

AUSTRALIAN PAEDIATRIC SURVEILLANCE UNIT ANNUAL REPORT, 2008 AND 2009

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Background

National active surveillance of rare diseases of childhood, including infectious and vaccine preventable diseases, genetic disorders, childhood injuries and mental health conditions is conducted by the Australian Paediatric Surveillance Unit (APSU). The study of communicable and vaccine-preventable diseases is supported in part by the Department of Health and Ageing through its communicable diseases program. In 2008 and 2009, APSU conducted national surveillance for the following infectious diseases or vaccine preventable conditions:

- acute flaccid paralysis (AFP): a major clinical presentation of poliomyelitis;¹
 - acute rheumatic fever (ARF): occurs due to group A streptococcal (GAS) infection and repeat GAS infections, if not treated, may lead to heart valve damage and rheumatic heart disease;²
 - congenital cytomegalovirus infection: a leading cause of congenital abnormality in Australia;³
 - congenital rubella: an extremely rare condition leading to birth defects;⁴
 - perinatal exposure to HIV: the most frequently reported source of HIV infection in Australian children;⁵
 - neonatal herpes simplex virus (HSV) infection: a very rare, but serious infection that may cause chorioretinitis, intracerebral calcification and birth defects;
 - neonatal group B streptococcus (GBS) infection: the most common cause of life threatening infections in neonates;
 - intussusception: the most common cause of bowel obstruction in infants and young children that has been associated with rotavirus infection and previous rotavirus vaccines;^{6,7}
 - congenital and neonatal varicella: a rare infection that may result in birth defects.⁸
- severe complications of varicella: a range of rare but serious complications; genotyping of samples will inform future vaccine and policy development;⁸ and
 - severe complications of influenza infection: complications such as pneumonia, encephalitis, myocarditis, rhabdomyolysis, disseminated coagulopathy, transverse myelitis, polyneuritis and Guillain-Barré syndrome have a significant burden among children aged less than 15 years.⁹

Methods

The APSU study protocols are developed with collaborating investigators and/or institutions that have expertise in each of the conditions studied. Detailed protocols including case definitions for each condition under surveillance and contact details of the expert investigators for each condition are available at www.apsu.org.au. The APSU sends monthly report cards listing the conditions under surveillance to approximately 1,300 paediatricians and child health clinicians around Australia. Report cards are returned whether the clinician has a case to report or not, and the rate of returned report cards provides a measure of participation. In 2009 approximately 80% of clinicians chose to receive and respond to the APSU report card via e-mail. All reported cases are followed-up by a questionnaire requesting de-identified data on the child's clinical presentation, treatment and short-term outcome. Clinicians were asked to return all questionnaires by fax as soon as children who met criteria for severe complications of influenza were identified during 2008 surveillance for seasonal influenza and during 2009 surveillance for seasonal and pandemic influenza.

The APSU aims to provide epidemiological information that is representative of the Australian child population and maximal case ascertainment is a high priority. Despite a representative mailing list (92% of all paediatricians in active clinical practice in Australia participate in monthly surveillance) and high response rates (average 96% per annum since 2000), complete case ascertainment is unlikely.¹⁰ This is particularly relevant in remote communities where children have limited access to paediatricians or when hospital admission is brief.

However, for most conditions studied by the APSU no alternative national data are available to allow an estimate of completeness of ascertainment. The APSU encourages the use of complementary data sources where available and reporting by a range of specialists to maximise case identification.^{10,11} Reported rates for conditions ascertained through the APSU therefore represent a minimum estimate of the incidence of these conditions in the relevant Australian child populations.

To further enhance surveillance for childhood conditions where hospital stays are minimal; where biological samples are required; and where a detailed history might be needed from parents or caregivers, the APSU, in collaboration with the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, initiated and coordinates the Paediatric Active Enhanced Disease Surveillance (PAEDS) system.¹² This is a hospital-based surveillance system reliant on active case ascertainment by specialist surveillance nurses. Since August 2007, PAEDS has operated in 4 tertiary paediatric hospitals in 4 states: New South Wales, Victoria, South Australia, and Western Australia (www.apsu.org.au)

All data are provided after review by the expert investigators responsible for each surveillance study and are accurate as at May 2010. However, it is possible that some notifications may be reclassified at a later date as additional clinical data for existing notifications, or additional notifications, are received.

Results

In 2008 and 2009, 1,318 and 1,340 clinicians respectively participated in the monthly surveillance of the 11 communicable or vaccine preventable diseases under surveillance. Consistent with previously reported high rates of participation by paediatricians,¹⁰ the report card return rate was 94% in 2008 and 91% in 2009. Enhanced data on diagnosis, clinical management and short-term outcome were available for more than 85% of all cases notified. The Table shows the number of confirmed cases ascertained in 2008 and 2009 and for the whole study period, and the reported rate per 100,000 of child population for each condition.

