

## New Research and Understanding of the Causes of Cerebral Palsy - Towards Future Prevention

Presented by Professor Alastair MacLennan

Cerebral palsy is a global health issue. In 2008, 337,000 children were born with cerebral palsy worldwide. Findings from an Access Economics analysis, suggest the financial and lost wellbeing cost of cerebral palsy (CP) in Australia alone in 2008 was \$3.74 billion. This was made up of \$1.34 billion (0.13% of GDP) in financial costs and \$2.4 billion for costs associated with lost wellbeing. With a major proportion of these costs borne by the individual and their families there is an imperative to alleviate these costs and their impact on the medical, health and legal systems.

### What is cerebral palsy?

Cerebral palsy results from damage to the developing brain, usually before birth and is a permanent, physical condition that affects movement. More than 65% of people with cerebral palsy will require a wheelchair and 25% of children will be unable to walk. People with cerebral palsy may have seizures and other impairments affecting their speech, vision, hearing or intellect.

Cerebral palsy often presents when children fail to reach movement milestones.

### What are the contributing factors that cause cerebral palsy?

Evidence based risk factors can be genetic or environmental.

#### Maternal Risk Factors

Maternal age  
Maternal nutrition  
Maternal race  
Susceptibility to infection  
Thrombophilia  
Hypothyroidism

#### Obstetric and Foetal Risk

Preterm delivery  
Intra uterine growth restriction  
Acute or chronic hypoxia  
Multiple pregnancies  
Infection  
Antepartum Haemorrhage  
Tight nuchal cord

#### Neonatal Risk Factors

Early life brain injury  
Genetic disorder  
Infection  
Near drowning

### Myth

Most cases of cerebral palsy are due to problems in labour e.g. foetal distress in labour, birth asphyxia or birth trauma.

### Reality

- Most cases of cerebral palsy start during pregnancy.
- Most cerebral palsy infants are born following an uncomplicated delivery.
- To date, there are no proven interventions to prevent cerebral palsy in term infants. These include elective caesarean section, quicker emergency caesarean, induction of labour, electronic foetal monitoring and avoidance of instrumental delivery.

*MacLennan, Nelson, Hankins, Speer. JAMA 2005;294:1688-90*

## The 7 myths of cerebral palsy

1. CP is usually due to acute intrapartum hypoxia.
2. Meconium, CTG changes, low Apgars and neonatal encephalopathy = acute hypoxia.
3. Electronic Foetal Monitoring can prevent CP.
4. Reversible neuropathology can be seen on a CTG.
5. "Immediate" or fast delivery is always possible.
6. Earlier delivery in labour will prevent CP.
7. MRI can show the cause and intrapartum timing.

**ALL INCORRECT!**

## The South Australian Cerebral Palsy Research Group

This research group is a multidisciplinary team led by Professor Alastair MacLennan, who is Head of the Discipline of Obstetrics and Gynaecology in the School of Paediatrics and Reproductive Health at the University of Adelaide. The group is based at the Women's and Children's Hospital, Adelaide and is a collaboration between The University of Adelaide, and other institutions, including several of the Women's and Children's Hospital Departments, the South Australian Cerebral Palsy Register and the SA Department of Health. Collaboration now occurs with CP groups in all states, especially NSW.

Professor MacLennan and his team have been investigating whether genetic susceptibility factors and adverse environmental triggers interact during pregnancy to contribute to the neuropathology of cerebral palsy. It has been the largest study to date where they have used blood spots taken from stored baby heel prick tests, studied the DNA within them, and then correlated that data from CP, birth defects and pregnancy outcome registers.

This study has led to three new concepts in cerebral palsy causal pathways. They are:

### *Genetic clotting disorders*

Inherited mutations increase the risk of blood clotting in the placenta; this clot travels directly to the developing baby's brain and causes a foetal stroke which causes hemiplegic cerebral palsy.

### *Abnormal genetic immune responses*

This is where the immune system response is too strong and self inflicts damage to developing brain tissue, or the complete opposite where the response is not strong enough and fails to fight off infection.

### *Viral infection*

Many viruses are capable of causing brain damage; they can cross the placenta and infect the baby during pregnancy.

**Interactions between these factors can also occur, multiplying the risk of cerebral palsy.**



## Research Directions

To further test these new factors, a wider study has been recommenced involving an Australia wide survey of CP cases/mothers vs controls/mothers. Mouth swabs are being taken to collect DNA and a survey is being undertaken to collect extensive epidemiological data. Where possible neonatal blood spots will be used for viral detection.

Future possible applications of this research include:

- Early detection of maternal and foetal genetic vulnerability
- Intervention possibilities:
  - Genetic screening of germ cells, embryo, foetus
  - Gene therapy
  - Anti-cytokine agents
  - Thrombolytics
  - Avoidance of infection
  - Immunisation against viral infections

**It has already been discovered that magnesium sulphate for women at risk of preterm birth reduces cerebral palsy risk.**

*Doyle et al, Cochrane Review 2009*

## Have you the cheek to help cerebral palsy research and help find other possibilities?

Professor MacLennan is looking for participants to help in his research. The team is seeking support from mothers with children aged between 5 and 18 years who are Caucasian and do NOT have cerebral palsy to assist in a trial. The mother would be required to complete a simple survey and provide mouth swabs from herself and one child. Kits will be sent to the participant's home and results from the final study can be forwarded if desired. Cerebral palsy occurs in all ethnic groups, however for statistical and scientific reasons, it is only feasible for us to study Caucasian families in this particular study.

For further information or to enrol

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**Call** 1800 800 254

**SMS** your name and address details to 0439 201 795 **or**

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