

Paediatrics, University of Adelaide

Head: Professor Don Robertson
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The Department of Paediatrics, University of Adelaide, has research interests in basic science, clinical paediatrics, public health relevant to children and young people, and in education. Many of the projects are undertaken in conjunction with other research groups in the WCH, the University of Adelaide, and national and international collaborators. The following research reports represents the interests and research activities of the staff and students of the Department.

1 Maternal perceptions of medical student interviewing skills

M O'Keefe

The opinions of mothers regarding medical student or doctor interviewing skills are rarely sought. This is despite the fact that mothers are active participants in most paediatric interviews. In this study, mothers attending paediatric medical outpatients with their children were shown videotaped interviews of a medical student interviewing a mother (both actors). There were 4 versions of the interview. Mothers could distinguish between levels of student competence, and between levels of interest in the mother's viewpoint shown by the student. Mothers preferred a more competent student, and one who took more account of their perspective of the child's health problem. Mothers could assist in the assessment of medical student interviewing skills and possibly feedback on doctor interviewing skills.

2 An interactive model for integrating knowledge in child health clinical skills

*DJ Bates; with MA Seidel,
DG Thomas (Centre for
Education)*

We are developing a model for integrating knowledge in child health clinical skills encompassing video demonstration and the capacity to interact and engage in clinical reasoning exercises, applicable as a tutorial session and as a self-paced computer aided learning module. For the latter we have utilised the DOCENT computer application developed at the University of Adelaide, which provides the ability to analyse free-text responses to questions and deliver immediate appropriate feedback.

The model is innovative in that students are not prompted with predetermined answers and must apply their own knowledge, which is reinforced by viewing video of a practicing clinician and by receiving feedback directly relating their responses to those of an experienced clinician (expert knowledge). A database of potential student responses (obtained by questionnaires during a tutorial session) has been used to generate a subset of regular expressions for breaking the student input into fragments for matching against core-concepts.

3

Prospective immunological study of children with increased risk of IDDM

*JJ Couper, S Beresford, A Pollard,
T Powell; PG Colman,
LC Harrison (Walter & Eliza Hall
Research Institute, Royal
Melbourne Hospital)*

Approximately 450 babies who have a first degree relative with insulin dependent diabetes are being followed prospectively to determine environmental factors and the sequence of autoimmune changes which precede the development of IDDM. Transient autoimmunity has been noted in some infants; the incidence of autoimmunity is substantially higher than the predicted incidence of IDDM. The ten infants who have progressed to IDDM have shown autoimmunity to multiple target antigens.

We have shown no prospective relationship between breast feeding, and introduction of cow's milk, with the development of autoimmunity. The relationship of enteroviral infection (Coxsackie B1-6 and rotavirus) and islet autoimmunity has been studied. A temporal relationship with rotavirus infection (but not coxsackie B1-6 infection) has been shown for the first time.

4

Homocyst(e)ine and endothelial dysfunction in children with type 1 diabetes

*E Wiltshire, JJ Couper; with
DW Thomas (Chemical
Pathology);
R Gent (Radiology)*

This is a longitudinal study of homocyst(e)ine (genotype and phenotype) dietary factors and endothelial dysfunction in 100 children with type 1 diabetes and controls. (10% of the risk of coronary artery disease in the general population is attributable to homocyst(e)ine and this can be reduced with folate supplementation). We have found lower homocyst(e)ine levels in the children with diabetes, which is partly explained by higher folate, B12 and B6 status. The relationship of homocyst(e)ine levels to ultrasound changes of endothelial dysfunction (flow mediated dilatation) has been studied. Children with type 1 diabetes have early endothelial dysfunction and for the first time we have shown a relationship with folate stores. This finding has prompted a folate intervention study.

5

The relationship of blood pressure in type 1 diabetes to changes in albuminuria

*J Nairn, JJ Couper; TW Jones
(Princess Margaret Hospital)*

This is an ongoing prospective study in approximately 600 children and adolescents with type 1 diabetes to determine whether blood pressure rises (within the normal range) precede rises in albumin excretion, the earliest sign of diabetic renal disease. The findings have relevance to the timing of interventional therapy.

