

Intrapartum Fever and Unexplained Seizures in Term Infants

Ellice Lieberman, MD, DrPH*; Eric Eichenwald, MD‡; Geeta Mathur, MD‡;
Douglas Richardson, MD, MBA‡; Linda Heffner, MD, PhD*; and Amy Cohen, BA*

ABSTRACT. *Objective.* Early-onset neonatal seizures are a strong predictor of later morbidity and mortality in term infants. Although an association of noninfectious intrapartum fever with neonatal seizures in term infants has been reported, it was based on only a small number of neonates with seizures. We therefore conducted a case control study to investigate this association further.

Methods. All term infants with neonatal seizures born at Brigham and Women's Hospital between 1989 and 1996 were identified. For this study, cases consisted of all term neonates with a confirmed diagnosis of seizure born after a trial of labor for whom no proximal cause of seizure could be identified. Infants with sepsis or meningitis were excluded. Four controls matched by parity and date of birth were identified for each case. The rate of intrapartum maternal temperature $>100.4^{\circ}\text{F}$ was compared for case infants and controls. Potential confounding was controlled in logistic regression analysis.

Results. Cases comprised 38 term infants with unexplained seizures after a trial of labor. We identified 152 controls. Infants with seizures were more likely to be born to mothers who were febrile during labor (31.6% vs 9.2%). In almost all cases, the fever developed during labor (94.7% cases, 97.4% controls). At admission, mothers of infants with seizures were not significantly more likely to have factors associated with concern about infection such as a white blood cell count $>15\,000/\text{mm}^3$ (28.9% vs 19.1%) and premature rupture of the membranes (15.8% vs 17.8%). In a logistic regression analysis controlling for confounding factors, intrapartum fever was associated with a 3.4-fold increase in the risk of unexplained neonatal seizures (odds ratio = 3.4, 95% confidence interval = 1.03–10.9).

Conclusion. Our data indicate that intrapartum fever, even when unlikely to be caused by infection, is associated with a fourfold increase in the risk of unexplained, early-onset seizures in term infants. *Pediatrics* 2000;106:983–988; neonatal seizures, fever, labor, epidural.

ABBREVIATIONS. CNS, central nervous system; OR, odds ratio; CI, 95% confidence interval; IL, interleukin.

From the *Center for Perinatal Research, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Harvard Medical School; and the ‡Joint Program for Neonatology, Harvard Medical School, Boston, Massachusetts.

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Reprint requests to (E.L.) Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, MA 02115. E-mail: elieberman@partners.org

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A 1985 Consensus Conference of the National Institutes of Child Health and Human Development concluded that seizure was the best predictor of later neurologic damage in the term infant.¹ Several studies have linked the occurrence of early-onset neonatal seizures to perinatal events,^{2–5} most commonly asphyxia.^{4,5} More recently, it has been suggested that maternal infection during labor might be a risk factor for cerebral palsy among term infants.⁶

Concern about intrapartum fever has been related largely to the possible presence of maternal infection that could be harmful to the fetus. However, in low-risk women at term, most fever during labor is not related to infection but to the use of epidural analgesia.⁷ Although the causes of epidural-related fever have not been definitively established, it is believed to be associated with altered thermoregulation rather than infection.

Recently, we reported that epidural-related intrapartum fever, though not associated with neonatal infection, is associated with adverse neonatal outcomes.⁸ Infants of women with intrapartum fever were significantly more likely to have low 1-minute Apgar scores, to need bag and mask resuscitation, to be hypotonic after birth, and to need oxygen therapy in the nursery. Overall, 18% of the infants of febrile women had at least one of these adverse events. We also found that infants of women with intrapartum fever were more likely to have neonatal seizures. However, although that finding was statistically significant, it was based on only a small number of neonates with seizures ($N = 4$). We therefore conducted a case control study to further investigate the association of maternal fever in labor with unexplained neonatal seizures among term infants.

