

The Causation of Cerebral Palsy is Evolving

During the past year the leading American paediatric neurologist, Karin B. Nelson, has written two seminal articles^{1,2} on the causation of cerebral palsy. Her primary conclusion is that electronic fetal monitoring (EFM) has not reduced the rates of cerebral palsy. One graph illustration¹ shows that over the period 1980 – 2009 the rates of cerebral palsy remained unchanged 2 per 1000 births despite the caesarean section increasing to over 30% (fivefold rise). Cerebral palsy is an important cause of physical disability in children and is commonly accompanied by cognitive deficits and epilepsy. The expectation was that within a short period of time the application of EFM monitoring would virtually eliminate cerebral palsy.

Nelson states that the current hypothesis on the causation of cerebral palsy is blinkered and that a new approach is needed. The challenge is how to recalibrate our current hypotheses in order that better preventive measures and therapies can be produced.

The commonly held theory is that cerebral palsy is caused by lack of oxygen during labour. It is believed that this lack of oxygen can and should be detected by electronic fetal monitoring. When there is an abnormal trace, a caesarean section or operative delivery should be performed. Some authors³ have emphasised the urgent nature of the procedure, stating that in acute asphyxia brain damage begins to develop after 10 minutes. The belief is that early detection and prompt action can prevent infants developing cerebral palsy. It hasn't worked. Since the introduction of electronic fetal monitoring the number of caesarean sections has risen sharply but there hasn't been a corresponding reduction in the numbers of children with cerebral palsy. This is an important issue for obstetricians and neonatologists. If our working model on the causation of cerebral palsy is incomplete, preventive strategies will be hampered. Nelson describes in some detail the Dublin fetal monitoring undertaken 25 years ago⁴. This large study randomised 13,079 low risk women to EFM or intermittent auscultation during labour. At 4 years follow-up the rates of cerebral palsy were not lower in the children who were monitored electronically. There was however a 55% reduction in neonatal seizures in the EFM group. The authors, at the time, postulated that the seizures prevented by the EFM monitoring might not have been caused by intrapartum asphyxia. The paper concluded that developments in perinatal care have greatly reduced the risk of death but that cerebral palsy rates had changed little over the previous 30 years.

There appears to be an agreement that EFM is an overly sensitive tool and a poor indicator of fetal neurological status³. However it is argued that once the outcome is known the EFM tracing is often the

only tool available to make a temporal reconstruction of any fetal decline.

Nelson maintains that EFM hasn't worked because it was based on a number of erroneous assumptions. When it was first introduced to identify fetal asphyxia during labour, it was expected that timely intervention would prevent cerebral palsy. It hasn't. On the other hand, it has led to a significant increase in the number of caesarean sections. Nelson points out that the abnormalities on EFM have a false positive rate of 99.8%, so most findings are false positive results.

Most cases of cerebral palsy in term babies are not caused by asphyxia during labour. The alternative causes are congenital malformations, fetal growth restriction, infection, placental inflammatory processes, and other unknown factors. There is an emerging focus on aberrant fetal growth with abnormal neurological outcome. In one large population based study, 91.5% of term infants with cerebral palsy had no recognized asphyxia event during the birth. Another report concluded that birth asphyxia has a role in approximately 10% of cases with cerebral palsy. The other 90% of cerebral palsy cases are not related to intrapartum events. There are of course readily recognizable obstetric sentinel events that are associated with birth asphyxia such as cord prolapse, uterine rupture, placental abruption, and fetal-maternal bleed. EFM is important in identifying these perinatal events.

The role of the placenta in the causation of cerebral palsy is gaining recognition. It has been coined 'the black box of the pregnancy'. The 2 major subcategories of placental inflammation are chorioamnionitis/ funisitis caused by infection and chronic villitis caused by an immunological response related to the breakdown of maternal-fetal tolerance⁵. Both subcategories are associated with an increased risk of neonatal encephalopathy. The rate of chronic villitis increases with gestational age. Another important condition that originates in the placenta is fetal growth restriction. Emboli from the placenta near the time of delivery have been suggested as a cause of neonatal stroke.

It is accepted that infants who suffer from hypoxia during labour develop neonatal encephalopathy prior to the subsequent evolution of cerebral palsy. The encephalopathy occurs in the first hours and days after birth. The features are difficulty in initiating respiration, abnormal level of consciousness, hypotonia, diminished reflex responses, seizures, and acidosis. Therapeutic hypothermia is a promising treatment for infants with neonatal encephalopathy. It reduces the risk of cerebral palsy by 12%. The important question is why the other infants with encephalopathy do not benefit. It suggests that many infants have a different underlying aetiology. It raises the question whether therapeutic hypothermia should be administered to these infants. The difficulty is in trying to identify the non-responders prior to starting cooling.

In order to significantly reduce the rates of cerebral palsy the underlying pathophysiology needs to be intensely studied and researched. Understanding the different causations will serve a platform for new therapies. The study of infants with neonatal encephalopathy who don't respond to therapeutic

hypothermia may be a useful place to start.

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Editor

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