

*Improving the health and wellbeing of ...*



PREVENTION  
INNOVATION  
DEDICATION



*every child*

Annual Report **2006 - Scientific Supplement**

# Telethon Institute for Child Health Research

## Who we are

The Telethon Institute for Child Health Research is Western Australia's only research facility dedicated to child health. Like the childhood illnesses and diseases we investigate, our team is diverse, consisting of some of Australia's, and the world's, leading experts in their fields.

We are housed in a purpose-built research facility on the edge of the Perth CBD and have close to 500 staff and students.

The Institute is a non-Government, not-for-profit organisation with strong affiliations with the State children's hospital and all the major WA universities.

## What we do

Our focus is on children, young people and their families.

We investigate the most complex, costly and devastating health problems facing our children in the 21st century. We approach these problems with dedication and innovation as we try to achieve our overall goal - prevention.

We work together. We work with others. We work hard to improve the life chances for all children.

You will find information about our broad range of research programs in the following pages.

## Our mission

To improve and to promote the health and wellbeing of all children through the unique application of multidisciplinary research.

## Our aims

- To conduct high quality research.
- To apply research findings to improve the health of children, adolescents and families.
- To teach the next generation of health researchers.
- To be an advocate for research and for children.

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# Every child



*At the Telethon Institute for Child Health Research we know that many children suffer through childhood from poor physical or mental health and disadvantaged environments.*

*Our dedicated team of close to 500 researchers and staff are committed to unravelling the complex issues that are affecting the health and wellbeing of our children.*

*Our unique multidisciplinary approach means that we explore these issues from many angles -- what are the genetic, environmental, biological, social and economic factors that are affecting the physical and emotional development of children?*

*Why do some children grow strong while others are sick?*

*Why do some succeed and others struggle?*

*What does it take for a child to grow up healthy and happy?*

*The answers are important for*  
**every child,**  
**every family,**  
**every community.**

*Our research themes reflect our broad approach:*

- Asthma, allergies and respiratory disease
- Cancer
- Healthy development
- Infectious disease
- Social and emotional wellbeing
- The early years
- Understanding disability
- Aboriginal child health

*We believe that **every child** should be given **every chance** to reach their full potential*

**PREVENTION**

**INNOVATION**

**DEDICATION**

# Division of Cell Biology

## Overview

The principal focus of research in the Division of Cell Biology continues to be the cellular and molecular mechanisms underlying resistance and susceptibility during childhood to inflammatory diseases in the respiratory tract, in particular those caused by allergy and infections. Earlier work from the Division has established an important paradigm in paediatric medicine, notably that risk for postnatal development of atopy and asthma and related diseases is determined primarily by maturational factors which control the transition of the immune system from the low activity state which is characteristic of fetal life, to the fully functional state seen in latter childhood. The key to this transition is the maturation of a variety of cytokine driven effector functions which are suppressed *in utero* in order to protect the placenta from inflammatory damage. These same mechanisms are necessary for resistance to both infections and allergy, and we have shown that the rate at which they mature functionally during the preschool years is a key determinant of risk for allergy, respiratory infection and asthma. Much of the work of the Division is targeted at more detailed definition of these mechanisms, with the aim of development of early intervention strategies to reduce disease susceptibility, ideally to prevent disease onset. A key component of these studies has recently reached the translational stage, in the form of a multinational trial on prevention of atopic asthma in high risk infants, coordinated in our labs in collaboration with the Division of Clinical Sciences, and funded by the US National Institutes of Health. A complementary stream of research in our Division is aimed at elucidation of the mechanisms that regulate the cell populations responsible for triggering the "late phase response" in asthma. This part of the asthmatic response is due to activation of T lymphocytes in the airway mucosa, and is largely responsible for progression from acute to chronic disease. Earlier work from the Division has identified the principal cellular trigger of this response, airway mucosal Dendritic Cells, and most recently we have shown that their pro-inflammatory functions are in turn controlled locally by T regulatory cells. Our ongoing studies in this area are aimed at development of new therapeutic strategies to dampen the pro-inflammatory functions of these Dendritic Cells in asthmatics.

## Aetiology and Pathogenesis of Atopy and Asthma

### Immunoprophylaxis of asthma and atopy

PG Holt in collaboration with PD Sly, Clinical Sciences, TICHR, R Loh, Princess Margaret Hospital, P Robinson, Royal Children's Hospital, Melbourne, H Sampson, Mount Sinai School of Medicine, New York, B Björkstén, Allergy Centre, Karolinska Institute, Stockholm and U Wahn, Charité - Universitätsmedizin, Berlin

After three years of intensive planning, in July 2006 we initiated a multicentre clinical trial on asthma/allergy prevention in high risk children in Perth, Melbourne and New York, under the auspices of the Immune Tolerance Network of the US National Institutes of Health. The trial is testing a radical method for prevention of these diseases in "high risk" children, employing a vaccine-like approach which is conceptually a mirror image of that used for prevention of infectious disease i.e. stimulation of development of immunological tolerance as opposed to active immunity. This trial strategy is based on the results of research in TICHR and in other centres in Europe and USA, indicating that the basis for natural resistance to sensitisation to inhaled allergens, and hence resistance to atopic asthma, is the development during early childhood of a form of immunological tolerance to inhaled allergen. This process is driven by repeated allergen exposure of the mucosal surfaces of the oropharynx, the nose, and the large airways, and the overall efficiency of tolerance induction is directly related to exposure intensity. In the trial we are seeking to increase the efficiency of the tolerance process in children at risk of allergy, by repeated exposure of the oral mucosa over for a one year period to a mixture of the three most important aeroallergens known to be associated with asthma in the areas of the trial centres in Australia, USA, Sweden and Germany (notably house dust mite, cat and grass allergens). The aim of this initial trial is to reduce atopy and asthma prevalence in these children over a 3 year follow-up period by 50%. An important component of the trial design involves detailed investigations on underlying allergen-specific immune responses in the children throughout the study period, to provide definitive information on underlying mechanisms. In response to requests from the US Food and Drug Administration who set the safety parameters for the trial, we are taking an initial group of 50 children through the first 6 months of treatment in Australia and the US to prove safety and efficacy, prior to opening up the additional trial sites in Europe to recruit a further 150 subjects. This process is well underway and as yet no safety issues have emerged.

This research is funded by the US National Institutes of Health Immune Tolerance Network.

### **The W.A. Pregnancy Cohort 13 year old Asthma Study**

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E Hollams, CE Ladyman, A Sadowska, M Serralha, D Suriyaarachchi, BJ Holt and PG Holt in collaboration with PD Sly, Clinical Sciences, TICHR

We have recently completed the respiratory component of the 14 year follow-up of the W.A. Pregnancy Cohort which has been followed intensively since birth. In this phase of the ongoing study, we have recruited 1,400 cohort members, with the aim of elucidating asthma and allergy phenotypes in this age group. We are currently analysing data on clinical history, genetic profile, lung physiology and immunology of the participants. Immunological assays undertaken have included allergen skin prick testing, haematology, and measurement of IgE and IgG4 to seven different allergens, measurement of eosinophil cationic protein and soluble CD14 from plasma, and leukotriene metabolites in urine. In addition, we are investigating both allergen-specific T-cell immunity and global measures of immune competence, and have obtained genotypic information on a large panel of atopy/asthma candidate genes. Completion of the *in vitro* analyses is on target for February 2007. After completion of the main part of the lab component, the focus of the work will shift to statistical analysis and modelling of the data obtained, which we envisage will be completed by the end of 2007. The long term objective is integration of the information collected to identify biomarkers which discriminate asthma subgroups, with the aim of improving diagnosis and treatment in this age group.

This research is funded by the National Health & Medical Research Council of Australia.

### **Identification of novel Th2-associated genes in allergen-stimulated T cells**

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A Bosco, K McKenna, C Devitt and PG Holt in collaboration with PD Sly, Clinical Sciences, TICHR

We have completed initial genome wide expression profiling of allergen specific T-cell memory responses in a large group of atopics, utilising Affymetrix microarray technology, the results of which appeared in the *Journal of Immunology* in late 2006. Analysis of the microarray results by hierarchical clustering has identified two major atopy-associated gene clusters containing several novel genes that exhibited expression patterns similar to known Th2 index genes. In particular, an "early" cluster of genes peaking 6 - 24 hrs following allergen stimulation was identified, which have not previously been recognised as part of the Th2 response profile; this cluster was enriched for a range of genes involved in cell signalling. A second cluster peaking at 48 hrs was enriched for genes associated with pro inflammatory effector functions. The

preferential expression of these novel genes in atopics following allergen stimulation has been confirmed by quantitative RT-PCR in several independent patient populations, and localised principally to CD4<sup>+</sup> Th cells, but with many also expressed in the CD8<sup>+</sup> Th cell population. Follow up studies are in progress stratifying these atopic responses by age and stage of (atopic) disease, and by symptomatology. In particular, we are seeking genes associated with stabilisation of allergen-specific Th memory, which are likely to be associated with progression to chronicity, and also genes associated with disease severity, which would be likely targets for anti-inflammatory drug development. We are additionally expanding our analytical methodology to encompass network analysis of microarray expression profiling data, which holds the promise of identification of a further layer of asthma/atopy candidate genes which escape detection by conventional analytical methodology.

This research is funded by the National Health & Medical Research Council of Australia.

### **Genome-wide identification of novel genes involved in acute asthma exacerbation in children**

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LS Subrata, E Mamessier and PG Holt in collaboration with P Le Souef, Paediatrics and Child Health, UWA

Acute asthma is a severe airways inflammatory disease, with respiratory viral infection being the most common cause of exacerbations leading to hospital emergency admission. We are approaching completion of studies on consecutive PBMC samples collected from child patients (2 - 12yo, mean 6.5) during an acute asthma attack and at convalescence at least six weeks post exacerbation. Affymetrix microarray technology is being utilised to identify novel genes differentially expressed *in vivo* between acute and convalescent stages of the disease, with the aim of contributing to our understanding of mechanisms leading to unleashed inflammatory processes in acute asthma. Initial analysis of the microarray data suggest that there are approximately 3500 genes differentially expressed between acute and convalescent stages. Functional and pathway analysis indicates that these genes are involved in a number of relevant biological pathways which include arachidonic acid/eicosanoid/leukotriene pathways, toll-like receptor (TLR) system, natural killer cells, FcεRI, complement and coagulation cascades, and leukocyte extravasation. Validation studies are in progress to control for potential effects of steroids given at the time of admission, and to verify the expression characteristics of sets of genes of interest.

This research is funded by the National Health & Medical Research Council of Australia.

## Effects of severe respiratory syncytial virus (RSV) infection on early immune profile development during infancy

E Mamessier, LS Subrata and PG Holt in collaboration with PD Sly, Clinical Sciences, TICHR

Respiratory syncytial virus (RSV) is a major cause of severe lower respiratory infection in infants and young children, leading to diseases such as pneumonia and bronchiolitis. Young children with severe RSV infection have an increased risk of developing childhood asthma later in life. In this study we are investigating innate and adaptive immune functions in two groups of acute RSV bronchiolitis infants with low versus severe bronchiolitis. Patient samples were collected at ten days post-hospitalisation with ages ranging ~ 2-12 months (Visit 1), then three months later (Visit 2), and finally at the age of 18 months. In response to *in vitro* RSV stimulation, the severe bronchiolitis group showed more sustained inflammatory responses at least during the three months post-infection, with high levels of IFN $\gamma$ , IL5, IL13, TNF and IL6 cytokine production maintained at Visits 1 and 2, but not at 18 months. In contrast, the low-infection group produced only IL6 at Visit 1 at lower levels, which rapidly decreased at Visit 2. Ongoing studies are focusing on expression of TLR associated genes, and Treg associated genes, in particular IL-10.

This research is funded by the National Health & Medical Research Council of Australia.

## Pre- versus postnatal sensitisation to environmental allergens in a high risk birth cohort

J Rowe, D Suriyaarachchi, M Serralha and PG Holt in collaboration with M Kusel and PD Sly, Clinical Sciences TICHR.

The issue of whether primary sensitisation to environmental allergens occurs transplacentally or only after birth remains controversial, with resolution of this question being important in relation to the design of rational strategies for allergy prevention in childhood. To elucidate the kinetics of allergen sensitisation in children during their first 2 years of life, we prospectively studied house dust mite (HDM)-specific IgE and IgG4 antibody production and associated T-cell immunity in a cohort of 200 infants at high genetic risk of developing atopy. We observed that HDM-induced T-cell responses in cord blood, although common, were unrelated to subsequent sensitisation. In contrast, T-helper 2 (Th2) responses in PBMC from 6 months onwards, particularly IL-4 and IL-5, correlated increasingly strongly with sensitisation outcomes at 2 years of age, and a contrasting negative relationship was observed with IFN $\gamma$ . In those children

who remained non-atopic at 2 years of age, transient HDM-IgE and IgG4 production frequently peaked at 6 or 12 months, before returning to baseline, suggesting the onset of tolerance. In contrast, progressively increasing HDM-specific IgE titres were observed in children sensitised to HDM at 2 years of age. We conclude that priming of Th2 responses and associated HDM-specific IgE observed in atopics occurs completely postnatally, with responses in cord blood being non-specific, and likely related to the activity of immunologically naive recent thymic emigrant CD4<sup>+</sup> T cells characterised in some of our earlier studies.

## Innate Immunity

### Airway epithelial cells and regulation of dendritic cell function

A Rate, JW Upham and PG Holt

Dendritic cells (DC) are the major antigen presenting cells of the lung and are closely regulated by signals in their microenvironment. DC and their precursors are in intimate association with airway epithelial cells (AEC) and recent published data suggests that AEC can influence DC differentiation and maturation. The current study aims to further characterise and elucidate the mechanisms behind AEC regulation of DC maturation. We have developed an *in vitro* AEC line/monocyte co-culture system, whereby in the presence of IL-4 and GM-CSF, maturation of monocytes into DC can be monitored. At Day 5, DC co-cultured with AEC are less phenotypically and functionally mature, expressing lower levels of surface markers and reduced efficiency at antigen presentation to T cells than DC cultured in media alone. In contrast, these cells are adept at sampling and processing antigen, functions generally ascribed to their more immature precursors. In view of these results, we would hypothesise that in steady state conditions, AEC restrict the full maturation of monocytes into DC and thus tightly regulate the adaptive immune response in the lungs. Identifying the mechanisms behind AEC regulation of DC maturation and whether these regulatory processes are less efficient in children with asthma is the focus of ongoing studies and will involve the use of primary AEC derived from asthmatic and non-asthmatic individuals.

This research is funded by the National Health & Medical Research Council of Australia.

### **Functional genomics of toll-like receptor (TLR)-4 in host responses to respiratory syncytial virus (RSV) and bacterial LPS**

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MK Tulic, JW Upham and PG Holt in collaboration with RJ Hurrelbrink, Virology, TICHR, CM Prêle, Molecular Biotechnology, TICHR, IA Laing, Population Sciences, TICHR, P Le Souef, Paediatrics and Child Health, University of Western Australia and PD Sly, Clinical Sciences, TICHR

Severe bronchiolitis following respiratory syncytial virus (RSV) infection occurs in only a small subset of infected infants, and the basis for variations in disease severity is not understood. Innate immune responses to RSV are mediated by Toll-like receptor (TLR)-4, and the 299Gly and 399Ile alleles of the TLR4 gene have been linked epidemiologically with increased severity of RSV disease in children. TLR4 is the receptor involved in bacterial (LPS)-induced signal transduction and recently it has been shown to recognise the F-protein of RSV. TLR4 is extremely polymorphic. We hypothesized that cellular immune responses to RSV mediated by these variant forms of the receptor are defective relative to responses mediated via the common form of the receptor. Human bronchial epithelial (HBE) cells were transfected with TLR4 constructs encoding the common TLR4 gene sequence (299Asp/399Thr), or the 299Gly or 399Ile alleles, and cytokine responses to *in vitro* RSV challenge were analyzed in the different transfected cells. Follow up studies compared RSV induced responses in PBMC from children expressing these same TLR4 genotypes. HBE expressing 299Gly or 399Ile displayed normal levels of intracellular TLR4 but failed to efficiently translocate receptor to the cell surface. This was associated with reduced NF- $\kappa$ B signaling post TLR4 engagement, reduced production of interferons, IL-8, IL-10, IL-12p35, IL-18 and CCL8, and the absence of acute-phase TNF $\alpha$ . Similar inhibition was seen using UV-inactivated RSV suggesting viral replication was not required for this effect. These findings were mirrored by blunted PBMC responses to RSV in children expressing the same TLR4 variants. We propose that poor expression of TLR4 on PBMC from children heterozygous for the Asp299Gly or Thr399Ile results in decreased LPS binding which causes reduced NF- $\kappa$ B signaling and cytokine production. Compromised first-line-defense against RSV at the airway-epithelial surface of children expressing these TLR4 variants may thus confer increased susceptibility to severe infections with this virus.

This research is funded by the National Health & Medical Research Council of Australia.

### **Antigen presenting cells during infancy**

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JW Upham, B Zhang, and PG Holt in collaboration with M Kusel and PD Sly, Clinical Sciences, TICHR

Dendritic cells (DC) are antigen presenting cells that are fundamental to regulation of the immune response. Our studies have focussed on the way in which DC function changes with age, and how this is related to the development and perpetuation of asthma.

We have examined DC subsets at 6 months, 12 months, 2 years and 5 years of age in a large cohort of children, and have shown that the numbers of circulating plasmacytoid DC at age 6 months and 12 months are independent predictors of respiratory tract infections and doctor-diagnosed asthma within the first 5 years of life. Children with lower numbers of plasmacytoid DC during infancy are at greater risk of respiratory infections and asthma. Current studies are examining whether these alterations in DC subsets are present at birth, or whether they develop in early post natal life.

This research is funded by the National Health & Medical Research Council of Australia.

### **Inhibition of the allergic response by bacterial lipoproteins and lipopeptides**

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S Yerkovich and JW Upham in collaboration with P Hart (Molecular Biotechnology TICHR)

Various microbial components interact with toll-like receptors (TLRs), key molecules involved in innate and adaptive immunity. We have recently shown that lipoproteins and lipopeptides derived from Gram-positive bacteria markedly inhibit allergen-specific Th2 responses in atopic individuals, but have no effect on responses in non-atopic individuals, and do not inhibit responses to other antigens such as tetanus toxoid. This effect is associated with changes in the expression of a family of regulatory molecules known as suppressor of cytokine signalling (SOCS). Further work is needed to determine the specific mechanisms involved, but this work has the potential to provide a foundation for developing new methods to treat allergic diseases such as asthma.

This research is funded by the National Health & Medical Research Council of Australia.

## Vaccine Studies

### **Neonatal immunization with pneumococcal conjugate vaccine in Papua New Guinea**

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AHJ van den Biggelaar, MA Nadal-Sims and PG Holt in collaboration with D Lehmann (Population Sciences, TICHHR), P Richmond, UWA School of Paediatrics and Child Health, and S Phuanokoonnon, W Pomat and P Siba, Papua New Guinea Institute of Medical Research

Infants in Papua New Guinea (PNG) are at high risk for neonatal onset of dense respiratory tract pneumococcal (Pnc) colonisation (median age of colonization is 17 days), which is associated with increased risk of invasive pneumococcal disease. In order to protect these high-risk groups from early Pnc disease and mortality, neonatal immunization with pneumococcal conjugate vaccine (PCV) has to be considered. Our current study in the PNG highlands involves 312 newborns that will be randomised to receive PCV either at 1) birth-1mo-2mo, or 2) 1mo-2mo-3mo or 3) receive only routine immunizations (control group). It is aimed at providing proof-of-principle of the safety and immunological feasibility for such a vaccination strategy. In addition, bacterial carriage is assessed weekly for the first month of life and at regular intervals thereafter, and children are followed for respiratory and other diseases throughout the study, and venous blood samples to study cellular and humoral immunity will be collected at birth and 2, 3, 4, 9, 10 and 18 months of age. At the end of 2006, 232 (75%) children had been enrolled of which 153 had completed the 3 month follow up (first time point of venous blood collection for cellular immunology) and 8 children had completed the full 18-month follow-up period. The success rate of collecting venous blood samples for cellular immunological studies has been 85%. We will therefore be able to address in this cohort important questions regarding the basic immunological mechanisms underlying conjugate vaccine responses during the critical neonatal period, the effect of early carriage or invasive disease on the development of systemic immunity to Pnc infections, and provide insights into the interactions between the developing T-cell system and neonatal vaccines against a background of intense microbial stimulation.

This research is an International Collaborative Research Grant funded by the Wellcome Trust, UK and the National Health & Medical Research Council of Australia.

### **The effect of high microbial exposure on early immune development**

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AHJ van den Biggelaar and PG Holt in collaboration with SL Prescott, UWA School of Paediatrics and Child Health, and P Siba, Papua New Guinea Institute of Medical Research

The current paradigm relating to postnatal development of immune competence is that early microbial exposure drives the maturation of the neonatal immune system from predominantly T helper 2 (Th2) towards protective T helper 1 (Th1) responses. Although this pattern of immune development has been well described for children in developed countries, it is not known whether these mechanisms hold true for children in the developing world, where higher exposure to infectious pathogens has been associated with the activation of counter regulatory mechanisms. In order to test the general applicability of this paradigm, we are directly comparing immune responses in cord blood mononuclear cells obtained from births in Papua New Guinea (PNG), with those from newborns in the metropolitan area of Western Australia. Our main focus is on the Toll-like receptor (TLR) system, and its relationship to early T cell development. This study will provide timely data on neonatal immunological pathways that are central to resistance to infectious diseases and vaccine efficacy, in Third World paediatric populations who are at greatest risk of infectious diseases. In particular, it may provide insight into the choice of vaccine adjuvant strategies which are most relevant to Third World settings.

This research is an International Collaborative Research Grant funded by the Wellcome Trust, UK and the National Health & Medical Research Council of Australia.

### **Immuno-epidemiology of Bacille Calmette-Guérin (BCG) vaccination**

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AHJ van den Biggelaar, M Roponen and PG Holt in collaboration with SL Prescott, UWA School of Paediatrics and Child Health and P Siba, Papua New Guinea Institute of Medical Research

Infants in low-income countries are vaccinated with BCG, preferably within the first month of life. Although the underlying mechanisms are not clear, it has been shown that BCG can induce protective T helper 1-memory responses, probably by accelerating dendritic cell maturation in this young age group. However, the efficacy of BCG immunization appears to vary within and between populations. In addition, there are epidemiological indications that the age and consequently relative order in which BCG is given in relation to other childhood vaccines may be related to non-specific childhood mortality risk. The immunology that may underlie these observations



has, however, never been studied. One approach to address this problem is elucidation of the potential pro-inflammatory effects of BCG on innate immune responses of newborns in low versus high infection environments, typified by the PNG:Perth populations described above. Our first data from these comparisons show that *in vitro* BCG induced pro-inflammatory responses (type-I interferon, IL-6, TNF-alpha, IL-23p19) are reduced and anti-inflammatory responses (IL-10) increased, in PNG newborns relative to Perth newborns. This indicates that in high infectious environments BCG-induced innate immune responses are skewed towards negative immune regulation, which may increase the threshold to induce protective immune responses and hence limit vaccine efficacy. In our second approach we aim to address the issue of whether age and hence relative order in which BCG is given in relation to other childhood vaccinations modulates the immune responses induced by BCG and/or other vaccines. To address this question we will study T cell responses to *Mycobacteria* derived purified protein derivative (PPD), Hepatitis B antigen (HbsAg), Diphtheria toxoid and measles lysate in a cohort of PNG infants that received BCG vaccination at different ages varying from birth to 9 months.

This research is an International Collaborative Research Grant funded by the Wellcome Trust, UK and the National Health & Medical Research Council of Australia.

### **Infection site side effects following pre-school vaccination with diphtheria, tetanus, acellular pertussis: elucidation of related vaccine-specific Th2 memory responses**

J Rowe, O White and PG Holt in collaboration with P Richmond, UWA School of Paediatrics and Child Health

Recent studies from our laboratory have established a potential link between priming during infancy (2, 4, 6 and 18 months of age) with the diphtheria tetanus acellular pertussis (DTaP) vaccine and the incidence of large local reactions to the pre-school DTaP booster. Immunological studies on these children indicate that local reactions are associated with pre-existing and boostable T-helper 2 (Th2)-polarised immunological memory to vaccine antigens demonstrable in both the humoral (IgE) and cellular (IL-5, IL-6 and IL13) compartments. With the aim of reducing the incidence of large local reactions, while still maintaining immunological memory, the Standard Australian Vaccination Schedule has recently changed for DTaP to a 3 dose priming regime, with the removal of the 18 month dose. We are attempting to determine what effects removal of the 18 month DTaP dose has on the persistence of vaccine-specific memory and the incidence of local reactions seen following the pre-school dose. For this study, we are collecting blood samples from 100

children at the time of their pre-school DTaP booster, and again 6 weeks and one year later. Vaccine-specific humoral and cell-mediated immunity will be examined as per the forerunner study. In addition, we will use micro-array technology to gain further insights into the Th2 pathway of immune memory, and the inflammation associated with the large local reactions.

### **Meningococcal B vaccine trial**

J Rowe, O White and PG Holt in collaboration with P Richmond, UWA School of Paediatrics and Child Health

*Neisseria meningitidis* is an obligate human pathogen that is carried in the upper respiratory tract by around 5 - 10% of the population. Occasionally the bacteria disseminate to cause invasive disease such as bacteremia and meningitis, particularly in young children and teenagers/young adults. Whilst early antibiotic treatment is often successful, prevention through vaccination is the ultimate goal. Currently the only vaccine available is to serotype C (polysaccharide conjugate vaccine), although 50 -70% of disease in developed countries is caused by serotype B. However, vaccine development for meningococcal B has been difficult as the polysaccharide capsule is poorly immunogenic in humans and has structural similarities to human neural antigens, raising questions of safety. Consequently, Wyeth has developed a candidate meningococcal B vaccine (vaccine is based on a surface exposed lipoprotein) that is currently in Phase I clinical trials. As part of this trial, healthy adults have been given 3 doses of the meningococcal B vaccine (at 0, 1 and 6 months) and we have collected blood samples before and after each dose. We are examining the development of cell-mediated immunity to the lipoprotein contained in the meningococcal B vaccine, employing cryobanked PBMC collected during the trial. This data will be merged with data on humoral immunity obtained by Wyeth, in order to obtain a complete understanding of what effect this vaccine is having on immune function.

### **Animal Model Studies**

#### **Airway mucosal DC (AMDC) maturation is controlled by local T cell interaction following repeated antigen challenge**

DH Strickland, JA Thomas, PA Stumbles, PG Holt in collaboration with GR Zosky, DJ Turner and PD Sly, Clinical Sciences, TICHR

We have recently provided evidence linking the functions of AMDC and T regulatory cells (Treg) with the intensity and duration of airway mucosal T cell activation during the asthma late phase response (LPR), and the ensuing development of airways hyperresponsiveness (AHR). The

result of this rat model study, published recently in the *Journal of Experimental Medicine*, implicate Treg as integral components of the “off switch” in asthma exacerbations. A key finding in the study was the capacity of adoptively transferred Treg to inhibit AHR development in sensitised, aerosol (allergen) challenged recipient animals. This finding has significant therapeutic implications, as it suggests that Treg activated at sites outside of airway mucosa have potential for recirculation to sites of allergen-induced inflammation in the airways, to re-establish homeostasis. This possibly will be tested further during 2007.

This research is funded by the National Health & Medical Research Council of Australia.

### **Dendritic cells are activated in the airways prior to the onset of experimental allergic airways disease.**

C von Garnier, ME Wikstrom, PG Holt and PA Stumbles

In order to gain a better understanding the cellular interactions involved in the allergic reactions of the airways, we have been studying the activation of T cells and dendritic cells (DC) in the airways of allergic mice. Mice were sensitised by systemic immunisation with a model allergen (ovalbumin), and then exposed to three daily aerosol doses in order to elicit an allergic reaction in the airways. Twenty-four hours after the first challenge, we found evidence of hyper-responsiveness in the airways and an influx of eosinophils, indicative of an allergic reaction that continued to consolidate with subsequent challenge doses. When the expression of a range of activation molecules was examined on the surface of T cells and DC in the airways, we found that DC expressed high levels of CD40 twelve hours after the first aerosol challenge. This increase in DC activation coincided with a transient increase in the proportion of activated CD4<sup>+</sup> T cells in the airways, suggesting the two cell types had interacted prior to the onset of the allergic reaction at 24 hours.

This research is funded by the National Health & Medical Research Council of Australia.

### **Tracking the fate of airborne allergen in the airways during induction of allergic airways inflammation**

ME Wikstrom, SR Judd, PG Holt and PA Stumbles

Over the last twelve months we have continued tracking the fate of airborne allergens in mice. In our previous studies, we used tagged allergen preparations to identify migratory dendritic cells (DC) that had delivered an inhaled allergen to the draining lymph nodes. Using the same strategy, we examined the range of cell types

present in the airways that could capture the allergen within two hours of administration with some striking results. For example, one subpopulation of DC (which expresses high levels of CD11b) could capture reasonably large amounts of allergen, while another (which expresses low levels of CD11b), could not, suggesting they may be equipped to perform different functions. Interestingly, when the airways were sensitised by systemic immunisation with allergen, we observed a striking increase in allergen capture and processing by all airway DC as well as other antigen-presenting cells, such as B cells. This increase could be attributed to specific antibody contained in the serum of immunised mice, indicating that antibody may enhance immune activation in the airways by improving allergen capture and processing by local DC. Over the next twelve months, we will continue to characterise the influence of specific antibody on DC function in the airways.

This research is funded by the National Health & Medical Research Council of Australia.

### **Induction of immunological and physiological tolerance following prolonged allergen exposure in a mouse model of airways hyperresponsiveness**

J Burchell, ME Wikstrom, PD Sly, PG Holt, DJ Turner and PA Stumbles in collaboration with PD Sly, Clinical Sciences, TICHR

Airway hyperresponsiveness (AHR) is one of the primary features of allergic airways disease. However its pathogenesis remains unclear. The aim of this study has been to develop a murine model of physiological and immunological tolerance following multiple exposures to inhaled allergen, and to examine the roles of airway CD4<sup>+</sup> T cells in this process. BALB/c mice were systemically sensitised to ovalbumin and then given 1, 8 or 16 OVA aerosol challenges. A single OVA aerosol produced AHR (as measured by low-frequency forced oscillation technique) whilst multiple (x8) aerosols resulted in tolerance. Airway and parenchymal eosinophilia, allergen-specific IgE and IgG1, airway wall thickness and numbers of goblet cells within airway epithelium were maximal after 8 aerosols and reduced after 16. While similar proportions of CD4<sup>+</sup> T cells became activated following both aerosol regimes, total numbers of airway CD4<sup>+</sup> T cells were significantly decreased, and OVA-specific CD4<sup>+</sup> T cell proliferation in draining lymph nodes (DLN) was significantly reduced, after multiple (x8) as compared to a single aerosol challenge. Coinciding with this was a decrease in the capture and processing of allergen by antigen presenting cells (APC) in the airways (dendritic cells, B cells and interstitial macrophages) and by subsets of CD11b<sup>+</sup> DC in DLN. In conclusion, these data indicate

that the immunological and physiological tolerance induced by multiple OVA airway challenges is associated with inhibition of allergen-specific CD4<sup>+</sup> T cell division in the DLN and/or recruitment into the airways, the underlying mechanism of which is a generalised reduction in the capacity of airway APC to capture, process and traffic inhaled allergen. The mechanisms mediating the down-regulation in allergen capture and processing are currently under further investigation.

This research is funded by the National Health and Medical Research Council of Australia and the Asthma Foundation of WA.

### **Identification of a candidate progenitor cell(s) for dendritic cells and other antigen-presenting cells within in the mouse respiratory tract**

DH Strickland, C von Garnier, ME Wikstrom, M Smith, JA Thomas, PG Holt and PA Stumbles

Antigen-presenting cells (APC), including myeloid-origin dendritic cells (mDC), are central to antigen surveillance in the respiratory tract (RT). It is unclear at present if RT-APC are recruited from the blood differentiated as early precursors, or whether resident pluripotential progenitors exist in the RT. The latter would provide at the same time both a close proximity to the respiratory tract environment and a readily available source of strongly immunogenic mDC. We have previously characterised antigen-presenting cell populations in different respiratory tract compartments and identified a novel rapid turn-over precursor region confined to lung parenchymal tissue. The surface phenotype of this population was CD11c<sup>low</sup> MHCII<sup>-</sup> CD11b<sup>+</sup> F4/80<sup>+</sup> Gr-1<sup>+</sup>, CD34<sup>-</sup> c-kit<sup>-</sup> and a proportion of cells within this region also expressed Sca-1. As shown by electron microscopy, ultra-structural characteristics of this cell population were those of a DC/monocytic progenitor. *In vitro* T cell activation by cells within the CD11c<sup>low</sup> MHCII<sup>-</sup> region was delayed by 72h compared with other lung APC, suggesting that a maturation and/or differentiation step was required during the culture period to achieve full immunostimulatory capacity. Following exposure to GM-CSF, the CD11c<sup>int</sup> MHCII<sup>-</sup> candidate progenitor region gave rise to both CD11c<sup>+</sup> MHCII<sup>+</sup> mDC and CD11c<sup>+</sup> MHCII<sup>int</sup> macrophage populations. Cells within this population therefore represent candidate progenitor cell(s) for mDC and other APC populations in lung parenchymal tissue.

This research is funded by the National Health and Medical Research Council of Australia

## *Staff and Students*

### **Head of Division**

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Patrick G Holt PhD FRCPATH DSc FRCPI MD(Hon) FAA  
Deputy Director, Telethon Institute for Child Health Research

Adjunct Professor, Centre for Child Health Research, UWA

Senior Principal Research Fellow, National Health & Medical Research Council of Australia

### **Research Staff**

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Karen Coster

Catherine Devitt BSc

Lan Doan Grad Dip (Sci)

Elysia Hollams PhD

Barbara Holt BSc

Samantha Judd BSc(Hons)

Claire Ladyman BSc DipEd (FSc)

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### **Postgraduate Students**

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Anthony Bosco BSc(Hons) PhD candidate

Jacinta Francis BSc(Hons) MSc candidate

Angela Rate BSc PhD candidate

Rebecca Taylor BSc MSc candidate

### **Visiting Research Fellows**

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Dr Emilie Mamessier PhD, Pathologie respiratoire liée à l'environnement, Université de la Méditerranée, Marseille, France.

Dr Marjut Roponen PhD, Department of Environmental Health, National Public Health Institute, Kuopio, Finland.

### **Research Support**

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Anne Amourgis

## *Theses passed*

Angela Taylor PhD University of Western Australia: Allergy Prevention Studies: The role of probiotics in allergy prevention in high-risk infants.

## *External Committees*

### **International**

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Patrick Holt. NIH Program Grant advisory panel - URECA study, University of Wisconsin.

Patrick Holt. NIH Program Grant advisory panel - Harvard Medical School/GIT flora study.

Patrick Holt. NIH Expert Committee on Food Allergy.

Patrick Holt. Chair, International Scientific Advisory Board, Centre for Translational Medicine, James Connolly Memorial Hospital, Dublin.

### **National**

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Patrick Holt. Sectional Committee for Biochemistry, Molecular Biology & Immunology, Australian Academy of Sciences.

Philip Stumbles. Member, National Health & Medical Research Council of Australia Training Award Committee.

Philip Stumbles. Australasian Society for Immunology (WA Branch) Student Symposium Committee.

Philip Stumbles. Australian Society for Medical Research, WA Medical Research Week Symposium Committee.

John Upham. National Health & Medical Research Council of Australia Training Award Committee.

John Upham. National Health & Medical Research Council of Australia, Grant Review Panel.

John Upham. Asthma Foundations of Australia, Medical & Scientific Advisory Committee.

John Upham. Education and Research Subcommittee, Thoracic Society of Australia & New Zealand.

## *Invited Presentations*

Patrick Holt. NIH Expert Committee on Food Allergy, Bethesda, Maryland, March, 2006.

Patrick Holt. Primary prevention of atopic asthma by oral mucosal immunoprophylaxis - 6th Symposium on Specific Allergy, Copenhagen, March, 2006.

Patrick Holt. The role of T regulatory cells in immunotherapy 6th Symposium on Specific Allergy, Copenhagen, March, 2006.

Patrick Holt. Probiotics and the Hygiene Hypothesis - FASEB Symposium, San Francisco, April, 2006.

Patrick Holt. Mechanisms of Inflammation - Keystone Symposium on Allergy, Allergic Inflammation and Asthma, Breckenridge, April, 2006.

Patrick Holt. Novel genes in human Th2 responses - 26th Symposium of Collegium Internationale Allergologicum, Malta, May, 2006.

Patrick Holt. Regulation of T cell immunity to inhaled antigens: programming of allergen responder phenotype during childhood - American Thoracic Society Congress, San Diego, May, 2006.

Patrick Holt. The immunology of tolerance and allergy - Karolinska Institute Symposium in honour of Bengt Björkstén, Stockholm, June 2006.

Patrick Holt. Clinical perspectives of early exposure to allergens - XXV Congress of the European Academy of Allergy & Clinical Immunology, Vienna, June 2006.

Patrick Holt. Development of improved multiplex profiling techniques for use in diagnosis and management of Allergic Disease - XXV Congress of the European Academy of Allergy & Clinical Immunology, Vienna, June 2006.

Patrick Holt. Programming of persistent atopic asthma in early childhood - Joint meeting of British Society for Immunology/Irish Society of Immunology, Belfast, September, 2006.

Patrick Holt. Regulation of the induction and expression of T cell immunity in the respiratory tract - Immunology and Infectious Diseases Research Group, University of Saskatchewan, October, 2006.

Patrick Holt. Aetiology and pathogenesis of atopic asthma - Department of Immunology, University of Manitoba, October, 2006.

Patrick Holt. Contemporaneous maturation of

immunologic and respiratory functions during early childhood: early programming for resistance or susceptibility to atopic asthma - 56th Annual Meeting of Japanese Society of Allergology, Tokyo, November, 2006.

Patrick Holt. Early intervention strategies for primary prevention of atopic disease - 56th Annual Meeting of Japanese Society of Allergology, Tokyo, November, 2006.

Patrick Holt. The role of novel Th2 and Th1 genes in atopic responses - 56th Annual Meeting of Japanese Society of Allergology, Tokyo, November, 2006.

Patrick Holt. The role of infant RSV infection in asthma pathogenesis - International Symposium on RSV infection in infancy, Chiba, November, 2006.

Deborah Strickland. Dendritic cells and the immunological homeostasis of the lung - ERS Annual Conference, Munich, September, 2006.

Philip Stumbles. The role of airway dendritic cells in the induction of allergic airways inflammation - 8th Annual MMRI Dendritic Cell Symposium, Brisbane, July 2006.

Philip Stumbles. Allergen uptake and processing at airway mucosal surfaces during induction of allergic airways inflammation - 9th International Conference on Dendritic Cells, Edinburgh, September 2006.

# Division of Children's Leukaemia and Cancer Research

## Overview

Paediatric cancers comprise many diseases. More than half of them affect cells of the immune system and the central nervous system, while only a minority involve epithelial cells. Thus, the most common malignancy in children is leukaemia, followed by brain tumours. In order to find better therapies for children with cancer, the Oncology Total Care Unit at Princess Margaret Hospital (PMH) and our division at the Institute are both members of the largest study group into these diseases, the US-based Children's Oncology Group (COG).

The research program of the Division focuses on childhood leukaemia and brain tumours. The main goals are the identification of genetic alterations that lead to childhood cancers and the application of this knowledge to the prognosis and improved therapeutic approaches for patients. In order to examine the genetic lesions present in the various types of cancer, we make use of the microarray technology to determine gene expression profiles. The initial studies involved our panel of established leukaemia cell lines since they are ideal tools for subsequent testing of potential new drugs for the treatment of patients. Currently, a large study on primary patient specimens is in progress with the ultimate aim to achieve improved risk stratification for acute lymphoblastic leukaemia (ALL) patients and to understand the genetic basis for chemoresistance.

## Leukaemia

### **Prediction of relapse in paediatric acute lymphoblastic leukaemia (ALL) using 3-gene defined diagnostic classifiers**

K Hoffmann, NG Gottardo, JR Freitas, AH Beesley and UR Kees in collaboration with MJ Firth, KU Perera and NH de Klerk, Division of Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research and DL Baker, Department of Haematology-Oncology, Princess Margaret Hospital, Perth, Western Australia.

Despite the high cure rates, resistant forms of childhood ALL constitute a leading cause of cancer-related morbidity and mortality in children. The clinical outcome measured as 5 year event-free survival (EFS) has reached up to 85% for patients classified as standard risk (SR) and 64-75% for high risk (HR) patients. However, a substantial number of patients currently classified and treated as SR patients continue to relapse, highlighting an urgent need for a more comprehensive risk stratification at the time of diagnosis. We examined the use of gene expression profiles (GEPs) to predict long-term clinical outcome in children with ALL. We initially analysed GEPs from 55 pre-B ALL patients using HG-U133A arrays. Subsequently, a multigene classifier for outcome prediction was developed and confirmed by quantitative RT-PCR (qRT-PCR). In an independent cohort of 46 pre-B ALL patients this multigene classifier was tested using qRT-PCR. In the test cohort (n=55) supervised outcome-prediction analysis identified 18 genes that predicted outcome with a high accuracy (89%). This 18-gene classifier (18-GC) was not only significantly linked to clinical outcome, but was also more predictive of outcome than conventional parameters currently used for risk stratification. After feature selection and validation of expression levels by qRT-PCR, a defined diagnostic 3-gene classifier (3-GC) was developed based exclusively on data from the test cohort. This 3-GC was able to predict outcome in an independent validation cohort (n=46). We subsequently applied the same methodology to a cohort of T-cell ALL (T-ALL) patients and were able to identify a 3-GC to predict relapse in these patients. These studies demonstrate the feasibility of building a prognosis predictor based on GEP, to improve risk stratification in childhood ALL. This is particularly important for the identification of patients currently stratified as SR for whom more intensive up-front treatments are already available. Currently a larger study is in progress to extend these findings. It focuses on a cohort of 50 T-ALL patients who were all treated on the same COG therapy protocol. The GEPs for these specimens were generated using the most recent and comprehensive HG-U133 Plus 2.0 microarrays (54,657 probe sets).

This work was funded by the US National Institutes of

Health and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **The relevance of cell lines as a model for drug-resistance in acute lymphoblastic leukaemia**

AH Beesley, ML Palmer, J Ford, RE Weller, AJ Cummings, JR Freitas and UR Kees in collaboration with MJ Firth, KU Perera and NH de Klerk, Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research.

Cell lines are important models for drug resistance in acute lymphoblastic leukaemia (ALL) but are often criticized as being unrepresentative of primary disease. There are also doubts regarding the authenticity of many lines. We have characterized a panel of ALL cell lines for growth and drug resistance and compared the data to that published for primary patient specimens. In contrast to the convention that cell lines are highly proliferative, those established in our laboratory grow at rates similar to estimates of leukaemic cells *in vivo* (doubling time 53-442 hours). Authenticity was confirmed by genetic fingerprinting, which also demonstrated the potential stability of long-term cultures. *In vitro* glucocorticoid resistance correlated well with that measured *ex vivo* but all lines were significantly more sensitive to vincristine than primary specimens. Sensitivity to methotrexate was inversely correlated with that of glucocorticoids and L-asparaginase, indicating possible reciprocity in resistance mechanisms. A cell line identified as highly methotrexate resistant (IC<sub>50</sub> >8000-fold higher than other lines) was derived from a patient receiving escalating doses of the drug, indicating *in vivo* selection of resistance as a cause of relapse. Many of these lines are suitable as models to study naturally occurring resistance phenotypes in paediatric ALL.