METHODS

Using a neonatal database, we identified all singleton, term infants (≥ 37 weeks gestation) weighing at least 2500 g born at Brigham and Women's Hospital between 1989 and 1996 with a diagnosis of possible or definite seizure. The records of 116 (98%) of the 118 infants identified were reviewed by a neonatologist (E.E. or D.R.) to confirm the diagnosis of a neonatal seizure. The neonatologists making this determination were blind to the characteristics of maternal labor. The diagnosis of seizure was confirmed only if the event was observed by 2 people, including an attending neonatologist, or if the diagnosis was confirmed by electroencephalogram or neurology consultation. The 2 unreviewed cases were not included in the analysis.

Because our investigation focused on unexplained seizures, the neonatal review also included a determination of whether other conditions likely to represent sufficient proximal cause for a seizure were present. Seizures determined to have an identified proximal cause were excluded from our analysis. Inclusion of

those seizures (particularly if they represent a high proportion of seizure cases) could obscure identification of risk factors for seizures with unidentified causes. Neonatal conditions considered likely to explain the neonatal seizure were determined before record review and included central nervous system (CNS) infections, congenital anomalies, metabolic diseases, recognized syndromes, skull trauma, and maternal drug use (see Table 1 for complete list). Some obstetric or fetal complications, such as uterine rupture and hydrops fetalis, were also considered to represent sufficient proximal cause for a neonatal seizure. However, some events during labor were not considered sufficient proximal cause, despite an expected association with neonatal seizures. Specifically, labors complicated by fetal distress and meconium-stained amniotic fluid during labor were not excluded because these complications could occur more frequently or be exacerbated if fever resulted in increased metabolic demands on the fetus. In addition, abnormal imaging results (such as focal brain infarct or hypoxic-ischemic brain injury) were not considered as explanatory factors because these abnormalities are the result of the insult rather than the precipitating event. Finally, because we were investigating the association of seizures with fever during labor, we excluded women who were not permitted to undergo a trial of labor.

The final group of seizure cases comprised all neonates with a confirmed diagnosis of seizure born after a trial of labor for whom no proximal cause of seizure could be identified. Four controls were selected for each case. Controls were the next 4 women delivering a term infant after a trial of labor who were of the same parity category (nulliparous or multiparous). If the number of women delivering after the case was insufficient on a given day, women delivering on the same day but before the case were chosen, beginning with the delivery closest in time to the case. Finally, if there were not 4 suitable deliveries on the same day, then controls were chosen from women delivering the next day, in order beginning with the first delivery of the day.

Data related to the pregnancy and labor characteristics of the women were abstracted from the maternal medical record by abstractors masked to the case or control status of the infants. Fetal distress during labor was as diagnosed by physicians during labor. Data on infant outcome were abstracted from the infant medical record.

The occurrence of intrapartum maternal temperature $>100.4^{\circ}\text{F}$ was determined for cases and controls. Cases and controls also were compared with regard to baseline characteristics including demographic information, characteristics of the pregnancy including birth weight and gestational age, and clinical conditions at admission to labor and delivery such as maternal WBC and temperature and the presence of premature rupture of the membranes (defined as rupture before the onset of contractions). Intrapartum factors compared included induction of labor, length of labor, time of membrane rupture, the presence of meconium-stained amniotic fluid, maternal intrapartum fever, the use of forceps and vacuum extraction, fetal tachycardia, epidural use, and the diagnosis of fetal distress. We did not evaluate the association of cesarean

TABLE 1. Proximal Cause of Seizure for 34 Excluded Infants

Condition	No. of Infants
Central nervous system anomaly	9
Skull trauma	5
Meningitis	4
Major syndrome	3
Fetomaternal hemorrhage	3
Metabolic disease	2
Uterine rupture	2
Hydrops	1
Toxoplasmosis, other infections, rubella, cytomegalovirus, and herpes simplex infection	1
Tuberous sclerosis	1
Aortic thrombosis	1
Idiopathic hypoglycemia	1
Maternal drug use	1
Documented sepsis	0
Chromosomal anomaly	0
Total	34

delivery with seizures. Previous studies in term infants have reported that only emergency cesareans, for indications such as fetal distress, are associated with seizures.^{3,5} In our study, nearly half of cesareans (6 of 13) for case infants were for fetal distress. These cesareans are likely to represent a response to adverse intrapartum events rather than an independent risk for adverse neonatal course.³

Cases and controls were compared with regard to demographic and pregnancy characteristics. The statistical significance for crude comparisons of continuous variables was determined using *t* tests. Categorical variables were compared using a χ^2 test or Fisher's Exact test where the expected value in any cell was <5 .

