

## —Short Review—

## Neonatal Encephalopathy and Cerebral Palsy

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In year 2000, the American College of Obstetricians and Gynecologists (ACOG) formed a task force called The ACOG Task Force in Neonatal Encephalopathy and Cerebral Palsy. This was in response to the increasing threat of malpractice claims against physicians whenever brain damaged infants are born. Such brain damaged infants have been the greatest threat for the practice of obstetricians. The work of the task force resulted in the publication of Neonatal Encephalopathy and Cerebral Palsy: defining the pathogenesis and pathophysiology. This book was published by ACOG and the American Academy of Pediatrics.

I presented a special lecture on this subject at Nippon Medical School on Nov 9, 04. Prior to the lecture, in mid-2004, the book was translated into Japanese and published in Japan under a license granted by ACOG. I was one of the three translators of this book, hence I am familiar with this subject. The entire lecture was solely based on this book.

In the United States, malpractice litigation is very common and the awards to the plaintiffs are becoming increasingly larger. The awards or compensation to the plaintiff commonly exceed one million dollars, of which the attorneys take a share of 1/2~1/3.

Reflecting this trend, premiums for malpractice insurance have soared as high as \$60,000/year, even in relatively rural Hawaii. In many states of the U.S., the premiums have exceeded \$100,000 per year for coverage of \$1 million. This trend has inevitably jeopardized practitioners. Among the members of ACOG, about 25% are limiting the intake of high-risk obstetrics, 12% have cut the number of

deliveries and 9% have stopped the practice of obstetrics altogether. Among the suits filed against obstetricians and gynecologists, 34% are related to brain damaged infants.

A 19<sup>th</sup> century English physician, William John Little, once described that the cause of cerebral palsy is a hypoxic episode during delivery. This description has been accepted without scientific basis and has not been challenged until recent times. However, it has been accepted among not only physicians but also the general public including people in the legal profession as well as lay people.

According to this theory, brain damage to the fetus is preventable if the obstetrician can identify hypoxic episodes during labor and deliver expeditiously enough by perform a cesarean section. Most attorneys argue during trials that if the hypoxic episodes had been found in a timely manner and delivery of the fetus done by cesarean section without delay, the infants could have been saved and that therefore, brain damage of the infants is the result of negligence by the physicians.

As the results of many studies and researches accumulated, it has become more clearer that this practice of blaming physicians for their actions during labor was actually wrong. The common misconception that the physicians' handling errors were the cause has come to be challenged by recent evidence.

On current evidence, it is estimated that in about 10% of brain damaged infants, the cause is hypoxia during labor. In the rest, the causes of brain damage arise from such conditions as cerebrovascular accident, infection, developmental brain malformation,

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metabolic defects, autoimmune and coagulation disorders, infection, and hypoxia in the fetus and newborn.

### Neonatal Encephalopathy

Neonatal encephalopathy is defined in term (>37 wks) and near-term (>34 wks) infants. It is a clinically defined syndrome of abnormal neurological findings including the following: abnormal states of consciousness, tone and reflexes, and respiratory function graded by severity of signs and symptoms, with the most severe state characterized by severe hypotonia, apnea, coma and seizures.

An estimate of the maximal possible contribution of intrapartum hypoxia to neonatal encephalopathy was, according to Badawi of Australia, 29%. Most infants with mild to moderate hypoxia develop normally. Those with severe neonatal encephalopathy are more likely to sustain long-term neurological morbidity.

Neonatal encephalopathy and cerebral palsy are rarely caused by perinatal asphyxia.

However, it can be said with certainty that the pathway from an intrapartum hypoxic-ischemic injury to subsequent cerebral palsy must progress through neonatal encephalopathy.

### Neuropathology

The neuropathology of intrapartum hypoxic-ischemic injury may be considered in the context of five basic anatomic subtypes.

(1) Parasagittal injury is caused by critical decreases in cerebral blood flow. Manifestation of this injury is spastic quadriplegia. (2) Injury to the basal ganglia follows acute near-total intrauterine asphyxia and usually involves the thalamus, caudate nucleus, globus pallidus, and putamen. (3) Periventricular white matter injury is the principle lesion found in the preterm infant, with the classic manifestation being spastic diplegia. (4) Focal and multifocal necrosis and (5) Selective neuronal necrosis.

### Cerebral Palsy

Cerebral palsy is a common disability of central nervous system characterized by aberrant control of movement and posture, appearing early in life and not as a result of progressive neurologic disease. Research shows that spastic quadriplegia, especially with an associated movement disorder, is the only type of cerebral palsy associated with acute interruption of blood supply. Purely dyskinetic or ataxic cerebral palsy, especially where there is an associated learning difficulty, commonly has a genetic origin and is not caused by intrapartum or peripartum asphyxia.

### Apgar Score

Apgar score is a standardized mini-examination of brain stem function assessing the clinical status of newborns in the first minutes after birth. There are numerous factors that can influence Apgar score such as preterm birth, maternal sedation or anesthesia, congenital malformations, and the individual assigning the score. It is well established that the 1- or 5-minute Apgar score is a poor predictor of long-term neurological outcome in the individual patient. Even a score of 0~3 is limited as an indicator and correlates poorly with future neurological outcome. An apgar score of 0~3 at 5 minutes is associated with an increased risk of cerebral palsy in only 0.3~1% of term infants. Almost 90% of infants with a 10-minute Apgar score of 0~3 do not have subsequent cerebral palsy. Conversely, 75% of children with cerebral palsy had normal Apgar scores at birth.

Criteria to define an acute intrapartum hypoxic event sufficient to cause cerebral palsy.

