as a result of the vulnerability of the periventricular region to injury due to immaturity.[38] The premature baby is less able to modify blood pressure and adapt to ischemia, making them more vulnerable to injury in the setting of ischemia.[39] Arguably, in the management of labour involving premature babies, there ought to be less tolerance for evidence of possible impaired oxygenation. As an aside, with regard to considering a claim for

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[27] *Id.* at 349.
[28] *Id.*
[29] *Id.* at 354.
[30] *Id.* at 358.
[31] *Id.* at 356.
[32] *Id.*
[33] *Id.* at 359.
[34] Anna Perez, et al., *Long-Term Neurodevelopmental Outcome With Hypoxic-Ischemic Encephalopathy*, 163 The Journal of Pediatrics, 454 (2013). This is contrary to the 2003 ACOG green book.
[35] Volpe, *supra* note 26, at 363.
[36] *Id.* at 364.
[37] *Id.* at 365.
[38] *Id.* at 370.
[39] *Id.* at 373.

damages for cases involving premature babies, there is a tendency not to pursue these cases as PVL is seen as a risk of prematurity. My concern is that meritorious cases may be missed. PVL merely reflects the vulnerability of the premature baby, but mismanagement of care may well explain the development of PVL. In other words, the special vulnerability of these babies must be considered in the management of the complication that results in their early delivery. Premature babies are less able to tolerate hypoxic stress, so that the threshold for intervention should be lower than in term babies.

Leaving the causal mechanism aside for the moment, the possible explanations for neonatal neurologic injury include:

1. Established antenatal brain injury;
2. Genetic causes;
3. Perinatal (and possibly intrapartum) injury with or without evidence of asphyxia;
4. Antenatal insults that make the brain vulnerable to intrapartum injury;
5. Neonatal injury.

In 2000 Cowan noted that the majority of infants with a clinical history of intrapartum asphyxia followed by neonatal encephalopathy and seizures had evidence of acute insult on neuroimaging.[40] The causal link between intrapartum asphyxia and NE is unmistakable. Crucially, evidence for established antenatal brain damage is rare in infants after evidence of intrapartum asphyxia, and these infants almost always have evidence of acute or sub-acute brain injury.[41] According to Cowan, this includes infants with acute ischemic infarctions[42] and although antenatal conditions may predispose some to these types of injury, this does not rule out intrapartum mismanagement as a contributing cause. This and other studies, implicate intrapartum events as important causes of newborn neurologic injury.

While the WI and BN patterns of injury have been thought to be caused by some form of reduction of blood supply to the brain globally, perhaps related to hypotension, this mechanism of injury cannot explain all of the patterns of acute brain injury in newborns. In particular, unilateral lesions and lesions or infarcts related to stroke cannot be explained by global hypotension. These kinds of focal white matter injury (WMI) are necessarily the result of ischemia caused by interruptions to blood flow in particular vessels that must be either thrombotic, embolic or by compression of the affected vessel. While beyond the scope of this paper, the issue of head compression as a cause to interrupted cerebral blood flow is an underappreciated cause of acute brain lesions in the newborn. There is considerable resistance in the obstetrical community to accepting head

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[40] Frances Cowan, *Outcome After Intrapartum Asphyxia in Term Infants*, 5 Seminars in Neonatology 128 (May 2000).
[41] *Id.*, at 129.
[42] *Id.*

compression as a mechanism of injury despite the prominence of excessive Oxytocin use in labour in many cases that go to litigation.

There is plenty of reliable literature establishing that WI and BN injury are not the only injuries associated with intrapartum hypoxia ischemia.[43] This points out the need for more interest in stroke and head compression as a cause of newborn injury and for an updated understanding of the mechanisms that can lead to injury. Even if the precise mechanism remains poorly understood in some cases, the timing of injury does not. Since neuroimaging can establish timing (within days), and intrapartum risk factors are associated with acute injury, a causal connection can be made between the two.

If acute newborn neurologic injury is associated with intrapartum risk factors and occurs without a severe metabolic acidosis resulting in focal lesions, then there must be multiple pathways to injury. The fetal hypotension associated with a metabolic acidosis is only one mechanism of injury. Though the precise mechanism may be less clear, it is quite clear that injury occurs around the time of birth.

In a study by Massaro and others (2015)[44] short-term outcomes after HIE were reviewed. There were 945 infants included with perinatal HIE.[45] The criteria used to establish the diagnosis of HIE clearly implicated intrapartum events as the cause for the newborn encephalopathy. Of the 945 infants studied, 160 had mild encephalopathy, 492 had moderate encephalopathy and 293 had severe encephalopathy. Less than half of the infants with mild encephalopathy (40.8%) had normal brain imaging on MRI scan. In the mild group, 2.3% had infarct or stroke. For the moderate encephalopathy group, even fewer had normal scans (37.1%), with 8.8% suffering infarct or stroke. Not surprisingly, the severe encephalopathy group had many fewer normal outcomes (only 10.90%), with 8.2% suffering infarct or stroke. The study supports a connection between intrapartum visit factors and stroke.

