Preface for Neonatal Encephalopathy and Neurologic Outcome

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In 2000, Dr. Frank Miller, then president of the American College of Obstetricians and Gynecologists (the College), initiated the Task Force on Neonatal Encephalopathy and Cerebral Palsy. At that time, Dr. Miller issued the following mission statement: “To create a multidisciplinary task force to review and consider the current state of scientific knowledge about the mechanisms and timing of possible etiologic events which may result in neonatal encephalopathy. The purpose of such review will be to produce a consensus statement, report or monograph for Fellows of the College which will succinctly summarize the neuroscience of neonatal encephalopathy and provide a framework for explaining to patients and the general public, in understandable language, medicine’s ability and capacity (and limitations) to detect, treat or in any way affect the pathophysiologic mechanisms which result in neonatal encephalopathy.”

The College collaborated with the American Academy of Pediatrics and published the final report in 2003. The task force acknowledged that the publication was a work in progress and would require updating.

Dr. Richard Waldman became President of the College in 2010. This revision was one of his presidential initiatives. The charge was simple and straightforward: “to update the document to the current state of scientific and clinical knowledge relating to neonatal encephalopathy and neurologic outcomes.” This charge was accomplished over 2 years.

I. Methods

The second Task Force on Neonatal Encephalopathy was convened in 2010 and comprised several physicians with expertise in different aspects of this issue, along with liaison members from the American Academy of Pediatrics, the Centers for Disease Control and Prevention, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Beginning in 2010, the task force met three times over the span of 2 years. At the first meeting, members outlined the subject matter to be covered, identified clinicians and scientists with particular expertise in the field, and agreed to edit solicited written contributions based on an extensive review of the literature from those individuals. At subsequent meetings, the task force reviewed and edited the draft manuscripts and deliberated to achieve consensus on the recommendations included in this report. Throughout the process, primary source documents were cited to the fullest extent possible.

Significantly more consultants were used in creating this document than in the report of the first task force, including an increased number of international contributors. There were 17 task force members and 88 consultants who collectively reviewed almost 1,500 references as part of an extensive undertaking to review the evidence and present new findings and recommendations to update the first report. Furthermore, the report in 2003 refined criteria from the International Cerebral Palsy Task Force that published a consensus statement in The British Medical Journal in 1999. Because the International Cerebral Palsy Task Force report has not been updated since 1999, it is our hope that this document will have global value.

Once the initial draft was completed, the following federal agencies and professional organizations endorsed the current report and provided their support of the task force’s review of the evidence and its recommendations:

• American Academy of Family Physicians
• American College of Nurse Midwives
• American Gynecological and Obstetrical Society
II. Task Force Goals

The task force identified five specific goals:

1. To continue to broaden the understanding of neonatal encephalopathy by summarizing the best available primary-source scientific data and expertise of highly qualified individuals who have been major contributors to the field.

2. To develop recommendations for evaluation of a newborn with encephalopathy to assist the clinician in defining both the cause and timing of that disorder.

3. To identify areas in which further research is needed and to incorporate those recommendations in each chapter.

4. To continue to raise awareness of the need for standardization of terminology and precision in its use, which is imperative for the interpretation of meaningful research on neonatal encephalopathy and its neurologic outcome.

5. To review the criteria for determining the presence of hypoxic insult during the intrapartum period outlined in the first report and make recommendations for change if needed based on new insights obtained over the past decade.

III. Changes in the Current Document

The title of this report has been changed from Neonatal Encephalopathy and Cerebral Palsy: Defining the Pathogenesis and Pathophysiology to Neonatal Encephalopathy and Neurologic Outcome to indicate that an array of developmental outcomes may arise after neonatal encephalopathy in addition to cerebral palsy.
The focus of the current edition is on moderate and severe neonatal encephalopathy in infants born at or beyond 35 weeks of gestation. Several new chapters have been added and all of the previous chapters have been significantly updated.

Chapter 1 provides a definition of neonatal encephalopathy in the infant born at or beyond 35 weeks of gestation, and a diagram to demonstrate the different causal pathways to cerebral palsy. The task force prefers the general term neonatal encephalopathy to hypoxic–ischemic encephalopathy, which is a cause specific subset of neonatal encephalopathy, and highlights the continued absence of precise terminology in the literature since the publication of the 2003 document. In particular, there is great disparity in the literature in the usage of the term “asphyxia.” The task force defines asphyxia as marked impairment of gas exchange leading, if prolonged, to progressive hypoxemia, hypercapnia, and significant metabolic acidosis. The term asphyxia, which describes a process of varying severity and duration rather than an end point, should not be applied to birth events unless specific evidence of markedly impaired intrapartum or immediate postnatal gas exchange can be linked to neurologic illness in the neonate. Throughout the report, the terms “asphyxia” and “birth asphyxia” and their variations appear in quotes when used in reference to a particular study to emphasize the wide variation in study definitions of asphyxia. Chapter 1 also discusses two very different perspectives on risk, timing of adverse events, and neurodevelopmental outcome in neonatal encephalopathy based on epidemiologic evidence, which was relied on heavily in the previous document versus data from neuroimaging studies that have been published since 2003.

Chapter 2 is a new contribution that reviews basic science studies specific to hypoxic–ischemic encephalopathy. These demonstrate that maintenance of cerebral perfusion is an essential prerequisite for long-term neuronal survival and that some neural cells are particularly vulnerable to primary energy failure. The neurotoxic cascade of molecular events that result in secondary brain injury is described in detail, and the cofactors of bacterial infection, inflammation, and chronic fetal substrate deprivation that have been shown to alter or make the fetus more vulnerable to hypoxia are discussed.

