Cerebral palsy and neonatal encephalopathy

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Abstract

A retrospective cohort study was carried out to test the hypothesis that children born at term with cerebral palsy with signs of neurological dysfunction preceded by depression at birth (termed neonatal encephalopathy) differ from those without such signs in the frequency of antenatal and perinatal factors, and in the severity and characteristics of their impairment and disability.

The study was carried out in the area covered by Oxford Regional Health Authority. Antenatal, intrapartum, neonatal factors, and the later clinical status of the two groups of children were used as the main outcome measures.

Although most maternal and antenatal characteristics were similar in the two groups, the mothers of children with a history of neonatal encephalopathy were more likely to be primigravidae (odds ratio (OR) 2·0; 95% confidence interval (CI) 1·0 to 4·3) and to have a pregnancy of greater than 41 weeks' gestation (OR 3·5; 95% CI 1·0 to 12·1). Intrapartum complications were more frequent in the neonatal encephalopathy group: meconium staining of the amniotic fluid (OR 3·5; 95% CI 1·5 to 7·8), an ominous first stage cardiotocograph (OR 10·2; 95% CI 2·9 to 36·4), with a longer median duration of abnormality (200 *v* 48 minutes). At 5 years of age those with neonatal encephalopathy were more likely to have developed spastic quadriplegia (OR 4·8; 95% CI 2·2 to 10·5), to have visual impairment (OR 3·0; 95% CI 1·0 to 8·6), and to be non-walking (OR 4·0; 95% CI 1·8 to 8·8) than those without neonatal encephalopathy.

Children with cerebral palsy who were born at term and have neonatal encephalopathy are more likely to have had signs of intrapartum asphyxia and are more likely to have a more severe form of cerebral palsy than those without a history of neonatal encephalopathy. Although this group represents only one in 10 of all cases of cerebral palsy, some of these may be obstetrically preventable.

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Cerebral palsy is used to refer to a spectrum of motor disorders of differing aetiology and clinical manifestation. A number of predisposing antepartum, intrapartum, and postnatal factors have been identified.[1] In children with cerebral palsy born after 37 weeks' gestation and who have no congenital anomaly, the neurological deficit is often attributed to an acute intrapartum hypoxic episode, possibly obstetrically preventable.[2] In some term infants who later develop cerebral palsy, however, there are pre-existing genetic or developmental factors which could have resulted in damage to the developing brain in the antenatal period, or which may have altered the vulnerability of the fetus to the normal stress of labour.[3 4]

The challenge is to identify those infants who show the effects of an acute intrapartum hypoxic-ischaemic injury as opposed to an earlier antenatal insult. Neuropathological study of infants who die may help to distinguish the two groups by identifying the age and characteristics of the lesions in the brain. In term infants acute asphyxia typically produces damage in the hippocampus, thalamus, brain stem, and anterior horn cells of the spinal cord.[5–9] Earlier antenatal ischaemic injury affecting the less mature brain tends to produce more severe damage in the white matter of the cerebral hemispheres with relative sparing of the cerebral cortex.[10 11]

In life, this distinction may not be made so clearly. Neuroimaging, such as ultrasound, may not detect mild diffuse lesions of antenatal origin and may also be unreliable soon after an acute hypoxic injury.[12] Newer techniques such as magnetic resonance imaging[13 14] and computed tomography,[15–17] though more discriminating, have not been available for routine use until recently.

