

# Cerebral Palsy and the Application of the International Criteria for Acute Intrapartum Hypoxia

Eva M. M. Strijbis, Inge Oudman, Phillipa van Essen, MPH, and Alastair H. MacLennan, MD

**OBJECTIVE:** To apply objective criteria for the identification of acute intrapartum hypoxia in a cohort of cerebral palsy cases and to identify other cerebral palsy-related pathologies.

**METHODS:** A cohort of all 235 neonates with cerebral palsy from a single Australian tertiary care center born between 1986 and 2003. Cases were identified from the South Australian Cerebral Palsy Register. Maternal and pediatric case notes were audited with application of the 2003 American College of Obstetricians and Gynecologists/American Academy of Pediatrics criteria to identify acute intrapartum hypoxia.

**RESULTS:** Data were available for analysis in 213 cases (91%). Major antenatal or pediatric cerebral palsy-related pathologies were identified in 98.1% of all these cases. An isolated acute intrapartum hypoxic event was defined as likely in only 2 of the 46 neonates born at term and none born preterm. Neonatal nucleated red blood cell counts were often high in neonates born preterm and following antenatal pathologies.

**CONCLUSION:** Cerebral palsy was seldom preceded by acute intrapartum hypoxia but antenatal cerebral palsy-related pathologies are often detectable. The objective American College of Obstetricians and Gynecologists/American Academy of Pediatrics criteria are useful to audit cerebral palsy

causation and exclude primary intrapartum hypoxia. (*Obstet Gynecol* 2006;107:1357–65)

**LEVEL OF EVIDENCE:** II-3

Cerebral palsy describes a group of disorders of movement and posture as a result of a defect or lesion of the immature brain.<sup>1</sup> The worldwide prevalence of cerebral palsy ranges between 2 to 2.5 per 1,000 live births and is the most common neurological congenital disorder.<sup>2</sup> Historically it was thought that cerebral palsy was often caused by an acute intrapartum hypoxic event. However, epidemiological studies suggest that only about 10% of cerebral palsy cases show possible signs of intrapartum fetal compromise, which may have had recent or longer-standing origins.<sup>3–7</sup> The longer-standing pathologies associated with the development of cerebral palsy are shown in the first box. More recently, associations have been found with hereditary thrombophilias, viral exposure, and cytokine polymorphisms.<sup>8–11</sup>

There is currently no clinical obstetric policy that has been shown to reduce the risk of cerebral palsy in term infants including electronic fetal heart rate monitoring and increased cesarean delivery rates.<sup>38,39</sup> Nevertheless, expert witnesses for the plaintiff can still be found who will opine, without supporting published data, that the cause of a plaintiff's cerebral palsy was acute intrapartum "birth asphyxia" which could have been recognized in time to deliver the infant at a stage when the neuropathological process was still reversible and preventable.<sup>40</sup>

In reaction to the above and to advances in cerebral palsy research, a multidisciplinary International Cerebral Palsy Task Force of scientists and clinicians working in this area was convened and published a consensus statement in 1999, which set out the objective criteria necessary to define in retrospect that an acute intrapartum hypoxic event had occurred before the onset of cerebral palsy.<sup>38</sup> This did not define that the acute hypoxic event was prevent-

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*From the Discipline of Obstetrics and Gynaecology, the University of Adelaide, and the South Australian Birth Defects Register, Department of Genetic Medicine, at the Women's and Children's Hospital, Adelaide, South Australia.*

*A.H.M. was Chair of the 1999 International Cerebral Palsy Task Force and wrote the foreword to the 2003 American College of Obstetricians and Gynecologists/American Academy of Pediatrics Cerebral Palsy Task Force Report.*

*Corresponding author: Professor Alastair MacLennan, the Discipline of Obstetrics and Gynaecology, School of Paediatrics and Reproductive Medicine, the University of Adelaide, at the Women's and Children's Hospital, 72 King William Road, North Adelaide, South Australia 5006, Australia; e-mail: alastair.maclennan@adelaide.edu.au.*