Analyses evaluating the association of fever with seizure took into account the matching by parity category (nulliparous or multiparous). Because combining all participants with identical values for matching variables into a single stratum decreases variance with no loss of validity, the data were analyzed as 2 strata (nulliparous and multiparous).⁹ Tests for homogeneity across the strata were performed using the Breslow-Day test. A pooled estimate of effect was determined using Mantel-Haenszel methods. Conditional logistic regression analyses taking matching into account were performed to evaluate the associations under study while controlling for potentially confounding factors. Odds ratios (OR) were calculated from regression coefficients and 95% confidence intervals (CI) from the standard errors of those coefficients.

RESULTS

The diagnosis of definite seizure was confirmed in 80 (69%) of 116 cases. A likely proximal cause of the seizure was identified in 34 (43%) of those infants (Table 1). The most common reasons identified were CNS structural anomaly ($N = 9$), skull trauma ($N = 5$), and culture-positive meningitis ($N = 4$), which together accounted for more than half of the explained seizures. Seven infants whose mothers did not have a trial of labor and 1 infant whose mother's temperature was not recorded (because labor lasted only .5 hour) were also excluded from the analysis.

After these exclusions, there were 38 term infants with unexplained seizures after a trial of labor and 152 controls. All seizures occurred within 48 hours of birth. Demographic and pregnancy characteristics of the cases and controls are shown in Table 2. The mothers of case and control infants were similar with

TABLE 2. Demographic and Pregnancy Characteristics of Seizure Cases and Controls

	Case Infants ($N = 38$)	Control Infants ($N = 152$)	<i>P</i>
Demographic characteristics			
Maternal age (y)			
<20	3 (7.9%)	11 (7.2%)	.3
20-29	11 (29.0%)	54 (35.5%)	
30-34	13 (34.2%)	59 (38.8%)	
≥ 35	11 (29.0%)	28 (18.4%)	
Receiving public assistance	8 (21.1%)	28 (18.4%)	.7
Smokers	1 (2.6%)	8 (5.3%)	.7
Alcohol use	1 (2.6%)	1 (.7%)	.4
Pregnancy characteristics			
Birth weight (g)			
<3000	9 (23.7%)	23 (15.1%)	.7
3001-4000	25 (65.8%)	111 (73.0%)	
4001-4500	3 (7.9%)	14 (9.2%)	
>4500	1 (2.6%)	3 (2.6%)	
Diabetes			
Gestational	1 (2.6%)	4 (2.6%)	.1
Pregestational	2 (5.3%)	1 (.7%)	
Hypertension			
Chronic	1 (2.6%)	4 (2.6%)	1.0
Pregnancy-induced	2 (5.3%)	9 (5.9%)	

regard to maternal age, the percentage receiving welfare, and the percentage reporting smoking at admission and alcohol use during pregnancy. The gestational ages, birth weights, and occurrence of pregnancy complications known at admission to labor and delivery also did not differ between groups. All infants weighed at least 2500 g because this was one of the eligibility criteria for the study.

Infants with seizures were more likely to be born to mothers who were febrile during labor (31.6% vs 9.2%, $P = .001$; Table 3). In almost all cases, the fever developed during labor. Only a small number of women were admitted with a temperature above 99.5°F, and that proportion was similar for cases and controls (5.3% cases, 2.6% controls, $P = .4$). The Breslow–Day test did not indicate heterogeneity across parity strata ($P = .4$). The Mantel–Haenszel odds ratio for the association of intrapartum fever with neonatal seizure was 5.1 (95% CI = 2.1–12.1).

