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Amplitude-Integrated Electroencephalography Coupled With an Early Neurologic Examination Enhances Prediction of Term Infants at Risk for Persistent Encephalopathy

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Amplitude-Integrated Electroencephalography Coupled With an Early Neurologic Examination Enhances Prediction of Term Infants at Risk for Persistent Encephalopathy

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ABSTRACT. *Objectives.* **The objectives of this study were to determine, first, whether an early neurologic examination could predict a persistent abnormal neonatal neurologic state comparable to the amplitude-integrated electroencephalography (a-EEG) and, second, whether a combination of the 2 methods would further enhance early identification of high-risk infants.**

Methods. **Fifty term infants were enrolled prospectively when they had evidence of intrapartum distress, Apgar score ≤5 at 5 minutes, or cord arterial pH ≤7.00 and were admitted to intensive care. Each enrolled infant underwent an early neurologic examination using a modified Sarnat staging system (stages 2 and 3 were regarded as abnormal) and a blinded simultaneous a-EEG measurement. Predictive values were calculated for a short-term abnormal outcome defined as persistent moderate to severe encephalopathy beyond 5 days.**

Results. **An abnormal short-term outcome was present in 14 (28%) of 50 infants. The neurologic examination was performed at 5 ± 3 hours after delivery. A short-term abnormal outcome occurred in 9 (53%) of 17 infants with initial stage 2 and in both infants with initial stage 3 encephalopathy. In addition, 13 infants manifested features of both stage 1s and 2 and post hoc were classified (S1–2). Three of the latter infants (23%) developed an abnormal short-term outcome. The a-EEG was abnormal in 15 (30%) infants, 11 (73%) of whom developed an abnormal outcome. An abnormal a-EEG was more specific (89% vs 78%), had a greater positive predictive value (73% vs 58%), and had similar sensitivity (79% vs 78%) and negative predictive value (90% vs 91%) when compared with an abnormal early neurologic examination. A combination of abnormalities had the highest specificity (94%) and positive predictive value (85%).**

Conclusion. **The combination of the a-EEG and the neurologic examination shortly after birth enhances the ability to identify high-risk infants and limits the number of infants who would be falsely identified compared with either evaluation alone.** *Pediatrics* **2003;111:351–357;** ***amplitude-integrated electroencephalography, hypoxia-ischemia, neuroprotective therapies.***

ABBREVIATIONS. a-EEG, amplitude-integrated electroencephalography; MRI, magnetic resonance imaging.

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The early and accurate assessment of cerebral function in newly born term infants at risk for hypoxic-ischemic cerebral injury is an important clinical problem, because these infants may be amenable to specific brain-oriented interventions.[1] A therapeutic window exists for neuroprotective interventions; however, the duration is unknown and may extend to only a few hours after birth.[2,3] Novel neuroprotective treatments may be associated with serious side effects in critically ill newborns, which further emphasizes the importance of early and accurate identification. Strategies to identify such infants have used variables such as fetal heart rate abnormalities, thick meconium-stained amniotic fluid, low Apgar scores, need of resuscitation, fetal acidemia, evidence of encephalopathy by neurologic examination, and the amplitude-integrated EEG (a-EEG). However, examination of specific individual variables in infants thought to have experienced perinatal hypoxia-ischemia consistently reveals poor predictive ability for long-term neurologic outcome.[4–7] This has prompted evaluation of a combination of variables to improve prediction. For example, the combination of a low umbilical artery pH, need for intubation, and a low 5-minute Apgar score had a sensitivity of 80%, a specificity of 99%, and a positive predictive value of 80% for the development of neonatal seizures.[8] Moreover, the age of onset of breathing, administration of chest compressions, and the age of onset of seizures predicted death or a major neurosensory impairment with a sensitivity of 80%, a specificity of 68%, and a positive predictive value of 69%.[9] Although the latter observations are encouraging, they clearly justify additional studies to improve the early prediction of adverse cerebral effects after perinatal hypoxia-ischemia.