Is stroke HIE or merely IE? In other words, a severe hypoxia resulting in a fetal metabolic acidosis is often not present in stroke. Arguably, a severe metabolic acidosis is not always present in asphyxia. Certainly some degree of hypoxia is present in many stroke cases as these infants inevitably have FHR changes consistent with hypoxia. If hypoxia potentiates the formation of thrombosis or embolus in a cerebral vessel, then the hypoxic component should remain in

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[43] Vann Chau, et al., *Comparison of Computer Tomography and Magnetic Resonance Imaging Scans on the Third Day of Life in Term Newborns With Neonatal Encephalopathy,* 123 Pediatrics 319 (Jan. 2009).

[44] Massaro, AN, et al., *Short-Term Outcomes After Perinatal Hypoxic Ischemic Encephalopathy: A Report From the Children's Hospitals Neonatal Consortium HIE Focus Group,* 35 J(2015) J. Perinatal 290 (Apr. 2015).

[45] *Id.* at 291. Perinatal HIE clearly refers to intrapartum events as described in this study. See Table 1.

describing all patterns of injury. If compression of a cerebral vessel explains the brain lesion, then the injury may be purely ischemic. It seems, based on the literature, that injury is almost always accompanied by hypoxia and therefore HIE should be used to describe all brain lesions occurring intrapartally.

Cowan also points out that term infants with focal infarction will usually demonstrate either antenatal or intrapartum complications.[46] These are the same complications that one sees with the classic asphyxia injury.

A 2003 study by Cowan found strong support for the cause of neonatal brain injury to be attributed to perinatal injury rather than early antenatal insults.[47] Cowan studied 351 infants: 261 with NE; and, 90 without NE, but with seizures within 72 hours of birth. The NE group had the hallmarks of intrapartum asphyxia.[48] While most of the NE children had bilateral lesions classically associated with intrapartum asphyxia, 8 of the 261 infants had focal infarction. In the seizure group of 90 children, 35 (more than 1/3) had focal cerebral infarction. In both groups the vast majority of children had evidence of acute findings only.[49]

Indeed, more than 90% of term infants were found to have perinatally acquired injury without any established antenatal injury. Cowan does not rule out possible antenatal factors as contributors to perinatally acquired injury. This study refutes the common assertion in much of the medical literature that antenatal factors are mostly responsible for NE. The study also takes issue that the unfounded assertion that the injurious process occurs antenatally. Intrapartum risks factors are prominently implicated as a cause of newborn neurologic injury.

Stroke is due to a focal interruption in blood supply. It involves the sudden rupture or occlusion of cerebral vessels that lead to neuronal death to tissue perfused by the affected cerebral vessel and later neurologic deficits.[50] Strokes can result from vasoconstriction or direct compression of intracranial vessels.[51] Neonatal Arterial Ischemic Stroke (NAIS) is caused by vascular occlusion. The understanding of the role of birth asphyxia in the development of neonatal stroke has evolved over the last couple of decades. The cause of perinatal stroke has

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[46] Cowan, *supra* note 40, at 135.
[47] Cowan, F., et al., *Origin and Timing of Brain Lesions in Term Infants With Neonatal Encephalopathy*, 361 Lancet 736 (Mar. 2003).
[48] *Id.* at 736. In addition to abnormal tone, feeding or alertness, these children had at least three of: late decelerations or meconium staining; delayed onset of respirations; arterial cord pH less than 7.1; Apgar scores less than 7 at 5 minutes; and, multiorgan failure.
[49] *Id.* at 738.
[50] Nelson, KB & Lynch, JK, *Stroke in Newborn Infants*, 3 Lancet Neurol 150 (Mar. 2004).
[51] *Epidemiology and Classification of Perinatal Stroke*, 14 Seminars in Fetal and Neonatal Medicine 245 (Oct. 2009).

been called "poorly understood"[52], but recent literature has recognized a clear correlation between intrapartum risk factors and NAIS.[53]

With stroke, neuroimaging can determine if the injury is acute since evidence of change to brain tissue often takes more than 18 hours to develop.[54] Therefore, when looking for an underlying cause for stroke, like asphyxia, one must look to the window of opportunity for injury established by neuroimaging. Changes associated with stroke, like those associated with more diffuse injury from systemic hypotension, have a similar timeline for evolution, getting worse over the ensuing 3 to 5 days, and thereafter resolving to the final injured state.[55]

Newborns with neonatal encephalopathy may suffer from focal or diffuse injury occurring during labour.[56] It is important to make the distinction between focal (and multifocal) interruptions of cerebral blood flow (caused by occlusion or insufficiency) and those resulting from a more generalized systemic reduction in circulation.[57] The former occur, for our purposes, as a result of vascular occlusion (which may be thrombotic, or embolic compressive). The objective is to determine the likely reason for the vascular insufficiency that leads to the lesion.

Importantly, the majority of lesions due to stroke are unilateral.[58] This means that these acute brain lesions cannot be explained by a systemic hypotension. If systemic hypotension explained these lesions one would expect bilateral damage.

