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Australian Paediatric Surveillance Unit (APSU) Annual Surveillance Report 2022

Suzy M Teutsch, Carlos A Nunez, Anne Morris, Guy D Eslick, and Elizabeth J Elliott, on behalf of Chief Investigators of APSU surveillance studies on communicable disease and complications of communicable disease

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Australian Paediatric Surveillance Unit (APSU) Annual Surveillance Report 2022

Suzy M Teutsch, Carlos A Nunez, Anne Morris, Guy D Eslick, and Elizabeth J Elliott, on behalf of Chief Investigators of APSU surveillance studies on communicable disease and complications of communicable disease

Abstract

For 30 years the Australian Paediatric Surveillance Unit (APSU) has conducted national surveillance of rare communicable diseases and rare complications of communicable diseases. In this report, we describe the results of thirteen such studies surveyed by the APSU in 2022, including reported case numbers and incidence estimates, demographics, clinical features, management and short-term outcomes. Conditions described are: acute flaccid paralysis (AFP); congenital cytomegalovirus (cCMV); neonatal and infant herpes simplex virus (HSV) infection; perinatal exposure to human immunodeficiency virus (HIV) and paediatric HIV infection; severe complications of influenza; juvenile-onset recurrent respiratory papillomatosis (JoRRP); congenital rubella infection/syndrome; congenital varicella syndrome (CVS) and neonatal varicella infection (NVI); and the new conditions dengue; Q fever; and severe acute hepatitis. In 2022, cases of severe complications of influenza were reported to the APSU for the first time since 2019. This likely reflects the easing of government-mandated restrictions imposed in 2020–2021 to curb the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the re-emergence of a range of infectious diseases. As previously, AFP surveillance by the APSU contributed to Australia achieving a minimum target incidence of one AFP case per 10^5 children aged less than 15 years. Cases of JoRRP and NVI were reported in 2022. This indicates potential gaps in human papillomavirus (HPV) and varicella vaccination coverage respectively, especially in high-risk groups such as young migrant and refugee women of childbearing age from countries without universal vaccination programs. Paediatric HIV case numbers resulting from mother-to-child-transmission (MTCT) of HIV remain low in Australia due to use of effective intervention strategies. However, there has been an increase in the number of imported cases of HIV in children (mainly perinatally-acquired) from countries with a high HIV prevalence. Without effective vaccines, there has been no decline in the incidence of congenital CMV and neonatal HSV, indicating the importance of early identification and management to reduce morbidity and mortality. The first cases of dengue, Q fever and severe acute hepatitis were received by APSU in 2022, including two cases of acute hepatitis in which aetiology has not been confirmed to date. The APSU has an important ongoing role in monitoring rare childhood infections.

Keywords: Australia; child; communicable disease; emerging infectious diseases; public health surveillance; rare disease

Introduction

Since 1993, the surveillance of rare communicable diseases and rare complications of communicable diseases in children has been an important activity of the Australian Paediatric Surveillance Unit (APSU).[1] In this report, we present the results of APSU surveillance in 2022 for thirteen communicable diseases or complications of communicable diseases, namely: acute flaccid paralysis (AFP); congenital cytomegalovirus (cCMV); neonatal and infant herpes simplex virus (HSV) infection; perinatal exposure to human immunodeficiency virus

(HIV) and paediatric HIV infection; severe complications of influenza; juvenile-onset recurrent respiratory papillomatosis (JoRRP); congenital rubella infection/syndrome; congenital varicella syndrome (CVS) and neonatal varicella infection (NVI); dengue; Q fever; and severe acute hepatitis.