The stage of encephalopathy in the first week of life is the single best clinical predictor of long-term outcome after acute perinatal asphyxia.[10] However, clinical assessment of encephalopathy in the initial hours after birth has never been examined rigorously in infants who are at risk of developing hypoxic-ischemic brain injury. The a-EEG, which is an electrical measure of cortical state, has been the best single laboratory predictor of long-term outcome after acute perinatal asphyxia. It provides a continuous recording of background voltage cerebral activity, is easily interpreted at the bedside by clinical staff, and correlates well with neurodevelopmental outcome.[11–13] The early clinical assessment of encepha-

lopathy and the a-EEG recording have not been compared to determine whether 1 method is superior to the other or whether the 2 evaluations complement each other for prediction of neurologic abnormalities in high-risk infants shortly after birth. Thus, this study had the following 2 objectives: to determine whether an early neurologic examination could predict a persistent abnormal neurologic state in the neonatal period comparable to the a-EEG and to determine whether a combination of the 2 methods would further enhance early identification of high-risk infants.

METHODS

The study was conducted during a 20-month period, from August 1999 through March 2001. Fifty infants were enrolled prospectively within the first 12 hours after birth. All infants were born at Parkland Memorial Hospital, a large county facility with 26 101 deliveries and 1748 admissions to the neonatal intensive care unit during the 20-month study period. Infants were considered eligible for study when they met all of the following criteria: delivery at term or near term (≥36 weeks' gestation), admission to the neonatal intensive care unit, intrapartum distress as evidenced by fetal heart rate abnormalities or meconium staining of the amniotic fluid, and either an Apgar score ≤5 at 5 minutes or severe fetal acidemia (umbilical cord arterial pH ≤7.00 or base deficit ≥16 mEq/L). Informed consent was obtained from the parents of eligible infants, and the study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center at Dallas.

Neurologic Evaluation

Each enrolled infant underwent a detailed neurologic examination by 1 of 2 examiners (A.L. or J.P.) within the first 12 hours after birth. Each investigator was blinded to the simultaneous a-EEG recording by use of a screen. The examination evaluated 6 components: level of consciousness (hyperalert, lethargy, stupor, or coma); activity (normal, decreased, or absent); posture (normal, complete extension, or decerebrate); tone (normal, hypotonic, or flaccid); primitive reflexes (normal, decreased, or absent); and autonomic dysfunction of the pupils (constricted, skew deviation, or nonreactive), heart rate (bradycardia or variability), and respirations (periodic breathing or apnea). The clinical examination was used to characterize infants into modified Sarnat stages as follows:[14]

Stage 1 (S1): hyperalert, normal tone and activity, exaggerated Moro, absence of autonomic dysfunction

Stage 2 (S2): lethargy, decreased activity, hypotonia, weak primitive reflexes, constricted pupils, bradycardia or periodic breathing

Stage 3 (S3): stupor, coma, decerebrate posture, absent spontaneous activity, flaccid, absent reflexes, and nonreactive pupils or apnea

Abnormalities of 3 of the 6 components of the examination were required to categorize an infant within a specific Sarnat stage. The Sarnat stages S1, S2, and S3 correspond to mild, moderate, and severe encephalopathy.[14,15] For this study, S2 or S3 was considered to represent an abnormal neurologic examination. Infants with an initial abnormal neurologic examination were evaluated daily in the first week of life, and all infants had a neurologic examination at the time of hospital discharge.

a-EEG

The a-EEG was recorded by 1 investigator (L.S.) for all enrolled infants, using a Lectromed cerebral function monitor (CFM 5330; Olympic Biomedical, Seattle, WA) from 2 frontoparietal adhesive electrodes and displayed on an integral printer at 6 cm/hour (Fig 1). The a-EEG was acquired either simultaneously or within 1 hour of the neurologic examination. At least 30 minutes of tracing was recorded, and the most abnormal section of the tracing persisting for 30 minutes was analyzed. Administration of anticonvulsants or sedatives and patient manipulation were directly recorded on the tracing. Tracings within 30 minutes of such events were excluded from analysis. The a-EEG provides a band of activity representing the amplitude of the background voltage of the brain, which was recorded on a semilogarithmic scale from 0 to 100 μV. The criteria of Naqueeb et al[16] was used for interpretation of the a-EEG (Fig 2) by drawing lines through the upper and lower margins of the band of activity and scoring the pattern as follows: normal amplitude, the upper margin >10 μV and the lower margin >5 μV; moderately abnormal amplitude, the upper margin >10 μV and the lower margin <5 μV; and suppressed amplitude, the upper margin <10 μV and the lower margin <5 μV. A moderately abnormal or suppressed amplitude was considered to represent an abnormal a-EEG.