This work was funded by the NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### ***In vitro* cytotoxicity of nelarabine, clofarabine and flavopiridol in paediatric acute lymphoblastic leukaemia**

AH Beesley, ML Palmer, J Ford, RE Weller, AJ Cummings, JR Freitas and UR Kees in collaboration with MJ Firth, KU Perera and NH de Klerk, Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research.

The *in vitro* efficacies of three new drugs - clofarabine (CLOF), nelarabine (NEL) and flavopiridol (FP) - were assessed in a panel of acute lymphoblastic leukaemia (ALL) cell lines. The IC<sub>50</sub> for CLOF across all lines was 188-fold lower than that of NEL. B-lineage, but not T-

lineage lines, were >7-fold more sensitive to CLOF than cytosine arabinoside (ARAC). NEL IC<sub>50</sub> was 25-fold and 113-fold higher than ARAC in T- and B-lineage respectively. T-ALL cells were 8-fold more sensitive to NEL than B-lineage but there was considerable overlap. FP was more potent *in vitro* than glucocorticoids and thiopurines and at doses that recent Phase I experience predicts will translate into clinical efficacy. Potential cross-resistance of CLOF, NEL and FP was observed with many front-line ALL therapeutics but not methotrexate or thiopurines. Methotrexate sensitivity was inversely related to that of NEL and FP. Whilst NEL is particularly effective in T-ALL, a subset of patients with B-lineage ALL may also be sensitive. CLOF appears marginally more effective in B-lineage than T-ALL and has a distinct resistance profile that may prove useful in combination with other compounds. FP should be widely effective in ALL if sufficient plasma levels can be achieved clinically.

This work was funded by the NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **Markers of drug-resistance in acute lymphoblastic leukaemia**

AH Beesley, ML Palmer, J Ford, RE Weller, JR Freitas, UR Kees in collaboration with MJ Firth, KU Perera and NH de Klerk, Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research.

A significant number of patients with acute lymphoblastic leukaemia (ALL) continue to relapse and for these the outlook is dismal due to the development of drug-resistance. Over the past 20 years our laboratory has developed a panel of paediatric ALL cell lines that retain critical features of the primary disease. Using the MTT viability assay we have measured the sensitivity of these cell lines to 13 commonly used ALL chemotherapeutic agents and have measured gene-expression profiles by Affymetrix HG-U133A microarray. In contrast with many of the cell lines that are available commercially, our cell lines generally grow at slow rates similar to the growth of leukaemic blasts *in vivo*. Their drug-resistance profile parallels the spectrum of resistance that has been observed in primary patient specimens, particularly in regard to dexamethasone. We have correlated drug-resistance and gene-expression profiles to generate an extensive database of drug-gene signatures that are currently being analysed for biological function. From this we have identified a link between glucocorticoid resistance and the expression of *MLL*, a commonly translocated gene in ALL. Comparison of drug-gene signatures with the publicly available Connectivity Map has provided potential drug-leads that are under test in our laboratory. We are also in the process of developing

a gene expression-algorithm based on our *in vitro* drug-gene resistance data that can predict outcome in primary patient specimens. Currently, using microarray data generated from our cohort of T-ALL patient specimens, we can predict relapse with >80% accuracy using a 7-drug model derived from our cell line drug-gene profiles. It is anticipated that the genes and pathways identified here will generate novel drug-leads that may contribute to the treatment and prognosis of patients with ALL.

This work was funded by the NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **A novel role for the *MLL* gene in steroid resistance in acute lymphoblastic leukaemia**

AH Beesley, ML Palmer and UR Kees in collaboration with MJ Firth, KU Perera and NH de Klerk, Biostatistics and Genetic Epidemiology, Telethon Institute for Child Health Research.

Rearrangements of the *MLL* gene, located at chromosome 11q23, are associated with aggressive leukaemias. All children with *MLL*-associated ALL (most of whom are infants) have extremely poor prognosis, although there remains considerable clinical heterogeneity within this cohort. Through its regulation of *HOX* genes, wild-type *MLL* is essential for normal mammalian development and haematopoiesis, yet the locus is highly unstable, with translocations occurring with >30 partner genes on various chromosomes. We have recently studied the resistance of a panel of ALL cell lines to a number of clinically relevant drugs including the steroids dexamethasone and methylprednisolone. Steroids are among the most important classes of drugs used to treat childhood ALL and elevated resistance to them is a feature of relapse. Steroid resistance is also prominent in patients with *MLL* disease. By correlating *in vitro* resistance profiles with gene expression data generated using Affymetrix U133A microarrays, we have identified a negative correlation between steroid resistance and *MLL* mRNA expression (i.e. high resistance, low *MLL* expression). This was evident in both B- and T-lineage cell lines, but was particularly strong for T-ALL cells ( $p < 0.0001$ ). No karyotypic 11q23 abnormalities were identified in the T-ALL cell lines, consistent with the fact that *MLL* translocations are rare in this lineage. Thus, we hypothesise that steroid resistance is related to reduced expression of the wild-type *MLL* protein. The well-documented steroid resistance observed in patients with *MLL*-rearrangements may therefore result from a decrease in the expression of wild-type *MLL* following the loss of one allele during translocation. Investigations are underway to more precisely define the *MLL* status of our panel of 22 ALL cell lines, focusing on genetic changes and

gene expression. We are altering the expression of the gene in these cells to monitor the effect on resistance to steroids and other clinically relevant ALL drugs. We are also using a bioinformatics approach to identify genes and pathways that are regulated by *MLL* using our existing microarray data on primary specimens and cell lines. The link between *MLL* expression and steroid resistance is relevant for all patients with ALL, not just those with *MLL* rearrangements, and has important implications for risk stratification and the design of therapeutic protocols.

This work is funded by the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **Paediatric brain cancers**

#### **The identification of deregulated genes and pathways involved in the pathogenesis of primitive neuroectodermal tumours**

PB Dallas, DJ Holthouse, C Bertram, S Egli and UR Kees

The greatly improved outlook for children with leukaemia, the most common paediatric cancer, is a major success story in cancer biology. Unfortunately, this success has not been matched for childhood brain tumours, the second most common type of paediatric cancer. Five-year survival rates have remained in the 50-70% range for at least 20 years, and the prognosis remains particularly dismal for those with recurrent or metastatic disease. In addition, brain tumour survivors often face serious long-term quality of life issues that can be devastating for both child and family.

The relatively poor outlook for children with brain tumours can be largely explained by the fact that the molecular pathogenesis of primitive neuroectodermal tumours of the central nervous system (CNS-PNETs), the most common type of brain tumour affecting children, is only partly understood. The main priority of the brain tumour research program is to address this problem, and ultimately develop safer and more effective drugs and treatment strategies that are urgently required. To achieve this goal we are employing a variety of approaches to investigate the molecular biology of CNS-PNETs.

Chromosomal abnormalities are a common feature of PNET cells, including rearrangements, duplications, deletions, and amplifications. These and other data reflect the complexity of PNET biology and suggest that multiple genes involved in the coordination of proliferation and differentiation in cells of the developing brain are deregulated during PNET development. As part of our approach to identifying these genes, we have analysed chromosomal aberrations in a panel of PNET cell lines using cytogenetic analyses, representational difference analysis (RDA), and microsatellite mapping. This latter



work was undertaken in collaboration with the Cancer Genome Project at the Sanger Centre, Cambridge, UK. In addition, in collaboration with Prof. Paul Meltzer from the National Human Genome Institute at the National Institutes of Health in the USA we have assessed our PNET cell lines using array-CGH, a relatively high-resolution genetic analysis technique. To further refine our focus to specific regions of the human genome, we have correlated our extensive cytogenetic data with the gene expression profiles of our five PNET cell lines and a panel of 23 primary PNET specimens, generated using Affymetrix HG-U133A microarrays. These analyses have led to the identification of several genes of interest that function in the regulation of the cell cycle, embryogenesis, and proliferation. Some of these genes have not previously been linked to PNET pathogenesis and represent promising new leads for ongoing study.

This work was funded by NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **A neural stem cell for the study of CNS-PNET pathogenesis**

C Bertram, S Egli, UR Kees, and PB Dallas

Recent data suggest that many, if not most, cancers arise through the deregulated proliferation of stem cells. Some of the strongest evidence supporting the cancer stem cell hypothesis was reported recently by two independent research groups who isolated a small population of cells from primary CNS-PNETs that had phenotypic and functional similarities to neural stem cells (NSCs). Critically, the capacity to initiate new tumours was restricted to this minority population, indicating that these cells were cancer stem cells (CSCs). In collaboration with Dr Martin Pera and Dr Susan Hawes at the Australian Stem Cell Centre at Monash University we are addressing the relationship between NSCs and brain tumour CSCs in more detail. As a first step, we are comparing the gene expression profiles of NSCs and CNS-PNETs with the aim of identifying deregulated genes and/or pathways that are linked to CNS-PNET pathogenesis. We are also extending this work to the analysis of CSC populations that we have identified in our CNS-PNET cell lines. We anticipate that the NSC model system that we are developing will lead to a clearer understanding of the molecular pathways involved in PNET pathogenesis, and ultimately to the design of new and improved treatment strategies

This work was funded by NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

### **The roles of *EZH2* and *FOXO1A* in CNS-PNET pathogenesis**

PB Dallas, DJ Holthouse, L Genovesi, S Egli, and UR Kees

Our comprehensive molecular analysis of our panel of primary CNS-PNETs and CNS-PNET cell lines identified an oncogene, *EZH2*, and a tumour suppressor gene, *FOXO1A*, which were simultaneously deregulated in the majority of tumour specimens. These two genes function in pathways that regulate critical aspects of cell growth and differentiation. In collaboration with Dr Martin Pera and Dr Susan Hawes at the Australian Stem Cell Centre at Monash University we are assessing the roles of these genes in the regulation of proliferation and differentiation of normal human neural stem cells (NSCs), a cell type from which CNS-PNETs are thought to arise. The manipulation of target gene expression levels in CNS-PNET cell lines and NSCs is being undertaken using adenovirus based over-expression or RNAi knockdown procedures. A detailed understanding of the roles of *EZH2* and *FOXO1A* in CNS-PNET pathogenesis may provide important new clues about molecular approaches to treatment that target biochemical pathways regulated by these two genes.

This work was funded by NHMRC and the Children's Leukaemia and Cancer Research Foundation (CLCRF), Western Australia

## *Staff and Students*

### **Head of Division**

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Ursula R Kees PhD

Adjunct Professor University of Western Australia

Consultant, Department Haematology/Oncology, Princess Margaret Hospital for Children

### **Research Staff**

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Alex H Beesley, PhD, Adjunct Senior Lecturer UWA

Peter B Dallas, PhD, Adjunct Senior Lecturer UWA

Simone Egli, BSc (Hons)

Joseph R Freitas, BSc (Hons)

Wayne K Greene, PhD, Senior Lecturer Murdoch University

Saranga Senanayake, BSc (Hons)

Renae Weller, BSc (Hons)

Mathew Welch BSc (Hons)

### **Postgraduate Students**

---

Joanne Boag, BSc (Hons), PhD candidate

Nicholas G Gottardo, MB ChB (Leeds, UK), PhD candidate

David J Holthouse, MBBS (Hon), BmedSci (Hon), PhD candidate

Misty-Lee Palmer, BSc (Hons), PhD candidate

Cornelia Bertram, MBs, PhD candidate

### **Honors Student**

---

Laura Genovesi, Honours student.

### **Research Support**

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Stewart Cattach

Daniella Shigrov

## *Theses passed*

Laura Genovesi, BSc (Hons, Class I), Murdoch University. The development of an optimised RNA interference (RNAi) protocol for the knockdown of target gene expression in brain tumours.

## *External Committees*

### **International**

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Ursula Kees. COG-B946, Children's Oncology Group, USA Chair (2000-)

Ursula Kees. COG-B969, Children's Oncology Group, USA Chair (2000-)

### **Regional**

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Ursula Kees. Cancer Council of Western Australia

## *Invited Presentations*

Ursula Kees. Developing molecular classifiers in leukaemia. New Directions in Leukaemia Research Conference, Sunshine Coast, Queensland, April 2006.

Ursula Kees. High expression of connective tissue growth factor in paediatric pre-B acute lymphoblastic leukaemia. 4th International Workshop on the CCN family of genes. Okayama, Japan, October 2006.

Peter Dallas. Microarray expression analysis in paediatric cancer research. Lotterywest forum on "The Impact of the Genomic Era on Society". Perth, October 2006.

# Division of Clinical Sciences

## Overview

The Divisional activities centered around three main themes:

### 1. Asthma

- a. Studies on the mechanisms underlying the development of asthma, both in our cohort studies and mechanistic studies in laboratory animals. These studies are largely conducted as part of the Asthma Program Grant and involve collaboration between the teams headed by the Program Grant PIs: Peter Sly (Clinical Sciences), Pat Holt (Cell Biology); Wayne Thomas (Molecular Biotechnology), Peter Le Souef (UWA School of Paediatrics and Child Health), Steve Stick (Clinical Sciences and PMH Department of Respiratory Medicine), John Upham (Cell Biology) and Phil Stumbles (Cell Biology and Murdoch University). Details of these studies can be found in the sections on Respiratory Physiology and Clinical Asthma Studies.
- b. During 2006 we launched the first true trial of primary prevention of asthma that will be based on sound immunological theory. This trial, known as the Global Prevention of Asthma in Children (GPAC) is funded by the Immune Tolerance Network and the National Institute of Allergy and Infectious Diseases, USA and uses oral mucosal immunoprophylaxis (hence forth known as OMIP). This project represents a major collaborative venture between Peter Sly and Pat Holt (Cell Biology). Clinical sites recruiting children are in Perth, Melbourne (Royal Children's Hospital) and New York (Mt. Sinai Hospital). Further details can be obtained from the Division of Cell Biology report.

### 2. Early Detection of Lung Disease in Cystic Fibrosis

This project, funded largely by the Cystic Fibrosis Foundation Trust, USA, combines the data collected from the clinically-directed disease surveillance program conducted by the Department of Respiratory Medicine, PHM with the research conducted within Clinical Sciences. The Program is coordinated by Dr. Siobhain Brennan and is run as a collaboration between the Perth Centre (Clinical Sciences and Respiratory Medicine) and the CF clinic at the Royal Children's Hospital Melbourne. The primary aims of this project are to translate research findings into improved clinical care for children with CF and to determine optimal outcome variables for clinical intervention trials.

### 3. WHO Collaborating Centre for Research on Children's Environmental Health.

The Division of Clinical Sciences was designated as a

WHO Collaborating Centre for Research on Children's Environmental Health in July for an initial period of four years. We are very proud to be one of only two Centres worldwide to include Children's Environmental Health in their designation. The main aims of the Centre are:

- a. To conduct high quality research aimed at understanding the mechanisms underlying the developmental origin of environmental origin in children, with a special emphasis on respiratory diseases.
- b. To build the research capacity of researchers and health care professionals by providing access to high quality education and training.
- c. To develop programs and curricula to increase awareness about environmental threats, with special emphasis on respiratory diseases, asthma and allergies in children.
- d. To develop methods for translating research findings into public policy and intervention strategies.

The Centre is housed in the Division of Clinical Sciences and affiliated with Curtin University through the Department of Public Health, Division of Health Sciences. The initial Centre staff include: Peter Sly (Director), Felicity Flack (Executive Officer), Merci Kusel (Cohort Studies), Peter Franklin (Environment), Leith Sly (Education and Training), Steve Zubrick (Policy and Planning) and Sue Phillips (Administration). One notable achievement is the development of a Graduate Certificate in Children's Environmental Health, the first such course of its kind anywhere. Information about the course can be obtained by emailing "CEH@curtin.edu.au".

## Respiratory Physiology

### **Ventilator-associated lung injury in mice: influence of physiological maturity and pre-existing lung injury.**

Graeme Zosky, Vincenzo Cannizzarro, Zoltan Hantos, Peter Sly.

Mechanical ventilation after respiratory failure can be a life-saving intervention. However, mechanical ventilation is known to injure the lungs. In infants and young children, ventilator-associated lung injury (VALI) is a significant problem with long-lasting consequences for the children and their families. VALI is thought to occur as the result of repetitive overstretching and collapsing of the lung, and inflammation. This project was initiated in 2006 with the aim being to develop rodent models of VALI on mice of various ages with and without background lung injuries or complications. We measured lung parameters in adult, 2

week and 4 week old BALB/c mice which were exposed to one of two ventilation protocols (one injurious and one conventional). We found that injurious ventilation caused lung damage in both adult and younger mice (evidence of over distension of the lungs), however conventional ventilation was only damaging to the lungs of adult mice ('stiffening' of the lungs). Preliminary data from this work will be presented at the American Thoracic Society meeting in 2007, as well as forming the basis of two manuscripts to be submitted for publication in early 2007. Future directions for this project include investigation into the effects of viral infection and neutrophils on ventilator-associated lung injury, using both BALB/c mice and neutrophil enzyme deficient (129/Sv) mice. In addition we plan to investigate whether high concentrations of oxygen increase lung injury in mechanically ventilated mice by examining the impact of oxygen on different age groups (i.e. infantile, juvenile and adult mice) and studying whether an antioxidant-enriched diet may attenuate the harmful effects of oxygen in combination with mechanical ventilation.

### **Allergen-sensitization and environmental exposures in early life interact synergistically to alter lung growth.**

Elizabeth Bozanich, Alexander Larcombe, Rosa Gualano<sup>1</sup>, Gary Anderson<sup>1</sup>, Debra Turner, Peter Sly. (<sup>1</sup>University of Melbourne.)

Asthma develops as the result of complex interactions between genetic susceptibilities and environmental exposures. Approximately 40% of 6-year-old children in Perth are sensitized to inhaled allergens. However, only half of these have asthma. Allergic sensitization per se is therefore insufficient for the development of persistent asthma. A "second hit", associated with lung inflammation in early life, increases this risk several fold. This "second hit" could come from viral infection or from other inflammatory stimuli such as exposure to cigarette smoke, air pollutants and vehicle exhaust emissions. The timing of this second hit may well be important, particularly if it is early while the lungs are still growing and developing. Determining the roles viral infection and environmental pollution have early in life may provide us with a strategy for intervention that could prevent life-long changes in respiratory function and airway hyperresponsiveness. The aim of this project is therefore to examine interactions between allergen sensitization and exposure to environmental hazards in early life using a mouse model of allergic inflammation. We will test the hypothesis that the combination of allergic sensitization and viral infections in early life alter lung growth, airway function and airway hyperresponsiveness. In contrast, we propose the combination of allergic sensitization and exposure to non-viral irritants, such as air pollutants, can not provide

the "second hit" required to induce persistent asthma.

In 2005/2006 we developed the novel model of neonatal allergic sensitization which forms the basis of this project. BALB/c mice are sensitized with ovalbumin (OVA) via the nose on the day of birth and boosted with nasal OVA 4 weeks later. Subsequent exposure to OVA aerosols at 8 weeks of age (ie as an adult) results in heightened airway responsiveness. Recent work has shown that the 'window of opportunity' in terms of successful sensitization is limited to the 48hrs post birth. This preliminary data has formed the basis of a successful three year NHMRC funded project (2007-2009) and will be submitted for publication early in 2007.

### **Mechanisms underlying acute changes in lung function and airway hyperresponsiveness following respiratory viral infections.**

Alexander Larcombe, Elizabeth Bozanich, Rosa Gualano<sup>1</sup>, Gary Anderson<sup>1</sup>, Debra Turner, Peter Sly. (<sup>1</sup>University of Melbourne.)

This study will investigate the mechanisms responsible for the increased airway responsiveness seen during respiratory viral infections to the common viruses of influenza (flu) and respiratory syncytial virus (RSV). Respiratory viral infections alter lung function and increase airway responsiveness in man. In addition, respiratory viral infections early in life are a risk factor for the subsequent development of asthma. The mechanisms responsible for this are unknown. Both the infecting virus and "host" factors, such as age of infection, gender and genetic predisposition, are likely to be important. These studies will provide a comprehensive assessment of the effects of acute viral respiratory infections on lung function and airway responsiveness using cutting edge techniques developed in our labs. The results will provide new insights into how these infections cause lung disease and may provide clues for new approaches to prevent the adverse effects of these common respiratory viral infections.

We have recently developed mouse models of RSV and flu. Exposure to both viruses results in AHR to methacholine (MCh), although the pattern of AHR differs depending on the way the MCh is delivered. RSV infected mice show AHR when the MCh is delivered as an aerosol, while infection with flu is associated with AHR to both inhaled and intravenous delivery of MCh. Organ bath studies were able to demonstrate that there was no change to the airway smooth muscle following infection with either virus. Viral titre assays have been able to confirm both excellent levels of infection and clearance in the mice. We have also conducted a number of assays which have given us further insight into the immunology of the model. Data generated from this project formed the basis of a successful NHMRC grant which was awarded

late in 2006.

### **Assessment of respiratory mechanics in rodents.**

Graeme Zosky, Alexander Larcombe, Elizabeth Bozanich, Tibor Janosi<sup>1</sup>, Debra Turner, Zoltan Hantos, Peter Sly. (<sup>1</sup>University of Szeged, Hungary.)

This study has been an ongoing collaboration with Prof Zoltan Hantos from the University of Szeged, Hungary, to develop a technique for accurately measuring lung volume in sedated mice and rats using a custom designed whole body plethysmograph. The measurement of lung volume using plethysmography in humans is complex but well established. It was first described by DuBois et al in 1956 (J Clin Invest 1956;35:322-326). Plethysmography involves placing a person in a chamber and having them take several breaths against a closed shutter using normal breathing. Changes of pressure in the box, brought about by compression and rarefaction of the gas within the chamber during inspiratory efforts, are related to changes in tidal volume. Plethysmography measures the volume of all the gas in the lungs, including any air trapped by closed or narrow airways, thereby providing a valuable method of measuring absolute lung volume and resting end expiratory lung volume, also known as functional residual capacity (FRC). Lung volume has been shown to alter with disease state, airway smooth muscle constriction, anaesthetic level, inflammation and a number of other factors. Assessment of lung volumes using whole body plethysmography in infants has assisted in the study of normal growth and development of pulmonary function and helped the study of therapeutic intervention in various respiratory diseases. Measurements of FRC provide valuable information about alteration of lung function in the disease state. In our laboratory we routinely use rodents to assess the long and short term influences of allergen, virus and bacteria exposure, fibrosis and bronchoconstrictive agents on the lung, but to date we have not been able to measure lung volume in these murine models of airways disease. In 2005 Prof Zoltan Hantos developed a whole body plethysmograph for the mouse and a separate one for the rat. Studies in the mouse proved very successful and we now incorporate the technique into our routine lung function assessment. In 2006 Prof Hantos made modifications to the rat plethysmograph that resulted in successful measurements of lung volume and the subsequent incorporation of lung volume measurements into our routine lung function assessment in the rat. The ability to successfully measure lung volumes in both the mouse and rat provides us with a powerful tool to enhance and improve our standard lung function measurements and provide valuable information on disease induced lung volume changes in our animal models.

### **Murine models of allergic airways inflammation.**

Graeme Zosky, Alexander Larcombe, Elizabeth Bozanich, Jennifer Burchell, Debra Turner, Patrick Holt, Deborah Strickland, Matt Wikstrom and Peter Sly.

Murine models have become increasingly popular over recent decades in order to elucidate the pathobiology of asthma. There are a number of variations in the methods for inducing allergic airways sensitisation in mice that involve systemic antigen sensitisation and subsequent antigen challenge of the airways. This work encompasses two main components; the first looking at allergen derived early and late phase responses, and the second to assess subsequent development of airway hyperresponsiveness to inhaled methacholine, in a commonly used mouse and rat model of asthma. To date we have shown early phase responses (ie within 10 mins) to allergen in sensitised BALB/c mice, but no late phase bronchoconstriction by 8 hours post allergen exposure. In a continuation of this work, we measured lung mechanics 12 and 24 hours after allergen exposure in BALB/c mice. However, no late phase bronchoconstriction was seen after a single nor multiple (4 or 6) OVA aerosols. Similarly, no late phase responses were seen in PVG/c rats 4 or 6 hours after a single allergen exposure, nor in BN rats 2, 4 or 6 hours after a single allergen exposure. In addition, BN and PVG/c rats failed to exhibit an early phase response after one OVA aerosol. As a model of early and late phase allergen responses is desirable, future work in 2007 may consider different time points or the effect of multiple aerosols.

In a second arm of the study, cumulative methacholine challenges were performed on 129/Sv mice and C57BL/6 mice to characterise lung mechanics and airway hyperresponsiveness. The data from these 2 strains were compared with data generated in 2005 using BALB/c mice. Quite marked strain-related differences were seen in the pattern of physiological, inflammatory and immunological responses. The mechanisms behind these strain-related differences are being investigated further in 2007.

### *Internal collaborations.*

Throughout 2006 we have been involved in several ongoing collaborative research projects within the Telethon ICHR. These projects are written up in greater detail elsewhere within this annual report by our collaborators, noted in parenthesis below. In brief we have assessed airway and tissue mechanics in the following collaborative studies;

- Immunomodulatory effects of ultraviolet B (UVB) radiation in mice (with Dr Prue Hart, Division of Molecular Biotechnology)

- Airway mucosal DC maturation is controlled by local T cell interactions following repeated antigen challenge (with Deborah Strickland and Patrick Holt, Division of Cell Biology)
- Characterisation of mouse respiratory tract antigen presenting cell (RT-APC) populations and their response during allergic airway inflammation (Matt Wikstrom and Phil Stumbles, Division of Cell Biology)
- Interface of T regulatory cells, physiology and cytokines in a murine model of asthma (PhD work of Jennifer Burchell in collaboration with Matt Wikstrom and Phil Stumbles, Division of Cell Biology)

## Clinical Asthma Studies

### Role of early, repeated viral respiratory infections and the development of atopy in childhood (The Childhood Asthma Study).

Merci MH Kusel, Peter D Sly, Patrick G Holt & Richard Loh

This prospective cohort of children at high genetic risk of asthma and atopy was recruited between 1996-98 and followed till the children reached 5 years of age. Extensive data on early respiratory infections, wheezing and development of atopic diseases such as eczema and asthma was collected during the first phase of the study which was completed in 2003. We commenced the 10-year old follow-up visit in July 2006 and at this visit, children undergo extensive lung function tests as well as blood and skin prick tests to determine their atopic status. Data on exposure to environmental pollutants such as pesticides as well as dietary information will also be collected in face to face interviews. Data collected during this follow-up visit will further enhance our understanding of innate and adaptive immune processes as well as factors determining the development and maturation of the immune system.

We acknowledge the tremendous contribution by the study children and their families in this study

### The Role of viral lower respiratory infections in allergy and asthma

Cathy Pienaar, Claudia Calogero, Carlie Dunford, Jessica Lynch, Jenny Tizard, Barbara Holt and Peter D Sly.

A proportion of infants hospitalised with wheezing illnesses continue to have recurrent episodes of wheeze and become asthmatics in later childhood. This study commenced in 2001 to determine how wheezy illnesses caused by RSV/Parainfluenza alter lung function and

to assess associations between immunological status, infection severity and eventual atopic outcome. Of the original 105 infants recruited, 85 (80.9%) were still currently enrolled in the study at the end of 2006. A total of 52 children were seen during 2006. 48 children continued to be assessed at their annual review which included the completion of a questionnaire as well as attempting preschool lung function testing using FOT (Forced Oscillation Technique). Four children completed their final visit of the study (visit 6) which included lung function measures (FOT and spirometry), skin prick testing and a blood sample.

### HPA axis responsiveness in adolescents

Lisha van Reyk, Marie Deverell, Sven Silburn, Nick de Klerk, Merci MH Kusel & Peter D Sly

The western world has seen a dramatic increase in the prevalence of asthma in the past few decades, and while there is no doubt that factors associated with the "western way of life" are involved, the precise cause of the increase remains elusive. While environmental, lifestyle and physical factors have been associated with increased rates of disease, psychosocial factors may play a part.

Epidemiological studies have found associations between stress in early life and atopic diseases such as asthma. One possible link between psychosocial stress and physical disease may involve the Hypothalamic-Pituitary-Adrenal (HPA) axis. Evidence suggests that an appropriate HPA-axis response to stressful stimuli is important in the development and control of the immune system, with an altered HPA axis response being associated with immune diseases such as rheumatoid arthritis and atopy.

This study has developed and validated the CO<sub>2</sub> inhalation test as a suitable method for assessing HPA axis responsiveness to stress in adolescents. The test is well tolerated and results in a significant increase in salivary cortisol levels. A total of 1468 adolescents completed the HPA axis responsiveness test as part of the 14 year follow-up in the West Australian Pregnancy Cohort.

Preliminary analysis showed associations between anxiety and HPA responsiveness with some gender differences identified. Further analyses are being undertaken to determine any associations between early life factors, asthma & atopy and HPA responsiveness.

### Risk factors for persistent asthma in adolescents

Marie Deverell, Lisha van Reyk, Smilja Dragovic, Merci MH Kusel, Patrick Holt & Peter D Sly

Asthma is a chronic and complex disorder and despite

our increase in the understanding of the genetics, pathology and mechanisms underlying asthma, a gold standard definition of asthma does not exist. Prospective longitudinal birth cohort studies have increased our understanding of the natural history and risk factors for asthma, yet we are still not able to accurately predict which children will go on to have asthma as adults.

Risk factors predicting the development and persistence of asthma and intermediate phenotypes (bronchial hyperresponsiveness, airway inflammation and atopy) may be influenced by gender and may also vary between childhood and adolescence.

As part of the Western Australian Pregnancy cohort, subjects participated in two respiratory assessments (spirometry, methacholine challenge and skin prick tests) at 6 and 14 years. A total of 1587 subjects completed the respiratory component at 14 years. 4% of the cohort developed new asthma during adolescence while over 6% of the cohort had persistent asthma. Analyses revealed that during adolescence risk factors for asthma and intermediate phenotypes differ between the sexes. Different mechanisms are likely to be involved in determining asthma in boys and girls and shed new light on the recognised switch in the gender balance in asthma prevalence from the male predominance in childhood to the female predominance in adult life.

## *Infant and Preschool Lung function studies*

### **Measurement of lung function in infants and preschool diagnosed with cystic fibrosis**

Graham L Hall (PMH), Gary Nolan, Catherine Gangell, Cindy Thamrin, Siobhain Brennan, Stephen M Stick and Peter D. Sly

This project aims to characterise the onset of early lung disease in infants and young children with cystic fibrosis. We are monitoring lung function in all infants diagnosed with cystic fibrosis at birth in conjunction with the Royal Children's Hospital Melbourne. A uniform and standardised protocol for both infant and pre-school lung function testing is now well-established. In infants lung function testing involves the multiple breath washout test (MBW), and the low frequency forced-oscillation technique (LFOT). From these two tests, information regarding lung volume, ventilation inhomogeneity, airway resistance and tissue mechanics have been deduced. In pre-school children lung function is measured using the forced oscillation technique (FOT). The FOT requires minimal co-operation from young children and can be routinely used in a clinical setting. Both cross-sectional and longitudinal data have been obtained. Data are being compared with bronchoscopies, bronchial alveolar lavage

and computed tomography scans as well as blood, genetics and urine sampling.

### **Antecedents of childhood asthma: measurements of infant lung function and airway inflammation**

Peter Franklin (SPACH), Vaska Stavreska (PMH), Graham L. Hall (PMH), Stephen M. Stick (PMH) and Peter D. Sly

Exhaled nitric oxide may reflect airway inflammation in asthma. We have developed a technique for measuring exhaled nitric oxide in infants as it is possible that this may be a useful test for asthmatic wheeze in this age group. We measured  $FE_{NO}$  and lung function in over 100 wheezy and non-wheezy infants. These children are being re-assessed at age 7. The aim of the study is to investigate if measurements of lung function and airway inflammation in infancy are predictive of the development of childhood asthma at seven years of age. To date approximately 80 children have returned for lung function, nitric oxide and allergy tests.

### **Assessment of lung function testing in healthy preschool-aged children using forced oscillations**

Graham L. Hall (PMH), Peter D Sly, Takayoshi Fukushima, Merci M. Kusel, Peter J. Franklin (SPACH), Friedrich Horak Jr. (PMH), Hilary Patterson, Catherine Gangell (SPACH) and Stephen M. Stick (PMH)

Monitoring of respiratory function is important in the diagnosis and management of respiratory disease. The forced oscillation technique requires minimal patient cooperation and is ideal for the determination of respiratory function in young children. This study aimed to develop reference ranges and to document the repeatability in healthy young children using commercially available forced oscillation equipment. Respiratory function was obtained in 158 healthy children, aged 2 to 7 years and between 92 and 127 cm in height. Reference ranges for respiratory impedance variables in healthy children between 2 and 7 years of age were created.

### **Assessment of bronchodilator responsiveness in preschool children using forced oscillations**

Cindy Thamrin, Catherine L Gangell (SPACH), Kanokporn Udomittipong, Merci MH Kusel, Hilary Patterson, Takayoshi Fukushima, André Schultz (PMH), Graham L Hall (PMH), Stephen M Stick (PMH) and Peter D Sly

Few data exist on respiratory function changes measured using forced oscillations following inhaled bronchodilators (BD) in healthy young children, limiting clinical applications of BD testing in this age group. We aimed to determine the most appropriate method of quantifying BD responses using FOT in healthy young children, and those with

common respiratory conditions, including cystic fibrosis (CF), neonatal chronic lung disease (nCLD), and those with a diagnosis of asthma and/or current wheeze. Significant BD responses (BDR) were seen in all groups. Absolute changes in BDR were related to baseline lung function while relative changes in BDR were less dependent on baseline and independent of height in healthy children. We concluded that BD responses assessed by the FOT in preschool children should be expressed as a percent change from baseline. The limits for a positive BD response of -40% and 65% for Rrs and Xrs, respectively, are recommended.

## Cystic Fibrosis

### Early detection of inflammation in cystic fibrosis.

Siobhain Brennan, Kaye Winfield, Peter D Sly, Stephen M Stick(PMH), Graham L Hall(PMH), Phil Robinson, Colin Robertson, Sven Thonell.

In 2006 this research group continued investigations on early development of inflammation and infection in cystic fibrosis. This project has now been extended to include a site at the Royal Children's Hospital in Melbourne and has received funding from the US Cystic Fibrosis Foundation. This project aims to investigate the following

1. To characterise the inflammatory response in the lungs of infants and young children with CF and to correlate this with bacteriology, clinical status and lung function.
2. To determine whether the inflammatory markers assessed are predictive of long term outcome in these children.
3. To investigate the nature of the relationship between markers of lung disease and the breakdown products of lung tissue excreted by the kidneys.

Our findings to date are outlined below:

- Over four hundred broncho-alveolar lavage fluid samples have been collected from over 100 children with CF. Inflammation is evident in virtually all of the lavage fluids collected, even in the very young infants (from four weeks of age) with no apparent clinical symptoms or infection.
- It appears that once acquired, inflammation consistently tracks with infection.
- The level of acquisition of *Staphylococcus* and *Haemophilus* is lower in this cohort than compared with other national CF centres for the same age group. This may be a consequence of the

prophylactic antibiotic policy in the WA paediatric clinic.

- Whilst there appears to be no difference in the age of acquisition in *Pseudomonas* in our clinic compared with the other national CF centers, the lavage program has demonstrated some success at eradicating *Pseudomonas aeruginosa* in young children with CF.

We have constructed a working database for the analysis of this data, and have begun to analyse longitudinal trends of disease progression.

Numerous collaborations (national and international) have resulted from this ongoing study.

### Inflammation in cystic fibrosis: friend or foe?

Peter D Sly, Siobhain Brennan, Kaye Winfield.

In cystic fibrosis, inflammation and infection occur concurrently, the role of inflammation is to attack invading pathogens and to effectively remove them from the host. In CF, for various reasons, inflammation overwhelms the lungs and the abundant neutrophils release excessive levels of enzymes (such as elastase) that can also attack lung tissue proteins elastin and collagen. It is this collateral damage from inflammation and infection that initiates fibrotic lesions, leading to long term irreversible lung damage and pulmonary function decline. In 2001, we initiated a new study that we believe may provide important information to the CF community about when inflammation begins to attack lung tissue. This study may provide a solid rationale for the use of anti-inflammatory therapy in CF and may also provide a non-invasive method that could be used to determine the point in disease when that anti-inflammatory therapy is warranted.

The study involves the recruitment of children with CF and children with no history of lung disease for our control population. We have recruited children for this study from both our Perth clinics and schools, as well as other national CF centres. We have investigated the breakdown products of elastin and collagen fibres found in urine and measured by high performance liquid chromatography (HPLC) to see if they correlate with the inflammation measured from sputum or bronchoalveolar lavage in patients at times of stable clinical health and at times of exacerbation of disease. We are also investigating whether current iv treatments, or anti-inflammatory therapies currently being trialed in the CF community locally and nationally, will influence these levels.

This study received funding from the National Cystic Fibrosis Association for 2002 and the first journal article outlining the validation of the technique and describing the effect of age in a non-CF pediatric population has



been written by Ms Kaye Winfield and accepted for publication in the Annals of Clinical Biochemistry. Further submissions for journals resulting from these studies are currently being compiled.

Collaborations that have resulted from this work include:

- (1) Investigation of correlation of biochemical markers of oxidative stress in patients with CF. Working with Dr Tony Kettle of Christchurch New Zealand, we have established a collaboration to concurrently assess markers of tissue damage alongside established markers of oxidative stress (tyrosine residues). This will provide us with further information about the process of early inflammation-led damage in children with CF.
- (2) Collaboration with Dr Yvonne Belis, Westmead Children's Hospital investigating the effect of reflux on markers of lung inflammation.

Ms Winfield submitted her masters thesis which resulted from this work in October and her thesis was subsequently passed.

### **Immune Surveillance in cystic fibrosis- the role of macrophages and dendritic cells**

Siobhain Brennan, John Upham, Matt Wikstrom, Steve Stick, Peter Sly

In collaboration with Dr. John Upham, of the Cell Biology Division, we have investigated the role of antigen presenting cells in the early stages of cystic fibrosis lung development. This study involves assessment of blood dendritic cells and monocytes, as well as macrophages found in the bronchoalveolar lavage fluid of children with CF. Children with CF have recurrent infections, which are often difficult to clear and we hypothesise that one reason for this is that there is a dysregulation of the "surveillance" system, which involves the antigen presenting cells in the airways- the dendritic cells and macrophages. With the assistance of the respiratory fellows in Respiratory Medicine (Dr Tonia Douglas, Andres Shultz and Paul McNemara) we use cells from BAL and collect blood from children with CF undergoing BAL, and will also be collecting blood from non-CF children undergoing surgery for non-respiratory related reasons. This study investigated the presence of macrophages in the lungs and the presence of dendritic cells and monocytes in the blood using flow cytometry and in-vitro culture techniques. We also investigated the presence of chemokines (proteins responsible for recruiting macrophages and dendritic cells to the lungs) and found these highly elevated in young uninfected children with CF. In addition we have investigated the expression and activity of TLR2 and TLR4 receptors on monocytes in the blood and on macrophages in the lung.

This study began in late 2003, and received funding from the Australian Cystic Fibrosis Research Trust for 2004. The findings of this study are being prepared as two publications.

### **The value of serum antibodies to *Pseudomonas aeruginosa* Exotoxin A as markers of early *Pseudomonas* infection in young children with cystic fibrosis**

Tonia Douglas, Siobhain Brennan, Peter Sly

This pilot study aimed to investigate the value of *Pseudomonas aeruginosa* antibody levels as markers of early respiratory infection with *Pseudomonas aeruginosa* and response to treatment in young children with cystic fibrosis (CF). *Pseudomonas aeruginosa* (*Ps a*) is a primary CF pathogen that accelerates lung disease and increases mortality. Initial "intermittent" infection with *Pseudomonas* is potentially treatable if detected before chronic infection is established. Currently detecting early respiratory infection reliably in young children with CF requires bronchoscopy under general anaesthesia. Less invasive methods of sampling respiratory secretions in children such as oro-pharyngeal swabs are insensitive and do not reflect lower respiratory bacteria accurately. Infection with *Ps a* stimulates the production of antibodies to *Ps a* proteins and toxins that are detectable in the serum. Levels of these antibodies in children were found to be sensitive markers of early *Pseudomonas* infection in the lungs, and response to anti-pseudomonas treatment. They may be useful in management of lung disease and may reduce the need for more invasive surveillance. However, studies investigating the potential of these markers in young children are scarce. The Respiratory Department at PMH has an established bronchoscopy program for all children in WA with CF and offers each child an annual bronchoscopy and bronchial lavage (washings) until around the age of 6 years. This unique program permits the study and treatment of respiratory infection and inflammation in children too young to expectorate or cooperate with conventional methods of lung surveillance. The potential of antibodies to *Pseudomonas* as markers of respiratory infection can therefore be assessed and, in this study, compared with the "gold standard" of bronchial lavage throughout early childhood. Data from this study will determine whether a larger prospective study is warranted and the sample size required.

This pilot study was funded by the Princess Margaret Hospital seeding grants scheme, and formed the basis of a successful postgraduate diploma project which was conducted in 2006 by Mr Charles Goh, through the Department of Pathology, UWA.

This pilot study was used to form the basis of a National CF Research Trust grant, submitted in June 2006, which was successfully funded for 2007. The grant was extended to include analysis of all Perth samples and to analyse

samples collected from a national CF BAL program for antibody titres to *Pseudomonas aeruginosa*.

### **Investigating markers of oxidative stress in young children with cystic fibrosis: a driving mechanism of pulmonary inflammation?**

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Siobhain Brennan, Tony Kettle

Previous preliminary data collected in association with Prof Kettle (NZ) on the presence of oxidative stress in young children with CF was used in a recent grant submission to the Australian Respiratory Council. The success of this grant application for 2007 will allow us to further investigate the role of oxidative stress in driving pulmonary disease by measuring biomarkers of reactive oxygen species and antioxidants in the lungs of young children with cystic fibrosis (CF) and relating these to pulmonary inflammation, infection and clinical outcome. Based on our preliminary data we believe that oxidative stress is initiated very early in CF and that it contributes significantly to the high inflammatory burden so common in lungs of children with CF. Recent pilot studies also report that inhalations of the anti-oxidant glutathione (GSH) are associated with improved lung function in older children and young adults with CF. The usefulness of such a therapy would be optimal if implemented at the time of when oxidative stress begins. Therefore a full understanding of the functional maturation of antioxidant defences and of the development of oxidative stress in these preschool children from birth is essential.

## *Other Research*

### **Promoting assent: involving children in the decision-making process in therapeutic clinical trials.**

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Angela Allesandri, Linda Kristiansen<sup>1</sup>, Peter D Sly. <sup>1</sup>Curtin University of Technology.

Dr. Angela Allesandri, a clinical oncologist at PMH, is undertaking studies towards a PhD in the important area of children's assent to participate in therapeutic clinical trials. While this is a new area of research for the Division, it builds on the interests and involvement of Peter Sly in the human ethics committee at PMH.

