

BREAK THROUGH



Cerebral Palsy
ALLIANCE
RESEARCH FOUNDATION

THE RESEARCH FOUNDATION OF CEREBRAL PALSY ALLIANCE NEWSLETTER – NOVEMBER 2012

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FROM THE Chairman

Welcome to our final edition of Breakthrough for 2012.

In the seven years since the establishment of the Research Foundation of Cerebral Palsy Alliance, there have been many important steps made towards finding the answers about cerebral palsy.

Led by internationally renowned neonatologist, Professor Nadia Badawi, the Research Foundation has earned an international reputation as a world leader in cerebral palsy research. Professor Badawi not only has extensive experience working in the field of cerebral palsy, she has also authored some of the most cited cerebral palsy research papers in the world.

To date, the Research Foundation has supported more than 40 Australian and international research projects including an important study investigating the link between a common virus, cytomegalovirus (CMV) and cerebral palsy (page 4). The work of these researchers is not only improving our understanding of and the

way we treat this complex condition, it's also giving hope to people living with cerebral palsy and their families that life-changing breakthroughs are possible.

In particular, two recent research discoveries, magnesium sulphate and hypothermia, are fueling this hope. There is now scientific evidence to support both these treatments as preventative strategies for babies at risk of developing cerebral palsy. The impact of these exciting breakthroughs is now evident in official figures obtained from the Australian Cerebral Palsy Register, which reveal a decline in the incidence of cerebral palsy for the first time in 60 years (page 9).

Our efforts to galvanise the research community to focus its attention on prevention, cure, early diagnosis and early intervention for cerebral palsy has been realised with the success of last year's inaugural Prevention and Cure Cerebral Palsy Summit (page 8) and the world-wide success and international regard of many Australian researchers.

In the past 12 months, our researchers were invited to present keynote papers at the world's leading conferences including the Australasian and American Academies of Cerebral Palsy and Developmental Medicine and the International Child Neurology Conference. Topics covered included assistive technology, risk factors for cerebral palsy in children born at full term, the Australian Cerebral Palsy Register; causal pathways; and the CP Check Up program (as first reported in Breakthrough 2011).

I firmly believe the projects you are helping us fund are pivotal to shaping the future direction of cerebral palsy research in Australia and overseas.

Collaboration is the key to breakthroughs in intervention and prevention strategies and cure of cerebral palsy.

There is no better time to join our alliance in cerebral palsy research.

Thank you
Bill Bartlett



Governor Spotlight

For the past 30 years, Paul Masi has worked in executive roles

within the Financial Services industry. His previous roles have included Group Chief Executive Officer and Managing Director of Austock Group Limited, CEO and Country Head at BofA Merrill Lynch and Head of Equities and Equity Trading for Merrill Lynch Asia Pacific Ltd.

Paul's most recent role was as Chief

Executive Officer and Managing Director of Octa Phillip Ltd. He is now pursuing non-executive duties and focusing on private investments, and is currently a Non-Executive Director of SHAW Stockbroking.

In 2007, Paul joined the Council of Governors for the Research Foundation of Cerebral Palsy Alliance. Paul and his wife Anne have four children, including a daughter who has cerebral palsy. Like many families, they hope the answers

to cerebral palsy will be found in their life-time, and believe society can play a huge part in accelerating research breakthroughs.

'With community support, researchers can continue their important work to not only investigate the prevention and cure of cerebral palsy, but also improve therapy and interventions that make life easier and more comfortable for people with cerebral palsy and their families.'

Research Awards



Two Australian researchers were awarded for presenting the best research papers into the prevention and cure of cerebral palsy.

Associate Professor Eve Blair and Dr Margaret Wallen were the dual recipients of the 2012 Cerebral Palsy Alliance Research Foundation Award at the Australian Academy of Cerebral Palsy and Developmental Medicine conference.

In her award-winning paper entitled 'Cerebral palsy in term and late preterm born singletons and macroscopically identified placental infarction', Assoc. Prof Eve Blair, from the Telethon Institute of Child Health in Western Australia, presented data on role of placental infarction, or scarring on the placenta due to interruption in blood supply, in causal pathways to cerebral palsy.

In this study, Eve and her colleague Karin Nelson compared the rates of placental infarcts between a total population of children in Western Australia with cerebral palsy, and children without cerebral palsy.