Surveillance method

Prospective national surveillance was conducted during 1 January – 31 December 2022 as previously described, with monthly clinician-reporting.[2,3] The exceptions were surveillance for dengue and Q fever (1 February – 31 December 2022) and for severe acute hepatitis (1 September – 31 December 2022). Briefly, the APSU distributes a report card in electronic (96%) or paper format (4%) each month to an average of 1,385 paediatricians and other clinicians in active child health practice and registered with the APSU (known as 'APSU Contributors'). The report card lists 16 rare conditions under APSU surveillance, including the 13 communicable diseases and complications described in this report (see case definitions in Appendix A). APSU Contributors are asked to report any cases newly diagnosed with one or more of the conditions listed and to return the card whether or not they have reported a case. This allows for calculation of annual response rates and identifies negative reports. Clinicians who notify a case are asked to provide data using an online or paper case report form (CRF). The CRF requests minimal individual patient details (to allow identification of duplicate reports), demographic and clinical data, and information on risk factors, vaccination status, management and short-term outcomes. Data entered online are stored in the secure research electronic data capture (REDCap) platform[4,5] hosted by the University of Sydney and data from paper forms are manually entered into REDCap by APSU staff. De-identified data are downloaded from REDCap into MS-Excel for simple descriptive analyses. Incidence estimates and 95% confidence intervals (CIs) are calculated using standard formulae and population denominators from the Australian Bureau of Statistics (ABS)[6] for children aged < 17 years (acute hepatitis), < 16 years (dengue; paediatric HIV; Q fever) and < 15 years (AFP; influenza; JoRRP), and from the Australian Institute of Health and Welfare (AIHW)[7] for live born neonates and infants (cCMV; neonatal and infant HSV; perinatal exposure to HIV; congenital rubella; CVS; neonatal varicella). Ethics approval for APSU surveillance studies was obtained from the Sydney Children's Hospitals Network and the University of New South Wales Human Research Ethics Committees.

Results

Representativeness of reporting and response rates

An average of 1,385 APSU Contributors received the monthly APSU report card in 2022. APSU Contributors came from every Australian state and territory, were distributed across metropolitan, rural and remote areas, and worked in hospitals and in community or private practice.

As in 2021,[2] the overall return rate of monthly APSU report cards was 81% (includes case notifications and 'nothing to report' responses). Prior to the coronavirus disease 2019 (COVID-19) pandemic (i.e., from 1993 to 2020), the response rate was consistently ≥ 90%.[3]

Total notifications, confirmed cases and incidence estimates

A total of 250 notifications was received for the thirteen communicable diseases and complications under surveillance in 2022. Of these, 184 were confirmed as cases; 23 were classified as duplicates; 18 were classified as reporting errors (administrative errors, cases outside study definition, missing CRFs) or provided insufficient data to confirm cases; and 25 were identified as historical (prevalent) cases not previously reported (Table 1).

Table 2 summarises the number of confirmed cases and incidence estimates (with 95% CIs)

Table 1: Notifications received in 2022 of communicable diseases and complications of communicable diseases under surveillance by the APSU, and their categorisation

Disease or complication under surveillance	Total notifications	Confirmed cases	Duplicates	Errors[b]	Other[c]
Acute flaccid paralysis[a]	**96**	**81**	**12**	**3**	0
Congenital cytomegalovirus	**55**	**33**[d]	**4**	**3**	**15**
Neonatal herpes simplex virus infection	**15**	**10**	**4**	**1**	0
Perinatal exposure to HIV	**27**	**20**	**1**	0	**6**
Paediatric HIV infection	**3**	0	0	0	**3**
Severe complications of influenza	**36**	**27**	**1**	**6**	0
Juvenile-onset recurrent respiratory papillomatosis	**1**	**1**[d]	**0**	0	0
Congenital rubella syndrome	0	0[d]	0	0	0
Congenital varicella syndrome	0	0[d]	0	0	0
Neonatal varicella infection	**1**	**1**	0	0	0
Dengue (commenced February 2022)	**2**	**2**[d]	0	0	0
Q fever (commenced February 2022)	**7**	**1**[d]	0	**5**	**1**
Severe acute hepatitis (commenced September2022)	**9**	**8**	**1**	0	0
Total	**250**	**184**	**23**	**18**	**25**

a Includes all cases of acute flaccid paralysis (AFP) reported via the APSU/National Enterovirus Reference Laboratory (NERL) and PAEDS surveillance systems. All confirmed cases have been classified by the Polio Expert Panel (PEP) as 'non-polio AFP' according to World Health Organization criteria.[8] Fifteen cases were reported via APSU/NERL, with three of these cases confirmed and ten cases duplicated by PAEDS.

b Includes administrative errors, cases outside of study definition, missing case report forms or insufficient data provided to confirm.

c Historical (prevalent) cases not previously reported.

d Includes both confirmed and probable cases.

reported for each condition in 2022 and from surveillance commencement to the end of December 2022.

