PAEDS
Paediatric Active Enhanced Disease Surveillance
ncirs NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE
apsu Australian Paediatric Surveillance Unit

newsletter
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IN THIS ISSUE

WELCOME

Welcome to the second newsletter of the PAEDS network. PAEDS is now in its 7th year since beginning as a pilot project under the leadership of NCIRS and APSU in 2007.

In the last 12 months there has been considerable growth in our national active hospital-based surveillance of important paediatric conditions related to vaccine preventable diseases. Last year our 5th paediatric hospital, the Royal Children's Hospital in Brisbane, joined PAEDS. Thanks to the leadership of Professor Michael Nissen and the hard work of research nurse Sonia Dougherty, we are now recruiting cases in Queensland. We hope to continue this expansion and include more new hospitals soon.

PAEDS has added 3 new conditions for surveillance in the last 12 months. These are:

- Pertussis
- Febrile seizures
- Encephalitis (NSW pilot project)

Capturing clinical details on these conditions and relevant biological samples will enable a better understanding of these conditions in Australia. The data will also allow us to examine disease morbidity and long-term outcomes (for pertussis and encephalitis) and to examine any potential relationships with vaccination (for febrile seizures and encephalitis). Surveillance for these conditions is described more below.

2012 also saw publication of a paper overviewing PAEDS activities led by A/Prof Yvonne Zurynski and published in the Journal of Paediatrics and Child Health, it describes the development and early achievements of PAEDS.

Surveillance for the 3 established PAEDS conditions – acute flaccid paralysis (AFP), intussusception and varicella – is ongoing. Last year saw PAEDS publish the first major Australian study of the impact of universal varicella vaccination in children, which has been funded under the Australian National Immunisation Program (NIP) since 2005. This publication, in the *Pediatric Infectious Disease Journal,* and led by A/Prof Helen Marshall, demonstrated a 68% reduction in varicella hospitalisations and a 40% reduction in herpes zoster in children since vaccine introduction. The results emphasised the importance of vaccination according to the NIP, as many recruited children were unvaccinated. Further analysis is planned, including formal assessment of vaccine effectiveness and correlations of disease severity with varicella genotype. PAEDS continues to notify the majority of AFP cases reported in Australia to the Polio Expert Panel (PEP) while providing stool samples to VIDRL for testing for enteric pathogens. Surveillance for intussusception (IS) is ongoing, with studies globally now reporting a similar risk of IS post rotavirus vaccination, as first reported internationally by PAEDS in 2011.

Importantly, PAEDS has undertaken a review of governance and operations and improved processes and structures are being implemented as we grow. Details are provided below on our exciting planned transition to WebSpirit, a web-based data management platform.

We hope you enjoy the rest of this newsletter and can join us in celebrating the ongoing success of the PAEDS network.

Members of the PAEDS Coordinating Centre at our weekly meeting.

NEW CONDITIONS UNDER SURVEILLANCE

Successful competitive grants and additional funding from the Department of Health and Ageing have resulted in the inclusion of 3 new conditions to PAEDS in the last 2 years.

Adding new conditions to PAEDS requires a sustained team effort from investigators and nurses. Everyone involved in the development of the new protocols and operating procedures deserves a huge THANK YOU! We would particularly like to acknowledge our skilled surveillance nurses for their excellent efforts during this busy time.

Pertussis

Pertussis (whooping cough) is a preventable respiratory illness caused by the bacterium *Bordetella pertussis.* Despite the availability of new acellular pertussis vaccines and immunisation coverage approaching 90%, pertussis continues to cause significant morbidity and mortality. In the past decade, a resurgence of pertussis has been identified in Australia, the USA and more recently the UK, all countries with long-established pertussis immunisation programs. This resurgence has been mainly in older children (due to waning immunity) and in infants under 3 months of age who are too young to have received more than 1 dose of pertussis-containing vaccine. One additional potential contributing factor to the resurgence is vaccine-driven adaptation of *B. pertussis.*

PAEDS aims to examine hospitalised pertussis in Australia, with special emphasis on disease severity, the need for intensive care, death and disability. This study also aims to examine the contribution of co-infections and other co-morbidities, and disease transmission in households (by checking the immunisation history of patients, family members and 'coughing contacts'). These factors will also be correlated with the genetic sub-types identified in *B. pertussis* positive cultures. Recruitment commenced in January 2012.