6
**Family environmental
 and treatment factors
 which influence the
 quality of life of children
 with chronic illness**

*M Sawyer, JJ Couper; with
 D French (University of WA);
 P Baghurst (Public Health
 Research Unit)*

This is a longitudinal study examining the impact of key risk factors and protective factors on the quality of life children of chronic illness, viz diabetes, cystic fibrosis and malignancies. The focus of the research is on the effect of treatment tasks that these children perform on their quality of life. Recruitment is complete.

7
**The effects of
 intrauterine growth
 restriction on postnatal
 lung structure and
 function**

*JD Kennedy; with A Wilson,
 AJ Martin, DW Parsons
 (Pulmonary Medicine); J Lipsett
 (Histopathology); IC McMillen,
 JA Owens (Physiology, Adelaide
 University)*

This project is examining the link between intra-uterine growth restriction and postnatal lung function and structure. Sheep from multiple pregnancies have been studied as a model of IUGR and new infant lung function techniques have been utilised. The animal studies for this project are complete and results are being analysed.

8
**Effects of single and
 multiple dose antenatal
 steroids on lung
 development in the
 intra-uterine growth
 restricted sheep**

*JD Kennedy; with A Wilson,
 AJ Martin, DW Parsons
 (Pulmonary Medicine); J Lipsett
 (Histopathology); JA Owens
 (Physiology, Adelaide University)*

This project is investigating the effects of antenatal corticosteroids on lung structure and function in IUGR. Intra-uterine growth restriction is induced by removing potential implantation sites from the mother's uterus prior to conception, thus restricting the size of the placenta. The sheep are delivered pre-term and ventilated, lung function tests are performed and the lungs are the harvested for morphometric analysis. This study is currently in progress.

9

Antenatal insulin-like growth factor-I and perinatal growth, survival and function of the growth restricted fetus

JD Kennedy; with A Wilson, AJ Martin, DW Parsons (Pulmonary Medicine); J Lipsett (Histopathology); JA Owens (Physiology, Adelaide University)

Antenatal administration of insulin-like growth factor-1 is a potential treatment for IUGR. This is part of a larger study currently being conducted by Dr Owens examining the effects of such treatment on a number of organ systems. Our group will concentrate on the effects of this treatment on lung structure and function. This study commenced in late 2000.

10

Pathogenesis of asthma in the REECH (Respiratory Events in Early Childhood) cohort

JD Kennedy, DJ Bates; with AJ Martin (Pulmonary Medicine); JE Marley, H Miles, R Ruffin (The Queen Elizabeth Hospital)

We have finished the analysis concerning the outcome of gastro-oesophageal reflux (GOR) and its relationship with respiratory disease and have unique data for publication. We are now turning our attention to the "Hygiene hypothesis" ie what is the effect of infection etc upon the prevalence of asthma.

11

Quality of life of children with asthma

JD Kennedy; with N Spurrier, M Sawyer (Public Health Research Unit); AJ Martin (Pulmonary Medicine)

Results have been analysed and a paper on the quality of life of children with asthma submitted and accepted for publication in the Journal of Asthma and Quality of Life Research.

12

The prevalence of snoring in children visiting a general practitioner

JD Kennedy; with B Lorenzen (Northern Division of General Practice); K Lushington (University of South Australia)

This study evaluated the prevalence of snoring as a presentation in General Practice. To date over 600 children and their parents have completed a sleep questionnaire and a subgroup of snoring children and matched controls are currently having their neurocognitive function assessed. The preliminary results are in agreement with our previous studies. We also are examining the awareness of sleep problems in children in General Practice.