Acute flaccid paralysis

Australia reported a non-polio AFP rate of 1.5 per 100,000 children aged less than 15 years in 2008 and 1.2 per 100,000 in 2009, exceeding the World Health Organization (WHO) AFP

surveillance target of 1 case per 100,000. This is due to additional cases reported via the PAEDS system developed jointly by the APSU and the National Centre for Immunisation Research and Surveillance. The most common diagnosis of non-polio AFP was Guillain-Barré syndrome (39% in 2008 and 34% in 2009). Adequate faecal specimens (2 within 14 days of onset of paralysis) were obtained for 31% of cases, which was well below the 80% WHO target. The importation of a type 1 wild poliovirus in an adult into Australia in 2007¹⁴ and the continued detection of cases of wild polio internationally, highlight the need for continued national surveillance.

Acute rheumatic fever

Between October 2007 and December 2009 cases of ARF were reported in all states and territories of Australia, except for Tasmania, suggesting the need for a national approach to the control of ARF and rheumatic heart disease. Almost all children were born in Australia (98%); 1 child was born in New Zealand and one in Papua New Guinea. The majority of children with ARF were Aboriginal or Torres Strait Islander, however, a small number of Caucasian children were reported from 5 states (New South Wales, Victoria, South Australia, Western Australia, and Queensland). These include the southern states where ARF is not recognised as a priority. Approximately 70% of all children reported resided in small rural towns or remote areas, with approximately 30% residing in urban or suburban areas.

Congenital cytomegalovirus infection

Congenital cytomegalovirus (cCMV) is the most common infectious cause of congenital malformations in Australia. APSU data show that cCMV infection is not associated with maternal illness in approximately one-third of cases, and should be considered regardless of maternal history.¹⁵ cCMV remains under-diagnosed. Although most cases are diagnosed by urine culture, use of polymerase chain reaction for urinary screening for CMV may increase diagnostic yield. Universal neonatal hearing screening programs may also help identify new cases. The total of 159 cases confirmed by the end of 2009 includes 6 cases that were notified between 2004 and 2007, but only confirmed recently.

Congenital rubella (with defects)

In 2008 there were three notifications, of which one was confirmed as a case. This was a child born to an immigrant woman from India whose

Table: Confirmed cases identified for 2008 and 2009 and for the total study period to December 2009 including reported rates per 100,000 of the relevant child population

Condition	Date study commenced	Questionnaire response (%) for total study period	Number of confirmed cases		Reported rate (per 10 ⁵)		Number of confirmed cases for total study period	Reported rate for total study period (per 10 ⁵ per annum)*
			2008	2009	2008	2009		
Acute flaccid paralysis (AFP)	March 1995	92	63†	50†	1.5‡	1.2‡	560†	0.9‡
Congenital cytomegalovirus	Jan 1999	74	34	32	11.5§	10.6§	159	5.5§
Acute rheumatic fever	October 2007	88	48	40	1.2‡	1.0‡	104	1.0‡
Congenital rubella (with defects)	May 1993	95	1	0	0.02	0.0	51	0.1
Perinatal exposure to HIV	May 1993	87	36	33	12.1§	11.0§	424	9.8§
Neonatal herpes simplex virus infection	Jan 1997	96	9	10	3.0§	3.3§	117	3.4§
Neonatal B group streptococcus Infection¶	July 2005	82	18	-	12.1§	-	150	18.0§
Congenital varicella	May 2006	100	0	0	0.0	0.0	2	0.2§
Neonatal varicella	May 2006	77	0	1	0.0	0.3§	15	1.5§
Severe complications of varicella	May 2006	69	7	4	0.2‡	0.1‡	30	0.2‡
Intussusception	May 2007	80	69	40	12.2**	6.8**	154	10.8**
Severe complications of influenza	July to Sep 2008	100	59	-	5.7‡	-	59	N/A
	May to Sep 2009	97	-	100	-	9.5‡	100	N/A

* All reported rates based on child population estimates published by the Australian Bureau of Statistics.¹³

† All cases of AFP reported via the Australian Paediatric Surveillance Unit or the Paediatric Active Enhanced Disease Surveillance system that have been classified by the Polio Expert Committee were 'non-polio AFP' according to World Health Organization criteria.

‡ Based on population of children aged less than 15 years.

§ Based on number of births.

|| Based on population of children aged less than 16 years.