Febrile seizures

Febrile seizures (FS) usually occur in children aged 6 months to 6 years, peaking in the 2nd year of life, and are triggered by a sudden change in temperature. They are usually caused by a viral illness but can also occur following fever associated with vaccination. Two new vaccines: the 13-valent pneumococcal conjugate vaccine (PCV13) and the combined measles, mumps, rubella, varicella (MMRV) vaccine have recently been added to the NIP. A meningococcal B vaccine for infants has also recently been registered in Australia and may be added to the NIP in the future. In pre-licensure vaccine trials all 3 vaccines have been associated with somewhat high rates of fever under certain circumstances, and therefore a risk of FS. Approximately 1 in 30 children aged 6 months to 6 years will have a FS at some time in their life and for most (70%) this is limited to only one FS. Any recurrent seizures usually occur within 1 year. However, the long-term clinical outcomes and risks of recurrence of a FS following vaccination are not well described.

This important PAEDS study will gather enhanced clinical and epidemiological information on FS and will determine if there is an increased risk of FS with the new vaccines. It will also describe the clinical and revaccination outcomes of children who have experienced a febrile seizure. Recruitment across all 5 sites commenced in early 2013.

In addition, in 4 PAEDS sites, children with FS identified under the PAEDS study will be offered enrolment into an NHMRC funded study, led by Dr Nicholas Wood, to compare the genetic susceptibility to seizures among children with FS that follow vaccination and FS not related to vaccines.

NHMRC Project Grant (1049557): Febrile seizures following vaccination in children: How common are they and what is the long term clinical outcome? Wood N, Buttery J, Gold M, Richmond P, Crawford N, Barton B, Macartney K.

Childhood encephalitis

The Australian Childhood Encephalitis (ACE) study led by Prof Cheryl Jones and Dr Philip Britton will collect data on encephalitis cases via PAEDS. A 6-month trial of surveillance began in May at the CHW site only. Results from this trial will be used to inform the roll-out to other states next year.

Encephalitis is a complex neurological syndrome caused by inflammation of the brain. Children are among those most severely affected. However, there is limited contemporary information about the causes of encephalitis in children worldwide. While viruses are the major known cause of infectious encephalitis, a cause is not found in up to 70% of cases using current standard methodologies. Australia has unique wildlife and vectors (mosquitoes, ticks, bats, etc) and therefore potentially unique sources and transmission of infections leading to encephalitis that are not described elsewhere. There is also increasing awareness of immune-mediated causes of encephalitis, but these have not been systematically studied in children. The ACE study has the potential to describe the incidence, aetiology, clinical characteristics, potential risk factors and short-term outcomes among Australian children hospitalised for encephalitis, thereby informing the development of standardised diagnostic guidelines.

Key upcoming dates for PAEDS

The annual PAEDS face-to-face meeting will be held at the University of Sydney campus on 28 and 29 November 2013. This is attended by all PAEDS staff and representatives of the PAEDS stakeholders, including the Australian Government Department of Health and Ageing and state health departments. The first meeting of our PAEDS Reference Group will be in **October 2013**, prior to the face-to-face meeting. The Reference Group will assist PAEDS in its growth and development.

CELEBRATING PAEDS SUCCESS

Surveillance of hospitalisations for pandemic influenza

When the NHMRC called for research applications on the H1N1 influenza pandemic in 2009, PAEDS was ready! We modified the APSU influenza surveillance protocol and wrote a successful NHMRC application. Supplementary funding from NSW Health enabled surveillance in 2 additional hospitals in NSW.

PAEDS provided unique data on the impacts of pandemic influenza H1N1-09 on Australian children and on paediatric hospitals by conducting surveillance for all laboratory confirmed influenza hospitalisations in 6 tertiary paediatric centres:

- The Children's Hospital at Westmead, NSW
- Sydney Children's Hospital, Randwick, NSW
- John Hunter Children's Hospital, Newcastle, NSW
- Royal Children's Hospital, Melbourne, Vic
- Women's and Children's Hospital, Adelaide, SA
- Princess Margaret Hospital, Perth, WA

Data on 601 cases was collected from the 6 centres resulting in 7 journal publications and numerous conference presentations. Congratulations particularly go to Dr Gulam Khandaker who was the lead author on many of these and received his PhD for thesis work in 2013.