They found that placental infarctions were most likely to be identified in the births of infants who went on to have cerebral palsy, especially those with spastic quadriplegia. However, they noticed different patterns of events that lead up to an infarct for children with cerebral palsy compared with children who did not go on to develop cerebral palsy.

This research builds on Assoc. Prof Eve Blair's internationally recognised work into cerebral palsy risk factors which aims to uncover the unique series of events, or causal pathways, that result in cerebral palsy for some children. It is only by mapping out these complex causal pathways that researchers can identify the best ways to prevent the condition, and Eve Blair's work on placental infarction is an important step towards this goal.

Dr Margaret Wallen from The Children's Hospital at Westmead in Sydney was recognised for her research paper entitled 'Modified constraint-induced therapy compared with intensive occupational therapy for children with hemiplegic cerebral palsy: results of a randomised trial' that looked at effective treatments leading to a reduction in the severity of cerebral palsy and improved quality of life.

Constraint-induced therapy (CIMT) is an intervention for people with hemiplegia that aims to improve use of the affected arm by constraining the dominant, unaffected arm using a mitt, sling or cast. Research has proven that CIMT is effective in improving upper limb function in children with cerebral palsy, but it can also be intensive and demanding to implement.

In this study, Dr Margaret Wallen and her colleagues tested whether a modified form of CIMT that had children wearing a mitt on their dominant hand for two hours per day while doing therapy exercises with their affected hand was as effective as standard intensive occupational therapy for improving use of the affected arm. They found that modified CIMT and intensive occupational therapy were equally effective in achieving this aim.

Thanks to Dr Wallen's research, we now know that both approaches are effective ways of improving children's use of their upper limbs, and can help in improving their participation in everyday activities.

Both Assoc. Prof Blair and Dr Wallen were recipients of a Research Foundation of Cerebral Palsy Alliance's *Innovation in Research* grant in 2006.



TOP: ASSOC. PROF. EVE BLAIR
BOTTOM: DR MARGARET WALLEN

Virus Link to Cerebral Palsy



A team of Australian researchers are investigating the links between a common virus and cerebral palsy.

Researchers have long recognised that the transmission of certain viruses from the mother to the developing fetus can increase the risk of birth defects and poor developmental outcomes.

Rubella, or German Measles, is a well-known cause of disability after infection in pregnancy, but thanks to a universal vaccination program, it is now rarely seen in Australia.

Cytomegalovirus (CMV) is a common virus that circulates in our community, which, unlike Rubella rarely causes symptoms in healthy people. As a result, the virus remains virtually unknown by the community and to date there has been little research into developing a vaccine to limit its transmission.

CMV is transmitted through close person-to-person contact with infected secretions such as in urine and saliva. However, when CMV is transmitted to the fetus during pregnancy, it can sometimes cause stillbirth, premature birth and neurological conditions such as cerebral palsy.

To prevent congenital CMV in Australia, we first need to understand how common it is, and this data is not readily available. The number of infants born in Australia with congenital CMV each year is not well known because most babies have no signs of the infection at birth, and we do not routinely screen for the virus at birth. Testing for fetal CMV infection after the newborn period is also not precise. The most accurate estimates we have of infection are from studies of immunity to CMV in women of child-bearing age, that suggest approximately one in every 200 babies are born with CMV every year in Australia.

Data from international studies suggest

that approximately one in 10 CMV infected babies are born with or later develop neurological problems. The number of these infants who will go on to develop cerebral palsy is unknown.

To understand more about this causal pathway to cerebral palsy, research is being undertaken by a collaboration between the University of Sydney, Cerebral Palsy Alliance and The Children's Hospital at Westmead.

Hayley Smithers-Sheedy, PhD student at Sydney University and Research Officer at Cerebral Palsy Alliance is working together with Professor Cheryl Jones, Dr. Camille Raynes-Greenow, Professor Nadia Badawi and Professor Alison Kesson to investigate the prevalence and clinical profile of cerebral palsy caused by congenital CMV.

Together the team will analyse data related to children born with cerebral palsy caused by congenital CMV on the Australian Cerebral Palsy Register (ACPR) to evaluate the impact and outcomes of cerebral palsy resulting from CMV.