We therefore have to turn to clinical observations to distinguish when brain injury might have occurred. For many years it has been assumed that intrapartum clinical signs of fetal distress such as changes on a cardiotocograph or meconium staining of amniotic fluid indicate acute hypoxic stress. It has become clear, however, that these signs may also reflect earlier antenatal ischaemic damage and this non-specificity limits their usefulness as markers of recent hypoxic events.[18] It has been suggested that signs of neonatal neurological abnormality in the first hours after birth are the most reliable indicator of a recent period of hypoxia.[19 20] This view has been adopted to the extent that the term 'hypoxic-ischaemic encephalopathy' has been used to describe infants with abnormal neonatal neurological signs. Over the last few years a consensus has evolved that, to attribute cerebral palsy to intrapartum hypoxia, the infant must be both depressed at birth and have signs of neonatal neurological abnormality.[21] It is likely that not all infants with neurological signs have had intrapartum hypoxia and a more general term such as neonatal encephalopathy is preferable.[22] In this study we have used the term neonatal encephalopathy to describe infants who have neonatal neurological dysfunction and

depression at birth. We assume that this group of infants includes those most likely to have had a recent hypoxic episode.

If this is so, children with cerebral palsy without neonatal encephalopathy might be expected to differ in a number of ways from those with encephalopathy. For example, those without neonatal encephalopathy would have: (a) a higher frequency of adverse maternal and antenatal factors (as they are more likely to have cerebral palsy of antenatal origin); (b) a lower frequency of acute events in labour such as haemorrhage and less severe signs of fetal distress (as measured by the frequency and duration of abnormalities on a cardiotocograph); and (c) a different pattern and distribution of motor and associated sensory and intellectual deficits. Those without neonatal encephalopathy (cerebral palsy assumed to be of antenatal origin) are more likely to have signs reflecting white matter damage, which predominantly affects motor tracts. Those with neonatal encephalopathy (cerebral palsy assumed to be of acute intrapartum origin) would be more likely to have evidence of extensive deep grey matter damage in addition to the white matter being affected, manifest as severe motor deficits with associated intellectual and sensory impairment.

We tested these hypotheses by comparing the antenatal histories, intrapartum events, the duration of stress in the fetus, and the clinical status of the surviving children between two groups derived from a total birth population. These two groups are: (1) children with cerebral palsy born of a singleton pregnancy after 37 completed weeks' gestation without congenital anomaly and who did not have neonatal encephalopathy (no neonatal encephalopathy group); and (2) children with cerebral palsy born of a singleton pregnancy after 37 completed weeks' gestation without congenital anomaly and who did have neonatal encephalopathy (neonatal encephalopathy group).

Methods

CHILDREN WITH CEREBRAL PALSY

Children with cerebral palsy born between 1984 and 1987 who were singleton deliveries after 37 completed weeks' gestation were identified from the Oxford regional register of early childhood impairment. This register includes children of mothers who are resident within the Oxford health region at the time of delivery. Multiple sources of ascertainment are used to compile the register and the status of children is determined at 3 and 5 years. We excluded children in whom a major congenital anomaly was diagnosed. This comprised a mixed aetiological group; some had well recognised syndromes such as the 'prune belly' syndrome, others had evidence of intrauterine infection such as congenital varicella, and some a genetically determined disorder such as X linked spastic paraplegia. In addition, children in whom there was a definite postnatal cause for cerebral palsy, such as neonatal meningitis or trauma, were excluded.

The children with cerebral palsy were divided into those with signs of neonatal encephalopathy and those without. This was based on information recorded in the neonatal case notes. We defined neonatal encephalopathy as depression at birth, based on a one minute Apgar score of less than or equal to six, followed by evidence of neonatal neurological abnormality such as lethargy, coma, impaired respiration, seizures, and/or tone changes. Infants with transient jitteriness were excluded. We did not attempt to grade or allocate a level of encephalopathy. Not all infants with seizures were allocated to the neonatal encephalopathy group. Infants who had seizures but who appeared neurologically normal between seizures (that is not lethargic or hypotonic) and who were not depressed at birth were not included in the neonatal encephalopathy group.

The Oxford regional register uses a standard system for describing children with central motor deficit.[23] On the basis of this, the clinical characteristics of the children in the study were described in terms of the distribution of tone changes, as walking or non-walking, and with or without intellectual deficit, vision loss, seizures, involuntary movement, or bulbar signs such as difficulty in swallowing.

