

# AUSTRALIAN PAEDIATRIC SURVEILLANCE UNIT

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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 (DoHA). In addition to conducting ongoing surveillance, the APSU has demonstrated readiness to respond rapidly to emerging diseases, epidemics and pandemics that have severe impacts in children.<sup>1</sup> In 2010, the APSU conducted national surveillance for rare infections or vaccine preventable conditions resulting in significant impacts on the child and family. The conditions included: acute flaccid paralysis (AFP), acute rheumatic fever (ARF), congenital cytomegalovirus infection (cCMV), congenital rubella, perinatal exposure to HIV, neonatal herpes simplex virus (HSV) infection, congenital and neonatal varicella, severe complications of varicella, and severe complications of influenza infection. Surveillance for intussusception (IS) was conducted in response to the introduction of new rotavirus vaccines in Australia as IS was initially linked with the receipt of older rotavirus vaccines.<sup>2</sup> The APSU, together with the National Centre for Immunisation Research and Surveillance (NCIRS) coordinates the Paediatric Active Enhanced Disease Surveillance (PAEDS) system. PAEDS is a hospital based surveillance mechanism including four tertiary paediatric hospitals in four states, and complements surveillance conducted by the APSU for AFP and IS.<sup>3</sup>

### Methods

The APSU study protocols and case definitions are developed in collaboration with groups of investigators who have expertise in each of the conditions under surveillance. Detailed protocols, case definitions and contact details of the expert investigators for each condition are available at [www.apsu.org.au](http://www.apsu.org.au) The APSU sends monthly report cards listing the conditions under surveillance to approximately 1,300 paediatricians and other 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.<sup>1,4</sup> In 2010,

approximately 85% of clinicians chose to receive and respond to the APSU report card via email. All reported cases are followed up by a questionnaire requesting de-identified data on the child's demographics, clinical presentation, treatment and short-term outcome. During surveillance for severe complications of influenza, clinicians were asked to return all questionnaires by fax as soon as children were identified, ensuring timely data collection. All questionnaires are reviewed by the study investigators before classification according to case definition criteria.

It is estimated that 92% of all paediatricians who have graduated with a Fellowship of the Royal Australasian College of Physicians (FRACP) and who are in active clinical practice in Australia, participate in the APSU. Lists of clinicians are updated to include new FRACP graduates and the APSU clinician database is constantly updated as clinicians change contact details, move out of clinical practice or retire. Despite high response rates to the report cards (average 96% per annum since 2000) complete case ascertainment is unlikely.<sup>1,4</sup> This is particularly relevant in remote communities where children have limited access to paediatricians or when hospital admission is brief and the child may not be seen by a paediatrician. The APSU encourages the use of complementary data sources where available, and reporting by a range of specialists to maximize case identification.<sup>1,4</sup> 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 as reported by the Australian Bureau of Statistics.<sup>5</sup>

The PAEDS<sup>3</sup> system developed by the APSU and the NCIRS complements data collected for several conditions, including AFP and IS. PAEDS enhances the surveillance effort, especially where hospital stays are minimal, where biological samples are required, and where a detailed history might be needed from parents or caregivers.

### Results

In 2010, 1,330 clinicians participated in APSU surveillance. Consistent with previously reported high rates of participation, the report card return rate was 95%. Enhanced data about diagnosis, clinical management and short-term outcome were

available for more than 90% of all notified cases. The reported rate per 100,000 per annum of the relevant child population for each condition was calculated for 2010 as was an overall annual rate for the whole study period (Table).

All data are provided after review by the expert investigators responsible for each condition and are accurate as at May 2011. However, it is possible that some notifications may be reclassified at a later date, additional clinical data for existing notifications, or

additional late notifications may be received and this will have an effect on final case counts reported over the last 12 months.

### Acute flaccid paralysis

The introduction of the PAEDS hospital-based surveillance system has strengthened Australia's AFP surveillance for case ascertainment and has contributed to Australia achieving the World Health Organization (WHO) surveillance target of a non-polio AFP rate of  $\geq 1$  per 100,000 children

**Table: Confirmed cases identified in 2010 and for the total study period, and reported rates per 100,000 of the relevant child population**

Condition	Date study commenced	Questionnaire response rate (%)	Number of confirmed cases 2010	Reported rate for 2010 (per 100,000)	Number of confirmed cases for total study period*	Reported rate for total study period (per 100,000 per annum)†
Acute flaccid paralysis	Mar 1995	100	41*	1.0‡	598*	0.9‡
Congenital cytomegalovirus	Jan 1999	93	31	10.5§	191	5.8§
Acute rheumatic fever	Oct 2007	96	39	0.9‡	151	1.1‡
Congenital rubella (with defects)	May 1993	No notifications	Nil	Nil	50	0.1
Perinatal exposure to HIV**	May 1993	97	52	17.6§	437	9.2§
HIV infection**			5	1.7	77	1.6
Neonatal herpes simplex virus infection	Jan 1997	100	4	1.3§	121	3.2§
Congenital varicella	May 2006	No notifications	Nil	Nil	2	0.2§
Neonatal varicella	May 2006	50¶	1	0.3§	15	1.3§
Severe complications of varicella	May 2006	92	9	0.2‡	45	0.2‡
Intussusception	May 2007 to May 2010	88	9	2.5***	163	5.2**
Severe complications of Influenza	Influenza season each year since 2008††	90	25	1.8‡	179	1.8‡

\* Includes all cases of acute flaccid paralysis (AFP) reported via the Australian Paediatric Surveillance Unit or the Paediatric Active Enhanced Disease Surveillance. All have been classified by the Polio Expert Panel as 'non-polio AFP' according to World Health Organization criteria.