Our study showed that even previously healthy children were admitted to hospital with serious complications such as pneumonia, encephalitis and other neurological complications. Only about a half of children received oseltamivir, and only 6% of children with predisposing chronic conditions had been vaccinated for influenza as recommended and funded under the NIP. This resulted in awareness raising among health professionals to vaccinate such children. This study also supported the recommendation for annual vaccination of healthy children who have no predisposing medical conditions.

By conducting this surveillance for these 4 months in 2009, PAEDS has demonstrated its capacity to collect timely, detailed clinical and laboratory data as well as information about complications and outcomes of influenza in children. With additional funding, PAEDS will be ready to provide such unique data during every influenza season; data essential to support influenza vaccination policy and for health services planning during influenza epidemics.

NHMRC Project Grant (633028): Characterisation of H1N1 influenza 09 in hospitalised children using Paediatric Active Enhanced Diseases Surveillance. Elliott E, Booy R, McIntyre P, Zurynski Y, Buttery J, Richmond P, Gold M, Marshall H, Royle J, Wood N.

PAEDS contribution to the Global Vaccine Safety Surveillance Collaborative

This year saw publication of the results of an international study conducted across 10 countries that assessed the risk of Guillain–Barré syndrome (GBS) following pandemic influenza vaccination (Dodd et al, *Vaccine* 2013). Results showed a very small increased risk of developing GBS in the 6 weeks post vaccination. This study was conducted via a new WHO-led global collaboration for the assessment of vaccine safety in which a number of PAEDS members are involved. PAEDS utilised our existing surveillance to capture GBS cases for a 12-month period across 2009 and 2010, and together with a GBS study that was conducted in Victoria (published in Crawford et al, *MJA* 2012), contributed 60 cases from Australia to the international study. This is another important example of how the PAEDS network can respond quickly to provide internationally important data and collaborate on a wide scale.

HOW DOES PAEDS WORK?

Dedicated and experienced research nurses are employed specifically to conduct PAEDS surveillance work at each hospital site. They scan ED and hospital admission records and other sources, such as microbiology and radiology records each day, to detect cases that potentially fulfil the criteria for the conditions under active surveillance. Our PAEDS nurses obtain consent for inclusion of the child's details in PAEDS during or shortly after the child's hospital presentation and we have a very high consent rate. Clinical data and immunisation history (verified on the ACIR) relevant to the child's condition, are recorded in a de-identified database at each hospital and then securely transmitted on a weekly basis to the PAEDS coordinating centre main database. PAEDS investigators at each site clarify clinical case presentations and liaise with hospital clinicians and laboratories to ensure surveillance is optimal. Epidemiologic analysis is routinely conducted to review and answer study questions on each condition. Where relevant, clinical specimens taken for patient management may be analysed further – such as genotyping of varicella-zoster virus and *B. pertussis.*

In 2013, PAEDS is moving to a new and exciting web-based data management system called "WebSpirit". This new platform, developed and supported by the Paediatric Trials Network Australia, will enable PAEDS data to be entered via a secure web portal by all centres around Australia, thereby avoiding the previously cumbersome task of exporting and importing data to the master database. The system includes quality assurance and monitoring features and user-friendly data extraction facilities. The system is being developed by the coordinating team at CHW and is estimated to go live by the end of the year.

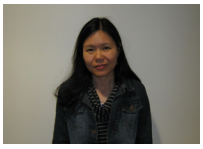
WELCOME NEW STAFF

The PAEDS network welcome **Prof Cheryl Jones** and **Dr Philip Britton** who are involved in the NSW pilot surveillance on encephalitis and planned roll-out of this across the network.

We also welcome some other new members:

Sonia Dougherty, originally from NZ, is a Registered Nurse with postgraduate qualifications. She has a background in mental health, paediatrics and research and is passionate about public health issues and preventative medicine. After spending 5 years in Melbourne working as a research nurse for the Baker IDI Heart and Diabetes Research Institute, craving the warmer weather and a more relaxed lifestyle, she moved to Brisbane with her family where PAEDS came to life.