Demographic, clinical, management and outcome data

Clinical features, management/treatment, outcome, trends in disease incidence and APSU outputs for each communicable disease or complication under surveillance are presented below. Table 3 presents the geographic location and Aboriginal and Torres Strait Islander status of confirmed cases for each communicable disease and complication.

Acute flaccid paralysis

APSU surveillance of acute flaccid paralysis (AFP, a clinical presentation of acute poliomyelitis) commenced in 1995 at the request of the Australian Government and was continued after the Western Pacific Region, including Australia, was declared polio-free by the World Health Organization (WHO) in 2000.[8] Since 2007, the national AFP program has also included cases identified through the Paediatric Active Enhanced Disease Surveillance (PAEDS) network, as previously described.[9] AFP cases are also reported directly to the National Enterovirus Reference Laboratory (NERL) by clinicians using the APSU case report form.[2]

Table 2: Confirmed cases identified by APSU surveillance during the period 1 January – 31 December 2022 and for the total study period, and estimated incidence per 100,000 children of the relevant population/age per annum, by communicable disease or complication of communicable disease

Communicable disease or complication of communicable disease	Surveillance study date of commencement	Confirmed cases for January–December 2022	Incidence estimate per 100,000 per annum and 95% CI for 2022	Confirmed cases for the whole study period to December 2022	Incidence estimate per 100,000 per annum for the whole study period to December 2022
Acute flaccid paralysis	March 1995	81[a]	1.70 [1.37-2.11][b]	1327	1.12 [1.06-1.18][b]
Congenital cytomegalovirus	Jan 1999	33[c]	11.15 [7.93-15.68][d]	529[c]	7.69 [7.07-8.38][d]
Neonatal herpes simplex virus	Jan 1997	10	3.38 [1.82-6.28][d]	239	3.24 [2.85-3.68][d]
Perinatal exposure to HIV	May 1993	20	9.80 [6.81-14.10][d]	992	11.80 [11.09-12.56][d]
Paediatric HIV infection	May 1993	0	0	101	0.07 [0.06-0.09][e]
Severe complications of influenza[f]	2008 (flu season only)	27	0.57 [0.39-0.83]	722	1.07 [1.00-1.15][b]
Juvenile-onset recurrent respiratory papillomatosis	Sep 2011	1[c]	0.02 [0-0.15][b]	21[c]	0.04 [0.03-0.06][b]
Congenital rubella infection/syndrome	May 1993	0	0	54[c]	0.64 [0.49-0.84][d]
Congenital varicella syndrome	May 2006	0	0	4[c]	0.08 [0.03-0.21][d]
Neonatal varicella	May 2006	1	0.34[d]	32	0.63 [0.44-0.88][d]
Dengue	Feb 2022	2[c]	0.04 [0.01-0.16][e]	2[c]	0.04 [0.01-0.16][e]
Q fever	Feb 2022	1[c]	0.02 [0-0.15][b]	1[c]	0.02 [0-0.15][b]
Severe acute hepatitis	Sep 2022	8	0.15 [0.07-0.30][g]	8	0.15 [0.07-0.30][g]

a Includes all cases of acute flaccid paralysis (AFP) reported via the APSU/National Enterovirus Reference Laboratory (NERL) and PAEDS surveillance systems. All cases have been classified by the Polio Expert Panel (PEP) as 'non-polio AFP' according to World Health Organization criteria.
b Based on population of children aged < 15 years.[6]
c Includes both confirmed and probable cases.
d Based on number of live births.[7]
e Based on population of children aged < 16 years.[6]
f Influenza surveillance was conducted each year during the influenza season, from July to September (inclusive) for 2008 and 2010–2015; June to October (inclusive) in the 2009 H1N1 influenza pandemic year; June to September (inclusive) 2016–2019 and 2022; and May to September (inclusive) in the 2020–2021 SARS-CoV-2 coronavirus pandemic years.
g Based on population of children aged < 17 years.[6]