To disrupt flow there must be either a blockage or an occlusion, whether extrinsic (compression) or intrinsic (thrombus or embolus). Despite the fact that some investigations done after fetal or newborn death have not revealed evidence of thrombus, it appears that Volpe posits only thrombus or vascular mal-development as explanations for stroke[59], without allowing for the possibility of compression or some other hypoxia-induced cause. The old way of thinking allowed the majority of neonatal strokes to be attributed to "idiopathic" causes[60], but recent technology has allowed a better appreciation for the fact that there is much more acute neonatal stroke than historically contemplated. It is time to abandon idiopathic non-explanations as a cause of newborn neurologic injury.

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[52] Ramaswamy, V., et al., *Perinatal Stroke in Term Infants With Neonatal Encephalopathy*, 62 Neurology 2088 (June 2004).
[53] Miriam Martinez-Biarge, et al., *Risk Factors for Neonatal Arterial Ischemic Stroke: The Importance of the Intrapartum Period*, 173 The Journal of Pediatrics, 62 (June 2016).
[54] Volpe, *supra* note 26, at 379.
[55] *Id.* at 380.
[56] Ramaswamy, *supra* note 52, at 2088.
[57] Volpe, *supra* note 26., at 383.
[58] *Id* at 380.
[59] *Id.* at 383.
[60] *Id.*

Volpe recognizes the association between intrapartum evidence of asphyxia[61] and neonatal stroke, but ponders how a generalized disturbance of cerebral perfusion (due to hypotension) can lead to a unilateral focal injury.[62] He posits that asphyxia, as a sympathetic stimulator, might induce vasoconstriction of the affected vessel.[63] Notably a systemic fetal metabolic acidosis is not part of this analysis. While the precise mechanism of unilateral focal brain injury may remain enigmatic for some[64], as will be discussed below, there is a clear correlation between neonatal stroke and intrapartum risk factors. This inevitably means that many of the variables some scientists feel are important to the asphyxia causation analysis, like cord gases and multi-organ involvement, are far less important. That is to say, asphyxia does not need to be severe enough to cause a severe metabolic acidosis in order to trigger brain lesions.

In Volpe's leading text on newborn neurology the following statement is made:

> The clinical settings for neonatal hypoxic-ischemic encephalopathy are dominated by the ultimate occurrence of ischemia (i.e., diminished blood supply to brain), usually but not necessarily preceded or accompanied by hypoxemia (i.e., diminished amount of oxygen in the blood supply). Hypoxemia leads to brain injury principally by causing myocardial disturbance and loss of cerebrovascular autoregulation, with ischemia the major consequence.[65]

This excerpt makes some important observations and raises an unanswered question. Significantly, it recognizes that ischemia is not only the cause of neonatal neurologic injury, but that brain ischemia can occur without hypoxemia. In other words, ischemia can occur without the myocardial disturbance that leads to hypotension and the disruption in the ability of the fetal brain to adjust blood pressure to diminished perfusion (loss of autoregulation). The unanswered question is concerned with how intrapartum events give rise to ischemia in the absence of hypoxemia or where hypoxemia is insufficient to result in hypotension and globally reduced cerebral perfusion.

According to Volpe three features must be present to establish that a newborn's brain injury was caused by an intrapartum insult. They are:

1. Evidence of fetal distress (e.g., fetal heart rate abnormalities, meconium-stained fluid);
2. Depression at birth; and

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[61] *Id.* at 389. Like prolonged second stage, fetal heart rate abnormalities, cord complications, etc.
[62] *Id.* at 388.
[63] *Id.* at 385.
[64] Though compression of the vessels seems to make much more sense.
[65] Volpe, *supra* note 26, at 400.

3. An overt neonatal neurological syndrome in the first hours and days of life.[66]

These criteria do not require: fetal hypotension; a particular topography of injury; a systemic fetal metabolic acidosis; multi-organ dysfunction; or a particular kind of resulting disability. I contend that the three criteria offered by Volpe are the only essential criteria. Once these conditions are present, a prima facie case is made out. This paper covers some of the other variables that tend to support or refute an intrapartum cause. While helpful, none of these other variables should be thought as determinative of cause. Moreover, the entire antenatal, intrapartum and neonatal clinical picture must be evaluated in order to determine causation.

It has also been posited that extremes of neck extension or rotation, as might occur with the operative vaginal delivery, may cause vascular distortion leading to intrauterine stroke.[67] Even if this sort of trauma explains some stroke, there is still a correlation between hypoxia and stroke, but the pathway to injury is not well understood. Arguably, much of the injury from trauma is also avoidable, but that is the subject matter for another paper.

Where the lesions are acute, it should follow that the diagnosis can be made from the imaging itself. That is certainly the situation with stroke. In other words, with a focal lesion there is no need to correlate the imaging with other clinical evidence. The finding of an acute focal lesion in the setting of intrapartum risk factors is enough. Some of the conventional thinking with asphyxia has been that acute brain lesions on imaging that have a more diffuse pattern require clinical correlation, usually with evidence of a severe metabolic acidosis in cord blood. That is, a focal lesion can be acute with a normal pH in cord blood, but with asphyxia the lesions need to be associated with an abnormal pH in cord blood. Are the mechanisms of injury different for focal lesions than more diffuse lesions, or is it time to re-think causation in asphyxia cases?[68] After all, both stroke and HIE are ischemic lesions, that, in the scenarios under consideration, are peripartum developments. How often do we see cases with classic acute asphyxial brain lesions, poor tracings, mismanaged intrapartum care and relatively good gases? The importance, or really the unimportance, of umbilical cord gas results needs to be revisited. Fetal hypotension must not be the only pathway to newborn neurologic injury and therefore cardiac ischemia leading to hypotension is only one pathway to injury, but not exclusively so.