Apart from fever, no differences were observed between cases and controls in clinical factors usually associated with concern about the presence of maternal infection during labor. Specifically, mothers of case infants were not more likely than mothers of controls to be admitted with an elevated WBC ($>15\,000/\text{mm}^3$; 28.9% vs 19.1%, $P = .2$). In addition, the presence of an elevated WBC at admission did not predict the development of an intrapartum fever. Among cases, 33.3% of women with an admission WBC $<15\,000/\text{mm}^3$ and 27.3% of women with a higher admission WBC became febrile ($P = 1.0$).

TABLE 3. Intrapartum Events for Seizure Cases and Controls

	Case Infants (<i>N</i> = 38)	Control Infants (<i>N</i> = 152)	<i>P</i>
At admission			
Premature rupture of membranes	6 (15.8%)	27 (17.8%)	.8
White blood count $>15\,000/\text{mm}^3$	11 (28.9%)	29 (19.1%)	.2
Temperature $>99.5^\circ\text{F}$	2 (5.3%)	4 (2.6%)	.3
Labor			
Labor induction	9 (23.7%)	36 (23.7%)	1.0
Membranes ruptured (h)*			
<12	24 (64.9%)	104 (70.8%)	.8
12–24	10 (27.0%)	33 (22.4%)	
≥ 24	3 (8.1%)	10 (6.8%)	
Length (h)			
<6	9 (23.7%)	48 (31.6%)	.07
6–12	9 (23.7%)	56 (36.8%)	
12–18	12 (31.6%)	23 (15.1%)	
≥ 18	8 (21.1%)	25 (16.5%)	
Fever $>100.4^\circ\text{F}$	12 (31.6%)	14 (9.2%)	.001
Meconium	22 (57.9%)	27 (17.8%)	.001
Fetal tachycardia	8 (21.1%)	9 (5.9%)	.003
Fetal distress	7 (18.4%)	4 (2.6%)	.001
Epidural analgesia			
≤ 4 cm	26 (68.4%)	65 (42.8%)	.01
>4 cm	3 (7.9%)	36 (23.7%)	
None	9 (23.7%)	51 (33.6%)	
Delivery			
Forceps applied	4 (10.5%)	8 (5.3%)	.3
Vacuum applied	2 (5.3%)	6 (4.0%)	.7
Occiput posterior position	5 (13.2%)	4 (2.6%)	.02
Nuchal cord	8 (21.1%)	22 (14.5%)	.3
Shoulder dystocia	4 (10.5%)	2 (1.3%)	.02

* Length of rupture missing for 1 case and 5 controls.

Although the overall rate of fever was lower, there was no association of admission WBC with later fever among controls (8.9% WBC $<15\,000/\text{mm}^3$, 10.3% WBC $>15\,000/\text{mm}^3$, $P = .7$). Finally, mothers of case infants were not more likely to be admitted with premature membrane rupture (15.8% vs 17.8%, $P = .8$). Clinicians' response to the fever was similar for mothers of case and control infants. Among febrile case infants 41.7% (5 of 12) received intrapartum antibiotics, compared with 50% (7 of 14) of febrile controls ($P = .7$).

Infants with seizures were more likely to have a diagnosis of fetal distress during labor (18.4% vs 2.6%, $P = .001$), meconium-stained amniotic fluid (57.9% vs 17.8%, $P = .001$), occiput posterior position at delivery (13.2% vs 2.6%, $P = .02$), and shoulder dystocia (10.5% vs 1.3%, $P = .02$). Although fetal tachycardia was also associated with the occurrence of seizures (21.1% vs 5.9%, $P = .003$), in both case infants and controls it occurred only in the presence of temperature elevation. In 58.8% (10 of 17) of women with a diagnosis of fetal tachycardia, maternal temperature exceeded 100.4°F, and no episode of tachycardia occurred with a maternal temperature $<99.0^\circ\text{F}$.

One potential explanation for our findings is that women with longer labors are more likely to have a fever and that it is the long labor, rather than the fever, that is associated with a higher risk of seizure. We therefore examined the association separately for women with shorter (<12 hours) and longer (≥ 12 hours) labors. Intrapartum fever was more common in infants with seizures regardless of length of labor (Fig 1). For labors ≥ 12 hours, intrapartum fever occurred in 50% of case infants and 22.9% of controls ($P = .03$). A similar association existed for shorter labors: intrapartum fever occurred in 11.1% of case infants but only 2.9% of controls ($P = .1$). The lack of conventional statistical significance in the short labor group probably results from the small number of women with short labors ($N = 5$) who become febrile.