INFORMATION ON ANTENATAL AND INTRAPARTUM EVENTS

The obstetric notes of mothers included in the study were obtained. All information about the outcome of the infant was masked by a researcher who did not participate in the review of the notes. Information was abstracted about the antenatal period and events during labour, delivery, and immediately after birth. Information was collected about the antenatal and intrapartum characteristics blind to the condition of the neonate and later development.

Gestation was estimated from accurate menstrual data or by ultrasound assessment before 20 weeks' gestation. If there was a discrepancy of greater than 14 days between the two, the ultrasound estimate was used.

FETAL HEART RATE MONITORING

At the time of birth of the subjects, continuous electronic fetal heart rate monitoring was widely used in all 10 obstetric units in the region. Some of the mothers in the study who did not have continuous electronic fetal heart rate monitoring had an admission cardiotocograph with intermittent monitoring during labour; the remainder had intermittent auscultation. It was accepted practice that if there were signs of fetal heart rate abnormality on intermittent auscultation, continuous electronic fetal heart rate monitoring was started.

The original traces were reviewed for the study and the presence and duration of ominous changes were noted. The terminology used to describe and classify the cardiotocograph was that used in the Dublin trial of continuous fetal heart rate monitoring.[24]

Table 1 Characteristics of mothers of children with cerebral palsy with and without neonatal encephalopathy (NE)

Maternal characteristic	No (%) without NE (n=100)	No (%) with NE (n=41)	Odds ratio (95% CI)
Unmarried	11 (11)	4 (10)	0·9 (0·3 to 2·9)
Maternal disease	12 (12)	3 (7)	0·6 (0·2 to 2·2)
Primigravida	34 (34)	21 (51)	2·0 (1·0 to 4·3)
Recurrent abortion	2 (2)	1 (2)	1·2 (0·1 to 13·9)
Poor obstetric history	5 (5)	3 (7)	1·5 (0·3 to 6·6)
Previous preterm labour	2 (2)	2 (5)	2·5 (0·4 to 18·5)
Maternal smoking	25 (25)	7 (17)	0·6 (0·2 to 1·6)
Mean age (years)	26·5	26·5	0 (−1·83 to 1·83)*
Mean length of menstrual cycle (days)	30·8	29·1	1·8 (−1·1 to 4·7)*

*Difference of means (95% confidence intervals).

Table 2 Antenatal factors in mothers of children with cerebral palsy with and without neonatal encephalopathy (NE)

Antenatal factor	No (%) without NE (n=100)	No (%) with NE (n=41)	Odds ratio (95% CI)
Antenatal infection	4 (4)	2 (5)	1·2 (0·2 to 7·0)
Premature rupture of membranes	1 (1)	2 (5)	5·1 (0·5 to 57·6)
Pre-eclampsia	33 (33)	13 (32)	0·9 (0·4 to 2·1)
Severe pre-eclampsia	8 (8)	3 (7)	0·9 (0·2 to 3·6)
Antepartum haemorrhage	3 (3)	1 (2)	0·8 (0·1 to 8·0)
Previous infertility	10 (10)	3 (7)	0·7 (0·2 to 2·7)
Induced conception	4 (4)	2 (5)	1·2 (0·2 to 6·9)
Raised maternal serum α fetoprotein	3/54 (6)	1/23 (4)	0·8 (0·1 to 8·0)
Polyhydramnios	2 (2)	1 (2)	1·2 (0·1 to 13·9)
Oligohydramnios	3 (3)	1 (2)	0·8 (0·1 to 8·0)
Reduced fetal movement	11 (11)	4 (10)	0·9 (0·3 to 2·9)
Complicated antenatal course	51 (51)	20 (49)	0·9 (0·4 to 1·9)

Table 3 Intrapartum factors in mothers of children with and without neonatal encephalopathy (NE)

