



Welcome to the first edition of the Paediatric Active Enhanced Disease Surveillance (PAEDS) newsletter. Although excellent national laboratory and public health surveillance systems are currently operating in Australia, very few provide timely, detailed clinical data or the opportunity for simultaneous collection of biological specimens. To address this gap, the Australian Paediatric Surveillance Unit (APSU) and the National Centre for Immunisation Research and Surveillance (NCIRS) developed a hospital-based active surveillance system - PAEDS.

PAEDS commenced in 2007 as a pilot project and has grown substantially over the last 5 years. Landmark studies arising from PAEDS surveillance to date have demonstrated a small but significant risk of intussusception (a rare form of bowel blockage) following rotavirus vaccination, and described the clinical burden of pandemic influenza in children. We are currently in a growth phase, which has seen the introduction of a formal governance structure, the planned addition of a PAEDS site in Queensland and inclusion of new conditions under surveillance, such as pertussis. We hope you enjoy our introductory newsletter, and look forward to sharing more of our work with you.

Director APSU, Professor Elizabeth Elliott
Director NCIRS, Professor Peter McIntyre

OVERVIEW

The PAEDS network conducts active, hospital based surveillance to collect enhanced data on serious vaccine-related childhood conditions for which data are not readily available using existing surveillance mechanisms.

PAEDS consists of a network of clinicians and public health researchers in four Australian tertiary paediatric

IN THIS ISSUE

Overview	1
Key Activities	1
Additional surveillance activity	2
Planning for new studies	2
PAEDS team past and present	3
Current PAEDS staff members	4
Publications and presentations	4

hospitals:

The Children's Hospital at Westmead, Sydney; Royal Children's Hospital, Melbourne; Women's and Children's Hospital, Adelaide; and Princess Margaret Hospital, Perth. PAEDS is currently working with investigators in Queensland to establish a fifth PAEDS surveillance site at the Royal Children's Hospital from July 2012.

The PAEDS system is based on the Canadian Immunisation Monitoring Program Active (IMPAct) which is well suited to the Australian environment. Similar to Canada, Australia has a geographically dispersed population but a large majority of children with serious illnesses are referred and admitted to large paediatric hospitals, enabling ease and completeness of case ascertainment.

PAEDS is funded by the Australian Government Department of Health and Ageing. In addition, from mid 2011, the state health departments of the participating sites, New South Wales, Victoria, Western Australia, South Australia also agreed to contribute annual funding to PAEDS. Queensland Health will join from mid 2012. This has enabled the expansion of PAEDS activities, including addition of new conditions for surveillance and increased capacity to rapidly respond to urgent issues.

KEY ACTIVITIES OF PAEDS

Conditions under surveillance

Acute flaccid paralysis

Surveillance for acute flaccid paralysis (AFP) has been conducted in PAEDS centres since 2007 and these centres contribute the majority of cases to the Polio Expert Panel of the Department of Health and Ageing. This data has contributed to Australia fulfilling requirements for WHO-required AFP surveillance as part of the Global Polio Elimination Strategy. It is planned that AFP surveillance be broadened to include potential

neurological Adverse Events Following Immunisation (AEFI).

Intussusception (IS)

PAEDS has monitored cases of intussusception (a rare form of bowel blockage) since 2007 when rotavirus vaccines were introduced to the National Immunisation Program (NIP). Surveillance has been important because a vaccine used in the USA in the late 1990's was associated with an increased risk of IS, although this was not found in prelicensure studies of the currently available vaccines. Analysis of the PAEDS data conducted in 2010 suggested an increased risk of intussusception among young infants following the first, but not subsequent, doses of both brands of rotavirus vaccine. In 2010 this data was presented to peak immunisation advisory committees, including the Australian Technical Advisory Group on Immunisation (ATAGI), the World Health Organization Global Advisory Committee on Vaccine Safety (GACVS) and the US Advisory Committee on Immunization Practices (ACIP).

This PAEDS study was the first to be published showing an association between the currently registered rotavirus vaccines and IS (refer to publication list). Together with emerging data from studies in other countries (e.g. Mexico, Brazil and the USA), this data was used to formulate national and international recommendations about the risk-benefit profile and continued use of rotavirus vaccines.

The use of rotavirus vaccines in Australia has averted >7000 hospitalisations in children under 5 years. The benefit in continuing to vaccinate babies offsets the small increased risk of IS (see advice at www.immunise.health.gov.au). A study commissioned by the Therapeutic Goods Association (TGA) will further examine the association between rotavirus vaccines and IS in 2012 and will incorporate PAEDS data.

Hospitalised varicella

Approximately 90% of varicella cases occur in children less than 15 years of age with at least 1% of these experiencing severe complications including secondary



bacterial infections, central nervous system manifestations, pneumonitis and death. PAEDS provides the only systematic prospectively collected data on hospitalised varicella in Australia, including risk factors

and vaccination status. This, together with the collection of biologic samples to perform virus genotyping, will allow for a better understanding of the epidemiology of varicella since the introduction of varicella vaccines to the National Immunisation Program in 2005 and is also a potentially important means to estimate vaccine effectiveness. Analysis obtained to date was presented at the 7th World Congress of the World Society for Paediatric Infectious Diseases (WSPID) in Melbourne in November 2011 and has been submitted for publication.