### **The role of psychosocial stress in the development and expression of chronic childhood asthma.**

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Jackie M Cesareo<sup>1</sup>, Davina French<sup>1</sup>, Sven Silburn, Peter D. Sly. <sup>1</sup>Department of Psychology, UWA

This project is using longitudinal data collected from

the Raine cohort to examine the interactions between psychosocial stress and asthma in children. Specifically, the role stress and family functioning can play in the induction of asthma is a major focus. We are also investigating whether the psychosocial profile of the child and family can influence the severity of asthma, as well as the effects of persistent asthma on the child and family. Preliminary results suggest that psychosocial stressors play a role in the induction of asthma in children. In addition, 2 year old children who wheeze and who experience stressful life circumstances demonstrate worse asthma when they are 6 years old. Jackie submitted her PhD in late 2006.

## *Staff and Students*

### **Head of Division**

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Peter D Sly MD MBBS DSc FRACP

Professor, School of Paediatrics & Child Health, University of Western Australia

Senior Principal Research Fellow, National Health & Medical Research Council

Director, Clinical Research & Education, Princess Margaret Hospital for Children

Respiratory Physician, Princess Margaret Hospital for Children

### **Research Staff**

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Elizabeth Bozanich BSc (Hons)

Siobhain Brennan PhD

Claudia Calogero MD

Vincenzo Cannizzarro MD

Tonia Douglas MBChB MRCPCH

Carlie Dunford BSc

Felicity S Flack PhD

K.E (Bill) Finucane (Emeritus Professor)

Zoltan Hantos PhD (Perpetual Visiting Professor, Adjunct Professor UWA)

Merci Kusel MBBS PhD

Alex Larcombe (PhD)

Hilary Patterson BE (Hons) BSc

Cathy Pienaar BSc (Nursing) MSc (Med)

Nina Sturges BSc(Hons)

Debra J Turner PhD

Kaye Winfield BSc

Graeme Zosky PhD

### **Postgraduate Students**

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Angela Alessandri MBBS FRACP (Paeds), MBioeth PhD Candidate

Jackie M Cesareo BA (Hons) PhD Candidate (in conjunction with UWA Psychology)

Marie Deverell BSc (Hons) PhD Candidate

Tonia Douglas MBChB (Hons), MRCPCH (UK) PhD Candidate

Raewyn Mutch MBChB DipRACOG FRACP PhD Candidate

Cindy Thamrin BE (Hons) BSc PhD Candidate

Lisha van Reyk BSc(Hons) PhD Candidate

Jennifer Burchell BSc(Hons) PhD Candidate

Kaye Winfield BSc. Masters Candidate

### **Research Support**

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Cameron Brooke

Smilja Drogovich BPsych

Samantha Gard Dip Tech (Applied Science)

Jessica Lynch BSc

Susan Phillips BA

## *Theses passed*

Cindy Thamrin (PhD student) "Measurement of lung function using broadband forced oscillations"

Raewyn Mutch (PhD Student) "Familial associations of asthma and atopy"

## *Awards*

Jennifer Burchell. 2006 Harasawa Fellowship / Young Investigator Award from the Japanese Respiratory Society to attend and present at the annual Asian Pacific Society of Respiriology Conference, Kyoto, Japan.

Jennifer Burchell. 2006 Western Australian Immunology Travel Prize (Australasian Society for Immunology)

Jennifer Burchell. 2006 Thoracic Society of Australia and New Zealand (W.A. Branch) Travel Award

Jennifer Burchell. 2006 Animal Resources Centre Student Oral Presentation Prize, Combined Biological Sciences Meeting, Perth, W.A.

Jennifer Burchell. 2006 Thoracic Society of Australia and New Zealand (TSANZ) travel award to attend the national conference, Canberra, ACT

## External Committees

### International

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Peter Sly. Joint American Thoracic Society - European Respiratory Society Task Force on Standards for Infant Respiratory Function Tests.

Peter Sly. European Respiratory Society Task Force on Forced Oscillation

Peter Sly. World Health Organisation advisor on asthma and lung diseases in children

Peter Sly. Long Range Planning Committee, Pediatric Assembly, American Thoracic Society

Peter Sly. International Task Force, Pediatric Assembly, American Thoracic Society

### National

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Peter Sly. GlaxoSmithKline: Paediatric Asthma Advisory group

### Regional

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Peter Sly. Asthma Foundation of Western Australia Medical Advisory Committee

Peter Sly. Human Ethics Committee, Princess Margaret Hospital for Children

Peter Sly. Chairman Scientific Advisory Subcommittee, Human Ethics Committee, Princess Margaret Hospital for Children.

Peter Sly. Institute for Child Health Research Executive Committee

Peter Sly. Princess Margaret Hospital Strategic Management Committee

Peter Sly. Research Committee, Arthritis Foundation of WA

R Mutch. TSANZ (WA Branch) Executive Committee

R Collins. TSANZ (WA Branch) Associates Subcommittee.

Debra Turner Board of Directors, Scitech, Western Australia

## Invited Presentations

Peter Sly. Wheezing in Infants and Children. The 16th Congress of Interasma Japan/North Asia. Tokyo. April 2006

Peter Sly. Effects of adverse environmental exposures on respiratory and immune development in children. Symposium "Environmental Threats to the Health of Children", Telethon Institute for Child Health Research, Perth, April 2006

Peter Sly. Wheezing in infants and young children: predicting who will develop persistent asthma and how they should be treated. RJ 06 Children Asthma and Allergy Forum, Shanghai, May 2006

Peter Sly. Managing Difficult Asthma in Children. RJ 06 Children Asthma and Allergy Forum, Shanghai, May 2006

Peter Sly. Immunoepidemiology of Childhood Asthma and T Cell Response Patterns. American Thoracic Society International Conference. San Diego, May 2006

Peter Sly. Translating infant/preschool research into asthma prevention strategies. Respiratory Workshop, Rotorua, July 2006

Peter Sly. Effect of postnatal steroids on early lung development, Respiratory Workshop, Rotorua, July 2006

Peter Sly. Early detection of lung disease in Cystic Fibrosis. Cystic Fibrosis Association meeting, Perth August 2006

Peter Sly. Susceptibility of children to environmental pollutants: respiratory immune system development. European Respiratory Society Annual Congress, Munich, Sept 2006

Peter Sly. Epigenetics and respiratory disease. European Respiratory Society Annual Congress, Munich, Sept 2006

Peter Sly. Current Research Trends in Asthma. Asthma Australia, Oct 2006

Peter Sly. Management of Paediatric Asthma. Asthma Australia, Oct 2006

Peter Sly. Combination therapy with ICS and LABA in Asthmatic Children: Scientific and Clinical Rationale. GSK Paediatric Asthma Expert Panel Meeting. Barcelona Nov 2006

# Division of Molecular Biotechnology

## Overview

Research in the Division of Molecular Biotechnology encompasses studies on the mechanisms of inflammation and allergy and the development of methods to treat or prevent diseases resulting from these processes.

The allergy research group has traditionally focused on the characterisation and production of allergens and antigens so that the immune responses can be accurately and reproducibly studied. The specificity of the responses also identifies the allergens that need to be targeted for the development of more effective immunotherapy and molecularly defined diagnostic tests. The differences between immune responses induced by potent allergens, weak allergens and non-allergenic proteins is also being used to pinpoint the events that lead to allergenicity and the range of immune responses that the body makes to inhaled antigens. Recent studies have studied the type of responses found in children admitted into the Emergency Department for asthma attacks. House dust mite and cat allergens are being studied because they constitute the most important indoor allergens in our region. They induce quite different types of immune responses, and thus provide an opportunity to explore different types of healthy and unhealthy responses. The characterisation of the allergens produced by cats is also a neglected area of investigation resulting in poor assessments of the allergy of people without large responses to the one known major cat allergen. It is becoming clearer that immune responses to other allergens are important for the development of allergic disease. Many investigators have been studying the effect of common respiratory viruses on the development of asthma. Our recent studies of responses resulting from the subclinical colonisation of the respiratory mucosal with bacteria have shown that this is also an important area of study, and given the recurrent and protracted nature of these infections they could have abundant opportunity to interact with responses to inhaled antigens.

Members of the inflammation research group are elucidating the molecular mechanisms that regulate the production of inflammatory cytokines by macrophages and other cells of the monocyte lineage. It is important to determine which of the possible regulatory mechanisms are used by human cells exposed to regulatory cytokines such as interleukins-4 and -10 and how these differ during the maturation of the cells along different functional pathways. The studies have concentrated on examining the suppressor of cytokine signalling (SOCS) and signal transducer and activator of transcription (STAT) regulatory pathways. The importance of these investigations has been clearly demonstrated by showing that STAT3 and SOCS3, found to be critical in mouse studies, do not have the same importance for the

regulation of tumour necrosis factor in human cells. The regulation of inflammatory responses *in vivo* is also being analysed by studying the inhibitory effects of ultraviolet light (UV) on systemic immune responses in mice. This model explores how inflammation is regulated as well as providing knowledge about a significant and complex environmental health issue. A reduction in UV exposure is important to reduce skin cancer but its suppressive effects can reduce immune responses and even, as is being studied here, could be used therapeutically for asthma. UV irradiation has been shown to be a powerful inducer of regulatory T cells that are, at least in part, dependent on signalling from the histamine type 2 receptor. Vitamin D induced by UV exposure is being studied because topical supplementation can both reverse some of the effects of UV damage, but also activate regulatory T cells by a process similar to that shown for UV. Vitamin D may play an integral role in the pathophysiological response of skin to UVB irradiation.

## Allergy

### Origins of defective anti-bacterial responses of asthmatic children in infancy

B. J. Hales, L. J. Pearce, L. A. Hazell, W. R. Thomas with M.M.H. Kusel, P. D. Sly and P. G. Holt from Cell Biology and Clinical Sciences

It was previously discovered that half of people allergic to house dust mites had a Th2 component to their antibody response to the common nasopharyngeal colonising bacteria *Haemophilus influenzae*. Instead of their IgG antibody response to the protective P6 antigen being exclusively of the Th1-dependent IgG1 subclass they also made IgG4 antibodies. This discovery was made possible by the development of quantitative IgG microtitre assays using a purified antigen, recombinant P6, and by focussing on responses induced by subclinical nasopharyngeal colonisation instead of rare systemic bacterial infections. It adds a new dimension to the study of interaction of infection, allergy and asthma showing that a broader perspective is required rather than simply focussing on the epidemic childhood viral infections. Indeed since subclinical bacterial infections persist for months they may have a larger influence on the mucosal immune responses than acute viral episodes. Further study has now shown that infants who develop house dust mite allergy fail to produce the Th1 dependent IgG1 anti P6 responses in infancy and that the first antibody they develop is dominated by the IgG4 subclass. Children who made the IgG4 antibody responses to P6 were also the children who made IgG4 to the house dust mite allergens. The lack of a Th1 response to a bacterial antigen and the early production of Th2 responses shows a very significant

aberration in the early immune responses to bacteria and from its timing it may result from an underlying primary susceptibility of the children to developing Th2 responses and not be a secondary effect due to the allergy.

Funded by NHMRC

### **Anti-allergen and anti-bacterial antibody responses in asthma exacerbations and recovery.**

B J Hales, L J Pearce, L A Hazell, W Smith, W R Thomas with Dr A Martin Princess Margaret Hospital and Professor P N LeSouef, Dr I A Laing and Dr C M Hayden UWA School of Paediatrics and Child Health.

Children attending the Emergency Department for the treatment of asthma attacks typically showed an anti house dust mite allergen response with 50-60% of the IgE focussed on the Der p 1 and 2 allergens and a further 20-30% of the mid-potency allergens Der p 4, 5 and 7. IgE binding to other allergens, even if frequent, was low. The only difference from responses of children with stable asthma was an almost complete absence of IgG1 and IgG4 antibody. The antibody responses to the house dust mite allergens and the P6 protein were followed up after 2-4 months. IgE immunoglobulin and IgE anti house dust mite antibodies decreased. About half of the exacerbations were associated with a rhinovirus infection but there was no difference in the IgE responses with and without infection. There was no increase or consistent change in the IgG antibody titres to the allergens, or to the P6 antigen. There was however a consistent and often marked increase in the IgE antibody titre to the P6. It is possible that the IgE increase could be dependent on a recrudescence or acquisition of a *H. influenzae* infection or be due to non-antigen-specific effects on an ongoing immune response. The size of the titres reached high levels of over 15 ng/ml, which shows the potential for the pathophysiological involvement of the anti bacterial responses in the progression of allergic disease.

Funded by NHMRC

### **T-regulatory functions in responses to house dust mite allergens**

B. J. Hales, N.N.R. Chu, L. A. Hazell, W. Smith, T. K. Heinrich, W. R. Thomas with AL Taylor and S. L. Prescott, UWA School of Paediatrics and Child Health

The transcription of the FOXP3 transcription factor, which is produced by regulatory T cells, is activated by the stimulation of peripheral blood mononuclear cells with the house dust mite allergens Der p 1, Der p 2 and Der p 7. Counterintuitively the major allergens induce the highest level of transcription and people allergic to house

dust mite make higher levels than people without the allergy. For the mid-range Der p 7 allergen, the amount of FOXP3 transcription correlated with the IgE titre of the donor. The FOXP3 was shown to be produced by CD25+ CD4+ T cells in keeping with the known surface phenotype of regulatory cells. The higher responses to the major allergens in allergic people and the demonstration that the transcription was induced by them show a potential feedback mechanism. The depletion of CD25+ cells however did not increase cytokine responses. FOXP3 transcription was inhibited by the addition of anti-IL-2 antibodies but this did not inhibit the transcription of mRNA for the Th2 cytokines and the interleukin-4 receptor. An inhibitory function of the FOXP3 therefore cannot be defined at this stage, but it is a marker of allergy that can be detected within hours of T-cell activation. The possible participation of the regulatory IL-10 and TGF- $\beta$  cytokines was examined by the addition of neutralising antibodies to the cultures stimulated with Der p 1 and house dust mite extract. Anti-IL-10 had little effect on the induction of cytokine or IL-4 receptor mRNA whereas anti-TGF- $\beta$  stimulated the responses but only in cells from allergic people. Ongoing studies are examining the difference in the regulation of responses to the major and mid-range allergens and to house dust mite proteins with little allergenicity.

Funded by NHMRC

### **Natural group 2 house dust mite allergens**

W. R. Thomas, W. Smith, L. A. Hazell with S. Piboonpocanun and P. Vichyanond, Mahidol University, Bangkok and with K. Meno ALK-Abello, Denmark

The group 2 house dust mite allergens were the founding members of the ML-domain family of lipid binding proteins. The solution of the structure of the recombinant polypeptide determined by X-ray crystallography and nuclear magnetic resonance was found to be different suggesting flexibility of the molecule. The flexibility is possibly required for the putative lipid binding activity and this is especially important for the natural allergens. This has been emphasised by the finding of Dr Piboonpocanun that recombinant polypeptides show undiminished IgE binding in the absence of their expected secondary structure. Natural Der f 2 and Der p 2 have therefore been purified by non-denaturing chromatography techniques for two collaborative studies. One is compare the serology and circular dichroism of the natural allergens in comparison with recombinant and denatured and refolded allergen with Dr Piboonpocanun and colleagues and other is to solve the structure of natural Der f 2 with Dr Meno and colleagues including the structure of the natural ligand. Small crystals have successfully been grown for the latter.

Funded by NHMRC

### **BASE a new cat allergen**

S. E. O'Neil, L. A. Hazell, B. J. Hales, W. R. Thomas, T. K. Heinrich and W. Smith

A clone from a cDNA library from the salivary gland of the cat was shown to produce a polypeptide that bound IgE from cat-allergic subjects. The sequence showed that the IgE-binding protein was homologous to the breast and salivary expressed (BASE) protein, which is a product of healthy salivary glands and is also similar to the major Equ c 4 latherin allergen described in horses. The IgE binding profile of recombinant BASE produced in *Escherichia coli* showed it bound IgE in 57% of the cat allergic subjects and that the binding was higher than the known major Fel d 1 allergen and the salivary lipocalin allergen Fel d 4 in 46 % of cat-allergic subjects. It therefore makes a very significant contribution to the IgE responses induced by cat allergens especially those with low titres of anti Fel d 1.

Funded by NHMRC

### **Allergen vaccination with B-cell epitopes**

T. K. Heinrich, C. E. Elliot, P.T. Cunningham, L. A. Hazell B. J. Hales W. R. Thomas

Phage display was used to identify amino acid residues 69-82 as the core of the epitope recognised by the anti-Der p 2 monoclonal antibody 10B2. Fusion polypeptides of glutathione-S-transferase of *Schistosoma japonica* and residues 69-82 were able to immunise mice to induce antibodies that reacted with the Der p 2 allergen. The ability of immunised mice to respond to repeated intranasal administration of house dust mite extract spiked with extra Der p 2 was examined. Mice vaccinated with the glutathione-S-transferase fusion protein but not the unmodified glutathione-S-transferase has markedly reduced IgE and IgG anti-Der p 2 antibody responses. The vaccination did not induce T-cell responses to Der p 2 or a synthetic 69-82 peptide in keeping with the known location of the T-cell epitopes in other sequences. Vaccination with a modified but serologically active sequence also inhibited the response. The results show that B cell responses to a single epitope can protect from allergic responses to inhaled aeroallergen.

Funded by NHMRC

### **Mucosal desensitisation of allergic responses to cysteine protease antigens**

P.T. Cunningham, C. E. Elliot and W. R. Thomas with P.G. Holt Cell Biology

The major Der p 1 allergen of the house dust mite is a cysteine protease. The biochemically similar, but

commercially available papain and ficin enzymes have been used to study allergic sensitisation and desensitisation therapy for this type of allergen. This provides a model that is not dependent on the supply of custom made reagent and can be used by laboratories that do not specialise in the production of allergens. It is particularly relevant because the intranasal sensitisation induces persistent IgE antibody and lung inflammatory responses. Previous studies have demonstrated the ability of feeding and sublingual administration of allergen to prevent the induction of the allergy. Desensitisation of previously primed mice can also be achieved, manifest by a reduced ability to produce IgE antibody responses to further boosts of allergen. The sublingual and oral regimens show for first time that mucosal tolerance can be used to inhibit responses induced at the respiratory mucosa. Decreased release of interleukin 5 into the bronchoalveolar lavage fluids could be observed but the cellular infiltration was unaffected. In the regimens tested to date the desensitisation could not be specifically enhanced by immunostimulatory oligonucleotides or by chitosan nanoparticles. The sublingual administration of peptide containing the T-cell epitope however desensitises for both IgE antibody and the cellular infiltrate. The allergen-induced production of the inflammatory chemokines TARC, MDC and TSLP has been studied as well as the production of vascular endothelial growth factor. These will be used for the study of longer-term desensitisation. Experiments using a mixture of ficin and papain as allergen showed an absence of a bystander effect produced by sublingual administration of papain on the response to ficin.

Funded by ALK Abello

### **Interaction of allergic sensitisation and *Pasteurella pneumotropica* infection in mice.**

S. B. See and W. R. Thomas

*Pasteurella pneumotropica* naturally infects the mucosa of mice in a similar fashion to the infection of humans with *Haemophilus influenzae*. The interaction of allergic sensitisation and immunity to the outer membrane protein antigens is being studied. DNA encoding the homologues of reported protective antigen of *H. influenzae*, P6, P26 and D15 has cloned recombinant polypeptides produce in *Escherichia coli*. Another antigen homologue P4 has also been cloned for expression. Vaccination of mice with the P6 antigen and to a lesser extent P26 has been shown to protect mice from developing pneumonia after intranasal infection. Interestingly P6 induced a similar titre of antibodies following intranasal vaccination with and without an immunostimulatory oligonucleotide adjuvant while the other proteins required adjuvant. Protection with P6 vaccination did however require adjuvant.

Mice made allergic to the papain allergen by intranasal sensitisation showed an increased susceptibility to infection.

Funded by the Asthma Foundation of Western Australia & NHMRC

## Inflammation

### Immunomodulatory effects in mice of UVB radiation

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PH Hart, S Gorman, JJ Finlay-Jones, J McGlade, J Lee, A Kuritzky

UVB immunomodulatory effects have been implicated not only in skin cancer development but also in the initiation and progression of autoimmune and infectious diseases in experimental animals. UV rays cannot penetrate beyond the outermost layer of skin. In our studies, the effects of UVB on systemic immunomodulation are studied; the shaved dorsal skin of mice is irradiated whilst a second body site (for example the ventral skin) provides the site for antigen sensitisation several days later. The immunomodulatory effects of UVB result in reduced swelling of the ears when they are challenged by surface painting with the same antigen after a further five days. To better understand the molecular mechanisms involved, lymph node cells draining sites of UVB irradiation and/or antigen sensitisation have been isolated and examined phenotypically and functionally. Using several experimental systems and two different antigens, we have not found any difference in the phenotype or function of antigen presenting dendritic cells from control and UVB-irradiated mice. We now have evidence that UVB irradiation of mice on their shaved backs for a time equivalent to about 20 minutes in noon in summer in Perth causes an accumulation of regulatory T lymphocytes in skin-draining lymph nodes and these regulatory cells can reduce subsequent immune responses in those nodes. We are seeking the phenotype and function of these regulatory cells. Are new regulatory T cells induced or are we measuring an accumulation of regulatory T cells in the lymph nodes draining UV-irradiated skin? Many experiments involve transfer of cells from a UVB-irradiated mouse into a naïve mouse subsequently challenged with antigen. Is regulatory T cell activation in donor mice sufficient for subsequent expression of activity in recipients? Alternatively do regulatory T cells require reactivation in the recipient mice, or in tissue culture? Thirdly, is T-Cell Receptor involvement important for their accumulation/activity? Is there any evidence that reduced immune responses to 'introduced' antigens is due to bystander suppression by UVB-associated T regulatory cells responding to UV-induced alteration of skin-derived antigens? These questions are being studied.

Funded by Cancer Council WA and NHMRC

### Immunomodulatory effects of topical vitamin D3 application

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PH Hart, S Gorman, A Kuritzky

Upon irradiation with UVB, 7-dehydrocholesterol in skin converts to pre-vitamin D which then isomerises to vitamin D with body heat. Skin keratinocytes have an autonomous vitamin D pathway and can produce substantial amounts of 1,25 (OH)<sub>2</sub> vitamin D<sub>3</sub>, the hormonally active form of vitamin D<sub>3</sub>. We propose that any effects of vitamin D associated with acute UV exposure are dependent on 1,25 (OH)<sub>2</sub> vitamin D<sub>3</sub> produced by keratinocytes and immune cells at the irradiated site. Hence we are studying the effects of 1,25 (OH)<sub>2</sub> vitamin D<sub>3</sub> applied directly to skin. Based on studies in human skin, local levels of 1,25 (OH)<sub>2</sub> vitamin D<sub>3</sub> in the order of 2-5 nM can be achieved following erythral UVB exposure. Using such levels painted onto skin, we have detected activation of T regulatory cells in the draining lymph nodes. Upon transfer to new mice, these T regulatory cells can suppress responses to several experimental antigens. Studies are ongoing in which vitamin D<sub>3</sub>-induced T regulatory cells are being phenotyped and further characterised and comparisons made with UVB-induced T regulatory cells.

Funded by Cancer Council WA and NHMRC

### Effect of UVB radiation and vitamin D3 on murine asthma models

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PH Hart, J McGlade, WR Thomas, D Strickland, J Thomas, D Turner, G Zosky

We have previously analysed the effect of UVB exposure on models of contact hypersensitivity, a response in mice dependent on type 1 or Th1 immune cells and production of cytokines like interferon- $\gamma$ . The effect of a single exposure to UVB on two asthma models in mice is being examined, the expression of these responses being dependent on type 2 or Th2 immune cells and production of cytokines like interleukins-4, -10 and -13. In the first model, mice are UVB-irradiated on their shaved backs three days before sensitisation, resensitisation and challenge intranasally with the cysteine protease, papain. In the second model, mice are irradiated on their shaved backs three days before sensitisation, and resensitisation, intraperitoneally with ovalbumin mixed with alum. The mice are subsequently challenged by aerosolised ovalbumin. Airways hyperreactivity is significantly reduced by skin exposure to UVB. The levels of inflammatory cytokines in lavage fluid, as well as antigen-specific responses by cells from the lung-draining lymph nodes, are reduced. These studies illustrate the systemic effects of UVB administered to one site but affecting immune responses at another, in this case in lungs. Studies are ongoing to gain a



better understanding of the mechanism by which UVB radiation can modify some of the important pathological components of asthma. The contribution of UVB-induced vitamin D3 to these responses is being assessed.

Funded by WA Asthma Foundation

### **Use of adenoviral vectors for dissection of cytokine mechanisms in activated human monocytes and macrophages**

PH Hart, CM Prêle, E Woodward, A Keith-Magee

Due to their phagocytic and poorly proliferative nature, it has been difficult to transfect human monocytes and macrophages isolated from human peripheral blood. This has been a stumbling block for use of primary monocytes and macrophages for study of cytokine signalling pathways relevant to the development and resolution of inflammation. Adenoviral vectors have recently allowed transduction of a high percentage of human macrophages. We have now optimised this methodology using human monocytes isolated by elutriation from human blood kindly provided by the Perth Red Cross Blood Bank and an adenoviral vector encoding green fluorescent protein (AdV-GFP). After 24 h incubation with M-CSF (20 ng/ml) and a further 24 h incubation with AdV-GFP, the number of cells expressing GFP is approximately 65% with significant GFP expressed per transduced cell. The viability of the cells is not compromised. We are particularly interested in the mechanisms by which monocytes/macrophages are activated and then how IL-4 and IL-10 suppress monocyte/macrophage inflammatory cytokine production. We have cloned the plasmids for wild type STAT 3 (a potentially important signalling molecule), a dominant negative (mutated) STAT 3, and SOCS1 and SOCS3 (molecules important in regulating cytokine production in mouse macrophages) into pAdTrack-CMV vectors (which also code for GFP). They were then recombined with the pAdTrack-CMV vector in bacteria before infection of mammalian HEK-293 cells that allowed replication of the virus. We have confirmed expression of all transgenes in human monocytes and macrophages by Western blot. The overexpressed STAT3 is phosphorylated in monocytes incubated with IL-10. Overexpressed SOCS 1 regulates LPS activation whilst SOCS3 regulates the activation of STAT3 by interleukin-6. Mechanisms by which IL-4 and IL-10 negatively regulate pro-inflammatory mediator production by human monocytes and macrophages may not be the same as those published for murine macrophages. Results of infection of human monocytes with adenoviruses expressing SOCS3, STAT3 and a dominant negative STAT3 have been published in 2006.

Funded by NHMRC

## *Staff and Students*

### **Head of Division**

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Wayne R Thomas, PhD

Allergy and Immunology Group

### **Research Staff**

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Allergy Group

Dr Susan Aulfrey PhD

Paula T Cunningham PhD

Claire E Elliot BSc Hons

Belinda J Hales BSc Hons PhD

Lee A Hazell Dip Appl Sci

Tatjana K Heinrich PhD

Angelika Kutasi BSc (Hons)

Leigh J Pearce BSc (Hons)

Wendy-Anne Smith BSc Hons PhD

Inflammation Group

Prue H Hart BSc (Hons) MSc PhD, NHMRC Principal Research Fellow

John Finlay-Jones BSc (Hons) PhD

Shelley Gorman BSc (Hons) PhD

Cecilia Prêle BSc (Hons) PhD

April Keith-Magee BSc MSc (till April 2006)

### **Postgraduate Students**

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Jacqueline McGlade BSc, PhD Candidate

Eleanor Woodward BSc, PhD Candidate

Serena O'Neal BSc, PhD Candidate

Jessica Lee BSc, Hons Candidate

### **Visiting Student**

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Alexandra Kuritzky BSc (Hons), medical student from University of Toronto, from July 2006.

### **Research Support**

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Daniella Shigrov

## *Theses passed*

Jessica Lee, Hons I Murdoch University: The effects of Ultraviolet-B radiation on murine bone marrow

## *Awards*

S. E. O'Neil, Perron Meritorious PhD Scholarship

S. E. O'Neil, Indoor Biotechnology Travel Award

S. E. O'Neil, Friends of the Institute Travel Award

S. Gorman. Qantas Young Investigator Award, TICHR, November 2006.

J. McGlade. University of WA Pro-Vice Chancellor Research and Innovation Award, Medical Research Week Symposium, Perth, June 2006

## *Invited Presentations*

W. R. Thomas. 2006. From Molecular Structure to Allergen Nomenclature. European Academy of Allergy and Clinical immunology, Vienna

PH Hart, Seminar, Curtin University, May 2006

PH Hart, Symposium Chair, Speaker and Organiser, American Society for Photobiology, Puerto Rico, July 2006

PH Hart, Symposium Speaker, 3rd Asian and Oceanian Conference on Photobiology, Beijing, November 2006

PH Hart, Symposium Speaker, Australian Health & Medical Research Congress, Melbourne, November 2006

## *External Committees*

W. R. Thomas. NHMRC Peer Review Advisory Committee

W. R. Thomas. Chairman of International Allergen Nomenclature Committee

PH Hart, Member, Medical Advisory Board, Sylvia & Charles Viertel Charitable Foundation

# Division of Population Sciences

## Highlights

Western Australian Aboriginal Child Health Survey – Launch of Volume Three and Volume Four and dissemination of findings.

Rio Tinto Child Health Partnership – National Symposium

Oddy WH. 'Ten of the Best' – NHMRC #007090 'Nutritional epidemiology of childhood asthma' 2000-2004. This project was selected by peer review from 800 NHMRC projects, programs and fellowships as one of Ten of the Best for 2004. Award presented in Sydney, September 2006 by Tony Abbott, Commonwealth Minister for Health.

A study, which described 23 years of total population data, and highlighted the increasing disparities between Aboriginal and non-Aboriginal WA born infants, especially in remote communities was published in the Lancet in 2006. This paper described the patterns and trends of infant mortality and the disparity that persists between Aboriginal and non-Aboriginal children. Jane Freemantle (Population Sciences) and colleagues analysed mortality data for the total population of Aboriginal and non-Aboriginal infants born in Western Australia between 1980 and 2001. They found that overall infant mortality fell in both populations, but less so in the Aboriginal than non-Aboriginal infants. Further, the main causes of death among Aboriginal infants were preventable. The authors called for immediate action to improve access to health care and living conditions for Aboriginal people. The findings draw attention to the increasing disparities in death rates between Aboriginal infants and their non-Aboriginal peers, which provide an important indicator of the overall health and wellbeing of Aboriginal communities and the long-term effect that racism, discrimination, and dispossession, have had on Aboriginal people. The authors also recommended that implementation and assessment of policies to reduce the continuing social and economic disadvantage faced by Aboriginal families in partnership with Aboriginal communities is vital to address these inequalities.

An important highlight in 2006 was the Council's success in winning a \$1.13 million National Suicide Prevention Strategy competitive research grant (2007-2009) to develop and evaluate an innovative proactive bereavement support service. This project will be carried out in conjunction with the WA Coroner's Counselling Service, the WA Police Service and Divisions of General Practice in the Southern Metropolitan area of Perth and the Samaritans.

## Aboriginal Health Research

### **Kulunga Research Network**

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Hayward C

During 2006, Kulunga consolidated its team which is larger and more stable than at any other time in its history. Several new members of staff have been appointed adding significantly to Kulunga's capacity to consolidate its role in the Institute in leading and progressing research for Aboriginal children, families and communities. Appointments include Dr Roz Walker as Research Manager, Dr Clair Scrine and Daniel McAullay as Senior Research Officers, Karina Aiberti as Research Assistant and Jennine Pickett as Administrative and Research Assistant.

Throughout 2006, Kulunga continued to progress its work to enhance its profile and outputs including the implementation of strategies to increase Aboriginal research capacity, and Institute-wide endorsement of Kulunga's research principles and protocols.

On the 24 March 2006, Volume Three of the Western Australian Aboriginal Child Health Survey (WAACHS) - *Improving the Educational Experiences of Aboriginal Children and Young People* was successfully launched. Mr Ernie Dingo was emcee of this event with the then WA Minister for Education and Training, the Honourable Ljiljanna Ravlich, officially launching the Volume. The launch was attended by over 100 invited guests including representatives from the Aboriginal community and the Australian and State Governments. This event received substantial media coverage through radio, newspaper and television with State and national coverage.

On 9 -10 May 2006 the Rio Tinto Child Health Partnership hosted its inaugural national symposium that focused on promoting healthy pregnancy in Indigenous communities – *Start Out Strong: A Healthy Beginning in Life*. Over 170 delegates attended the symposium representing a wide range of organisations and communities involved in different ways in promoting healthy pregnancies in Indigenous communities. The keynote Speaker was Dr Caroline Tait - Assistant Professor at the Indigenous Peoples' Health Research Centre at the University of Saskatchewan, Canada. The outcomes and future directions that arose from the symposium's workshops established a clear message about how best to promote healthy pregnancies in Indigenous communities that has been used to inform a range of stakeholders and advocate for program and policy change.

On 22 November 2006, Volume Four of the WAACHS - *Strengthening the Capacity of Aboriginal Children, Families and Communities* was successfully launched. Local Aboriginal media personality, Narelda Jacobs, was emcee for the event and the then Western Australian

Minister for Community Services, the Honourable David Templeman (MLA) officially launched the Volume. More than 150 invited guests including representatives from the Aboriginal community and the Australian and State Governments attended the launch. There was extensive radio, newspaper and television media coverage of the Launch and the Volume Four findings at State and national levels. A promotional video was produced for the launch which will also be used as a communication tool for community stakeholders to carry out workshops and staff development and inductions.

### **Kulunga Communication Strategy**

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Hayward C, Edwards T

All activities in Kulunga's Communication Strategy are coordinated by Kulunga's Communication Officer and have a range of policy implications in the areas of maternal and child health in Indigenous communities. Kulunga's Communication Strategy enables its work to have an impact on many stakeholders and policy makers and provides direct access to an array of information via its electronic resources.

In 2006, substantial progress was made towards the design and implementation of promotional materials to build the profile of Kulunga and its research projects. Pull-up banners were designed in consultation with the Institute's Public Relations Manager to complement the Institute's own promotional banners. Kulunga has also developed its own website where electronic versions of newsletters, reports and other publications are made available. The production of the website ensures that Kulunga's research outputs are in an accessible format for the Indigenous community and raises awareness of its work within the Institute. There was also ongoing development of Kulunga's circulation database which by the end of 2006 had over 300 contacts including State and Australian Government departments, Indigenous community organisations, corporations and members of the wider community. Kulunga's quarterly newsletter, 'commUNITY' – Bringing Us Together was produced and distributed via email and through its website.

This project is funded by Department of Health and Ageing (coordinated through the Office for Aboriginal and Torres Strait Islander Health).

### **Rio Tinto Child Health Partnership**

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Hayward C, Param R, Scrine C, Edwards T, Pickett J

The Rio Tinto Child Health Partnership is an innovative and collaborative undertaking between the Telethon Institute for Child Health Research (the Institute), Rio Tinto Services Ltd (and its consortium of contributors),

the Alcohol Education and Rehabilitation Foundation (AER Foundation) and the governments of the Northern Territory, Western Australia and Queensland.

In 2006, the Partnership underwent a consolidation phase with new staff recruited to assist with the project management. These include Kulunga Communications Officer, Ms Tracey-Lee Edwards and Dr Clair Scrine who assumed the executive coordination duties. Associate Professor Ted Wilkes continued as the Partnership Leader and Associate Professor Colleen Hayward continued as Partnership Manager.

A number of sites across each of the jurisdictions were identified to progress the Partnership's key objectives - reducing alcohol and tobacco consumption in pregnancy and Indigenous community health workforce development. Activities undertaken within the nominated sites included, developing ways to enhance and increase the Aboriginal and Torres Strait islander workforce in child and maternal health, the provision of culturally appropriate antenatal care and engagement of women at an early stage of their pregnancy, delivery of services that reflect a holistic approach to the mother, baby and family that is culturally appropriate and in accordance with best practice processes.

This project is funded by Rio Tinto Services Ltd, The Alcohol Education and Rehabilitation Foundation (AER Foundation), Western Australian Government, through the WA Department of Premier and Cabinet, Northern Territory Government, through the NT Department of Health and Communities, Queensland Government, through the Qld Department of Health.

### **Social and Cultural determinants of health and well being of Aboriginal children and young people in Western Australia: "Does culture have an impact on the health and wellbeing outcomes of Aboriginal children and young people?"**

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A Masters project by Adele Cox and supervised by Helen Milroy and Jianghong Li.

This Master project aims to explore the concept of cultural participation and continuity and how it is related to the health and wellbeing of Aboriginal children and young people in the Western Australian context, using a combination of quantitative and qualitative methods. The quantitative data comes from WAACH and qualitative data will be collected in July 2008, using focus group interviews, in-depth interviews at individual level (children, youth, carers and community leaders and health workers), review of written documents and observation and participation in local cultural events.

The specific objectives of the quantitative analyses are:

- 1) To identify dimensions (indicators) of the Aboriginal cultural continuity at both the individual and community levels, which are conducive to health and wellbeing;
- 2) To assess the association between cultural participations and physical and mental health among Aboriginal children and adolescents, and to establish the extent to which cultural continuity may buffer the negative effects of economic and social disadvantage on health and wellbeing;
- 3) To identify mediating factors that link cultural participations to health and wellbeing.

The qualitative study has the following objectives:

- 1) To further explore the concepts of cultural continuity, identity and resilience.
- 2) To explore and identify factors that may inhibit the transfer of Aboriginal traditions and values from the Elders to the younger generation and that impact on feelings of belonging and connectedness among youth;
- 3) To assess the extent to which the experience of the stolen generations and racism have negatively impacted on cultural continuity;
- 4) To gain knowledge of Indigenous perspectives on the root causes of the pervasive health and social problems in Aboriginal populations and effective solutions to the problems; to identify factors that Aboriginal people themselves consider critical for regenerating hope, self-esteem and wellbeing.

### **NHMRC Aboriginal and Torres Strait Islander Healthy Start To Life Research Project “Restor(y)ing Aboriginal Parenting”**

Zubrick S, Silburn S, Donovan R, D’Antoine H, Kickett-Tucker C, Milroy H, Milroy J, Lawrence D, Wilkes E, Cox A, Pearson G, Williams A

This five year NHMRC Research project commenced in 2006 supported by a budget of \$2,104,620, with contributions from NHMRC \$1,612,793, and Curtin University \$491,827)

The project aims to develop, deliver and evaluate a universal early intervention for parents of Aboriginal children aged 12 – 36 months, and seeks to address some of the long-term consequences of Australia’s past policies of forced separation on the social transmission of Aboriginal identity, cultural knowledge and skills in parenting.

In the first year the team has; 1) Established an project management steering committee, a project governance structure, and a cultural security process which will

ensure the cultural integrity and acceptability of the project methodology, program content, implementation evaluation and dissemination of findings; (2) Conducted two workshops with the research team to support data analysis and cultural interpretation of the data.

The research plan has; 1) Examined the data from the Western Australian Aboriginal Child Health Survey to confirm the target focus and identify modifiable risk and protective factors associated with parenting and children’s behavioural, social and academic outcomes; (2) Reviewed the Australian and international literature on parenting interventions proven efficacious and /or effective in targeting highly disadvantaged communities to identify good practice principles, program elements, and interventions that inform the next phase of research and program development; (3) Employed and trained two Aboriginal researchers from the Noongar community to conduct in depth interviews and focus groups with Aboriginal caregivers and elders residing in the Perth Metropolitan area.

The qualitative research phase has identified community issues, concerns, goals, values, beliefs, parenting behaviours, family practices and routines, and recommendations for successful program delivery. Data from each phase (1) –(3) has built and consolidated an evidence base and established clear intervention targets on what, who, when, where, and how best to intervene. Each phase has progressively informed the approach, the context for program delivery, program strategies, curriculum content, as well as perceived barriers to program uptake and project sustainability.

### **Swimming Pool Project - Impact of swimming pools on children’s health in remote Aboriginal communities**

Lehmann D, Tennant M, Silva D, Jacoby P, Johnston J, Smith J, Kulunga Research Network, Stanley F in collaboration with Wright H (Port Hedland Regional Hospital), Coates H, Lannigan F (Princess Margaret Hospital), Weeks S (Professional Hearing Services)

Swimming pools were built in four remote Aboriginal communities in Western Australia in 2000. A before and after study of children in two of these communities showed a reduction in burden of skin infections and otitis media.

We examined data collected at local clinics in Jigalong and Mugarinya to see if there has been any change in clinic attendance and antibiotic treatment since the pools were opened. We found a reduction in antibiotic prescription and in clinic attendance for middle ear infections, respiratory infections and skin infections. A paper for publication is in draft form.

A highly successful swimming carnival was held in Jigalong in February 2006 which was attended by the Olympic Swimming champion, Shane Gould.

This study is funded by the WA Department of Housing and Works.

### **Qualitative studies of smoking and breast-feeding - Early weaning, smoking, stress and resilience among young Aboriginal women**

Nichols F, Stokes A, Johnston J, Monck R, Jeffries-Stokes C, Lehmann D in collaboration with Ngunytju Tjitji Pimi Inc, Bega Garibirringu Health Services Aboriginal Corporation

This largely qualitative project, a subset of ICHR's Kalgoorlie Otitis Media Research Project, investigated maternal smoking and breastfeeding patterns and characteristics; and Aboriginal perceptions of related social determinants and appropriate interventions. Results were drawn from both our cohort study (100 Aboriginal and 180 non-Aboriginal mothers) and from qualitative data collected during interviews with 55 Aboriginal women.

Results indicated that, in line with national figures, smoking was common among both Aboriginal and non-Aboriginal mothers—with higher rates in the Aboriginal population. Infant feeding patterns indicated that exclusive breastfeeding among Aboriginal mothers was below national and international targets. Maternal smoking and infant feeding characteristics indicated that different factors may influence the decisions of Aboriginal and non-Aboriginal mothers regarding these behaviours. Study findings pointed consistently to stress (and by way of stress-response, to freedom-seeking behaviour) as a pervasive component in the lives of many Aboriginal people and as a central social determinant of early weaning and smoking behaviour. Related interventions should therefore include strategies to address stress-related causes. Local proposals included multi-faceted young mothers' support, activity and education centres. Some of these activities are already underway. A manuscript documenting our findings is being finalised for publication.

This study is funded by Healthway.

### **Western Australian Aboriginal Child Health Survey (WAACHS)**

Hayward C, Walker R, Pearson G, Edwards TL, Cox A

Throughout 2006, Kulunga was responsible for all aspects of the completion and implementation of Western Australian Aboriginal Child Health Survey (WAACHS) Volumes Three and Four. This included managing business development, communicating with funding and other

key stakeholders, coordinating the WAACHS Steering Committee meetings and Reference Group meetings. On the 24 March 2006, Volume Three *Improving the Educational Experiences of Aboriginal Children and Young People* was successfully launched at the Institute. On 22 November 2006, Volume Four of the WAACHS - *Strengthening the Capacity of Aboriginal Children, Families and Communities* was also successfully launched at the Institute

In 2006, the WAACHS Team and Kulunga staff were also involved in several projects that utilised the Survey findings and recommendations including their application at a broader, strategic policy level for use by the Department of Education and Training as well as the Australian Education Systems Officials Committee (AESOC) Senior Official Working Party on Indigenous Education - a key policy group responsible for setting directions in Indigenous education. Kulunga was also involved in designing and contributing to key research projects based on the translation of Survey findings.

