

# Asphyxia from the eyes of the obstetrician

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## Proceedings

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*The last ten years, the next ten years in Neonatology*

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## Abstract

Nowadays it is well recognized that there are multiple potential pathways causing hypoxic-ischemic events that may lead to cerebral palsy in term infants. The signs and symptoms of neonatal encephalopathy may range from mild to severe, depending on nature and timing of brain injury. The incidence of cerebral palsy has not changed over the last 30 years and one of the obstetricians' challenge is how to recognize babies at intrapartum risk both before and during labour.

A detailed description of prepartum and intrapartum risk factors is available. A close surveillance of labour and intrapartum time should be mandatory as the valuation of all available data from obstetrical examination, cardiotocography, ultrasound and labour progression to reach the correct diagnosis with the lowest possible rate of error. The close monitoring should not exclude a humanized and compliant attitude versus labouring women and their families. We analysed the Cagliari Neonatal Intensive Care Unit (NICU) activity during the last four years considering 22 asphyxiated babies (coming from 9 different hospitals) who underwent hypothermia treatment. The main result was that the need to resuscitation procedures at birth correlates with adverse outcomes.

Asphyxia still remains a matter of great concern also as medico legal claims.

Considering that neonatal encephalopathy is a heterogeneous condition, it is unlikely that it will be eradicated. However, a comprehensive evaluation

of all risk factors and of intrapartum surveillance available tools may reduce as much as possible adverse events.

### Keywords

Asphyxia, neonatal encephalopathy, cerebral palsy, hypoxic-ischemic events, comprehensive obstetrics, medico-legal claims.

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### Introduction

Perinatal asphyxia is the main cause of death or brain damage in term infants who develop neonatal encephalopathy admitted to Neonatal Intensive Care Unit (NICU). Neonatal encephalopathy is a clinical syndrome of disturbed neurologic function of the term and late preterm infant. Clinical aspects include: a subnormal level of consciousness or seizures often accompanied by difficulty with initiating and maintaining respiration and depression of tone and reflexes. It represents a major contributor to cerebral palsy, long-term disability and neurodevelopmental sequelae.

A condition of impaired blood gas exchange, may cause a progressive fetal hypoxemia and hypercapnia, with a significant metabolic acidosis, which may lead to an asphyxiated baby who may develop neonatal encephalopathy [1].

Even if many efforts have been made to reduce these dramatic events it still represents a big concern for both obstetricians and neonatologists.

It has been estimated that moderate or severe hypoxic-ischemic encephalopathy (HIE) occurs in 0.5-1 per 1,000 live births. About 50% of these infants will die and at least 25% of survivors will have neurodevelopmental consequences [2, 3].

The rate of perinatal asphyxia, at birth, and in the first minutes of life, is commonly considered a sensitive mark of the quality of care provided in the perinatal period, both to the pregnant woman and

to the newborn. Although for a long time it was believed that intrapartum asphyxia was the main cause for the development of cerebral palsy, it's not possible to clearly determine the exact timing of hypoxia or ischemia onset nor a single causal mechanism.

Neither the widespread use of electronic fetal monitoring (EFM) and the increasing rate of cesarean sections, nor the improved neonatal intensive care had contributed to further reduce this rate in the last three decades [4].

Although asphyxia cannot always be linked to peri-partum substandard care, it has become the dominant cause of medico-legal litigation in developed countries. Malpractice claims (**Tab. 1**), are directed against health service involving both obstetricians and neonatologists, determining increasingly defensive medical behaviours [5].

### Diagnosis and timing of neonatal encephalopathy

There have been various consensus statements addressed to outline criteria to establish a causal link between intrapartum hypoxic-ischemic events and cerebral palsy [6-8].

The latest one recognizes that “knowledge gaps still preclude a definitive test or set of markers that accurately identifies, with high sensitivity and specificity, an infant in whom neonatal encephalopathy is attributable to an acute intrapartum event” [8].

In order to determine the possibility that an acute hypoxic-ischemic event that occurred within close temporal proximity to labour and delivery contributed to neonatal encephalopathy, it is recommended that a comprehensive evaluation should be performed of neonatal status and all potential contributing factors, including maternal medical history, parity and obstetric history, intrapartum factors (including fetal heart rate [FHR] monitoring and events related to the delivery itself), placental pathology and developmental outcome.

It has been proposed to consider the following categories:

1. neonatal signs consistent with an acute peripartum or intrapartum event;
2. type and times of contributing factors that are consistent with an acute peripartum or intrapartum event;
3. developmental outcome of neonatal encephalopathy in spastic quadriplegia or dyskinetic cerebral palsy [8].

**Table 1.** List of factors mainly leading to malpractice claims against obstetricians and neonatologists (modified from: Donn et al., 2014 [5]).