13

Production of monoclonal antibodies to *Haemophilus influenzae* type B capsular polysaccharide

*AP Kodituwakku, DM Roberton;
H Zola (Child Health Research
Institute)*

Haemophilus influenzae type b (Hib) is an important pathogenic bacterial organism in children. The majority of infections occur during early childhood. The bacterium enters the blood stream from the upper respiratory tract and disseminates to distant body sites. The immunity to Hib infection depends on the level of antibody response to PRP capsular polysaccharide of the bacterium. Children less than two years of age mount a poor natural antibody response to PRP antigen due to the immaturity of the immune system.

We have produced mouse monoclonal antibodies against Hib PRP capsular polysaccharide. These antibodies will be used to study the B lymphocyte involvement in the development of antibody response to PRP antigen in children. We hope that this information will be useful to provide a better understanding of the antibody response to Hib infections in children.

14

Combination RSV/PIV3 nasal drop vaccine study

*DM Roberton, MS Gold,
H Marshall, L Dinan*

The Vaccine Research Unit has participated in an international, multiculture Phase 1 RSV/PIV3 combination vaccine study trial. Eleven healthy children aged 6-18 months were enrolled in this study at our site. Subjects were vaccinated with either respiratory syncytial virus (RSV) vaccine or parainfluenza type 3 (PIV3) or RSV and PIV3 combined live attenuated vaccine or placebo. Subjects were closely monitored with frequent clinical review and nasal washes performed to detect any viral shedding post vaccination. Serology samples were also obtained prior to and 6 weeks following vaccination. Serology results are not yet available. The total of 60 children enrolled has been achieved from Australian and American sites.

15

“FluMist” vaccine nasal spray study

*DM Roberton, MS Gold,
H Marshall, M Busuttill*

FluMist vaccine is an intra-nasal vaccine spray that has been extensively trialed in adults and children in Australia and overseas. The study we are currently conducting is a Phase 3 safety, tolerability and immunogenicity study to determine if there is any interference when FluMist nasal spray vaccine is given concurrently with measles, mumps, rubella and varicella vaccines. Children are randomised to one of three groups. Group 1 receive MMRII and VARIVAX with a placebo spray followed by 2 doses of FluMist, group 2 receive MMRII and VARIVAX with 2 doses of FluMist spray and group 3 receive 2 doses of FluMist spray followed by MMRII and VARIVAX four weeks later. Fifty-one children have currently been enrolled to the study at our site.

16

Recombinant RSV nasal drop study in adults and seropositive children

*DM Roberton, MS Gold,
H Marshall, L Dinan, M Busuttill*

The Vaccine Research Unit in association with WyethLederle Pharmaceuticals is involved in assessing the potential development of potential RSV vaccines for use in children. Several recombinant strains are currently being tested. Our Unit has been involved in the assessment of a particular RSV strain sequentially in adults and seropositive children. Two adults were enrolled to this multicentre international Phase 1 study at our site. After FDA approval of the adult data we were able to enrol 1 child to the seropositive cohort after screening the child for the presence of RSV antibodies. The seropositive data from 17 subjects enrolled in Australia and South Africa will be available soon for FDA review and if favourable we will progress to the seronegative cohort.

17

Combination measles, mumps, rubella, varicella study

DM Robertson, MS Gold, H Marshall, L Dinan, M Busuttill

The development of combination vaccines is an important aspect of vaccine research and development. The Vaccine Research Unit has been involved in a Phase III international, safety and immunogenicity study to compare a combination measles, mumps, rubella, varicella vaccine with measles mumps, rubella and varicella vaccines given as separate injections at the same time or six weeks apart. One hundred and seventy-five children were enrolled to this study at our site, which has recently been completed. Serology was obtained prior to and 6 weeks after vaccination.

18

The protective efficacy of adversely stored pertussis vaccines

CA Boros, MS Gold, DM Robertson

Storage of vaccines below 0°C occurs frequently at vaccine provider sites. Such adverse storage of pertussis vaccines can affect their immunogenicity. The effect of adverse storage on the protective efficacy of pertussis vaccines against respiratory challenge has not yet been reported. In general adverse storage did not decrease the protective efficacy of DTPw or DTPa. It will be important to determine how this model of vaccine protective efficacy relates to vaccine immunogenicity and to immunisation responses.