To date their research has identified an unexpectedly high number of children with severe disability in the group with known CMV. Children with cerebral palsy and CMV were more likely to have spastic quadriplegia, severe functional mobility limitations and a range of associated impairments including epilepsy, deafness, vision impairment and moderate to severe intellectual impairments than children born with cerebral palsy but without CMV.

To ensure their findings represent the true impact of cerebral palsy due to CMV, the team are investigating whether congenital CMV infection is accurately diagnosed and identified in

children with cerebral palsy.

To do this, they are currently seeking permission from families of children born with cerebral palsy to retrospectively test for the presence of CMV DNA in their child's newborn blood spots which are taken at birth as part of the routine 'heel prick' test. These blood samples are stored as standard practice in hospitals throughout Australia.

With an established link between CMV and cerebral palsy, it is important that effective screening, treatments and preventative strategies for this common virus be investigated.

One research project that is looking at ways to prevent CMV is a large USA study involving 150,000 participants. This study will investigate whether CMV immunoglobulin (including the product from the Australian company CSL) is able to reduce or prevent the maternal transmission of CMV during pregnancy. It also hopes to identify whether administration of immunoglobulin reduces the severity of outcomes for babies who are born with CMV.

If effective, this treatment may pave the way to prevent or reduce the severity of cerebral palsy for cases of pregnant women with new CMV infection.

However, until the study results are known, the best means of minimising the risk of getting CMV infection during pregnancy is careful attention to hand hygiene.

These strategies are especially important for individuals caring for young children, who are thought to be at an increased risk of CMV infection through activities such as nappy changing.

Left: Macquarie Group Foundation Chair Of Cerebral Palsy, Prof. Nadia Badani And Prof. Cheryl Jones.

Front cover (from L-R): Ms Hayley Smithers-Sheedy, Prof. Nadia Badawi, Prof. Cheryl Jones and Dr Camille Raynes-Greenon.

The Research Foundation of Cerebral Palsy Alliance is supporting the work of Hayley Smithers-Sheedy through a scholarship funded by Eagle Boys Pizza.



Under The MICROSCO

Dr Cally Tann

Clinical Research Fellow, London School of Hygiene & Tropical Medicine

Honorary Senior Research Associate, Institute for Women's Health, University College London

2012 Research Foundation of Cerebral Palsy Alliance
Innovative Research Grant
\$35,513 over 2 years

Nearly a quarter of all newborn deaths throughout the world are a result of a brain injury that occurred around the time of birth. In addition, each year an estimated one million survivors of newborn brain injury go on to develop cerebral palsy, seizure disorders or other neurological impairment

The vast majority of this health burden falls on families in the poorest of countries but to date research into the prevention and treatment of cerebral palsy in developing countries has not been a high priority.

Few studies have looked at the causes of cerebral palsy in Africa. One of the main causes of newborn brain injury (neonatal encephalopathy) is lack of oxygen to the baby's brain during a difficult birth. This is particularly common in places like Uganda where access to a skilled birth attendant, or to emergency obstetric care if there is a complication of labour, can be problematic.

In addition, treatments like therapeutic cooling that are proven to improve outcomes in these babies are difficult to achieve in places where there is no or limited access to newborn intensive care facilities. However, in recent years some studies have suggested that certain

infections occurring during pregnancy or at the time of delivery may increase the chance of newborn encephalopathy suggesting that there may be other ways in which we may help prevent newborn brain injury.

Since September 2010, Dr Cally Tann and her team in Uganda have been recruiting mothers and their newborns to a research project at Mulago Hospital in Kampala, Uganda, called the 'ABAaNA study' (abaana means 'young child' in the local language, Luganda).

The study aims to help us understand which infections and other risk factors, during pregnancy and delivery, might be important in the development of newborn brain injury in Africa and elsewhere. The study compares two groups of term babies: one group with newborn brain injury (the cases), and another group of well term newborns (the controls).

It aims to examine the effects of a whole range of infections in the mother, the newborn and in the placenta including bacterial infections, viral infections, like HIV, cytomegalovirus and herpes virus, and other infections more common in Africa such as malaria and syphilis.

In November 2012, Dr Tann and her ABAaNA study team will start a new phase of their research to compare childhood development and disability at 12-15 months of age between these two groups.