Obstetrics factors	Resuscitation care factors	Post-resuscitation care factors
Failure to consider past obstetrical history	Failure to arrange for pediatric/neonatal at delivery	Failure to transfer the baby to a neonatal unit in a timely manner
Failure in cephalo-pelvic disproportion prediction	Late arrival of the neonatal health care provider	Failure to be vigilant for seizures
Failure to act when admission findings suggest an already compromised fetus	Faulty equipment	Failure to recognize/treat hypoglycemia
Injudicious use of oxytocin to induce or augment labor	Substandard resuscitation technique	Failure to be vigilant for infection
Failure to recognize lack in labor progression		Failure to initiate therapeutic hypothermia in a timely manner
Failure in mal-presentation diagnosis		
Delay or failure in fetal distress diagnosis – failure to recognize anomalous CTG patterns		
Delay in carrying out cesarean section or operative delivery		
Substandard operative technique		

CTG: cardiotocography.

1. Neonatal signs consistent with an acute peripartum or intrapartum event:

- Apgar score < 5 at 5 minutes and 10 minutes. Apgar abnormality score correlates with risk of cerebral palsy, paradoxically most infants with low Apgar score will not develop cerebral palsy. If Apgar score at 5 minutes is almost 7, it is improbable that peripartum hypoxia-ischemia played a major role in causing encephalopathy;
- fetal acidemia with umbilical artery pH < 7, BE ≥ -12 mmol/l or both. The presence of metabolic acidemia does not define timing of a hypoxic-ischemic event;
- neuroimaging evidence of acute brain injury consistent with hypoxia-ischemia;
- presence of multisystemic organ failure (MOF).

2. Type and timing of contributing factors that are consistent with an acute peripartum or intrapartum event:

- sentinel hypoxic or ischemic event occurring immediately before or during labour and delivery, such as a ruptured uterus, complete abruption placentae, umbilical cord prolapse;
- FHR patterns, such as a category II (nonreassuring) FHR pattern lasting at least 60 minutes with minimal persistent or absent variability and lacking accelerations, even

in absence of decelerations, is suggestive of a previously compromised or injured fetus. It should be performed a great distinction between a patient who initially presents an abnormal FHR pattern and one who develops an abnormal FHR pattern during labor;

- timing and type of brain injury based on imaging studies consistent with an etiology of an acute peripartum or intrapartum event. There are typical brain injury patterns at cranial ultrasound, computer tomography, magnetic resonance that are well encoded in terms of timing of a cerebral insult;
- no evidence of other proximal or distal factors that could be contributing factors. The presence of other significant risk factors, such as abnormal fetal growth, maternal infection and sepsis, could be more probably the causal factor of neonatal encephalopathy instead of an acute intrapartum event.

3. Developmental outcome of neonatal encephalopathy is spastic quadriplegia or dyskinetic cerebral palsy. Other subtypes of cerebral palsy or developmental abnormalities may occur, but they are not specific to acute intrapartum HIE. When more elements from each of the item categories are met, it has been suggested the increasingly likelihood that peripartum or intrapartum hypoxia-ischemia played a role in the pathogenesis of neonatal encephalopathy [8].

## Fetal heart rate and relationship with hypoxic-ischemic events

Evaluation of FHR is the main tool available for obstetricians to survey fetal wellbeing during labour.

FHR variations started to be studied about fifty years ago. It was firstly noticed the possible link between bradycardia and risk of fetal death [9].

During the 1970s the FHR monitoring was introduced in clinical practice.

The expected goal was an early detection of a fetal hypoxic status to expedite delivery to reduce morbidity and mortality [10].

During labour, a healthy fetus with a previous normal EFM, which undergoes a hypoxic-ischemic insult, will exhibit a characteristic sequence of FHR patterns related to fetal adaptation to hypoxemia. If hypoxemic factors are allowed to persist a potential brain injury may occur.

Four distinct patterns of intrapartum hypoxia have been proposed: slowly evolving hypoxia, subacute hypoxia, acute hypoxia, pre-existing hypoxia.