19

Antibody responses to immunisation in premature and term infants

CA Boros;with A McPhee (Neonatal Medicine); MS Gold, DM Robertson; M Hanlon (Children's Hospital, Sydney)

Little is known regarding the immune response of premature infants to immunisation. Premature infants may be at higher risk of infection from vaccine preventable diseases. Premature infants generally had lower antibody responses to immunisation antigens at both 2 and 7 months of age. At 7 m, Geometric Mean Concentrations (GMCs) for DT, TT and PRP reached protective levels in both groups. Although responses to term infants to pertussis antigens were generally significantly higher at 2m and 7m, there is no serological correlate of protection against pertussis. Continued follow up of these infants will determine if the differences in antibody levels to vaccine antigens persist.

Staff participating in research

University Funded Staff

Prof DM Robertson
MD, FRACP, FRCPA, Head

Dr RH Burnell
MBBS, FRACP, Senior Lecturer

Prof DW Thomas
MB, MS, MMedSci (Hons), FRACP, FRCPA, MAACB, Head of Chemical Pathology

Dr RTL Couper
MB, ChB, FRACP, Senior Lecturer

Dr JL Penfold
MBBS,FRACP, Senior Lecturer, Head of Diabetes and Endocrinology

A/Prof JJ Couper
MBBS,MD,FRACP, Senior Lecturer, Deputy Head of Diabetes & Endocrinology

Dr JD Kennedy,
MD, FRCP, FRACP, Senior Lecturer and Deputy Head

Dr M Gold

MD, FRACP, FACP, Senior Lecturer

Dr M O'Keefe

FRACP, DCCH, Lecturer

Dr DG Thomas

MD, FRACP, Senior Lecturer, Director of Physician Training

Dr DJ Bates

BSc (Hons), PhD, Principal Research Officer

Hospital Funded Staff

Dr H Marshall

MBBS, DCH, Senior Medical Officer – Vaccine Research Unit

Ms J Aldis

CertMedLabSci, Technical Officer

Ms M Busuttil

BAppSci (MedLabSci), Technical Officer

Dr H Huynh

MBBS, Clinical Research Fellow

Mrs S Nobbs

DipMedLabSci, Technical Officer

JJ Couper

Australian Diabetes Society, Cairns, Aug 2000
 American Diabetes Society, San Antonio, June 2000
 Paediatric Endocrine Genes Satellite of ICE, Sydney, Oct 2000

JL Penfold

Copenhagen, May 2000:

- *Childhood Diabetes – From Epidemiology to Molecular Genetics*

Mrs L Dinan

BSc, M PublHealth, Project Manager – Vaccine Research Unit

Mr GJ Harvey

DipMedLabSci, Laboratory Manager

Mrs A Pollard

Technical Assistant

Grant Funded Staff

Dr C Boros

MBBS, FRACP, Postgraduate Student

Dr A Kodituwakku

MBBS, Postgraduate Student

Mr M Bawden,

Research Assistant (CRC)

Ms J Nairn

RN, Research Nurse, Endocrine

Dr D Petchell

MBBS, FRACGP, Postgraduate Student

Dr E Wiltshire,

JDFA, FRACP, Research Fellow

International and Interstate Travel and Presentations

JD Kennedy

World Sleep Congress, Sydney March 2000:

- *Neurocognitive function in children* (invited speaker)

Stanford University Pediatric Sleep Disorders

Course, April 2000

**International and
Interstate Visitors**

Professor Georges Grau

Professor of Physiology, University de la Mediterranee, Marseille, visited

December:

- *Tumor necrosis factor*

**Other Research-related
Activity**

JJ Couper

program organising committee, Australian Diabetes Society, Annual Scientific Meeting

JD Kennedy

reviewer, *Paediatric Pulmonology, J Paediatrics and Child Health*; reviewer NH&MRC and Channel 7 Children's Research Foundation