A conditional logistic regression analysis was performed to examine the association of fever with unexplained neonatal seizure while taking into account matching and controlling for the potentially con-

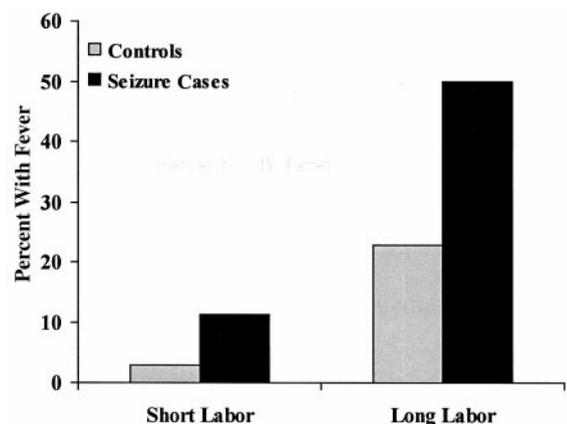


Fig 1. Proportion of case infants and controls with fever according to length of labor.

foundings effects of fetal distress, meconium-stained amniotic fluid, epidural use, occiput posterior position at delivery, shoulder dystocia, maternal age, forceps or vacuum use, birth weight, and length of labor. In that model, fever was associated with a 3.8-fold increase in the risk of seizures (OR = 3.4, 95% CI = 1.03–10.9).

Neonatal evaluation and treatment related to infection were examined for infants with seizures born to febrile ($N = 12$) and afebrile ($N = 26$) mothers. All infants in the case group were evaluated for infection at the time of the seizure. In addition to negative bacterial cultures, 50% (19 of 38) had negative viral cultures (58.3% with febrile mother vs 46.2% with afebrile mother, $P = .5$). In 4 infants, all with hypoxic-ischemic brain injury (1 with febrile mother, 3 with afebrile mother), lumbar puncture was not performed. For 1 additional infant, no cerebrospinal fluid cell counts were available because the specimen tubes broke.

None of the infants included in the case series were diagnosed with meningitis because this was an exclusion criterion. There was also no difference in the cerebrospinal fluid WBC analysis between the groups. All infants with seizures were treated with antibiotics, but for most (86.8%) treatment was continued for <3 days (83.3% with febrile mothers, 92.3% with afebrile mothers). Only 2 infants, both of febrile mothers, were treated for 7 days. No infants were treated for 14 days, the usual course of treatment for meningitis in our institution.

Laboratory evaluations also did not suggest greater evidence of non-CNS infection in the infants with seizures born to febrile mothers than in those born to afebrile mothers. No infants were diagnosed with sepsis because this was an exclusion criterion. Only 1 infant (of an afebrile mother) had a WBC <5000/mm³, and infants of febrile mothers were no more likely to have an elevated (>.2) immature to total neutrophil ratio (16.7% febrile, 26.9% afebrile, $P = .5$).

The specific brain lesions diagnosed did not differ for the infants of febrile and afebrile mothers (Table 4). Only 2 case infants died, 1 born to a febrile and 1 to an afebrile mother.

DISCUSSION

Our data indicate that intrapartum fever, even when unlikely to be caused by infection, is associated with an increase in the risk of unexplained, early-onset neonatal seizures in term infants. Infants whose mothers were febrile during labor had about 3.5 times the risk of seizure of infants whose mothers

were afebrile. This association remained in a multivariate model controlling for potentially confounding factors including fetal distress and other predictors of seizure such as meconium-stained amniotic fluid.