- Slowly evolving hypoxia: in a healthy fetus with a normal EFM the episodes of hypoxemia result first of all in reduction of FHR (decelerations) associated with uterine contractions. Amplitude and length are related to the hypoxic stress itself. If the stress insult continues, fetus reacts with cardiac output increment, with FHR increase (compensatory tachycardia). In adults, the same aim can be obtained with stroke volume augmentation being cardiac output reassumed by the formula: cardiac output = stroke volume x heart rate [11]. Slowly evolving hypoxia allows fetus to make metabolic adjustments and so a fetus, which does not develop metabolic acidemia, can compensate it almost indefinitely. However, if the stress still continues, the fetus may go beyond compensatory mechanism and FHR is forced to reduce or lose variability and fall out in a persistent bradycardia.
- Subacute hypoxia: EFM shows variable decelerations, with minimum deep amplitude of 60 bpm, lasting 90 seconds or more. If after a deceleration there are less than 60s to begin another one, time may be not enough to recover normal aerobic metabolism, and respiratory followed by metabolic acidosis starts to occur [12].
- Acute hypoxia: bradycardia lasting in the baby for more than 3 minutes could be related to acute

hypoxia. During acute hypoxia  $PO_2$  fall down rapidly, causing a redistribution of blood flow to preserve as much as possible noble tissues. If FHR fall out to less than 80 bpm for more than 3 minutes with loss of variability, or after a period of slowly evolving hypoxia or subacute hypoxia, it's strongly recommended to deliver the fetus.

- Pre-existing hypoxia: EFM shows a substantial invariable baseline; there is no FHR cycling activity. Sometimes tachycardia can be pointed out, more pronounced in case of recent damage. After a hypoxic insult, FHR decelerations may appear in response to uterine dynamics. At birth these babies may show MOF, seizures, cortical brain injuries, meconium aspiration syndrome, pulmonary hypertension [8-16].

Notwithstanding its proven correlation with changes in FHR, the widespread implementation of EFM in the developed world didn't reach its aim.

Primarily this is due to the high rate of inter/intra observer interpretation and the frequency of falsely non-reassuring EFM patterns. However, even if newer methods are under evaluation, EFM still remains the predominant method of intrapartum fetal surveillance [13].

The need to expedite delivery in cases of pathologic or suspected "non-reassuring fetal status" had certainly contributed to the increased cesarean sections rate without a significant reduction in neonatal morbidity and mortality [15].

## Intrapartum care for a safe and humanized childbirth

Intrapartum care should be strongly addressed to increase safety for the mother and the baby, to reduce adverse outcomes and to result in a positive experience of childbirth for the woman, her family and clinicians too [16].

Once established that fetal surveillance in labour by intermittent or continuous EFM is recommended to all women, even though its limits, it's relevant to consider which management options during labour and delivery may concur to reduce adverse outcomes.

Neonatal encephalopathy recognizes specific risk factors. They can be classified in before conception risk factors, antepartum and intrapartum ones, as summarized in **Tab. 2** [17, 18].

Careful detection and analysis of before conception and antepartum risk factors at admission to the delivery ward may improve identification of

**Table 2.** Neonatal encephalopathy risk factors (modified from: Badawi et al., 1998 [17, 18]).

Before conception risk factors	Antepartum risk factors	Intrapartum risk factors
Socio-demographic factors	Maternal thyroid diseases (likely linked to fetal neuronal development disorder)	Maternal pyrexia
Maternal medical conditions (e.g. family history of seizures or other neurological disorders)	Viral infections (possibly linked to hyperthermia or other inflammatory mediators)	Chorioamnionitis (due to cerebral sepsis or via inflammatory mediators)
Severe obesity	Fetus growth restriction (FGR)	Prolonged labour (e.g. persistent occipito-posterior position)
Infertility treatment	Abnormal placentation	Acute intrapartum event (e.g. cord accident, uterine rupture, bleeding from vasa previa, placenta abruption, oxytocin abuse, maternal collapse, shoulder dystocia)
	Severe pre-eclampsia	Instrumental vaginal delivery and emergency cesarean section
	Moderate or severe vaginal bleeding during pregnancy	Meconium stained amniotic fluid
	Abnormal and nonreassuring EFM patterns	

EFM: electronic fetal monitoring.

babies at increased risk of asphyxia and consequently allowing the best decisions about timing, mode and place of delivery [19].

Detection and appropriate management of intrapartum risk factors represents an important goal to achieve.

Intrauterine infections and inflammation may worsen the effect of any intrapartum hypoxic/ischemic event during labour. It has been proposed that cytokines may be the final common mediators of brain injury. Back to physiology, perinatal asphyxia decreases oxygen saturation thus allowing shift from aerobic to anaerobic metabolism with lactate accumulation, acidosis and cell death. The possible re-oxygenation induces oxidative stress with DNA damage. This event causes pro-inflammatory and anti-inflammatory cytokines activation. Their balance determines cell survival or death [20].

Obstetric evaluation of fetal situation, presentation and position is crucial to anticipate and to adequately treat prolonged labour.

Intrapartum ultrasound at present represents an increasingly useful tool to assess both fetal head and body position and progression during labour [21].

In deciding when and how to intervene, it is important to consider parity, duration of labour, fasting and hydration, epidural analgesia effects, pain relief other than epidural analgesia, adequacy of pushing effort, maternal and fetal status, progress in fetal rotation and descent, and women's preferences, feelings and emotions.