This project is funded by Department of the Premier and Cabinet, Department of Education and Training, Department of Health, Department of Community Development, Disability Services Commission, West Australian Drug Strategy, Department of Justice, Department of Housing and Works, Department of Health and Ageing (coordinated through the Office for Aboriginal and Torres Strait Islander Health), Department of Education, Science and Training, Office of Indigenous Policy Coordination, Attorney General's Department, Department of Family, Community Services and Indigenous Affairs.

### **WAACHS Communication Strategy**

Hayward C, Walker R, Pearson G, Edwards T, Cox, A

The Communication and Dissemination Working Group provided support and direction for the ongoing development, refinement and implementation of the WAACHS Communication and Dissemination Strategy.

On 10 July 2006, a new Research Manager, Dr Roz Walker, was appointed to Kulunga to take responsibility for the implementation of the Communication and Dissemination Plan for Volumes Three and Four. In 2006, a total of 37 forums and presentations were provided involving 1704 Aboriginal community representatives and key agency stakeholders. Other dissemination activities included the production of a Community Booklet, promotional video, power point presentations, Summary Booklet and nine Regional Profiles specific to each of the Indigenous Coordination Centre regions and all based on the findings of Volume Three. In addition, the WAACHS team and Kulunga staff responded to various media requests.

During 2006, a targeted promotional strategy was also established with the aim of increasing WAACHS Volume sales and disseminating the supplementary materials free of charge. Over 750 Regional Profiles and 1000 Community Booklets for Volume Three and Summary Booklets for all three Volumes were distributed to identified stakeholders involved with Indigenous education and social services throughout the nine regions within the Survey.

This project is funded by Department of the Premier and Cabinet, Department of Education and Training, Department of Health, Department of Community Development, Disability Services Commission, West Australian Drug Strategy, Department of Justice, Department of Housing and Works, Department of Health and Ageing (coordinated through the Office for Aboriginal and Torres Strait Islander Health), Department of Education, Science and Training, Office of Indigenous Policy Coordination, Attorney General's Department, Department of Family, Community Services and Indigenous Affairs.

## *Epidemiology Of Infectious Disease*

### **Pathways to hospitalisation with infection**

Lehmann D, Moore H, Jacoby P, Carville K, de Klerk N, McMinn P in collaboration with Burgner D, Richmond P (School of Paediatrics and Child Health, University of Western Australia), Smith D (Division of Microbiology and Infectious Diseases, PathWest Laboratory Medicine WA)

In 2005, extensive work was carried out utilising the population-based WA Data Linkage System to investigate the principal reasons young WA children are admitted to hospital, focusing on admissions for infection. Between 1990 and 2000, infections were the main cause of hospital admission in children aged less than 2 years, with admission rates for infection 4.6 times higher in Aboriginal children than in non-Aboriginal children. Admission rates changed significantly over time between 1992 and 2000, especially for acute lower respiratory infections where there has been a real increase in incidence of bronchiolitis for infants aged less than 12 months. Rates for pneumonia have declined in Aboriginal children but increased in non-Aboriginal children. A diagnostic shift was also noted between bronchiolitis, bronchitis and asthma for children in their second year of life. Additionally, admission rates for meningitis have dropped by more than 70% in WA children over the study period. Disseminating these results was one of the focuses for 2006. We have two major journal articles in press, one published letter to the editor and have presented results at several local and national conferences including the 15th Annual Meeting of the Australasian Epidemiological Association held in

Melbourne.

Plans for further investigation of acute lower respiratory infections also became a focus for 2006. The primary objective of this new project is to describe the burden, aetiology and antecedents of acute lower respiratory infections in WA Aboriginal and non-Aboriginal children. This project is an extension of the analysis that was conducted in 2005 and includes investigation of a wider range of age groups, emergency department presentations and laboratory data to identify pathogen-specific episodes of acute lower respiratory infections. We have been negotiating with the custodians of the Ultra Laboratory Database System and the Emergency Department Data Collection with a view to linking these data to other core datasets in the WA Data Linkage System. This study will provide the essential baseline data on which to identify, recommend and evaluate appropriate preventative measures for acute lower respiratory infections in Aboriginal and non-Aboriginal children.

We have been investigating seasonal and temporal trends of respiratory viruses. A Quality Activity Proposal was approved by the Pathology Committee in December 2006 to extract data on all respiratory viral testing conducted at Princess Margaret Hospital between 1996 and 2005. We will receive the de-identified data in early 2007.

This study is funded by the NHMRC, as part of NHMRC Program Grant.

### **Causal pathways to Otitis Media - The Kalgoorlie Otitis Media Research Project - An investigation into the causal pathways to otitis media in Aboriginal and non-Aboriginal children**

Lehmann D, Jacoby P, Watson K, Jeffries- Stokes C, Stokes A, McAullay D, Elsbury D, Finucane J, Monck R, Stanley F in collaboration with Bega Garbarringu Health Services Aboriginal Corporation, Ngunytyu Tjitji Pimi Inc, Coates H (Senior ENT Surgeon, Princess Margaret Hospital), Riley TV (Department of Microbiology, University of Western Australia), Weeks S (Audiologist, Professional Hearing Services), Cripps AW (Griffith University, Queensland), Kyd J (Central Queensland University, Rockhampton), Bowman J, Taylor A, Smith D (Division of Microbiology and Infectious Diseases, PathWest Laboratory Medicine WA), Murphy D (Public Health Bacteriology Laboratory, Brisbane), Leach A (Menziess School of Health Research, Darwin), Pingault N (University of Western Australia)

Otitis media (OM, middle ear infection) can seriously affect childhood development, school performance and subsequent social and economic wellbeing. The Kalgoorlie Otitis Media Research Project was established in 1999 to investigate the causal pathways to OM and, specifically,

to identify demographic, socio-economic, environmental, microbiological and immunological risk factors for OM in Aboriginal and non-Aboriginal children in order to develop appropriate interventions. We followed 100 Aboriginal and 180 non-Aboriginal children from birth to age two years. Field work was completed in 2004 and data cleaning was completed in April 2005.

The burden of OM remains very high in the Kalgoorlie-Boulder area with a peak prevalence of 72% in Aboriginal children aged 5-9 months and 40% in non-Aboriginal children aged 10-14 months. Furthermore, 29% of Aboriginal children and 5% of non-Aboriginal children have had a perforated ear drum at least once by age 2 years, and 65% of Aboriginal children and 23% of non-Aboriginal children have some degree of hearing loss at age 12-17 months.

A series of papers and presentations were prepared during 2006. We have submitted a paper detailing the rationale, methods, population characteristics and ethical considerations of the project. We have found that for optimal isolation of *S. pneumoniae* and *H. influenzae*, transit time from collection in the field in Kalgoorlie to a -70°C freezer in Perth should be less than 72 hours and that *H. influenzae* grew better from nasopharyngeal aspirates than from nasal swabs. We have reported high rates of upper respiratory tract (URT) carriage of the three major OM pathogens (*Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Haemophilus influenzae*), with higher rates in Aboriginal than non-Aboriginal children. Carriage also begins at a young age in Aboriginal children. There is seasonal variation in carriage in non-Aboriginal but not in Aboriginal children and we have found a negative association between carriage of *Staphylococcus aureus* and pneumococcal serotypes included in 7-valent pneumococcal conjugate vaccine, which may have implications with regard to effectiveness of the vaccine.

Rhinoviruses and adenoviruses are commonly identified in the URT, more commonly in Aboriginal than non-Aboriginal children and are frequently associated with bacterial carriage. Using mathematical models we have differentiated between host-level and pathogen-level interactions between different bacterial and viral pathogens which are relevant to determining the types of interventions required to reduce carriage and disease.

We found that exposure to environmental tobacco smoke is associated with increased risk of OM. Results have been presented at local, national and international conferences including the Fifth International Symposium on Pneumococci and Pneumococcal Diseases in Alice Springs.

This study is funded by Healthway; and the NHMRC as part of NHMRC Program Grant.

### **Vaccine Impact Surveillance Network (VISN) - Enhanced Surveillance of Invasive Pneumococcal Disease through the Vaccine Impact Surveillance Network**

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Lehmann D, Moore H, Willis J, Harrison C, Rooney K, Bayley K, Brown L in collaboration with Keil T (Department of Microbiology, Princess Margaret Hospital), Murphy D (Public Health Bacteriology Laboratory, Brisbane), Richmond P (School of Paediatrics and Child Health, University of Western Australia), Giele C (WA Department of Health) for the VISN Network

The Vaccine Impact Surveillance Network (VISN) was established in 1996 to collect and analyse information on vaccine-preventable diseases and evaluate the impact of vaccines and vaccination programs on these diseases. Invasive Pneumococcal Disease (IPD) is the disease caused by *Streptococcus pneumoniae* (pneumococcus) invading a normally sterile site such as blood and cerebrospinal fluid. IPD is a major cause of pneumonia, septicaemia, bacteraemia and meningitis worldwide. Although IPD only became a notifiable disease in Australia in 2001, VISN has collected epidemiological and microbiological data on all reported cases of IPD since 1996 through review of hospital records and reporting from Public Health and Infection Control Units. Data collected include the clinical diagnosis, management, risk factors, vaccination history, outcome, pneumococcal serotype and antibiotic resistance.

A 23-valent pneumococcal polysaccharide vaccine (Pneumovax) has been recommended since 1986 for Aboriginal adults aged 50 years or more, for younger Aboriginal adults with known risk factors and non-Aboriginal Australians aged 65 years or more, and since 2005 has been fully funded by the Federal Government. In 2001, the 7-valent conjugate pneumococcal vaccine (Prevenar) was licensed for use in Aboriginal and Torres Strait Islander children and other children with known risk factors. Since January 2005 all Australian children are offered Prevenar.

During 2006, updating and cleaning of all data has continued, with the bulk of the work largely complete. We have continually updated databases with new reports of IPD cases. At 31 December 2006, covering a period of nearly 11 years from 1 April 1996, there were a total of 1666 episodes of IPD on the VISN database. In 2006 there were 131 reported cases of IPD and 10 deaths in the 114 records checked so far (9% case fatality rate); this compares with 140 cases and 21 deaths in 2005. IPD reported in children aged less than 5 years fell from 21 cases in 2005 to 18 cases in 2006.

In April 2006, we presented 10 years of epidemiological data on IPD at the 5th International Symposium on Pneumococci and Pneumococcal Diseases in Alice Springs.



We found that IPD incidence in children aged less than 2 years declined from 192 in 1996-2001 to 124 per 100,000 per annum in 2002-2005 in Aboriginal children and from 70 to 56/100,000/annum in non-Aboriginal children. Incidence of IPD due to serotypes included in Prevenar vaccine declined from 118 to 43/100,000/annum in Aboriginal children and from 59 to 45/100,000/annum in non-Aboriginal children, with no increased incidence of disease due to non-vaccine serotypes. A paper documenting the effect of the seven-valent pneumococcal conjugate vaccine in Western Australia was published in the journal *Vaccine*.

Continued surveillance is essential to detect emergence of disease due to non-vaccine serotypes and any decline in adult incidence due to herd immunity.

This study is funded by the WA Department of Health through the Collaboration for Applied Research and Evaluation.

#### **Neonatal immunisation in PNG - NHMRC/ Wellcome International Collaborative Research Grant Neonatal immunisation with pneumococcal conjugate vaccine in Papua New Guinea**

Lehmann D, van den Biggelaar A, Holt P in collaboration with Reeder J, Siba P, Pomat WS, Phuanukoonnon S (Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea) and Richmond P (School of Paediatrics and Child Health, University of Western Australia)

Throughout the world an estimated one million children die annually from pneumococcal disease, the majority in early infancy. This study is designed to investigate the safety, immunogenicity and priming for immunologic memory of pneumococcal conjugate vaccine (PCV) in 300 Papua New Guinean infants at 1-2-3 months of age and to find out whether neonatal immunisation in the first week of life will provide earlier protective antibody responses. The study is assessing the impact of PCV on early pneumococcal nasopharyngeal colonisation and on the incidence of acute respiratory infections in the first year of life. We are investigating the development of mucosal and T-cell immunity to non-capsular pneumococcal protein antigens and how this may be affected by early onset of colonisation. The study will also assess the impact of neonatal immunisation on humoral and cellular immune responses to concomitant vaccines (diphtheria toxoid, tetanus toxoid and measles) and whether PCV interferes with normal maturation of the immune system. Ms Jacinta Francis from the Papua New Guinea Institute of Medical Research has come to our institute to undertake a Masters degree and will be investigating maternal and neonatal immune responses to *Streptococcus pneumoniae* and how these responses relate to early URT carriage in

children in this study.

Recruitment into the study began in May 2005 and 233 babies were enrolled by the end of 2006.

In an extension of this project, D Lehmann is co-supervising a post-doctoral research fellow (IA Laing), who is investigating the contribution of human genetic susceptibility to nasal bacterial carriage, development of immune/vaccine responses and the incidence of pneumonia in this population. Dr Laing has an Australian Respiratory Council Ann Woolcock Research Fellowship and genetics studies are supported through a grant from the University of Western Australia Research Grants Scheme 2006.

This study is funded by the NHMRC International Collaborative Research Grant, and the Wellcome Trust (UK).

#### **Non-specific beneficial effects of vaccination in PNG - Impact of routine immunisations on childhood survival in Tari, Southern Highlands Province, Papua New Guinea**

Lehmann D, de Klerk N, Firth M in collaboration with Alpers MP (Centre for International Health, Curtin University of Technology)

Following a report of increased risk of death associated with diphtheria tetanus pertussis (DTP) and oral polio vaccination of children living in rural areas of Guinea-Bissau, the World Health Organization Department of Vaccines and Biologicals sought proposals to determine the effects of routine infant immunisation on survival in areas of high mortality. We investigated the impact of routine immunisations on childhood survival in Tari, Southern Highlands Province, Papua New Guinea. Continuous monthly demographic surveillance enabled us to identify births, deaths, migrations, and immunisation status of all children born in Tari between 1989 and 1994. The study determined the effect of DTP, BCG and measles vaccinations on mortality in the first two years of life and found no deleterious effects of infant immunisations. Our findings have been published in an international journal.

There has also been an investigation into some statistical methodology issues concerning longitudinal and observational data sets such as this one. A paper comparing the potential impact of the varying assumptions that different studies have made around the world has been submitted for publication.

This study is funded by the World Health Organization; and the NHMRC, as part of NHMRC Program Grant.

## **Effectiveness of pneumococcal vaccines - An effectiveness study of pneumococcal polysaccharide vaccine among children in the highlands of Papua New Guinea**

Lehmann D, de Klerk N, Firth M in collaboration with Alpers MP (Centre for International Health, Curtin University of Technology)

In the 1980s pneumococcal polysaccharide vaccine was found to be efficacious in reducing mortality and severe morbidity due to acute lower respiratory infection when given from the age of 6 months onwards to young children in the highlands of Papua New Guinea. An effectiveness study of a 23-valent pneumococcal polysaccharide vaccine was subsequently undertaken between 1991 and 1995 when the vaccine was offered to all children aged 8-23 months attending rural child health clinics. The effectiveness of this vaccine in reducing mortality and hospitalisation for pneumonia is being evaluated.

This study is funded by the World Health Organization; and the NHMRC, as part of NHMRC Program Grant.

## **The Meningitis Centre**

2006 was another great year for The Meningitis Centre. Enquiries continue to attract from across Australia and internationally from people requiring information. ([www.meningitis.com.au](http://www.meningitis.com.au)) is proving very popular with many people adding the site to their list of 'favourites'. Popular information includes disease information sheets, general immunisation information and stories from individuals and families who have experienced meningitis.

The Centre's continuing efforts to raise awareness of all forms of meningitis has resulted in the development of new materials including a meningitis and septicaemia wallet sized symptom card, a poster and an updated Recovering from Meningitis brochure. Many of the Centre's volunteers also continued to raise awareness by giving talks to hospital staff and students about their experience of the disease.

The past year also saw three new volunteer parents added to our committee. They have been an asset to the Centre and have come with new ideas and energy. It is a pleasure to welcome Michael Danzi and Mike and Yvonne Graham to our committee.

In June 2006 we conducted a national text (txt) campaign to remind young people who had not received Meningococcal C immunisation to get the free meningococcal C vaccine as part of the catch up programme and to consult their doctor for information about eligibility and immunisation.

The Centre was also keen to see that the Vaccine Trials Group in Princess Margaret Hospital are conducting a new study looking at a Meningococcal B vaccine and The Centre continues to offer support to the Vaccine Trials Group.

In 2006 The Friends of The Institute for Child Health Research Margaret River awarded funding for The Centre's book project and visited the Centre to meet staff. The Centre would like to thank the Friends of The Institute for Child Health Research Margaret River for all their fund raising efforts and continued support.

The Meningitis Centre has been consolidating its connection with the international Confederation of Meningitis Organisations (COMO). COMO is an organisation of medical and charity leaders from across the world united to increase the international profile of meningitis. COMO launched its website [www.comoonline.org](http://www.comoonline.org) this year and increased its membership. A member's web site was also launched which includes resources such as the COMO toolkit and a member list.

Bruce Langoulant, the Chairman of The Meningitis Centre in Australia and currently President of the international Confederation of Meningitis Organisations (COMO), visited New Zealand to support the Meningitis Trust's efforts in NZ to have their government fund the pneumococcal vaccine for all New Zealand children under two on the back of our lobbying success of 2004 in Australia.

Bruce attended another successful conference in New York in mid September 2006. The Conference succeeded in recruiting three new groups out of the U.S. and cementing relationships between existing member groups and saw the development of an action plan for COMO's third year of operation.

The dedicated 2006 Meningitis Centre Management Committee

Mr Bruce Langoulant – Chairman, Mrs Treacy Elliott – Support/Project Officer, Ms Linda Gibbs- Coordinator, Mr Bob Ginbey, Dr Tony Keil, Prof Deborah Lehmann, Ms Jude Willis, Ms Heather D'Antoine, Ms Jan Adams, Ms Melanie Trainor, Dr Julie Dockerty, Mr Michael Kailis, Mr Barry Thornton, Mr Michael Danzi, Mr Mike Graham, Mrs Yvonne Graham, Mrs Sarah Johnston

## Developmental Epidemiology

### Twins and Singletons with Specific Language Impairment (LOOKING at Language)

Rice M (Institute for Lifespan Studies, University of Kansas), Zubrick S, Taylor K (Centre for Developmental Health, Curtin University of Technology and Telethon Institute for Child Health Research)

The five-year study is investigating genetic, neurobiological and environmental risks for Specific Language Impairment (SLI) in twins and singletons from 2-6 years. This condition is called 'Specific Language Impairment' because, primarily, language is impaired, although the condition affects children's learning and social/emotional development. Children with SLI face many challenges at school, with half behind in their reading and a third with social/emotional difficulties. The project addresses two of the four NIH priority areas for research in communication disorders: (1) Determining factors that contribute to or cause normal and disordered communication and (2) developing and refining diagnostic criteria to facilitate early diagnosis of communication disorders. Seven percent of children with normal hearing and intelligence struggle to learn to talk and we don't know why. In WA, this equates to 7000 children in Kindergarten to Year Two with Specific Language Impairment (SLI). Knowledge about pathways to language, learning and social/emotional disorders in children 2-9 years will inform health and education policies on how to provide services that promote good developmental outcomes for children with language difficulties.

This study is funded by the National Institute of Deafness and Communication Disorders Award R01 DC05226-01A1.

### The WA Twin Child Health (WATCH) Study.

The aim of the WATCH study was to collect data from families of multiples who belonged to the WA Twin Register, to examine the roles that genes and the environment play in the link between childhood asthma and atopy, and exposure to environmental tobacco smoke. Over 90% of eligible families of multiples born between 1980 and 1995 have been contacted and invited to join the WATCH study. Completed questionnaires have been received from nearly 2,500 families (57%), resulting in data from over 13,000 individuals.

Using the questionnaire data, we were able to examine a number of asthma and atopy endpoints, including wheezing ever, wheezing in the last 12 months, current asthma, hay fever and eczema. They all showed greater concordancy in MZ twins compared with DZ twins, suggesting evidence of a genetic component. After

adjusting for age, boys had a significantly higher prevalence of current asthma ( $p=0.021$ ), wheezing ever ( $p<0.001$ ) and current wheeze ( $p<0.001$ ), when compared with girls, but showed no difference in the prevalence of hay fever, and eczema. However, our results indicate that exposure to ETS had little effect on the prevalence of asthma, hay fever and eczema, but that twins with older siblings had a higher rate of asthma than twins who were the first born in their families.

The WATCH study is one of a few twin-family studies of asthma and atopy in the world. Asthma in WA twin families was found to have a strong genetic component, with shared family environment playing little part. New statistical methods have been developed to analyze twin-family data which allow the critical assumptions of the classic twin method to be tested. These have been described by Janice Hansen, Study Coordinator, who has submitted her PhD on the WA Twin Register and Asthma in twin families.

### "WATCH for Asthma" Study

The "WATCH for Asthma" study commenced in 2000 using a grant from the NHMRC. Its main aim was to explore the complexity of the asthma phenotype in WA twin families by collecting detailed clinical asthma phenotype data on a sample of twins born in WA between 1990 and 1995, and their families. Families, consisting of the twins, their biological parents and any of their siblings aged 7 and over, were invited to attend one of our Clinics to undergo a series of standard breathing, allergy and blood tests. We also offered a free zygosity test to families who are unsure of the zygosity of their twins.

Two hundred and thirty nine families, comprising 1040 individuals, have completed testing at our clinics at PMH, Busselton, Geraldton, Merredin, Northam, Bunbury and Albany. Data collection has been completed, and we are now in the process of analysing the large amount of data that has been collected.

Results from this study have shown that exhaled nitric oxide (eNO) was influenced age, sex, body mass index (BMI) and smoking status. There was a strong relationship between eNO and doctor-diagnosed asthma, increased serum IgE levels, increased airway responsiveness and increased blood eosinophils. In addition, it was shown these relationships were strongly modified by an individual's atopic status, with a positive relationship being shown in atopic individuals, whereas non-atopic individuals showed no relationship. Exhaled nitric oxide was shown to have a significant genetic contribution, with heritability estimates in this population ranging from 34-80%. To our knowledge, this is the first study to show that eNO has a separate genetic pathway as well as sharing some genetic pathways with IgE and airway responsiveness. Future

directions for this study will include the genotyping of all study participants using stored DNA.

Study co-ordinator, Dr Kerryn Coleman submitted her Master of Public Health (MPH) dissertation on the genetic epidemiology of exhaled nitric oxide in "WATCH for asthma" families, and was awarded an MPH with high distinction. A number of papers are being prepared for publication.

### **The Western Australian Pregnancy Cohort (Raine) Study**

The Raine Study Executive: Professor Ian Puddey (Chair), Professor Fiona Stanley, Professor Lawrie Beilin, Professor Lou Landau, Professor John Newnham, Associate Professor Garth Kendall, Raine Medical Research Foundation Representative & Raine Study Coordinator

The Raine Study 13yr follow up (Physical Activity Levels in Early Adolescence: Antecedents and Consequences) examined patterns of behaviour that develop from a very early age, and circumstances that are related to levels of physical activity and the consequences of inactivity, such as obesity, elevated blood pressure, diabetes, low back pain, and "high risk" behaviour. Intensive assessment of Raine Study teenagers at 13 years of age included objective measurement of physical activity, physical fitness, motor competence, and dietary intake, as well as markers of cardiovascular health, low back pain, and mental health. In addition, teenagers underwent a test of lung function, a methacholine response test, skin prick tests for allergies, and a hypothalamic – pituitary-adrenal axis response test. Parental information was also updated with respect to measurement of height and weight, blood pressure measurements, measures of serum lipids, physical activity level, dietary intake and self reports on smoking, alcohol intake and medications using standardised questionnaires. Data collection was completed in May 2006.

The Raine Study 13yr follow-up was funded by the NHMRC, Telstra Foundation, Healthway and the Raine Medical Research Foundation.

The Raine Study 16yr follow-up (mental health, spinal pain, the metabolic syndrome, the hypothalamic-pituitary-adrenal axis, and hepatic disease in middle adolescence) commenced in June 2006. Some of the major themes of this latest follow-up include: Developmental health; physical, lifestyle and psychosocial determinants of spinal pain in adolescence; Cardiovascular health and the metabolic syndrome; Gene-environment interaction in Hypothalamic-Pituitary-Adrenal axis functioning; Hypothalamic-Pituitary-Adrenal Axis and cognition and mental health (Fetal HPA); Non-alcoholic fatty liver disease; and the fetal and early childhood origins of Polycystic Ovary Syndrome.

Consumer and Community Participation has also become an important component of the 16yr follow-up. Established in May 2006, the Raine Study Youth Reference Group provides a forum for participants to have an input into the management and direction of the Study.

The Raine Study 16yr follow-up is funded by the NHMRC and the Telstra Foundation.

### **Reproductive pathology in women with severe mental illness and early offspring outcomes**

Jablensky A, Morgan V, Zubrick S, Bower C, Yellachich L

We have ascertained the incidence of complications of pregnancy, labor and delivery, and the neonatal period, through a population-based study of 3662 women who had given birth in Western Australia 1980-1992. The cohort included all women with diagnoses of schizophrenia (N=382 women, 618 births), bipolar disorder (N=763 women, 1301 births) and unipolar depression (N=686 women, 1255 births) on the Western Australian Mental Health Information System, as well as a random comparison sample (N=1831 women, 3129 births) with no recorded psychiatric diagnosis. The analysis revealed significant overall increases of pregnancy complications in women with schizophrenia, bipolar disorder and unipolar depression, and of neonatal complications in women with schizophrenia only. Our work has detailed the complex interplay of maternal demographic (age, marital status), social (socioeconomic disadvantage, lack of social support), and behavioural (poor nutrition and self-care, smoking, substance use) vulnerability factors for sub-optimal reproductive outcomes, likely to be exacerbated by psychotic symptoms. This study is advancing our understanding of genetic and environmental factors associated with adverse obstetric and early offspring outcomes for women with psychoses. While genetic liability and gene-environment interactions may account for some outcomes, maternal risk factors, as well as biological and behavioral concomitants of severe mental illness, appear to be major determinants of adverse outcomes.

This study is funded by the Stanley Foundation (US); NHMRC and the March of Dimes (US).

### **Developmental pathways for the high-risk children of parents with severe mental illness**

Jablensky A, Morgan V, Zubrick S, Bower C, Croft M, Valuri G, Woodman R, Dean J, Duggan P, Griffith J

This study extends work undertaken in the study of reproductive pathology in women with severe mental illness. In this continuation of the project, we have extended our cohort to 249,119 mothers with 466,937

children born 1980-2001, including 14,418 children born to women with schizophrenia or affective psychoses. A total of 272,257 children have had any hospital admission and 19,762 children have had one or more in- or outpatient contacts with the mental health services, at which ICD diagnoses of mental and behavioural disorders were made; this includes 1314 children with at least one recorded diagnosis of psychosis (303 with schizophrenia).

All high-risk children, born to mothers with schizophrenia and affective psychoses, have been followed up through the various administrative databases and registers (Mental Health Information System, midwives' records, hospital morbidity, mortality, birth defects, intellectual disability, cerebral palsy and cancer), and the data have been collated as person-related "events", linked over time by a unique identifier. In addition to the electronic data linkage, detailed diagnostic and developmental data are being extracted manually from the clinical case records of the children with diagnoses of psychoses and coded on a behavioural checklist and a modified version of the Diagnostic Interview for Psychosis (DIP) to establish valid research diagnoses. Important new data sets have been added to: (i) identify siblings of the index offspring on the project database; (ii) identify fathers. Follow-up of this cohort of children will increase substantially our capacity to provide definitive answers to presently unresolved questions about the relative contributions of reproductive pathology and genetic liability to the incidence of major mental disorders and the community burden of disease and disability. In addition to new knowledge on disease causation, the study will provide a unique evidence base for better informed preventative interventions and management strategies including risk reduction for the high-risk children of parents with severe mental illness through targeted antenatal and postnatal interventions.

This study is funded by the Stanley Foundation (US); NHMRC and the March of Dimes (US).

## *Birth Defects*

### **Folate and the prevention of neural tube defects**

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Bower C, Miller M, Payne J, Serna P, Oddy W, de Klerk N, Hickling S, Ambrosini G, Flicker L, Geelhoed E, Milne E

As part of a contract for Food Standards Australia and New Zealand, we estimated the effect of incremental increases in folic acid intake on the incidence of neural tube defects in Australia and New Zealand. We used available data on prevalence of neural tube defects in Australia and New Zealand, folic acid supplement use and serum folate to put into a published model to estimate the number of neural tube defects that could be prevented in Australia and New Zealand with increments

of folic acid intake from 0.1mg daily to 1mg daily. We estimated that an increase of 0.2mg folic acid per day would result in the prevention of 49 (95%CI 27, 84) neural tube defects per year in Australia and 11 (95%CI 6, 18) in New Zealand. A separate estimation for Indigenous Australians found that 0.2mg of folic acid daily could prevent 7 (95%CI 4, 11) neural tube defects in Indigenous infants per year. The estimates are imprecise because of limitations in the data used in the model. More representative and precise data on neural tube defects, serum folate levels and use of folic acid supplements from all Australian states and New Zealand are needed to refine the output from the model and to provide a baseline assessment of folate status against which to measure the effects of any future interventions to prevent neural tube defects.

### **Epidemiology of hypospadias in Western Australia**

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Nassar N, Bower C, Barker A (PMH)

This project involves a number of studies investigating the incidence and trends, risk factors and health outcomes associated with hypospadias in Western Australia (WA). Hypospadias is a urogenital birth defect occurring in infant boys and is the second most common birth defect in WA.

The first study investigating hypospadias involved the examination of the prevalence and trends of hypospadias in WA between 1980 and 2000. Findings showed a total of 1788 cases were registered during the study period with hypospadias diagnosed on average for one in every 285 births. Results also highlighted that the rate of hypospadias increased by 2% per annum from 28 per 10,000 births in 1980 to 43 per 10,000 births in 2000 and, in particular, the rate of moderate or severe hypospadias (which occurs in 11% of all cases) almost doubled. There was also a consistent rise both in infants diagnosed with isolated hypospadias and infants who also had other co-existing anomalies, although infants with co-existing anomalies were more likely to have a severe form of hypospadias. The results from this study have been accepted for publication in the Archives of Disease in Childhood.

Studies currently underway include an investigation of maternal and paternal reproductive health and genetic risk factors that may be associated with hypospadias; and another study to investigate the health status, outcomes and health service utilisation of infants with hypospadias and those who have had surgical repair in WA between 1980 and 2003. A further study is also being conducted in collaboration with investigators from the Children's Hospital Boston to determine the association between first trimester maternal serum levels of human chorionic gonadotropin and the risk of hypospadias or other urogenital anomalies.

## *Fetal Alcohol Syndrome in Australia*

### **Alcohol consumption during pregnancy in non-Indigenous West Australian women**

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Bower C, Elliott E, Haan E

High alcohol intake in pregnancy has been linked to abnormal fetal development. We analysed the responses from the pregnancy stage of the RASCALS, an annual survey of women and their children up to the age of eight years. The women were a random sample of 10% of all births in WA during 1995-1997. 46.7% of the women had not planned their pregnancy. Most women (79.8%) reported drinking alcohol in the three months before pregnancy, with 58.7% drinking alcohol in at least one trimester of pregnancy. Women generally reduced their average alcohol consumption and the number of standard drinks on a typical occasion as their pregnancy progressed, although 10 to 14% were drinking outside the current guidelines for pregnancy. It is important that all women of child-bearing age are aware, well before they consider pregnancy, of the risks of drinking alcohol during pregnancy so they can make informed decisions about their alcohol consumption in pregnancy.

This study is funded by Healthway and the NHMRC.

### **Alcohol and Pregnancy Project**

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Bower C, Elliott E, Henley N, O'Leary C, D'Antoine H, Bartu A, Blum L, Giglia R, Hammill J, James R, Jeffries-Stokes C, Mahony A, McAullay A, McKenzie A

The Alcohol and Pregnancy Project builds on our previous research where we identified that health professionals' lack knowledge about alcohol use during pregnancy and its consequences. Health professionals reported their need for resources such as written materials for themselves and for distribution to clients.

The Alcohol and Pregnancy Project will seek to provide WA health professionals with evidence-based health promotion resources to support their knowledge and advice to pregnant women and women of child-bearing age about alcohol use during pregnancy. The aim of the project is to increase the proportion of WA health professionals who routinely ask and advise women about alcohol use during pregnancy and its consequences.

In 2006, we conducted a synthesis of international and national literature and resources. This synthesis provided the evidence-base for the content of the Alcohol and Pregnancy resources. Issues relating to the communication of information on alcohol use during pregnancy were explored through focus groups and interviews with health professionals (Aboriginal health workers, nurses, allied health professionals, general practitioners, obstetricians

and paediatricians) in metropolitan Perth and country areas. We also gathered qualitative data from Aboriginal and non-Aboriginal women of child-bearing age about the communication of alcohol consumption during pregnancy and its effects.

This evidence-based information and qualitative data from WA health professionals and women shaped the development of the *Alcohol and Pregnancy: Health Professionals Making a Difference* information pack. The information pack contains four resources, a comprehensive booklet and a fact-sheet for health professionals, wallet cards for health professionals to hand to women after they have asked and advised them about alcohol use during pregnancy, and a desk calendar.

The resources were pre-tested with health professionals and women to ensure that they were acceptable, comprehended and would be suitable for health professionals to use as the basis for their advice. The resources were well received by both health professionals and women.

The information packs will be disseminated to health professionals throughout WA in early 2007 and will be evaluated in late 2007.

### **Alcohol and Pregnancy: Women's knowledge, attitudes and practice**

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Payne J, Bower C, Elliott E, Henley N, O'Leary C, D'Antoine H, Bartu A

This project aims to describe Western Australian (WA) women's knowledge, attitudes and practice regarding alcohol use in pregnancy. In 2006, a computer assisted telephone interview was used to collect data from a random, representative sample of 600 WA women aged 18 to 45 years on their knowledge, attitudes and practice regarding alcohol use in pregnancy and Fetal Alcohol Spectrum Disorder. These data are currently being analysed.

## *Assisted Reproduction Outcomes*

### **Assisted Reproduction and Birth Defects**

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Hansen M, Bower C, Kurinczuk J, Petterson B, Sullivan E, Jequier A, Burton P, Junk S, Yovich J

National assisted reproductive technology (ART) registers that rely on practitioners' reports of birth defects have consistently reported lower proportions of children with birth defects than record linkage studies that link ART infants to birth and malformation registers. We compared the birth defect data reported to the national Australian ART Register by practitioners at three Western Australian

ART clinics with the birth defect data identified on the Western Australian Birth Defects Registry (WABDR) through record linkage of all the pregnancies conceived at these clinics to the WABDR. We found that the national Australian ART Register significantly underestimated the prevalence of birth defects in WA-born ART infants. Less than one third of ART children identified with a major birth defect on the WA Birth Defects Registry were reported to the National ART Register. National ART registers provide valuable information on pregnancy rates and short-term pregnancy outcomes such as multiple birth and birth weight, but we believe that, if possible, information used for patient counselling about birth defects in ART children should come from large studies that have used record linkage to high quality birth defect registers.

## Rett Syndrome

### National - Rett syndrome: determinants of outcome and burden (AussieRett)

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Leonard H; Bower C; deKlerk N; Silburn S; Christodoulou J; Ellaway C; Fyfe S; Hall S; Msall M; Dr Nagarajan L; Reilly S; Woodhead H.

AussieRett, as the Australian Rett Syndrome Study is now known, is a population-based study following over a five year period a cohort of Australian Rett syndrome cases born since 1976. The study aims to describe the natural history of Rett syndrome and assess the impact of the condition on resource utilisation as well as to examine the economic and social burden for families and the community.

Questionnaires are administered to families on enrolment to the study and then every two years. Information is collected at each questionnaire on their child's functional ability in daily living, behaviour, hand function, medical conditions, and use of health and education services and every four years on family health and functioning. The fourth follow-up questionnaire was administered to families in the final months of 2006 and is being completed by mail or over the internet.

Genetic and clinical data are also collected as part of the project. The latter include clinical assessments, EEGs, ECGs, and bone densitometry. Organisation of the first round of bone densitometry assessments is now almost complete with 104 undertaken using Lunar prodigy densitometers and a further 23 using other types of equipment.

Another important and innovative source of data for this study is video footage provided by the subjects' families. During 2006 coding of the mobility component of the video material was completed and further work undertaken on the oromotor function domain. This

involved a multi-disciplinary approach which included input from psychologists, physiotherapists and speech therapists and national collaborations with the Children's Hospital at Westmead, Sydney and the Royal Children's Hospital, Melbourne. International collaborations also continued with Professor Walter Kaufmann from Johns Hopkins University, Professor Alan Percy from the University of Alabama and Professor Michael Msall from the University of Chicago.

In 2006 we continued to run meetings of our Consumer Reference Group which involves regular teleconferences with families across Australia. Mid year we published the 2006 Australian Rett Syndrome Report which was distributed to all participating families and clinicians and is available on the web.

Analytical investigations using data relating to different aspects of the study continue to be undertaken and during 2006 ten articles relating to the study were published. The work covered a range of topics from the general epidemiology (ie how common is Rett syndrome and what is the associated life expectancy) to complex aspects of the genetics. We were also able to describe the behavioural characteristics of Rett syndrome and some of the variability in these as well as examine the factors associated with onset of seizures and scoliosis. We have also been able to report on the process of collection and coding of the video material that has occurred over the last few years.

Genetic studies included an investigation of the influence of X-chromosome inactivation on clinical severity in subjects with the two commonest *MECP2* (Rett syndrome genetic) mutations. In conjunction with Professor David Ravine at the Western Australian Institute for Medical Research we identified a rare exon 1 *MECP2* mutation in one of our cohort and were able to describe the clinical characteristics in this case. Finally we have also been able to describe the role of *MECP2* in newborn encephalopathy in males (that is in some baby boys who develop neurological problems very early in life).

### International: InterRett

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Leonard H, Anderson A, Bebbington A, De Klerk N, Fyfe S, Ravine D

During 2006 the AussieRett group continued to manage the international phenotype database InterRett. Funded by the International Rett Syndrome Association (IRSA) InterRett collects data from families and clinicians around the world through online and paper based questionnaires. In May 2006 Dr Helen Leonard and InterRett project coordinator Alison Anderson were invited to participate in a Clinical Trials in Rett Syndrome Workshop in San Francisco. The workshop ran in conjunction with the

IRSA annual Family Conference which Helen and Alison also attended. They recruited over 50 new families to the project. A meeting with the IRSA research committee secured a further three years funding that will allow the project to continue through to December 2009. This funding provided the opportunity for a new member to join the team on a part-time basis in 2007.

On their return journey from the US Helen and Alison met with Dr Nadia Bahi-Buisson from the Necker children's hospital in Paris and the French Rett syndrome family association. This meeting resulted in the signing of a Memorandum of Understanding between InterRett and the two French parties that will result in approximately 300 French cases being added to the database. To date the database contains over 1100 cases from 30 countries satisfying the prime objective of creating a sufficiently large sample size to allow comparison of genetic with phenotypic characteristics. An important paper validating the 'representativeness' of this international cohort was recently submitted to a peer-reviewed journal. The validation was obtained by replicating an analysis of genotype-phenotype relationships carried out in the Australian cohort. Results from the international cohort mirrored those obtained using the Australian population-based cohort.

During 2006 the InterRett team were also successful in obtaining two small grants. The first grant, from UWA, aims to test the feasibility of assessing workplace exposure to genotoxic agents using an adaptation of a protocol currently used in the research of childhood cancer (AUS-ALL study). The second grant from the Department of Education Science and Training provides travel funds to promote collaborative work between China and Australia. This initiative involves the creation of a Mandarin version of the InterRett website and online data collection tools, the participation of six Australian researchers in a workshop in Beijing in 2007 and an Australian workshop to be held in 2008 attended by our Chinese partners and hopefully other international collaborators.

## *Down Syndrome*

### **Down Syndrome (NOW) Study**

Leonard H, Bower C, de Klerk N, Silburn S, Fyfe S, Hall S, Msall M, Bourke J, Dyke P, Jacoby P, Hogan D, Maley A

Down syndrome is the most common known cause of intellectual disability, affecting 14-15% of people with intellectual disability registered with Disability Services Commission (DSC) in Western Australia. The Down Syndrome Needs Opinions Wishes (NOW) study aims to document the current health, functioning, needs (including psychosocial, employment, and accommodation needs), and behavioural features of children and young adults with

Down syndrome; to track changes in health, functioning and needs of these children and young people over time; and to estimate the social and economic burden of Down syndrome on affected families and the community. The study involves 363 families with a child aged 25 years or under in 2004 who completed a comprehensive questionnaire.

In 2006 a grant was received from DSC to release the findings from the Down Syndrome NOW study as a report. The Down Syndrome Association of Western Australia (DSAWA) is a partner in this project, which aims to distribute the report both to relevant stakeholders and participating families. It is anticipated that the report will translate the information collected in 2005 from the families throughout WA, reflecting the current needs and status of these children and young adults and their families. To ensure the report includes information relevant to the main stakeholders a number of focus groups were organised in conjunction with the DSAWA. The aim of the focus groups was to determine which elements of the research findings will provide the most relevant information for families and other stakeholders. The focus groups were comprised of parents, DSC Local Area Coordinators, therapists, paediatricians and other service providers. The report is expected to be completed by September 2007.

Analysis of the child and family factors which impact on the mental and physical health of the mother of a child with Down syndrome is currently being undertaken. In a collaboration with Professor Dennis Hogan from Brown University, Rhode Island we are also using the questionnaire data to examine the post-school experiences of the young adults with Down syndrome. In a local collaboration with DSC we are investigating the prevalence of autistic features in children with Down syndrome.

## *Child Nutrition and Development*

### **Dietary patterns and mental health**

Oddy WH, Silburn S, DeKlerk NH, Sloan N, Li J, Kendall GE.

Work continued intensely on this project throughout 2006. Two draft papers have been written and are awaiting submission for publication. Briefly, it is important to develop indicators to monitor the quality of diets of children and adolescents as a predictor of adolescent mental health morbidity. One of the roles of indexes of diet quality is to assess overall dietary patterns and may also be useful in relation to measures of adolescent mental health. The objective of this analysis was to investigate the association of dietary quality and mental health outcomes in a birth cohort of Western Australian



adolescents. Preliminary results showed that 23% of the sample reported externalising or internalising mental health problems some or all of the time and these were more likely to have a lower diet quality score as measured by our diet quality index ( $R = -.102$ ;  $p < 0.0005$ ). Thirteen year olds tended to have lower mean diet quality scores with the presence of externalizing problems ( $R = -.109$ ;  $p < 0.0005$ ) as well as internalizing problems ( $R = -.071$ ;  $p = 0.022$ ). Preliminary conclusions show that as the mean diet quality score increased, all domains of mental health improved, and that healthy diets should be encouraged in adolescent children for the benefit of their mental health and wellbeing.

Funding was received in late 2006 from the Australian Rotary Health Research Fund to continue this work looking at 'Dietary factors and trajectories of mental health from infancy to adolescence'.