They will examine which risk factors from pregnancy and birth might be important in the development of cerebral palsy and other neurological impairments.

The ultimate aim of the study is to provide important new information on the causes, timing and outcomes of brain injury-related cerebral palsy. The cohort of ABAaNA babies is the largest cohort infants of this kind to be followed in sub Saharan Africa and therefore should provide vital new information on risk factors for death and disability from neonatal encephalopathy in Uganda.

Researchers hope this information will help us develop intervention strategies to prevent death and disability from newborn brain injury.

For more information on supporting cerebral palsy research, please phone Tracey Jordan on (02) 9479 7200.

OPE



Associate Professor Nick Evans,
Head of the Department of Newborn Care at the
Royal Prince Alfred Hospital and Clinical Assoc. Prof,
University of Sydney

Dr Angela McGillivray
Royal Prince Alfred Hospital, Sydney

2012 Research Foundation of Cerebral Palsy Alliance
Innovative Research Grant
\$58,300 over 2 years

International research shows that severe jaundice may be re-emerging in some parts of the world including developed countries such as the United States and parts of Europe. Is it so in Australia and if so, why? Assoc. Professor Evans and Dr McGillivray hope to find out.

Jaundice is a yellowing of the skin caused by raised levels of bilirubin in the blood. About half of all newborn babies become jaundiced and, in almost all, it is benign. In a few babies, bilirubin levels in the blood become dangerously high and can damage the brain. Some children who develop cerebral palsy have had severe jaundice at birth or very soon afterwards, in the newborn period.

Researchers already know that conditions such as premature birth, infections, and certain blood conditions can increase the risk of severe jaundice. Many of these risk factors can be managed early and thus, high levels of jaundice can often be prevented.

In 2009, Assoc. Professor Nick Evans and Dr Angela McGillivray began

work on a two-phase research project to ascertain the incidence of severe neonatal jaundice and the spectrum of developmental outcomes in Australia. In the first phase of the project, the first nationwide survey of severe jaundice was conducted in collaboration with the Australian Paediatric Surveillance Unit (APSU).

The aim of this initial phase study is to establish the current incidence of severe jaundice in Australian-born babies and the associated causes and clinical risk factors of this condition.

Phase 1 of the study is due to be finalised by 2013. To date, this study has revealed 63 confirmed cases of severe neonatal jaundice.

Phase 2 of this project will entail a national neurodevelopmental follow-up program of children born with severe jaundice at one and three years of age. The aim is to establish the spectrum of long-term neurodevelopmental outcomes among affected children and confirm whether these outcomes correlate with MRI

brain findings. By analysing this data, the study will help the research team define the contributory factors leading to disability. It is anticipated that this data will inform the development of important future prevention strategies including screening initiatives and education programs for parents, care-providers and health professionals.

This study also aims to inform future improvements to the continuity and co-ordination of newborn care, particularly after hospital discharge as well as to inform risk reduction strategies for severe neonatal jaundice and associated disabilities.

Assoc. Professor Evans is also Chair of the NSW Perinatal Services Network NICU Managers Committee and on the executive of the Australian and New Zealand Neonatal Network.

Prevention and Cure Cerebral Palsy Summit Update



With your support, cerebral palsy researchers can continue looking for answers and offer new hope to families.

At last year's historic Prevention and Cure Cerebral Palsy Summit, 29 of the world's leading cerebral palsy researchers collaborated to identify 31 global research projects they believe had the best chance of bringing us closer to finding a prevention and cure for cerebral palsy.

Below is an overview of two of those vital research projects which are still awaiting funding. Your support to fund or part fund any of these projects will change the lives of future generations.

RESEARCHERS

Dr Yvonne Wu, Dr Roberta Ballard, Dr Sandra Juul, Dr Rod Hunt, Dr Iona Novak, Dr Helen Liley, Dr Sue Jacobs, Dr Jane Pillow

PROJECT

Neonatal Erythropoietin and Therapeutic Hypothermia

Hypoxic-ischemic encephalopathy (HIE), or decreased blood and oxygen delivery to the brain, is an important cause of newborn brain injury leading to cerebral palsy. Erythropoietin (EPO – a hormone produced by the kidney and liver) has been shown in animal studies to reduce brain injury and promote repair following HIE.

