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The Royal Women's Hospital presents

Annual Research Symposium

- Cool Topics in Neonatology

Abstracts and Biographies

Tuesday 10 November 2009
9.00am – 5.00pm

Bio 21 Research Institute
30 Flemington Road
Parkville Victoria 3052

www.thewomens.org.au/annualresearchsymposium2009

Cool Topics in Neonatology Program

Tuesday 10 November 2009

8.15am – 9.00am	Registration
9.00am – 10.30am	Life Before Birth Chair: Prof Bob Gibson
9.00am – 9.30am	Prof Caroline Crowther Antenatal Corticosteroids – Unresolved Questions
9.30am – 10.00am	Prof Lex Doyle Magnesium Sulphate for Neuroprotection of the Fetus
10.00am – 10.30am	Prof Maria Makrides Maternal Nutrition – Effects on the Fetus and Child
10.30am – 11.00am	Morning tea
11.00 am – 12.30pm	Coming to Grips Chair: Prof Lex Doyle
11.00am – 11.30am	Dr Sue Jacobs Therapeutic Hypothermia in Hypoxic-Ischaemic Encephalopathy (HIE)
11.30am – 12.00noon	Dr Jeanie Cheong Diagnostic and Prognostic Tools in HIE
12.00noon – 12.30pm	Panel Discussion When to Withdraw Care in Severe HIE?
12.30pm – 1.30pm	Lunch
1.30pm – 3.00pm	Gently Does It! Chair: A/Prof Carl Kuschel
1.30pm – 2.00pm	Ms Sally Murray Nursing Practices and Developmental Care in the NICU
2.00pm – 2.30pm	Dr Carol Newnham Reducing Stress in Parents and Their Premature Babies
2.30pm – 3.00pm	Dr Alicia Spittle Supporting Developmental Care in the NICU and Beyond
3.00pm – 3.30pm	Afternoon tea
3.30pm – 5.00pm	A Breath of Fresh Air Chair: Prof Peter Davis
3.30pm – 3.50pm	Dr Louise Owen Non-Invasive Ventilation: What We Know, What We Need to Know
3.50pm – 4.10pm	Dr Risha Bhatia Is it possible to understand the regional behaviour of the newborn lung at the bedside?
4.10pm – 4.30pm	Dr Georg Schmoelzer Respiratory Monitoring During Neonatal Resuscitation
4.30pm – 5.00pm	Prof Colin Morley Controversies in Neonatal Resuscitation and Ventilation

Antenatal Corticosteroids – Unresolved Questions

Professor Caroline Crowther

Professor Caroline Crowther is a maternal fetal medicine subspecialist and Director of ARCH: the Australian Research Centre for Health of Women and Babies, in the Discipline of Obstetrics and Gynaecology at The University of Adelaide.

She has extensive experience in the design, conduct and analysis of systematic reviews randomised clinical trials and has co-ordinated many large, multicentre trials that focus on the evaluation of new maternal perinatal therapies or care practices including the use of antenatal corticosteroids

Abstract

Professor Caroline Crowther

ARCH for Women and Babies, Discipline of Obstetrics and Gynaecology, The University of Adelaide.

Children born preterm have a higher than average risk of dying in the first weeks of life and survivors experience higher rates of neurosensory disability than children born at term. There is strong evidence that antenatal corticosteroids given to women at risk of preterm birth substantially improve short-term neonatal health, increase the chance of the baby being discharged home alive, and reduce childhood neurosensory disability, with known efficacy and safety into adulthood.

Although there was initial reluctance to implement this life saving therapy, antenatal corticosteroids are now widely used, with clinical practice guidelines for them developed by many colleges and institutions throughout the world.

One of the major advances in maternal fetal medicine over the last 35 years has been the evaluation and implementation into clinical practice of administration of antenatal corticosteroids to women at risk of preterm birth. However there remain important clinical questions on the use of antenatal corticosteroids that are unanswered, as highlighted in the three relevant Cochrane systematic reviews (Roberts & Dalziel 2006; Brownfoot et al 2007; Crowther and Harding 2008).

These include: What is the best corticosteroid to use – dexamethasone or betamethasone? What should the treatment regimen for administration be? What is the optimal dose? Do women with a multiple pregnancy require a higher dose? Should the corticosteroids be repeated if the risk of preterm remains and, if so, after what time interval? What is the long term health outcome related to antenatal corticosteroid use?