For determining interagreement for categorizing the a-EEG, 3 independent observers received an instruction manual describing Naqueeb's criteria for interpretation of the a-EEG and scored the a-EEG recordings from the 50 infants. These evaluations were

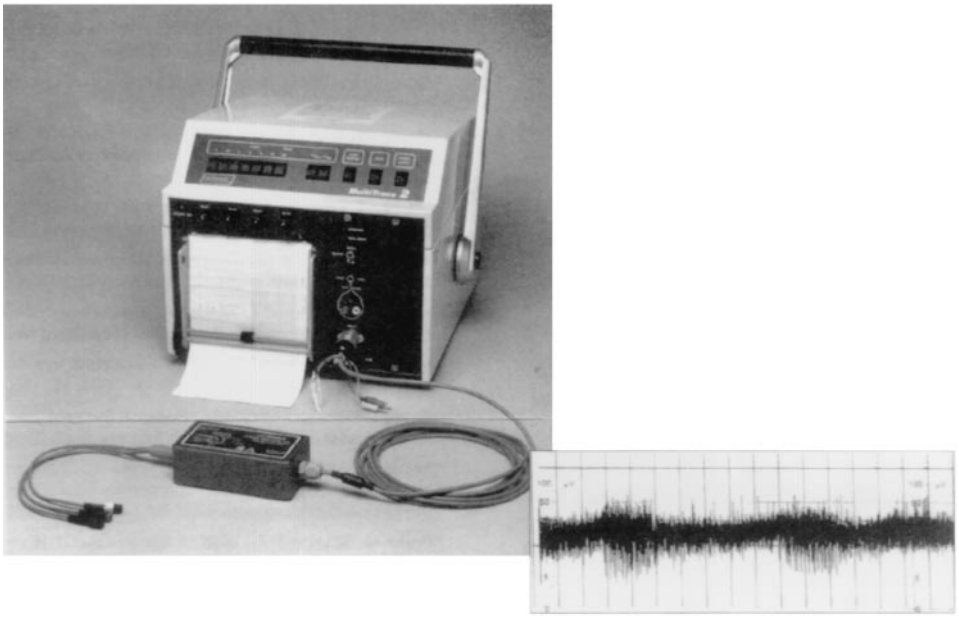

Fig 1. Cerebral function monitor used for determination of the a-EEG. The cerebral function monitor record shows a continuous normal voltage background with a normal sleep wake cycling. (Picture provided courtesy of Olympic Medical, Seattle, WA.)

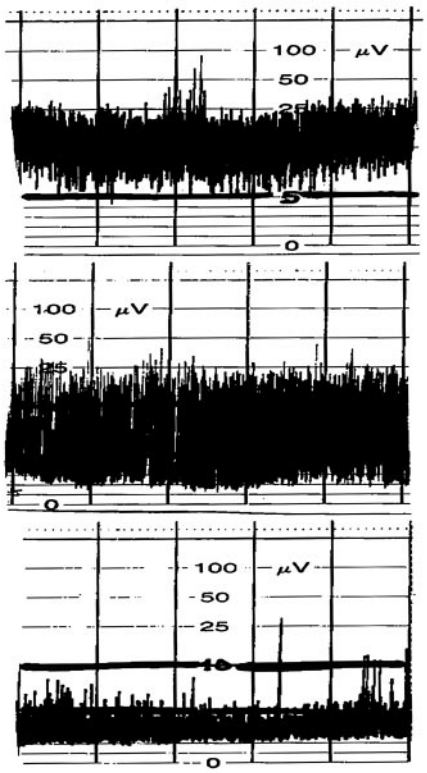

Fig 2. Classification of a-EEG abnormalities. Top tracing is representative of a normal recording, the middle tracing is representative of a moderately abnormal pattern, and the bottom tracing is representative of severe suppression.

done without specific training or knowledge of other pertinent clinical information. There was a 100% agreement among the 3 observers in the classification of a normal versus abnormal a-EEG recording. There were 2 disagreements in the interpretation of the a-EEG, and these were confined to differentiating a moderately abnormal from a suppressed pattern.