† Includes 3 cases due to perinatal exposure and 2 cases due to exposure during medical procedures abroad.

‡ Based on population of children aged < 15 years.

§ Based on number of births.

|| Based on population of children aged < 16 years.

¶ Two notifications only; one questionnaire received.

\*\* Based on number of children aged  $\leq 24$  months.

†† Influenza surveillance was undertaken each year since 2008 during the influenza season, July to September except in the pandemic year (2009) when surveillance occurred from June to October.

All the figures were correct at the time of submission. As additional information becomes available cases may be reclassified for the current year and for previous years.

<15 years in 2010 for the third year in a row. After review of all cases by the Polio Expert Panel, the most common diagnoses of non-polio AFP was Guillain-Barré syndrome (36%) and acute disseminated encephalomyopathy (12%). Faecal specimens (2 within 14 days of onset of paralysis) were taken for 34% of cases however, only 22% were adequate for analysis by the National Polio Reference Laboratory. This is well below the WHO target, which is set at 80% of all reported cases—a target that is seldom achieved in developed countries. The importation of a type 1 wild poliovirus in an adult into Australia in 2007<sup>6</sup> and the continued detection of cases of wild polio internationally highlight the need for continued national surveillance to keep Australia polio-free.

### **Acute rheumatic fever**

Between October 2007 and December 2010, 151 confirmed cases of ARF were reported from all states and territories of Australia, except for Tasmania and the Australian Capital Territory, suggesting the need for a national approach to the control of ARF and rheumatic heart disease. The majority of children identified as Aboriginal or Torres Strait Islander (87%), however there were 10 Caucasian children and 8 children of Pacific Islander ethnicity. A similar breakdown of ethnicity was noted in an audit of a tertiary children's hospital in Sydney.<sup>7</sup> Approximately 66% of all children residing in small rural towns or remote areas, with the other 34% resided in urban or suburban areas. The most common presenting symptoms in children diagnosed with ARF included carditis, polyarthritis and fever. All children were prescribed long-term prophylactic treatment with Benzathine Penicillin G to prevent recurrences and progression to rheumatic heart disease (RHD). The newly established organisation, Rheumatic Heart Disease Australia (<http://www.rhdaustralia.org.au/>) will further develop a national approach to ARF and RHD control in Australia.

### **Congenital cytomegalovirus infection**

cCMV is the most common infectious cause of congenital malformations in Australia.<sup>8</sup> 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.<sup>8</sup> There were 191 cases confirmed by the end of 2010, however cCMV remains under-diagnosed. Polymerase chain reaction analysis of newborn screening cards may retrospectively identify additional cases to further describe the impact of cCMV. Universal neonatal hearing screening programs may also help identify new cases. Despite most infants (90%) being symptomatic very few are treated with antivirals (8%).<sup>9</sup> This study continues to inform the ongoing debate about the need for routine screening of mothers and infants.

### **Congenital rubella (with defects)**

There were no notifications of congenital rubella in 2010 supporting the effectiveness of the rubella vaccination program. In 2008 and 2009 there were 3 notifications of congenital rubella to the APSU. At the time of publication in 2010, detailed clinical data were not yet available,<sup>10</sup> however it is now known that two of these notifications were prevalent rather than incident cases. The other child, notified in 2008 was confirmed as an incident case of congenital rubella. The child was born in Australia to an immigrant woman from India whose vaccination history was unclear. The risk of congenital rubella remains, particularly among immigrant women born in countries with poorly developed vaccination programs, justifying continued surveillance.<sup>11</sup> Such women should have serological testing for rubella after arrival in Australia, and vaccination when appropriate. Travel to rubella endemic countries in the first trimester by women with no prior rubella immunity poses a risk of congenital rubella to the foetus.