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[66] *Id.* at 401.

[67] Volpe, *supra* note 26, at 385.

[68] The thoughts expressed in this paragraph are not entirely my own. This analysis arises out of discussions I have had with Dr. Barry Schifrin, an obstetrician, who I admire as one of the leading authorities in the world on this subject. Dr. Schifrin astutely asks why stroke is a neuroradiological diagnosis while asphyxia requires clinical correlation. As both involve ischemic lesions, why can't they share a common cause?

There are limited possibilities for explaining the lesions associated with both asphyxia and stroke. As I stated, both injuries are ischemic. Flow to the brain must be diminished to cause ischemia and resulting necrosis. Logically, reduced flow is due to hypotension, blockage of the cerebral vessels upstream from the damage (thrombus or embolus), or compression of the cerebral vessels. Not all acute brain lesions can be attributed to hypotension, as stroke demonstrates. Therefore, a severe metabolic acidosis is not an essential component of the causation analysis.

There has been an assumption, one that I hope to demonstrate is mistaken, that stroke (a more common cause of cerebral palsy than global hypoxia-ischemia) cannot be attributed to the mismanagement of intrapartum care. The correlation between intrapartum risk factors and stroke suggests that there is an opportunity to intervene and prevent stroke in some cases.

Focal ischemic stroke and the more diffuse injury attributed to hypotension share much in common, including the delay in anoxic neuronal change often for 18 hours or more after injury.[69] The evolution of injury is very similar in both. This is important for two critical reasons: first, it indicates the timing of injury (likely peripartum); and, second, it suggests that both focal and diffuse injury share causal pathways. Significantly, the focal injury (stroke) is most often a local ischemic injury and can occur in the absence of hypotension. A severe metabolic acidosis is not a condition precedent of all intrapartum cerebral ischemic injury.

Medical literature recognizes that events in the perinatal period[70] can lead to stroke.[71] The perinatal period includes labour. There is now an appreciation that some stroke is caused during the intrapartum period and may be preventable. While many clinical variables have been found to be associated with stroke, included in the variables are intrapartum risk factors.[72] As early as the 1980s it was recognized that a significant percentage of focal lesions in newborns were related to perinatal asphyxia. [73]

In a 2005 study by Lee et al intrapartum complications were more common in infants suffering from NAIS.[74] The study notes that 6 infants diagnosed with

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[69] Volpe, *supra* note 26, at 380.

[70] Grunt, S., et al., *Incidence and Outcomes of Symptomatic Neonatal Arterial Ischemic Stroke*, 135 Pediatrics e1220-1228e1221.

[71] The perinatal period is defined as occurring between 20 weeks gestation and postnatal day 28. *Id.* at e1221.

[72] *Id.*

[73] Volpe, *supra* note 27, at 383 (and his footnotes 178-189).

[74] Lee, J., et al., *Maternal and Infant Characteristics Associated With Perinatal Arterial Stroke in the Infant*, 293 JAMA 723-729, 728 (Feb. 9, 2005). Although the study went on to say that complications such as fetal heart rate abnormalities were no longer independently associated with

stroke and with asphyxia had focal arterial infarction "as opposed to the more typical…hypoxic-ischemic injury, such as deep gray-matter or arterial-watershed injury, reminding us that the clinical diagnosis of birth asphyxia is not specific for any single pathogenetic mechanism of brain injury". This means that asphyxia can result in multiple pathways to injury and a variety of lesions, not necessarily diffuse or bilateral.

Intrapartum risks like prolonged second stage labour, fetal heart rate abnormalities, signs of perinatal asphyxia, and cord complications resulting in a generalized disturbance of systemic circulation with impaired brain perfusion have long been recognized as related to NAIS.[75] Yet Volpe asks how the more common unilateral lesions caused by stroke in the distribution of a single cerebral vessel can occur in the presence of a generalized disturbance of perfusion. In other words, where flow to the brain generally is affected, one would expect more diffuse and bilateral injury. Volpe speculates that variations in the development of cerebral vessels or their responses to regulatory effectors might account for this. The problem with this theory is that acute perinatal stroke can occur in the absence of a generalized reduction in brain perfusion. The causes postulated by Volpe fail to address other ways of inducing vasoconstriction.[76] It also fails to explain more recent research that has found newborn injury in cases of mild neonatal encephalopathy without significant metabolic acidosis and cardiac involvement.

We should keep in mind other causes of stroke. For example, trauma may cause perinatal stroke during operative vaginal delivery (forceps or vacuum). Extremes of neck extension or rotation can impair blood flow in the vertebrobasilar system or in the carotid system.[77] Hyperextension of the head can also lead to injury.