Answers are needed to these unresolved questions to be able to make better evidence-based recommendations about care for women who are at risk of preterm birth.

Magnesium Sulphate for Neuroprotection of the Fetus

Professor Lex Doyle

Professor Lex Doyle trained as a neonatal paediatrician in Melbourne in the 1970s, and then did a fellowship at McMaster University in Canada from 1979 to 1982, where he completed a MSc in Clinical Epidemiology and Biostatistics. He then returned to the Royal Women's Hospital in Melbourne as a neonatal paediatrician in 1983, and also a senior lecturer at the University of Melbourne.

He succeeded Bill Kitchen as the Convenor of the Victorian Infant Collaborative Study Group in 1991, a research group that has evaluated the long-term health of the tiniest and most immature survivors in the state of Victoria born in the 1970s, 1980s, 1990s, and 2000s. He was made a professor of neonatal paediatrics in the University of Melbourne in 2003.

He stopped working as a neonatal paediatrician in 2006 to concentrate on full time research and teaching, and is now Head of Clinical Research Development at the Royal Women's Hospital. His major research interest is in improving the long-term health of tiny or very preterm babies.

Abstract

Lex W Doyle^{1,2,3}

Royal Women's Hospital, Melbourne, ²Department of Obstetrics and Gynecology, and Pediatrics, University of Melbourne, and ³Murdoch Children's Research Institute, Melbourne Australia.

As survival rates have improved, it is clear that the rate of long-term neurological impairments and disabilities has remained too high relative to term controls. Magnesium sulphate has been observed in human studies to be associated with reductions in cerebral palsy in very low birth weight (VLBW, birth weight < 1500 g) survivors. Experimental data support its role as a possible neuroprotective agent.

There have been 5 randomised controlled trials completed of magnesium sulphate given to pregnant women where long-term outcomes for infants have been reported. In four of these trials the primary intent was to use magnesium to protect the unborn baby's brain. Synthesising the data from these trials has shown that magnesium sulphate before birth reduces the risk of cerebral palsy by approximately one-third, and increases the rate of survival free of cerebral palsy. Approximately 50 mothers need to be treated with magnesium before birth to prevent one case of cerebral palsy. This is achieved without any major side-effects to either the mother or baby. There remain many unanswered questions before it can be recommended for routine practice, including the following: Which women need treatment? With what dose? For how long?

Magnesium sulphate promises to be an effective treatment in improving long-term outcomes for very preterm infants, but it should not be given outside of high-risk maternity hospitals who are experienced in its use.

Maternal Nutrition – Effects on the Fetus and Children

Professor Maria Makrides

Professor Maria Makrides is a NHMRC Senior Research Fellow and Director of the Child Nutrition Research Centre, a joint venture between the Women's & Children's Health Research Institute, University of Adelaide, Flinders Medical Centre & Children, Youth, and Women's Health Service, Adelaide, South Australia.

She currently serves on the Board of Directors of the International Society for the Study of Fatty Acids and Lipids (ISSFAL), is a member of the Nutrition Committee, Australian Academy of Science and is a scientific advisor to Food Standards Australia and New Zealand for infants and young children.

Abstract

Maria Makrides and Robert A Gibson

Women's and Children's Health Research Institute, North Adelaide, SA 5006 and University of Adelaide, SA 5005

The maternal diet can be a source of nutrients to the fetus by active transport mechanisms across the placenta. In fact the last trimester of pregnancy represents one of the most active periods of nutrient deposition and growth. The fetus will double in size during this time and key protein, fat and micronutrient stores are laid down. There are two potential nutritional stresses to the fetus/infant:

- During pregnancy if the maternal dietary intake falls short of the recommended intakes, placental transfer of nutrients maybe less than optimal.
- Following preterm birth the infant is denied the usual placental transfer of nutrients and is at risk of multiple nutrient deficiencies because current feeding practices often fall short of meeting their high nutrient requirements and their low nutrient stores provide little buffer from deficiency.

The presentation will provide several examples of nutritional interventions designed to address shortfalls in micronutrient, protein and fatty acid supply. The specific examples chosen include iron, iodine, protein and fatty acids. Iron requirements during pregnancy have been under debate for some time and long term follow-up of our randomized trial of iron supplementation suggest that routine iron supplementation is not warranted and may in fact be harmful for women who are not anemic during pregnancy.