¶ Group B streptococcus sepsis study finished in June 2008.

** Based on number of children aged 24 months or younger.

N/A Due to the limited surveillance period a reported rate was not calculated.

vaccination history could not be confirmed. Serological testing was not performed. In 2009 there were no notifications. The risk of congenital rubella remains, particularly among immigrant women born in countries with poorly developed vaccination programs, justifying continued surveillance.⁴ Such women should have serological testing for rubella after arrival in Australia, and vaccination when appropriate. For women with no prior rubella immunity, travel to rubella-endemic countries in the first trimester poses a risk of congenital rubella to the foetus. Perinatal exposure to HIV and HIV infection

In 2008 there were 36 perinatal exposures to HIV in Australia, and 33 in 2009. Antenatal diagnosis of the mother's HIV infection and use of interventions including antiretroviral treatment during pregnancy, caesarean delivery and avoidance of breastfeeding, continues to minimise the risk of mother-to-child HIV transmission.⁵

Neonatal herpes simplex virus infection

A significant number of cases of neonatal herpes simplex virus (HSV) infection continue to be confirmed, with a preponderance in females. Presentation with skin, eye and mouth disease occurred in half of confirmed cases, whereas disseminated HSV infection occurred in a quarter of confirmed cases. Among cases with disseminated infection, more than half were diagnosed with encephalitis and a third with pneumonitis. More than 20% of confirmed cases had died before notification, with almost half of these diagnosed at post-mortem examination.

Intussusception

The small number of cases ascertained suggests under-reporting and the APSU data will be greatly supplemented by cases identified by PAEDS. There was a small number of cases of intussusception observed in infants who received a rotavirus vaccine but a temporal association between either Rotarix[®] or RotaTeq[®] vaccines and intussusception could not be confirmed using APSU data alone. Accepting the limitation of under-reporting of intussusception and limited vaccination data on confirmed cases, ongoing intussusception surveillance is better justified through the PAEDS system rather than the APSU, to further explore in detail any possible relationship between the number of observed intussusception cases, the age at vaccination, dose and vaccine given.

Neonatal and infant *Streptococcus agalactiae* (group B streptococcus) sepsis

The number of notifications received over the total study period are consistent with other available data. Over half (59%) of the confirmed cases of *Streptococcus agalactiae* group B (GBS) sepsis had early onset disease (EOD: at younger than 8 days of age). Pre-term birth was more common in mothers of infants with late onset disease (LOD: at 8 days of age or older) than in mothers of infants with EOD (58% versus 28%). Infant death was more common in those with LOD than in those with EOD (8% versus 4%). A detailed final report is in preparation for peer review publication by the investigators for this study.

Severe complications of varicella infection

In 2008, 7 children hospitalised with severe complications of varicella were reported, compared with 4 cases in 2009. The complications in 2008 included septic arthritis, focal purulent collection, osteomyelitis, and ataxia, while in 2009 there were 3 cases of ataxia and one of bacteraemia. Median stay in hospital was 12.5 days in 2008 compared with 3.5 days in 2009. All of the reported children were unvaccinated and family members were the infecting contacts.

Congenital and neonatal varicella

There were no cases of neonatal varicella reported in 2008 and only 1 case in 2009. This was an infant born to a woman who experienced symptoms of varicella infection 1 day after delivery. The infecting contact was identified as the woman's husband who had been told that the illness he was experiencing was not chicken pox. No cases of congenital varicella were reported in 2008 and 2009.

Severe complications of influenza

In 2008, influenza B was the dominant influenza type among the 59 children hospitalised with severe complications of influenza and reported to APSU. In 2009, the dominant strain was pandemic influenza H1N1 2009 among 100 children reported to APSU. A range of complications were reported with x-ray-confirmed pneumonia the most common during both years. However, in 2009 serious complications such as encephalitis and rhabdomyolysis were more common than in 2008. Admission to paediatric intensive care was more common in 2009 (38%) compared with 2008 (29%) and 7 (7%) of the reported children died in 2009 compared with only 1 child (2%)

in 2008. Vaccination for seasonal influenza was uncommon during both 2008 and 2009, even among children with pre-existing chronic disorders who were eligible for vaccination according to current recommendations.

Conclusions and future directions

APSU data contribute significantly to the national surveillance effort, providing valuable information for clinicians, policymakers and the community.^{10,11,16} The APSU is often the only source of national data that includes clinical and/or laboratory details, and data on both inpatients and outpatients.^{10,11}

After demonstrating the feasibility of the APSU to respond rapidly to an outbreak of influenza in 2007, it has conducted surveillance for seasonal influenza in 2008 and surveillance for both seasonal and pandemic influenza in 2009. The APSU will again conduct surveillance for the severe complications of influenza from June to September in 2010.