In a study by Grunt et al[78], 96 neonates with NAIS were reviewed. The associated clinical variables for this cohort were divided into 3 categories: maternal conditions; birth complications; and, neonatal comorbidities. Among the birth complications were: forceps; birth asphyxia; neonatal resuscitation; pathologic cardiotocography; meconium stained fluid; and, Apgar scores. Significantly, 68% of the cohort studied had birth complications. This study found an association between NAIS and the 3 categories of complications identified. The study did not offer any explanation for how any of these complications caused NAIS. The importance of this, and other studies, is the association between NAIS and birth complications. Though there is no comment on the pathway from birth complications to NAIS, it should be clear that the pathway is not the same as that induced by fetal metabolic acidosis and subsequent

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PAS after adjustment for maternal variables. However, many other studies have found that there is a correlation between fetal heart rate abnormalities and stroke.

[75] Volpe, *supra* note 26, at 388.

[76] Like head compression.

[77] Volpe, *supra* note 27, at 384.

[78] *Supra* note 70.

systemic hypotension associated with the classic asphyxial injury. A different causal pathway is at play, but one nevertheless associated with intrapartum risk factors.

A 2005 study by Lee et al[79] examined pregnancy complications associated with NAIS. In that study, 16% of the infants studied had a clinical diagnosis of birth asphyxia or HIE despite evidence of brain injury attributed to stroke. The study remarked how these asphyxiated infants had focal arterial infarction rather than the more typical (WMI or BN) injury associated with asphyxia.

A study by Harteman et al[80] examined the risk factors for NAIS[81] in symptomatic full-term infants. Despite the literature that relates HIE to diffuse brain damage and not focal infarction, this study suggests that perinatal asphyxia plays a role in the development of NAIS.[82] In this study 32% of the infants with NAIS were admitted to the NICU as a result of perinatal asphyxia. The study refers to multiple publications that have found an association between intrapartum hypoxia-ischemia and NAIS. In terms of causation, the Harteman study posits that hypoxia-ischemia might play a role in activating thrombogenesis.[83] The study also found that intrapartum maternal pyrexia is associated with NAIS. This suggests that intervention may be appropriate in the presence of hypoxia and elevated maternal temperature to prevent focal injury.

An important study by Chau et al[84] looked at CT and MRI patterns of brain injury on day 3 of life for newborns with NE. The cohort of term babies (36 weeks or more gestational age) with NE in this study had inclusion criteria typical for intrapartum asphyxia. These included: fetal distress at delivery; requirement for resuscitation at birth; Apgar scores of 5 or less at 5 minutes; or, metabolic acidosis. Interestingly, the patterns of brain injury identified in this study included: watershed injury/white matter injury (WMI); basal nuclei injury (BN); total injury (WMI and BN); and focal-multifocal injury (stroke).[85] Of particular interest is the finding that some of these neonates with acute injury had stroke. In the total cohort of 48 newborns, 13 were found to have stroke. It is significant to note that out of the 13 newborns with stroke, 11 had evidence of fetal distress. In that same group the median cord pH was 7.0, revealing evidence of a metabolic acidosis. The median cord base excess was -14.3. It is clear that newborns with stroke have some of the same factors at play as those suffering the more classic asphyxial patterns of brain injury.[86] While not the aim of this

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[79] Lee, *supra* note 74,.
[80] Harteman, Johanna, *Risk Factors for Perinatal Arterial Ischemic Stroke in Full-Term Infants: A Case- Control Study*, 97 Arch Dis Child Fetal Neonatal F411-16, F414 (Mar. 2012).
[81] The study called it PAIS – perinatal arterial ischemic stroke.
[82] Harteman, *supra* note 80, at F414.
[83] *Id*.
[84] Chau, *supra* note 43.
[85] Chau, *supra* note 43, at page 320.
[86] *Id. See also* Table 1 and page 324.

study, the findings support the contention that intrapartum asphyxia can lead to focal brain injury. Again it supports the need to rethink the pathophysiology of neonatal neurologic injury.

Another study by Chau in 2012[87] studied a cohort of 48 neonates. The inclusion criteria for this cohort was evidence of NE consistent with intrapartum hypoxia ischemia. The subjects of the study were classified according to their predominant pattern of brain injury. Significantly, 13 of the 48 neonates had focal-multifocal injury. Of these 13 neonates, 9 had white matter injury, 3 had stroke, and 2 had white matter injury and stroke. There were 3 more subjects with focal-multifocal abnormalities combined with basal nuclei damage.[88] This article points out that "focal and multifocal lesions such as strokes are increasingly recognized to occur concomitantly with NE".[89]

Recent studies have identified the correlation between intrapartum risk factors and stroke. Consequently, caution must be exercised in accepting assertions that there are no reliable predictors of NAIS.[90]

It is not clear exactly how hypoxia that does not evolve into a systemic hypotension will cause lesions in the fetal or newborn brain. Having said that, two things should be abundantly clear: first, neuroimaging can identify acute lesions in the newborn brain that can present as diffuse only, focal only, or both diffuse and focal (as well as unilateral or bilateral); and, second, that there is a correlation between these acute brain lesions and intrapartum hypoxic stress. It follows that relieving or responding to intrapartum hypoxic stress has the potential to prevent both asphyxial injury and stroke. This means that there is potential to prevent acute brain lesions of any description by responding to evidence of intrapartum hypoxia or fetal stress.[91] Certain fetal heart rate changes suggest hypoxic stress, making the fetal heart tracing a vital tool for narrowing the timing of injury within the window of opportunity identified by neuroimaging.