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## Major Pathologies Associated With Cerebral Palsy

Prematurity<sup>12,13</sup>

Antepartum hemorrhage<sup>14–16</sup>

Complication of multiple pregnancy<sup>17,18</sup>

Genetic disorders<sup>19</sup>

Intrauterine infection, for example, chorioamnionitis, funisitis, villitis, cytomegalovirus, toxoplasmosis<sup>20–23</sup>

Intrapartum fever<sup>20,24,25</sup>

Intrauterine growth restriction<sup>26–28</sup>

Maternal and fetal coagulopathies<sup>8,9,10</sup>

Multiple congenital anomalies<sup>29,30</sup>

Maternal disease, for example, hypothyroidism, diabetes, drug abuse, severe preeclampsia, viral illness<sup>31,32</sup>

Placental pathology, for example, major infarction, thrombotic vasculopathy<sup>33–35</sup>

Tight nuchal cord<sup>36</sup>

Childhood causes<sup>37</sup>

Other causes, for example, fetal hemorrhage, rhesus disease<sup>2</sup>

able or that it was the primary cause of the cerebral palsy but rather it defined the few cases of cerebral palsy that might have been associated with acute intrapartum hypoxia. In 2003 the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) updated the literature on the pathogenesis and pathophysiology of neonatal encephalopathy and cerebral palsy and slightly revised the 1999 template.<sup>39</sup> The new template describes nine criteria to be sought to define an acute intrapartum hypoxic event sufficient to cause cerebral palsy: four essential criteria which help prove the existence of severe hypoxia at birth and five criteria that if present together suggest an intrapartum timing, but by themselves are nonspecific to asphyxial insults (second box). All four of the essential criteria must be met before an intrapartum hypoxic cause of cerebral palsy can be considered. At least three of the additional five criteria have to be present to suggest a possible acute event rather than longer-standing hypoxia or other chronic pathology.

The primary objective of this study was to apply the ACOG/AAP 2003 template of criteria in a large cohort of cerebral palsy cases to document cases with clear evidence of acute intrapartum hypoxia and those with evidence of other possible causes for cerebral palsy. In recent years better data are more often being collected on high-risk pregnancies and neonates, for example, cord blood gases, placental histology, and neonatal brain imaging which may allow better insight into some of the potential antenatal causes of cerebral palsy. Secondary objectives were to identify the availability of information needed to retrospectively apply the 2003 ACOG/AAP criteria for defining acute hypoxia and to correlate avail-

able neonatal nucleated red blood cell (RBC) counts with detectable acute and chronic pathologies. Previous studies have shown that nucleated RBC counts are significantly higher in neonates exposed to intrauterine hypoxia.<sup>41–43</sup> These studies have suggested that there may be a relationship between the timing of the asphyxial event and the number and changing profile of neonatal nucleated RBCs. Such patterns have not been studied in a large series of cases with a cerebral palsy outcome.

## PARTICIPANTS AND METHODS

An audit of obstetric, neonatal, and pediatric case notes was performed in a cohort of cerebral palsy cases identified from the South Australian Cerebral Palsy Register. This register includes all children diagnosed with cerebral palsy before 5 years of age, living in South Australia.<sup>44</sup> The register includes post-neonatally acquired cerebral palsy providing that the brain injury occurred before 2 years of age. A pediatric specialist confirmed the diagnosis in all cases. Children are included in the register when it is clear that cerebral palsy is present and the type and severity can be determined. Cases in which the child dies before the age of 5 years are still included.