Table 3: Demographic characteristics of confirmed cases reported to the APSU during the period 1 January – 31 December 2022, by communicable disease and complication of communicable disease

Communicable disease or complication of communicable disease	Confirmed cases N	Geographic distribution by state/ territory[a]	Indigenous N
Acute flaccid paralysis	81[b]	ACT: 1; NSW: 28; NT: 2; Qld: 9; SA: 5; Tas.: 0; Vic.: 29; WA: 7.	8
Congenital cytomegalovirus	33[c]	ACT: 0; NSW: 13; NT: 0; Qld: 7; SA: 0; Tas.: 0; Vic.: 2; WA: 11.	1
Neonatal herpes simplex virus	10	ACT: 0; NSW: 2; NT: 0; Qld: 5; SA: 0; Tas.: 0; Vic.: 4; WA: 0.	2
Perinatal exposure to HIV	20	ACT: 0; NSW: 5; NT: 0; Qld: 8; SA: 0; Tas.: 0; Vic.: 2; WA: 5.	0
Paediatric HIV infection	0	—	—
Severe complications of influenza	27	ACT: 1; NSW: 18; NT: 0; Qld: 2; SA: 0; Tas.: 0; Vic.: 5; WA: 1.	2
Juvenile-onset recurrent respiratory papillomatosis	1[c]	ACT: 0; NSW: 0; NT: 0; Qld: 0; SA: 0; Tas.: 0; Vic.: 0; WA: 1.	0
Congenital rubella infection/syndrome	0	—	—
Congenital varicella syndrome	0	—	—
Neonatal varicella	1	ACT: 0; NSW: 1; NT: 0; Qld: 0; SA: 0; Tas.: 0; Vic.: 0; WA: 0.	N/A[d]
Dengue	2[c]	ACT: 0; NSW: 1; NT: 0; Qld: 1; SA: 0; Tas.: 0; Vic.: 0; WA: 0.	0
Q fever	1[c]	ACT: 0; NSW: 1; NT: 0; Qld: 0; SA: 0; Tas.: 0; Vic.: 0; WA: 0.	0
Severe acute hepatitis	8	ACT: 0; NSW: 4; NT: 0; Qld: 3; SA: 0; Tas.: 0; Vic.: 1; WA: 0.	1

a ACT: Australian Capital Territory; NSW: New South Wales; NT: Northern Territory; Qld: Queensland; SA: South Australia; Tas.: Tasmania; Vic.: Victoria; WA: Western Australia.

b Includes all cases of acute flaccid paralysis (AFP) reported via the APSU/National Enterovirus Reference Laboratory (NERL) and PAEDS surveillance systems. All cases have been classified by the Polio Expert Panel (PEP) as 'non-polio AFP' according to World Health Organization criteria8

c Includes both confirmed and probable cases.

d N/A: not applicable.

Data on AFP cases collected by the three different surveillance sources are collated by the NERL, reviewed and classified by the Polio Expert Panel, and reported to the WHO.[2,3]

In 2022, a total of 96 AFP notifications was ascertained jointly by APSU/NERL and PAEDS, with 15 contributed by APSU/NERL alone. Eighty-one cases were confirmed as non-polio AFP and twelve were duplicates (Table 1), affirming Australia's polio-free status. The other three cases were classified as errors (not AFP). The incidence estimate was 1.70 (95% CI: 1.37–2.11) AFP cases per 100,000 children less than 15 years of age (Table 2), which met the WHO annual surveillance target of at least 1 AFP case per 100,000 children aged < 15 years. 'Adequate' stool samples (which WHO defines as two stool samples collected at least 24 hours apart and within 14 days of onset of paralysis in ≥ 80% of cases) were collected from 58/81 children with confirmed AFP (72%).

