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Australian Paediatric Surveillance Unit (APSU) Annual Surveillance Report 2019

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Australian Paediatric Surveillance Unit (APSU) Annual Surveillance Report 2019

Suzy M Teutsch, Carlos A Nunez, Anne Morris, Skye McGregor, Jonathan King, Julia ML Brotherton, Daniel Novakovic, Robert Booy, Cheryl A Jones, William Rawlinson, Bruce R Thorley and Elizabeth J Elliott

Abstract

The Australian Paediatric Surveillance Unit (APSU) has been prospectively collecting national data on rare childhood conditions since 1993, with monthly reporting of cases by paediatricians. In this report we describe annual results from studies for ten communicable diseases and complications of communicable diseases that were conducted using APSU surveillance in 2019 and place these in an historic context. Results are reported on acute flaccid paralysis, congenital cytomegalovirus infection, neonatal herpes simplex virus infection, perinatal exposure to HIV, paediatric HIV infection, severe complications of seasonal influenza, juvenile onset recurrent respiratory papillomatosis (JoRRP), congenital rubella syndrome, congenital varicella syndrome and neonatal varicella infection. APSU provides rich clinical data to complement data collected from other surveillance systems and to improve understanding and response to rare childhood infections.

Keywords: Australia, child, public health surveillance, rare diseases, communicable diseases

Introduction

For over 26 years the Australian Paediatric Surveillance Unit (APSU) has conducted national monthly surveillance of rare medical conditions in childhood, including communicable and non-communicable diseases. APSU facilitates surveillance and collection of prospective national data on several conditions simultaneously using an active mechanism, with reporting by paediatricians. Each month paediatricians are prompted to notify newly diagnosed cases of conditions currently under surveillance; those who notify cases are then asked to provide detailed demographic, clinical and outcome data. These unique data have filled knowledge gaps, enabled estimation of disease incidence and analysis of disease trends over time, and contributed to research, clinical practice and policy development.¹ In 2019, APSU conducted surveillance for eight communicable diseases and complications of communicable diseases; the results are detailed in this report.

Characteristics of the APSU surveillance system

The APSU surveillance mechanism is well-established, robust and flexible (Text box 1). APSU is able to respond rapidly to changing public health priorities, such as inclusion in 2008 of a study on severe complications of seasonal influenza surveillance following a surge in childhood admissions and deaths.^{2,3} We maintain currency of the database of contributors through our relationship with the Royal Australasian College of Physicians. Individual clinicians and researchers and research groups may apply for inclusion of a study for APSU surveillance. We convene a national investigator group to develop the study protocol, review and classify cases, analyse and report results. APSU data are collected from metropolitan, rural and regional clinicians, include children seen as both in- and out-patients, are clinically rich, and complement data collected by existing surveillance systems. Electronic reporting and the low

Text box 1. Characteristics of the APSU surveillance system

- Surveillance and research resource available to researchers, research groups nationally
- Targets rare childhood disorders, including communicable and vaccine-preventable disease
- Flexible and responsive to public health needs
- Dedicated, updated, relevant and representative database of paediatricians
- Prospective, national surveillance using monthly 'active' reporting mechanism
- Includes inpatients and outpatients in urban/regional/rural/remote/very remote regions
- Internationally recognised diagnostic criteria and study protocol provided to contributors
- Simple reporting process, acceptable to contributing paediatricians, with minimal workload
- Electronic report card used by 95% of clinicians: high response rate to monthly card (> 90%)
- Data capture using secure REDCap system: high completion rate of case report form
- Data are timely, sensitive: enhance and complement other surveillance systems
- Member of the International Network of Paediatric Surveillance Units

frequency of rare conditions requires minimal workload for paediatricians, as reflected in their high and sustained participation rate: over 90% (333,003/352,944) of all monthly report cards sent in the first 25 years were returned. APSU has been evaluated using CDC criteria for surveillance systems⁴ and met criteria for usefulness, simplicity, acceptability and representativeness, sensitivity and timeliness of data quality. Clinicians support the APSU, reporting that it is valuable for generating knowledge (81%), identifying research priorities (78%), guiding clinical practice (70%) and informing public health policy (70%). Similar responses were received from researchers and public health professionals.⁴

Surveillance method

The APSU surveillance method has been described in detail elsewhere.⁵ Between 1 January and 31 December 2019, a report card listing 14 rare medical conditions in children was distributed each month, either by email (95%) or as a reply-paid paper card (5%), to 1429 paediatricians located across Australia. These clinicians were registered with the APSU as 'contributors' and were considered to be 'active' (i.e. they worked as clinicians, had agreed to report to the APSU and were not on leave). The 14 conditions listed on the 2019 report card (Figure 1) could be categorised as either rare

communicable diseases or complications of rare communicable diseases, rare genetic disorders or uncommon injuries and other conditions.

The ten rare communicable diseases and complications of rare communicable diseases under APSU surveillance in 2019 and listed on the report card were: acute flaccid paralysis, congenital cytomegalovirus infection, neonatal herpes simplex virus infection, perinatal exposure to HIV, paediatric HIV infection, severe complications of seasonal influenza, juvenile onset recurrent respiratory papillomatosis (JoRRP), congenital rubella syndrome, congenital varicella syndrome and neonatal varicella infection.

Upon receipt of the monthly APSU report card (Figure 1), paediatricians were asked to notify *whether or not* they had seen a child with one or more of the conditions listed on the card during the previous month and to return the card to the APSU. Paediatricians who notified a case were sent the link to a case report form (also available on the electronic card) requesting de-identified demographic, clinical, laboratory, treatment and outcome data on the child. Data from case report forms are collected using the secure REDCap system and automatically downloaded into a database for checking and safe storage. Case report forms were forwarded to study investigators with expertise in each of the specific conditions so that cases could be confirmed.