Permission to retrieve data from medical records was obtained from the institutional Research Ethics Committee (REC 1607/8/2007). The case audit was conducted under the auspices of the hospital's Perinatal Mortality Committee and was legally privileged under Section 64D of the South Australian Health Commission Act. In this study, only children with cerebral palsy born between 1986 and 2003 in the Adelaide Women's and Children Hospital and at its location before 1995 in the Queen Victoria Hospital



## Criteria to Define an Acute Intrapartum Event Sufficient to Cause Cerebral Palsy

### Essential criteria

1. Evidence of a metabolic acidosis at birth (pH < 7.00 and base deficit  $\geq$  12 mmol/L)
2. Onset of neonatal encephalopathy within 24 hours
3. Cerebral palsy of the spastic quadriplegic or dyskinetic type
4. Exclusion of other pathologies associated with cerebral palsy

### Criteria that together suggest intrapartum timing but are nonspecific to asphyxial insults

5. A sentinel hypoxic event occurring immediately before or during labor
6. A sudden and sustained fetal bradycardia or other evidence of a nonreassuring fetal status, usually after a hypoxic sentinel event when the pattern was previously normal
7. Apgar scores of 0–3 beyond 5 minutes
8. Multisystem failure within 72 hours of birth
9. Early imaging study showing evidence of acute nonfocal cerebral abnormality

were included. As gestational age is a risk factor for cerebral palsy, the cases were subanalyzed in three groups: less than 32 weeks, 32 to less than 37 weeks and 37 or more weeks of gestation.<sup>12</sup>

Available obstetric and neonatal variables of significance for this study were extracted from the medical records of the 235 cerebral palsy cases to identify the presence of the nine criteria as defined in the ACOG/AAP 2003 consensus statement.<sup>39</sup> The proportion of cases meeting each of the nine criteria was determined. The criteria were also applied to estimate the proportion of cases in which either a chronic or acute intrauterine hypoxia may have occurred. Each record was searched for the presence of major pathologies associated with cerebral palsy (second box.). Intrauterine growth restriction (IUGR) was defined as under the 10th percentile of weight for

gestation at birth, using Australian Commonwealth charts that allow for gender, birth order, and maternal height. An intrapartum fever was defined as a temperature more than 37.2°C recorded during established labor. Nucleated RBC counts are expressed per 100 white blood cells with our laboratory normal range being 0–7 in cord blood at term.

Relative risks and exact confidence limits were calculated using Epi Info 6 (Centers for Disease Control and Prevention, Atlanta, GA).

### RESULTS

Seven maternal and 15 pediatric medical records could not be traced. All missing medical records were from births before 1995 when the hospital moved to a new location. Cases were excluded from analyses if essential maternal or neonatal data were missing.

**Table 1. Presence of the American College of Obstetricians and Gynecologists /American Academy of Pediatrics 2003 Template Criteria**

	Gestation			
	< 32 wk (n = 119, 55.9%)	32 to < 37 wk (n = 48, 22.5%)	$\geq$ 37 wk (n = 46, 21.6%)	All (n = 213, 100%)
<b>Essential criteria</b>				
PH < 7.00 and BD $\geq$ 12	2 (1.7)	2 (4.2)	4 (8.7)	8 (3.8)
Neonatal encephalopathy	NA	NA	13 (28.3)	NA
Quadriplegic or dyskinetic cerebral palsy	23 (19.3)	17 (35.4)	12 (26.1)	52 (24.4)
Associated cerebral palsy pathology	119 (100)	48 (100)	42 (91.3)	209 (98.1)
<b>Nonspecific criteria</b>				
Sentinel hypoxic event	0	0	2 (4.3)	2 (0.9)
Bradycardia or NRFS	6 (5.0)	6 (12.5)	14 (30.4)	26 (12.2)
Apgar score < 4 after 5 min	1 (0.8)	0 (0)	5 (10.7)	6 (2.8)
Multisystem failure	7 (5.9)	3 (6.3)	7 (15.2)	17 (8.0)
Acute nonfocal cerebral abnormality	5 (4.2)	6 (12.5)	9 (19.6)	20 (9.4)

BD, base deficit; NA, not applicable, NRFS, nonreassuring fetal status.  
Data are presented as number (percentage).



Among the 22 excluded cases, 15 had major antenatal risk factors for cerebral palsy. Eleven neonates were born preterm, three were born at term, and in eight cases the gestation was not known.