A careful analysis of data compiled over 25 years shows that intrapartum complications are less common causes of cerebral palsy than previously thought. The criteria are based on the statement, "a template for defining a causal relationship between acute intrapartum events and cerebral palsy," published in the British Medical Journal in 1999.

The criteria consist of two parts: part 1.1 and part

## 1.2.

Part 1.1 of criteria presents four essential criteria that are necessary before an intrapartum hypoxic event can be considered as a cause of cerebral palsy. If any one of the 4 essential criteria is not met, this provides strong evidence that intrapartum hypoxia was not the cause of cerebral palsy.

Par 1.2 of the criteria presents a set of five criteria that collectively suggest an intrapartum timing. With the exception of the first criterion of an acute hypoxic sentinel event occurring immediately before or during labor, all the other four criteria described are weakly associated with acute intrapartum hypoxia. It is not necessary for all five criteria to be present to establish a relationship between acute intrapartum hypoxia and cerebral palsy. Accordingly, contrary evidence such as a reassuring fetal heart rate pattern, a normal Apgar score of 7 or more at 5 min, or an early MRI study inconsistent with a recent global hypoxic or ischemic event excludes an injurious event during labor.

The use of these criteria will help to evaluate the probability that the pathology causing cerebral palsy occur during labor.

## 1.1: Essential criteria (all four must be met)

1. Evidence of metabolic acidosis in fetal umbilical cord arterial blood obtained at delivery ( $\text{pH} < 7$  and base deficit  $> 12$  mmol/L).

2. Early onset of severe or moderate neonatal encephalopathy in infants born at 34 or more weeks of gestation.

3. Cerebral palsy of the spastic quadriplegic or dyskinetic type.

4. Exclusion of other identifiable etiologies, such as trauma, coagulation disorders, infectious condition, or genetic disorders.

1.2: Criteria that collectively suggest an intrapartum timing (within close proximity to labor and delivery, eg. 0~48 hours) but are nonspecific to asphyxial insult.

1. A sentinel (signal) hypoxic event occurring immediately before or during labor.

2. A sudden and sustained fetal bradycardia or the absence of fetal heart rate variability in the presence of persistent late or variable deceleration, usually after a hypoxic sentinel event when the pattern was

previously normal.

3. Apgar score of 0~3 beyond 5 minutes.

4. Onset of multisystem involvement within 72 hours of birth.

5. Early imaging study showing evidence of acute nonfocal cerebral abnormality.

Some explanations of the criteria.

## Criteria 1.1

1. Metabolic acidemia at birth must be present to establish that a potentially damaging intrapartum hypoxic event is a cause of cerebral palsy. It is important to remember even when this pH threshold of less than 7 is used to define significant acidemia, most newborns in this category will be neurologically normal with no apparent morbidity.

2. If an intrapartum insult is severe enough to result in ischemic cerebral injury, abnormalities will be noted in the neurological examination within 24 hours of birth. Outcome is related to the maximum grade of severity. Thus, for infants with mild encephalopathy (stage 1), outcome is invariably favorable. Moderate encephalopathy (stage 2) is associated with an abnormal outcome in approximately 20 ~ 25% of cases. Severe encephalopathy (grade 3) is associated with a poor outcome in all cases.

3. Spastic quadriplegia and, less commonly, dyskinetic cerebral palsy are the only types of cerebral palsy associated with acute hypoxic intrapartum events. Spastic quadriplegia is the most common type of cerebral palsy associated with acute hypoxic intrapartum events, but it is not specific to intrapartum hypoxia. Neither hemiplegic cerebral palsy, spastic diplegia, nor ataxia have been associated with acute intrapartum hypoxia.

4. A large proportion of cerebral palsy cases are associated with maternal and antenatal factors, such as preterm birth, intrauterine growth retardation, intrauterine infection, maternal or fetal coagulation disorders, multiple pregnancy, antepartum hemorrhage, breech presentation, and chromosomal or congenital abnormalities.

## Criteria 1.2

1. A sentinel hypoxic event usually includes ruptured uterus, placental abruption, umbilical cord prolapse, amniotic fluid embolism, maternal

cardiopulmonary arrest, and fetal exsanguination from either vasoplevia or massive fetomaternal hemorrhage.

2. The most frequently observed fetal heart rate patterns associated with cerebral palsy are those with multiple late decelerations and decreased beat-to-beat variability. However, the false positive rate for these patterns is 99%.

3. It is well established that the 1- or 5-minute Apgar score is a poor predictor of long-term neurologic outcome. There is a good correlation between an extremely low Apgar score at 15 and 20 minutes and subsequent neurologic dysfunction. A score of less than 3 at 15 minutes was associated with a 53% mortality rate and a 36% cerebral palsy rate. When the low score persisted at 20 minutes, mortality was almost 60% and 57% of survivors had cerebral palsy.

4. With initial hypoxemia, fetal cerebral vascular resistance can decrease by at least 50% to maintain cerebral blood flow with minimal impact on oxygen

delivery. The clinical manifestations of the redistribution of cardiac output during severe asphyxia reflect the involvement of multiple organs (eg, necrotizing enterocolitis, persistent pulmonary hypertension, hypoglycemia, disseminated intravascular coagulopathy, release of nucleated blood cells, oliguria and anuria, hyponatremia, and fluid retention.)

5. Early brain edema suggests recent insult. MRI is the optimal method for the evaluation of early injury.

#### Source of information

The entire lecture is based on the publication "Neonatal Encephalopathy and Cerebral Palsy" published by the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, Washington, D.C. 2004.

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