Cerebral Palsy- An Expensive Enigma

Rhona Mahony
National Maternity Hospital

“A group of permanent disorders of the development of movement and posture, causing activity limitation that are not attributed to progressive disturbances that occurred in the developing fetal or infant brain”

Rosenbaum et al 2006
Two thirds of cerebral palsy arises in 97% of singletons born at or after 35 weeks gestation.

Little WJ. (1862) “On the influence of abnormal parturition, difficult labours, premature birth and asphyxia neonatorum on the mental and physical condition of the child.”

Freud. (1897) “Infantile cerebrallhmun”

The major cause of cerebral palsy and mental retardation was intrapartum "brain damage"
Asphyxia

- Intrapartum hypoxic ischaemia is characterised by progressive hypoxaemia and hypercapnoea accompanied by the progressive development of metabolic acidosis.
- Ultimately leads to cellular damage and death and damages the neonatal brain.
- There were two main models described: acute profound and prolonged partial injury.

Criteria defining an acute intrauterine asphyxic event

- Evidence of a sentinel event
- Severe metabolic acidosis (arterial pH < 7.00, base deficit > 12 mmol/L)
- Early onset of moderate to severe neonatal encephalopathy in infants greater than 34 weeks
- Apgar score 0-3 for greater than 5 mins
- Imaging studies showing involvement of the thalamus, basal ganglia, putamen, brainstem
- Development of extrapyramidal neurological abnormalities
- May or may not have multiorgan dysfunction

International Cerebral Palsy Task Force MacLennan.
1999 BMJ 319,1054
Criteria defining a prolonged partial asphyxic intrauterine event

- Development of a nonreassuring fetal heart rate pattern where an assuring pattern has been present. (weak correlation)
- Severe metabolic acidosis (arterial pH < 7.00, base deficit > 12 mmol/L)
- Early onset of moderate to severe neonatal encephalopathy in infants greater than 34 weeks
- Apgar score 0-3 for greater than 5 mins
- Imaging studies showing watershed-type lesions in cerebral cortex
- Development of quadriplegia or dyskinesia
- Usually has multiorgan dysfunction

International Cerebral Palsy Task Force MacLennan. 1999 BMJ 319:1054

Brain MRI Neonatal HIE

Conditions causing neonatal depression and /or neonatal encephalopathy that mimic “perinatal asphyxia”

- Neonatal sepsis
- Chorionamnionitis without documented neonatal sepsis
- Congenital infection – TORCH
- Congenital abnormalities of brain
- Neuronal migration disorders
- Congenital myotonic disorders including congenital myasthenia gravis
- Metabolic conditions causing lactic acidosis
- Thrombophilic conditions-Protein S and C, Factor V Leiden deficiency, anticardiolipin antibodies etc.
- Hypoglycaemia/calcaemia/magnesemia.

What is the contribution of Asphyxia to Cerebral Palsy in Term Infants?

The Cerebral Palsy Debate

- In the past three decades many epidemiological and clinical studies have suggested that most cases of CP are not related to intrapartum asphyxia.

- Estimated that approximately 10% -20% of cases of CP are attributable to events in labour and delivery.
Origin and timing of brain lesions in term infants with neonatal encephalopathy.

- 90% of infants with NNE, seizures or both had evidence of acute perinatally acquired insults.
- Low rate of established brain injury acquired before birth


<table>
<thead>
<tr>
<th>Contribution of Labour and Delivery to Cerebral Palsy</th>
<th>CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecedents of cerebral palsy and perinatal death in term and late preterm singletons.</td>
<td>Small</td>
</tr>
<tr>
<td>How much of encephalopathy is due to birth asphyxia? - How often do perinatal events at full term cause cerebral palsy?</td>
<td>0.55/1,000</td>
</tr>
<tr>
<td>How much of encephalopathy is due to birth asphyxia? - How much of encephalopathy is due to birth asphyxia?</td>
<td>Small</td>
</tr>
<tr>
<td>Assessing the contribution of birth asphyxia to cerebral palsy in term singletons.</td>
<td>20%</td>
</tr>
<tr>
<td>Relationship of intrapartum and delivery room events to long-term neurologic outcome.</td>
<td>Small</td>
</tr>
</tbody>
</table>

The association of cerebral palsy with birth asphyxia: a definitional quandary

John H ElKhonsy, Karin B Nelson

11/4/2014
Antecedents of Cerebral Palsy and Perinatal Death in Term and Late Preterm Singletons

Sarah Mehmet, MRCOG, FFPM, Eve Blyth, MD, NAFA, Nadia Badawi, FRCPCH, FFPM, John Korch, FRCPCH, and Harris N. Nelson, MD

OBJECTIVE: To examine the antecedents of cerebral palsy and perinatal death in singleton born at or after 37 weeks of gestation, we identified the birth and perinatal risk factors and HIE/Encephalopathy.