Hospitalised pertussis

During 2011, PAEDS investigators developed a protocol for active surveillance of hospitalised pertussis, including gathering data on the clinical and laboratory features of such cases. In addition, information on the vaccination history of pertussis cases and their contacts will be collected and analysed, and clinical samples will be obtained for genetic analysis (to be done at the University of New South Wales). Enhanced clinical and epidemiological data on pertussis is important to further inform vaccine strategies in the management of Australia's sustained pertussis epidemic. Hospitalised Pertussis surveillance will commence at the PAEDS sites in 2012.

Additional surveillance activity

H1N1 Pandemic 2009

In June 2009 the PAEDS network was able to quickly respond to the H1N1 2009 Pandemic with the support of an NHMRC H1N1 Special Initiative Grant, and an additional grant from NSW Health which enabled surveillance in 2 additional hospitals in NSW, John Hunter Children's Hospital, Newcastle and Sydney Children's Hospital, Randwick. PAEDS demonstrated capacity to ramp-up the surveillance effort at relatively short notice, by bringing additional resources into play: in the 4 months June to September 601 children hospitalised with influenza were recruited. This is likely to be the largest case series of children admitted to hospital with laboratory confirmed influenza. A report was presented to the NHMRC in December 2009 and to date five publications have resulted.

Analysis of influenza vaccine adverse events



The PAEDS network helped gather data on fever and febrile convulsions in children presenting to the four participating hospitals in March-April 2010 to contribute to the analyses conducted during the investigation into the unexpected adverse events following seasonal influenza

vaccine in 2010. The high risk of fever and febrile convulsions was only associated with one brand of influenza vaccine (Fluvax®, CSL Biotherapies), which is no longer recommended for use in young children.

New analysis of this data using the self-controlled case series method will also be presented at the Public Health Association of Australia National Immunisation Conference in July 2012; this method provides an excellent model for conducting assessment of the incidence of serious adverse events related to influenza or other vaccines in children.

Guillain Barré syndrome

The World Health Organization (WHO), in collaboration with the US Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA), began a novel worldwide collaborative study on the incidence of Guillain Barré syndrome (GBS) following pandemic

H1N1 vaccine in early 2010. As part of this study, the PAEDS group has submitted data on GBS cases (confirmed using Brighton criteria) from each PAEDS site. It is anticipated that data from more than a dozen countries will be included in the final data set; results of the analysis are expected in 2012.

Planning for new studies

Acute Childhood Encephalitis

Encephalitis is a complex neurological syndrome caused by inflammation of the brain, which is usually infection-related ("infectious encephalitis"). Children are among those most severely affected. However, there is limited contemporary information about the causes of encephalitis in children worldwide. It is critical to collect this information actively and prospectively because while viruses are the major known cause of infectious encephalitis, using current standard methodologies, a diagnosis is not made in up to 70% of cases. This study will provide information on psychological and physical disease burden, with scope for studies of long term outcome, economic impact and genetic susceptibility.

PAEDS team past and present

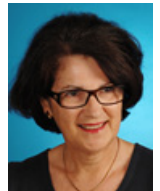


The PAEDS team includes staff at The Children's Hospital at Westmead (CHW), the Royal Children's Hospital Melbourne (RCH), the Women's and Children's Hospital Adelaide (WCH), Princess Margaret Hospital Perth (PMH) and the Royal Children's Hospital Brisbane (From July 2012). The Coordinating centre for PAEDS is located at the Children' Hospital Westmead, Sydney.

PAEDS warmly welcomes new staff members Dr Marie Deverell, Ms Jenny Murphy and Ms Jocelynn McRae who have joined the PAEDS coordinating centre at the Children's Hospital Westmead. Marie joined the PAEDS group in January 2012 as a Senior Research Officer for PAEDS and the Australian Paediatric Surveillance Unit (APSU). Marie hails from Western Australia and has a PhD in Paediatrics and Child

health. She has previously worked at the Public Health Advocacy Institute of Western Australia, the Western Australia Audit of Surgical Mortality and the Telethon Institute for Child health Research. Ms Jenny Murphy has been acting in the role of PAEDS Nurse Coordinator since December 2011. She holds a Bachelor of Applied Science from Sydney University. Jenny has an extensive background in Immunisation research, and has worked at the Children's Hospital Westmead for over 20 years. Ms Jocelynn McRae joined PAEDS in May 2012. Jocelynn has held recent clinical research appointments in areas including infectious diseases and childhood cancer. Jocelynn holds a Master of Health Science (Clinical data management, University Sydney) and is currently part way through a Master of Public Health (University Sydney). Jocelynn's clinical background includes over 10 years as an intensive care nurse and laboratory science.