Protein and fatty acids will be the focus of interventions for preterm infants. These examples will highlight that fact that for some nutrients, such as the fatty acid DHA, the maternal diet determines the breast milk DHA composition so maternal dietary intervention post-birth offers an intervention strategy; while in other cases, such a protein quality, the maternal diet has little influence on the

protein composition of breast milk. Both higher DHA and higher protein interventions offer significant potential in improving the growth and developmental outcomes of preterm infants.

Therapeutic Hypothermia in Hypoxic – Ischaemic Encephalopathy (HIE)

Dr Sue Jacobs

Dr Sue Jacobs is a Consultant Neonatologist and Director of the Newborn Intensive and Special Care Nurseries at the Royal Women's Hospital, Melbourne.

Sue is the Principal Investigator of the NHMRC funded ICE (Infant Cooling Evaluation) trial that has recently been completed. The results are being analysed to be submitted for her MD thesis and will be presented at PSANZ in 2010.

Sue is also the first author on the Cochrane Review: Cooling for newborns with hypoxic ischaemic encephalopathy.

Abstract

Peripartum asphyxia complicated by moderate or severe hypoxic-ischaemic encephalopathy (HIE) is a devastating global health issue. A therapeutic 'window of opportunity' exists after resuscitation of the asphyxiated newborn and before the delayed phase of neuronal loss. Animal studies demonstrate that neuronal injury following hypoxia-ischaemia can be prevented or reduced by a mild reduction in brain temperature.

Human infant pilot studies confirmed feasibility, without major adverse effects. Randomised trials and systematic reviews comprising term infants with moderate or severe HIE have established the neuroprotective benefit of therapeutic hypothermia. Cooling reduces mortality or major disability to 18 months of age. Importantly, mortality is reduced without any increase in major neurodevelopmental disability in survivors, and with only minor adverse effects. Inclusion of data from the recently published TOBY trial in the Cochrane review, 'Cooling for newborns with HIE', demonstrates that therapeutic hypothermia also significantly reduces cerebral palsy, as well as neuromotor and cognitive delay.

Current evidence supports the implementation of therapeutic hypothermia within strict protocols into standard care in tertiary NICUs to improve the outcome for term and near term newborns with moderate or severe HIE. Equally strict protocols in non-tertiary nurseries are being developed to enable earlier initiation of cooling under guidance of the regional NICU and transport team.

Diagnostic and Prognostic Tools in HIE

Dr Jeanie Cheong

Dr Jeanie Cheong is a neonatologist based at the Royal Women's Hospital Melbourne who has a special interest in Perinatal Neurology and Neuroimaging.

She completed her basic medical training at the University of Melbourne and completed her Fellowship of the Royal Australasian College of Physicians in 2002.

She spent 3 ½ years at the Hammersmith Hospital and University College London Hospital working towards an MD where her work focussed mainly on magnetic resonance neuroimaging in term infants with hypoxic-ischaemic encephalopathy. She is a co-investigator of the Victorian Infant Brain Studies team based at the Murdoch Children's Research Institute and maintains an active involvement in research involving perinatal brain injury, its consequences and correlation with neuroimaging.

Abstract

Hypoxic-ischaemic encephalopathy (HIE) is an important cause of mortality and morbidity in term-born infants. Clinical assessment and cranial ultrasound have low sensitivity in diagnosis and prognosis.

The availability of bedside amplitude-integrated EEG (aEEG) and magnetic resonance imaging (MRI) and spectroscopy (MRS) have refined diagnostic and prognostic ability in HIE. Background patterns on aEEG in the first 12 hours after birth are highly predictive of outcome, and prognostic sensitivity is improved when combined with clinical evaluation.

Patterns of brain injury on MRI assist in confirming the diagnosis and the extent of brain injury has a strong correlation with pattern and severity of neuromotor outcome.

MRI changes on diffusion weighted images appear early whereas changes on conventional MRI become more apparent towards the end of the first week. Increased lactate and decreased N-acetyl aspartate on proton MRS correlate with severity of injury and prognosis. The optimal timing of MRI and MRS has been around 5-7 days, but this will need re-evaluation in the era of hypothermia as standard of clinical care.