Chapter 4 is a new contribution on placental pathology and umbilical cord abnormalities, which highlights the fact that clinical correlation with those entities has been difficult because the placenta has often been discarded when neonatal encephalopathy is identified. The information presented underscores the need for population-based studies that include detailed pathologic correlation of the placenta and other antenatal and perinatal risk factors with neuroimaging studies and possible genetic markers of neonatal encephalopathy.

Chapter 6 addresses the issue of standardization of the terminology used in intrapartum monitoring. Also discussed is the association of various electronic fetal heart patterns with fetal and neonatal acidemia.

Chapter 8 is a new contribution that discusses focal ischemic fetal and neonatal strokes. Magnetic resonance imaging (MRI) is the neuroimaging investigation of choice in all perinatal stroke syndromes, and despite a lengthy list of putative associations, a true causative factor cannot be found in most cases. Perinatal strokes are the predominant cause of hemiplegic cerebral palsy, and many children affected have additional abnormalities.

Because of the significant advances in neuroimaging over the past decade, several experts were asked to collaborate on Chapter 10, and Dr. Terri Inder provided the lead on this very substantial effort. Magnetic resonance imaging has been found to be the neuroimaging modality that will best define both the nature and extent of cerebral injury in neonatal encephalopathy. Early MRI performed between 24 hours and 96 hours of life is most sensitive for the delineation of the timing of the perinatal cerebral injury, whereas an MRI examination obtained optimally at 10 days of life (but with an acceptable window, between 7 days and 21 days of life) will best delineate the full extent of the cerebral injury.
Chapter 11 is a new contribution on the subject of neonatal interventions. The implementation of hypothermia for the treatment of neonatal encephalopathy is a milestone in neonatal medicine and represents the culmination of research spanning decades that has proved the potential for neural rescue following perinatal asphyxia. The recognition that this therapy improves early childhood outcomes has accelerated the pace of investigations to find other brain-oriented treatments, which also are described in the chapter.

Chapter 12 is a new contribution from several obstetricians, including maternal–fetal medicine specialists, and neonatologists reviewing patient safety efforts 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. A template is provided for performing a root cause analysis as part of this process. Furthermore, because many obstetricians and pediatricians who practice in small hospitals will not be expected to encounter many cases of neonatal encephalopathy, an obstetric and neonatal data collection tool is provided to serve as a guide for obtaining necessary information to learn from these cases.

In the first edition of this report, the task force outlined essential criteria necessary to establish a causal link between intrapartum hypoxic events and the subsequent development of cerebral palsy. Chapter 13 reflects the broader perspective championed by the current task force and includes a proposed comprehensive multidimensional assessment tool of neonatal status to determine the likelihood that an acute hypoxic–ischemic event that occurred within close temporal proximity to labor and delivery contributed to neonatal encephalopathy.

In 2003, the task force identified the following four essential criteria required to define an acute intrapartum hypoxia event as being sufficient to cause cerebral palsy: 1) severe acidemia at birth, 2) early onset of neonatal encephalopathy, 3) cerebral palsy of spastic quadriplegic or dyskinetic type, and 4) exclusion of other identifiable etiologies. These criteria were useful for several reasons. It was important to recognize that neither spastic diplegic nor hemiplegic cerebral palsy is likely to have its origin in birth hypoxia. It was also useful to stress that moderate degrees of academia and low Apgar scores are relatively common in infants with normal subsequent neurologic outcomes. Nevertheless, one of the goals of the current guideline was to review these criteria for possible revision and to assess their utility in light of new knowledge. Despite the many advances highlighted in the new and updated chapters in this document, new epidemiologic data on neonatal encephalopathy and hypoxic–ischemic encephalopathy have been very limited since the publication of the report in 2003. There have been no population-based studies of the incidence of neonatal encephalopathy or hypoxic–ischemic encephalopathy with updates from more recent birth cohorts since the mid 1990s, and very few reports on risk factors based on studies with larger sample sizes than the Western Australia study published in the late 1990s. Despite standardizing fetal heart rate interpretation systems, we still lack reliable assessment tools of fetal and neonatal status, which are both sensitive and specific to an intrapartum insult that correlates with long-term outcome. The critical hypoxic or ischemic threshold for neuronal necrosis in the developing brain remains unknown. Clinical and epidemiologic studies of risk factors often appear discordant. The timing of contributory events and developmental outcome is unclear. Confusion persists in the terminology relating to neonatal encephalopathy and hypoxic–ischemic encephalopathy used in the scientific literature. Laboratory studies of etiology continue to focus almost exclusively on the hypoxia–ischemia pathway. All of these factors underscore existing knowledge gaps.

For the current edition, the task force concluded that a broader perspective might be more fruitful. We simply do not have a definitive test or set of markers that reliably identify an infant in whom neonatal encephalopathy is attributable to an acute intrapartum event. Nevertheless, the task force felt there was strong justification for undertaking steps to assess the probability that an acute hypoxic–ischemic event that
occurred within close temporal proximity to labor and delivery, was solely responsible for or significantly contributed to an episode of neonatal encephalopathy.

The Executive Summary and Chapter 13 outline the information necessary for making this assessment, which can be derived from a comprehensive evaluation of all the potential contributing factors to any case of neonatal encephalopathy, including the maternal medical history, obstetric antecedents, intrapartum factors (including fetal heart rate monitoring patterns), and placental pathology. Subsequent analysis of all that information will produce a number of benefits that extend far beyond the provision of a single probability estimate.

IV. This Document

The task force acknowledges that like its predecessor, this publication is a work in progress. It incorporates concepts as they are currently understood, and we hope that it will serve as another building block that leads toward a complete understanding of neonatal encephalopathy.

Endnotes

* The Royal College of Obstetricians and Gynaecologists has reviewed and approved the task force report and provided its official designation of “support” in lieu of endorsement.

** The findings and conclusions in this task force report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.