### **Perinatal exposure to HIV and HIV infection**

In 2010 there were 52 cases of perinatal exposure to HIV, three of which acquired HIV infection perinatally. In addition, there were 2 children with HIV infection who were exposed to contaminated blood products overseas. HIV infection was diagnosed prior to, or at the birth of the child in 46 (85.5%) of the mothers, enabling use of interventions including use of antiretroviral treatment (n=45), and avoidance of breast-feeding (n=43). HIV infection among children remains a rare occurrence in Australia, however, the number of reported cases of perinatal exposure has increased and may possibly be attributed to the availability of interventions to minimise the risk of mother-to-child transmission among women who know their HIV status prior to pregnancy. Of concern is the small number of mothers whose HIV infection was not known until after the birth of their child, precluding the use of interventions to minimise the risk of mother-to-child HIV transmission.<sup>12,13</sup>

### **Neonatal herpes simplex virus infection**

Significant numbers of cases of neonatal HSV continue to be confirmed, with preponderance in female infants. The incidence over the last 14 years has remained steady, however there is a trend to improved survival of infants. This may be due to changes to recommendations for treatment with the use of higher doses of antiviral agents recommended since 2003.<sup>14</sup> Furthermore, the method of diagnosis has changed over the last 14 years with a move to more sensitive molecular techniques, which may potentially lead to earlier accurate diagnosis enabling earlier treatment. This study has also demonstrated

a change in the HSV strain causing infection in recent years, with an increasing number of cases due to HSV-1, whereas previously HSV-2 was mostly detected in cases of neonatal HSV in Australia.<sup>15</sup> There is a need for ongoing surveillance to describe potential relationships between early detection and treatment with outcome.

### **Intussusception**

There were 162 cases reported to the APSU during the period May 2007 to May 2010. Adequate information about immunisation status was available for only 80 cases, 14 of whom received a rotavirus vaccine within 14 days of developing IS. As the number of reports through the APSU was very small, the data were combined with cases collected via the PAEDS system. The combined data showed that there was a slightly elevated risk of IS following the 1st dose of a rotavirus vaccine, among young infants aged 1–2 months.<sup>2</sup>

### **Severe complications of varicella infection**

In 2010, 9 children hospitalised with severe complications of varicella were reported. The complications included septic shock, focal purulent collection, and ataxia. Median stay in hospital was 8 days and 6 children were admitted to a paediatric Intensive Care Unit. All of the reported children were unvaccinated and most of the infecting contacts were close family members or other children in the school and pre-school setting.

### **Congenital and neonatal varicella**

There was only 1 case of neonatal varicella reported in 2010. The incidence rate of neonatal varicella for the current surveillance study period (2006–2010) was 1.3 per 100,000 live births per annum—a considerable reduction when compared with the previous surveillance study conducted by the APSU during 1995–97, when the incidence was estimated at 5.8 per 100,000 live births per annum.<sup>15</sup> No cases of congenital varicella have been reported since 2008, supporting the effectiveness of the varicella vaccination program, which began at the end of 2005.

### **Severe complications of influenza**

In 2010, 25 children hospitalised with severe complications of influenza were reported to the APSU and most (68%) had influenza A H1N1 2009, 24 had influenza A but not further subtyped and 8% had influenza B. In contrast, in 2009, 100 children with severe complications were reported to the APSU; and 77% had pandemic influenza H1N1 2009, but H3N2 was also detected. A range of complications were reported with x-ray confirmed pneumonia

most common during both years. However, in 2009 serious complications such as encephalitis and rhabdomyolysis were more common than in 2010. Although a smaller number of children were reported in 2010 compared with 2009, a similar proportion was admitted to a paediatric Intensive Care Unit (44% in 2010 compared with 38% in 2009). There were 2 deaths in 2010 compared with 7 deaths in 2009. Vaccination for seasonal influenza was uncommon in 2010 even in the 2 children with pre-existing chronic disorders and eligible for free vaccination.<sup>17</sup>

## **Conclusions and future directions**

APSU data contribute significantly to the national surveillance effort, providing valuable information for clinicians, policymakers and the community.<sup>9,10,16</sup> The APSU is often the only source of national data that includes clinical and/or laboratory details, and data on both inpatients and outpatients.<sup>9,10</sup>

After demonstrating the feasibility of the APSU to respond rapidly to an outbreak of influenza in 2007, the APSU has conducted surveillance for influenza in 2008, 2009, and 2010, providing a unique and detailed dataset on severe complications of influenza in children and a publication describing the impact of the severe complications of influenza from 2008 to 2010 is in preparation. The APSU will once again conduct surveillance for the severe complications of influenza from June to September 2011.

Surveillance for juvenile respiratory papillomatosis will commence in the second half of 2011. Respiratory papillomatosis is a rare but devastating condition in children aged less than 12 years, and is thought to be perinatally transmitted.<sup>17</sup> 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.

APSU currently conducts surveillance for other rare conditions of childhood ([www.apsu.org.au](http://www.apsu.org.au)) and is also involved in the study of impacts of rare diseases

on families, clinicians and health services. This endeavour will be further supported by an Australian Research Council Linkage Grant (LP110200277).

The APSU has advocated for the development and adoption of a coordinated national plan for rare diseases in Australia and drafted a rationale for such a plan ([www.apsu.org.au](http://www.apsu.org.au)) with the support of the Australian Research Alliance for Children and Youth. The APSU collaborated with the Department of Population Genomics, Western Australian Department of Health to organise the *Awakening Australia to Rare Diseases Symposium*, a first national symposium on rare diseases in Australia, held in April 2011 and attended by people affected by rare diseases, patient support groups, researchers, clinicians, government representatives and industry. A significant outcome of the symposium was the establishment of the National Rare Diseases Coordinating Committee, which will advocate for the further development and adoption of a national plan for rare diseases.

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