Several studies have reported an association of intrapartum fever with adverse neurologic outcome. However, in these studies fever was viewed exclusively as a marker for an infection that was responsible for the adverse outcome. For example, a recent case control study by Grether and Nelson⁶ suggested that maternal infection during labor may be associated with the occurrence of unexplained cerebral palsy in infants weighing >2500 g, even in the absence of neonatal infection. In their definition of "infection," however, isolated fever greater than 100.4°F was sufficient for a woman to be classified as infected. Similarly, Adamson et al¹⁰ reported that intrapartum maternal fever was a risk factor for neonatal encephalopathy among term infants but hypothesized that the association was related to the presence of sepsis. However, our previous work indicates that for term low-risk, nulliparous women, most intrapartum fever is not caused by infection. Rather, it is associated with the use of epidural analgesia for pain relief.⁷ In that population, 15% of women receiving epidural analgesia became febrile, compared with <1% of women not receiving epidural. Because the manifestations of the febrile response are similar regardless of whether the causative agent is infectious or noninfectious,¹¹ it is possible that the reported associations reflect physiologic changes that are part of the febrile response independent of infection.

Evidence suggests that maternal fever may be of concern for the fetus, even if not infectious in origin. In primates, hyperthermia in the absence of infection has been directly associated with the development of fetal hypoxia, metabolic acidosis, and hypotension.¹² Other animal studies have demonstrated that an increase in brain temperature of even 1°C or 2°C increases the degree of brain damage resulting from an ischemic insult.^{13–15} Among adults admitted with stroke, higher body temperature at admission is associated with an increase in stroke severity, infarct size, and mortality.¹⁶ Conversely, cooling the newborn head during ischemia has been demonstrated to be neuroprotective in animal models^{17,18} and is being investigated actively as a treatment to attenuate perinatal brain injury.¹⁹ These findings suggest that maternal intrapartum fever could injure the fetus by increasing the risk of neurologic injury independent of infection. Fetal temperature may reach fever levels more often than indicated by maternal temperature because studies in humans indicate that fetal temperature is 0.5°C to 0.9°C higher than maternal temperature.^{12,20–24}

It is important to address whether maternal or undiagnosed neonatal infection could explain the association of intrapartum fever with seizure that we observed. The main infectious cause of seizures in neonates is CNS infection. All neonates with seizures were evaluated for infection, and no infants included in our analysis had positive blood or cerebrospinal

TABLE 4. Brain Injury Diagnoses for Infants With Seizure Born to Febrile and Afebrile Women

	Febrile ($N = 12$)	Afebrile ($N = 26$)	P
Hypoxic-ischemic encephalopathy	50.0% (6/12)	57.7% (15/26)	.8
Intracerebral hemorrhage	16.7% (2/12)	19.2% (5/26)	
Infarct	25.0% (3/12)	11.5% (3/26)	
Unknown	8.3% (1/12)	11.5% (3/26)	

fluid cultures because this was an exclusion criterion for the study. However, one must also consider the possibility that some infants had an infection that was undetected by culture because of intrapartum maternal treatment with antibiotics or because specific culture techniques are needed for some organisms. Several factors suggest that such undetected infection is not the likely explanation for our findings. First, these infants were evaluated extensively in a tertiary care intensive care unit, and the neonatologists providing treatment did not conclude that an infection was present. Although all infants of febrile mothers with seizures were treated with antibiotics, 10 of 12 were treated for <3 days, and 2 were treated for only 7 days. The usual course of treatment for presumed meningitis in our institution is 14 days. Shorter treatments, particularly for <7 days, would be unlikely to provide effective treatment for meningitis. In addition, laboratory tests did not suggest the presence of infection. Infants of febrile mothers were no more likely to have an elevated immature to total neutrophil ratio or low WBC count (or cerebrospinal fluid abnormalities) than the infants of afebrile mothers. Finally, of the 80 infants with seizures during the study period, only 4 (5%) had positive cultures for meningitis, and 12 of the 38 infants with unexplained seizure were born to mothers who were febrile during labor. This suggests that for undetected infection to account for our findings, the rate of undetected infection would have to be far higher than the rate of detected infection.