Karen Orr is a Clinical Nurse Consultant who has completed post-graduate qualifications and experience in immunisation and paediatrics. She joined the National Centre for Immunisation Research and Surveillance in 2013 after 12 years of experience as Immunisation Coordinator for the South Eastern Sydney Public Health Unit. Karen's current role with PAEDS is in the follow up of children following febrile convulsions.



Dr Lieu Trinh has a PhD in Clinical Epidemiology. Her previous studies have been in the area of antenatal care, sexual and reproductive health and quality use of medicines. She also has experience with data linkage. Lieu has recently joined NCIRS and will be assisting PAEDS with data analysis.

PAEDS PUBLICATIONS*

- Zurynski Y, McIntyre P, Booy R, Elliott EJ, on behalf of the PAEDS Investigators Group. Paediatric Active Enhanced Disease Surveillance: a new surveillance system for Australia. *Journal of Paediatrics and Child Health* 2013;49:588-94.
- Marshall HS, McIntyre P, Richmond P, Buttery JP, Royle JA, Gold MS, Wood N, Elliott EJ, Zurynski Y, Toi CS, Dwyer DE, Booy R. Changes in patterns of hospitalized children with varicella and of associated varicella genotypes after introduction of varicella vaccine in Australia. *Pediatric Infectious Disease Journal* 2013;32:530-7.
- Esterman EE, Lahra MM, Zurynski YA, Booy R, Elliott EJ. Influenza infection in infants aged <6 months during the H1N1-09 pandemic: a hospital-based case series. *Journal of Paediatrics and Child Health* 2013;49:635-40.
- Dodd CN, Romio SA, Black S, Vellozzi C, Andrews N, Sturkenboom M, Zuber P, Hua W, Bonhoeffer J, Buttery J, Crawford N, Deceuninck G, de Vries C, De Wals P, Garman P, Gimeno MV, Heijbel H, Hur K, Hviid A, Kelman J, Kilpi T, Chuang SK, Macartney K, Rett M, Lopez-Callada VR, Salmon D, Sanchez FG, Sanz N, Silverman B, Storsaeter J, Thirugnanam U, van der Maas N, Yih K, Zhang T, Izurieta H. International collaboration to assess the risk of Guillain Barré syndrome following influenza A (H1N1) 2009 monovalent vaccines. *Vaccine* 2013;31:4448-58.
- Campbell S, Crawford NW. Varicella infection in infants less than 12 months. *Vaccine.* 2013;31:295-6.
- Crawford NW, Cheng A, Andrews N, Charles PG, et al. Guillain-Barré syndrome following pandemic (H1N1) 2009 influenza A immunisation in Victoria: a self- controlled case series. *Medical Journal of Australia.* 2012;197:574-8.
- Khandaker G, Zurynski Y, Buttery J, Marshall H, Richmond PC, Dale RC, Royle J, Gold M, Snelling T, Whitehead B, Jones C, Heron L, McCaskill M, Macartney K, Elliott EJ, Booy R. Neurologic complications of influenza A(H1N1)pdm09: surveillance in 6 pediatric hospitals. *Neurology* 2012;79:1474-81.
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- Elliott EJ, Zurynski YA, Walls T, Whitehead B, Gilmour R, Booy R. 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;48:235-41.
- Buttery JP, Danchin MH, Lee KJ, Carlin JB, McIntyre PB, Elliott EJ, Booy R, Bines JE, for the PAEDS/APSU Study Group. Intussusception following rotavirus vaccine administration: post-marketing surveillance in the National Immunization Program in Australia. *Vaccine* 2011;29:3061- 6.
- Khandaker G, Zurynski Y, Lester-Smith D, Kesson A, Heron L, Dwyer DE, Elliott EJ, Booy R. Clinical features, oseltamivir treatment and outcome in infants aged <12 months with laboratory-confirmed influenza A in 2009. *Antiviral Therapy* 2011;16:1005-10.
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- Elliott EJ. Pregnancy and pandemic flu [comment on Hewagama S, et al. 2009 H1N1 influenza A and pregnancy outcomes in Victoria, Australia. Clin Infect Dis. 2010;50:686-90]. *Clinical Infectious Diseases* 2010;50:691-2.

***This list includes all primary PAEDS publications and selected studies that include PAEDS data.**

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