Intrapartum factor	No (%) without NE (n=100)	No (%) with NE (n=41)	Odds ratio (95% CI)
Breech presentation	4 (4)	1 (2)	0·6 (0·1 to 5·5)
Pregnancy duration ≥42 weeks' gestation	5 (5)	6 (15)	3·5 (1·0 to 12·1)
Induction of labour	24 (24)	17 (42)	2·2 (1·0 to 4·9)
Induction of labour in primigravidae	9/34 (27)	12/21 (57)	3·7 (1·2 to 11·7)
Augmentation of labour	13 (13)	6 (15)	1·2 (0·4 to 3·3)
First stage >12 hours	13/84 (16)	7/35 (20)	1·4 (0·5 to 3·8)
Second stage >2 hours	6/82 (7)	8/31 (26)	4·4 (1·4 to 14·0)
Meconium stained amniotic fluid	17 (17)	17 (42)	3·5 (1·5 to 7·8)
Haemorrhage in labour	2 (2)	1 (2)	1·2 (0·1 to 13·9)
Spontaneous vaginal delivery	66 (66)	10 (24)	0·2 (0·1 to 0·4)
Forceps delivery	16 (16)	16 (39)	3·4 (1·5 to 7·7)
Breech delivery	1 (1)	1 (2)	2·5 (0·2 to 40·5)
All caesarean sections	16 (16)	14 (34)	2·7 (1·2 to 6·3)
All emergency caesarean sections	9 (9)	14 (34)	5·2 (2·1 to 13·4)
All emergency caesarean sections in labour	4 (4)	10 (24)	7·7 (2·3 to 26·4)

ETHICS APPROVAL

Approval for the study was obtained from the ethics committees of all eight health districts in the Oxford region.

STATISTICAL ANALYSIS

Analysis of categorical data was performed by comparison of characteristics of those with neonatal encephalopathy and those without neonatal encephalopathy expressed as odds ratios and their 95% confidence intervals. Continuous data were analysed comparing the difference between means and 95% confidence intervals for data with a normal distribution and the Mann-Whitney test for non-normally distributed data.

Results

There were 339 children with cerebral palsy on the regional register who were born between 1984 and 1987 to mothers resident in the Oxford region. Of these 27 (8%) had a postnatal cause for their disability and 123 (36%) were born before 37 completed weeks' gestation. Of the remainder, 42 (22%) had evidence of major congenital anomaly and two were term multiple births. The remaining 145 children were eligible for inclusion in the study. There was insufficient information in the case notes of four, three of these being born outside the region, and these were excluded.

Of the 141 children with cerebral palsy in the study, 100 (71%) had no sign of neonatal encephalopathy and 41 (29%) had evidence of neonatal encephalopathy.

MATERNAL AND ANTENATAL CHARACTERISTICS

Existing maternal disease occurred more often in the group without neonatal encephalopathy and previous preterm labour more often in the neonatal encephalopathy group; numbers were small, however, and confidence intervals wide (table 1). The only maternal factor which differed at the 5% level between the two groups was primigravidity, which was more frequent in the neonatal encephalopathy group (odds ratio (OR) 2·0; 95% confidence interval (CI) 1·0 to 4·3).

Overall, half of the mothers of infants without neonatal encephalopathy (51/100) and mothers of infants with neonatal encephalopathy (20/41) had one or more complicating antenatal factors (table 2). The frequency of other individual complicating antenatal factors did not differ at the 5% level between the two groups.

INTRAPARTUM CHARACTERISTICS

Pregnancy which continued after 41 completed weeks' was more frequent in the neonatal encephalopathy group (OR 3·5; 95% CI 1·0 to 12·1) (table 3), particularly in primigravidae (OR 11·0; 95% CI 1·2 to 102·5).

Induction of labour (OR 2·2; 95% CI 1·0 to 4·9), particularly in primigravidae (OR 3·7; 95% CI 1·2 to 11·7), was more frequent in the neonatal encephalopathy group. A second stage of labour exceeding two hours (OR 4·4; 95% CI 1·4 to 14·0) and meconium staining of the amniotic fluid were all more frequent in the neonatal encephalopathy group (OR 3·5; 95% CI 1·5 to 7·8).