The full audit was conducted on 213 complete sets of case notes (91%). In 127 of these cases all nine criteria from the ACOG/AAP template could be assessed. The percentage of cases meeting each criterion, grouped by gestational age, is shown in Table 1. Blood gases near birth were available in 152 cases. A severe metabolic acidosis at birth was confirmed in 8 of these cases (3.8% of the total). Neonatal encephalopathy was present in 28.3% of cases at term and 98.1% of all cases had at least one major pathology associated with cerebral palsy (Table 2). Less than 1% of all cases had a hypoxic sentinel event during labor. Histologic examination of the placenta was performed in 144 cases.

None of the 46 cases born at term ( $\geq 37$  weeks of gestation) met all of the ACOG/AAP criteria for severe acute intrapartum hypoxia as a possible cause of cerebral palsy. In most cases, the criteria clearly ruled out acute intrapartum hypoxia. Some cases met some of the criteria and are potentially contentious. These are discussed in detail below to explain their adjudication. Most cases at term (91%) were associated with at least one major antenatal pathology associated with cerebral palsy (Table 2). Nearly 9% of the cases met the criteria for a severe metabolic acidosis at birth, more than twice the proportion seen in preterm deliveries. Sustained fetal bradycardia before birth was described in 30% of cases at term. This was significantly greater than the rate of brady-

cardia seen in the less-than-32-weeks-of-gestation group, relative risk 6.04 (95% exact confidence interval 2.67–27.92). Fewer than 20% of cases at term had early imaging evidence of an acute nonfocal cerebral abnormality but this was a higher rate than seen in the very preterm group, RR 4.66 (95% exact CI 1.54–22.17). Placental examination was not performed in 13 cases. Cord or early neonatal blood gas analysis was performed in 25 (54%) of cases.

Two cases described below had an intrapartum sentinel hypoxic event and were adjudged in this study to probably have experienced acute intrapartum hypoxia despite a lack of corroborating blood gas evidence.

In the first case, placental abruption occurred during labor. The baby was delivered by emergency cesarean delivery because of severe fetal bradycardia. The Apgar scores were 1 and 2 at 1 and 5 minutes, respectively. Neonatal encephalopathy and nonfocal cerebral edema and quadriplegic cerebral palsy were recorded. Placental histologic examination showed a retroplacental hematoma. Other antenatal risk factors could not be detected. No cord or early neonatal blood gases were available. In this case, criteria 2, 3, 5, 6, 7, and 9 were met. Thus, although confirmatory blood gases were not available, severe acute intrapartum hypoxia was likely and probably followed the antepartum hemorrhage.

In the second case, uterine rupture was discovered during an emergency cesarean delivery, which was performed because of severe sustained fetal bradycardia and maternal hypotension during labor. The fetal pH measured during labor did not show a

**Table 2. Major Cerebral Palsy–Associated Pathologies Present by Gestational Age Group**

	Gestation			
	< 32 wk (n = 119, 55.9%)	32 to < 37 wk (n = 48, 22.5%)	$\geq 37$ wk (n = 46, 21.6%)	All (n = 213, 100%)
Prematurity	119 (100)	48 (100)	0	167 (78.4)
Antepartum hemorrhage	42 (35.3)	9 (18.8)	7 (15.2)	58 (27.2)
Multiple pregnancy	33 (27.7)	8 (16.7)	2 (4.3)	43 (20.2)
Genetic disorders	0	0	1 (2.2)	1 (0.5)
Intrauterine infection	39 (32.8)	11 (22.9)	10 (21.7)	60 (28.2)
Intrapartum fever	14 (11.8)	8 (16.7)	6 (13.0)	28 (13.1)
Intrauterine growth restriction	40 (33.6)	21 (43.8)	12 (26.1)	73 (34.3)
Maternal thrombophilia	1 (0.8)	0	0	1 (0.5)
Multiple congenital anomalies	5 (4.2)	7 (14.6)	14 (30.4)	26 (12.2)
Maternal disease	28 (23.5)	16 (33.3)	14 (30.4)	58 (27.2)
Severe placental pathology	28 (23.5)	11 (22.9)	5 (10.9)	44 (20.7)
Tight nuchal cord	0	1 (2.1)	2 (4.3)	3 (1.4)
Cause in infancy	0	2 (4.2)	4 (8.7)	6 (2.1)
Other causes	2 (1.7)	0	0	2 (0.9)
Total with one or more	119 (100)	48 (100)	42 (91.3)	209 (98.1)