Figure 1. Example APSU monthly report card in 2019

APSU REPORT CARD: AUGUST 2019B

NOTHING TO REPORT? Please select reply and type 'NTR' in the subject line of this email

Study Updates:

APSU has CEASED surveillance for Stroke in children <2 years old: Please ensure all outstanding case reports have been completed and returned to APSU as soon as possible. Cases diagnosed between June 2017 and July 2019 and not yet notified to APSU can still be reported. Questionnaires can be completed via the SECURE ONLINE FORM by following this secure link: [Online Stroke in Children < 2 years old Questionnaire](#) or by printing out the form by following this link: [PDF Stroke in Children < 2 years old Questionnaire](#), completing and returning via email to SCIN-APSU@health.nsw.gov.au or fax to (02) 9845 3082.

2019 Severe Complications of Influenza surveillance for the Commonwealth Department of Health commenced on 1st June 2019 through to 30th September 2019. Please report cases as soon as possible – you do not need to wait for the monthly APSU email.

- * Questionnaires can be filled out online by following this secure link: [ONLINE Severe Complications of Influenza Questionnaire](#)
- * Study protocol and printable questionnaire can be accessed on the APSU website: [PRINTABLE Severe Complications of Influenza Questionnaire](#)

DO YOU HAVE A CASE TO REPORT? Select reply and type the number of cases you are reporting in the space provided in the table below. Please return completed Case Report Form(s) to the APSU or complete case report forms ONLINE by selecting the relevant study link. *If you report a case, please record patient details for later reference*

NEWLY DIAGNOSED CASES ONLY – Please report cases diagnosed within study period only

Study case report forms and online case report forms are available through the hyperlinks below or via the APSU website <http://apsu.org.au/studies/current/>

No of Cases	Case Report Forms – link to PRINTABLE PDF form (return by email or fax)	ONLINE Case Report Forms – secure link to complete form ONLINE
[]	Acute flaccid paralysis **	Online Severe Complications of Influenza 2019
[]	Severe Complications of Influenza 2019	Online Severe Indoor Trampoline Park Injury Admitted to Hospital Questionnaire
[]	Severe Indoor Trampoline Park Injury Admitted to Hospital	Online Severe Injury Related to Disc Battery Questionnaire
[]	Severe Injury Related to Disc Battery	Online Fetal Alcohol Spectrum Disorder Questionnaire
[]	Fetal Alcohol Spectrum Disorder	
[]	MECP2 Duplication Syndrome	
[]	Juvenile onset Recurrent Respiratory Papillomatosis	
[]	Congenital varicella	Online Congenital Varicella Questionnaire
[]	Neonatal varicella	Online Neonatal Varicella Questionnaire
[]	Rectal stricture	
[]	Congenital cytomegalovirus infection – NSW – Other States	
[]	Neonatal Herpes Simplex Virus Infection	Online Herpes Simplex Virus Infection Questionnaire
[]	HIV Infection and Perinatal Exposure to HIV in Australia – Mother – Child	Online HIV Infection and Perinatal Exposure to HIV in Australia – Mother – Child
[]	Congenital rubella	Online Congenital Rubella Questionnaire

See your protocol sheet for details regarding stool/serum specimens.

Please ALSO report cases of acute flaccid paralysis immediately by telephone to the National Enterovirus Reference Laboratory on (03) 9342 9607 or email enterovirus@nhb.org.au.

Results

Representativeness of mailing list

In 2019 the number of children aged 0–14 years who were living in Australia was 4.7 million or 19% of the total population.⁶ Of the children, 51% were boys, 5.9% were Aboriginal or Torres Strait Islander ; 70% lived in major cities and 2% lived in remote/very remote regions; 21% live in the lowest and 20% in the highest socioeconomic areas; and 82% lived in couple families.⁶ The distribution of the child population by state is shown in Table 1.⁷

In 2019, the 1,429 paediatricians reporting to the APSU ('APSU Contributors') worked in every Australian state and territory. This number represents approximately 90% of paediatricians in clinical practice in Australia and all hold a Fellowship of the Royal Australasian College of Physicians or equivalent. The proportion of paediatricians and other specialists by state/territory was similar to the proportion of resident children (Table 1). Contributors were based in major cities, inner and outer regional and remote areas. They included general and sub-specialist paediatricians (Table 2) and some other specialists (e.g. paediatric surgeons and psychiatrists) working in child health in both inpatient and outpatient settings.

The overall return rate by paediatricians of the monthly APSU report card was 91.8% in 2019. This includes case notifications and 'nothing to report' responses. In comparison, the response rate has been over 90% for 26 years and in 2018 was 92.0%.⁵

Conditions under surveillance

Table 3 lists the communicable diseases currently under surveillance and shows the duration of the study, and the total number of cases identified, the number of cases confirmed in 2019 and an estimate of minimum incidence for both 2019 and the entire study period.

Acute flaccid paralysis (AFP)

Since 1995, the APSU has conducted AFP surveillance at the request of the Australian Government. AFP is the clinical presentation for, and thus a marker of, acute poliomyelitis; surveillance and investigation of AFP cases is critical to ensure that Australia retains its polio-free certification by the World Health Organization (WHO).

Suspected cases of AFP in children aged less than 15 years were reported to the National Enterovirus Laboratory (NERL) at the Victorian Infectious Diseases Reference Laboratory via one of two separate but complementary mechanisms: by individual clinicians, who notified a case to APSU or NERL and completed the APSU case report form, or via the Paediatric Active Enhanced Disease Surveillance system (PAEDS). PAEDS employs research nurses at seven designated paediatric hospitals to identify new cases of AFP in inpatients and to complete a case report form based on the APSU form. Stool samples were collected via both surveillance mechanisms. WHO defines an adequate stool sample as being two stools of sufficient quantity for laboratory analysis and collected at least 24 hours apart, within 14 days after the onset of paralysis. All reported AFP cases were confirmed and classified by the Polio Expert Panel (PEP) at bi-monthly teleconference meetings for reporting to the WHO. APSU has membership of the PEP.