This randomized placebo-controlled clinical trial will determine whether 5 doses of Epo, given to infants with HIE who are receiving cooling therapy, reduces the risk of death or moderate to severe neurologic disability including cerebral palsy.

FUNDING REQUESTED - \$69,001 for year 1

RESEARCHERS

Dr Suzie Miller, Prof Graham Jenkin, A/Prof Michael Fahey, Prof Euan Wallace, The Ritchie Centre, Monash Institute of Medical Research, Monash University, VIC

PROJECT

Cord blood stem cell treatment following birth asphyxia.

Some babies suffer a severe reduction in oxygen around the time of birth, with adverse effects on the developing brain. This project will examine whether cord blood stem cells migrate to the injured brain and reduce damage. This project will also explore the mechanism(s) by which cord blood stem cells are able to reduce injury, providing foundation knowledge to inform future clinical application.

FUNDING REQUESTED - \$178,800 over 2 years

For further information contact Tracey Jordan on 02 9975 8762 or at tjordan@cerebralpalsy.org.au

GLOBAL ACTION TO CHANGE THE WORLD FOR PEOPLE WITH CP



More than 7000 participants from the United States, Canada and Australia recently participated in September – a 4-week activity based challenge that raised money to support people with cerebral palsy.

To date, September has raised more than \$700,000 around the world. Global leader in the fundraising stakes was a team from ING Direct, which had 52 teams (an incredible 20% of its Australian workforce) taking part in September.

September was launched on the inaugural World Cerebral Palsy Day (4 September), celebrated by disability organisations from 28 countries including the USA, Canada, India, Australia and Netherlands.

As part of World CP Day celebrations, people were asked to submit ideas for inventions that could change the world for people with cerebral palsy. Ideas ranged from the simple (like brand-name jeans with elastic waists so people with CP could



Tanya Taylor (centre), whose 3 year old son Daniel has cerebral palsy, organised 19 teams from Willoughby Public School to participate in September.

easily get them on and off), to the more complex (like a solar powered wheelchair).

The World CP Day Committee

will soon select an idea to be seed funded and put to inventors to turn into reality by next year's World CP Day.



MILLA, SUZAN, SCOTT AND LUCA

Light at the end of the tunnel

By **Adam Cresswell**
Health Editor, The Australian

Recent breakthroughs have led to a historic drop in cerebral palsy cases

Milla Griffin is a bright child. She loves to build things with her Lego, and play music to her one-year-old brother. The fascination with Lego makes her mother, Suzan, wonder if Milla might one day want to become an architect, or perhaps a designer. In her five-year-old's world, where every idea retains the heady whiff of possibility, Milla dreams of being a doctor.

But Milla's parents know her dreams are more fragile than most others, for Milla is severely affected by cerebral palsy, which means she cannot feed or dress herself, has difficulty communicating and lacks core strength to such a degree that she can't sit for long unsupported.

"She tried very hard, but she has a tendency to fall to one side,"

explains Suzan, who since Milla's birth has remained out of the full-time workforce to ensure her daughter gets the help she needs.

Suzan, who gave birth to her second child, Luca, last year, is frank about the challenges involved in caring for a child with cerebral palsy. Cerebral palsy is lifelong, and Milla relies on her parents for everything – "to be fed, to be washed, to brush her teeth."

"Unless there's a miracle out there, she will never outgrow that, whereas a normal child will out-grow that," Suzan said.

The miracles have certainly been few and far between for patients and families affected by cerebral palsy. Official figures suggest its rate has remained static for decades,

at between two and 2.5 cases for every 1,000 live births.

All that is about to change. Iona Novak is head of research for Cerebral Palsy Alliance and oversees the research activities of the Cerebral Palsy Register, the largest whole-country register of cerebral palsy cases in the world.

"We run a report every two years (based on the register) and this year we are expecting to see the rate dip down for the first time in 60 years," Novak tells *The Australian*.

Expectations that this year's report will show a historic drop in the cerebral palsy rate hang on the success of two treatments: magnesium sulphate, discovered in the past few years almost by accident, and hypothermia.