Grants

Sawyer M, Couper JJ, Baghurst P, French D

Family environmental and treatment factors which influence the quality of life of children with chronic illness

NH&MRC

\$78,000

Wiltshire E, Thomas DW, Couper JJ

Homocyst(e)ine and endothelial dysfunction in children with type 1 diabetes

Channel 7 Children's Research Foundation

\$36,000

Wiltshire E

Juvenile Diabetes Foundation of Australia

\$55,000

Wiltshire E, Couper JJ

Novo Nordisk

\$10,000

Wiltshire E, Couper JJ

Eli Lilly (AZA Research)

\$15,000

Wilson AC, Kennedy JD, Martin AJ, Lipsett J, Parsons DW

The effects of intrauterine growth restriction on postnatal lung structure and function

Channel 7 Children's Research Foundation

\$7,500

Lorenzen B, Lushington K, Kennedy J

The prevalence of snoring in children visiting a general practitioner
Northern Division of General Practice
\$17,500

Zola H, Macardle P, Robertson D

Immaturity of the human infant immune response to cellular and molecular mechanisms and clinical consequences
NH&MRC
\$97,811

Publications

Badcock NR, Couper RTL, Aldis JJE, Staugus RE, Parsons DW

Vitamin E peroxidative and non-peroxidative free radical damage markers, and sample collection timing in children and adolescents with cystic fibrosis. *Aust J Nutr Dietet* (2000) 57: 79-83

Bates DJ, Thomas DG, Seidel MA

An interactive model for integrating knowledge in child health clinical skills. In Pradhan M, Warren J, Chu S, Coiera E and Zelmer ACL (eds) (2000) Health Informatics Society of Australia, Victoria

Blunden S, Lushington K, Kennedy D, Martin J, Dawson D

Behaviour and Neurocognitive Performance in Children Aged 5-10 Years Who Snore Compared to Controls. *J Clin Exp Neuropsychol* (2000) 22: 554-568

Boros CA, Kay D, Gold MS

Parent reported allergy and anaphylaxis in 4173 South Australian children. *J Paed Child Health* (2000) 36: 36-40

Couper JJ, Couper RTL

Prader-Willi Syndrome. *Lancet* (2000) 356:673-657

Colman PG, Steele C, Couper JJ, Beresford SJ, Powell T, Kewming K, Pollard A, Gellert S, Tait B, Honeyman M, Harrison LC

Islet autoimmunity in infants with a Type I diabetic relative is common but is frequently restricted to one autoantibody. *Diabetologia* (2000) 43: 203-209

Couper JJ, Kallincos N, Pollard A, Honeyman M, Prager P, Harrison LC, Rischmueller M

Toxic shock syndrome associated with newly diagnosed type I diabetes. *J Paed Child Health* (2000) 36: 279-282

Coulson BS, Honeyman M, Stone N, Gellert S, Goldwater P, Steele C, Couper JJ, Tait B, Colman P, Harrison L

Association between rotavirus infection and pancreatic islet autoimmunity in children at risk of type 1 diabetes. *Diabetes* (2000) 49 :1319-1325

Couper RT, Huynh H, Butler RN

Gene encoded antibacterial activity in *Helicobacter pylori*. *J Ped Gastroenterol Nutr* (2000) 31: 327-8

Couper RTL

Exocrine Pancreatic Function testing. In Durie PR, Hamilton JR, Walker WA, Walker-Smith J and Watkins J (eds) *Pediatric Gastrointestinal Disease* (3rd Edition) (2000) BC Dekker Inc, Philadelphia, PA, Vol 2, pp 1515-1528

Couper RTL

Methaemoglobinaemia secondary to topical lignocaine/prilocaine in a circumcised neonate. *J Paed Child Health* (2000) 36: 406-407

Couper RTL, Couper JJ

Prader-Willi syndrome. *Lancet* (2000) 356: 673-675

Elliott SR, Robertson DM, Zola H, Macardle PJ

Expression of the costimulator molecules, CD40 and CD154, on lymphocytes from neonates and young children. *Human Immunol* (2000) 61: 378-388