In 2019, there were 83 AFP notifications via the APSU/NERL and PAEDS surveillance mechanisms for all of which case report forms were provided. There were 14 duplicates and six errors (did not fulfil the case definition, including three cases outside the age range) and 63 confirmed AFP cases. Seven cases were reported by paediatricians who work outside hospitals surveyed by PAEDS and would otherwise have been missed.

Of the 63 confirmed AFP cases, all were classified as non-polio AFP by the PEP. Thus, Australia's non-polio AFP rate in 2019 was 1.34 per 10⁵ children under 15 years of age. This meets the

Table 1. Number and proportion of APSU Contributors (n = 1,429) and of children aged 0–14 years by Australian state and territory

APSU contributors n = 1,429	n (%) contributors	Children 0–14 years	% children 0–14 years
Australia			
Paediatricians	1,334 (93.4%)	4,741,629	100
Other specialties ^a	95 (6.6%)		
New South Wales (NSW)			
Paediatricians	498(34.8%)	1,499,863	31.7
Other specialties	41 (2.9%)		
Victoria (Vic)			
Paediatricians	322 (22.6%)	1,201,923	25.3
Other specialties	20 (1.4%)		
Queensland (Qld)			
Paediatricians	227 (15.9%)	989,916	20.9
Other specialties	12 (0.8%)		
Western Australia (WA)			
Paediatricians	139 (9.7%)	511,842	10.8
Other specialties	9 (0.6%)		
South Australia (SA)			
Paediatricians	85 (6.0%)	308,953	6.5
Other specialties	4 (0.3%)		
Tasmania (Tas)			
Paediatricians	26 (1.8%)	94,123	2.0
Other specialties	3 (0.2%)		
Australian Capital Territory (ACT)			
Paediatricians	20 (1.4%)	81,390	1.7
Other specialties	6 (0.4%)		
Northern Territory (NT)			
Paediatricians	17 (1.2%)	52,840	1.1
Other specialties	0 (0%)		

a Other specialties include surgery, psychiatry, anaesthetics, general practice, nuclear medicine, obstetrics, sexual health medicine.

Table 2. Distribution of paediatricians^a contributing to APSU by specialty (n = 1,334)

Specialty	1,334 (%)
Paediatric subspecialty (other)	451 (33.8%)
General paediatrics	424 (31.8%)
Neonatology	186 (13.9%)
Community child health/Developmental	183 (13.7%)
Emergency	69 (5.2%)
Intensive Care	17 (1.3%)
Clinical pharmacology	2 (0.1%)
Clinical epidemiology	1 (0.1%)
Forensics	1 (0.1%)

a The other 95 APSU contributors belong to other specialties e.g. surgery, psychiatry.

WHO reporting target for sensitive AFP surveillance of 1 per 10⁵ children aged < 15 years per annum.⁸ Adequate stool samples were collected from 31 cases (49%).

All 63 children with AFP were Australian-born and eight (12.7%) were Indigenous. Ethnicity was not recorded for two children. Of the confirmed cases, 23 were reported in New South Wales, 18 in Victoria, 11 in Queensland, four in Western Australia, two each in South Australia, Tasmania, and the Northern Territory and one in the Australian Capital Territory.

The most common diagnoses in AFP cases were: Guillain-Barré syndrome (GBS) in 18 cases (29%), transverse myelitis in 11 cases (18%), acute disseminated encephalomyelitis (ADEM) in five cases (8%) and spinal cord compression in two cases (3%), which is consistent with previous years.⁵ One case of acute flaccid myelitis was recorded.

Since AFP surveillance commenced 24 years ago, 1,132 cases have been confirmed. The case rate has continuously remained above 1 per 10⁵ children aged less than 15 years each year since 2008,⁹ contributing to Australia's status as polio-free.⁸ We have recently reported the newly described entity acute flaccid myelitis using the AFP database.¹⁰

In 2019, a report of Australian AFP cases was published each fortnight in the *WHO Regional Office for the Western Pacific Polio Bulletins*; these cases contributed to the 2019 National Certification and Regional Certification Committee reports¹¹ that enable Australia to be declared polio-free. AFP data were also published in the PAEDS annual report to *Communicable Diseases Intelligence* in 2019.¹² Ongoing surveillance of AFP in Australia remains important as poliomyelitis persists in several countries and Australia remains at risk of imported infection.⁸

Congenital cytomegalovirus infection (cCMV)

Congenital CMV infection is transmitted from infected mothers to their unborn children during pregnancy. It is often asymptomatic but can result in severe sequelae, notably hearing loss and developmental delay,¹³ justifying screening for CMV in children with sensorineural hearing loss.¹⁴ There is no vaccine available to prevent CMV infection; however, antiviral treatment including ganciclovir and valganciclovir is recommended for symptomatic cCMV and is thought to be effective in improving developmental and hearing outcomes.¹⁵ APSU surveillance of cCMV infection commenced in 1999.

In 2019, there were 16 notifications. One case report was not returned. Twelve neonates in the

first three weeks of life had confirmed cCMV infection (mostly diagnosed by PCR on urine or Guthrie blood spot) and three who presented later with symptoms had suspected cCMV. Based on 15 cases, the incidence estimate was 5.28 per 10⁵ births in 2019. Ethnicity was reported for 14 infants: two were Indigenous. Six infants were reported from Queensland, five from NSW, and two each from Victoria and the Northern Territory. No infant with cCMV was reported from South Australia, Western Australia, Tasmania or the Australian Capital Territory.

Clinical characteristics of the 15 infants included: deafness (6), small for gestational age (6), jaundice (5), petechiae or purpura (4), thrombocytopenia (3), microcephaly (3) and anaemia (2). Hepatitis and developmental delay were each reported in one infant. Six of the 15 infants were treated with valganciclovir and all were alive at the time of reporting.