### **Childhood Precursors of Adult Cardiovascular Disease, Obesity and Diabetes- 16 year follow up of a Longitudinal Cohort**

Beilin LJ, Palmer L, Oddy WH, Mori T, Kendall G, Hands B

In June the 13-year nutritional epidemiological follow-up of the Western Australian Pregnancy Cohort was completed including data entry of 898 three-day food diaries, 1629 food frequency questionnaires (FFQ) by CSIRO and 1324 red blood cell (RBC) analyses at Royal Perth Hospital. The 16 year nutrition follow-up of the Western Australian Pregnancy Cohort (approx 2000 16-year-olds) commenced using validated methods following ethics approval. The NHMRC project grant (2006 Prof L Beilin CI-A) was funded to implement the 'Childhood Precursors of Adult Cardiovascular Disease, Obesity and Diabetes- 16 year follow up of a Longitudinal Cohort' project within the Raine Study cohort to investigate diet, nutrition and cardiovascular risk factors.

### **Nutrition-related behaviour as a mediating factor underpinning socioeconomic inequality in health**

Li J, Henderson S, Oddy W, Kendall G, Downie J, Landsborough L.

Work commenced on the 'Socioeconomic patterning of diet quality in a cohort of adolescents in Western Australia' project in 2006. The quality of diets in children and adolescents is important because early adoption of healthy eating habits may contribute to lower incidence of obesity and cardiovascular diseases in adulthood. While measures of diet quality have been created in other developed countries to enable research on diet quality as an outcome as well as a predictor of a range of health outcomes, no such work has been conducted in Australia. The purpose of this project is to investigate the

association of social, economic and demographic factors with diet quality in a cohort of adolescents followed from pregnancy to age 13, using a diet quality index developed at the Institute for Child Health Research. In preliminary analysis we concluded that maternal education impacts on the diet quality of their adolescent. Further analysis will examine occupation, family income and the socioeconomic status of residential areas and their association with the diet quality index.

### **Obesity and fast food: the Growth and Development Study**

Oddy WH, Byrne, S, Watt FJ, Blair E, Davis EA. Fast food and its association with obesity in children.

A poster abstract was submitted to the 10th International Congress on Obesity, Sydney, Australia 3-8 September 2006. This poster was awarded the Most Outstanding abstract selected as Poster Presentation within theme and received the President's Poster Award. An Honours student will work on this project in 2007 to investigate the psychological and physical health risks associated with fast food consumption.

### **Promoting Optimal Infant Nutrition: The Perth Breastfeeding Scoping Project**

Oddy WH, Hauck Y, Henley N, Ellies P, Hart B, Binns CW.

Funding was received in late 2006 to implement this 'seeding' project of literature reviews, focus groups of mothers and key stakeholders, in preparation for a large Breastfeeding Health Promotion Campaign planned for the next decade.

This study is funded by the West Australian Health Promotion Foundation to commence in 2007.

### **Causal pathways to eating disorders: a prospective analysis using data from the Western Australian Pregnancy Cohort (Raine) Study.**

Byrne S, Oddy WH, Forbes D, Allen K.

Funding was obtained from the Australian Rotary Health Research Fund in late 2006 to commence a study investigating the causal pathways to eating disorders applying data collected within the West Australian Pregnancy Cohort Study in the 13 year follow-up.

### **Maternal obesity and the risk of birth defects.**

Bower C, Oddy WH, DeKlerk NH.

Data analysis is continuing on this project and it will be

written up for scientific publication in 2007.

### **Early child development and breastfeeding**

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Oddy WH, Kendall GE, Dixon G, De Klerk NH, Zubrick S.

Data analysis is continuing on this project and will be written up for scientific publication in 2007 continuing into 2008.

### **Breastfeeding and its effect on the risk of Sudden Infant Death Syndrome**

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Espaignet E, Oddy WH, Firth M, DeKlerk NH.

Data analysis is complete on this project and it is being written up for scientific publication.

### **Nutrition and mental health: Fatty Acids and Depression Project**

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Oddy W, Kendall G, Silburn S, Zubrick S, Blair E, Miller M

We examined the association of 'Docosahexanoic acid and mental health morbidity in a population study of adolescents'. A growing body of evidence indicates the potential importance of fatty acid nutrition to the healthy functioning of the human brain, suggested by the high concentration of docosahexanoic acid (DHA) in neural tissue. In the Western Australian Pregnancy Cohort Study our aim was to examine the association between mental health morbidity and DHA levels. We showed that the mean (+SD) DHA level in erythrocytes was 4.35 (1.05) µg/mL (range 1.05-9.91). The prevalence of mental health morbidity was 26% at year 13. A reduced amount of DHA was associated with total mental health morbidity ( $p=0.052$ ), aggressive behaviour ( $p=0.034$ ) and attentional deficits ( $p=0.074$ ) at 13 years. Following adjustment for maternal factors: age, education and happiness DHA was no longer associated with any mental health domain. The fatty acid associations with mental health morbidity in adolescents will be examined in detail in 2007/2008.

### **The Childhood Growth and Development Study**

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Byrne S, Davis E, Blair E, Zubrick S, Jones T, Silburn S

The primary aim of the study is to identify the biopsychosocial factors, and their causal pathways, that contribute to the development and persistence of childhood obesity, so that these pathways may be targeted in prevention programmes. The study involves three groups of children (a community sample of overweight/obese children, a community sample of healthy weight children, and a treatment-seeking sample

of obese children) and their parents. A comprehensive assessment protocol is used to assess a broad range of factors (biological, psychological and social/environmental) that may influence the development and persistence of childhood obesity. Children and their parent(s) are assessed, separately, immediately upon enrolment into the study, and then at six-monthly intervals for at least three years. This design will enable both longitudinal and cross-sectional data to be examined. Assessments include the collection of height and weight data, and measures of a broad range of biological, psychological and social/environmental factors that are purported to influence the persistence of childhood obesity into adolescence and adulthood.

At the end of 2006, the Growth and Development Study has 1408 children taking part. This year the new schools we visited were Yale and Maddington and our returning families came from East Wanneroo, Mount Pleasant, Dianella Heights, Lance Holt, Ferndale, Como, East Claremont and Subiaco. To date, 468 initial interviews have been completed with children, as well as 339 with parents. So far, over 300 children have come back for their one year follow-up interviews and some families are even moving on to their 3-year follow-ups. In 2007, we will continue to follow-up all our families as well as recruiting new families. In 2006, the Childhood Growth and Development Study were grateful for the support of Healthway.

This study is funded by Healthway.

## *Databases and Information Technology for Population Studies*

### **Record linkage and the Maternal and Child Health Research Database**

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Cosgrove P, Wood M, Berinson M, Laubsch Y

The Maternal and Child Health Database is a linked database of maternal and childhood population data that has been an important resource within the division as well as being a key component of various collaborations with other external groups and researchers.

The record linkage collaboration with the Data Linkage Unit continues. The collaboration involves record linkage work previously done at ICHR being carried out at the DLU, co-location of staff on a part-time basis to the DLU and the provision of an annual de-identified snapshot of linked health data being provided by the DLU and the WA Department of Health to the Institute.

The DLU System is governed by best practice privacy-sensitive protocols that have been developed in WA and are designed to optimize linkage efficiency with minimum

risk for individual privacy. The collaboration is working well, with feedback from ICHR researchers helping the Data Linkage Unit to continue to ensure the high quality of their linkage.

The Maternal and Child Health Database has been updated with linked health records for all children born in WA between 1980 and 2003. This has been supplemented with data from the Australian Bureau of Statistics. Procedures have been put in place to determine and store additional information often required by researchers, such as which hospital admissions belong to a single episode of care.

Work is continuing on the development of in-house web-based computer applications for use in the area of meta-data management and knowledge management. Metadata is 'data about data' and these systems are designed to allow data in the Maternal and Child Health Research Database to be used as efficiently as possible, giving researchers easy access to associated key information on the data and also to a knowledge base containing contributions by other researchers using these important data resources.

2006 has also seen the increased use of the in-house questionnaire development and processing software called "Teleforms". This computer software and accompanying computer hardware facilitates the streamlining of the data collection process by studies at the Institute that collect data using questionnaires.

### **The Western Australian Twin Register**

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Hansen J, Alessandri P, Coleman K, de Klerk N, Croft M, James A, Burton

The WA Twin Register (WATR) was established in 1997 using a grant from the WA Health Promotion Foundation (Healthway), and initially comprised data on all WA multiple births between 1980 and 1992 inclusive. The main purpose for establishing the Register was to invite families to participate in the WA Twin Child Health (WATCH) study which examined the roles that genes and the environment play in the link between childhood asthma and atopy, and exposure to environmental tobacco smoke. The Register has since been extended to include 1993-1997 births, using part of a grant from the National Health and Medical Research Council (NHMRC) for the "WATCH for Asthma" (WFA) study. This study aimed to collect detailed clinical asthma phenotype data on twins born between 1990 and 1995, and their families, and to investigate and describe the familial aggregation of childhood asthma and atopy. A total of 11,188 multiple birth children, born in WA between 1980 and 1997 inclusive, have been identified, representing 2.5% of all births during that time. They comprised 5,340 sets of

twins, 166 sets of triplets, quadruplets and quintuplets. Forty-eight families had two sets of multiples during the time period. The WATR is the only population-based register of multiples in Australia, and one of only a few anywhere in the world.

The WATR has been extended to include multiples born between 1974 and 1979 (a WAIMR initiative), and we are awaiting approval to extend the childhood component of the Register to include all WA multiples born from 1998 onwards.

### **Western Australian Mortality Database for infants, children and young people**

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Freemantle CJ, Read AW, DeKlerk NH, Divitini M, Woods M, Cosgrove P, Anderson IP (University of Melbourne), Officer K, Stanley FJ.

Work continues on the expansion of the mortality database to include deaths up to 2005. Information describing deaths for the years 2002 and 2003 has been collected. However, release of information describing deaths where there has been a coronial enquiry is dependent on the release of the information from the Coroner for these deaths. This has meant that there has been a delay in accessing the information on deaths in the more recent years. Thus, the information describing deaths for years 2004 and 2005 has only been partially collected. The protocol developed for the collection of the information includes review of the information and coding of the deaths by three independent experts. These reviews have been completed for years 2002 and 2003. This information has been collated and added to the Mortality Database.

In 2006, important collaborations were initiated with colleagues in Alaska and New Zealand and comparative analyses of infant mortality and mortality attributed to Sudden Infant Death Syndrome (SIDS) have been commenced. These analyses will compare the patterns and trends of mortality of Australian Aboriginal infants and children with those of Alaska Native and Maori infants and children. These analyses which use total population data will be the first of their kind and will provide important information about the differing antecedents to and causes of mortality in each of the populations.

The Western Australian Mortality Database for infants, children and young people continues to inform policy and identify areas of critical need. An excellent example of the application of the information contained in the data base is the Preventing SIDS in Aboriginal Communities project. The analysis of the mortality data, 1980-2001, identified the significantly increased risk of deaths attributed to SIDS for Aboriginal infants compared with non-Aboriginal infants. These data also identified

geographical regions of greatest risk. Working with SIDS and Kids Western Australia, the Preventing SIDS in Aboriginal Communities project has used a grass-roots, community consultation approach in accordance with the principles of participatory action-research. One of the exciting aspects of this research is the collaboration of non-Aboriginal and Aboriginal researchers, health professionals, community members and those working in areas of policy development, resource allocation and the development of health strategy. One of the aims of this research is to develop better ways and processes of transforming our known research into policy and practice through the development of interventions to prevent SIDS. The Project Advisory Group will not only provide advice to guide the analyses of the data, but members of the reference group will act as a conduit through which to report the results to the Aboriginal Community. The project is being led and run by Aboriginal researchers and community members.

Work has also continued on investigating associations between prior hospital admission and death in childhood, with particular focus on quantifying the disparities between Indigenous and non-Indigenous children in Western Australia. This research has been funded by Healthway WA. A significant component of this research has been the investigation of the association of deaths due to suicide and prior hospital admission. These data are currently being analysed with a view to identifying possible patterns of hospitalisation associated with suicide.

### **WA Family Connections Genealogical Project**

Glasson E, Nielsen L, Johnston M, de Klerk N

Due to the genetic complexity of many health conditions, population-based data are often necessary as sampling frames for research. The aim of the Family Connections project is to create and store electronic links between genealogically related individuals in WA for use in familial or genetic research projects. Genealogical relationships are defined from information recorded on birth, death and marriage registrations as well as other data sources that are used at the Data Linkage Unit for data linkage activities related to health research projects. The project methodology uses the same best-practice protocols and procedures that were developed for the WA Data Linkage System. The genealogical properties are stored as separate data using software tools designed and built specifically for the project.

Phase One of the project involves creating genealogical links from all available electronic registrations ( $n = 1.2$  million records). These exist from 1974 for births, and 1984 for deaths and marriages. Phase Two will create

genealogical links from registrations since 1950 that are currently held as paper records (0.9 million records). To date, most children born since 1974 (approximately 754,000 records) and most marriage partners (approximately 234,000 records) have had genealogical links created from available electronic data.

Data linkage between the WA Family Connections project, health datasets and tissue registers are possible with appropriate ethical approval and compliance with legal requirements. This represents significant potential to analyse genetic variants with respect to phenotype or patterns of disease history for the WA population.

### **ARC Linkage Grant: Developmental Pathways in WA Children**

Changing socioeconomic inequalities in neonate, infant and child health and development

PhD candidate: Langridge AT

Supervisors: Kendall G, Li J, Zubrick S, Codde J

A multi-level approach to childhood literacy and numeracy: Developmental pathways and the role of early health

PhD candidate: Malacova E

Supervisors: Li J, de Klerk N, Leonard H, Humphry S

Towards Prevention – A population health approach to child abuse and neglect: A measurement model and the identification of antecedent causal pathways

PhD candidate: O'Donnell M

Supervisors: Kendall G, Stanley F, Leonard H, Patterson Y, Mathews R

Do you see what I see? Discerning the perceptions of how Aboriginal and White Western Australians see themselves, each other and the effect of these perceptions on service provision and utilisation within the human service sector of the Perth metropolitan area of Western Australia

PhD candidate: Pearson G

Supervisors: Freemantle J, Vicary D, Silburn S

Impact of abuse and/or neglect that has resulted in care and protection: Effect on mental health and developmental outcomes in adolescence and early adulthood

PhD candidate: Northey K

Supervisors: Kendall G, Li J, Silburn S

On the dimensions and development of juvenile delinquency. A population-based study of the prevalence and frequency of offending and the influence of individual, family and community factors on delinquency in Western Australian children

PhD candidate: Ferrante A

Supervisors: Indermaur D, Kendall G, Zubrick S, Jessop M.

The ARC Linkage Grant continues to progress its innovative linkage of population-level data across multiple disciplines and WA government agencies. Collaborative partnerships and working relationships between the University of Western Australia (Centre for Child Health Research and Crime Research Centre) and six government jurisdictions in Western Australia (the Departments of Health (DOH), Education and Training (DET), Community Development (DCD), Corrective Services (DoCS), Disability Services Commission (DSC) and Office of Children and Youth (OCY)) have substantially progressed this landmark project over the past year.

At the beginning of 2006 it was identified that the project would benefit from a 'Communication Strategy' to guide communications between researchers, key stakeholders, consumer representatives and the general public. With the assistance of the Public Relations Office of the Telethon Institute for Child Health Research, a 'Communications Workshop' was held in February 2006 with all researchers, Industry Partners, and their respective public relations staff members in attendance. Addressing the stakeholders' and the project's communication requirements and expectations, a 'Communication Strategy' was drafted, discussed at all levels of governance, and is currently being implemented. One of the actions of the 'Communication Strategy' was to give the project a name that reflects the nature of the research. The project has since been named "Developmental Pathways in WA Children Project". The involvement of consumer representation and community participation on the project has been supported and is being developed under the guidance of the Institute's Consumer Research Liaison Officer, Anne McKenzie. Each of the PhD candidates' studies will proceed with consultation of community members, including Aboriginal representatives.

The four APAI recipient PhD candidates and two self funded PhD candidates on the project have continued to make substantial progress towards completing their studies. Ethics approvals have been obtained, and the candidates continue to work on their literature reviews and methodology while commencing data analyses. A number of the candidates have undertaken additional

post-graduate units at the University of Western Australia including epidemiology, biostatistics and data linkage, as well as a number of courses aimed at assisting them in the process of their PhD. With the restructure of the Department of Justice in 2006 (to the Department of Corrective Services (DoCS) and the Department of the Attorney General (DoTAG)), and a review of the Department's financial contributions to this project, a new PhD scholarship was created. This 'Justice' themed PhD scholarship will be taken up by candidate Ms Jocelyn Jones in April 2007.

Two of the PhD candidates, one Chief Investigator (Dr Garth Kendall) and one Partner Investigator (Dr Jane Freemantle) went on an international research trip, travelling to New Zealand, Canada and the United States in June 2006. The trip was a unique opportunity to showcase the project internationally; to acquire up to date knowledge of similar research that is being conducted around the world; and to establish and strengthen existing and new international networks and collaborations. As part of the research trip, the researchers participated in the New Investigators Network (NIN), which was developed by the Canadian Institute for Advanced Research to support the career development of promising young scholars in the area of human development. This was a most successful trip and the PhD candidates reported their experiences to the interested Industry Partners and members of the wider research community in September 2006.

Other project team members have been involved in a number of conferences and presentations, both nationally and internationally, including but not limited to a presentation at the Australian Society for Medical Research Symposium in Perth; poster presentation at the ESRC Cambridge Network SCoPiC Conference (The Social Contexts of Pathways in Crime: Assessing the Role of Individual Differences and the Environment in Crime Causation) in Cambridge; and a presentation on data linkage at the 15th Annual Meeting of the Australasian Epidemiological Association at the University of Melbourne.

In addition to the restructure of the Department of Justice, over the past year the project has witnessed a number of other departmental restructures and staff changes. This has contributed to a delay in receiving linked data. It is acknowledged, however, that this project is breaking new grounds in the linkage of a number of new data sets, and that the data have required a degree of preparation prior to linkage. Legal constraints have also prevented the release and linking of some data, and new procedures and legislation have been necessary to enable such data linkage.

Given the complexity of linking data from multiple government agencies, the Data Linkage Unit (DLU)

ected to draft individual data agreements with the various departments to facilitate the process of data linkage. By August 2006 the DET data, which consisted of all Western Australian Literacy and Numeracy Assessment (WALNA) data from 1998 to 2005, had been linked at the DLU. Staff changes and data management time at the DET meant that the data was not extracted and provided to the project until January 2007. Linkage of DSC data was close to completion by December 2006. The linkage process for DCD data will commence in 2007, with an anticipated completion date of April 2007. A data agreement is in final draft between DLU and DoCS and the DoCS linkage is anticipated to commence in April/May 2007, pending finalisation of legislation changes.

## *Autism Spectrum Disorders (ASD)*

### **WA Register for Autism Spectrum Disorders**

Dixon G, Glasson E, Bower C, Wray J

Autism spectrum disorders include autism, Asperger syndrome, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS). They are characterised clinically by significant impairment in social interaction and communication, and by a restricted or repetitive range of interests. Symptoms may be apparent before 30 months of age, but diagnosis is tentative before this time. Many children have difficulties integrating into society and each require varying degrees of supervision and support in daily living. Our current understanding of the aetiology and intervention strategies for autism spectrum disorders is limited. The WA Autism Register serves as a primary resource to researchers, clinicians and service providers to provide knowledge of the diagnostic patterns of these complex disorders.

Since January 1999, the WA Register for Autism Spectrum Disorders has collected demographic and diagnostic information on newly diagnosed cases in WA. Annual summaries are made of the number and ages of people diagnosed, the severity of their disability, and some biological, diagnostic and developmental features. To date, the Register has collected information for more than 1400 children, adolescents and some adults who were newly diagnosed with an autism spectrum disorder. After eight years of operation, the data can be used to calculate diagnostic prevalence rates for the WA population. The Register continues to be approached by varying agencies and individuals for information about its data and data collection management. In 2006 information about the methodology and success of the Register, which has been described as an internationally unique resource, was presented to an international autism meeting in Montreal, Canada.

## *Cerebral Palsy*

### **WA Cerebral Palsy Register**

Watson L, Blair E, de Groot J, Stanley F

Cerebral palsy (CP) is a chronic neurological condition affecting movement and posture, ranging in severity from barely noticeable to severely disabling. As there is no cure, prevention and effective management are top priorities. The longstanding WA CP Register is used to monitor the occurrence of CP in WA and carry out research to investigate its causes and evaluate treatment strategies. In 2006 a 5-year report was produced presenting Register data up to birth-year 1999.

### **Australian Cerebral Palsy Register (ACPR)**

Blair E, Watson L, de Groot J, F Stanley and the ACPR national collaboration

Our lack of knowledge regarding the extent and distribution of CP across Australia led to the setting up of a national collaboration to combine CP data from all States and Territories. The ACPR has been co-ordinated by WA CP Register staff since its inception in 2002. Coverage of the national live birth population has increased from 45% at the outset to almost 100% in 2006, with only the Northern Territory still seeking funding. An internet website donated to the NSW CP Register by Macquarie Bank and Accenture, further developed and maintained as a donation by Paul Novak of Compots, provides all States with facilities for data entry, management and transfer, also making it possible for the public to directly contribute data.

An essential aspect of data pooling is the need to address intra- and interstate differences in classifying CP. The WA team was mandated to design a standardised method of recording clinical data, and the resulting CP Description form which incorporates an instrument to measure spasticity newly developed by S Love and N Gibson - the Australian Spasticity Assessment - was trialled nationally in 2006. With funds donated by PLAN Australia, motor assessment videos of children were produced for trialling the new form, and this DVD will form the basis of a reference and training manual for ongoing use. Eve Blair's invited presentation of this work at a meeting of the SCPE, a European network of CP Registers, in Vilnius and Paris in early October generated considerable interest.

A meeting of all State and Territory representatives held in Brisbane in late October 2006 again provided the opportunity for a national CP Description seminar at which results of the trials of the new form were presented. ACPR progress and data consistency issues were addressed on the second day, the most pressing

matter being the need to secure funding and establish formal links between the States and the AIHW. To this end the collaboration will consider moving the clearing house from TICHR to a centre with ready access to the business expertise required to establish the necessary groundwork.

### **Case-control studies of cerebral palsy in term and preterm infants**

Blair E, Stanley F, de Groot J, Hepworth A, Watson L

CP refers to a collection of conditions having in common a motor disorder due to cerebral pathology acquired early in development, implying a variety of ways in which CP may be caused. The aetiology is far from clear in the majority of cases. The few causes that are fully understood can now be prevented, and are routinely prevented in developed countries. It is now known that less than 10% of CP cases in developed countries can be attributed to events that occur during birth. Many factors associated with CP, such as preterm birth, multiple pregnancy, growth restriction and a variety of complications of pregnancy, nonetheless are seldom followed by CP. This has given rise to the idea that combinations of factors may be required in order to cause CP. The case control study of CP in term and preterm infants seeks to identify some of these combinations.

Antenatal and perinatal data have been collected from medical records for all children born in WA between 1980 and 1995 who are registered on the WA CP Register. Similar data have also been collected for an equal number of neonatal survivors who are not on the register, and for perinatal deaths. These comprehensive data have now been computerised, and analysis and documentation of results are in progress.

### **Cerebral Palsy Management Studies**

Love S, Gibson N, Blair E

Two PhD projects looking at the use of botulinum toxin A in the management of cerebral palsy in children are currently in progress.

## *Intellectual Disability*

### **IDEA (Intellectual Disability Exploring Answers) Database**

IDEA Advisory Council 2006: Bourke J, Bower C, Leonard H (TICHR), Petterson B, Valentine J (PMH), Morgan V (UWA), Sanders R (Dept of Education and Training), Mathews A (DSC), Stopher K (DSC), Chauvel P (Consultant), Rowe P (SCDC), Rook C (Consumer)

Annual notifications of children identified with an intellectual disability are received from the Department of Education and the Disability Services Commission. These are linked by the Western Australian Data Linkage Unit to each other and to all current notifications on the database. This is in keeping with best practice protocols and should minimise the possibility of duplications. The linkage process is nevertheless quite complex with the possibility of children being notified through both sources and in different years. Changes to the protocol in 2006 have resulted in delays in the process but it is hoped that this will be rectified in 2007.

In 2006 the IDEA database received applications for linkage from a number of studies investigating a range of topics including mental health problems in children, pathways to health and education, child abuse and neglect, autism and alcohol in pregnancy. The IDEA database continues to be one of the few population-based resources internationally which can provide deidentified data on intellectual disability to researchers.

It is recognised that the two principal causes of low birth weight are preterm delivery and intra-uterine growth retardation. The latter can occur in both pre-term and term infants. In 2006, a study on the association between intrauterine growth and subsequent intellectual disability in the child was completed, using data on children born between 1983 and 1992. The association of intrauterine growth with risk of intellectual disability was investigated by assessing percentage of optimal birth weight by level of intellectual disability and compared with infants without intellectual disability. Findings from this study will provide important information for clinicians and parents in the follow-up, screening and management of infants most at-risk of intellectual disabilities and the possibility of early intervention to reduce poor developmental outcomes in children in the future.

## Childhood Cancer Epidemiology

### **Australian Study of Causes of Acute Lymphoblastic Leukaemia in Children (AUS-ALL)**

Milne E, Bower C, de Klerk N, Kees U, in collaboration with Armstrong B (University of Sydney), van Bockxmeer F (Haematology, Royal Perth Hospital), Baker D (Princess Margaret Hospital), Fritschi L (Viertel Centre for Research in Cancer Control, Queensland Cancer Fund) Thompson J (WA Cancer Registry), Lockwood L (Royal Children's Hospital, Brisbane), Rice M (Women's and Children's Hospital, Adelaide), Stevens M (Children's Hospital Westmead, Sydney), Smibert E (Royal Children's Hospital, Melbourne), Suppiah R (Mater Children's Hospital), Alvaro F (John Hunter Hospital), Downie P (Monash Medical Centre), Haber M, Norris M (Children's Cancer Institute Australia for Medical Research), Scott R (Hunter Area Pathology Service), Attia J (University of Newcastle), Marshall G (Sydney Children's Hospital), Miller M (Marg Miller Consulting).

Researchers in the Childhood Cancer Epidemiology program have now completed the fourth year of a five-year (2003-2007) NHMRC funded national case-control study into the causes of childhood acute lymphoblastic leukaemia (ALL). The primary hypothesis of this study is that maternal folate supplementation during pregnancy protects against ALL in the offspring, with the effect modified by genetic factors in folate metabolism. This study addresses the actions and interactions of supplemental and dietary folate, environmental exposures, and genetic polymorphisms in parents and children in determining the risk of childhood ALL. The team is multidisciplinary, bringing together molecular biologists, geneticists, oncologists and epidemiologists. Case subjects comprise 350 children (0-14 years) newly diagnosed with ALL in Australia between 2003 and 2006. They are identified through all the paediatric oncology centres in Australia. Two controls are selected for each case, frequency matched by age, gender and State of residence, a total of 700. Controls are identified using random digit dialing. Data collection instruments were specifically developed for use in the study: self administered exposure questionnaires for each parent and food frequency questionnaires for the mother (during pregnancy and breastfeeding), the father (in the 12 months prior to the pregnancy), the child's current diet (completed by the parent) and their diet as an infant. Telephone follow-up interviews ask about occupational and other exposures. An occupational exposure expert, blinded to case/control status, is examining all the occupational information and will allocate probability and amount of exposure to the chemicals with reference to a custom designed database of jobs and exposures. Blood and buccal samples are taken

from the case child (in remission), and blood samples are taken from his/her parents. The study is well under way. To date, 517 cases have been notified to us, 513 (99%) of whom have achieved remission and are thus eligible to participate. 453 of the cases in remission have been invited to participate, of whom 379 (84%) have consented, 49 have declined (11%), two died prior to consent and the rest are yet to consent. DNA collection is complete for 363 (96%) recruited cases, and 323 (85%) case families have completed questionnaires. To date 658 (48%) recruited control families have completed food questionnaires (77% of those sent), and 495 (47%) have provided DNA samples. Genotyping has been completed in 1927 specimens. In total, data from 800 families have undergone occupational exposure assessment. Data cleaning is well under way, as are plans for the analysis of the final datasets.

This study is funded by the NHMRC.

### **Australian Study of Causes of Childhood Brain Tumours (AUS-CBT)**

Milne E, Bower C, de Klerk N, Dallas P, in collaboration with Armstrong BK (University of Sydney), van Bockxmeer F (Haematology, Royal Perth Hospital), Baker D (Princess Margaret Hospital), Fritschi L (Viertel Centre for Research in Cancer Control, Queensland Cancer Fund), Thompson J (WA Cancer Registry), Hassall T (Royal Children's Hospital, Brisbane), Kirby M (Women's and Children's Hospital, Adelaide), Kellie S (Children's Hospital Westmead, Sydney), Ashley D (Royal Children's Hospital, Melbourne & Monash Medical Centre), Pinkerton R (Mater Children's Hospital), Alvaro F (John Hunter Hospital), Ashton L, Norris M (Children's Cancer Institute Australia for Medical Research), Scott R (Hunter Area Pathology Service), Attia J (University of Newcastle), Cohn R (Sydney Children's Hospital), Miller M (Marg Miller Consulting).

Researchers in the Childhood Cancer Epidemiology program have now completed the first year of a NHMRC funded national case-control study into the causes of childhood brain tumours (CBT). It aims to investigate genetic, dietary and environmental risk factors for CBT. Cases are children aged 0-14 diagnosed with CBT at one of the 10 paediatric oncology units in Australia, and their parents. The study involves retrospective recruitment of cases diagnosed in 2005 as well as prospective recruitment of cases diagnosed in 2006 onwards. Recruitment began in March 2006. In total, 189 eligible cases (106 retrospective and 83 prospective) have been notified to us. To date, 126 (67%) of eligible cases have been invited to participate, of whom 73 (58%) have consented and 16 (8%) families have declined to participate. 11 (6%) cases will not be invited by the



treating oncologist for medical or psychosocial reasons. We are liaising with the clinicians regarding inviting the remaining eligible cases and obtaining consent from the families already invited.

Data collection is well under way; instruments include self-administered exposure questionnaires for each parent and food frequency questionnaires for the mother, father and child. Telephone follow-up interviews ask about occupational and other exposures. DNA samples (blood or buccal samples) are collected for genotype analysis. DNA collection is complete for 59 cases, while 49 families have completed questionnaires. DNA has been extracted from all specimens collected to date, and stored at Royal Perth Hospital ready for genotyping.

Cases diagnosed in 2005 & 2006 are being matched to controls recruited in AUS-ALL for whom data collection is well under way. More control families will be recruited in waves by random digit dialling throughout Australia starting in 2007.

This study is funded by the NHMRC.

### **Intra-uterine growth and risk of childhood leukaemia**

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Milne E, Bower C, de Klerk N, Blair E, in collaboration with Baker D (Princess Margaret Hospital), Thompson J (WA Cancer Registry)

The aims of the study are to look at the relationships between birth weight, intrauterine growth and gestational age at delivery and risk of childhood leukaemia and to describe these findings in relation to possible causal pathways. Population-based linked health data were used to meet the objectives of this study. Maternal and birth information, recorded on the Midwives Notification System for every person born in WA between 1980 and 2005, was linked to the WA Cancer Registry to identify cases who developed acute lymphoblastic or myeloblastic leukaemia in the first 14 years of life.

The primary analysis of the relationship between intra-uterine growth and risk of ALL has been completed, and the paper describing the results is in press with the American Journal of Epidemiology. The results showed a linear relationship between 'proportion of optimum birth weight' and risk of ALL, particularly in younger children. This finding indicates that risk of ALL is not related to birth weight *per se* (as previously reported), as the relationship was also observed in children who did not meet any definition of 'high birth weight'. This question has not been previously investigated. The next aim is to investigate whether the observed association extends to siblings of the index children, and to other maternal and birth-related factors. This analysis will provide further important information that will contribute to the

understanding of the causal pathways to childhood ALL.

This study is funded by the NHMRC.

### **Trends in Childhood Leukaemia in Western Australia 1958-2005**

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Milne E, Robertson L, de Klerk N, in collaboration with Thompson J (WA Cancer Registry)

In 2006, the Cancer Epidemiology group began the analysis of population-based data from the Cancer Registry WA and other sources to investigate the trends in incidence in childhood leukaemia since 1958. The analysis is still under way.

## *Social, Economic and Psychological and Cultural Determinants of Health*

### **The Australian Early Development Index (AEDI): Building Better Communities for Children**

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Brinkman S, Silburn S, Lawrence D & Zubrick S

The Australian Early Development Index (AEDI) is a national project involving collaboration between the Centre for Community Child Health (Murdoch Children's Research Institute) and the Telethon Institute for Child Health Research. The project's overall objective is to enable communities, State and Territory governments and the Australian government to monitor the progress of policies and services and to inform initiatives to enhance early child development which improve the proportion of children who arrive at school ready for school learning. Funded jointly by the Commonwealth Department of Family and Community Services and Shell Australia, the first three year phase of the project concluded in December 2006. The first three years of funding for this project supported the scientific development and validation of the AEDI community profiling process and the establishment of the AEDI national support centre and website. The AEDI's innovative web-based data-entry system has been used by teachers to assess over 30,000 children in 60 communities around Australia. This has enabled each of the participating communities being provided a comprehensive 28 page report showing how their children are performing on five dimensions of readiness for learning at school relative to state and national norms and their local socio-demographic characteristics. The AEDI national support centre is now supporting these communities to use this information as baseline data and as a community planning tool to ensure that appropriate services and supports are available for

families and pre-school children.

An important highlight for this project in 2006 was a request from the World Bank to assist the Government of Indonesia in developing a similar EDI capability. This resulted in Sally Brinkman being contracted as a consultant to assist in the evaluation design for a \$US120 million World Bank funded project which is establishing early child development services in 5000 of Indonesia's poorest communities. The consultancy services also include technical support in the adaptation of the EDI for use in the Indonesian context and advice in the development of the methods and instruments for baseline and follow-up evaluation of the project outcomes.

### **Formative study of discrimination and mental health of CALD Australian children**

Runions K, Dandy J, (School of Psychology, Edith Cowan University) Li J, Zubrick S, Silburn S, (Telethon Institute for Child Health Research) Cross D (Child Health Promotion Research Unit, Edith Cowan University).

This study aims to provide a preliminary examination of the relationship between perceived discrimination and internalising and externalising outcomes in Culturally and Linguistically Diverse (CaLD) children (aged 8-12) of Asian and Middle-Eastern descent. A select set of potential mediators and moderators of this relationship have been implemented, including measures of attribution tendencies and ethnic identity.

We have completed stages one (formation of an advisory group) and two (piloting of questions). Questions were piloted in a semi-structured interview format with 11 children between the ages of 7 and 15, from seven families. All instruments were understood by children, with the exception of the ethnic identity questions. Revisions of these items was undertaken for the third phase. This piloting indicated that all children noted having experienced one of the potentially discriminatory events at least once, the most common of which was being called names or insulted. Parent instruments were piloted as well, with no major revisions required.

Recruitment for the third stage presented greater difficulty than anticipated, and slowed progress. To date we have collected data on only a third of our anticipated sample size. Snowball sampling from our advisory group and pilot families resulted in low rates of recruitment. A school-based recruitment approach was developed, which will be expanded this year. We have received approval from Healthway to continue the study into 2007. The results of this work will support a larger research project and the development of programs to support resilient responses to discrimination for CaLD children.

This study is funded by Healthway.

### **Postdoctoral fellowship: Mailman School of Public Health, Columbia University in New York**

Mattes E

Dr Eugen Mattes was the inaugural NHMRC General Practice Fellow. In December 2006, he completed his 2 ½ year postdoctoral fellowship at the Mailman School of Public Health, Columbia University in New York in social epidemiology. His fellowship focused on cutting edge theories and methods required to investigate the social determinants of health especially related to the health and development of children. He was invited to be the first non-US citizen affiliate with their prestigious Health and Society Scholars Program funded by the Robert Wood Johnson Foundation and headed by Professors Bruce Link and Peter Bearman (<http://www.chssp.columbia.edu/>). The Program has provided him with the opportunity to meet and investigate the work of leading US scientists examining social inequalities in health. He was and remains affiliated with the Imprints Center for Genetic and Environmental Lifecourse Studies headed by Prof. Ezra Susser (<http://www.cumc.columbia.edu/dept/imprints/>).

Dr Mattes was also involved with the Psychiatric Epidemiology Training (PET) Program and the New York (Queens) Vanguard Center of the billion dollar National Children's Study. Upon his return in December 2006, Dr Mattes will continue working on a number of collaborations between Columbia University and the Institute for Child Health Research. Principally, he will examine the notion of biological embedding – how the early social and physical environments of children, primarily in the Raine Study, influence their trajectories in mental, neuroendocrine, respiratory and cardiovascular health.

### **Early life stress, adolescent brain development and risk for adverse cognitive and psychosocial outcomes**

Foster J (Edith Cowan University), van Eekelen J, McKeague I (Columbia University, USA), de Kloet R (University of Utrecht, The Netherlands), Mattes E

The aim of the study is to investigate the effect of early life stress on adolescent hypothalamic-pituitary-adrenal (HPA) axis functioning, mental health and cognition in the 16-year old children in the Western Australian Pregnancy Cohort (Raine) Study. One of the exciting aspects of the Raine Study is the availability of detailed information about the mother, the father and the child from mid pregnancy onwards. Specifically this study is investigating how early life stress influences perturbed neurodevelopmental processes during adolescence

which remodel the corticolimbic neural networks, which underlies adult cognition and emotion. Dr van Eekelen with Prof de Kloet will oversee the assessment of the HPA axis functioning and related genotyping of corticosteroid receptors. Associate Prof Foster will lead the investigation into the use of the pre-frontal cortex as the main executive brain centre in the cognitive performance using a combination of a computer game for cognitive testing and functional magnetic resonance imaging (fMRI) in collaboration with Princess Margaret Hospital. Dr Mattes and Prof McKeague will detail the trajectories of early life stress, family function and mental health and examine their impact on HPA and cognitive functioning at 16 years of age.

Funding from the NHMRC was awarded in 2006 and the project will commence in 2007.

### **Peel Regional Partnerships for Community Child Development**

McMurray A, Stanley F, Down B, Stumbles P, van Eekelen A, Li J, Simms M, Kendall G, Wadell B, Franklin P, Mattes E.

This innovative collaboration between community, research and government sectors will use multidisciplinary and multilevel research to identify essential elements of the 'enabling community': the psychological, social, cultural, educational, physical and economic conditions that maximise opportunities for children to reach their developmental potential. Interdependent streams of investigation into the psychosocial, biological and environmental pathways to child health and wellbeing will provide comprehensive understanding of children's development in the context of family and community life in one regional community. The study will investigate the relationship between health and place through three streams of interconnected analyses: *Community capacity, Social-Economic-Psychosocial (SEP) Determinants of Health, and Biological embedding*. The research will measure a child's relevant biological endowments (genetic and intrauterine) and their interactions with environmental and social exposures to produce the 'allostatic load'; a measurable outcome of how the child responds to stress. Substantial funding has been secured from various government sectors to recruit a cohort of children from 18 weeks of pregnancy and to follow them up till age 5 and to collect individual, familial and community level data at each of stage of child development. An ARC Linkage Project Grant is pending to seek further funding for the project.

## *Adolescent Development*

### **The Virtual Infant Parenting Program: A Randomised Controlled Trial**

Silburn S, Hart B, Codde J, Brinkman S, Hutton H

The Virtual Infant Parenting (VIP) program is a school based health promotion program, which aims to reduce adverse maternal and child health outcomes associated with unplanned teenage pregnancy and parenthood. All government and independent high schools in each of the Metropolitan Area Health Service regions were invited to take part in the study and 58 schools enrolled to participate. The program was delivered by School Health Nurses to groups of 5-6 girls with some sessions being delivered by General Practitioners. The program content covers health issues affecting infant and maternal health, such as smoking, nutrition, alcohol and other drugs, physical activity and support systems. A key component of the program involved students caring for the infant simulator over a weekend period. The infant simulator realistically replicates the sleeping and feeding patterns of a 6-week-old infant. The first three years of the project's operation was funded by Healthway and LotteriesWest with in-kind support from the Department of Health's Population Health and Community and Child Health Services. This has enabled 1277 girls to participate in the program and a further 1553 girls to participate as controls. The next phase of the study is being supported by the Department of Health and involves epidemiological register follow-up of the pregnancy outcomes of all consenting participants until they reach age 21 years. The maternal and child health status of participants identified as having live births during this time will also be assessed through home based interviews.

### **The Adolescent Health and Wellbeing Survey**

Silburn S, Kendall G and Austin R in collaboration with Toumbourou J, Patton G, Williams J and Homel R.

The Institute is collaborating with the Centre for Adolescent Health (University of Melbourne and the Royal Children's Hospital, Victoria) and Key Centre for Ethics, Law, Justice and Governance (Griffith University) in an ARC funded school-based survey of adolescent health and wellbeing in 30 different local government areas across Victoria, Queensland and Western Australia. The WA component of the study in 2006 involved the Institute supporting schools in the state's southwest in completing the survey. The information collected is designed to assist schools and communities in developing local programs that enhance the healthy development of young people. The study invites young people to report on their health behaviours including substance use and related problem behaviours and their social relationships and investigates

a range of social and individual factors that are known to influence health and wellbeing.

### **Role of Implanon (etonogestrel implants) in the prevention of repeat teenage pregnancy**

Skinner R., Hickey M., Doherty D

187 pregnant adolescents have been recruited to a 2 year longitudinal study (the Biopsychosocial antecedents of repeat teenage pregnancy), and 82 of these pregnant adolescents have opted to use the contraceptive implant Implanon following the birth of their child. The study is currently evaluating the acceptability and continuation rates of Implanon in this population and the role of Implanon in the prevention of repeat pregnancy. Participants are being surveyed at baseline, six weeks and then at three monthly intervals, to collecting data on contraceptive continuation, repeat pregnancy, and sexually transmitted infections.

This project is funded by the Raine Medical Research Foundation, the University of Western Australian and the Women's and Infants' Research Foundation.

### **Biopsychosocial antecedents of repeat teenage pregnancy**

Skinner R., Hickey M., Doherty D, Kendall, G.

This study is being run in parallel with the "Role of Implanon in prevention of repeat teenage pregnancy" and aims to collect comprehensive data on the bio-psychosocial risk factors for repeat pregnancy in the teenage years and the healthy adjustment to teenage parenting. Standardised instruments are being utilized to measure functioning in a range of domains. Data collected will be compared to population norms and will also be linked to WA Data Linkage System.

Of the 187 teenagers recruited 63 have withdrawn:

- 8 prior to baseline (either after seeing the baseline questionnaire or due to severe clinical complications).
- 32 at six weeks (28 of these teenagers were not booked for delivery at King Edward Memorial Hospital and only consented to complete the baseline questionnaire and have their medical records audited).
- 10 at three months.
- 3 at six months.
- 7 at nine months.
- 3 at 12 months.

Of the 151 teenagers for follow up (36 teenagers were

not eligible for follow up) 27 have withdrawn from the study. The main reason for withdrawal from the study is loss of contact or moving interstate or out of the Perth metropolitan area.