Definition of an Abnormal Short-Term Neurologic Outcome

An abnormal short-term outcome was defined prospectively as the persistence of either a moderate or a severe encephalopathic state beyond 5 days of age, or death in the first week attributable to hypoxic-ischemic cerebral injury. This outcome was used for statistical computations of the predictive values of the early neurologic examination alone, the a-EEG alone, and the combination of both.

Patient Demographics

Medical records of both the mother and the infant were reviewed, and the following data were collected: complications during pregnancy and labor; mode of delivery; delivery room interventions (bag and mask ventilation, intubation, chest compressions, medications); Apgar scores at 1, 5, and 10 minutes; cord arterial pH; need for mechanical ventilation; use of sedatives and anticonvulsants; and duration of hospital stay. Electrographic and neuroimaging studies were performed as part of patient care at the discretion of the medical team. The standard EEG was defined as abnormal in the presence of any of the following: generalized low voltage, seizures, or a burst suppression pattern. Magnetic resonance imaging (MRI) abnormalities included diffuse white matter and basal ganglia involvement and/or cortical changes consistent with an ischemic insult. Infants with abnormalities in their neurologic examination at discharge were considered high risk and were referred for follow-up to a clinic on the main campus designed to serve infants with serious health care problems during the first 18 months of life. Long-term outcome for high-risk infants was evaluated by 1 attending neonatologist, trained in follow-up assessments, at 6, 12, and 18 months of age. Evaluations included a detailed neurologic examination, an assessment of development using the Bayley Scales of Infant Development, and a visual and hearing evaluation. Cerebral palsy was defined as a nonprogressive motor disorder predominantly spastic in character. A composite score that incorporated all of these assessments was used to classify the infants as normal versus having moderate or severe developmental delay. The remainder of the cohort was referred to a system of primary care clinics that are neighborhood based, and follow-up data are less consistently available. All infants who were referred to neighborhood clinics had a normal neurologic examination on discharge from the hospital.

Statistical Analysis

Descriptive patient data were presented as mean ± standard deviation. The predictive values for determining an abnormal short-term outcome using the neurologic examination performed within the first 12 hours alone, the a-EEG alone, and combining the examination with the a-EEG were assessed by calculation of the sensitivity, specificity, positive and negative predictive values, and likelihood ratios.

RESULTS

The patient population comprised 50 term and near-term infants with a gestational age of 39 ± 2 weeks and a birth weight of 3950 ± 280 g. Infants were enrolled at 5 ± 3 hours, with 43 infants (85%) examined before 6 hours of age. There were 30 boys (60%) and 20 girls (40%). The ethnic composition consisted of 36 Hispanic (72%), 8 black (16%), and 6 white (12%). All infants had evidence of acute perinatal distress manifested by fetal heart rate abnormalities or thick meconium staining of the amniotic fluid. An Apgar score <5 at 5 minutes without fetal acidemia was present in 16 infants (32%), isolated severe fetal acidemia manifested by a cord arterial pH <7 or a base deficit >16 mEq/dL was present in 18 infants (36%), and a combination of both was present in 16 infants (32%). Delivery room resuscitation included intubation in 36 infants (72%) and chest compressions and epinephrine in 9 additional infants (18%). An abnormal short-term outcome was present in 14 infants (28%).