A surveillance study of juvenile respiratory papillomatosis is planned for late 2010. Respiratory papillomatosis is a rare but devastating condition in children aged less than 12 years, and is thought to be perinatally transmitted.¹⁷ Juvenile respiratory papillomatosis is difficult to treat, recurrences are common and may lead to airway obstruction. The human papillomavirus (HPV) vaccine, which protects against HPV6 and HPV11, is currently nationally recommended and it is hoped that the rates of juvenile papillomatosis among young children will reduce with increased vaccination rates.

The APSU continues to provide useful data and clinical and public health insights relating to infectious diseases in Australian children. Ongoing surveillance through the PAEDS system will continue to complement the work of the APSU, and both APSU and PAEDS provide a platform for the rapid response to potential emerging infectious diseases threatening Australian children.

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References

1. Roberts JA, Grant KA, Yoon YK, Polychronopoulos S, Ibrahim A, Thorley BR. Annual report of the Australian National Poliovirus Reference Laboratory, 2008. *Commun Dis Intell* 2009;33(3):291–297.

2. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis* 2005;5(11):685–694.
3. Rawlinson WD, Hall B, Jones CA, Jeffery HE, Arbuckle SM, Graf N, et al. Viruses and other infections in stillbirth: what is the evidence and what should we be doing? *Pathology* 2008;40(2):149–160.
4. Gidding HF, Young M, Pugh R, Burgess M. Rubella in Australia: can we explain two recent cases of congenital rubella syndrome? *Commun Dis Intell* 2003;27(4):537–540.
5. McDonald AM, Zurynski YA, Wand HC, Giles ML, Elliott EJ, Ziegler JB, et al. Perinatal exposure to HIV among children born in Australia, 1982–2006. *Med J Aust* 2009;190(8):416–420.
6. Bines JE, Patel M, Parashar U. Assessment of postlicensure safety of rotavirus vaccines, with emphasis on intussusception. *J Infect Dis* 2009;200(Suppl 1):S282–S290.
7. Haber P, Patel M, Izurieta HS, Baggs J, Gargiullo P, Weintraub E, et al. Postlicensure monitoring of intussusception after RotaTeq vaccination in the United States, 1 February 2006, to 25 September 2007. *Pediatrics* 2008;121(6):1206–1212.
8. Peadon E, Burgner D, Nissen M, Buttery J, Zurynski Y, Elliott E, et al. Case for varicella surveillance in Australia. *J Paediatr Child Health* 2006;42(11):663–664.
9. Zurynski YA, Lester-Smith D, Festa MS, Kesson AM, Booy R, Elliott EJ. Enhanced surveillance for serious complications of influenza in children: role of the Australian Paediatric Surveillance Unit. *Commun Dis Intell* 2008;32(1):71–76.
10. He S, Zurynski YA, Elliott EJ. Evaluation of a national resource to identify and study rare diseases: The Australian Paediatric Surveillance Unit. *J Paediatr Child Health* 2009;45(9):498–504.
11. Zurynski YA, Peadon E, Bower C, Elliott E. Impacts of national surveillance for uncommon conditions in childhood. *J Paediatr Child Health* 2007;43(11):724–731.
12. Pym M, Adams J, Booy R, Buttery J, Elia S, Elliott E, et al. The development and trial of paediatric active enhanced disease surveillance (PAEDS): A new surveillance mechanism for Australia. *J Paediatr Child Health* 2008;44:A16.
13. Australian Bureau of Statistics. Australian Demographic Statistics. September quarter 2009. Canberra: Australian Bureau of Statistics; 2010. Catalogue no: 3101.0
14. Carnie JA, Lester R, Moran R, Brown L, Meagher J, Roberts JA, et al. Public health response to imported case of poliomyelitis, Australia, 2007. *Emerg Infect Dis* 2009;15(11):1733–1737.
15. Howard J, Hall B, Brennan LE, Arbuckle S, Craig ME, Graf N, et al. Utility of newborn screening cards for detecting CMV infection in cases of stillbirth. *J Clin Virol* 2009;44(3):215–218.
16. Grenier D, Elliott EJ, Zurynski YA, Pereira RR, Preece M, Lynn R, et al. Beyond counting numbers: Public health impacts of national paediatric surveillance units. *Arch Dis Child* 2007;92(6):527–533.
17. Schaffer A, Brotherton J, Booy R. Do human papillomavirus vaccines have any role in newborns and the prevention of recurrent respiratory papillomatosis in children? *J Paediatr Child Health* 2007;43(9):579–580.