FETAL HEART RATE PATTERNS AND NEUROLOGIC INJURY

The medical literature reviewed above highlights the importance of fetal heart rate ("FHR") changes for the recognition of hypoxic stress and the potential to prevent or mitigate neurologic injury, whether focal or diffuse.

There is a considerable amount of medical literature published that tends to diminish the value of FHR patterns in identifying the hypoxic fetus and the need

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[87] See Chau 2012
[88] See Chau 2012 at page 322.
[89] See Chau 2012 page 324.
[90] For example, see Raju 2007.
[91] The intrapartum response to evidence of hypoxic stress is to reduce the stress (ie., discontinue Oxytocin with excessive uterine activity) or expedite delivery.

for intervention for suspected impaired oxygenation. But electronic fetal heart rate monitoring is the preferred method of surveillance of fetal well-being and is mandatory in high risk pregnancies. FHR patterns are vital tools both in the management of intrapartum care and refining the timing of injury in the causation analysis.

This section is primarily concerned with FHR patterns. I will not cover uterine activity in any detail, but a brief comment is warranted. Uterine activity is crucial to the interpretation of FHR patterns. Excessively frequent contractions, unduly prolonged contractions and inadequate rest between contractions must influence the clinical response to periodic changes in the FHR rate pattern. These patterns of uterine activity are also highly suggestive of hypoxia. Injudicious use of Oxytocin will exacerbate the ill-effects of abnormal uterine activity.

With regard to the fetal heart rate, the starting proposition is that a normal FHR tracing reflects a well-oxygenated fetus.[92] During the intrapartum period, evolution of the FHR pattern from normal (category I) to one that is atypical or abnormal (category II or III) assists in identifying the timing of insult and injury. A previously normal (category I) tracing that is later characterized by the presence of decelerations, diminished variability and changes in baseline, reflect hypoxic insult, though not necessarily injury.[93] On the other hand, a tracing that is abnormal (category III) at the outset might indicate a fetus already injured.

Certainly, the combination of an atypical or abnormal tracing (category II or category III) and evidence of a metabolic acidosis in cord blood at birth strongly suggests intrapartum asphyxia.

A complete analysis of the value of FHR interpretation in the timing of injury cannot ignore the controversy that arises over the sensitivity[94], specificity[95] and positive predictive value[96] of fetal heart rate interpretation. But these matters must be considered in the appropriate context. FHR tracings should not be used to predict the neurologically injured fetus, as that defeats the purpose of this tool. Rather, the objective is to recognize hypoxic stress and intervene before injury occurs. Electronic fetal monitoring is not used to predict which children will suffer from CP – it is to be used to prevent CP.

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[92] Schifrin, *supra* note 13, at 114.

[93] *Id.*

[94] Sensitivity is concerned with how often a test will result in a true positive. Sensitivity is the true positives divided by the sum of the true positives and the false negatives. The sensitivity of EFM is high.

[95] Specificity is concerned with true negatives. How often will a negative test be accurate. EFM has poor specificity. Specificity = true negatives/(true negatives + false positives).

[96] Positive predictive value is concerned with the probability that a condition will exists when the test result is positive for that condition. PV+ = true positive/(true positive + false positive). Negative predictive value is concerned with how often a person does not have a condition when the test result is negative.

The starting proposition must be that a normal fetal heart tracing during labour is almost assuredly an indication that the fetus is neither hypoxic nor acidotic.[97] Moreover, the intrapartum fetal heart pattern will never fail to warn of the presence of hypoxia by exhibiting decelerations, diminished variability or other changes associated with hypoxia.[98] Put another way, significant hypoxia will always result in a FHR tracing that deviates from normal (to category II or III), but it must be appreciated that things other than hypoxia can cause these same deviations.

As I said, there is insufficient appreciation for the importance of the FHR pattern during labour in the causation analysis. Where the FHR pattern on admission is entirely reassuring with normal baseline, moderate variability, the absence of decelerations, and the presence of accelerations, it is reasonable to assume that the fetus enters labour neurologically intact.[99] Where the FHR pattern subsequently changes to an atypical pattern or abnormal pattern (category II or III), particularly in the context of excessive uterine activity, there is strong evidence that an intrapartum insult is responsible for any newborn neurologic depression. Evolution of the FHR pattern showing deterioration during labour should be seen as reflecting mounting fetal stress and oxygen debt. Crucially, the FHR patterns must be assessed in the overall context of the labour (including the nature of the uterine activity, the progress of labour, fetal position and maternal complications such as fever).

Thus, a normal tracing on admission in a low risk pregnancy should be used as the baseline against which subsequent FHR patterns are to be compared in order to determine whether intrapartum hypoxia or ischemia explains a subsequent poor neonatal neurologic outcome. Importantly, proper interpretation of FHR patterns requires assessment over time and in the overall clinical context.