Early Neurologic Examination

The 50 infants underwent an early neurologic examination at 5 ± 3 hours after birth. The initial examination was normal without any signs of encephalopathy in 15 infants (30%), and 3 infants (6%) had features of mild encephalopathy. All 18 infants had a normal short-term outcome (Table 1). Thirteen infants had features of both mild and moderate encephalopathy and thus could not be categorized definitively as S1 or S2 encephalopathy. We refer to this ambiguous category (not predefined at study initiation) as S1–2. Three (23%) of the infants in this category subsequently progressed to moderate encephalopathy and had an abnormal short-term outcome. Seventeen infants (34%) were identified to have S2 encephalopathy by their early neurologic examination. Of these 17 infants, 5 (29%) infants remained moderately encephalopathic and 4 progressed to severe encephalopathy. Thus, 9 (53%) infants in this category had an abnormal short-term outcome. Two (4%) infants had severe encephalopathy on initial examination, and both died in the first week of life as a result of severe brain injury.

TABLE 1. Number of Infants Identified With an Abnormality by Neurologic Examination at <12 Hours of Age, a-EEG Alone, or by a Combination of Both Evaluations, and the Number of Infants With a Persistent Encephalopathy in Each Category

Method of Evaluation	Infants Identified	Persistent Encephalopathy
Neurologic examination		
Normal, S1	18	0
S1–2*	13	3
S2	17	9
S3	2	2
a-EEG		
Normal	35	3
Moderately abnormal	4	3
Severe suppression	11	8
Examination + a-EEG		
One or both normal	37	3
Both abnormal	13	11

* Refers to the category of infants with combined features of mild and moderate encephalopathy and was included as abnormal when the examination and a-EEG were combined.

A total of 19 infants had S2 or S3 encephalopathy (17 with S2 and 2 with S3; Table 1), and 11 developed an abnormal short-term outcome. Expanding the definition of an abnormal neurologic examination to include the newly described (S1–2) category ($n = 13$) yielded a total of 32 infants; 14 developed an abnormal short-term outcome.

a-EEG

A normal a-EEG recording was obtained in 35 (70%) infants. Of these infants, 3 (8.5%) had an abnormal early neurologic examination and developed an abnormal short-term outcome. An abnormal a-EEG recording was obtained in 15 infants (30%). The abnormalities included 4 infants with a moderate abnormal pattern and 11 infants with a severely suppressed pattern. Of the 15 infants with an abnormal a-EEG, 11 (73%) developed an abnormal short-term outcome and 4 (27%) did not (Table 1).

Combination of the Early Neurologic Examination and a-EEG

Thirteen infants were identified with a combination of any abnormality in the early neurologic examination (S1–2, S2, S3) and the a-EEG (moderate abnormal or suppressed amplitude). An abnormal short-term outcome developed in 11 (85%) of the 13 infants. Thirty-seven infants (74%) had either abnormalities of only 1 test or no abnormalities of either test. Three (8%) of these infants developed an abnormal short-term outcome (Table 1).

Summary of Predictive Values

The sensitivity, specificity, positive and negative predictive values, and positive likelihood ratios for an abnormal short-term outcome are summarized in Table 2. Thirty-two infants, including those in the S1–2 category, had abnormalities in the early neurologic examination. With the use of this examination, the sensitivity was 100%, specificity was 50%, positive predictive value was 44%, negative predictive value was 100%, and the likelihood ratio was 2. An abnormal neurologic examination as defined prospectively (S2, S3) was noted in 19 infants. With the use of this abnormal examination, the sensitivity was 78%, specificity was 78%, positive predictive value was 58%, negative predictive value was 90%, and the likelihood ratio was 3.5. An abnormal a-EEG alone was noted in 15 infants, which yielded a sensitivity of 79%, a specificity of 89%, a positive predictive value of 73%, a negative predictive value of 91%, and a likelihood ratio of 7. The combination of abnormalities in both the clinical examination and a-EEG narrowed the number of infants likely to develop an abnormal outcome to 13 with sensitivity of 78%, specificity of 94%, positive predictive value of 85%, negative predictive value of 92%, and a likelihood ratio of 13.