Seven infants without neonatal encephalopathy were delivered by elective caesarean section compared with none in the neonatal encephalopathy group; the indication to perform five of these seven was a previous caesarean section. Delivery by forceps or emergency caesarean section was more frequent in the neonatal encephalopathy group (OR 3·4; 95% CI 1·5 to 7·7), (OR 7·7; 95% CI 2·3 to 26·4) (table 3).

A total of 48% of mothers of infants without neonatal encephalopathy and 66% of mothers of infants with neonatal encephalopathy had a cardiotocograph available for analysis (table 4). Eight per cent of the group without neonatal encephalopathy and 48% of the neonatal encephalopathy group had signs of fetal distress with an increased likelihood of ominous

Table 4 Findings on cardiotocograph (CTG) in mothers of children with cerebral palsy with and without neonatal encephalopathy (NE)

CTG finding	No (%) without NE (n=100)	No (%) with NE (n=41)	Odds ratio (95% CI)
CTG performed	63 (63)	31 (76)	1·8 (0·8 to 4·1)
CTG missing	15 (24)	4 (13)	0·6 (0·2 to 2·0)
Ominous first stage CTG	4/48 (8)	13/27 (48)	10·2 (2·9 to 36·4)
Ominous second stage CTG	19/45 (42)	21/25 (84)	7·2 (2·1 to 24·4)
Median (range) duration of first stage abnormality (min)	48·5 (38–287)	200·0 (15–480)	0·3†
Median (range) duration of abnormal total CTG (min)*	38·0 (8–287)	100·0 (12–480)	0·003†

*Based on ominous CTG in either or both the first and second stages of labour.
†Mann-Whitney (p value).

Table 5 Outcome at 5 years for those with and without neonatal encephalopathy (NE)

Outcome at 5 years	No (%) without NE (n=100)	No (%) with NE (n=41)	Odds ratio (95% CI)
Quadriplegia	23 (23)	24 (58)	4·8 (2·2 to 10·5)
Hemiplegia	39 (39)	7 (17)	0·3 (0·1 to 0·8)
Diplegia	9 (9)	3 (7)	0·8 (0·2 to 3·1)
Hypotonia/varying tone	12 (12)	3 (7)	0·6 (0·2 to 2·2)
Other tone change	17 (17)	4 (10)	0·5 (0·2 to 1·7)
No independent walking	23 (24)	21 (55)	4·0 (1·8 to 8·8)
No useful vision	8 (9)	8 (22)	3·0 (1·0 to 8·6)
Severe intellectual delay	22 (23)	15 (43)	2·5 (1·1 to 5·7)
Involuntary movements	17 (17)	11 (27)	1·8 (0·8 to 4·3)
Swallowing difficulty	20 (20)	18 (44)	3·1 (1·4 to 6·9)

changes on the cardiotocograph in both the first (OR 10·2; 95% CI 2·9 to 36·4) and second (OR 7·2; 95% CI 2·1 to 24·4) stage on cardiotocograph in the neonatal encephalopathy group. The duration of ominous changes for the total labour was longer in the neonatal encephalopathy group than in the group without neonatal encephalopathy (median duration without neonatal encephalopathy 38 minutes, with neonatal encephalopathy 100 minutes; Mann-Whitney, p=0·003).

NEONATAL CONDITION

By definition, all infants who developed neonatal encephalopathy had a one minute Apgar score of less than six, but among those without neonatal encephalopathy 23 (23%) had a one minute Apgar score of less than six but did not go on to demonstrate neonatal neurological abnormality. The median Apgar scores at one and five minutes for those with neonatal encephalopathy were two and five respectively, whereas for those without neonatal encephalopathy the median Apgar scores at one and five minutes were nine and 10 respectively (Mann-Whitney; p<0·0001).