A symptomatic illness suggestive of CMV infection was reported during pregnancy in four of the 15 mothers (27%) and positive CMV serology was reported in 11/15 (73%). Serology was unknown or not tested in four mothers.

In 21 years of APSU surveillance for cCMV, a total of 362 confirmed cases was reported: 195 during the first 11 years, 1999–2009,¹⁴ and 167 during the next 10 years. APSU data collected from 1999 to 2016 showed no increase over time in the number of infants with symptomatic CMV infection but did show an increase in the number of symptomatic infants who received antiviral treatment.¹⁵ Over 40% of their mothers reported a symptomatic illness suggestive of CMV infection during pregnancy and this correlated with positive CMV serology in these mothers. Hearing loss and developmental delay were prevalent in both symptomatic and asymptomatic infants. Bartlett recommended the introduction of universal newborn screening for cCMV infection in infants.¹⁵

Most cases reported to the APSU are asymptomatic (71%) and thus surveillance is likely to underestimate the true incidence of cCMV

infection. APSU data do show that children with asymptomatic cCMV are at increased risk of hearing loss but have similar neurodevelopmental outcomes to healthy controls.¹⁶ APSU data have contributed to a range of educational resources for health professionals, carers and the community regarding prevention and management of cCMV disease,⁵ and have influenced clinical care and thinking about screening.^{14,15}

Neonatal herpes simplex virus infection (HSV)

HSV infection in neonates and young infants is transmitted either during birth or soon after delivery, most commonly from mothers with primary genital HSV infection.^{17,18} Neonatal HSV infection manifests either as disease localised to specific organs (e.g. the skin, eyes or mouth or the central nervous system) which ranges from mild to severe, or as disseminated disease which is more likely to result in severe outcomes including death or disability.^{18,19} There is no vaccine available to prevent neonatal HSV infection; however, antiviral treatment with acyclovir has been available and recommended for infants since the 1980s.²⁰ The APSU has conducted surveillance for this condition since 1997.

In 2019, there were nine notifications to the APSU of neonatal HSV infection in infants aged less than three months. Eight were confirmed as cases and for one child no case report form was received. The estimated incidence rate of neonatal HSV infection was 2.64 per 10⁵ births in 2019.

Of the eight confirmed cases, four had HSV-1 and four had HSV-2 infection. Two infants had disseminated disease with neurological involvement (one with HSV-1, who died, and one with HSV-2). Six of the infants had disease localised to the central nervous system, two of whom also had skin lesions, and both survived. All infants received antiviral treatment with acyclovir at diagnosis. The infant who died received acyclovir and antibiotics (benzylpenicillin and gentamicin) until the time of death.

Table 3. Confirmed cases identified by the APSU during the period 1 January – 31 December 2019 and for the total study period, and estimated incidence per 10⁵ children of the relevant population/age per annum, by condition

Communicable disease or complication of communicable disease	Surveillance study date of commencement	Confirmed cases for Jan–Dec 2019	Incidence estimate per 10 ⁵ per annum and 95% CI for 2019	Confirmed cases for the whole study period to Dec 2019	Incidence estimate per 10 ⁵ per annum for the whole study period to Dec 2019
Acute flaccid paralysis (AFP)	March 1995	63 ^a	1.34 [1.02–1.70] ^b	1,132	1.04 [0.98–1.10] ^b
Congenital cytomegalovirus	Jan 1999	15	5.28 [2.77–8.17] ^c	362	5.97 [5.37–6.62] ^c
Congenital rubella infection	May 1993	0	0	54	0.71 [0.53–0.93] ^c
Congenital varicella syndrome	May 2006	0	0	3	0.07 [0.01–0.21] ^c
<i>Congenital varicella syndrome</i>	1995–1997 ^d			6	0.80 [0.30–1.80] ^e
Neonatal varicella infection	May 2006	3	0.99 [0.20–2.90] ^c	31	[0.49–1.03] ^c
<i>Neonatal varicella infection</i>	1995–1997 ^d			44	5.80 [4.30–7.80] ^e
Juvenile-onset recurrent respiratory papillomatosis ^e	Sep 2011	0	0	17	0.04 [0.02–0.07] ^b
Neonatal herpes simplex virus (HSV) infection (< 3 months)	Jan 1997	8	2.64 [1.14–5.21] ^c	208	3.19 [2.78–3.66] ^c
Perinatal exposure to HIV	May 1993	59	19.49 [14.84–25.14] ^c	852	11.28 [10.53–12.06] ^c
Paediatric HIV infection	May 1993	0	0	87	0.07 [0.06–0.09] ^f
Severe complications of influenza ^g	2008 (flu season only)	62	1.32 [1.00–1.68] ^b	695	1.31 [1.22–1.41] ^b

a Includes all cases of acute flaccid paralysis (AFP) reported via the APSU/NERL and PAEDS. All cases have been classified by the Polio Expert Panel (PEP) as 'non-polio AFP' according to WHO criteria.

b Based on population of children aged < 15 years.

c Based on number of live births.

d See reference 38.

e Includes both confirmed cases (visualisation on endoscopy, histological confirmation) and probable cases (visualisation on endoscopy, no histology report).

f Based on population of children aged < 16 years.

g Influenza surveillance was conducted each year during the influenza season, from July to September for 2008 and 2010–2015; June to October in the 2009 pandemic year; and June to September 2016–2019

Two cases were reported from New South Wales, two from Victoria, three from Western Australia and one from Queensland. No cases were reported in South Australia, Tasmania, the Northern Territory or the Australian Capital Territory. Ethnicity was recorded for five cases and none was Indigenous.

In the 23 years since APSU surveillance for neonatal HSV commenced, a total of 208 confirmed cases has been reported, the annual frequency fluctuating over time. Case numbers were highest in 2015 (16 cases) and lowest in 2017 (two cases).