Clinical Characteristics of Infants With an Abnormal Short-Term Outcome

Summary of the information pertaining to events during labor, delivery room resuscitation, and follow-up for the 14 infants with persistent abnormalities of the neurologic examination beyond 5 days or death is shown in Table 3. Twelve of the 14 infants had a simultaneous recording of the a-EEG and the neurologic examination within the first 6 hours after birth, whereas 2 infants were studied between 6 and 12 hours after birth. Seven infants (50%) died in the first year of life from complications related to severe brain injury, and 3 of the 7 deaths occurred in the first week of life. All infants who survived to hospital discharge manifested abnormalities in their neurologic examination on discharge in the form of hypertonia ± clonus or hypotonia. Follow-up at 18 months in 6 of the 7 surviving infants showed moderate to severe developmental delay in 4 infants and a normal neurodevelopmental outcome in 2 infants. One infant has been lost to follow-up. For the 4 infants with developmental delay and the 1 infant lost to follow-up, there was evidence of global ischemic injury by MRI involving the basal ganglia and white

TABLE 2. Summary of Predictive Values for the Neurologic Examination and a-EEG Evaluations

	Sensitivity	Specificity	PPV	NPV	LR
Abnormal examination S1–2, S2, S3 ($n = 32$)	100%	50%	44%	100%	2
Abnormal examination ($n = 19$)	78%	78%	58%	90%	3.5
Abnormal a-EEG ($n = 15$)	79%	89%	73%	91%	7
Combination of abnormalities* ($n = 13$)	78%	94%	85%	92%	13

PPV indicates positive predictive value; NPV, negative predictive value; LR, positive likelihood ratio.
* The combination of abnormalities combines infants in the first ($n = 32$) and third ($n = 15$) groupings.

TABLE 3. Description of the 14 Infants With an Abnormal Short-Term Outcome

Complications of Labor	Mode of Delivery	Apgar Score			Cord pH	BD	IR	Neurologic Exam	a-EEG*	Postdischarge Outcome
		1 Minute	5 Minutes	10 Minutes						
Head entrapment	Stat CS	1	4	4	6.69	30	Yes	S2	3	Death
Decelerations	Stat CS	0	0	0	6.68	30		S3	3	Death
Decelerations	Stat CS	0	0	3	6.60	30	Yes	S3	3	Death
Decelerations	Stat CS	0	0	4	6.80	22	Yes	S2	1	Death
Decelerations	Stat CS	1	2	3	7.20	4	Yes	S2	3	Death
Decelerations	Vaginal	4	5	5	6.80	28	No	S2	3	Death
Decelerations	Vaginal	2	2	7	7.08	16	No	S2	3	Death
Bradycardia	CS	0	0	1	6.59	30	No	S2	2	No abnormalities
Decelerations	CS	0	0	0	7.15	20	Yes	S2	1	Lost to FU
Decelerations	Stat CS	2	5	8	7.30	12	Yes	S2	3	Moderate DD
Fetal bradycardia	Stat CS	1	4	5	6.80	30	No	S2	3	Severe DD
Decelerations	Vaginal	1	3	4	7.11	12	No	S (1–2)	2	Moderate DD
Decelerations	Stat CS	1	3	5	6.87	19	No	S (1–2)	2	Moderate DD
Precipitous delivery thick meconium	Vaginal	1	1	4	7.00	17	Yes	S (1–2)	1	No abnormalities

Stat CS indicates emergent cesarean section; BD, base deficit; IR, intensive resuscitation and chest compressions ± epinephrine; FU, follow-up; DD, developmental delay.
* 1 = normal, 2 = moderately abnormal, 3 = suppressed.

matter, ischemic cortical changes, and low-voltage electrical activity or burst suppression by standard EEG. The remaining 2 infants with normal outcome had subtle abnormalities on an initial MRI that normalized on a repeat MRI before discharge.

DISCUSSION

Current testing of neuroprotective therapies, such as modest reductions in brain temperature, in large, randomized, controlled trials of term infants with hypoxia-ischemia underscores the importance of patient selection.[17] Novel therapies such as hypothermia are likely to be associated with recognized and unrecognized adverse events and thus should ideally be evaluated in infants at greatest risk of progression to hypoxic-ischemic cerebral injury. Timely identification of these infants to allow initiation of therapy within the therapeutic window for potential rescue of newborns remains a challenge. This investigation focused on the neurologic examination shortly after birth and a simultaneously obtained a-EEG to delineate further the accuracy of patient identification for potential neuroprotective therapies. The results demonstrated that the a-EEG was more specific (89% vs 78%) and had a higher positive predictive value (73% vs 58%) when compared with the neurologic examination performed within 12 hours after delivery. Furthermore, the combination of abnormalities in both the early neurologic examination and the a-EEG yielded the highest specificity and positive predictive value for the short-term outcome of persistent encephalopathy (94% and 85%, respectively).