Collection of the data is managed through the use of an Access database program. This ensures that participants are visited / contacted at the correct time. To date the following questionnaires have been collected:

- 179 baseline questionnaires (data collection completed)
- 147 six week questionnaires (data collection completed)
- 137 three month questionnaires (data collection completed)
- 131 six month questionnaires
- 102 nine month questionnaires
- 83, twelve month questionnaires.

In October 2006 analysis of the baseline (n=179), six week (133), three month (n=118), six month (n=93), nine month (n=70) and twelve month questionnaires (n=49) was undertaken in relation to pregnancy intention and contraceptive use. This was in preparation for presentation at two conferences: 'The PMH Research and Advances Seminar' and 'The 5th Australian & New Zealand Adolescent Health Conference'.

This project is funded by the Raine Medical Research Foundation, the University of Western Australian and the Women's and Infants' Research Foundation.

### **Why do so many teenagers fall pregnant? Biopsychosocial antecedents of teenage pregnancy**

Skinner R, Zubrick S, Silburn, S., Kendall, G, Hickey M, Doherty D, Milroy H, Fyfe S, Fenwick, J (Chief Investigators) and; Param R, Ash J, Smith J, Austin R (Research Staff).

This two-stage project seeks to elucidate complex biological, psychological, and social pathways to unplanned pregnancy in the teenage years. In Phase One, perceptions, values and beliefs were explored in a qualitative study. Aboriginal and non-Aboriginal teenagers attending antenatal, termination and family planning clinics were interviewed. Data from these interviews are generating new hypotheses and a risk-scale measure evaluating teenage pregnancy risk in this age group. In 2006 phase one of the study was completed. A total of 69 individual, in-depth, semi-structured interviews were conducted across three groups of sexually active teenagers (never pregnant, pregnant-terminating and pregnant-continuing), including Indigenous adolescents.

Data collection is continuing with Aboriginal teenagers in an attempt to capture greater diversity in the sexual and reproductive experiences of this group. A conceptual model of teenage pregnancy risk was generated via a systematic approach to data analysis. A "Teenage Pregnancy Risk Scale" was developed directly from the interview data and will be validated within the larger phase two survey. This risk scale and a battery of validated measures relating to individual, familial and extrafamilial domains will be administered during the Phase Two survey of approximately 2000 young people from school and clinics, commencing in early 2007. Statistical analysis will be used to determine how multiple risk factors interact or combine to shape sexual and childbearing behaviour. This study will lead to new understandings of teenage pregnancy in Australia, and more effective teenage pregnancy intervention programs.

## *Suicide Prevention*

### **WA Ministerial Council for Suicide Prevention**

Silburn S (Chair), Phillips S (Executive Officer), Robertson D, Northey K Miller K, Mudgway N, Sayers M

The Institute's program of translational research in suicide prevention aims to ensure current policy and practice for the prevention of suicide and suicidal behaviour is informed by current scientific knowledge. The Council is administratively based at the Institute and reports to the Minister for Health. It includes senior representation of all government departments concerned with human services, non-government agencies, carers, consumers and other community stakeholders. The Council is responsible for advancing scientific and community understanding of suicide and its prevention and seeks to co-ordinate the efforts of government and community sector services in reducing the morbidity and mortality associated with suicide and self-harm.

With funding from the Margaret River Friends of the Institute, the MCSP developed and piloted an Information Resource Pack for family friends caring for a young person recovering from a suicide attempt or an episode of acute suicidal behaviour. This built on the knowledge gained from a large-scale consultation study involving carers, consumers and service providers. Further funding from the Office of Children and Youth in 2006 has enabled the pack to be published for routine State-wide dissemination through all government and non-government services having contact with seriously suicidal individuals and their families. It is now also available on-line through the MCSP website. This is the first Australian publication of its kind and addresses a major gap in the information resources currently available to families and friends who play such a vital role in the months and years following a suicidal

crisis. There has been significant interest in this publication from elsewhere in Australia and internationally.

An important highlight in 2006 was the Council's success in winning a \$1.13 million National Suicide Prevention Strategy competitive research grant (2007-2009) to develop and evaluate an innovative proactive bereavement support service. This project will be carried out in conjunction with the WA Coroner's Counselling Service, the WA Police Service and Divisions of General Practice in the Southern Metropolitan area of Perth and the Samaritans.

## *Capacity Building Grants in Population Health*

### **Indigenous Capacity Building Grant - Not Just Scholars But Leaders: Learning Circles in Indigenous Health Research**

Barrow J, Hayward C, Lehmann D, Stanley FJ, Eades S, de Klerk N, Gilles M, Gray D, Larson A, Slack-Smith L, Thompson S and Watson C; Bessarab D, Brown N, Coffin J, Hammill J, Jones J, Kickett-Tucker C, McAullay D, Milroy H, Wilkes ET and Wright M

Commencing in February 2005, this NHMRC funded capacity building grant aims to build the capacity of 10 Indigenous researchers over five years to be able to conduct Indigenous specific population health research. The ICBG looks to build the capacity of the team investigators by working within four broad and overlapping research themes. These themes have been identified from the research interests of the named Lead Applicants and Team Investigators. They are:

Theme 1 – Commitment to Indigenous Communities

Theme 2 – Health Services Research

Theme 3 – Lifestyle, Behaviour and Susceptibility to Disease

Theme 4 – Pathways to Resilience and Wellbeing

2006 saw the second year of operation of the Indigenous Capacity Building Grant (ICBG). There were numerous highlights and achievements throughout the year including two team workshops to assist in the presentation of study proposals and/or major works to date, concentrated time with supervisors & mentors, professional development in the areas of grant submissions and study proposals and many networking and advocacy opportunities. Also of note, Two Team Investigators were successful in their applications for PhD scholarships and another team Investigator submitted a Doctoral Thesis.

With a solid background support group continuing to be in place, 2006 has been an outstanding second year

for the ICBG. Further notable outcomes have been the 19 publications to date that have been accepted with a further 30 publications either already submitted or nearing submission. Other highlights for 2006 also include the 38 various presentations made by members of the ICBG as well as the number of State, National and International bodies and committees that members are representative upon, some 32 different groups.

This project is funded by the NHMRC - \$2.5 million over five years with additional funding provided from Curtin University.

### **BHP Pilbara Health Partnership - Substance Use Reduction Program**

Hayward C, Walker R, Scrine C

BHP Billiton, through its Pilbara Health Partnership with the WA State Government, has engaged the Kulunga Research Network to establish links between key service providers and other local and regional stakeholders in the Pilbara to coordinate the approach to lessening substance abuse by Aboriginal young people and improve their access to an appropriate range of health and wellbeing services. Ultimately, the project aims to enhance the capacity of Aboriginal young people and their families and communities to benefit from and contribute to the future social, cultural and economic development in the Pilbara.

In 2006 preliminary activities to progress this project included: the formal signing of a Memorandum of Understanding between BHP Billiton Iron Ore and the Institute; engaging relevant Government agencies, non-Government organisations and service providers to secure their assistance with the development and implementation of the project, and to support existing health and educational programs working to address and lessen substance use among Aboriginal young people living in the Pilbara region.

This project is funded by the BHP Billiton Iron Ore Pilbara Health Partnership

### **BHP Pilbara Health Partnership – Australian Early Development Index**

Hayward C, Walker R, Scrine C

BHP Billiton, through its Pilbara Health Partnership with the WA State Government, has engaged the Kulunga Research Network to coordinate and work with families, schools, local government and other stakeholders in the Port Hedland and Newman areas to assist in the coordination and implementation of the Australian Early Development Index (AEDI), and provide the support and training required to undertake the first stage of

the AEDI's associated community planning process. Kulunga will work to enhance the capacity of local organisations to utilise the information provided by the AEDI community profile and to develop and implement evidence based interventions, establish networks between the relevant stakeholders, and the local Aboriginal and non-Aboriginal communities of the region. Over the long term, the project aims advance the cognitive and physical development and the social, emotional, and behavioural wellbeing of children living in the Pilbara so they are in a position to maximise their learning potential and the opportunities available to them in the region.

In 2006 preliminary activities to progress this project included: the formal signing of a Memorandum of Understanding between BHP Billiton Iron Ore and the Institute, engaging relevant Government agencies, non-Government organisations and service providers to ensure their support and commitment to working with Kulunga and to assisting with the implementation of the AEDI in participating schools.

This project is funded by the BHP Billiton Iron Ore Pilbara Health Partnership.

### **Wheatbelt Aboriginal Health Service Review**

Scrine C, Jones J

The Kulunga Research Network was engaged by the WA Country Health Service to prepare an evaluation framework and qualitative research plan for the Wheatbelt Aboriginal Health Service to assist in measuring Aboriginal people's uptake of and access to mainstream primary health care services across six sites in the Wheatbelt region, and the impact on their health outcomes.

The methodological approach to this project involved collating a set of quantitative and qualitative data that outlines:

- The health status and major health issues experienced by Aboriginal people;
- Aboriginal people's access and utilisation of mainstream primary health care services.

In 2006, a series of focus groups, key informant interviews and community meetings were undertaken to obtain a range of qualitative data to establish the key issues and needs of the Aboriginal population across the six sites. A report was commenced based on the key findings arising from the qualitative and quantitative data obtained.

This project is funded by WA Country Health Service.

## *The Applied Research Projects in Child Health*

## Health and Wellbeing Themed Reports

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Clark K, Smith G

In 2006 a series of brief reports were prepared to profile child and maternal health and wellbeing indicators for the State. The primary source of the indicator data was the Department of Health's Health and Wellbeing Surveillance System. The HWSS is an ongoing series of telephone surveys of Western Australian households. The HWSS incorporates a range of foci, including one which relates to the health of children in the 0-15 year age range. The reports prepared by TICHHR were designed for use by health system decision makers, with an emphasis on policy and planning regional child health services. Separate reports were prepared for each of the nine Department of Health administrative regions/areas on a range of topics, including health care utilisation, health behaviours, chronic conditions and family wellbeing.

## Evaluation of Future Directions in Maternity Care Consultation

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Jackiewicz T, Fisher C (ECU)

The Maternity and Neonatal Clinical Network is undertaking a consultation process for the Future Direction in Maternity Care Plan (FDMC) in Western Australia. This consultation process, to be undertaken over a period of 18 months, aims to assist in presenting a way forward for maternity care in WA over the next five years. The DOH has developed a three staged consultation process with the overall aim of ensuring that real input into decision making is facilitated, and to confirm the credibility of the consultation exercise. Consultation contributes to decision making and is part of good policy development and implementation. Communicating with people affected by a decision is more likely to increase the acceptability of that decision.

The Health Policy and Clinical Reform Division, has engaged the Telethon Institute for Child Health Research to undertake an evaluation of the DOH consultation process with the view of developing Best Practice Guidelines for the Department of Health to be used in future consultations. The aim of the evaluation is to determine whether the stated aims and objectives of the Consultation Plan for the Future Directions in Maternity Care have been met and to make a judgment as to how well they have been met as per best practice consultation.

This project will result in the following outputs:

1. A final report including background information on the consultation, the outcomes of the consultation process and recommendations as to the evaluation of the process.
2. A report on best practice principles for

consultation in the Western Australian Health System based on the results of the evaluation and the fit between the consultation and the available literature.

The project is currently in the field putting in place processes to collect appropriate information to inform the evaluation. The TICHHR evaluation team has prepared a project management plan, submitted ethics approval documents to the PMH Ethics Committee for ethics approval to collect data, commenced the preparation of a literature review of the area, developed data collection tools and undertaken a qualitative evaluation of the Future Directions in Maternity Care Workshop held on early December 2006. Data collection will continue into 2007 and the project is expected to be completed by the middle of next year.

This project is funded by the Western Australian Department of Health.

## Obstetric and Neonatal outcomes for Women with Serious Mental Illness

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Hauck Y (Curtin), Jackiewicz T

Translating research results into better services for women with serious mental illness is the aim of a partnership project between the Centre for Clinical Research in Neuropsychiatry (CCRN) and the Telethon Institute for Child Health Research (TICHHR). The project seeks to improve pregnancy outcomes for women with schizophrenia and bipolar disorder, through developing and delivering an antenatal care resource package. The project follows major research led by CCRN Director Professor Assen Jablensky and Professor's Steve Zubrick and Carol Bower (TICHHR) that identified significantly increased risk of pregnancy complications and poor neonatal outcomes for this group. This Record Linkage Study of Schizophrenia (investigating pathways from conception to disease including any foetal origin of the disease in adults) found women with schizophrenia and with bipolar disorder to have increased risk of bleeding during pregnancy, placenta praevia, cord complications, foetal distress and low birthweight babies. Further, women with schizophrenia were also more likely to be single mothers, have no partner available as a co-carer of the child and be socioeconomically deprived.

The purpose of this project is to produce a primary prevention package with the aim of reducing the likelihood of obstetric complications in women with SMI which has the potential to reduce the potential risk loading for schizophrenia in their offspring. The package targets risk factors amenable to intervention such as early and ongoing compliance with attendance at an antenatal care agency, smoking moderation or cessation, nutritional

advice and links to appropriate support services at the earliest opportunity.

A qualitative exploratory study was conducted between June and November 2006 which involved consultation with key stakeholders, an environmental scan to determine current service delivery issues, and a review of the literature. Individual and focus group interviews were undertaken with community mental health clinicians, consumers, and midwives. This study resulted in the development of an antenatal intervention package for community mental health clinicians as a strategy to reduce risks and improve the reproductive outcomes for women with SMI.

In 2007, a pilot study of the Clinical Guidelines will be conducted with a small cohort of Case Managers in the Perth North Metropolitan Area Health Service. The Clinical Guidelines will be revised and refined based upon feedback obtained during the pilot review. A formal implementation process will then commence with the final Clinical Guidelines for Community Mental Health Clinicians being introduced throughout the Perth North Metropolitan Area Health Service. Ongoing clinical monitoring of outcomes of clients with serious mental illness will then be undertaken to determine the impact of these Clinical Guidelines on maternal and child health.

This primary preventive intervention has the potential to significantly improve obstetric and neonatal outcomes for this high-risk cohort. The focus on this project was the antenatal period. However, there is potential for ongoing development of resources to cover the entire childbearing continuum for women with SMI, which would include pre-conception planning and postnatal support into the early and vulnerable childhood years.

This project is funded by the North Metropolitan Area Mental Health Service.

### **Consultancy support to Department of Health**

Jackiewicz T

The Institute has provided consultancy support and research information to the Director of Population Health, Department of Health in relation to the development of a health promotion framework for the early years and the development of a strategic direction for health promotion.

The Institute provided the DOH with two reports, the first a brief snapshot of services in the Western Australian community that focus on the early years, and secondly, the development of a framework for health promotion in the early years. The TICHR also provided input into the development of the Department of Health's Strategic Directions for Health Promotion Policy.

This project is funded by the Western Australian Department of Health.

### **ADHD Case Study Project**

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Pathway to a diagnosis of ADHD in children.

There has been controversy about the rates of children being diagnosed with ADHD and the subsequent prescription of stimulant medications. In Australia, Western Australia (WA) has been identified as having a higher rate of stimulant prescription than any other state. In WA only highly trained specialists (Paediatrician or Child, Adolescent Psychiatrist or Paediatric Neurologist) are able to initiate treatment with stimulant medicines in children with a diagnosis of ADHD. There are strict guidelines that these specialists apply when making this diagnosis. Despite this, ADHD is an emotive topic for many families and one that is fuelled by media interest. To date there has been a significant amount of research into the general area of ADHD; however, gaps remain.

In 2006 members of the CARE team, the WA DOH and other interested professionals commenced discussions to develop a research agenda for the Institute in the area of ADHD in WA. A three phase research agenda was proposed with the findings of the initial phase to inform the subsequent phases. Phase one of the ADHD research agenda has been submitted to PMH ethics and awaits approval. This initial phase of the research agenda focuses on describing the pathways to diagnosis taken by families in Western Australia with a child that has been diagnosed with ADHD and prescribed stimulant medication. The sample for this research will be derived from the DOH Stimulant Register. The research will describe the characteristics of the pathways to diagnosis. It will explore what influences parents to seek help for their child's behavioural issues, where do they seek initial advice, does this advice impact their decision about where to go for help, who influences their decisions? In order to collect this exploratory type of data a qualitative project that will give rich family centered data has been developed. The findings from this study should provide insight into ways the system can support families of these children along the pathway to diagnosis. Furthermore the findings from phase one will be used to inform future stages of the ADHD research agenda.

### **Commonwealth Department of Family and Community Services**

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Indigenous Child Care Plan

Jackiewicz S.

It is well known that many Indigenous children and families are living in less than ideal circumstances and are experiencing significant disadvantage. Some of this disadvantage could be turned about through the participation in quality early childhood programs. However, Indigenous children are still significantly underrepresented in government funded children's



services. Enrolment of Indigenous children in appropriate children's services could have long term benefits both socially and economically.

The National Indigenous Child Care Plan consultations were commissioned by the Department of Families, Community Services and Indigenous Affairs. The project was a collaborative project between the Institute, Edith Cowan University, Charles Darwin University, Royal Children's Hospital Melbourne and Queensland University of Technology. The aim of the consultations was to provide information to be utilised in the development of a National Indigenous Child Care Plan.

The project involved conducting consultations with Indigenous communities across Australia about their child care requirements. Consultations took place in metropolitan, rural and remote locations around the country. The Secretariat of National Aboriginal and Indigenous Child Care provided the researchers with entry to many of the communities. They also provided support and advice throughout the process. Participants at each of the consultations were asked to discuss their views of child care for Indigenous children. Some communities were able to discuss child care across a broad community approach while others focussed on the child care provision in their community. All consultations provided valuable insight into the child care requirements of the varied Indigenous families of Australia. The consultations culminated in a national workshop held in South Australia. At this workshop the findings from the consultations and the recommendations were presented to those attending. This included both government and Indigenous representatives.

The findings from these consultations were reported to FaCSIA in 2006. The reporting was a face to face brief with the Minister and a written report followed by a summary report. The outcomes of this research are pending.

### **Phase I of Longitudinal Study of Australian children: Parenting and Families in Australia**

Smith G, Zubrick S and Jackiewicz T

The Longitudinal Study of Australian Children (LSAC) is a questionnaire-based study that aims to track the development of young people from birth to adulthood. The study includes a sample that is representative of the Australian population and includes the families of approximately 5000 infants and 5000 four year olds. These families will be followed for seven years, with questionnaires being collected at two year increments. The questionnaires contain a large number of questions that explore family and social issues relevant to the development of children and address topics such as family

functioning, health and wellbeing, non-parental care, and education.

The Longitudinal Study of Australian Children was initiated and is funded by the Australian Government Department of Families, Community Services and Indigenous Affairs (FaCSIA) as part of its Stronger Families and Communities Strategy. FaCSIA are currently publishing a series of theme papers based on the data available from first wave of LSAC. This series is being published with the intent of informing policy decisions. Two of the papers that will form part of the series are *Parenting and Families in Australia* and *Child Care in Australia*.

### **Longitudinal Study of Australian Children: Theme Papers**

Parents and Families in Australia

Zubrick S, Smith G, Nicholson J (Griffith University), Sanson A (University of Melbourne), Jackiewicz T

Researcher from TICHR, Griffith University, and The University of Melbourne were contracted to prepare the theme paper *Parenting and Families in Australia* using data available from the first wave of the LSAC.

The paper examines a wide range of topics in relation to infants and children in Australian families such as; a) parental feelings of stress and sources of social support, b) parenting styles and family functioning, c) factors influencing parents' feelings and perceptions about the way they parent their children, d) the roles and contributions of parents who do not live with their children, and e) the relationship between parent wellbeing, family functioning, and parenting practices and the outcomes for children. Each of the above areas is examined in detail. The findings are then integrated and the implications for policy and future research are discussed.

This paper has been through peer review and has been accepted for publishing.

Funded by the Department of Families, Community Services and Indigenous Affairs (FaCSIA).

### **Child Care in Australia**

Harrison L (Charles Sturt University), Ungerer J (Macquarie University), Smith G, Zubrick S, Wise S (AIFS) with Press F (Charles Sturt University) and Waniganayake M

Researchers from TICHR, Charles Sturt University, Macquarie University, and Australian Institute of Family Studies were contracted to prepare the theme paper *Child Care in Australia* using data available from the first wave of the LSAC to explore the child care and education settings to which Australian families send their infants and 4-5

year-old children.

The paper examines a number of topics related to non-parental care/education such as; a) patterns of non-parental care use and the reasons for care choice, b) the relationship between care type and the characteristics of the child, their family, and their community, c) the quality of child care/education settings, and d) the relationship between child care/education and a child's physical wellbeing, socio-emotional wellbeing, and cognitive functioning. The paper examines each of these areas in detail and goes on to provide a summary of the findings along with the major policy implications.

This paper is currently in its final draft form and will be submitted for peer review in the near future.

Funded by the Department of Families, Community Services and Indigenous Affairs (FaCSIA).

## *Centre for Developmental Health*

Silburn S & Zubrick S (Co-Directors), D Lawrence, K Taylor

The Centre for Developmental Health is a joint venture between Curtin and ICHR for the establishment of a centre of expertise in developmental health research. The Centre promotes the integration of knowledge of human growth and development across traditional discipline boundaries and the application of this knowledge for the advancement of children's developmental outcomes. Our goal is to develop a knowledge base to assist society to move towards greater equality of health and opportunity for children and young people—i.e. improve health and the develop their capacities and skills, and to promote a competent population at all socio-economic levels.

Highlights in 2006 include the promotion of Dr David Lawrence to Associate Professor at Curtin University and the successful completion of a number of postgraduate students supervised by CDH staff [H Fearnley, PhD (Curtin), J Caesario, PhD (UWA) and F. Eades, MAE (ANU)]. With a number of newly funded projects entering periods of high activity, the Centre has recently undergone significant expansion. This has necessitated new accommodation being located at the Curtin University's Shenton Park campus for the Healthy Start to Life- Aboriginal parenting program while the Proactive Bereavement Support Project and some MCSP staff will be located on the Bentley Campus.

## Staff and Students

### Head of Division

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Professor S Zubrick MSc, MA, PhD

### Kulunga Network Manager

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Associate Professor C Hayward BEd, B Sc (Community Management and Development)

### Head of Epidemiology

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Clinical Professor C Bower MBBS, MSc, PhD, FAFPHM, DLSHTM

### Head of Biostatistics and Genetic Epidemiology

---

Professor N de Klerk BSc, MSc, PhD

### Research Staff

---

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K Alpers

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J Barrow

S Baxendale BHSc

K Bayley BSc

M Berinson BSc (Hons) MPH

D Biddle Dip Marketing Management

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A Cox

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J Hansen MPH, BSc (Hons)

M Hansen BSc MPH

C Harrison RN

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A Hepworth BSc hons (Psych). BSc hons (Math&Stat)

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D Houston BA / MSocWk

A Howard BSc (Psychology) Hons

A Italiano BPsych

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Dr I Laing BSc, PhD

C Laurvick BA MPH

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S Lee

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Dr J Li BA, MSc, PhD

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Dr E Mattes MBBS, MPH, PhD, FRACGP

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Dr E Milne BAppSc (Physio), MPH, PhD

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H Moore BSc (Hons I) GradDipClinEpid

N Mudgway

V Muniandy BEd (Early Childhood)

F Nichols PhD

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C O'Leary RN, BSc, MPH

Dr W Oddy BAppSci (Nutrition) MPH, PhD, NHMRC Population Health Research Fellow, University of Western Australia Adjunct Research Fellow, Telethon Institute for Child Health Research Honorary Research Fellow

K Officer BSc BVMS

R Param

J Payne SRN(UKCC), P Grad Dip (Hlth Admin), MSc (Pub Hlth)

G Pearson

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D Silva MBBS FRACP MPH

N Sloan BSc Hons

C Smargiassi Data Entry Clerk

J Smith MBBS

G Smith BPsych, M Psych

M Stone BA(Psych), MSc(SpPath)

Associate Professor K Taylor BAppSc, PGradDipHlthSc, PhD, FSPA

M Tennant RN RM BAppSc MPH

A Thompson BSc CN

Dr R Walker

A Watkins BPsych, PGradDip. (Psych).

K Watson BHlthSc (Hons)

L Watson

F Watt B.Psych

Dr K Watts BSc (Hons) PhD

K Webb BSc Hons

Associate Professor E Wilkes BA (Social Science)

A Williams BEd (PhysEd)

M Williams

J Willis BAppSc GradCertPubHlth GradDipHlthSc

M Wood BA(Hons), MA, MBCS, CITP

D Wood BAppSc (Phys Ed) Dip Ed, Grad Dip HN

T Yarran

Professor S Zubrick MSc, MA, PhD

## Postgraduate students

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K Allen B.A. (Hons) PhD Candidate  
F Broomfield B.A. (Hons) M.Psych (Clinical)  
L Colvin BCom, MPH, PhD candidate  
A Cox DipAppSc, MMedSci Candidate UWA  
A Ferrante BA, Dip Ed, PhD candidate  
N Gibson BAppSc(Phys)(Honours);  
PostGradDip(Phys)(Dev Paeds); MSc (Phys Dev Paeds)  
M Hansen B.Sc. (Hons), MPH. PhD candidate  
Dr A Haynes MBBS, MPH candidate  
A Langridge BSc (Hons), PhD candidate  
S Love BApp Sc(phys), PostGradDip Phys(Dev Paeds)  
E Malacova BSc (Hons), MSc (Applied Statistics), PhD  
candidate  
L Mercer B.A. (Hons)  
G Miners B.A. (Hons) M.Psych (Clinical)  
H Monteiro BA SocSci, MPH candidate  
K Northey BAppSc (Psych), RMHN, PGradDipHlthSc, MSc  
(Pub Health), PhD Candidate  
M O'Donnell BPsych (Hons), MPsych, DipEd, PhD  
candidate  
C O'Leary RN, BSc, MPH, PhD candidate  
G Pearson BA, Masters candidate  
N Pingault BSc(MedSci)(Hons I) MASM MAIMS PhD  
Candidate  
WS Pomat BSc(Hons) MSc PhD Candidate  
M Robinson BA (Hons) Psych, Grad Dip Comm, M.Psych  
(Clinical) candidate  
F Watt B.Psych M.Science Candidate

## Honorary Research Fellows

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Associate Professor G Kendall RN, MPH, PhD  
Dr R Skinner MBBS PhD FRACP

## Theses passed

Dr E Hagemann PhD Curtin University of Technology  
2006. The genetics of Attention-Deficit/Hyperactivity  
Disorder and associated psychopathologies  
L Mercer B.A. (Hons), UWA 2006. Predictors of thin-ideal  
internalisation in children.  
G Miners B.A. (Hons) M.Psych (Clinical), UWA 2006. Body

perception in children.

J Sein B Health Sci, UWA 2006. Calibration of a short  
food frequency questionnaire to assess folate intake in a  
case-control study of childhood leukaemia.

## Awards

Clinical Professor C Bower NHMRC Principal Research  
Fellowship 2005-2009  
Clinical Professor C Bower Consumers' Council (WA) Inc.  
Certificate for Excellent Services to Consumers, 2006  
Dr S Byrne Finalist Healthway Award – Research project  
grants focussing on capacity building  
Ms A Ferrante ARACY ARC/NHMRC Research Network  
General Scholarship (SCoPIC), August 2006  
Ms A Ferrante Australian Postgraduate Award (APA),  
December 2005  
Dr E Hagemann ARACY ARC/NHMRC Research Network  
Early Career Researcher Scholarship (ISSBD), July 2006  
M Hansen 2006 Prizes for Higher Degree by Research  
Achievements (UWA). Best publication in the Clinical  
Medicine and Dentistry category.  
Dr D Lehmann Public Health Association of Australia  
Community Award, October 2006  
Dr J Li Curtin University Research Fellowship December  
2006 (2007-2011)  
Dr E Mattes NHMRC General Practice Fellowship (2002-  
6)  
K Northey Certificate of Recognition for being in the  
top 100 students at Edith Cowan University, 2006 (Re-  
registration of Mental Health Nursing Course)  
Dr W Oddy NHMRC Population Health Career  
Development Award 2005 to 2009 (\$425,250)  
Dr W Oddy 'Ten of the Best' – NHMRC #007090  
'Nutritional epidemiology of childhood asthma' 2000-  
2004. This project was selected by peer review from 800  
NHMRC projects, programs and fellowships as one of  
Ten of the Best for 2004. Award presented in Sydney,  
September 2006 by Tony Abbott, Commonwealth Minister  
for Health.  
Dr W Oddy NHMRC Grant Review Panel. WH Oddy  
invited to participate as panel member of an NHMRC  
Grant Review Panel, Melbourne July 31st to August 4th  
Dr W Oddy President's Poster Award. 10th International  
Congress on Obesity, Sydney, Australia 3-8 September  
2006. Poster: Oddy WH, Byrne, S, Watt FJ, Blair E, Davis  
EA. Fast food and its association with obesity in children.

This poster was awarded the Most Outstanding abstract selected as Poster Presentation within theme.

Dr W Oddy Community network. Journal of College of Lactation Consultants (major article February 2006)

Dr W Oddy Community network. Public Health Association of Australia Newsletter (Feb 2006)

Dr K Watts National Heart Foundation Pediatric Postdoctoral Research Fellowship 2007-2008

Dr K Watts Finalist Healthway Award – Research project grants focussing on capacity building

## External Committees

### State

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Dr E Blair Shaken Baby Syndrome Steering Committee

Clinical Professor C Bower WA Perinatal and Infant Mortality Committee Member 1993-

Clinical Professor C Bower WA Confidentiality of Health Information Committee, deputy member 2003-

Clinical Professor C Bower Scientific Sub-Committee of the Human Research Ethics Committee, Curtin University of Technology 2000-

Clinical Professor C Bower Western Australian Genetics Council, Department of Health WA, 2001-

Clinical Professor C Bower Prenatal Diagnosis Committee, Department of Health WA, 2001-

Clinical Professor C Bower Western Australian Neurosciences, Foundation Member of Board, 2005-

Dr J Freemantle Member Princess Margaret Hospital Mortality Review Committee

Dr J Freemantle Observer, Victorian Consultative Council on Obstetric and Paediatric Mortality and Morbidity, 2004-

Dr J Freemantle Ministerial Advisory Council on the Prevention of Death in Children and Young People

Dr J Freemantle Member Scientific Advisory Council SIDS and Kids, (WA)

Dr J Freemantle Member of the WA Board of the Australian Council on Smoking and Health

Dr J Freemantle Member WA Branch Executive of the Public Health Association of Australia

Dr J Freemantle Jalaris Aboriginal Corporation – Adviser to programs, evaluation and funding

Dr J Freemantle Convenor and Chair of the Caitlyn Anne Foundation Working Group

Dr J Freemantle Fellow of Guildford Grammar Council

Dr D Lehmann Vaccine Impact Surveillance Network Committee (1998 –)

Dr D Lehmann Meningitis Centre Committee (1998-)

Dr D Lehmann Princess Margaret Hospital Ethics Committee (2005-)

Dr D Lehmann Perinatal and Infant Mortality Committee, Ministry for Health, WA (2005-)

A McKenzie Deputy Chair and Board Member, Health Consumers' Council WA Inc. 2003-ongoing

A McKenzie Member, Health Consumers Council WA Inc. 1994- ongoing

A McKenzie Consumer Representative, Primary Health Care Research Evaluation and Development Unit Advisory Committee. University of Western Australia, Notre Dame University and Combined Universities Centre for Rural Health. 2005-ongoing

A McKenzie Consumer Representative Royal Perth Hospital Intensive Care Research. 2005-ongoing

A McKenzie Consumer Representative Child & Youth Health Network Advisory Group. 2006-ongoing

A McKenzie Consumer Representative Child & Youth Health Clinical Network. 2006-ongoing

A McKenzie Lay Member, Silver Chain Ethics Committee, Perth. 2005-ongoing

A McKenzie Consumer Representative Western Australian Audit of Surgical Mortality Management Committee, Royal college of Surgeons. 2006 ongoing

A McKenzie Consumer Representative WA Department of Health Community Data Awareness Working Group. 2005-2006

Dr E Milne WA Confidentiality of Health Information Committee, member (2003-6)

Dr E Milne Cancer Council WA Skin Cancer Control Steering Committee, (2001-6)

Dr E Milne Cancer Council WA Research Committee (2005-6)

Dr E Milne Perth Epidemiology Group, committee member (2003-6)

K Northey Board Member, Ministerial Council for Suicide Prevention (2006 - )

Dr W Oddy Chairperson, Baby Friendly Hospital Initiative Advisory Committee (WA), 2003-current.

Dr W Oddy Treasurer, Local Organising Committee, International Society for Research into Human Milk and Lactation. International conference to be held in Perth, Western Australia 2008.

Professor S Silburn Mental Health Network Coordinating Committee

Professor S Silburn WA Mental Health Safety Action Group

### **National**

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Professor C Bower Intergovernmental Fetal Alcohol Spectrum Disorder Working Party

Dr S Byrne Member of The Australian Child and Adolescent Obesity Research Network (ACAORN) (2004)

Dr S Byrne Co-chair of the ACAORN Longitudinal Studies Special Interest group (2004)

Dr S Byrne Member of the Australian Eating Disorders Research Interest Group (2004)

Dr E Blair Australasian Academy of Cerebral Palsy and Developmental Medicine

Clinical Professor C Bower Australian Birth Defects Society Committee member 1999 -

Clinical Professor C Bower Australian Paediatric Surveillance Unit Scientific Review Panel 1998-

Clinical Professor C Bower Australian Paediatric Surveillance Unit Board 1998-, Chair (2003-)

Clinical Professor C Bower National Child Health Information Advisory Committee (AIHW) 1998-

Clinical Professor C Bower National Perinatal Statistics Unit, National Birth Anomalies Steering Committee member 2004-

Clinical Professor C Bower Intergovernmental Committee on Drugs Working Party on Fetal Alcohol Spectrum Disorder – member 2006-

Clinical Professor C Bower Food Standards Australia New Zealand, Folate Fortification Scientific Advisory Group 2006-

Dr J Freemantle Member of Australian Mortality Data Group

Dr J Freemantle Member National Child Death Review Group

Dr J Freemantle Vice-President (policy) Public Health Association of Australia

Dr D Lehmann Data Safety Monitoring Board for the Maternal pneumococcal immunisation study in the Northern Territory ('PneuMum')

Dr E Mattes Royal Australian College of General Practitioners (RACGP) Curriculum Review Project , Member of the Critical Thinking and Research Working Group (2005-6)

A McKenzie Member, Consumers' Health Forum of Australia (CHF), Canberra. 2002-ongoing

A McKenzie Consumer Representative CHF, Community Quality Use of Medicines Steering committee. 2004-ongoing

A McKenzie Consumer Representative CHF, National Prescribing Service Pharmaceutical Decision Support Working Group. 2005-ongoing

A McKenzie Consumer Representative CHF, Medicines Australia – Code of Conduct Appeals Committee. 2006 - ongoing

A McKenzie Consumer Representative CHF, National E-health Transition Authority (NeHTA) Consumer and Clinical Discussion Forum. 2006 ongoing

A McKenzie Consumer Representative CHF, National Prescribing Service New Drugs Working Group 2006-ongoing

Dr E Milne NHMRC Grant Review Panel Member (2005-6)

### **International**

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Dr E Blair Editor with responsibility for Cerebral Palsy, Cochrane Review Group for Movement Disorders, Lisbon.

Clinical Professor C Bower International Clearinghouse for Birth Defects Surveillance and Research. Vice Chair (2006-)

Dr J Freemantle Member International Society of Perinatal and Infant Death, Epidemiology Working Group

Dr J Freemantle Member of the International Indigenous Measurement Group

Dr D Lehmann Co-Director of the 5th International Symposium on Pneumococci and Pneumococcal Diseases, Alice Springs, 2006

Dr J Li Associated Editor (Since 2005), Rural Sociology published by American Rural Sociological Association

Dr E Mattes Member of Imprints Center for Genetic and Environmental Lifecourse Studies, Columbia University (2005-)

Dr E Mattes Affiliate, Robert Wood Johnson- Health and Societies Scholars Program, Columbia University (2004-6)

Dr E Milne Working party for the development of international studies of embryonal cancers in children, WHO International Agency for Research into Cancer, Lyon, France Member (2006-)

Dr E Milne Working party for the development of international studies of adolescent bone tumours, WHO International Agency for Research into Cancer, Lyon, France, Member (2006-)

Dr W Oddy Nominated Executive Committee Member, International Society for Research into Human Milk and Lactation, 2006-2007

## *Invited Presentations*

Dr E Mattes Is public health articulating a realisable utopia? If so, what is it? Research Seminars in the Robert Wood Johnson's Health and Societies Scholars Program. Mailman School of Public Health, Columbia University, New York, January 2006.

Allen K, Byrne S, Davis EA. Longitudinal Study of Binge Eating and Eating Disorder Symptoms in Overweight and Obese Children: Findings from the Childhood Growth and Development Study. 10th International Congress on Obesity, Sydney NSW.

Dr E Blair Sexual health behaviours of Aboriginal Adolescents – the WAACHS. Quarterly forum on sexually transmissible infections (HDWA). Wed. March 2006

Dr E Blair Cerebral Palsy at TICHR. PLAN Fund raising dinner. Joondalup Country Club

Dr E Blair Nordmark, E, McIntyre, S, Novak, I, Blair E. Establishing cerebralpalsy REGistryS: what have we learned. 1 hour breakfast session, American Academy of Cerebral palsy and Developmental Medicine, Boston, September 2006

Dr E Blair The Western Australian CP Register; Surveillance of Cerebral Palsy in Europe (SCPE) Annual meeting. Vilnius Lithuania, October 2006

Dr E Blair Reliable description and classification process in CP Children. Vilnius, Lithuania. October 2006.

Dr E Blair Quantifying the risks of CP associated with perinatal factors – methodological pitfalls. Vilnius, Lithuania October 2006.

Dr E Blair An Update on the Epidemiology of CP. INSERM, Paris, France

Dr E Blair Methodological problems in the study of perinatal risk factors of CP, including the question of IUGR. INSERM, Paris, France

Dr E Blair Reliable description and classification process in CP Children. Brisbane Australian Cerebral Palsy Register (ACPR). October 2006

Dr E Blair Methodological issues in quantifying the risk of CP: using PET as an example. Brisbane ACPR. October 2006.

Dr E Blair Sexual health behaviours of Aboriginal Adolescents – the WAACHS. Quarterly forum on sexually transmissible infections. Tradewinds Hotel,

Fremantle. November 2006

Professor C Bower Fetal Alcohol Syndrome. Goldfields Weekend 2006: Bush Babies. Kalgoorlie, May 2006.

Clinical Professor C Bower Prenatal diagnosis of birth defects in WA. Women's and Infants' Research Foundation Rising Stars Symposium

Clinical Professor C Bower Fetal abnormality and stillbirth. SIDS and Kids and PSANZ Mortality Group.

Clinical Professor C Bower Fetal Alcohol Syndrome. Goldfields weekend – Goldfields Division of General Practice.

Clinical Professor C Bower Fetal Alcohol Spectrum Disorder – report of the IGCD FASD Working Party. Ministerial Council on Drugs Strategy.

Clinical Professor C Bower Modelling NTD prevention. Food Standards Advisory Group, Food standards Australia and New Zealand.

N Brown Australian Indigenous Delegation to the United Nations Permanent Forum on Indigenous Issues (UNPFII). - Prepared Aboriginal and Torres Strait Islander health briefing for presentation to entire delegation. New York City, May 2006

N Brown University of Wollongong, Faculty of Medicine features forum, August, 2006.

N Brown Committee of Deans of Australian Medical Schools, Melbourne, October, 2006.

N Brown Invited presentation on health and human rights, plenary session to Pacific Region Indigenous Doctor's Congress, Rotorua, December 2006

Dr S Byrne The psychology of dieting: Eating and weight disorders in modern society. Invited Lecture. The Karrakatta Club Annual Lecture. Perth, W.A.

Dr S Byrne Tackling the problem of childhood obesity. Invited lecture. The Mike Schon-Hegrad Annual Lecture. Perth, W.A

Dr S Byrne Obesity and Depression: What is the nature of the relationship? Invited symposium. 10th International Congress on Obesity, Sydney, Australia

H D'Antoine Alcohol use in pregnancy: a thumbnail sketch. Community Health Services Workshop, Kununurra, February 2006.

H D'Antoine Alcohol use in pregnancy: a thumbnail sketch. Community Health Services Workshop, Kununurra, February 2006.

A Ferrante Criminology Research Council Biennial Strategic Planning Meeting, Canberra, April 2006.

Fordham, R; Northey, KA; Lawrence, DR; Silburn, SR; Williams, AW & Zubrick, SR A cost-effectiveness analysis



- of a Behavioural Family Intervention in preventing behaviour problems in children. NIFTeY 2006 Conference: Prevention: Invest Now or Pay Later, University of New South Wales, 8-9 February, 2006.
- Dr J Freemantle University of Saskatchewan, Saskatoon. Making Research Count in the Early Years – improving Indigenous health in Western Australia
- Dr J Freemantle The University of British Columbia. The Challenge of Improving Indigenous Health – from a Western Australian perspective
- Dr J Freemantle Alaskan Native Health Consortium, Anchorage. Organising total population death information to inform policy and practice and to assist in guiding the prevention of death of infants, children and young people
- Dr J Freemantle Statistics Canada, Ottawa 2006 The strategic use of databases
- Dr J Freemantle Understanding Mortality Data - QUT School of Public Health International Health Summer School. 2006
- Dr J Freemantle Measurement of Indigenous Mortality Workshop, Australian Bureau of Statistics, Sydney, 2006
- Freemantle J, de Klerk, N., Read, A., Stanley, F. 9th SIDS International Conference, Yokohama, Japan Sudden Infant Death Syndrome – trends and disparities among Western Australian Aboriginal and non-Aboriginal infants, 1980-2001
- Freemantle J, de Klerk, N., Read, A., Stanley, F. Public Health Association of New Zealand Annual Conference The Challenges of Change: improving infant and child health
- Freemantle J, de Klerk, N., Read, A., Stanley, F. 18th International Symposium on the Forensic Sciences, Perth From Court Room to Classroom – using data to prevent deaths among Western Australian infants, children and young people
- Freemantle J, de Klerk, N., Read, A., Stanley, F. Perinatal Society Australia and New Zealand, Perth The Challenges of Improving Indigenous Health – in the beginning... making the early years count
- Gibson L, Byrne S, Blair E, Davis EA The psychological burden of childhood obesity. 10th International Congress on Obesity, Sydney NSW.
- J Hammil Rio Tinto Child Health Partnership, National Symposium – Human rights & human biology, May 2006
- J Hammil Presentation to the International Society of Biomedical Research on Alcoholism, Sydney, September, 2006
- J Hammil FASD Workshop, Bunbury SWAMS. October, 2006
- Associate Professor C Hayward “Reaching for Rights and Recognition: Women in Rural, Remote and Regional Areas”, key-note address to Port Hedland women’s gathering for International Women’s Day. March 2006:
- Associate Professor C Hayward “Well Women’s Centre, Centres Well”, address to open the Hedland Well Women’s Centre. March 2006
- Associate Professor C Hayward “Partners in a Learning Culture – the Way Forward”, presentation to the WA Aboriginal Training Seminar. May 2006
- Associate Professor C Hayward “Ensuring a Healthy Future – Educating Aboriginal Children and Young People”, address to the Women’s College Leadership Seminar. May 2006
- Associate Professor C Hayward “... If He Hollers, Let Him Go...” Symposium presentation to the International Society for the Study of Behavioural Development. July 2006
- Associate Professor C Hayward “What Does Sustainability and Development Look Like?”, keynote address to the Sustainability in Indigenous Communities Conference. July 2006
- Associate Professor C Hayward “An Indigenous Perspective on Community Wellbeing”, presentation to Leadership WA’s Program, ‘Towards Healthier Communities’. September 2006
- C Hayward “Rio Tinto Child and Maternal Health Partnerships” Presentation at the AER “Changing the Way we Drink” National Conference. September 2006
- J Jones Audit and Best Practice for Chronic Disease – Systems assessment. Geraldton, Regional Aboriginal Medical Service
- C Kickett-Tucker Building Community Capacity and Resilience. Indigenous Community Forum. Office of Crime Prevention, Perth Western Australia, February, 2006.
- C Kickett-Tucker Not Just Scholars But Leaders: Learning Circles in Indigenous Health Research, February, 2006.
- C Kickett-Tucker NHMRC Indigenous Researchers Network Workshop. Yalgorup, Western Australia.
- C Kickett-Tucker Success Not Shame: Obstacles and Lessons Learned. Aboriginal Employees Forum. Woodside Energy, Perth, Western Australia. March 2006
- C Kickett-Tucker Aboriginal Carers’ Perceptions of School: Year 2 Report. Swan Education District Office, Education Department of WA, Perth, Western Australia, March 2006
- C Kickett-Tucker Indigenous Australian Women in Sport. Centre for Aboriginal Studies, Curtin University, Western Australia. May, 2006
- C Kickett-Tucker Self-esteem and identity of Urban Aboriginal Children. Healthy Start to Life Project. May,

2006

C Kickett-Tucker 19th Biennial Meeting of the International Society for the Study of Behavioural Development (2006). Poster Symposium Presenter. "Moorditj Nyoongahs: Aboriginal Carers' Perceptions of Their Children's Schooling at an all-Aboriginal Urban, Government Primary School." 2006

C Kickett-Tucker 19th Biennial Meeting of the International Society for the Study of Behavioural Development (2006). Poster Symposium Co-convenor. "Culture, Parenting and Child Well being among Indigenous Australian and African American Families. 2006

C Kickett-Tucker 5th Australian and New Zealand Adolescent Health Conference (2006). Presenter. Indigenous Racial Identity & Self Esteem: Risk and Protective Factors 10-12 year old West Australian Aboriginal school children

Dr D Lehmann Kalgoorlie Otitis Media Research Project. Bush Babies: Pregnancy, birth and early childhood in the Goldfields, Kalgoorlie WA, May 2006

Dr D Lehmann Kalgoorlie Otitis Media Research Project. Bush Babies: Pregnancy, birth and early childhood in the Goldfields, Kalgoorlie WA, May 2006

Dr J Li Social and Gender Inequality and Vulnerability to HIV/AIDS. Invited to speak at World AIDS Day-China, Tianjing, 1-2 December 2006 but unable to attend.