A customized management of obstetric assistance during labour is mandatory. Extending the paradigm of medicine "diagnosis before treatment" to intrapartum care will surely contribute

to reduce the widespread injudicious use of oxytocin and/or operative deliveries during prolonged labour, cervical and mechanic dystocia [22, 23].

Guidelines, procedures and protocols may guide clinicians in diagnosis and treatments. They need to be applied estimating globally that woman, in that moment, in that place. They are otherwise completely useless if merely applied to avoid suits [24, 25].

Supporting the woman, taking into account maternal feelings and emotions, involving her in the decision-making process have been proven to be essential to give her a safer and positive experience of childbirth and to reduce medical legal litigations too.

All in all only a comprehensive obstetric approach may lead to a correct diagnosis and correct following actions.

Availability of adequate human and structural resources which allow one-to-one midwifery care, regularly trained caregivers, comfortable delivery rooms, operative theatre inside the delivery ward are obviously necessary to ensure appropriate care and expedite delivery when needed [26].

### The Cagliari experience on asphyxiated babies

Between July 2010 and May 2014, 22 term asphyxiated newborns from singleton pregnancies, coming from 9 different deliveries settings, have been admitted at the NICU of Cagliari to undergo to hypothermia treatment:

- newborns birth weight ranged from 2,860 g to 4,500 g;
- 10/22 babies were delivered with an emergency cesarean section (45.45%);

- 4/22 with vacuum extractor application (18.18%);
- 8/22 with spontaneous vaginal delivery (36.36%);
- all newborns had Apgar score < 7 at 5 minutes (100%);
- babies with pH < 7 were 6/22 (27.27%);
- 16/22 babies had > -12 BE (72.72%);
- delivery room resuscitation and/or intubation was necessary in 17/22 newborns (77.27%);
- 5/22 babies had psychophysical disability (tetraparesis and mental retardation, 22.72%);
- 4/22 babies died (18.18%).

Our data compared with a prospective observational multicentric study data performed in different Obstetrics Units in the North of Italy [27] were consistent with the study conclusions. In singleton term pregnancies that end up with an asphyxiated newborn, the need for intubation or resuscitation procedures represents the most unfavourable prognostic index and the prognosis is even more adverse if 5-minute Apgar score was less than seven. Operative deliveries and emergency cesarean sections themselves didn't contribute to reduce rates of adverse outcomes. The inability to breath spontaneously at birth, often determined by other causes than acidosis, correlates with adverse outcomes, more than pH and BE values considered individually. Death and long term disability may sadly occur despite neonatal intensive care efforts.

## Discussion and conclusion

Several investigations and claim analysis suggested that a significant proportion of asphyxia rates could be considered as preventable, but which subtype of intrapartum asphyxia can be prevented by improved care is still controversial [26].

In many circumstances it has been suggested to be a gap between knowledge and clinical practice. Considering that neonatal encephalopathy is a heterogeneous condition, caused by multiple potential pathways leading to cerebral palsy, it is unlikely that it will be eradicated. The American College of Obstetricians and Gynaecologists (ACOG) has recently stated that multiple potential pathways lead to cerebral palsy in term infants and that signs and symptoms of neonatal encephalopathy may be related to the nature and the timing of brain injury. They proposed five causal pathways including possible occurring factors from conception to neonatal period and childhood. Moreover just to evaluate the possible role of an

acute hypoxic-ischemic event occurring during labour or delivery, it has been proposed to consider elements from three categories of related factors [8].

It seems obvious that improving intrapartum care to reduce perinatal asphyxia needs a comprehensive approach to childbirth, evaluating the woman history, risk factors related to the pregnancy and previous obstetric experiences, socioeconomical status and emotional condition to achieve the best and safer personalized approach to labour and delivery.

At admission to delivery ward caregivers have to be aimed at offering a safe and positive childbirth experience to women and their families.

Further tireless efforts should be done to reduce neonatal encephalopathy and related adverse outcomes.

The need to provide a safe and humanized childbirth is strictly related to kindness and respect, proper diagnosis and accurate selection of therapeutic options in obstetric care to avoid overtreatment without expected benefits.

Continuous delivery ward team training, obstetrics and neonatal audit associated to data collection may provide necessary information to learn from these cases [28].

This may reduce legal proceedings for redress and mainly contribute to improve positive experiences of childbirth for mothers, families and physicians too.

We completely agree with the ACOG sentence directed at preventing neonatal encephalopathy: "Enhancing patient safety requires changing the culture of health care delivery from one that names and blames to one that is dedicated to reducing medical errors through a constructive, nonthreatening, and professional process" [8].

## Declaration of interest

The Authors declare that there is no conflict of interest.

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