This study used persistent signs of moderate to severe encephalopathy beyond 5 days as the measure of an abnormal short-term neurologic outcome. All infants with such abnormalities demonstrated an abnormal neurologic examination at the time of hospital discharge, 50% died, and more than two thirds of the survivors evaluated had significant disability at follow-up. The absence of long-term follow-up data on infants with a normal neurologic discharge examination is a limitation to this report. However, several large reports consistently identified persistent neonatal neurologic abnormalities as the strongest predictor of long-term neurodevelopmental abnormalities in infants subjected to hypoxic-ischemic injury.[14,18–21] Thus, Sarnat and Sarnat initially described stages of neonatal encephalopathy in 21 infants with a hypoxic-ischemic insult and assessed neurodevelopmental outcomes at 1 year of age. The prognosis was good in the absence of severe encephalopathy and when the total duration of moderate encephalopathy was less than 5 days.[14] These observations were further supported by Robertson and Finer,[19] who reported that infants with moderate or severe encephalopathy in the first week of life or with an abnormal neurologic examination at the time of hospital discharge had significantly more long-term physical and mental impairment as well as reduced school performance when compared with infants with mild encephalopathy or a normal neurologic examination. In a third report, the prognostic value of an abnormal neurologic examination on hospital discharge in relation to the presence of cerebral palsy at 7 years of age was demonstrated in the Collaborative Perinatal Project, which evaluated >40 000 newborns in the neonatal period.[18] Infants with neurologic abnormalities at the time of hospital discharge had a 99-fold increased risk of cerebral palsy when compared with infants without abnormalities.

This investigation is the first to evaluate rigorously an early neurologic examination as a potential surrogate for abnormal long-term outcome. This proved to be more complex than anticipated. Attempts to categorize the early neurologic findings shortly after birth revealed a constellation of abnormalities not easily classified by the Sarnat stages, in particular, in the least affected infants. Thus, approximately 25% of infants could not be readily grouped into stage 1 or 2 , and were grouped post hoc as S1–2. This is an important group because 3 of 13 progressed to moderate encephalopathy and developed an abnormal short-term outcome. In all 3 infants, the a-EEG accompanying the examination was abnormal and therefore would have facilitated identification in a

timely manner. Additional studies with a larger number of infants focusing on the early neurologic examination will be needed to define this category further, the frequency of progression to more severe neurologic manifestations, and its prognostic implications. If similar findings are replicated, then this might lead to modifications in the Sarnat stages immediately after birth, which are often used as entry criteria for neuroprotective trials. The present study also demonstrated the value of a definitive abnormal neurologic examination (S2, S3) with regard to short-term outcome. Thus, 53% of infants with moderate encephalopathy (S2) and 100% of infants with severe encephalopathy (S3) progressed to an abnormal short-term outcome. These observations are consistent with the long-term prognostic studies by Robertson and Finer[22] in which none of the infants with mild encephalopathy had any handicap, 25% of infants with moderate encephalopathy had a handicap or died, and all of the infants with severe encephalopathy died or had profound disability on long-term follow-up. Furthermore, survivors of moderate encephalopathy had reduced school performance with more than 1 grade level delay when compared with their unaffected peers at 8 years of age.[23]