Magnesium sulphate treatment is now written into Australia's official National Health and Medical Research Council guidelines, which outline what treatments should be given for premature birth. Incredibly, although Novak estimates that the number of cerebral palsy cases in Australia would be cut by 90 each year if every hospital used magnesium sulphate in very preterm births, not every hospital is providing it.

"Our plea to hospitals is to use this new research data. It's a win for families, but it's also a win for obstetricians, when they have been maligned as a cause of cerebral palsy when they are not."

The second recent breakthrough involves the use of induced hypothermia in babies who are born at full term but who are clearly sick – unconscious, floppy and showing characteristics of a condition known as neonatal encephalopathy, which is known to confer a very high risk of cerebral palsy.

Novak says lowering the babies' body temperature by about 2C, as part of a controlled procedure carried out under anaesthetic, prevents cerebral palsy for about one in six babies. But looking to the future, there are at least three further developments on the horizon that Novak says could help the rate to fall further in decades to come.

One involves stem cells, which are

already known to help fight blood cancers such as leukaemia. Novak thinks more promising still are two other treatments about to start human trials in Australia: one using a chemical involved in the brain's sleep-wake cycle, called melatonin, and the other being erythropoietin (EPO), a hormone involved in red blood cell production.

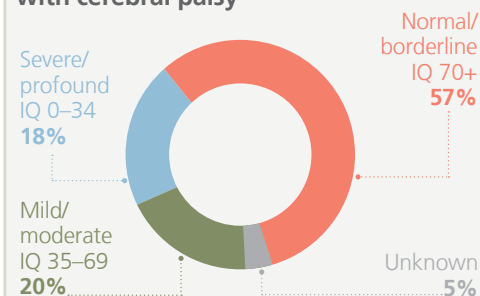
EPO, which is used illegally by some athletes in a bid to boost performance, also has been observed to be present in the brain immediately after a brain injury, and appears to help recovery.

Novak is about to be involved in a study of 440 high-risk babies in Sydney, Melbourne, and Brisbane, that is expected to reduce the rate of cerebral palsy in the treated group by between 10 per cent and 14 per cent.

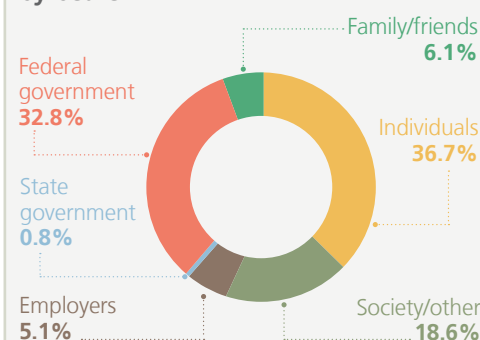
"On top of the cooling and magnesium sulphate, it's the most important probable breakthrough for the prevention of CP, and I would be bold enough to use the word cure because EPO appears to cause brain regeneration, not just halt the injury," Novak says.

This is an edited version of an article published in *The Australian* on 12 July 2012. To read the complete version of this article, visit www.theaustralian.com.au/news/features and search for 'Milla Griffin'.

Rates of impairment in people with cerebral palsy



Financial costs of cerebral palsy, by bearer



Prevalence comparison

Arthritis	3,848,304
Asthma	1,356,620
Type II diabetes	1,073,459
Coronary heart disease	309,726
Dementia	167,378
Intellectual disability	131,024
ADHD	130,006
Type I diabetes	97,440
Autism spectrum disorders	80,675
Cerebral palsy	33,797
Appendicitis	26,170
Road traffic accidents	25,381
Eating disorders	23,464
Stroke	19,627
Multiple sclerosis	16,081
Bowel cancer	13,552
Breast cancer	12,359
Prostate cancer	11,899
Muscular dystrophy	3457

Source: Access Economics (data for 2003, 2005, 2007)



OCCUPATIONAL THERAPIST REBECCA MARTIN WITH MILLA AND SUZAN

Did you know that Australian children are 3 times more likely to be diagnosed with cerebral palsy than with cancer?

In fact, every 15 hours an Australian child is born with cerebral palsy.

And for most, the cause remains unknown.

By supporting cerebral palsy research, you can help us find the answers.

To find out how, visit www.cpresearch.org.au or phone 02 9975 8762



A gift from you today could help fund crucial research and help us come closer to a world without cerebral palsy
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