Only 15 infants in the study had umbilical cord gas analysis; all of the 10 with neonatal encephalopathy had an arterial pH of 7·2 or less, as did three of the five without neonatal encephalopathy; and arterial base deficit of −12·0 was found in all 10 of those with neonatal encephalopathy and two of four without neonatal encephalopathy. Among the infants with neonatal encephalopathy, 29% had evidence of renal failure and 10% had evidence of myocardial ischaemia. None of the group without neonatal encephalopathy had either renal failure or myocardial ischaemia. Eighteen (18%) of the infants with neonatal encephalopathy and eight (20%) of those with neonatal encephalopathy had a birth weight less than or equal to the 10th centile (OR 1·1; 95% CI 0·4 to 2·8) and 19 (19%) of those without neonatal encephalopathy and nine (22%) with neonatal encephalopathy had a head circumference less than or equal to the 10th centile (OR 1·2; 95% CI 0·5 to 2·9). The proportion of infants whose birth weight or head circumference was less than or equal to the 10th centile did not differ between the two groups.

Among the infants without neonatal encephalopathy were 13 who had neonatal seizures but no other signs of encephalopathy. Two had ominous cardiotocograph changes but all had an Apgar score at five minutes between eight and 10. Two of these infants were delivered by elective caesarean section.

TYPES OF CEREBRAL PALSY

At 5 years of age children with neonatal encephalopathy were more likely than those without neonatal encephalopathy to have quadriplegia (OR 4·8; 95% CI 2·2 to 10·5) and were less likely to have hemiplegia (OR 0·3; 95% CI 0·1 to 0·8) (table 5). The motor disability seemed more severe in the neonatal encephalopathy group with a higher proportion of children unable to walk independently at 5 years (OR 4·0; 95% CI 1·8 to 8·8). There was an increased frequency among those with neonatal encephalopathy of associated impairments; severe visual impairment (OR 3·0; 95% CI 1·0 to 8·6), severe intellectual delay (OR 2·5; 95% CI 1·1 to 5·7), and swallowing difficulty (OR 3·1; 95% CI 1·4 to 6·9). Although the frequency of involuntary movement was increased in the neonatal encephalopathy group this was not statistically significant at the 5% level (OR 1·8; 95% CI 0·8 to 4·3).

Discussion

In recent years there has been a considerable change in our understanding of the origin of cerebral palsy. The earlier view that most cerebral palsy was attributable to intrapartum hypoxia, much of which was obstetrically preventable, has been supplanted by a counter-view that 'birth asphyxia is a rare cause of cerebral palsy'.[25]

Although it is likely that in some infants who develop cerebral palsy, injury has been acquired around the time of birth, in others the insult occurs antenatally and in many the brain abnormality may have evolved over a long period of time. These concepts of the origins of fetal and neonatal brain injury are based on neuropathological,[5–11 26] radiological,[27–30] and epidemiological[31–33] evidence. It would be helpful to have a clearer understanding, according to the time of hypoxic insult, of the differences in the clinical characteristics of infants who later develop cerebral palsy. This would not only help to identify preventable factors, but also in deciding which infants may benefit from treatment which may reduce the secondary cell damage after acute intrapartum hypoxia.[34]

We used the clinical finding of depression at birth followed by neonatal neurological abnormality as the most reliable marker of an acute episode of intrapartum hypoxia. This finding was used as the basis for differentiating those children with a predominantly antenatal origin of cerebral palsy and those with a primarily intrapartum origin. We recognised, however, that this division may be rather crude. It is possible, for example, that within the group of children with cerebral palsy with neonatal encephalopathy there might be some whose encephalopathic signs reflected a longstanding neurological disorder. Further, it is possible that a more critical evaluation of neurological states in the first few days of life might help to identify different aetiological subgroups. For example, we were aware of a group of infants who had neonatal seizures but did not show any other signs of encephalopathy and who were not depressed at birth. This group of infants appeared to be aetiologically distinct from those with changes in consciousness and muscle tone between seizures. It was also of interest that in nine of the 13 infants in this group seizures began before the age of 48 hours. In the past it has been suggested that seizures which start in the first 48 hours of life are those most likely to reflect intrapartum hypoxia.[35] A large systematic study of infants with clinical signs of neurological dysfunction in the neonatal period together with neuroimaging would clarify these issues.