The prediction of persistent encephalopathy or early neonatal death using the a-EEG alone in the present study was consistent with previous a-EEG studies in infants with hypoxia-ischemia.[16,24–26] These studies reported that abnormalities of the a-EEG provided accurate prediction of adverse neurodevelopmental outcome during early childhood. For the present study, the criteria of al Naqeeb et al[16] was used to categorize the a-EEG results because these authors evaluated both normal and high-risk infants and derived the classification of abnormality on the basis of the normative data. Al Naqeeb et al reported on the use of the a-EEG in different groups of infants with encephalopathy, 1 of which consisted of 20 infants at high risk for birth asphyxia studied within 12 hours after birth. The reported specificity of 82% and positive predictive value of 81% were similar to our observed specificity of 89% and positive predictive value of 73%. A potential limitation of any evaluation performed shortly after birth is that data obtained at 1 time interval may not represent later times, because the process affecting the infant (eg, hypoxia-ischemia, infection) is not static. Toet et al[25] attempted to address this issue by examining the a-EEG at 3 and 6 hours after birth in neonates with hypoxia-ischemia. There was a change in the a-EEG pattern among 31% of the infants studied between 3 and 6 hours; however, the sensitivity (91% and 85%), specificity (77% and 86%), and positive predictive value (75% and 83%) were reasonably similar at 3 and 6 hours, respectively.[25] Our study, done at a mean age of 5 hours after birth, encompasses the age range described by Toet et al. Another potential limitation of the a-EEG is the need for invasive needle electrodes to obtain a quality recording with low impedance. However, this can be obviated by the technique used in this study, where the 2 electrodes were placed on the frontal-parietal area at the junction of hair growth. This allowed an easier seal using only adhesive paste. A frontal-parietal recording location should detect abnormal electrographic activity from the parasagittal or even diffuse areas of brain that would typically be affected in infants with moderate and/or severe encephalopathy.

This investigation also examined the combination of abnormalities in both the neurologic examination and the a-EEG to determine whether the predictive values could be enhanced when compared with either test alone. The combination of abnormalities in the neurologic examination and a-EEG had the highest predictive ability reflected by a specificity of 94%, a positive predictive value of 85%, a positive likelihood ratio of 13, and a significant decrease in the number of false-positive identifications. As indicated in Table 2, the number of infants identified to develop a persistent encephalopathy was reduced from 32 when any abnormality on the neurologic examination was considered (S1–2, S2, and S3), to 19 infants when only S2 and S3 abnormalities were considered on the neurologic examination, to 15 infants with the a-EEG alone, and to 13 infants with the use of both methods. The combination of the examination and the a-EEG helps to address the difficulty of interpreting a neurologic examination performed shortly after birth when abnormalities are evolving and the findings are difficult to categorize. Furthermore, the combination does not solely rely on an abnormal a-EEG because the neurologic examination should be consistent by manifesting abnormalities. Both evaluations can be performed by clinicians at the bedside without additional extensive formal training. Although the positive predictive value for an abnormal outcome is high using both the neurologic examination and a-EEG, no estimates can be made of the magnitude of risks justified by such a positive predictive value for experimental interventions. In part, this reflects the unknown hazards with any new neuroprotective therapy. Nevertheless, combining the early neurologic examination and a-EEG decreased the number of infants who would unnecessarily be treated by any new therapy and should reduce the sample size required for neuroprotective trials. This should facilitate more rapid completion of clinical trials and ultimately provide additional evidence to guide clinical practice.

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FOOD INSECURITY

"[A report] issued by the Center on Hunger and Poverty at the Heller School for Social Policy and Management at Brandeis University, Waltham, Massachusetts, states that >11 million households (10.77% of US households), containing >33 million individuals, reported experiencing food insecurity and that 3.3 million of these households (3.27%) reported the presence of hunger at home. As defined in the report, food insecurity occurs whenever the availability of nutritionally adequate and safe foods, or the ability to acquire acceptable foods in socially acceptable ways, is limited or uncertain. Hunger, in the report's language, does not mean simply the pangs that may beset anyone whose dinner is delayed, but refers to the uneasy or painful sensation caused by a recurrent or involuntary lack of food."

Mitka M. Not enough food (instead of too much) is also a problem in the United States. *JAMA.* 2002:288:1462

Editor's Note: A new problem you may not have known about defined by bureaucrats.

Noted by JFL, MD

Amplitude-Integrated Electroencephalography Coupled With an Early Neurologic Examination Enhances Prediction of Term Infants at Risk for Persistent Encephalopathy

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