Nursing Practices and Developmental Care in NICU

Ms Sally Murray

Nurse Educator, Neonatal Intensive and Special Care Nurseries, the Royal Women's Hospital, Melbourne.

Sally Murray has been nursing for 12 years, in Australia and London, working in neonatal intensive care units (NICUs) for the last 5 years, having undertaken a postgraduate certificate in neonatal intensive care at Latrobe University. She is currently the Clinical Nurse Educator on the neonatal unit at the Royal Women's Hospital.

Abstract

The main focus of this talk is to inform and educate staff on family centered and developmental care for neonatal patients and their families. A brief history, the main key concepts and elements of developmental care and how nursing staff can understand and promote organisation for preterm infants will be discussed.

Reducing Stress in Parents and Their Premature Babies

Dr Carol Newnham

Dr Carol Newnham works with two Melbourne research groups – the Parent-Infant Research Institute which develops evidence-based interventions for mothers and infants, and the Victorian Infant Brain Studies group, which focuses primarily on relationships between neural and functional development in at-risk infants.

Dr Newnham's primary research work involves assessing a comprehensive and intensive intervention delivered to mothers of hospitalised preterm infants in terms of its effect on infant development. The results of the first of three related projects was published this year, the second has been submitted and the third (for which NHMRC funding was granted thus ensuring a larger sample size) is nearing completion of the recruitment phase. The latest focus of Dr Newnham's research interest has been the effect of stress on brain development. She recently developed a measure of accumulated stress in hospitalised preterm infants which is now attracting attention from several overseas nurseries. She has presented her work at local and overseas conferences and has been an invited speaker at several workshops.

In addition to research work, Dr Newnham publishes a quarterly magazine for the parents of preterm infants (Premiepress), now in its tenth year, which presents recent and pertinent research results, theories and interventions (i.e. information) from different disciplines that might be helpful to information-hungry parents.

Abstract

Stress involves physical, psychological and social events that result in excessive reactions and difficulty in coping. It has behavioural, emotional and physiological outcomes. For the *mother* of a preterm infant, stress associated with the birth and medical recovery of her child can affect the critically important relationship with her infant and overall adjustment to parenthood, including mental health issues. The attachment between mother and infant, her sensitivity to the infant's needs and maternal mental health are all robust predictors of future child development. For the preterm *infant*, stress occurs before language or understanding of the world has occurred. Animal studies show that stress that occurs in the neonatal period (mediated by stress hormones) has a lasting, often whole-of-life impact on brain and functional development. Stress responses that occur repeatedly, over long periods of time, especially during early critical periods of development, exact an "allostatic load" or cost that can accelerate disease processes.

Thus behaviourally and emotionally, stress-impacted *mothers* and preterm *infants* can be poor social partners to each other. In addition, physiologically, it may be that acute and chronic stressors in the NICU affect *infant* neural development. Preterm infants may therefore have a double jeopardy: first

from their early birth and the sequelae of medical complications, and secondly from relationship and iatrogenic factors that increase stress. The results of two studies aimed at reducing and managing preterm infant stress will be presented:

- (i) A sensitivity intervention for mothers of still-hospitalised very preterm infants was applied in a randomised controlled study (n=45). Infants were scanned using Magnetic Resonance Imaging at 40 weeks and outcomes included volumes of different tissue types within 16 brain regions, along with diffusion tensor data, yielding measures of white matter connectivity. Results showed that infants of intervention compared with control mothers had improved white matter microstructure
- (ii) The results of a survey of 150 NICU doctors and nurses concerning their perceptions of the relative severities of preterm infant stress reactions to 44 acute and 24 chronic stressors will be presented. These results can be used to manage infants' allostatic loads.

Supporting Developmental Care in the NICU and Beyond

Dr Alicia Spittle

Dr Alicia Spittle is a physiotherapist who completed her PhD in early 2008 investigating the effects of a randomised controlled trial of early intervention on motor development of very preterm infants.

Alicia is the recipient of the first Cerebral Palsy Foundation Post-Doctoral Fellowship. Alicia also works clinically in the neonatal intensive and special care unit at the Royal Women's Hospital as part of the neonatal developmental therapy team and lectures at The University of Melbourne.