METHODS: From a total population of 1,000 singleton born at or after 37 weeks of gestation, we identified the birth and cerebral palsy and HIE in a matched control group. 184 maternal deaths, and 72 intrapartum stillbirths. (All deaths in selected birth years). Neonatal death and cerebral palsy were categorized as: -ecephalopathy, or after neonatal encephalopathy, or after neonatal encephalopathy considered hypoxic-ischemic, -HIE/Encephalopathy- considered hypoxic-ischemic, -Ventricular Enlargement - Neonatal death, Inflammation, Fetal Growth restriction, and Birth defects identified by age 6 years in each of these outcomes and by intrapartum stillbirths.

RESULTS: The birth-related cerebral palsy also potentially asphyxial birth events or inflammation were significantly increased in infants with CP (OR 1.8, 95% confidence interval 1.1-3.0).

Encephalopathy 66.5% 54%
Encephalopathy 12.4% 24%
HIE/Encephalopathy 21.2 22%

Risk Factors for CP following HIE

- Asphyxial Event 22%
- Inflammation 12%
- Fetal Growth restriction 15%
- Birth Defects 26%

In 40% of cases of CP no risk factor identified
Birth defects recognized in >50% of cases of CP without HIE

Significant proportion of CP and perinatal death associated with antenatal maldevelopment.

Conundrum

A template for defining a causal relation between acute intrapartum events and cerebral palsy: international consensus statement

International Cerebral Palsy Task Force, BMJ 319: 1054, 1999

"Epidemiologic studies suggest that in about 90% of cases intrapartum hypoxia could not be the cause of cerebral palsy."

Origin and timing of brain lesions in term infants with neonatal encephalopathy

"Although our data cannot exclude the possibility that antenatal and genetic factors might predispose some infants to perinatal brain injury, our data strongly suggest that events in the immediate perinatal period are most important in neonatal brain injury."
Cerebral palsy following neonatal hypoxic seizures in singleton term infants: the influence of parity.

<table>
<thead>
<tr>
<th></th>
<th>Primips 31,729</th>
<th>Multips 46,109</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral Palsy</td>
<td>12 (0.4%)</td>
<td>2 (0.04%)</td>
<td>0.0016</td>
</tr>
<tr>
<td>Developmental Delay</td>
<td>4 (0.12%)</td>
<td>3 (0.065%)</td>
<td>0.6189</td>
</tr>
<tr>
<td>Neurological Impairment</td>
<td>16 (0.55%)</td>
<td>5 (0.1%)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

Overall incidence of cerebral palsy and developmental delay (combined as neurological impairment) subsequent to seizures of presumed asphyxial etiology and analysed by parity.

Conclusion

- The incidence of unexplained early onset neonatal seizures was 10 times higher in primiparas compared with multiparas and was associated with a 10-fold increase in the incidence of cerebral palsy in primiparas (0.4% vs. 0.04%).
Medical Practitioners and the Courts: a case of mutual misunderstanding

The Dunne Case
<table>
<thead>
<tr>
<th>Transaction Date</th>
<th>2008 (€m)</th>
<th>2009 (€m)</th>
<th>2010 (€m)</th>
<th>2011 (€m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>41.2</td>
<td>53</td>
<td>81</td>
<td>97.8</td>
</tr>
</tbody>
</table>

Special Court Edition
Temporal and demographic trends in cerebral palsy - fact or fiction

“No data exist in the entire medical literature to demonstrate that intervention based on any single or combination of FHR patterns reduces the risk of CP”

Clark and Hankins Am J Obstet Gynecol 2003;188:628-33

Temporal and demographic trends in cerebral palsy - fact or fiction

“A test leading to an unnecessary major abdominal surgery in more than 95% of cases should be regarded by the medical community as absurd at best”

Clark and Hankins Am J Obstet Gynecol 2003;188:628-33

Human Error
System Failure
Wilful Misconduct
Moderate Hypothermia to Treat Perinatal Asphyxial Encephalopathy

Denis V. Azzopardi, F.R.C.P.C.H., Brenda Strohm, R.G.N.,
A. David Edwards, F.Med.Sci., Leigh Dyet, M.B., B.S., Ph.D.,
Henry L. Halliday, F.R.C.P.H., Edmund Jozefczak, M.Sc.,
Emma Porter, M.R.C.P.C.H., Marianne Thoresen, M.D., Ph.D.,
Total Body Cooling
The placenta is a fetal organ expressing a fetal genotype

Cerebral Palsy: Placental Possibilities

Sentinel events
Utero-placental Insufficiency—Decidual Vasculopathy
Fetal vasculopathy
Primary Placental Lesions—Perivillous Fibrin Deposition
Chronic Villitis
Choriomionitis
Abnormal intrauterine environment—Nucleated RBC
Chorangiosis