PAEDS would also like to acknowledge the valued contribution of our founding Nurse Coordinator, Mrs Margie Pym (2007 – 2008, pictured right) and also Ms Leanne Vidler (left) who was much valued in the role of PAEDS nurse coordinator from 2009 – 2011.



Publications & Presentations

Publications

Buttery JP, Danchin MH, Lee KJ, Carlin JB, McIntyre PB, Elliott EJ, et al. Intussusception following rotavirus vaccine administration: Post-marketing surveillance in the National Immunization Program in Australia. *Vaccine*.2011;29(16):3061-6.

Publications Including PAEDs Data

Elliott EJ, Zurynski YA, Walls T, Whitehead B, Gilmour R, Booy R, et al. Novel inpatient surveillance in tertiary paediatric hospitals in New South Wales illustrates impact of first-wave pandemic influenza A H1N1 (2009) and informs future health service planning. *Journal of Paediatrics and Child Health*. 2012;48(3):235-41.

Khandaker G, Zurynski Y, Buttery J, Marshall H, Richmond P, Dale R, et al. Neurologic complications of influenza A(H1N1) pdm09: surveillance in 6 pediatric hospitals. *Neurology*. 2012. In Press.

Khandaker GM, Dibben et al. Mania in a patient with H1N1: is oseltamivir the culprit or a red herring? [Letter]. *American Journal of Psychiatry*. 2010; 167: 1129-30

Khandaker GM, Zurynski Y, Lester-Smith D, et al. Clinical features, oseltamivir treatment and outcome in infants aged <12 months with laboratory confirmed influenza A in 2009. *Antiviral Therapy*. 2011; 16:1005-10.

Khandaker GM, Lester-Smith D, Zurynski Y, et al. Pandemic (H1N1) 2009 and seasonal influenza A (H3N2) in children's hospital, Australia. [Letter] *Emerging Infectious Diseases*. 2011;17: 1960-2.

Khandaker GM, Rashid H, Zurynski Y, Richmond PC, et al. Nosocomial versus community-acquired pandemic influenza A

(H1N1) 2009: a nested case-control study. Journal of Hospital Infection. In Press.

Presentations

Dodd CN. International Collaborative Case Series Safety Monitoring for Pandemic 2009 H1N1 Vaccines: Estimation of the Risk of Guillain-Barre Syndrome. ICPE: International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Barcelona Spain, August 22-26, 2012.

Current PAEDS staff members

Children's Hospital Westmead, Sydney



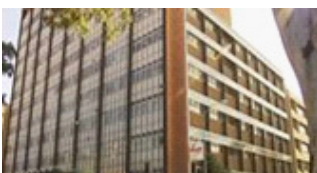
Professor Peter McIntyre - Director, NCIRS, Professor Elizabeth Elliott - Director, APSU, Professor Robert Booy - Head of Clinical Research, NCIRS, A/Professor Kristine Macartney - Deputy Director, of Government Programs, NCIRS
Dr Nick Wood - Clinical Research Fellow, NCIRS, A/Professor Yvonne Zurynski - Assistant Director, APSU
Ms Jenny Murphy - Research Nurse Coordinator, PAEDS, Ms Jocelyne McRae - Research Nurse Coordinator, PAEDS, Dr Marie Deverell - Senior Research Officer, APSU/PAEDS, Mr Manos Visvikis - Database Manager, APSU/PAEDS

Royal Children's Hospital, Melbourne



Dr Jim Buttery, Immunisation CCRE, Dr Jenny Royle, Paediatrician, Dr Nigel Crawford, Consultant Paediatrician, Alissa McMinn, Research Assistant, Julie Quinn, Surveillance nurse, Georgie Lewis, Surveillance nurse
Leonie Hickie, Surveillance nurse, Donna Lee, Surveillance nurse, Tammy Hutchinson, Surveillance nurse, Victoria Scott, Administration Assistant

Women's and Children's Hospital, Adelaide



A/Professor Mike Gold, Senior Lecturer, University, Department of Paediatrics, A/Professor Helen Marshall, Director Vaccinology & Immunology Research Trials Unit, Ms Christine Heath, Surveillance Nurse, Ms Mary Walker, Surveillance Nurse

Princess Margaret Hospital, Perth



A/Professor Peter Richmond, Dr Christopher Blyth, Paediatrician,
Ms Caroline Talbott, Surveillance Nurse
Ms Christine Robbins, Surveillance Nurse

Royal Children's Hospital, Brisbane



Associate Professor Michael Nissen.
Other personnel to be advised.

For More Information:

Paediatric Active Enhanced Disease Surveillance (PAEDS)
Kids Research Institute, The Children's Hospital at
Westmead
Cnr Hawkesbury Rd and Hainsworth Street
Locked Bag 4001
Westmead NSW 2145
Sydney Australia

PAEDS website coming soon!

Marie Deverell
E: marie.deverell@health.nsw.gov.au
P: 02 9845 3007