Given Grether and Nelson's⁶ suggestion that maternal intrapartum infection may be associated with adverse neurologic outcome for the infant (cerebral palsy), even in the absence of neonatal infection, we also examined the possible role of maternal intrapartum infection. In our study, mothers of case infants were no more likely than mothers of control infants to have an elevated temperature or a high WBC at admission and were also no more likely to have premature rupture of the membranes. Although this does not rule out the possibility of infection, there seems to have been no obvious indications of, or risk factors for, infection at admission. During labor, it is difficult to know whether a fever is of infectious origin because traditional markers are not useful. WBCs tend to be elevated^{25,26} and have been noted to be a poor marker for infection.²⁷ Although placental pathology information was not obtained routinely, this information may also be of limited value because in a study of women at term, bacteria have been cultured from only 22% of placentas with histologic chorioamnionitis.²⁸ In evaluating whether maternal infection could be responsible for our findings, it is also important to note that the authors of the study proposing this hypothesis⁶ considered the presence of fever sufficient evidence for diagnosis of maternal infection.

Several potential mechanisms could explain an association of noninfectious fever with neonatal seizures. Intrapartum asphyxia is considered a major contributor to the occurrence of early neonatal seizures.^{29,30} This is a potential mechanism of action for intrapartum fever. Both animal¹³⁻¹⁵ and human da-

ta¹⁶ suggest that the effects of oxygen deprivation may be augmented by even small temperature increases. A relative oxygen deficit could occur if higher temperatures resulted in increased metabolic activity and, as a consequence, higher oxygen requirements. Thus, it is plausible that any effect of hypoxia during labor might be exacerbated by the presence of intrapartum fever, making the fetus more vulnerable to neurologic injury. On the other hand, we found no increase in the diagnosis of fetal distress associated with intrapartum fever.

The encephalopathy that accompanies sepsis is thought to be related to the production of mediators such as cytokines.⁶ Maternal cytokine production in response to infection during pregnancy has also been hypothesized to be an important factor in initiating or supporting brain damage during fetal development.³¹ Epidural analgesia (the major cause of noninfectious fever during labor) has been associated with higher levels of maternal serum interleukin (IL)-6 at the time of delivery,³² and the monocytes of infants whose mothers received epidural have been demonstrated to have higher IL-1 β and IL-6 production.³³ It is therefore plausible that noninfectious fever may trigger at least some of the same physiologic events that occur with infection, resulting in similar neurologic injury.

Because seizure in term infants is rare (approximately 1.3 per 1000 births in our population and in the literature),^{2,5} a case control design is advantageous. However, because our study is retrospective, we do not have information on placental cultures that could establish the presence or absence of infection. This makes it difficult to evaluate the specific role of noninfectious fever. Although most noninfectious fever in term women is related to epidural analgesia,⁷ epidural use is a very indirect measure because only a small proportion of women receiving epidural (10% in our control group) develop intrapartum fever. Larger studies in which placental cultures are obtained are needed to evaluate more definitively the role of noninfectious fever.

Early-onset neonatal seizures have been noted repeatedly to be a strong predictor of later morbidity and mortality in term infants.¹ Our study indicates that intrapartum fever is a strong independent risk factor for unexplained seizures in term infants in the absence of documented neonatal infection. The physiologic mechanism for this association is uncertain but could reflect either an effect of cytokines or an increase in metabolic rate that exacerbates the effect of hypoxia.

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HIGH COSTS AS STATES DRAW AUTISTIC PUPILS

One family came from India, others from Greece, Italy, and Israel. An Australian family is thinking about coming. Compared with those migrants, Rob and Anne Mandel had it pretty easy, giving up his medical practice and a life they loved in Indiana to get their son, Sam, the help he needed in New Jersey.

Sam is autistic, and his parents' move made the Mandels part of a phenomenon in which families, desperate for the most sophisticated special education for their disabled children, have moved from other states and even other nations in search of care.

But, increasingly, the needs of parents with autistic children are clashing with the bottom lines of school districts that have to pay for enormously expensive services—often more than \$40,000 per child per year—for students who may never set foot in district classrooms, sent instead to private institutions at the public schools' expense . . . "It's driving the suburban school districts crazy," said James H. Lytle, the superintendent of Trenton's public schools. "If you have 8 kids who need to go to a special school, you have to go to your taxpayers for \$400,000. That's essentially like sending them all to Andover. . . "

Peterson I. *New York Times.* May 6, 2000

Noted by JFL, MD

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