Dr J Li Early Development Index and Indigenous children & culturally and linguistically diverse children. A guest lecture for Developmental Health Short Course (#561) by Garth Kendal, April 2006, PMH, Perth.

Dr J Li Political and economic determinants of health. A guest lecture for Developmental Health Short Course (#561) by Garth Kendal, April 2006, PMH, Perth

Dr E Mattes Social influences on mental and cardiovascular health, and brain growth Research Seminars in the Robert Wood Johnson's Health and Societies Scholars Program. Mailman School of Public Health, Columbia University, New York, November 2006

Northey, KA Using Linked Data to study child abuse. Short Course in Developmental Health, Princess Margaret Hospital, 6th April 2006.

Northey, KA. Crime Prevention – A Lifespan Developmental Approach using Population Health Strategies. Masters Course in Crime Prevention, Crime Research Centre, 1.5 hr lecture, September 2006.

Northey, KA. Crime Prevention – A Lifespan Developmental Approach using Population Health Strategies. Masters Course in Crime Prevention, Crime Research Centre, 1.5 hr lecture, September 2006.

C O'Leary Fetal alcohol syndrome – Australian health

professionals' knowledge and practice. Fetal Alcohol Spectrum Disorder Forum, Women's Referral and Access Project, New South Wales Health, Ballina, NSW. September 2006

C O'Leary Policy for the prevention of fetal alcohol syndrome in Australia and overseas. Fetal Alcohol Spectrum Disorder Forum, Women's Referral and Access Project, New South Wales Health, Ballina, NSW. September 2006

C O'Leary Parental Alcohol Misuse. Kimberley Workshop, Wyndham. Drug and Alcohol Office September 2006

C O'Leary Fetal alcohol syndrome – Australian health professionals' knowledge and practice. Fetal Alcohol Spectrum Disorder Forum, Women's Referral and Access Project, New South Wales Health, Ballina, NSW. September 2006

C O'Leary Policy for the prevention of fetal alcohol syndrome in Australia and overseas. Fetal Alcohol Spectrum Disorder Forum, Women's Referral and Access Project, New South Wales Health, Ballina, NSW. September 2006

C O'Leary Parental Alcohol Misuse. Kimberley Workshop, Wyndham. Drug and Alcohol Office September 2006

Dr W Oddy Best presentation award. International Society Hypertension meeting, Fukuoka Japan, October 2006. Inflammation and altered liver function is present in 13 year olds with features of the metabolic syndrome. Thomson RC, Mori TA, Stanley FJ, Kendall G, Palmer LJ, Oddy WH, Sloan N, Hands B, Beilin LJ.

Dr W Oddy Oral presentation. 6th Congress of the International Society for the Study of Fatty Acids & Lipids (ISSFAL) incorporating the 6th International Congress on Essential Fatty Acids & Eicosanoids & PUFA in Maternal & Infant Health Annual Scientific Meeting, Cairns, North Queensland, 23 – 28 July 2006. Docosahexaenoic acid and mental health morbidity in a population study of adolescents. Oddy WH, Mori TA, Beilin LJ, Kendall GE, Silburn SR, Zubrick SR, deKlerk NH.

Dr W Oddy Oral presentation. 6th Congress of the International Society for the Study of Fatty Acids & Lipids (ISSFAL) incorporating the 6th International Congress on Essential Fatty Acids & Eicosanoids & PUFA in Maternal & Infant Health Annual Scientific Meeting, Cairns, North Queensland, 23 – 28 July 2006. Patterns of fish consumption and levels of erythrocyte docosahexaenoic acid in a population study of adolescents. Oddy WH, Mori TA, Kendall GE, Beilin LJ, Huang RC, Silburn SR, deKlerk NH.

Dr W Oddy Oral Presentation. Oddy WH. Infant feeding and infections in the West Australian Aboriginal Child Health Survey. Start Out Strong: A healthy beginning to

life symposium, Perth, WA, 27 April 2006

Dr W Oddy Poster presentation. Di Candilo (Webb) K, Oddy WH, Miller M, Sloan N, Kendall GE. Breakfast Eating Habits of Adolescents: Implications for body weight. The 24th National Dietitians Association of Australia Conference, Sydney, May 2006.

Dr W Oddy Poster presentation. Di Candilo (Webb) K, Oddy WH, Miller M, Sloan N, Kendall GE. Breakfast Eating Habits of a Future Generation: A modifiable risk factor for child mental health. The 24th National Dietitians Association of Australia Conference, Sydney, May 2006.

Dr W Oddy Oral presentation. 15th Annual Meeting of the Australasian Epidemiological Association, Melbourne, 18-19 September 2006. Diet quality and mental health in a cohort of adolescents in WA. Oddy WH, Webb K, Kendall GE, Li, J, Robinson M, Silburn S.

Dr W Oddy Oral presentation. 15th Annual Meeting of the Australasian Epidemiological Association, Melbourne, 18-19 September 2006. Socioeconomic patterning of diet quality in a cohort of adolescents in Western Australia. Li J, Oddy WH, Webb K, Kendall GE, Huang RC, Beilin LJ.

Dr W Oddy Oral presentation. First World Congress of Public Health Nutrition World, Barcelona Spain, 28-30 September. Breastfeeding and mothers' return to paid employment. Binns CW, Scott JA, Oddy WH.

Dr W Oddy Oral presentation. 15th International Society for Research in Human Milk and Lactation, International Conference at Niagara-on-the-Lake, Ontario, Canada, Sept 22-26, 2006. Using data from household surveys to measure the association between exclusive breastfeeding and child morbidity in developing countries. Miharshahi S, Oddy WH, Thompson S, Peat JK.

Dr W Oddy Oral presentation. Local. Derbil Yerrigan. Pregnancy and Lactation. National Heart Foundation, Perth, April 12th 2006.

Dr W Oddy Lecture. Lactation Training Program, Baby Friendly Hospital Initiative, St John of God Hospital, Perth Western Australia, June 2006

Dr W Oddy Lecture. D'Antoine H. Notre Dam University. 1st Year Medical Students. Perth. April 2006. 'Failure to Thrive in Aboriginal Children.

Oddy WH, Byrne, S, Watt FJ, Blair E, Davis EA. Fast food and its association with obesity in children. 10th International Congress on Obesity, Sydney NSW.

G Pearson DET - Cannington District Education Officers - District Staff - including program managers, psyches and support staff, Perth, June, 2006

G Pearson Presentation of WAACHS Vol 3 findings to Canning District Office, Perth, August 2006

G Pearson Presentation of WAACHS Vol 3 findings to

Canning District Office, Perth, September 2006

G Pearson Presentation of WAACHS Vol 3 findings to Mental Health Promotion Action Link (MPHAL)- Kwinana Interagency group comprised of Health, Education and Mental Health providers, Perth, October 2006

G Pearson Presentation of WAACHS Vol 3 findings to Academics and education/community stakeholders, Perth, October 2006

G Pearson Christian Brothers Education Province Meeting - Edmund Rice Building - mainly principals and deputies. Fremantle, May 2006

G Pearson General Practice and Public Health Council Research Conference - Perth Convention Centre - - other researchers, GP's and health managers, July, Statewide

G Pearson DET - State Aboriginal Managers Forum - Mecure Hotel - District Aboriginal Managers, Central Office Policy Officers, July, Statewide

Pearson G, Walker R Presentation of WAACHS Vol 3 findings to Mental Health Promotion Action Link (MPHAL)- WASON building- Interagency group comprised of Health, Education and Mental Health providers, Perth, August 2006

Pearson G, Walker R Two Presentations of WAACHS Vol 3 findings to the senior staff at the Dare to Lead Aboriginal Education Conference, (Department of Education and Training), Kalgoorlie, Warburton, August 2006

Professor S Silburn Western Australian Primary Principal's Association Conference presentation on WAACHS, Perth, June 2006

Professor S Silburn WAACHS presentation to Fremantle Regional Managers Forum (DET), Fremantle, July 2006

Professor S Silburn WAACHS presentation Department of Indigenous Affairs, Perth, August 2006

Professor S Silburn Presentation of WAACHS Vol 3 findings to Yorgum (Aboriginal Community Stakeholders), Perth, August 2006

Professor S Silburn Presentation of WAACHS to City of Fremantle Council, Fremantle, Perth, September 2006

Professor S Silburn Presentation of WAACHS Vol 3 findings to South West Education Regional Administrators Conference, SW Region, November 2006

Professor S Silburn Catholic Education Presentation, Broome Kimberley

Silburn S, Stanley F Presentation of WAACHS Vol 3 findings to the Productivity Commission, Perth, August 2006

Silburn S, Zubrick S, Hayward C Confidentialised Briefing to Australian Government representatives. Canberra, February 2006

Silburn S, Zubrick S, Hayward C Confidential pre launch briefing to Aust and State Govt (video Conference Link-up). Perth, March 2006

Silburn S, Zubrick S, Hayward C WAACHS Vol 3 Launch. Perth, March 2006

Silburn S, Zubrick S, Hayward C WAACHS Vol 3 Launch. Canberra, April 2006

Silburn S, Zubrick S, Hayward C International Society for the Study of Behavioural Development – Symposium, Melbourne, July 2006

R Walker Meeting organised through DIA with Aboriginal groups and agencies - recommendation to combine groups, Port Hedland, November 2006

R Walker Presentation/Workshop of WAACHS Vol 3 findings to Derby Interagency Meeting, Derby, November 2006

R Walker Presentation/Workshop of WAACHS Vol 3 findings to AIEOs and Aboriginal Teachers at Derby District School, Derby

R Walker Presentation/Workshop of WAACHS Vol 3 findings to AETC representatives and Kids Matter project managers at DIA Kununurra, Kununurra Statewide

R Walker Discussion with Wanun Foundation Representatives and TAFE staff, Kununurra

R Walker Presentation of WAACHS Vol 3 to the Kimberley Interagency Group Meeting, Broome Kimberley

R Walker Discussion with Kimberley Education District Office with respect to embedding recommendations into Aboriginal Education Strategy within School Plans, Broome Kimberley Region

R Walker Presentation/Workshop of WAACHS Vol 3 findings to Principles and Senior staff in leadership and Policy roles in schools and Kimberley Education District Office at the Leadership Conference, Broome Kimberley Region

R Walker Discussion re relevance of WAACHS Vol 3 findings to the Broome Primary School School Parent Participation Initiative

R Walker Meetings with DCD, Pilbara Development Commission and Shire Council, Aboriginal Medical Service re links between Vol 3 findings and early years strategy and Substance Use and Attendance

Watt F, Byrne S, Blair E, Davis E. Obesity and adverse mental health outcomes in children. 10th International Congress on Obesity, Sydney NSW.

Watts K, Byrne S, Thompson A, Bell L, Jones T, Davis EA. Waist girth is strongly associated with cardiovascular risk factor profile in primary school-aged children. 10th International Congress on Obesity, Sydney NSW.

Associate Professor E Wilkes Derbarl Yerrigan Workshop, Club Capricorn. February, 2006

Associate Professor E Wilkes Senate Inquiry into petrol sniffing in remote Aboriginal communities, February, 2006

Associate Professor E Wilkes Next Steps - Indigenous Detoxification Unit, Perth. March, 2006

Associate Professor E Wilkes Invited Chair - UWA Berndt Museum consultations to house Indigenous collection Perth. March, 2006

Associate Professor E Wilkes Lecture: Leadership and Achievement, Curtin University, Perth, May, 2006

Associate Professor E Wilkes Presentation to staff of the Sexual Assault Referral Centre, SARC, Perth. June, 2006

Associate Professor E Wilkes Yorgum Health forum –Suicide and Child Abuse, Perth. July, 2006

Associate Professor E Wilkes Alcohol and Education Rehabilitation Foundation Workshop, Perth . August, 2006

Associate Professor E Wilkes Lecture on Aboriginal Terms of Reference Curtin University, Perth. August, 2006

Associate Professor E Wilkes Presentation to Fortescue Forum: Indigenous Developmental Health and mining, Perth & Port Hedland. September, 2006

Associate Professor E Wilkes APSAD Presentation of James Rankin Oration, Cairns. November 2006

Associate Professor E Wilkes Cultural welcome and presentation to Youth Reach South, Perth. December, 2006

Professor S Zubrick Presentation of WAACHS Vol 3 findings to the Australian Council for Children and Parents. Melbourne, June 2006

Professor S Zubrick Indigenous Post enumeration Survey of the Census 2006 – ABS, Perth, September 2006

Professor S Zubrick WAACHS Presentation to the Community and Child Health Council of Australia, Perth, November 2006

Zubrick S, Hayward C, Stanley F Key forum presentation of WAACHS Vol 3 findings GARMA, Gove, NT, August 2006

# Division of Cancer Biology

## Overview

Whilst the Cancer Biology Division closed in 2006, ongoing research focuses primarily on Scl, a gene which is essential for normal blood cell maturation and brain development. Without Scl, mice die due to a fatal lack of blood cells. Additionally, abnormally high amounts of Scl have been shown to be strongly correlated with T cell leukaemia in humans and in mice. Without Scl in the developing central nervous system, normal brain development is impaired.

We have engineered two types of genetically manipulated mouse models, which have Scl function specifically removed in early brain development, but not in blood development. It is hoped that these brain Scl knockout mice will provide new insights into how the brain develops.

Given that the ongoing research is more related to basic neuroscience than cancer biology, ongoing research will be accommodated in another Division from 2007.

## Basic Neuroscience

### Scl expression & function in the central nervous system

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Dr. JAM van Eekelen

Scl is a transcription factor that is expressed in the central nervous system (CNS). The aim of this project is to further investigate the role of this gene in the mouse brain based on the underlying hypothesis that a highly regulated and highly specific expression of the Scl-gene in CNS implies an important yet undefined function for Scl in brain cells.

Detailed investigation into the cellular phenotype of mature Scl-expressing neurons in midbrain and hindbrain elucidated the type of neurons that expresses Scl. This is thought to contribute to a better understanding of Scl function during embryogenesis and after birth. We have identified a change in cellular phenotype from developing to mature neurons, which supports the view that the role of Scl in neurons after birth is essentially different from its earlier role during brain development.

Our loss of function approach through conditional deletion of Scl during embryogenesis in neuronal-Scl deleted mice is an alternative way to unravel Scl function in CNS. We have shown that embryonic deletion of Scl results in a striking phenotype after birth. The survival rate of these mice after birth was severely affected. They were significantly growth retarded and displayed a hyperactive behaviour from p<sub>nw</sub>2 onwards. Moreover, lacZ reporter gene staining had disappeared almost completely from hindbrain and was significantly reduced in caudal thalamus and midbrain. These observations were quantitatively verified at weaning age. However, less intense LacZ

staining in the mid-hindbrain was already apparent at E12.5, indicating that some Scl null neurons are lost already early in brain development.

We studied a potential functional compensation by Tal2, a homologous bHLH factor to Scl, which could not be confirmed based on the absence of sufficient overlap in Scl and Tal2 expression during early neurogenesis. Furthermore, the functional implications of loss of Scl neurons were studied with a focus on control of respiration, anxiety and daily activity patterns. The overall research results in this study subscribe a crucial role for Scl as a neurogenic factor in neuronal differentiation of a specific population of mid-hindbrain GABA-ergic interneurons.

## Staff and Students

### Senior Scientist

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Dr. J. Anke M van Eekelen.

Adjunct Senior Lecturer, University of Western Australia.

### Postgraduate Students

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Elena Takano. B.Sc. M.Sc. Candidate (Thesis submission 1 March)

### Research Support

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Elena Takano. B.Sc. M.Sc. (from 1 April onwards)

### Theses passed

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Elena Takano M.Sc. University of Western Australia: Characterization of the transcription factor Scl in CNS: its potential role as a neurogenic factor.

### External Committees

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J.A.M. van Eekelen. Australian and New Zealand Society for Cell and Developmental Biology. WA representative.

J.A.M. van Eekelen, Conference organizing committee: 4th Summer conference on Molecular Mechanisms in Developmental, Perth 10th February 2006

### Invited Presentations

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C. Bradley, E. Takano, M. Hall, J. Göthert, A. Harvey, G. Begley, J.A. M. van Eekelen (presenter). The essential hematopoietic transcription factor Scl is also critical for neuronal development. 4th Summer conference on Molecular Mechanisms in Development, Perth 10th February 2006

J.A.M. van Eekelen, Developmental Health lecture at Curtin University, WA: Early life stress and adolescent brain development; risk for adverse cognitive and psychosocial outcomes. 4 April 2006

# Research collaborations

*Children's Allergy and Immunology Research Group (University of WA School of Paediatrics and Child Health)*

*In collaboration with Division of Cell Biology*

## Overview

Our research program focuses on early immune development, predominantly in the clinical context of allergic disease. With strong clinical and laboratory activities our group examines both immunological mechanisms, and clinically relevant applications for practical solutions. This includes a number of clinical intervention studies for the prevention of allergic diseases. In broad terms the projects focus on:

- Fetal immune responses which predispose to immune dysfunction (particularly allergy)
- Maternal influences on immune development (*in utero*)
- Early life environmental factors which may predispose or help prevent the development of asthma and allergic diseases

In collaboration with our colleague (Prof Tony Ferrante) in Adelaide, we have recently identified a novel neonatal predictor of allergic disease. This has recently been the subject of a provisional patent application (and is due to be published in the *J Allergy Clin Immunol* this year). Another novel aspect to our findings was that this marker could be modified by an antenatal intervention aimed at preventing allergic disease.

We have also just completed a larger intervention study examining the role of probiotics in allergy prevention, which did not demonstrate any benefit. In view of the wide acceptance of these products for disease prevention, this finding has been of international interest.

We have also had another NHMRC success, with a project grant to look at the ontogeny of Toll-like receptor (TLR) development in early life and for differences in children who go on to develop allergic disease. To our knowledge this has never been documented before.

## Allergy

### **Immunomodulatory effects of omega-3 polyunsaturated fatty acids : role in allergy prevention in infancy**

Susan L Prescott, Jan Dunstan, Charles Hii, Tony Ferrante

**Summary of objectives:** The aim of this study is to determine if the previously observed immunomodulatory effects of n-3 PUFA (NHMRC I39025) have a role in allergy prevention. In this study we are recruiting a cohort (n=360) of newborn infants at high risk of allergic disease (as determined by maternal allergic disease). These children are being randomized to receive 650mg of fish oil (containing 280mg DHA and 110mg EPA) or a placebo for the first 6 months of life. We are assessing the effects on immune function and the point prevalence of symptoms of sensitization and allergic disease are being determined at 6, 12 months (and subsequently 2.5 and 5 years) of age. Children in the "active" group receive a daily fish oil supplement.

**Progress:** Recruitment commenced in July 2006 (with 6 months delay because of a delay in the delivery of the fish oil capsules from Canada. At the time of this report (Feb 2007) 250 women and their infants have been recruited into the study, with 29 withdrawals. None of these was because of adverse effects. So far, 89 children have been reviewed at 6 months of age and 21 at 12 months (for blood collection, allergy testing and clinical review). Sample processing and storage is progressing well and assays will commence when all samples (at each age group) have been collected. All equipment and techniques are operating well. The first "2 year" clinical visits will commence in June 2007 (when further blood samples, skin prick testing and clinical data will be collected). The study is progressing well. No significant problems have been encountered.

### **The ontogeny of TLR mediated innate immune function in normal and atopic children**

Susan L Prescott

**Objectives:** This is the first study to document normal maturation of Toll like receptor (TLR) function in early childhood, and to compare this in allergic and nonallergic children. These innate pathways are believed to play a central role in environment-driven immune maturation. Functional differences (as a result of environmental or genetic factors) have been recently implicated in the rising rates of allergic disease. Using samples from existing cohorts (NHMRC I39025; 211942; 254528) we will:

1) assess the "normal" maturation of TLR pathways in

nonallergic children (n=95) followed from birth and subsequently at 12, 30 and 60 months of age,

2) compare the development of TLR mediated immune function in children who develop aeroallergen sensitisation by 5 years (n=95) compared to those do not (n=95).

3) examine relationships between TLR function and developing specific responses (to allergens and vaccines).

This project has just been funded to begin in 2007.

### **Effects of enteric flora on mucosal and systemic immune function in infants at risk of allergic disease.**

Susan L Prescott

Summary of objectives: The aim of this study was to assess the role of probiotic administration to children at high risk of allergic disease (maternal allergic disease) on allergy prevention. These children received either a probiotics ( $3 \times 10^9$  Lactobacillus acidophilus LAVRI per day) or a placebo from birth until 6 months of age.

Summary of immunological findings: We recruited 231 pregnant, allergic women in pregnancy. 178 infants completed the supplementation period and the subsequent follow up period. Children who received the probiotics showed reduced production of IL-5 and TGF- $\beta$  in response to polyclonal stimulation (P=0.044 and P=0.015 respectively). They also demonstrated significantly lower IL-10 responses to TT vaccine antigen compared with the placebo group (P=0.03), and this was not due to any differences in vaccination. However, there were no significant effects of probiotics on either Th1 or Th2 responses to allergens or other stimuli. In summary, although we did not see any consistent effects on allergen-specific responses, our study suggests that probiotics have immunomodulatory effects on vaccine responses. The significance and clinical relevance of this need to be determined in further studies.

Summary of clinical findings: At six months of age, the rates of atopic dermatitis were similar in the probiotic (n=23/89, 25.8%) and placebo (n=20/88, 22.7%) groups (p=0.629). This did not change when possible confounding effects of feeding practices and older siblings were accounted for in regression modelling. At 12 months there were also no significant differences in symptoms of allergic disease, and no differences in the rate of sensitisation (SPT) to common allergens (including egg, milk, peanut, cat, or house dust mite). Thus, early probiotic supplementation did not reduce the risk of allergic disease or sensitisation in the first year of life in these high risk infants. Further follow-up will examine for any effects on aeroallergen sensitisation or disease.

We have 7 publications from this so far and others in

preparation.

### **Fetomaternal immunological interactions in the aetiology of allergic disease.**

Susan L Prescott, Catherine Thornton

Summary of objectives: This novel study examined the role of maternal/fetal immune interactions as a plausible controlling mechanism for immune maturation in early life. To do this we recruited a cohort of 160 women, which included equal number of atopic and nonatopic women, and equal number of multigravid and primigravid women in each group.

Key findings so far (analysis ongoing):

- We observed that allergic outcomes in the offspring were associated more strongly with materno-fetal immune interactions than with a maternal history of allergy. Specifically, allergic disease at 6 years of age was associated with significantly higher maternal responses to fetal alloantigens (lymphoproliferation and both Th1 and Th2 cytokine responses). These influences appeared to be stronger than the influence of maternal allergy per se.
- Fetal Th1 IFN $\gamma$  alloantigen responses were significantly correlated with the degree of HLA mismatch (maternal HLA class II antibodies)
- The capacity of the fetus to produce IL-13 and IL-10 was directly related to the level of these cytokine produced by the mother in response to fetal antigens.
- Allergic mothers showed a non-significant trend for stronger lymphoproliferation to fetal alloantigens.
- The number of previous pregnancies (gravidity) was associated with stronger maternal responses to fetal alloantigens, as shown by lymphoproliferation and IFN $\gamma$  synthesis, but did not affect fetal responses to the various stimuli.
- Patterns of APC function and T cell signalling were associated with the risk of subsequent allergic disease.

Collectively these findings demonstrate that maternal responses to fetal antigens relate to fetal immune responses and subsequent allergy. This novel observation suggests that events at the materno-fetal interface have an important influence on early immune development and should be investigated further.

NB: This cohort has also facilitated other studies comparing neonatal responses of infants of atopic versus non-atopic women, and is likely to give rise to many future publications on this (as multiple aliquots of cord blood are still available on all subjects).

## **Role of maternal dietary omega 3 fatty acids in modulation of allergen-specific T cell responses in the offspring**

Susan L Prescott

The main objective was determine if maternal dietary supplementation with n-3 PUFA during pregnancy can modify immune responses in infants, in the context of developing future allergy prevention strategies. We observed significant effects on neonatal immune function, and preliminary evidence that this may influence allergy risk. Although the originally funded aspects of this project are complete, we are still generating data from this cohort (as it is followed further) and have had 7 further publications arising (total of 16) in peer review journals.

## **Lupin allergenicity in children.**

Susan L Prescott, Richard Loh

Summary of objectives: This study will investigate the rate of lupin sensitization in peanut allergic children. This is part of a multi-disciplinary investigation into the safety aspects of introducing lupin flour and products more widely in Western Australia as a low "GI" food.

It falls under the umbrella of a major research facility support for the Diabetes Research Program (DRP) within the Centre For Food & Genomic Medicine (CFGM). It is a collaborative research initiative targeting innovative dietary and genome-based health solutions and economic development opportunities.

## **The effects of maternal smoking on fetal and postnatal immune development**

Susan L Prescott, Paul Noakes

This study addressed the effects of two major maternal factors on early Toll-like receptor (TLR)-mediated microbial responses, namely maternal allergy and smoking in pregnancy. As well as first-line microbial defence, innate TLR-mediated pathways modulate subsequent specific immune response and are essential for normal immune maturation.

Summary of findings: Infants of smokers showed significantly attenuated TLR-mediated responses compared to infants of non-smokers, including lower responses following TLR2, TLR3, TLR4 and TLR9 activation. These infants also had significantly lower IL-6 responses to antigen-specific stimulation compared with infants of non-smokers. Maternal allergy did not have significant independent effects on TLR responses, although there was a trend for lower TLR2 (IL-6 and IL-10), TLR4 responses (IL-10) and PPD (IL-6) responses in neonates of atopic

mothers. However, the inhibitory effects of smoking on TLR responses were significantly greater if mothers were atopic. This potentiating effect of maternal allergy was most apparent for TLR2 (IL-6), TLR3 (TNF $\alpha$ ) and TLR4 (TNF $\alpha$ ) responses.

Conclusions: This demonstrates that in addition to effects on developing airways, maternal smoking in pregnancy also has significant immunologic effects that could contribute to increased risk of respiratory infections and asthma. These effects appear to be mediated through effects on TLR-mediated innate response pathways that also promote regulatory pathways in the inhibition of allergic immune responses. This highlights that other environmental interactions are highly relevant to the "hygiene hypothesis".

## **The effects of antioxidant supplementation on immune responses of allergic adults**

Jan Dunstan, Susan L Prescott

Summary of objectives: Antioxidants are of growing interest in early treatment and prevention of allergic diseases in early life, but the effects on allergen-specific immune responses need to be documented further before intervention studies in infants are undertaken. The aim of this study in adults was to determine the effects of dietary antioxidants on allergen-specific immune responses in sensitised individuals. In a randomized controlled trial, 54 allergic adults received an antioxidant supplement (n=36) comprising  $\beta$ -carotene (9mg/d), vitamin C (1500mg/d), vitamin E (130mg/d), zinc (45mg/d), selenium (76 $\mu$ g/d) and garlic (150 mg/d) or a placebo (n=18) for 4 weeks. Antioxidant capacity (AC), serum levels of vitamin C, vitamin E,  $\beta$ -carotene and selenium, peripheral blood responses, exhaled nitric oxide (eNO), as a marker of airway inflammation, and plasma F<sub>2</sub> isoprostanes, as a measure of oxidative stress, were measured before and after supplementation.

Summary of findings: Antioxidant supplementation resulted in significant increases in serum levels of vitamin C, vitamin E,  $\beta$ -carotene and selenium levels, compared to the placebo group (P<0.001). There was no change in serum AC, plasma F<sub>2</sub>-isoprostanes, eNO or immune responses following supplementation with antioxidants compared to placebo. In conclusion, supplementation with antioxidants resulted in significantly increased levels of vitamin C, vitamin E,  $\beta$ -carotene and selenium but no change in immune responses, serum AC or plasma F<sub>2</sub>-isoprostanes.



## Staff and Students

### Head of Group

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Susan Prescott, B.Med.Sci(hons), M.B.B.S., F.R.A.C.P., Ph.D.  
Associate Professor, School of Paediatrics and Child Health UWA

Paediatric Allergist and Immunologist, Princess Margaret Hospital

### Research Staff

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Jan Dunstan PGDip BAppSc (Hons), PhD

Lauren Westcott BSc (Hons)

Jenefer Wiltschut BSc (Hons)

Helen Currie BSc (Hons)

Miranda Smith BSc (Hons)

Postgraduate Students

Liza Breckler BSc (Hons) PhD Candidate

David Martino BSc(Hons) PhD Candidate

Suzi McCarthy BSc(Hons) PhD Candidate

Bonita Chow BSc(Hons) PhD Candidate

Angie Taylor Dip. Med.Tech., BSc (Med Sc) (Hons) PhD Candidate- completed 2006

Paul Noakes BSc (Hons) PhD Candidate – completed 2006

### Research Support

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Weibke Jung

## Theses passed

Paul Noakes PhD University of Western Australia:  
The effects of maternal smoking on infant immune development

Angie Taylor PhD University of Western Australia: Allergy Prevention Studies: The role of probiotics in allergy prevention in high-risk infants

## Awards

Jan Dunstan, Child Health Research Foundation Fellowship.

## External Committees

### International

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Susan Prescott. Advisor: Mead Johnson (monograph on dietary fatty acids)

Susan Prescott. Advisor: Council of Health Advisors, Gerson Lehrman group (New York)

### National

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Susan Prescott. National Asthma Council: Asthma Management Handbook Working party

Susan Prescott. Paediatric Interest Group: Australasian Society of Clinical Immunology and Allergy

Susan Prescott. Allergy Prevention Working Party: Australasian Society of Clinical Immunology and Allergy

Susan Prescott.: National Advisory Board for the use of hydrolysed milk formulae (Nutricia)

Susan Prescott.: Nestle Scientific Advisory Board

Susan Prescott.: ASCIA organising committee for National meeting

### Local

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Susan Prescott. Faculty of Medicine Research Committee

Susan Prescott. Convenor: UWA Research Grants Scheme

Susan Prescott. Electoral Committee, Princess Margaret Hospital

Susan Prescott. Graduate Research Board UWA.

Susan Prescott. Scientific Advisory Committee, ICHR

## Invited Presentations

Susan Prescott (Plenary) Role of T regulatory pathways in early development): Symposium on Specific Allergy, Copenhagen, Denmark.

Susan Prescott Effects of maternal smoking on fetal immune development. CIA 26th Annual meeting (Collegium Internationalle Allergologicum) St Julians, Malta.

Susan Prescott (Plenary: Role of fatty acid in early immune development): 7th Congress of the International Society for the Study of Fatty Acids and Lipids, Cairns, Australia

## Diabetes, Obesity and Metabolism

### Overview

Type 1 diabetes in childhood is a common chronic metabolic disease of unknown cause that can affect children of all ages. The incidence of Type 1 diabetes continues to increase. Type 2 diabetes is also on the increase as a consequence of the increasing prevalence of obesity in childhood. The diabetes research program addresses questions relevant to both these forms of diabetes.

The mainstay of management of Type 1 diabetes is insulin treatment, which attempts to restore blood glucose levels to as close to normal as possible to prevent the devastating long-term complications of the disease. Unfortunately this is difficult to achieve and insulin therapy is frequently associated with low blood glucose or hypoglycaemia. Hypoglycaemia results in unpleasant symptoms if mild and if severe, can produce convulsions or unconsciousness, this in turn impairs quality of life but importantly restricts attempts to control diabetes.

A major goal of our research is to address the problem of hypoglycaemia and examine ways to treat diabetes more effectively. The program of research brings together an active team of experienced investigators from different fields to address this important clinical problem. By improving diabetes control we anticipate that in turn this will contribute to diabetes complication prevention as well as reducing the burden of disease on the patient and on his or her family.

A second thrust of research in the diabetes division is to study the epidemiology of diabetes. In WA, every child with diabetes is managed at our centre. The causes of diabetes are as yet unknown and the reason for its increase is unknown. There are genetic influences on the aetiology of type 1 diabetes as well as an unknown environmental trigger. This research aims to study the pattern of type 1 diabetes development and factors that may be associated with it.

A third focus is childhood obesity and Type 2 diabetes. We are collaborating with other investigators at the Institute for Child Health Research to examine the causes of obesity in childhood. In addition the section is involved in several lines of research studying the pathophysiological derangements that develop in obese children. This research is headed by Dr Elizabeth Davis who aims to study the impact of exercise on the metabolic disturbances that develop in this group of children.

## Diabetes

### **Prospective evaluation of responses to hypoglycaemia in newly diagnosed young patients with type 1 diabetes: does intensive diabetes management prevent loss of glucagon response and hypoglycaemia awareness. 1015/EP**

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Dr Tim Jones and Dr Elizabeth Davis

Aim: To prospectively characterise glucagon responses and hypoglycaemia awareness in 2 groups of children which receive either conventional or intensive treatment.

Funders of the project: NHMRC/JDRF

### **Australian Childhood Diabetes DNA Repository. 1245/EP**

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Dr Tim Jones, Dr Elizabeth Davis.

Project Aim: To identify and recruit families affected by either type 1 or young onset type 2 diabetes; to develop and maintain a database and repository of DNA samples from these families.

Funders of the project: NHMRC

### **Epidemiology of childhood-onset type 1 diabetes in Western Australia. 800/EP**

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Dr Aveni Haynes, Dr Tim Jones, Dr Elizabeth Davis

Project Aim: To determine the incidence of childhood-onset type 1 diabetes in children aged 0-14 yrs, in WA and to analyse trends in incidence. To identify potential antenatal and perinatal antecedents to childhood-onset type 1 diabetes.

Funders of the project: NHMRC/JDRF.

### **The effects of nocturnal hypoglycaemia on sleep in pre-pubertal children with type 1 diabetes. 983/EP**

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Dr Andrew Wilson, Dr Tim Jones, Dr Elizabeth Davis

Project Aim: During sleep the body's usual hormonal responses to hypoglycaemia are absent. An important protective mechanism is then the ability to arouse from sleep during a hypoglycaemia. This study investigates the relationship between hypoglycaemia and sleep in children.

Funders of the project: NHMRC/JDRF

### **Management of glycaemia during early and late recovery from exercise in type 1 diabetes**

### **diabetes: measurements of hepatic glucose output and whole body glucose utilization.**

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Dr Luis Ferreira, Dr Paul Fournier, Dr Tim Jones, Dr Elizabeth Davis.

Project Aim: the goal of this study is to determine the response of skeletal muscle glucose utilisation and hepatic glucose production to a 10-second all-out sprint. The goal of this study is to explore further the mechanisms responsible for the observed exercise-mediated stabilisation.

Funders of the project: NHMRC/JDRF and 2006 JDRF Grant Award

### **Carbohydrate utilization during exercise as a predictor of the risk of late-onset post-exercise hypoglycaemia in adolescents with type I diabetes: the effect of glycaemic control.**

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Dr Paul Fournier, DR Luis Ferreira, Dr Tim Jones, Dr Elizabeth Davis

Project Aim: The goal of this study is to examine the effect of glycaemic control on the risk of post-exercise hypoglycaemia in adolescents with type I diabetes by comparing the differences in the amount of glucose that must be administered to maintain normal blood glucose levels between non-exercised and exercised diabetic subjects.

Funders of the project: NHMRC/JDRF

### **The effect of one month of scrupulous avoidance of hypoglycaemia using a continuous glucose monitoring system on the hormonal and symptomatic responses to hypoglycaemia in patients with hypoglycaemia unawareness**

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Dr Tim Jones, Dr Liz Davis, Dr Paul Fournier

Project Aim: Approximately 25% of patients with Type I Diabetes suffer from hypoglycaemia unawareness, a condition where the symptoms of a low blood glucose event are diminished or lost. The purpose of this study is to test whether using a continuous glucose monitoring system for one month in patients with hypoglycaemia unawareness will prevent episodes and restore the symptoms of hypoglycaemia.

Funders of the project: JDRF

## *Staff and Students*

### **Head of Group**

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Timothy W Jones MD DCH FRACP

Head of Department of Paediatrics, Endocrinology and Diabetes, Princess Margaret Hospital for Children

Clinical Associate Professor, Centre for Child Health Research, The University of Western Australia

### **Research Staff**

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Dr Elizabeth Davis FRACP, MBBS

Dr Jacqueline Curran MBBS

Dr Aris Sifarikas FRACP, MBBS

Dr Sarah McMahon MBBS

Dr Aveni Haynes MB BChir

Dr Patricia Gallego MD

Michael LePage BSc (Hons)

Margaret Ho B.A (Hons)

Jennifer Girschik BSc (Hons)

Danielle Philippe BSc (Hons)

Vanessa Baker BHSc

Niru Ratnam BSc (Hons), RN

Alisha Thompson RN, GC Ned

Leanne Youngs BSc(Hons)

Max Bulsara BSc (Hons) MSc

### **Postgraduate Students**

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Dr Aveni Haynes MB BChir PhD Candidate

Dr Sarah McMahon MBBS (Hons) FRACP PhD Candidate

Dr Elizabeth Davis FRACP, MBBS PhD Candidate

Max Bulsara BSc (Hons) MSc PhD Candidate

Dr Patricia Gallego MD PhD Candidate

### **Research Support**

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Max Bulsara BSc (Hons) MSc

Vanessa Baker BHSc

## *Awards*

AM Thompson, LM Bell, L Naylor, L Ferreira, N Ratnam, K Watts, L Youngs, V Baker, TW Jones, D Green and EA Davis. Obese Adolescents Benefit More From A Resistance Training Protocol Than From Traditional Circuit Training

Methods, Nursing, Allied Health and Laboratory Staffing Award, Research and Advances, Princess Margaret Hospital, 18-20th October 2006.

## Committees

TW Jones. Member Scientific Review Committee Diabetes Australia Research Trust 2004-

TW Jones. Endocrine Health Network Advisory Group, Department of Health 2006- current

## Invited Presentations

Jones TW. Invited Speaker. Consequences of hypoglycaemia. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Jones TW, Invited Speaker. Hypoglycaemia. Presented at the Diabetes Twenty Twenty Meeting, Melbourne, Australia. 2006

Jones TW. Invited Speaker. Hypoglycaemia in Early Diabetes. American Diabetes Association ASM, Washington US 2006.

EA Davis. Diabetes thru the ages. Australian Diabetes Educator Association State Conference- Keynote speaker, March 2006.

Ghevodian N, Nguyen HT, Jones TW, Siafarikas A, Ratnam N. Predicting hypoglycaemia non-invasively in type 1 diabetic adolescents using Hypomon®. Presented at the American Diabetes Association ASM, Washington US June 2006.

Nguyen H, Ghevondian N, Jones T. Neural network detection of hypoglycaemic episodes in children with type 1 diabetes using physiological parameters. Presented at the IEEE Engineering in Medicine and Biology Society, August 2006, New York USA.

Watts K, Byrne S, Thompson AM, Bell LM, Jones TW, Davis EA. Waist girth is strongly associated with cardiovascular risk factor profile in primary school-aged children. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Thompson Am, Bell LM, Naylor L, Ratnam N, Watts K, Youngs L, Baker V, Jones TW, Green D, Davis EA. Obese adolescents benefit more from a resistance training protocol that from traditional circuit training methods. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Curran JA, Johnston R, Beye P, Martin D, Jones TW, Davis EA. Acanthosis nigricans is a useful screening tool for

type 2 diabetes and insulin resistance in obese Australian Aboriginals. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Gallego PH, Bulsara MK, Davis EA, Jones TW. Declining trends of albumin excretion rate in children and adolescents with type 1 diabetes mellitus. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Gallego PH, Shephard N, Bulsara MK, van Bockxmeer FM, Powell BL, Beilby JP, Arscott G, Le Page M, Palmer LJ, Davis EA, Jones TW, Choong CSY. Association of angiotensinogen gene T235 variant with the development of persistent microalbuminuria in children and adolescents with type 1 diabetes mellitus. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Siafarikas A, Ratnam N, Loveday J, Marangou D, Elliot J, Bulsara M, Jones TW, Davis EA. A randomised trial of intensive therapy with pump therapy (CSII) vs multiple daily injections (MDI) in adolescents with onset type 1 diabetes mellitus. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Haynes A, Bower C, Bulsara MK, Jones TW, Davis EA. Perinatal risk factors for childhood type 1 diabetes in Western Australia-a population based study (1980-2002). Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Elliot J, Ratnam N, Loveday J, Marangou D, Clements B, Siafarikas A, Jones TW, Davis EA. Intensive insulin pump therapy for adolescents with type 1 diabetes form diagnosis: QOL, self-efficacy and adjustment over 6 months. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Thompson Am, Bell LM, Naylor L, Ratnam N, Watts K, Youngs L, Baker V, Jones TW, Green D, Davis EA. Obese adolescents benefit more from a resistance training protocol that from traditional circuit training methods. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Curran JA, Johnston R, Beye P, Martin D, Jones TW, Davis EA. Acanthosis nigricans is a useful screening tool for type 2 diabetes and insulin resistance in obese Australian Aboriginals. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Allen K, Byrne S, Davis EA. A longitudinal study of binge eating and eating disorder symptoms in overweight and obese children: Findings from the Childhood Growth and Development Study. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Oddy WH, Byrne S, Watt FJ, Blair E, Davis EA. Fast food and its association with obesity in children. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Watt F, Byrne S, Blair E, Davis E. Obesity and adverse mental health outcomes in children. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Gibson L, Byrne S, Blair E, Davis EA. The psychological burden of childhood obesity. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Watts K, Byrne S, Thompson AM, Bell LM, Jones TW, Davis EA. Waist girth is strongly associated with cardiovascular risk factor profile in primary school-aged children. Presented at the International Congress on Obesity Meeting, Sydney, Australia, September 2006.