Data are presented as number (percentage).





metabolic acidosis (7.29) but cord gases were not documented. The neonate's Apgar scores were 3, 4, and 4 at 1, 5, and 10 minutes, respectively. Neonatal encephalopathy ensued but there were no signs of multisystem failure, and repeated early brain imaging showed no abnormalities. The cerebral palsy was of a diplegic type. Major cerebral palsy-associated pathologies were not identified. Placental histology was not performed. In this case, essential criteria 2 and 4 were met. Evidence for criterion 1 was missing. Nonspecific criteria 5 and 6 were met, criterion 7 was almost met and criteria 8 and 9 were not met. Acute intrapartum hypoxia was assumed but not definitely confirmed.

Two cases met three of the essential criteria for hypoxia, but an acute timing of this could not be substantiated.

In the first case, criteria 1, 2, and 3 were met but several cerebral palsy-associated antenatal pathologies including intrauterine growth restriction were present. Placental histology showed a single umbilical artery, chronic villitis, placental hemangioma, and major infarction. The baby had multiple congenital abnormalities. Thus, criterion 4 was not met. There was no sentinel hypoxic event, intrapartum bradycardia occurred, and the Apgar scores were 1 and 1 at 1 and 5 minutes, respectively. There was multisystem failure in the neonatal period, but there was no nonfocal cerebral abnormality on imaging, although intraventricular hemorrhage occurred. Thus, three nonspecific criteria (6, 7, and 8) were met. The overall picture suggested chronic fetal compromise with ongoing hypoxia in labor.

In the second case, a severe metabolic acidosis, neonatal encephalopathy, and quadriplegic cerebral palsy were present, and thus criteria 1, 2, and 3 were met. The mother had gestational diabetes, and there was neonatal hypoglycemia. Placental histology showed an abnormal amount of infarction. The baby was delivered by an emergency cesarean, because of nonreassuring fetal heart rate patterns in the second stage of labor. The Apgar scores were 1 and 4 at 1 and 5 minutes, respectively, and thus criterion 7 was almost met. There was no sentinel hypoxic event and no evidence of nonfocal cerebral damage on neonatal brain imaging. Thus, criteria 4, 5, and 9 were not met. Because possible antenatal cerebral palsy-risk factors were present and the nonspecific criteria for acute hypoxia were equivocal, primary acute intrapartum hypoxia could not be confirmed or refuted although a continuing "acute on chronic" hypoxia was possible.

In three cases, no antenatal or pediatric cerebral palsy-associated pathologies could be retrospectively

detected, but either acute intrapartum hypoxia could not be substantiated or fetal stroke was clinically considered.

In the first case, the neonate was instrumentally delivered because of nonreassuring fetal heart rate patterns and meconium-stained liquor. The scalp pH during labor was 7.24. Cord arterial gas analyses showed pH 7.11 and base deficit  $-12$ . Apgar scores were 6 and 9 at 1 and 5 minutes, respectively. No neonatal encephalopathy or multisystem failure ensued. Brain imaging and placental histology were not performed. The cerebral palsy was diplegic. In this case, only criteria 4 and 6 were met. Severe acute intrapartum hypoxia as the primary cause of the cerebral palsy was not established, but an associated cause for the cerebral palsy could not be found.