Gold M, Goodwin H, Botham S, Burgess M, Nash M, Kempe A

Re-vaccination of 421 children with a past history of an adverse vaccine reaction in a special immunisation service. *Arch Dis Childhood* (2000) 83: 128-31

Gold MS

The prevention, diagnosis and management of allergic disease in childhood. *Curr Paed* (2000) 10: 137-144

Gold MS, Sainsbury R

First aid anaphylaxis management in children who were prescribed an epinephrine autoinjector device (EpiPen). *J Allerg Clin Immunol* (2000) 106: 171-176

Honeyman MC, Coulson BS, Stone NL, Gellert SA, Goldwater PN, Steele CE, Couper JJ, Tait BD, Colman PG, Harrison LC

Association between rotavirus infection and pancreatic islet autoimmunity in children at risk of developing type 1 diabetes. *Diabetes* (2000) 49: 1319-1324

Kennedy JD, Edward LJ, Bates DJ, Martin AJ, Nobbs S, Haslam RR, McPhee AJ, Staugas RE, Baghurst P

Effects of Birthweight and Oxygen Supplementation on Lung Function in Late Childhood in Children of Very Low Birth Weight. *Ped Pulmonol* (2000) 30: 32-40

Lipsett J, Cool JC, Runciman SC, Ford WDA, Parsons DW, Kennedy JD, Martin AJ

Effect of immediate versus slow intrauterine reduction of congenital diaphragmatic hernia on lung development in the sheep: A morphometric analysis of term pulmonary structure and maturity. *Ped Pulmonol* (2000) 30: 228-240

Lipsett J, Cool JC, Runciman SIC, Ford WDA, Kennedy JD, Martin AJ, Parsons DW

Morphometric analysis of preterm fetal pulmonary development in the sheep model of congenital diaphragmatic hernia. *Ped Develop Pathol* (2000) 3: 17-28

Manton ND, Lipsett J, Moore DJ, Davidson GP, Bourne AJ, Couper RTL

Non-alcoholic steatohepatitis in children and adolescents. *Med J Aust* (2000) 173: 476-479

Roberton D

Consultant paediatric workforce in Australia: numbers and needs. *J Paed Child Health* (2000) 36: 299-300

Spurrier NJ, Sawyer MG, Staugas R, Martin AJ, Kennedy D, Streiner DL

Association Between Parental Perception of Children's Vulnerability to Illness and Management of Children's Asthma. *Ped Pulmonol* (2000) 29: 88-93

Thomas DW

Biochemical Investigations. In Toouli J, Russell C, Devitt P and Ingham-Clark C (eds) *Integrated Basic Surgical Sciences* (2000) Edward Arnold, London, Chapter 29.2, pp 573-578

Turner MW, Dinan L, Heatley S, Jack DL, Boettcher B, Lester S, McCluskey J, Roberton D

Restricted polymorphism of the mannose-binding lectin gene of indigenous Australians. *Human Mol Genet* (2000) 9: 1481-6

Wilson AC, Moore DJ, Moore MH, Martin AJ, Staugas REM, Kennedy JD

Late presentation of upper airway obstruction in Pierre Robin sequence. *Arch Dis Childhood* (2000) 83: 435-438

Wiltshire EJ, Flaherty SP, Couper RTL

Hepatocyte growth factor in human semen and its association with semen parameters. *Human Reprod* (2000) 15: 1525-1528

Xian CJ, Couper R, Howarth GS, Read LC, Kallincos NC

Increased expression of HGF and c-met in rat small intestine during recovery from methotrexate-induced mucositis. *Br J Cancer* (2000) 82: 945-952

Post-graduate Degrees

P. Adamson

PhD
Child Health Research Institute
Paediatrics
University of Adelaide

P. Dewan

Urology, Royal Children's
Hospital
M Med Sci
Paediatrics
University of Adelaide

K. Friend

PhD
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Genetics
Paediatrics
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I. Lensink

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