Abstract

Spittle J Alicia,^{1,2,3}

¹Royal Women's Hospital, Melbourne, ²Murdoch Children's Research Institute, Melbourne, ³Physiotherapy, School of Health Sciences, University of Melbourne,

Advances in neonatal medicine over the past decades, have improved the survival rates for preterm infants, however, children born very preterm are at risk of a complex range of motor, cognitive, sensory, behavioural and health problems compared to children born at term. Rates of major disability for preterm infants have remained relatively constant with these advances in medicine, however, the incidence of infants with minor problems are increasing, especially for the smallest and most preterm infants. Developmental care both in the neonatal intensive and special care nursery aims to support the behavioural organisation of each individual infant, enhancing physiological stability, protecting sleep rhythms and promoting growth and maturation. These interventions include handling and positioning measures, reduction of noxious environmental stimuli, and cue based care.

Early interventions programs post hospital discharge aim to prevent the excessive rates of neurological impairments in very preterm infants; however, the evidence for these interventions is poorly understood. We conducted a systematic review of early intervention programs for preterm infants which demonstrated that although they have a positive influence on cognitive outcomes in the short to medium term, further research is needed on the longer-term effects of these programs and, in particular, for motor outcomes.

We conducted a randomised controlled trial of a preventative care program at home for infants born at less than 30 weeks' gestation. The intervention group (n=61) received the preventative care program consisting of 9 home visits over the first year from a physiotherapist and psychologist, focusing on the parent-infant relationship, parental mental health and infant development, with the control group (n=59) receiving standard care. Our results demonstrated that a preventative care program for very preterm infants and their families improved behavioral outcomes for infants and reduced primary caregiver anxiety and depression.

Non Invasive Ventilation: What We Know, What We Need to Know

Dr Louise Owen

Dr Louise Owen is a UK trained Neonatologist who came to the Royal Women's Hospital in 2006, having finished her specialist training, to embark upon a research degree.

Louise is now completing her research MD investigating the use of NIPPV in preterm infants. Louise has undertaken five separate studies in the NICU to try to answer questions about NIPPV and improve the way we deliver non-invasive respiratory support to premature babies. She has published several papers on this topic, including two reviews and a survey of current practice of NIPPV.

Louise does some clinical work in the RWH NICU and also works as a Consultant for NETS Victoria.

Abstract

Nasal intermittent positive pressure ventilation (NIPPV) is a form of non-invasive respiratory support consisting of CPAP with additional mechanical inflations. The technique has emerged as neonatal practice has recognised the importance of lung protective strategies of respiratory support. NIPPV appears to offer more support than standard CPAP and its use reduces the number of infants needing intubation or re-intubation. NIPPV may also protect babies from developing Chronic Lung Disease.

However the way in which NIPPV works remains unclear, we do not know how accurately the inflations we set are delivered, nor whether the inflations actually ventilate the baby. We do not know the optimal settings in terms of pressure, inflation rates or gas flow, and we do not know whether we should be synchronising the mechanical inflations with the baby's own respiratory effort. We do not know the best device or interface for NIPPV delivery, nor how to wean infants from it.

This presentation will review the evidence for NIPPV support and discuss current research and emerging data on this topic.

Electrical Impedance Tomography – Friend or Foe?

Dr Risha Bhatia

Dr Risha Bhatia is an Irish-trained neonatologist who completed her neonatal training in Melbourne since arriving in 2006. She has recently joined the RWH neonatal respiratory research team in order to pursue a higher research degree.

Her research interests lie in regional lung ventilation using different modes of ventilation. She will soon be starting some clinical studies looking to optimising nasal CPAP in preterm infants with early RDS and post-extubation.

Risha continues to do some clinical work in NICU and is part of the Victorian Neonatal Emergency Transport Team.

Abstract

Non-invasive monitoring of lung function is ubiquitous in neonatal intensive care and has the capacity to provide useful diagnostic information and guide therapy. Such monitoring, whilst useful, measures parameters outside the lung. It assumes that the mechanical properties of the lung are uniform. We now know that this assumption is incorrect and that there is considerable variability in the mechanical behaviour of different regions of the lung. It may be useful to detect these differences and a new generation of imaging techniques is required.