In the second case, the baby was spontaneously delivered with Apgar scores of 7 and 9 at 1 and 5 minutes, respectively. There was no neonatal encephalopathy. There was multisystem failure. Blood gas analyses, brain imaging, and placental histology were not performed. The cerebral palsy in this case was of a hemiplegic type and infantile stroke was considered. In this case, only criteria 4 and 8 were met with data for criteria 1 and 9 missing.

In the third case, labor was complicated by a shoulder dystocia for 2 minutes. There was no prior severe bradycardia during labor. The neonate was delivered vaginally with Apgar scores of 0 and 0 after 1 and 5 minutes, respectively. Early neonatal blood gas analysis, 45 minutes after delivery, showed a pH 7.01 and base deficit  $-20$ . There was neonatal encephalopathy but no multisystem failure. Brain imaging showed no early abnormalities. Placental histology was not performed. The cerebral palsy was of a hemiplegic type. Infantile stroke was considered possible but was not confirmed. Criteria 2 and 4 were met, and criterion 1 was almost met. Of the nonspecific criteria, only criterion 7 was met. Severe early neonatal hypoxia was present, but the nonspecific criteria suggest that the hypoxia was chronic, and clinically a fetal stroke was a possibility. Two minutes of shoulder dystocia may have created an "acute on chronic" picture making this adjudication difficult.

In all 48 cases in the group that had a gestation of 32 to less than 37 weeks, major cerebral palsy-associated pathologies other than prematurity could be defined (Table 2). In 34 cases (70.8%), placental examination was performed. In 34 cases (70.8%), blood gas analysis was performed. The international criteria were designed to detect intrapartum hypoxia in term births. Signs of neonatal encephalopathy can be imprecise in premature neonates, and prematurity



is a major risk factor included in criterion 4 of the ACOG/AAP template. However, the template was applied in neonates with prematurity (Table 1) for comparison.

There were three neonates born between 32 and less than 37 weeks of gestation with evidence of perinatal hypoxia. All three were associated with pathological events before labor.

In the first case, the neonate was delivered by emergency cesarean after spontaneous onset of labor began after a severe placental abruption. Criteria 1 and 7 were almost met, criteria 2, 3, and 8 were met, and criteria 4, 5, 6, and 9 were not met. The mixed chronic and acute perinatal hypoxic picture was compatible with fetomaternal hemorrhage occurring before and during labor.

In the second case, the neonate was also delivered by an emergency cesarean at 33 weeks of gestation because of a placental abruption after spontaneous onset of labor. Criteria 1, 5, and 6 were met. Perinatal hypoxia secondary to the placental abruption was the presumed cause.

In the third case, the neonate was delivered before labor by an elective emergency cesarean at 36 weeks of gestation because of decreased fetal heart rate variability after abdominal trauma, associated antepartum hemorrhage, and maternal hypertension. Only criteria 1 and 3 were met.

In all 119 cases of gestation of less than 32 weeks, there was a major risk of cerebral palsy because of extreme prematurity. However, additional cerebral palsy-associated pathologies such as antepartum hemorrhage, intrauterine infection, and intrauterine growth restriction were very common (Table 2). Placental histology was performed in 99 cases (82.9%), and blood gas analyses were performed in 94 cases (80%). Hypoxia at birth was very uncommon and only one neonate had a severe metabolic acidosis at birth. This neonate also had congenital anomalies, intrauterine growth restriction, and placental vasculopathy. Intraventricular hemorrhage was a common finding in this group of cases.

There was a high incidence of breech presentation (24.9%) at all gestations. The incidence of breech presentation was 35.3%, 14.6%, and 8.7% at less than 32 weeks of gestation, 32 to less than 37 weeks of gestation, and term births, respectively.

Neonatal nucleated RBC counts at birth were often high in the neonates delivered preterm and in the neonates with cerebral palsy-associated pathologies. However, there were insufficient cases in which acute intrapartum hypoxia may have occurred, or in which nucleated RBCs were measured in term neo-

nates who later were diagnosed with cerebral palsy, to find a predictable pattern.