Certain FHR patterns tend to be more frequently associated with fetal acidemia. While the focus of much of the medical literature is on acidemia, the real issue is the presence of hypoxic stress as acidemia is not necessary for intrapartum injury to occur. The presence of these FHR patterns is important to the causation analysis.

The importance of tachycardia as an indicator of possible fetal acidemia or hypoxia is under-appreciated. Fetal tachycardia is often dismissed as clinically unimportant in the presence of maternal pyrexia or the influence of certain medications. It is important to appreciate that there are other causes for fetal tachycardia, including hypoxia. There is a higher incidence of fetal acidemia where tachycardia is accompanied by decelerations, particularly severe variable

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[97] *Electronic Fetal Heart Monitoring – Risks, Benefits, Future and Strategies to Avoid Pitfalls,* US Obstetrics & Gynecology 60-62, 60 (2008).
[98] *Id.* at 61.
[99] Eden R.D., et al., *The Fetal Reserve Index: Re-Engineering the Interpretation and Responses to Fetal Heart Rate Patterns,*" Fetal Diagnosis and Therapy, 4 (June 8, 2017)4.

decelerations or late decelerations.[100] Reduced variability, in combination with these patterns, also points to a higher risk of fetal acidemia.

It is recognized that atypical (category II) tracings are the most frequently encountered patterns during labour and constitute a very wide range of patterns that can vary in their significance from benign to ominous.[101] The development of minimal or absent variability along with late or variable decelerations is the most consistent predictor of fetal acidemia (again, the concern ought to be hypoxic stress).[102] Likewise, the presence of fetal tachycardia with decelerations, especially if occurring more than 2 hours before delivery, is more likely to result in a depressed infant.[103]

Vintzileos (2016) and colleagues argue, appropriately, for the audit of all cases where a category I (normal) pattern on admission results in the birth of a depressed baby.[104] These authors point out that this analysis will often demonstrate a predictable deterioration in the FHR pattern characterized by the sequential development of loss of accelerations, significant decelerations, episodes of tachycardia or continuous tachycardia, poor variability and bradycardia. Intervention is required for this type of deterioration in the FHR pattern when either ominous category II (atypical) or category III (abnormal) patterns emerge.

A developing fetal metabolic acidosis is most often seen with category II (atypical) FHR patterns involving tachycardia, decelerations and diminished variability.[105] Atypical (category II) tracings are defined so broadly that there is precious little guidance about how to manage these patterns. The little guidance that does exist fails to give adequate attention to the broader clinical circumstances under which these changes occur (i.e., poor progress, abnormal uterine activity).

A 2014 study by Jonsson and colleagues looked at NE cases that evolved with evidence of a normal cardiotocographic (CTG) pattern on admission that became abnormal and resulted in metabolic acidemia at birth.[106] The study found that most of the cases of NE were caused by asphyxia that evolved during labour.

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[100] Holzmann, M., et al *Cardiotocography patterns and Risk of Intrapartum Fetal Acidemia*, 43 J. Perinat 473-79, 475 (July 2015).
[101] Anthony M. Vintzileos & John C. Smulian, *Decelerations, Tachycardia and Decreased Variability: Have We Overlooked the Significance of Longitudinal Fetal Heart Rate Changes for Detecting Intrapartum Fetal Hypoxia?*, 215 American Journal of Obstetrics and Gynecology 261-264, 261 (Sept. 2016).
[102] *Id.* at 262.
[103] *Id.*
[104] *Id.*
[105] *Id.* at 263, *see also* Holzmann, *supra* note 100.
[106] Jonsson, M., et al., *Neonatal Encephalopathy and the Association to Asphyxia in Labor*, 211 American Journal of Obstetrics and Gynecology 667e1-8 (Dec. 2014).

Importantly, the study also observed that normal admission CTGs provide an opportunity to intervene before injury occurs. Indeed the failure to respond to pathologic CTG patterns was common in NE cases, determined in this study to be HIE.[107]

This tells us that FHR patterns are useful in determining the timing of injury. As was stated earlier, neuroimaging establishes the window of opportunity for brain injury. Intrapartum data can then be used to narrow that window. The presence of a normal FHR tracing on admission that deteriorates over the intrapartum period, resulting in the delivery of a depressed neonate, establishes an intrapartum timing of injury, absent any other more compelling cause. For the healthy neurologically intact fetus entering labour with a normal FHR pattern, the presence of hypoxia will be reflected on the intrapartum tracing. While hypoxic insults are not necessarily injury, the injury invariably occurs after the onset of FHR patterns consistent with hypoxia. The issue becomes one of fetal tolerance to hypoxia, the ability to compensate for hypoxic insults and a mounting oxygen debt.

Importantly, the fact that expedited delivery for evidence of hypoxia on the FHR tracing often results in the delivery of a normal baby is not an argument against expedited delivery. Nor is it an argument against the utility of electronic fetal heart rate monitoring. This is often referred to in the literature as a false positive. It is my view that it is falsely referred to as a false positive. The purpose of FHR monitoring is not to identify the fetus with neurologic injury who will go on to suffer profound disability. Rather, the purpose of FHR monitoring is to intervene before serious injury occurs. Used properly, it should always yield a false positive. The word “positive” should not refer to the presence of a severe metabolic acidosis, but rather to the presence of risk factors that make safe vaginal delivery risky or unlikely.