In 2019, we conducted an analysis of 193 cases of neonatal HSV infection reported to the APSU over a 22-year period (1997–2018). Of these, 83 had neurological disease, either localised to the central nervous system or disseminated and caused by HSV-1 (55%) or HSV-2 (45%). Children with neurological disease were more likely to have disseminated disease, increased mortality, and abnormal neuroimaging compared with infants with HSV infection without neurological involvement (unpublished data).

Perinatal exposure to HIV and paediatric HIV infection

APSU surveillance for perinatal exposure to HIV in children born to women infected with HIV, and HIV infection in children aged less than 16 years, has been conducted since 1993 in collaboration with the Kirby Institute, previously the National Centre for HIV Epidemiology and Clinical Research.²¹ Mother-to-child transmission (MTCT) of HIV, although now uncommon (~2%), is the most frequent cause of HIV infection in Australian children.²¹ Prevention of perinatally-acquired HIV infection by MTCT includes maternal antiretroviral treatment during pregnancy; prophylactic antiretroviral treatment of the infant; caesarean section delivery; and avoiding breastfeeding.

In 2019, there were 63 notifications of perinatal exposure to HIV to the APSU. Four were duplicate reports; 59 cases of perinatal exposure

to HIV were confirmed. In two of these cases MTCT was confirmed; a rate of 3.38%. One child was born to a woman with undiagnosed HIV at birth (vaginal delivery, breast fed, no antiretroviral treatment). The mother of the second child was known to have HIV but did not receive antiretroviral treatment. HIV test results were not reported for 15 of the infants by the end of 2019. In 2019, the estimated incidence of perinatal exposure to HIV was 19.49 per 10⁵ births. The number of reported cases varies by year and in 2019 was double that reported in 2018 for perinatal exposure (29 cases) and perinatal transmission (one case).

All infants were born in Australia and three were Indigenous. Eighteen cases were confirmed in each of New South Wales and Western Australia, five in Victoria, four in the Australian Capital Territory and three in Queensland. No case was reported in South Australia, Tasmania or the Northern Territory. For 11 cases no geographic location was recorded.

Information on management was available for 34 mothers, 31 of whom received antiretroviral treatment during pregnancy. Mode of delivery was vaginal in 17, by emergency caesarean section in 9 and elective caesarean section in 5 infants. Three reports did not include the mode of delivery. Of the mothers, 23 were known to have been born overseas and 2 identified as Aboriginal.

Since surveillance commenced 26 years ago, a total of 852 confirmed cases of perinatal exposure to HIV and 87 confirmed cases of paediatric HIV infection have been reported to the APSU. During this time, we documented a fall in MTCT from 39% in the 5-year period 1985–1991 to 28% in 1992–1996 and 2% in 2012–2016.²¹

There were no reported cases of paediatric HIV infection in 2019, the last cases (three children born overseas) having been reported to the APSU in 2014.²²

Data on perinatal HIV exposure and perinatal HIV transmission in Australian-born infants

and paediatric HIV infections are routinely reported in the Australian Annual Surveillance Report on HIV, viral hepatitis and sexually transmissible infections,²³ and contribute to the National HIV Strategy.²⁴ Data are also routinely reported to the Joint United Nations Programme on HIV/AIDS (UNAIDS)²⁵ as part of international reporting on mother-to-child transmission of HIV.

Severe complications of influenza

APSU surveillance of severe complications of laboratory-confirmed influenza virus infection in hospitalised children aged under 15 years has been conducted during the Australian winter season (1 June to 30 September) since 2008. Children are vulnerable to developing severe complications, leading to high rates of hospitalisation, morbidity and mortality.²⁶

In 2019, 77 notifications were reported to the APSU, with case report forms completed for 76. There were 62 confirmed cases; the remainder were classified as duplicates (3) or errors (11). In contrast there were only 20 confirmed cases reported in 2018, which correlates with other reports of the severity of the 2019 influenza season.²⁷ The estimated incidence rate was 1.32 per 10⁵ children aged under 15 years.

Thirty-nine confirmed cases had influenza A infection (two with influenza A H1N1) and 23 cases had influenza B infection. Fifty-two children (84%) had no underlying medical condition.

The severe complications reported involved multiple organ systems, including the respiratory, central nervous, renal, musculoskeletal, cardiac, gastrointestinal and haematological systems. Pneumonia was the most common complication, recorded in 24 children (39%), followed by seizures in eight (13%), rhabdomyolysis in eight (13%), and bacterial co-infection in seven children (11%). Twenty children (32%) were admitted to an intensive care unit and seven (11%) required mechanical ventilation. Thirty-three (53%) required oxygen therapy.

Of the children, 28 (45%) received antiviral treatment (oseltamivir), and one received both oseltamivir and acyclovir. Forty-three children (69%) received antibiotics. Only five children were recorded as having received the seasonal influenza vaccine. The vaccination status was unknown for 41 children.

At the time of reporting to the APSU, two children had died and five remained in hospital. The two children who died were under five years of age and both had encephalitis/encephalopathy, one with seizures and the other with pneumonia. Both children were treated with oseltamivir and antibiotics. One child had influenza A and one child had influenza B. Neither child had an underlying medical condition or had been vaccinated against seasonal influenza.

Twenty-six cases were reported in New South Wales, 19 in Queensland, six in Victoria, six in Western Australia, three in the Australian Capital Territory and two in Tasmania. No cases were reported in South Australia or the Northern Territory. Ethnicity was recorded for 57 cases; two cases were Indigenous.

In the twelve seasons since APSU surveillance for severe complications of influenza commenced, a total of 695 confirmed cases have been reported. The annual number of cases has fluctuated: the highest number was reported during the 2009 H1N1 pandemic and in 2017 (106 cases in each year), and in 2015 (82 cases), while the lowest number of cases was reported in 2018 (20 cases). Data from ten years of APSU surveillance 2008–2017 will be submitted for publication in 2020. It showed that over half the children with severe complications were previously healthy, almost half required ICU, the most common complication was pneumonia, vaccination rates were very low, and antivirals were underutilised (unpublished).