Describing regional lung mechanics in infants at the bedside has been difficult. One exciting development in this field is Electrical Impedance Tomography (EIT), a relatively new imaging technique that has evolved over the past 25 years. Potentially of great value in clinical diagnosis, its main respiratory application currently is as a research tool in the investigation of regional lung function. EIT has the potential to improve our understanding of the complex tidal behaviour of the lung. It is a safe, non-invasive, radiation-free and portable technique which allows for the continuous monitoring of global and regional ventilation. Alternative imaging modalities such as computerized tomography (CT) and magnetic resonance imaging (MRI) deliver excellent resolution but are impractical because they require transport of the infant to the device and are expensive.

Recently we, and others, have shown that EIT is feasible in the newborn and may allow for more rapid alterations in ventilation strategy. It has the ability to identify adverse ventilatory events without the need for chest radiography and therefore an added radiation load. EIT is currently a research tool and more work needs to be done before it assumes a regular clinical role in the care of our patients. This presentation will discuss the potential of EIT in helping us understand the regional behaviour of the newborn lung at the bedside.

Respiratory Monitoring During Neonatal Resuscitation

Dr Georg Schmoelzer

Dr Georg Schmoelzer is an Austrian-trained Neonatologist who completed his neonatal training in Melbourne since arriving in 2007. He has joined the RWH neonatal respiratory research team in 2007 in order to pursue a higher research degree. His research interests lie in improving delivery room care using different methods of monitoring respiratory function. Georg continues to do some clinical work in NICU and is part of the Victorian Newborn Emergency Transport Team.

Abstract

Approximately, 3-6% of all newborn infants require respiratory assistance immediately after birth. An internationally agreed consensus statement and other guidelines that provide advice regarding techniques and equipment for neonatal resuscitation all agree that the key to successful neonatal resuscitation is the application of adequate positive pressure ventilation (PPV).

When preterm infants fail to breathe adequately immediately after birth, it is important to apply positive pressure ventilation in an appropriate, gentle way to create a functional residual capacity, facilitate gas exchange and minimize lung injury. However, the application of adequate PPV in the delivery room can be difficult because the assessment of whether the ventilation is effective is subjective and simply relies on an impression of adequate chest wall rise and an increase in heart rate. Applying the same technologies in the delivery room as those used in the neonatal intensive care units could improve the effectiveness of ventilation in preterm infants immediately after birth.

In contrast to the delivery room, ventilation in the neonatal intensive care unit is guided by ventilators which continuously display airway pressure, gas flow and tidal volume. Better delivery room care of preterm infants offers considerable potential for improving important short- and long-term outcomes.

Controversies in Neonatal Resuscitation and Ventilation

Professor Colin Morley

Professor Colin Morley is a clinician who can't stop doing research. He was educated at the University of Cambridge and trained in the UK. He was appointed a University Lecturer in Paediatrics and Consultant Paediatrician at the University of Cambridge and Addenbrookes Hospital in 1979. In Cambridge he developed a synthetic surfactant treatment for premature babies which was licensed and marketed in the UK, investigated the causes of cot deaths, developed Baby Check, a scoring system to help mothers and doctors evaluate the severity of an infant's illness, and studied neonatal ventilation.

In May 1998, he was appointed Professor/Director of Neonatal Medicine at The Royal Women's Hospital and The Royal Children's Hospital, Melbourne. His current research is investigating neonatal resuscitation, nasal CPAP, mechanical ventilation, hypoxic ischaemic encephalopathy, oxygenation and preventing infections. He has published over 240 manuscripts. He is a co-recipient of an NHMRC five year program grant to investigate lung disease in premature babies.

He retired from the Women's and Children's Hospitals in September 2008 but is still researching, writing and teaching.

Abstract

During this presentation I will discuss the problems with mask ventilation during resuscitation illustrating this by showing very instructive real time recordings with changes in ventilation pressure, flow, tidal volume, heart rate, oxygen saturation and inspired oxygen concentration. The talk will cover:

- Face mask position and hold
- Face mask obstructing the airway
- Face mask leak
- Adjusting the peak inflating pressure
- Positive end expiratory pressure (PEEP) and continuous positive airway pressure (CPAP)
- Bradycardia and changes in heart rate
- Hypoxia and oxygen saturation changes
- Adjusting the inspired oxygen concentration (FiO₂)
- Spontaneous breathing