DIAGNOSTIC SIGNIFICANCE OF UMBILICAL CORD GASES

The umbilical cord ordinarily contains two arteries and a single, larger vein. Determining pH, blood gases and base deficit from analysis of cord blood taken immediately after birth will allow some conclusions about fetal status immediately before delivery. Hypoxia of sufficient severity and duration can cause an increase in fetal metabolic acidosis that is best reflected in the analysis of arterial cord blood.[108]

There is a correlation between severe fetal metabolic acidosis and newborn neurologic injury. Severe fetal metabolic acidosis can lead to profound

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[107] *Id.* at 667.e6.

[108] It is necessary that a sample be taken from both the larger umbilical vein and one of the smaller umbilical arteries to ensure that the artery has indeed been sampled by comparing the results. Similar values on analysis may mean that the artery was sampled twice.

neurologic injury, including CP or cognitive and developmental deficits in the absence of motor dysfunction.

Cord blood gas analysis that demonstrates a severe metabolic acidosis supports an intrapartum cause for NE, really HIE. The lack of a metabolic acidosis in cord blood, however, does not refute an intrapartum cause for HIE. There are a number of scenarios where cord blood gas analysis will not demonstrate a metabolic acidosis despite compelling clinical evidence pointing to an intrapartum event as the cause of HIE. One example is related to events that tend to suddenly and substantially cut off flow to the cord. This can occur in cases of sentinel obstetrical emergencies, such as cord prolapse, shoulder dystocia, and uterine rupture.[109] Other scenarios involve sampling the vein twice (or only sampling a single vessel, when the vein is mistakenly sampled), tainted samples, lab errors, and events causing brain ischemia in the absence of systemic fetal metabolic acidosis.[110] Finally, to the extent that recent studies have established a correlation between stroke and intrapartum hypoxic stress, and that a metabolic acidosis is not present in many of these cases, it suggests that brain lesions can occur in the absence of a metabolic acidosis.

CONCLUSIONS

This paper has looked at the role neuroimaging as well as fetal heart rate patterns in determining the cause and timing of newborn neurologic injury. There are other important components of the causation analysis that have not been covered – in particular the role of antenatal, genetic and neonatal data. Genetic, antenatal and neonatal factors must be considered and the way they may have contributed to the outcome. Neonatal clinical and diagnostic data are very important in the causation analysis and must not be ignored. The need for neonatal resuscitation, the onset of seizures, EEG studies, haematological assessments, lactic acid accumulation, multi-organ dysfunction, and other neonatal conditions must be assessed and correlated clinically. Neonatal conditions like persistent pulmonary hypertension, meconium aspiration, and hypoglycaemia may all play a role. In the setting of an acute injury that follows a deteriorating intrapartum scenario, neonatal data will tend to support an intrapartum cause for injury. It may also be that intrapartum events are only contributing causes. There can be co-morbid causes to newborn neurologic injury.

This paper has also not dealt with standard of care issues. Obviously proving a breach of the standard of care is required of the plaintiff. Importantly, to succeed in the lawsuit, the breach of the standard of care must be proved to have occurred at a time when injury could have been prevented or mitigated. While some courts have called for proving a breach of the standard of care before

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[109] D'Alton, *supra* note 3 at 97.

[110] This would include stroke (thrombotic or embolic), and any event that would disrupt cerebral blood flow, including trauma and head compression.

exploring causation, it is my view that, at least in birth trauma cases, the first step is to establish causation. Only with an understanding of causation can you determine if a breach of the standard of care is causative.

Despite the importance of other clinical and diagnostic evidence, both neuroimaging and fetal heart rate data are crucially important to the causation analysis. Where neuroimaging establishes an acute injury, it is necessary to look for events during that window of opportunity that might explain the lesions on the newborn brain. Things like maternal hypertension, trauma, infection, preeclampsia, bleeding, and reduced fetal movement may provide clues and be part of the differential diagnosis. Antenatal factors, like intrauterine growth restriction and oligohydramnios, must also be considered as well as possible genetic factors. Using the genetic, antenatal, intrapartum and neonatal data, a list of possible causes for newborn neurologic injury must be formulated – the differential diagnosis. From that list, the more likely cause must be determined.

Following a normal pregnancy with a presumptively neurologically intact fetus, acute newborn brain lesions accompanied by a deteriorating intrapartum fetal heart rate pattern represent compelling evidence of intrapartum injury. As additional variables are added to this equation, support for an intrapartum injury will wax and wane, depending on the clinical significance of the diagnostic evidence. In the final analysis, one must rely on the preponderance of the medical evidence to tease out that diagnosis on the list of diagnoses considered that most likely explains the outcome. Having done that, causation will be established on a balance of probabilities. The mechanism may be obscure in some cases, but timing will be reasonably clear as will the opportunity to respond to avoid injury. In this way liability can be established.

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