Juvenile-onset recurrent respiratory papillomatosis (JoRRP)

JoRRP is a rare disease resulting from perinatal exposure of the airways to human papillomavi-

rus (HPV) in the maternal genital tract. In children who develop the disease, which is typically due to infection with Human Papillomavirus (HPV) types 6 or 11, the infection is not cleared by the immune system and persists in the child's respiratory tract, giving rise to the development and recurrence of benign papillomata, typically affecting the larynx and causing airway obstruction.^{28–30}

In 2007, Australia established a national HPV vaccination program for females aged 12–26 years of age, which includes protection against HPV types 6 and 11. Since the program commenced, rates of HPV6 and 11 infection and associated genital warts have fallen dramatically.^{31,32} Since October 2011, surveillance of JoRRP has been conducted by the APSU and, using this surveillance approach, Australia was the first country to demonstrate that JoRRP is preventable by vaccination of females of child-bearing age.³⁰ To ensure capture of JoRRP cases, specialist paediatric otolaryngologists who treat the disease were enrolled as contributors to monthly APSU surveillance. The aim of JoRRP surveillance is to monitor the incidence of the disease, describe the epidemiology of cases including maternal history, monitor the viral types associated with disease and describe treatment modalities in use.

In 2019, no cases of JoRRP were reported to the APSU in any Australian state or territory for the second consecutive year. Of two cases reported in 2017, one was a probable case of non-laryngeal JoRRP and the other occurred in a child who was not born in Australia. This suggests that widespread vaccination of females and, since 2013, routine vaccination of males, has interrupted community circulation of the causal HPV types for JoRRP and correspondingly dramatically reduced the risk of perinatal exposure and subsequent disease in Australia. In the eight years of JoRRP surveillance, 17 confirmed cases were reported, with one to four cases identified per year until the end of 2017.

Novel data from the APSU JoRRP study have been published³⁰ and were presented in 2019 by

Chief Investigator Associate Professor Daniel Novakovic at the World Phonosurgery Congress in Buenos Aires Argentina and at the ASEAN ORL-HNS Congress in Singapore.

Congenital rubella syndrome

Congenital rubella syndrome is a vaccine-preventable condition caused by maternal rubella infection during pregnancy, which can result in fetal death or congenital defects including heart disease, deafness and blindness, neurological abnormalities and developmental delay.³³

APSU surveillance of congenital rubella commenced in 1993. Paediatricians are asked to notify any cases in children or adolescents aged up to 16 years with definite or suspected congenital rubella infection with defects, based on history, clinical and laboratory findings.

In 2019, there were no cases of congenital rubella reported to the APSU in any Australian state or territory. This was consistent with the lack of notifications to the National Notifiable Disease Surveillance System in 2019. This is a passive surveillance system with reporting from laboratories and state/territory health departments. Together the two methods provide excellent case ascertainment.³⁴ No notifications of congenital rubella have been reported to the APSU since 2015, when two cases were reported, one with confirmed congenital rubella syndrome.³⁵

Since surveillance commenced, a total of 54 confirmed cases of congenital rubella infection have been reported to the APSU in 26 years, and 35 of these cases have been confirmed as having congenital rubella syndrome. Twenty-nine cases were reported during the first eleven years of surveillance (1993–2013) and five during the subsequent ten years (2004–2013),³² most likely due to increased uptake of rubella vaccination in young women and infants.

Rubella immunisation for adolescent women was introduced in Australia in 1971. Immunisation of infants at 12 months with the measles-mumps-rubella (MMR) vaccine was introduced

in 1989.³³ The majority of children identified with CRS during the study period have been born to women from countries without national vaccination programs,³³ thus ongoing vigilance is required. Conscientious objection to vaccination persists in specific regions of Australia and contributes to a lower than average uptake of the measles-mumps-rubella-varicella vaccine, putting unborn children at potential risk.³⁶

Neonatal varicella virus infection and congenital varicella syndrome

Varicella zoster virus infection in young infants can be acquired either congenitally or in the neonatal period. Congenital varicella syndrome can result in eye, neurological, cardiovascular, or gastroenterological abnormalities, developmental delay, blindness and typical cicatricial skin lesions.³⁷

Neonatal varicella infection occurs in the first month of life with rash and fever developing after either exposure to an infected person or through maternal infection in the last 4 weeks of pregnancy. APSU surveillance for congenital and neonatal varicella infection commenced in 2006, following the introduction of universal vaccination for infants in 2005.³⁸

In 2019, three cases of neonatal varicella infection were notified to the APSU. All presented with skin lesions consistent with varicella infection, all were hospitalised, two were treated with acyclovir and all were discharged well. Maternal infection was reported for one case. All of the infants were born in Australia: the mothers of two of the infants were born overseas and the country of birth was unknown for the mother of the third infant. In 2019, the estimated incidence rate was 0.99 per 10⁵ births.

A total of 31 cases of neonatal varicella infection have been reported to the APSU in the 14 years since the current surveillance commenced in 2006. This contrasts with APSU data collected in a previous study over three years (1995–1997),

prior to the introduction of varicella vaccination, when 44 cases of neonatal varicella were reported.

There were no notifications of congenital varicella syndrome reported to the APSU in 2019. A total of three confirmed cases have been reported to the APSU since surveillance commenced in 2006. The last confirmed case of congenital varicella was notified in 2017. This contrasts with APSU data collected in a previous study during 1995–1997, prior to the introduction of routine varicella vaccination, when six cases were reported.³⁸

Although the current Immunisation Schedule provides free vaccination to children, catch-up for adolescents to age 20 years and to refugee and humanitarian entrants to Australia,³⁹ ongoing surveillance of varicella is important to identify infants born to unvaccinated women born in Australia or overseas.