Gallego PH, Bulsara MK, Davis EA, Jones TW. Declining trends of albumin excretion rate in children and adolescents with type 1 diabetes mellitus. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

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Elliot J, Ratnam N, Loveday J, Marangou D, Clements B, Siafarikas A, Jones TW, Davis EA. Intensive insulin pump therapy for adolescents with type 1 diabetes from diagnosis: QOL, self-efficacy and adjustment over 6 months. Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Haynes A, Bower C, Bulsara MK, Jones TW, Davis EA. Perinatal risk factors for childhood type 1 diabetes in Western Australia-a population based study (1980-2002). Presented at the Australasian Paediatric Endocrine Group Annual Meeting, Tasmania, Australia September 2006.

Haynes A, Bower C, Bulsara MK, Jones TW, Davis EA. Perinatal risk factors for childhood type 1 diabetes in Western Australia-a population based study (1980-2002). Presented at the International Diabetes Epidemiology Group Conference. Stellenbosch November 2006, South Africa.

Bulsara MK, Gallego PH, Holman DJ, Davis EA, Beilby JP, Van Bockxmeer FM, Palmer LJ, Choong C, Jones TW. The relationship between ACE genotype and risk of severe hypoglycaemia in a population based cohort of children

with type 1 diabetes. Presented at the International Diabetes Epidemiology Group Conference, Stellenbosch, South Africa, 2006.

# 2006 Publications

## Total number of publications for 2006 - 169

- Ager S, Fyfe S, Christodoulou J, Jacoby P, Schmitt L, Leonard H. Predictors of scoliosis in Rett syndrome. *Journal of Child Neurology* 2006;21:809-13.
- Alfonso HS, Fritschi L, de Klerk NH, Ambrosini GL, Beilby J, Olsen N, Musk AW. Plasma vitamin concentrations and incidence of mesothelioma and lung cancer in individuals exposed to crocidolite at Wittenoom, Western Australia. *European Journal of Cancer Prevention* 2006;15:290-94.
- Allen KL, Byrne SM, Blair EM, Davis EA. Why do some overweight children experience psychological problems? The role of weight and shape concern. *International Journal of Pediatric Obesity* 2006;1:239-47.
- Anderson AW, Heptulla RA, Driesen N, Flanagan D, Goldberg PA, Jones TW, Rife F, Sarofin H, Tamborlane W, Sherwin R, Gore JC. Effects of hypoglycemia on human brain activation measured with fMRI. *Magnetic Resonance Imaging* 2006;24:693-97.
- Archer HL, Evans JC, Millar DS, Thompson PW, Kerr AM, Leonard H, Christodoulou J, Ravine D, Lazarou L, Grove L, Verity C, Whatley SD, Pitz DT, Sampson JR, Clarke AJ. NTNG1 mutations are a rare cause of Rett Syndrome. *American Journal of Medical Genetics Part A* 2006;140A:691-94.
- Badawi N, Dixon G, Felix JF, Keogh JM, Petterson B, Stanley FJ, Kurinczuk JJ. Autism following a history of newborn encephalopathy: more than a coincidence? *Developmental Medicine and Child Neurology* 2006;48:85-89.
- Badawi N, Novak I, McIntyre S, Edwards K, Raye S, deLacy M, Bevis E, Flett P, van Essen P, Scott H, Tungaraza K, Sealy M, McCann V, Reddihough D, Reid S, Lanigan A, Blair E, de Groot J, Watson L. Proposed new definition of cerebral palsy does not solve any of the problems of existing definitions. *Developmental Medicine and Child Neurology* 2006;48:78-78.
- Baldwin DN, Pillow JJ, Stocks J, Frey U. Lung-function tests in neonates and infants with chronic lung disease: tidal breathing and respiratory control. *Pediatric Pulmonology* 2006;41:391-419.
- Batterham R, Stanley F, Frost R, Tsoi AC, Finney K, Cathro W, Kotagiri R, Arthur E. From data to wisdom: pathways to successful data management for Australian science. Report of the working group on Data for Science to the Prime Minister's Science, Engineering and Innovation Council (PMSEIC). Canberra: Commonwealth Government of Australia; 2006 December.
- Beesley AH, Palmer ML, Ford J, Weller RE, Cummings AJ, Freitas JR, Firth MJ, Perera KU, de Klerk NH, Kees UR. Authenticity and drug resistance in a panel of acute lymphoblastic leukaemia cell lines. *British Journal of Cancer* 2006;95:1537-44.
- Binns C, Scott J, Nwafor N, Graham K, Oddy W, Lee A. Which mothers take folic acid and folate containing foods? *Asia Pacific Journal of Clinical Nutrition* 2006;15:335-40.
- Blair E. Trends in cerebral palsy prevalence in Northern Ireland, 1981-1997 (Editorial). *Developmental Medicine and Child Neurology* 2006;48:405.
- Blair E, Watson L. Epidemiology of cerebral palsy. *Seminars in Fetal Neonatal Medicine* 2006;11:117-25.
- Boag JM, Beesley AH, Firth MJ, Freitas JR, Ford J, Hoffmann K, Cummings AJ, de Klerk NH, Kees UR. Altered glucose metabolism in childhood pre-B acute lymphoblastic leukaemia. *Leukemia* 2006;20:1731-37.
- Bosco A, McKenna KL, Devitt CJ, Firth MJ, Sly PD, Holt PG. Identification of novel Th2-associated genes in T memory responses to allergens. *Journal of Immunology* 2006;176:4766-77.
- Bottcher MF, Jenmalm MC, Voor T, Julge K, Holt PG, Bjorksten B. Cytokine responses to allergens during the first 2 years of life in Estonian and Swedish children. *Clinical and Experimental Allergy* 2006;36:619-28.
- Botto LD, Lisi A, Bower C, Canfield MA, Dattani N, De Vigan C, De Walle H, Erickson DJ, Halliday J, Irgens LM, Lowry RB, McDonnell R, Metneki J, Poetzsch S, Ritvanen A, Robert-Gnansia E, Siffel C, Stoll C, Mastroiacovo P. Trends of selected malformations in relation to folic acid recommendations and fortification: An international assessment. *Birth Defects Research Part a-Clinical and Molecular Teratology* 2006;76:693-705.
- Bower C. Primary prevention of neural tube defects with folate in Western Australia: the value of the Western Australian Birth Defects Registry. *Congenital Anomalies* 2006;46:118-21.
- Bower C, de Klerk N, Milne E, Bailey H, Ambrosini G, Hickling S, Geelhoed E, Flicker L. Plenty of evidence on mandatory folate fortification. *Australian and New Zealand Journal of Public Health* 2006;30:81-82.
- Bower C, de Klerk N, Hickling S, Ambrosini G, Flicker L, Geelhoed E, Milne E, O'Leary P. Assessment of the potential effect of incremental increases in folic acid intake on neural tube defects in Australia and New Zealand. *Australian and New Zealand Journal of Public Health* 2006;30:369-74.
- Bower C, Miller M, Payne J, Serna P. Folate intake and the primary prevention of non-neural birth defects. *Australian and New Zealand Journal of Public Health* 2006;30:258-61.
- Bower C, Rudy E, Ryan A, Cosgrove P, Callaghan A.

- Report of the Birth Defects Registry of Western Australia 1980-2005. Perth: King Edward Hospital, Women's and Children's Health Service; 2006: 13.
- Bradley CK, Takano EA, Hall MA, Gothert JR, Harvey AR, Begley CG, van Eekelen JAM. The essential haematopoietic transcription factor Scl is also critical for neuronal development. *European Journal of Neuroscience* 2006;23:1677-89.
- Bryan DL, Forsyth KD, Hart PH, Gibson RA. Polyunsaturated fatty acids regulate cytokine and prostaglandin E2 production by respiratory cells in response to mast cell mediators. *Lipids* 2006;41:1101-07.
- Bulsara C, Styles I, Ward AM, Bulsara M. The psychometrics of developing the patient empowerment scale. *Journal of Psychosocial Oncology* 2006;24:1-16.
- Burgess SW, Wilson SSI, Cooper DM, Sly PD, Devadason SG. *In vitro* evaluation of an asthma dosing device: The smart-inhaler. *Respiratory Medicine* 2006;100:841-45.
- Bussau VA, Ferreira LD, Jones TW, Fournier PA. The 10-s maximal sprint - A novel approach to counter an exercise-mediated fall in glycemia in individuals with type 1 diabetes. *Diabetes Care* 2006;29:601-06.
- Calver J, Bulsara M, Boldy D. In-patient hospital use in the last years of life: a Western Australian population-based study. *Australian and New Zealand Journal of Public Health* 2006;30:143-46.
- Calver J, Horner B, Boldy D, Bulsara M. The burden of infectious diseases in Western Australian residential aged care facilities: a population-based record linkage study. *Australian Infection Control* 2006;11:1034-42.
- Carr J, Bell E, Pearson ADJ, Kees UR, Beris H, Lunec J, Tweddle DA. Increased frequency of aberrations in the p53/MDM2/p14(Arf) pathway in neuroblastoma cell lines established at relapse. *Cancer Research* 2006;66:2138-45.
- Creaney J, Christansen H, Lake R, Musk AB, de Klerk N, Robinson BWS. Soluble mesothelin related protein in mesothelioma. *Journal of Thoracic Oncology* 2006;1:172-74.
- Cripps AW, Leach AJ, Lehmann D. Pneumococcal vaccination in developing countries. *Lancet* 2006;368:644.
- Davey RJ, Ferreira LD, Jones TW, Fournier PA. Effects of exercise-mediated acidosis on determination of glycaemia using CGMS. *Diabetes Technology and Therapeutics* 2006;8:516-18.
- Donovan RJ, Henley N, Jalleh G, Silburn S, Zubrick S, Williams AA. The impact on mental health in others of those in a position of authority: a perspective of parents, teachers, trainers and supervisors. *Australian e-Journal for the Advancement of Mental Health (AeJAMH)* 2006;5.
- Dyke P, Leonard H. The Australian Rett Syndrome Study Report 2006. Perth, Western Australia: Telethon Institute for Child Health Research; 2006.
- Elliott EJ, Payne J, Haan E, Bower C. Diagnosis of fetal alcohol syndrome and alcohol use in pregnancy: A survey of paediatricians' knowledge, attitudes and practice. *Journal of Paediatrics and Child Health* 2006;42:698-703.
- English DR, Milne E, Simpson JA. Ultraviolet radiation at places of residence and the development of melanocytic nevi in children (Australia). *Cancer Causes and Control* 2006;17:103-07.
- Eppens MC, Craig ME, Jones TW, Silink M, Ong S, Ping YJ. Type 2 diabetes in youth from the Western Pacific region: glycaemic control, diabetes care and complications. *Current Medical Research and Opinion* 2006;22:1013-20.
- Franklin PJ, Hall GL, Moeller A, Horak F, Brennan S, Stick SM. Exhaled nitric oxide is not reduced in infants with cystic fibrosis. *European Respiratory Journal* 2006;27:350-53.
- Franklin PJ, Turner S, Mutch R, Stick SM. Parental smoking increases exhaled nitric oxide in young children. *European Respiratory Journal* 2006;28:730-33.
- Freemantle CJ, Read AW, de Klerk NH, McAullay D. Constructing a mortality profile of Western Australian born Aboriginal infants, children and young people using total population linked data. *Australasian Epidemiologist* 2006;13:9-14.
- Freemantle CJ, Read AW, de Klerk NH, McAullay D, Anderson IP, Stanley FJ. Patterns, trends, and increasing disparities in mortality for Aboriginal and non-Aboriginal infants born in Western Australia, 1980-2001: population database study. [Erratum appears *Lancet* 2006;368(9539):918-18]. *Lancet* 2006;367:1758-66.
- Freemantle CJ, Read AW, de Klerk NH, McAullay D, Anderson IP, Stanley FJ. Sudden infant death syndrome and unascertainable deaths: Trends and disparities among Aboriginal and non-Aboriginal infants born in Western Australia from 1980 to 2001 inclusive. *Journal of Paediatrics and Child Health* 2006;42:445-51.
- Freemantle J, Read A, de Klerk N, McAullay D, Anderson I, Stanley F. Infant mortality among Australian Aboriginals - Authors' reply. *Lancet* 2006;368:916-17.
- Gallego PH, Bulsara MK, Frazer F, Lafferty AR, Davis EA, Jones TW. Prevalence and risk factors for microalbuminuria in a population-based sample of children and adolescents with T1DM in Western Australia. *Pediatric Diabetes* 2006;7:165-72.
- Gappa M, Pillow JJ, Allen J, Mayer O, Stocks J. Lung function tests in neonates and infants with chronic lung disease: lung and chest-wall mechanics. *Pediatric Pulmonology* 2006;41:291-317.

- Gibson LY, Hogben JH, Fletcher J. Visual and auditory processing and component reading skills in developmental dyslexia. *Cognitive Neuropsychology* 2006;23:621-42.
- Giles-Corti B, Timperio A, Cutt H, Pikora TJ, Bull FC, Knuiman M, Bulsara M, Van Niel K, Shilton T. Development of a reliable measure of walking within and outside the local neighborhood: RESIDE's Neighborhood Physical Activity Questionnaire. *Preventive Medicine* 2006;42:455-59.
- Glasson E, Bolton H, Chauvel P, Cohen D, Cook H, Dixon G, Klinken J, McMullin B, Tender J, Wray J. WA Register for Autism Spectrum Disorders -2004 Report. Perth, Western Australia; 2006.
- Gorman S, Harvey NL, Moro D, Lloyd ML, Voigt V, Smith LM, Lawson MA, Shellam GR. Mixed infection with multiple strains of murine cytomegalovirus occurs following simultaneous or sequential infection of immunocompetent mice. *Journal of General Virology* 2006;87:1123-32.
- Gracey M, Bridge E, Martin D, Jones T, Spargo RM, Shephard M, Davis EA. An Aboriginal-driven program to prevent, control and manage nutrition-related "lifestyle" diseases including diabetes. *Asia Pacific Journal of Clinical Nutrition* 2006;15:178-88.
- Grimbaldeston MA, Finlay-Jones JJ, Hart PH. Mast cells in photodamaged skin: what is their role in skin cancer? *Photochemical and Photobiological Sciences* 2006;5:177-83.
- Hadlow NC, Hewitt BG, Dickinson JE, Jacoby P, Bower C. Community-based screening for Down Syndrome in the first trimester using ultrasound and maternal serum biochemistry. *Bjog-an International Journal of Obstetrics and Gynaecology* 2006;113:363-64.
- Hales BJ, Chu NR, Bosco A, Smith W, Heinrich TK, Thomas WR. Determinants of house dust mite allergenicity. *Allergy and Clinical Immunology International* 2006;18:65-70.
- Hales BJ, Martin AC, Pearce LJ, Laing IA, Hayden CM, Goldblatt J, Le Souef PN, Thomas WR. IgE and IgG anti-house dust mite specificities in allergic disease. *Journal of Allergy and Clinical Immunology* 2006;118:361-67.
- Haynes A, Bulsara MK, Bower C, Codde JP, Jones TW, Davis EA. Independent effects of socioeconomic status and place of residence on the incidence of childhood type 1 diabetes in Western Australia. *Pediatric Diabetes* 2006;7:94-100.
- Heidari M, Rice KL, Phillips JK, Kees UR, Greene WK. The nuclear oncoprotein TLX1/HOX11 associates with pericentromeric satellite 2 DNA in leukemic T-cells. *Leukemia* 2006;20:304-12.
- Heyworth JS, Glonek G, Maynard EJ, Baghurst PA, Finlay-Jones J. Consumption of untreated tank rainwater and gastroenteritis among young children in South Australia. *International Journal of Epidemiology* 2006;35:1051-58.
- Hicks CR, Crawford GJ, Dart JK, Grabner G, Holland EJ, Stulting RD, Tan DT, Bulsara M. AlphaCor: Clinical outcomes. *Cornea* 2006;25:1034-42.
- Hinwood AL, de Klerk N, Rodriguez C, Jacoby P, Runnion T, Rye P, Landau L, Murray F, Feldwick M, Spickett J. The relationship between changes in daily air pollution and hospitalizations in Perth, Australia 1992-1998: a case-crossover study. *International Journal of Environmental Health Research* 2006;16:27-46.
- Hoffmann K, Firth MJ, Beesley AH, de Klerk NH, Kees UR. Translating microarray data for diagnostic testing in childhood leukaemia. *Bmc Cancer* 2006;6.
- Holt PG. Th1-mediated inflammation as a potential pathogenic factor in allergic disease. In: Lowenstein H, Bienenstock J, Ring J, editors. *From Genes to Phenotypes. The Basis of Future Allergy Management*. Gottingen: Hogrefe & Huber; 2006. p. 7-10.
- Hopper JL, Treloar SA, de Klerk NH, Morley R. Australian Twin Registry: A Nationally Funded Resource for Medical and Scientific Research, Incorporating match and WATCH. *Twin Research and Human Genetics* 2006;9:707-11.
- Horton A, Murray F, Bulsara M, Hinwood A, Farrar D. Personal monitoring of benzene in Perth, Western Australia: the contribution of sources to non-industrial personal exposure. *Atmospheric Environment* 2006;40:2596-606.
- Hulskamp G, Pillow JJ, Dinger J, Stocks J. Lung function tests in neonates and infants with chronic lung disease of infancy: functional residual capacity. *Pediatric Pulmonology* 2006;41:1-22.
- Jahnsen FL, Strickland DH, Thomas JA, Tobagus IT, Napoli S, Zosky GR, Turner DJ, Sly PD, Stumbles PA, Holt PG. Accelerated antigen sampling and transport by airway mucosal dendritic cells following inhalation of a bacterial stimulus. *Journal of Immunology* 2006;177:5861-67.
- Janosi TZ, Adamicza A, Zosky GR, Asztalos T, Sly PD, Hantos Z. Plethysmographic estimation of thoracic gas volume in apneic mice. *Journal of Applied Physiology* 2006;101:454-59.
- Jarvis S, Glinianaia SV, Blair E. Cerebral palsy and intrauterine growth. *Clinics in Perinatology* 2006;33:285-300.
- Jian L, Nagarajan L, de Klerk N, Ravine D, Bower C, Anderson A, Williamson S, Christodoulou J, Leonard H. Predictors of seizure onset in Rett syndrome. *Journal of Pediatrics* 2006;149:542-47.
- Kankirawatana P, Leonard H, Ellaway C, Scurlock J, Mansour A, Makris CM, Dure LS, Friez M, Lane J, Kiraly-Borri C,



- Fabian V, Davis M, Jackson J, Christodoulou J, Kaufmann WE, Ravine D, Percy AK. Early progressive encephalopathy in boys and MECP2 mutations. *Neurology* 2006;67:164-66.
- Kendall GE, Schonert-Reichl K, Smith V, Jacoby P, Austin R, F. S, Hertzman C. The evaluation of "Roots of Empathy" in Western Australian Schools 2005. (For WA Department of Education and Training). Perth: Telethon Institute for Child Health Research; 2006.
- Kendall M, Mitchell TJ, Costigan G, Armitage M, Lenzo JC, Thomas JA, von Garnier C, Zosky GR, Turner DJ, Stumbles PA, Sly PD, Holt PG, Thomas WR. Downregulation of IgE antibody and allergic responses in the lung by epidermal biolistic microparticle delivery. *Journal of Allergy and Clinical Immunology* 2006;117:275-82.
- Khoo SK, Zhang G, Backer V, Porsbjerg C, Nepper-Christensen S, Creegan R, Baynam G, de Klerk N, Rossi GA, Hagel I, Di Prisco MC, Lynch N, Britton J, Hall I, Musk AW, Goldblatt J, Le Souef PN, and the Greenlandic Population Study Group. Associations of a novel IL4RA polymorphism, Ala57Thr, in Greenlandic Inuit. *Journal of Allergy and Clinical Immunology* 2006;118:627-34.
- Kicic A, Sutanto EN, Stevens PT, Knight DA, Stick SM. Intrinsic biochemical and functional differences in bronchial epithelial cells of children with asthma. *American Journal of Respiratory and Critical Care Medicine* 2006;174:1110-18.
- Koong B, Pharoah MJ, Bulsara M, Tennant M. Methods of determining the relationship of the mandibular canal and third molars: a survey of Australian oral and maxillofacial surgeons. *Australian Dental Journal* 2006;51:64-68.
- Kumar S, Middlemiss C, Bulsara M, Guibilato A, Morgan W, Tay-Kearney ML, Constable IJ, Yogesan K. Telemedicine-friendly, portable tonometers: an evaluation for intraocular pressure screening. *Clinical & Experimental Ophthalmology* 2006;34:666-70.
- Kurinczuk JJ, Hansen M, Bower C. Methodological considerations when designing studies to examine the health of children born following ART. In: Sutcliffe AG, editor. *Health and welfare of ART children*. London: Informa UK Ltd; 2006. p. 11-41.
- Kusel M, Sly PD. Acute respiratory tract infections in childhood. *Medicine Today* 2006;7:14-22.
- Kusel MMH, de Klerk NH, Holt PG, Keadze T, Johnston SL, Sly PD. Role of respiratory viruses in acute upper and lower respiratory tract illness in the first year of life - A birth cohort study. *Pediatric Infectious Disease Journal* 2006;25:680-86.
- Laing IA, Le Souef PN. Association studies in asthma. In: Postma DS, Weiss ST, editors. *Genetics of asthma and chronic obstructive pulmonary disease*. New York: Informa Healthcare; 2006. p. 239-72.
- Laurvick CL, de Klerk N, Bower C, Christodoulou J, Ravine D, Ellaway C, Williamson S, Leonard H. Rett Syndrome in Australia: A review of the epidemiology. *Journal of Pediatrics* 2006;148:347-52.
- Laurvick CL, Msall ME, Silburn S, Bower C, de Klerk N, Leonard H. Physical and mental health of mothers caring for a child with Rett Syndrome. *Pediatrics* 2006;118:e1152-64.
- Lenzo JC, Jarnicki AG, Gunn SR, Holt PG, Thomas WR. Inhalation allergy and desensitisation to a cysteine protease allergen. In: Lowenstein H, Bienenstock J, Ring J, editors. *From Genes to Phenotypes. The Basis of Future Allergy Management*. Gottingen: Hogrefe & Huber; 2006. p. 84-86.
- Leonard H, de Klerk N, Bourke J, Bower C. Maternal health in pregnancy and intellectual disability in the offspring: A population-based study. *Annals of Epidemiology* 2006;16:448-54.
- Li J, Zhang K, Tian L. Multiple facets of China's health inequality. *Lancet* 2006;367:1397.
- Martin AC, Laing IA, Khoo SK, Zhang G, Rueter K, Teoh L, Taheri S, Hayden CM, Geelhoed GC, Goldblatt J, LeSouef PN. Acute asthma in children: Relationships among CD14 and CCL6 genotypes, plasma levels, and severity. *American Journal of Respiratory and Critical Care Medicine* 2006;173:617-22.
- Martin DD, Davis EA, Jones TW. Acute effects of hyperglycaemia in children with type 1 diabetes mellitus: The patient's perspective. *Journal of Pediatric Endocrinology and Metabolism* 2006;19:927-36.
- Mattes E, Stacey MC, Marinova D. Predicting commercial success for Australian medical inventions patented in the United States: a cross sectional survey of Australian inventors. *Medical Journal of Australia* 2006;184:33-38.
- Mattes E, Stacey MC, Marinova D. Surveying inventors listed on patents to investigate determinants of innovation. *Scientometrics* 2006;69:475-98.
- McCormack GR, Giles-Corti B, Bulsara M, Pikora TJ. Correlates of distances traveled to use recreational facilities for physical activity behaviors. *International Journal of Behavioral Nutrition and Physical Activity* 2006;3:18.
- McCormack GR, Masse LC, Bulsara M, Pikora TJ, Giles-Corti B. Constructing indices representing supportiveness of the physical environment for walking using the Rasch measurement model. *International Journal of Behavioral Nutrition and Physical Activity* 2006;3:44.
- Measey MA, Li SQ, Parker R, Wang Z. Suicide in the Northern Territory, 1981-2002. *Medical Journal of Australia* 2006;185:315-19.

Milne E, de Klerk NH, van Bockxmeer F, Kees UR, Thompson JR, Baker D, Armstrong BK. Is there a folate-related gene-environment interaction in the etiology of childhood acute lymphoblastic leukemia? *International Journal of Cancer* 2006;119:229-32.

Milne E, Jacoby P, Giles-Corti B, Cross D, Johnston R, English DR. The impact of the kidskin sun protection intervention on summer suntan and reported sun exposure: Was it sustained? *Preventive Medicine* 2006;42:14-20.

Milne E, van Bockxmeer FM, Robertson L, Brisbane JM, Ashton LJ, Scott RJ, Armstrong BK. Buccal DNA collection: Comparison of buccal swabs with FTA cards. *Cancer Epidemiology Biomarkers and Prevention* 2006;15:816-19.

Mitrou F, Lawrence D, De Maio J, WAACHS team. Education of Aboriginal and Torres Strait Islander children and young people. In: *Australian Social Trends 2006*. Canberra: Australian Bureau of Statistics; 2006. p. 97-103. ABS Catalogue No 4102.0.

Moeller A, Horak F, Lane C, Knight D, Kicic A, Brennan S, Franklin P, Terpolilli J, Wildhaber JH, Stick SM. Inducible NO synthase expression is low in airway epithelium from young children with cystic fibrosis. *Thorax* 2006;61:514-20.

Moore HC, Lehmann D. Decline in meningitis admissions in young children: vaccines make a difference. *Medical Journal of Australia* 2006;185:404.

Musk AW, de Klerk NH. Malignant mesothelioma in Australia. In: O'Byrne K, Rusch V, editors. *Malignant Pleural Mesothelioma*. New York: Oxford University Press; 2006. p. 20-22.

Musk AW, Olsen NJ, Reid A, Threlfall T, de Klerk NH. Asbestos-related disease from recycled hessian superphosphate bags in rural Western Australia. *Australian and New Zealand Journal of Public Health* 2006;30:312-13.

Nassar N, Roberts CL, Barratt A, Bell JC, Olive EC, Peat B. Systematic review of adverse outcomes of external cephalic version and persisting breech presentation at term. *Paediatric and Perinatal Epidemiology* 2006;20:163-71.

Nassar N, Roberts CL, Cameron CA, Olive EC. Diagnostic accuracy of clinical examination for detection of non-cephalic presentation in late pregnancy: cross sectional analytic study.[see comment]. *BMJ* 2006;333:578-80.

Nassar N, Roberts CL, Cameron CA, Peat B. Outcomes of external cephalic version and breech presentation at term, an audit of deliveries at a Sydney tertiary obstetric hospital, 1997-2004. *Acta Obstetrica et Gynecologica Scandinavica* 2006;85:1231-38.

O'Leary C, Bower C, Payne J, Elliott E. Letter to the

Editor, Fetal Alcohol Syndrome. *Australian Family Physician* 2006;35:184.

Oddy WH. Fatty acid nutrition, immune and mental health development from infancy through childhood. In: Huang JD, editor. *Frontiers in nutrition research*. New York: Nova Science Publishers, Inc.; 2006. p. 177-211.

Oddy WH, Li J, Landsborough L, Kendall GE, Henderson S, Downie J. The association of maternal overweight and obesity with breastfeeding duration. *Journal of Pediatrics* 2006;149:185-91.

Oddy WH, Pal S, Kusel MMH, Vine D, de Klerk NH, Hartmann P, Holt PG, Sly PD, Burton PR, Stanley FJ, Landau LI. Atopy, eczema and breast milk fatty acids in a high-risk cohort of children followed from birth to 5 yr. *Pediatric Allergy and Immunology* 2006;17:4-10.

Oddy WH, Scott JA, Binns CW. The role of infant feeding in overweight young children. In: Flamenbaum RK, editor. *Childhood obesity and health research*. New York: Nova Science Publishers, Inc.; 2006. p. 111-33.

Oddy WH, Scott JA, Graham KI, Binns CW. Breastfeeding influences on growth and health at one year of age. *Breastfeeding Review* 2006;14:15-23.

O'Leary P, Breheny N, Dickinson JE, Bower C, Goldblatt J, Hewitt B, Murch A, Stock R. First-trimester combined screening for Down Syndrome and other fetal anomalies. *Obstetrics and Gynecology* 2006;107:869-76.

Olive EC, Roberts CL, Nassar N, Algert CS. Test characteristics of placental location screening by transabdominal ultrasound at 18-20 weeks. *Ultrasound in Obstetrics and Gynecology* 2006;28:944-49.

O'Neil SE, Heinrich TK, Hales BJ, Hazell LA, Holt DC, Fischer K, Thomas WR. The chitinase allergens Der p 15 and Der p 18 from *Dermatophagoides pteronyssinus*. *Clinical and Experimental Allergy* 2006;36:831-39.

Panegyres PK, Beilby J, Bulsara M, Toufexis K, Wong C. A study of potential interactive genetic factors in Huntington's disease. *European Neurology* 2006;55:189-92.

Panizza JA, James AL, Ryan G, de Klerk N, Finucane KE. Mortality and airflow obstruction in asthma: a 17-year follow-up study. *Internal Medicine Journal* 2006;36:773-80.

Piboonpocanun S, Malainual N, Jirapongsananuruk O, Vichyanond P, Thomas WR. Genetic polymorphisms of major house dust mite allergens. *Clinical and Experimental Allergy* 2006;36:510-16.

Pillai SG, Chiano MN, White NJ, Speer M, Barnes KC, Carlsen K, Gerritsen J, Helms P, Lenney W, Silverman M, Sly P, Sundy J, Tsanakas J, von Berg A, Whyte M, Varsani S, Skelding P, Hauser M, Vance J, Pericak-Vance M, Burns DK, Middleton LT, Brewster SR, Anderson WH, Riley JH.

- A genome-wide search for linkage to asthma phenotypes in the genetics of asthma international network families: evidence for a major susceptibility locus on chromosome 2p. *European Journal of Human Genetics* 2006;14:307-16.
- Pillow JJ, Frerichs I, Stocks J. Lung function tests in neonates and infants with chronic lung disease: global and regional ventilation inhomogeneity. *Pediatric Pulmonology* 2006;41:105-21.
- Prele CM, Keith-Magee AL, Yerkovich ST, Murcha M, Hart PH. Suppressor of cytokine signalling-3 at pathological levels does not regulate lipopolysaccharide or interleukin-10 control of tumour necrosis factor-alpha production by human monocytes. *Immunology* 2006;119:8-17.
- Ramelet AS, Abu-Saad HH, Bulsara MK, Rees N, McDonald S. Capturing postoperative pain responses in critically ill infants aged 0 to 9 months. *Pediatric Critical Care Medicine* 2006;7:19-26.
- Reid A, de Klerk NH, Ambrosini GL, Berry G, Musk AW. The risk of lung cancer with increasing time since ceasing exposure to asbestos and quitting smoking. *Occupational and Environmental Medicine* 2006;63:509-12.
- Robertson L, Hall SE, Jacoby P, Ellaway C, de Klerk N, Leonard H. The association between behavior and genotype in Rett Syndrome using the Australian Rett Syndrome database. *American Journal of Medical Genetics Part B-Neuropsychiatric Genetics* 2006;141B:177-83.
- Samanek AJ, Croager EJ, Gies P, Milne E, Prince R, McMichael AJ, Lucas RM, Slevin T. Estimates of beneficial and harmful sun exposure times during the year for major Australian population centres. *Medical Journal of Australia* 2006;184:338-41.
- Sanders SA, Herrero LJ, McPhie K, Chow SSW, Craig ME, Dwyer DE, Rawlinson W, McMinn PC. Molecular epidemiology of enterovirus 71 over two decades in an Australian urban community. *Archives of Virology* 2006;151:1003-13.
- Saxena A, de Lagarde D, Leonard H, Williamson SL, Vasudevan V, Christodoulou J, Thompson E, MacLeod P, Ravine D. Lost in translation: translational interference from a recurrent mutation in exon 1 of MECP2. *Journal of Medical Genetics* 2006;43:470-77.
- Schibler A, Pillow JJ. Clinically relevant early functional and diagnostic markers of lung disease in the paediatric intensive care unit. In: Frey U, Gerritsen J, editors. *European Respiratory Monograph: Respiratory Diseases in Infants and Children*. Sheffield: European Respiratory Society Journals Ltd; 2006. p. 142-52.
- Scott JA, Binns CW, Graham KI, Oddy WH. Temporal changes in the determinants of breastfeeding initiation. *Birth* 2006;33:37-45.
- Scott JA, Binns CW, Oddy WH, Graham KI. Predictors of breastfeeding duration: evidence from a cohort study. *Pediatrics* 2006;117:e646-55.
- Selgrade MK, Lemanske RF, Gilmour MI, Neas LM, Ward MDW, Henneberger PK, Weissman DN, Hoppin JA, Dietert RR, Sly PD, Geller AM, Enright PL, Backus GS, Bromberg PA, Germolec DR, Yeatts KB. Induction of asthma and the environment: What we know and need to know. *Environmental Health Perspectives* 2006;114:615-19.
- Shannon T, Giles-Corti B, Pikora TJ, Bulsara M, Bull F. Active commuting in a university setting: assessing commuting habits and potential for model change. *Transport Policy* 2006;13:240-53.
- Sharpe JA, Naylor LH, Jones TW, Davis EA, O'Driscoll G, Ramsay JM, Green DJ. Impact of obesity on diastolic function in subjects <= 16 years of age. *American Journal of Cardiology* 2006;98:691-93.
- Siafarikas A, Cherian S, Vicca N, Jones TW, Burgner D. Vitamin D Deficiency in Migrants. In: Stoltz VD, editor. *New Topics in Vitamin D Research*. New York: Nova Publishers; 2006. p. 199-221.
- Silburn SR, Zubrick SR, De Maio JA, Shepherd C, Griffin JA, Mitrou FG, Dalby RB, Hayward C, Pearson G. *The Western Australian Aboriginal Child Health Survey: Strengthening the capacity of Aboriginal children, families, and communities*. Perth: Centre for Developmental Health, Curtin University of Technology and Telethon Institute for Child Health Research; 2006.
- Slack-Smith LM, Read AW, Darby J, Stanley FJ. Health of caregivers in childcare. *Child: Care, Health and Development* 2006;32:111-19.
- Sly JL, Lombardi E, Kusel M, Sly PD. Piloting a web-based continuing professional development program for asthma education. *International Journal of Medical Informatics* 2006;75:708-13.
- Sly PD. Objective assessment of lung disease in wheezy infants: The time has come. *Pediatric Pulmonology* 2006;41:798-800.
- Sly PD, Collins RA. Physiological basis of respiratory signs and symptoms. *Paediatric Respiratory Reviews* 2006;7:84-88.
- Sly PD, Gerritsen J. Guest editorial: Physiology: the basis of normal function yet too often ignored. *Paediatric Respiratory Reviews* 2006;7:83.
- Soloff C, Lawrence D, Misson S, Johnstone R. Growing up in Australia. The longitudinal study of Australian children: an Australian Government Initiative. *LSAC Technical Paper No. 3. Wave 1 weighting and non-response*. Canberra: Australian Government, Australian Institute of Family Studies; 2006 May.

## Senior staff

- Stanley FJ, Maberly GF. Mandatory fortification of flour with folic acid: an overdue public health opportunity - Reply. *Medical Journal of Australia* 2006;184:199-99.
- Straker LM, Pollock CM, Zubrick SR, Kurinczuk JJ. The association between information and communication technology exposure and physical activity, musculoskeletal and visual symptoms and socioeconomic status in five year olds. *Child: Care, Health and Development* 2006;32:343-51.
- Strickland DH, Stumbles PA, Zosky GR, Subrata LS, Thomas JA, Turner DJ, Sly PD, Holt PG. Reversal of airway hyperresponsiveness by induction of airway mucosal CD4+CD25+ regulatory T cells. *Journal of Experimental Medicine* 2006;203:2649-60.
- Taylor RC, Richmond P, Upham JW. Toll-like receptor 2 ligands inhibit T(H)2 responses to mite allergen. *Journal of Allergy and Clinical Immunology* 2006;117:1148-54.
- Thomson AK, Glasson EJ, Bittles AH. A long-term population-based clinical and morbidity review of Prader-Willi Syndrome in Western Australia. *Journal of Intellectual Disability Research* 2006;50:69-78.
- Thomson AK, Glasson EJ, Bittles AH. A long-term population-based clinical and morbidity profile of Angelman syndrome in Western Australia: 1953-2003. *Disability and Rehabilitation* 2006;28:299-305.
- Tulic MK, Hamid Q. New insights into the pathophysiology of the small airways in asthma. *Clinics in Chest Medicine* 2006;27:41-52.
- Udomittipong K, Stick SM, Verheggen M, Oostryck J, Sly PD, Hall GL. Pre-flight testing of preterm infants with neonatal lung disease: a retrospective review. *Thorax* 2006;61:343-47.
- Upham JW, Hughes T. Dendritic cells. In: Laurent GJ, Shapiro SD, editors. *Encyclopedia of Respiratory Medicine*. Oxford, United Kingdom: Elsevier Academic Press; 2006. p. 10-15.
- Upham JW, Rate A, Rowe J, Kusel M, Sly PD, Holt PG. Dendritic cell immaturity during infancy restricts the capacity to express vaccine-specific T-cell memory. *Infection and Immunity* 2006;74:1106-12.
- Upham JW, Stick SM. Interactions between airway epithelial cells and dendritic cells: implications for the regulation of airway inflammation. *Current Drug Targets* 2006;7:541-45.
- von Ungern-Sternberg BS, Sly PD, Loh RK, Isidoro A, Habre W. Value of eosinophil cationic protein and tryptase levels in bronchoalveolar lavage fluid for predicting lung function impairment in anaesthetised, asthmatic children\*. *Anaesthesia* 2006;61:1149-54.
- Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, Michelangeli V. Subclinical thyroid dysfunction and blood pressure: a community-based study. *Clinical Endocrinology* 2006;65:486-91.
- Ward AM, de Klerk N, Pritchard D, Firth M. Correlations of siblings' and mothers' utilisation of primary and hospital health care: A record linkage study in Western Australia. *Social Science and Medicine* 2006;62:1341-48.
- Watson K, Carville K, Bowman J, Jacoby P, Riley TV, Leach AJ, Lehmann D. Upper respiratory tract bacterial carriage in Aboriginal and non-Aboriginal children in a semi-arid area of Western Australia. *Pediatric Infectious Disease Journal* 2006;25:782-90.
- Watson L, Blair E, Stanley F. Report of the Western Australian Cerebral Palsy Register – to birth year 1999. Perth: Telethon Institute for Child Health Research; 2006 December.
- Watt PM. Screening for peptide drugs from the natural repertoire of biodiverse protein folds. *Nature Biotechnology* 2006;24:177-83.
- Watt PM, Heinrich TK, Thomas WR. Protein silencing with Phylomers: a new tool for target validation and generating lead biologicals targeting protein interaction. *Expert Opinion on Drug Discovery* 2006;1:491-502.
- Watts K, Naylor LH, Davis EA, Jones TW, Beeson B, Bettenay F, Siafarikas A, Bell L, Ackland T, Green DJ. Do skinfolds accurately assess changes in body fat in obese children and adolescents? *Medicine and Science in Sports and Exercise* 2006;38:439-44.
- White GP, Hollams EM, Yerkovich ST, Bosco A, Holt BJ, Bassami MR, Kusel M, Sly PD, Holt PG. CpG methylation patterns in the IFN $\gamma$  promoter in naive T cells: variations during Th1 and Th2 differentiation and between atopics and non-atopics. *Pediatric Allergy and Immunology* 2006;17:557-64.
- Wiertsema SP, Khoo SK, Baynam G, Veenhoven RH, Laing IA, Zielhuis GA, Rijkers GT, Goldblatt J, Lesouef PN, Sanders EA. Association of CD14 promoter polymorphism with otitis media and pneumococcal vaccine responses. *Clinical & Vaccine Immunology: CVI* 2006;13:892-97.
- Wikstrom ME, Batanero E, Smith M, Thomas JA, von Garnier C, Holt PG, Stumbles PA. Influence of mucosal adjuvants on antigen passage and CD4(+) T cell activation during the primary response to airborne allergen. *Journal of Immunology* 2006;177:913-24.
- Win NN, Binns CW, Zhao Y, Scott JA, Oddy WH. Breastfeeding duration in mothers who express breast milk: a cohort study. *International Breastfeeding Journal* 2006;1:28 (22 December).
- Winfield KR, Gard S, Kent GN, Sly PD, Brennan S. Assay for urinary desmosines in a healthy pre-pubertal population

using an improved extraction technique. *Annals of Clinical Biochemistry* 2006;43:146-52.

Woodward EA, Prele CM, Finlay-Jones JJ, Hart PH. The receptor for cis-urocanic acid remains elusive. *Journal of Investigative Dermatology* 2006;126:1191-93.

Yeatts K, Sly P, Shore S, Weiss S, Martinez F, Geller A, Bromberg P, Enright P, Koren H, Weissman D, Selgrade M. A brief targeted review of susceptibility factors, environmental exposures, asthma incidence, and recommendations for future asthma incidence research. *Environmental Health Perspectives* 2006;114:634-40.

Yerkovich ST, Rate A, Upham JW. Dendritic cells in allergic disease: innocent bystanders or prime suspects? *Allergy and Clinical Immunology International* 2006;18:71-75.

Yong VK, Morgan WH, Cooper RL, Shaw M, Bremner AP, Bulsara M, Yu DY. Trends in registered blindness and its causes over 19 years in Western Australia. *Ophthalmic Epidemiology* 2006;13:35-42.

Zosky GR, Sly PD, Turner DJ. Mouse models of asthma: what physiological evidence are they based on? *Allergy and Clinical Immunology International* 2006;18:76-79.

Zubrick S, Lawrence D, de Maio J, Biddle N. Testing the reliability of a measure of Aboriginal children's mental health: An analysis based on the Western Australian Aboriginal Child Health Survey. Perth: Telethon Institute for Child Health Research, Australian Bureau of Statistics Canberra; 2006 2 March: ABS Catalogue No. 1351.0.55.011.

Zubrick SR, Silburn SR, De Maio JA, Shepherd C, Griffin JA, Dalby RB, Mitrou FG, Lawrence DM, Hayward C, Pearson G, Milroy H, Milroy J, Cox A. The Western Australian Aboriginal Child Health Survey: Improving the educational experiences of Aboriginal children and young people. Perth: Curtin University and Telethon Institute for Child Health Research; 2006.



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