## DISCUSSION

This cohort study tested the ACOG/AAP 2003 template of evidence for acute intrapartum hypoxia in a large series of cerebral palsy cases. The results show that, when data for all nine criteria were available, no case of cerebral palsy could be solely explained by an acute intrapartum hypoxic event. The consensus statement offers a template of evidence that can better define retrospectively acute intrapartum hypoxia. This study suggests that acute intrapartum hypoxia sufficient to cause a severe metabolic acidosis and cerebral palsy is rare and that there are nearly always antenatal pathologies or other events that would have contributed to a cerebral palsy outcome. Previous epidemiological studies have estimated that about 10% of cerebral palsy cases had evidence of possible perinatal asphyxia. However, these studies often had difficulty in defining the nature of the fetal compromise and the timing of events, and therefore hypoxia beginning during labor as the primary causative event could not be confirmed.

Severe metabolic acidosis at birth could be proven in only 3.8% of this cohort. Many of these were delivered before labor and in the others an antenatal pathology was present suggesting an antenatal onset of these biochemical changes. Two other cases were associated with a sentinel hypoxic event during labor. No blood gases were available to measure the severity of the presumed metabolic acidosis in these two cases. There were no retrospectively detectable antenatal or pediatric cerebral palsy-associated pathologies in these cases and thus intrapartum hypoxia and ischemia was presumed to have caused the cerebral palsy secondary to the sentinel hypoxic events. It is therefore probable that 2 of the 46 cases at term may have experienced de novo acute intrapartum hypoxia. This gives an incidence of about 4% in term neonates but no apparent cases among those born preterm. New possible causative factors such as hereditary thrombophilias, which are associated with both antepartum hemorrhage and cerebral palsy, viral exposure or cytokine mutations, have not been ruled out in any of the cases, highlighting the difficulty in assuming that intrapartum events were the primary cause of cerebral palsy.<sup>9-11,45</sup>

Other than prematurity, the most common associated clinical pathologies identifiable retrospectively from the case notes were intrauterine growth restriction (34.3%), intrauterine infection (28.2%), and antepartum hemorrhage (27.2%). Other pathology, such



as maternal disease, placental pathology, and multiple pregnancy, were often present in conjunction with these three main associations. These findings are in keeping with the epidemiological literature.<sup>3-7</sup>

Our data underline that many of the individual criteria from the ACOG/AAP template are not specific to “acute asphyxia” and may often be present in the presence of longer-standing pathologies such as intrauterine growth restriction and intrauterine infection. Without specific tests for infection and without placental pathology, in all cases it is likely that the role of intrauterine infection in this series is an underestimate.

The international criteria to detect acute intrapartum hypoxia were derived mostly from data on term infants. Increasing prematurity is a major risk factor for cerebral palsy and early neonatal encephalopathy cannot be clearly defined in preterm infants. Despite this limitation, it was an a priori decision to test the criteria in mildly premature neonates. All 48 cases of cerebral palsy born between 32 and 36 weeks of gestation were associated with other major cerebral palsy-related pathologies, for example, intrauterine growth restriction and infection. Cerebral white matter injury in preterm infants is commonly associated with infection and rarely with metabolic acidosis.<sup>46</sup> When prematurity and neonatal encephalopathy were excluded from the template, the criteria were consistent in suggesting a chronic pathology in the preterm infants. The international criteria were not applied in the very preterm infants. Other major antenatal cerebral palsy-associated pathologies were present in 98% of cases at gestations less than 32 weeks. Antepartum hemorrhage, intrauterine growth restriction, and maternal disease causing placental pathology in preterm neonates were other common associations in this and previous studies.<sup>4,7</sup> Multiple pregnancy was common in the very preterm group and has previously been described as an additional independent risk factor for cerebral palsy.<sup>17</sup>