Discussion and conclusions

The APSU provides a unique active surveillance mechanism that allows collection of detailed and timely clinical data on rare childhood disorders from a representative group of contributors (paediatricians and other child health specialists nationally). The surveillance mechanism is well-established and robust and complements other national data collections.

The participation rates by contributors is high and sustained. In 2019, 1426 contributors reported to the APSU with a monthly return rate of the surveillance card of 91.8%. A reporting rate of at least 90% was achieved over the last 25 years. General and sub-specialist paediatricians report cases from urban centres, regional and remote areas.

In 2019, 14 rare conditions, including eight communicable diseases or complications of communicable diseases (acute flaccid paralysis, congenital cytomegalovirus infection, neonatal herpes simplex virus infection, perinatal exposure to HIV and paediatric HIV infection,

severe complications of seasonal influenza, juvenile onset recurrent respiratory papillomatosis (JoRRP), congenital rubella syndrome, congenital varicella syndrome and neonatal varicella infection), were under surveillance. APSU confirmed cases of all conditions apart from JoRRP, congenital rubella syndrome and congenital varicella syndrome.

WHO's target for AFP incidence of at least 1 case per 10⁵ children aged under 15 years of age per annum was achieved in 2019, as has been the case for many years. Regular review and classification of AFP cases collected by APSU, NERL and PAEDS is undertaken by the Polio Expert Panel Committee. All 2019 cases were classified as non-polio AFP and reported to the WHO, contributing to Australia's status as polio-free. GBS, transverse myelitis and ADEM accounted for most cases of AFP and one case of the novel condition acute flaccid myelitis was identified. While there is a threat of importation of polio-myelitis, ongoing surveillance is required.

The number of children with severe complications of influenza was high in 2019, reflecting the high community prevalence of seasonal influenza. Few children in this group had documented seasonal vaccination, however influenza vaccination uptake in children aged six months to five years has increased nationally from <5% in 2017 to 39.7% in 2019 [Beard et al 2020]. This follows changes to the National Immunisation Program in 2018, which saw recommendations and funding for seasonal influenza vaccination in six Australian states and territories for all children aged under five years, and additionally to all Aboriginal and Torres Strait Islander children aged five to 14 years.⁴⁰ The fact that 60% of children admitted with severe influenza complications were previously healthy supports universal vaccination and identifies the need for ongoing education for the community and healthcare workers about the need to vaccinate children. Outcomes are worse for children with influenza and co-infection, and the convergence of the upcoming influenza season with the COVID-19 pandemic is of concern. The APSU can respond rapidly to this emerging disease threat and will

monitor co-infection with COVID-19 and influenza and its outcomes in children reported with influenza complications in 2020.

The frequencies of cCMV and neonatal HSV infection in infants have remained at similar levels since the late 1990s. These conditions are transmitted from mothers to infants and are not vaccine-preventable, however our results indicate a need for increased awareness by health professionals and the community, and for maternal screening for these infections in order to prevent potentially devastating outcomes including death and disability. The cCMV and neonatal HSV infection studies are the longest continuously-running surveillance studies of these diseases internationally and allow for a thorough analysis of trends over time in response to changes in policy, diagnostics, treatment and vaccination strategies.

Our longstanding collaboration with the Kirby Institute provides data collected since 1993 on over 852 confirmed cases of perinatal exposure to HIV infection. Trends over time include a significant fall in the number of women in whom HIV infection was not diagnosed before or during pregnancy and an accompanying increase in the number of LSCS deliveries, use of antiretrovirals in mother and infant, and exclusively bottle-fed babies. These interventions in turn have decreased in the number of cases of mother-to-child transmission to < 5%. Nevertheless, many perinatally exposed children are born in Australia to mothers who were born overseas, including 23/30 cases reported to the APSU in 2019 for whom the mother's birthplace was known. These data highlight that there remain high risk groups in whom screening for HIV during pregnancy should be universal.

There has been an ongoing decline in the numbers of cases of congenital rubella syndrome, neonatal varicella infection, congenital varicella and JoRRP reported to APSU since surveillance commenced for these conditions. This decline in case numbers for these conditions persisted in 2019 and reflects increased vaccine availability and uptake over time. Continued sur-

veillance is required as children of immigrant and refugee women from countries without vaccination programs remain vulnerable to these conditions. Although overall coverage of the measles-mumps-rubella-varicella (MMRV) vaccine was high in infants aged 24 months in Australia in 2017 (92%), lower coverage (< 85%) was observed in specific regions, leaving some groups vulnerable.³⁶

We thank all Australian paediatricians for their ongoing, voluntary contribution to APSU surveillance and for providing data to inform clinical care, policy and prevention. We also acknowledge the contribution and expertise of all researchers, clinicians and research groups who use the APSU mechanism.

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Appendix A. APSU conditions under surveillance