Many infants who later have signs of cerebral palsy do not appear to have abnormal neurological signs in the neonatal period. If neonatal encephalopathy is considered to be a condition of term infants, then only 12% (41/339) of all children with cerebral palsy born to residents of the area in the four birth years studied had evidence of neonatal encephalopathy. This once again emphasises the need to look at aetiological factors which may influence earlier intrauterine cerebral development, not just events related to labour, in the majority of children with cerebral palsy.

The search for clinical markers of adverse antenatal factors in populations of children with cerebral palsy, however, is fairly unrewarding. Although previous work has shown an increased risk of pre-eclampsia and intrauterine growth retardation among mothers of term infants with cerebral palsy compared with a control population,[36] this risk does not appear to be greater in the group without neonatal encephalopathy as we had hypothesised. Apart from a lower frequency of primigravidae, we were unable to find antenatal characteristics in the group without neonatal encephalopathy which differentiated these infants from the group with neonatal encephalopathy. It is likely that more sophisticated fetal neuroimaging techniques are needed to detect signs of antenatal ischaemic damage, whether focal lesions or the more diffuse white matter lesions described with intrauterine hypoxia.[10]

It was clear, however, that the clinical intrapartum course was different in the infants with and without neonatal encephalopathy. There was an increased frequency of induction of labour and of pregnancies of greater than 41 weeks' gestation among the mothers of infants who went on to develop neonatal encephalopathy. In addition, prolonged labour and signs of prolonged severe distress were more frequent in the neonatal encephalopathy group. This cluster of adverse intrapartum events were also described by Minchom *et al* in infants who developed early neonatal seizures.[37] Such associations do not, of course, imply a causal link.

This group (neonatal encephalopathy), however, includes those cases of cerebral palsy which are most likely to be obstetrically preventable. For example, it could be argued that reduction in the duration of fetal distress by expediting delivery might have altered the outcome. The greater frequency of fetal distress among those with neonatal encephalopathy, however, could equally reflect longstanding neurological dysfunction which is not, at present, obstetrically preventable.

The challenge is to find reliable ways of identifying the infant who is neurologically abnormal before or during labour. Several potential methods are being examined; for example, the use of near infrared spectroscopy in labour and antenatal biophysical assessment.[38–42] Using the latter, abnormal in utero behavioural states can be shown in some infants who later show abnormal neonatal neurological function. Neonatal evidence of damage to other organs may help to identify a recent acute hypoxic event. Ischaemic damage to the kidneys or myocardium in an infant with neonatal encephalopathy who subsequently has cerebral palsy provides supporting evidence of an intrapartum origin to the later neurological deficit.[43–45]

It has been previously suggested that clinical subgroups of cerebral palsy may have different aetiologies.[46] Our hypothesis that children with cerebral palsy who have a history of neonatal encephalopathy have more extensive motor impairment and associated sensory and intellectual disability was sustained. Further exploration of the relation between the neuropathology of the injury, the later clinical manifestations, and the appearance of the brain on neuroimaging may be useful in understanding the time of injury and hence in identifying those insults which are most likely to be preventable.

In conclusion, we consider that children with cerebral palsy and a history of neonatal encephalopathy (depression at birth followed by neonatal neurological dysfunction) are more likely than those without neonatal encephalopathy to have: (a) evidence of prolonged fetal distress as measured by the duration of cardiotocograph changes; (b) evidence of other organ damage; and (c) a severe and extensive form of motor deficit with intellectual and sensory involvement.

We suggest that this cluster of clinical signs indicates that the aetiology is likely to be an acute intrapartum insult, preventable or non-preventable. It follows that in the absence of this cluster of signs, intrapartum asphyxia is

unlikely to be the cause of a subsequent neurological deficit.

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