A second limitation is that the template only identifies acute intrapartum hypoxia as a possible cause of cerebral palsy. It does not identify the many possible antenatal causes which may not be apparent at birth.<sup>9-11</sup> Histologic examination of the placenta is not a specific criterion in either international evidence template, but in this series, placental histology often showed evidence of chorioamnionitis, funisitis, villitis, or extensive infarction. The value of sending the placenta for detailed examination in cases in which a neonate appears compromised in the perinatal period is great, as such placental abnormalities have been

strongly associated with perinatal stroke or subsequent periventricular leukomalacia or both.<sup>35</sup>

One limitation of this study is that data for all nine criteria were only available in 127 of the 213 cases audited. A lack of cerebral palsy-associated pathologies or data to judge the fulfilment of all the criteria made adjudication of the presence or absence of acute intrapartum hypoxia difficult in a few cases. In two cases born at term, evidence for the first essential criterion, that is, blood gases around birth, was missing; therefore the extent of metabolic acidosis during a known sentinel hypoxic event in these cases could not be confirmed or refuted. However, if the blood gas data had been available and both these cases had been confirmed as severe metabolic acidosis, the attributable risk of acute intrapartum hypoxia as a possible cause of cerebral palsy in this series of 213 cases would have been about 1%.

Another limitation of this study is that it was not a case-control study. There was an overrepresentation of cerebral palsy cases from preterm deliveries because the study hospital is a tertiary referral center. Although there was no control group, the prevalence of maternal diabetes (preexisting or gestational) in term deliveries in this cohort was higher (15.2%) than the rate seen for all South Australia (4.1%).<sup>47</sup> Breech presentation was also more common than expected at all gestations in this study and has been described as a possible independent risk factor for cerebral palsy.<sup>48</sup> Both of these factors may have been influenced by the tertiary status of the hospital.

A final limitation of the study is the sample size. Only two probable cases of acute hypoxia were identified, and there were not enough cases to estimate the incidence of acute asphyxia with reasonable precision in term cases. The estimate of 4% at term is compatible with slightly higher estimates in the literature where these strict criteria were not applied.

Previous studies have shown that nucleated RBC counts are higher at birth in neonates exposed to intrauterine hypoxia.<sup>41-43</sup> In this cohort, neonatal nucleated RBC counts were mostly high in preterm neonates and pregnancies exposed to detected chronic intrauterine pathology, for example, intrauterine growth restriction. However, such counts were available in only 13 of the 46 neonates born at term. In the two cases with a sentinel intrapartum hypoxic event and probable acute intrapartum hypoxia, the nucleated RBC counts at birth were borderline and were not repeated during the early neonatal period to see if there was a later rise in response to the presumed intrapartum hypoxia. Thus, in this first but incomplete series of nucleated RBC counts in associ-



ation with cerebral palsy, there were too few cases of proven acute intrapartum hypoxia to examine the usefulness of nucleated RBC counts as a surrogate for an intrapartum insult.

In summary, the ACOG/AAP template helped illustrate that, in this cohort, cerebral palsy was seldom preceded by acute intrapartum hypoxia. The criteria proved very useful in excluding primary severe intrapartum hypoxia in 99% of these cases. Other cerebral palsy-associated pathologies could be identified in 98% of cases leaving about 1% in which intrapartum causation was debatable. It is possible that newly detected hereditary and infective factors may increase vulnerability to perinatal hypoxia. Many of these factors are silent during pregnancy and are difficult to identify in retrospect especially if cord gases, placental histology, and neonatal investigations are not documented and cord blood stored. These are important data for a perinatal audit and should be collected on all neonates delivered with any signs of possible compromise. In the very few cases in which acute intrapartum hypoxia solely occurs, it will require new evidence and clinical trials to show if any clinical intervention can actually reduce the risk of cerebral palsy. The ACOG/AAP criteria are a useful template of evidence to collect to help understand the possible causation and timing of the neuropathology and in particular to define or rule out an acute hypoxic intrapartum event sufficiently severe to cause cerebral palsy. Understanding the etiology of cerebral palsy is important for the parents, for the staff involved, and for the future if we are to find ways to reduce the unchanged incidence of this serious condition, which remains the most common chronic motor disability of childhood.

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