Surveillance study – Case definition
<p>Acute flaccid paralysis (AFP) Any child less than 15 years of age with acute flaccid paralysis in one or more limbs or acute onset of bulbar paralysis. All cases reported through APSU, NERL and PAEDS are reviewed by the PEP and classified as: confirmed poliomyelitis; non-polio AFP, polio-compatible or non-AFP. The NERL determines whether there is an infectious cause of AFP including enteroviruses. The PEP secretariat reports all Australian cases to the World Health Organization (WHO).</p>
<p>Congenital cytomegalovirus (CMV) infection Congenital CMV: Any child from whom CMV is isolated in the first three (3) weeks of life, from urine, blood, saliva, or any tissue taken at biopsy. Suspected congenital CMV: any child up to 12 months of age, in whom CMV is isolated from urine, blood, saliva or any tissue taken at biopsy <i>and</i> /or a positive serum immunoglobulin M (IgM) is found <i>and</i> in whom clinical features exist that may be due to intrauterine CMV infection. Clinical features associated with congenital CMV infection include: prematurity, low birth weight, sensorineural deafness, other neurological abnormalities (encephalitis, microcephaly, developmental delay), seizures, microphthalmia, chorioretinitis, cataracts), hepatitis, hepatosplenomegaly, thrombocytopenia, pneumonitis or myocarditis.</p>
<p>Neonatal and young infant herpes simplex virus (HSV) infection Any neonate or infant aged less than 3 months of age (regardless of gestation) seen in the last month with laboratory confirmation of HSV infection <i>and</i> with either clinical evidence of HSV infection <i>or</i> laboratory confirmation of maternal perinatal HSV infection in an asymptomatic infant. Laboratory confirmation is by detection of HSV by polymerase chain reaction (PCR) in a surface swab, respiratory specimen <i>and</i>/or sterile site (cerebrospinal fluid [CSF] or blood) (or by virus isolation), or by immunofluorescence. Clinical evidence of neonatal HSV infection is one or more of: typical herpetic lesions of the skin, eye or mouth; evidence of disseminated infection (bleeding, bruising or coagulopathy, jaundice or elevated serum bilirubin, hepatosplenomegaly or elevated liver transaminases), pneumonitis (respiratory distress or chest radiograph) or encephalitis (lethargy, seizures, apnoea or abnormalities on neuroimaging or electroencephalogram [EEG]). Laboratory evidence of maternal perinatal HSV infection is provided by detection of HSV in maternal genital swab <i>and</i> /or mother seroconverted to HSV or IgM positive in pregnancy or early postnatal period.</p>
<p>Paediatric human immunodeficiency virus (HIV) infection and perinatal exposure to HIV in Australia Any child aged less than 16 years at diagnosis of HIV infection in Australia or any child born to a woman with diagnosed HIV infection. Children born to women with HIV infection and who are known to have been exposed to HIV perinatally, by <i>in utero</i> exposure or through breastfeeding, should be notified, even if they are subsequently confirmed as HIV antibody negative.</p>
<p>Juvenile onset recurrent respiratory papillomatosis (JoRRP) Any infant or child under the age of 15 years diagnosed with juvenile onset recurrent respiratory papillomatosis (JoRRP) confirmed by endoscopy of the larynx <i>and</i> by histology.</p>
<p>Severe complications of influenza in children < 15 years (June – September 2018) Any child aged less than 15 years with laboratory-confirmed influenza admitted to hospital with at least one of the following complications:</p> <ul style="list-style-type: none">• Pneumonia (confirmed on X-ray or microbiology)• Oxygen requirement• Mechanical ventilation requirement• Laboratory proven secondary bacterial co-infection; bacteraemia; septicaemia;• Encephalitis / encephalopathy• Seizures (including simple febrile seizure, prolonged or focal seizure or status epilepticus)• Transverse myelitis• Polyneuritis / mononeuritis• Reye syndrome• Myocarditis; pericarditis; cardiomyopathy• Rhabdomyolysis• Purpura fulminans• Disseminated coagulopathy• Shock (requiring > 40 ml / kg fluid resuscitation)• Acute renal failure• Death, including death at presentation to hospital• Guillain-Barré syndrome

Surveillance study – Case definition

Congenital rubella

Any child or adolescent up to 16 years of age who, in the opinion of the notifying paediatrician, has definite or suspected congenital rubella, with or without defects, based on history, clinical and laboratory findings.

Severe complications of varicella virus infection including neonatal and congenital varicella infection Neonatal varicella

Any infant who has neonatal varicella based on history, clinical and/or laboratory findings in the first month of life without features of congenital varicella syndrome.

Features of neonatal varicella infection include pox-like rash which may be papulovesicular, vesiculopustular or haemorrhagic, and fever. Other systemic symptoms may be present. Complications of neonatal varicella include bacterial superinfection, neurological and haematological problems and general visceral involvement.

The diagnosis of neonatal varicella can be made when an infant in the first month of life presents with clinical features of varicella infection. There may be a history of maternal varicella infection in the last 1–4 weeks of pregnancy or contact with a varicella-infected person after birth.

The diagnosis can be confirmed by laboratory tests to detect:

- Viral antigen/viral isolate from scrapings of the skin lesions or viral DNA from lesion fluid.
- Varicella-specific IgM in a serum sample from the infant (or from the contact).

Congenital varicella

Any stillbirth, newborn infant, or child up to the age of 2 years who, has definite or suspected congenital varicella infection, with or without defects and meets at least one of the following criteria:

- Cicatricial skin lesions in a dermatomal distribution and / or pox-like skin scars and / or limb hypoplasia.
- Development of herpes zoster in the first year of life.
- Spontaneous abortion, termination, stillbirth or early death following varicella infection during pregnancy.

Confirm varicella infection by one or more of the following:

- Detection of varicella-specific IgM antibodies in cord blood or in serum specimen taken in the first 3 months of life (only 25% of cases are positive).
- Persistence of varicella-specific immunoglobulin G (IgG) antibody in a child aged beyond 6 months of age.
- Identification of varicella virus in skin lesions or autopsy tissue.
- History of maternal varicella during pregnancy or maternal contact with varicella in pregnancy in the mother of an infant with congenital abnormalities.

The following clinical signs may also be present in cases of congenital varicella syndrome:

- Microcephaly, hydrocephalus, cerebellar hypoplasia, motor or sensory deficits, sphincter dysfunction and peripheral nervous system defects.
- Microphthalmia, cataracts, Horner's syndrome, chorioretinitis, nystagmus, retinal scars, optic atrophy.
- Gastrointestinal abnormalities including colonic atresia, hepatitis, liver failure.
- Genito-urinary abnormalities.
- Cardiovascular abnormalities.
- Intrauterine growth retardation.