Of the 81 confirmed AFP cases notified to the APSU, three were notified from sites outside the eight hospitals where PAEDS operates. Ten

additional cases were identified by both APSU and PAEDS surveillance. Duplicates often provide complementary data and are important for validating the effectiveness of AFP surveillance.

The most common diagnoses assigned by the PEP for the non-polio AFP cases were Guillain-Barré syndrome (GBS) (n = 26), transverse myelitis (TM) (n = 12), acute disseminated encephalomyelitis (ADEM) (n = 11), botulism (n = 3), and tick bite paralysis (n = 3). Two children were diagnosed with a recently described entity of interest, acute flaccid myelitis (AFM).[10]

Retrospective data analysis of 590 cases of AFP contributed by APSU/NERL and PAEDS surveillance systems over eleven years (2007–2017), published in 2022, showed that almost half of children presenting with AFP were aged < 5 years and that the most common diagnoses were GBS, TM and ADEM, with the latter occurring more often in winter.[11]

AFP data were also published in the Australian National Enterovirus Reference Laboratory's 2021 annual report in *Communicable Diseases Intelligence*,[12] and are published fortnightly by the WHO Regional Office for the Western Pacific in the Polio Bulletin 2022.[13] These data also contribute to the WHO's annual progress report on sustaining polio-free status in the Western Pacific Region.[14]

Congenital cytomegalovirus infection

APSU surveillance of congenital cytomegalovirus (cCMV) has been conducted since 1999.[2,3,15]

In 2022, there were 55 notifications of cCMV in infants, of which 33 were confirmed as cases (n = 31 definite and n = 2 probable) (aggregated); four were duplicates; three were errors (two were outside of case definition and one had insufficient data to classify); and fifteen were historic prevalent cases diagnosed prior to 2022 (Table 1). In comparison, 45 confirmed cCMV cases were reported in 2021 and 37 in 2020. Cases have been reported each year since surveillance commenced, with the highest number in 2021 (n = 45) and the lowest in 2003 (n = 7).[2]

Of the 33 confirmed cCMV cases in 2022, 12 (36%) were small for gestational age. Fifteen cases were symptomatic (45%), with the most common clinical conditions being small for gestational age (n = 12); jaundice (n = 10); thrombocytopaenia (n = 9); microcephaly (n = 6); and hepatitis (n = 5). Hearing impairment was diagnosed in 21 children (64%) and was sensorineural in 16 of them. Five children had developmental delay. Seven of the eight (88%) infants who had moderate to severe cCMV symptoms, including neurological symptoms or multiple symptoms, received antiviral treatment with valganciclovir or ganciclovir according to current recommendations,[16–18] and one of the eight infants died.

A symptomatic illness suggestive of maternal CMV infection was reported during pregnancy in six of 22 (27%) mothers for whom these data were available. A positive immunoglobulin G (IgG) and/or IgM for CMV infection was reported in eleven mothers.

In 2022, incidence data from APSU cCMV surveillance[19] were included in updated Australian clinical guidelines for the management of CMV infection in infants.[20]

Neonatal and infant herpes simplex virus infection

APSU surveillance of neonatal and infant herpes simplex virus (HSV) infection has been conducted since 1997.[2,3,21] In 2022, there were 15 notifications of HSV infection in infants reported to the APSU, of which ten were confirmed as cases, four were duplicates and one was an error (no CRF completed) (Table 1). In comparison, 14 confirmed HSV cases were reported to the APSU in 2021 and eight cases in 2020. HSV cases have been reported each year since surveillance commenced, with the highest confirmed case number reported in 2015 (17 cases) and the lowest in 2017 (two cases).[22]

Of the ten confirmed cases in 2022, all were neonates aged between one and 21 days; 30% (3/10) had disseminated disease, 30% had skin eye mucous membrane (SEM) disease and 60% (6/10) presented with central nervous system (CNS) disease (four of whom also had cutaneous disease). Of the three neonates with disseminated disease, one had encephalitis and cutaneous involvement and one had severe hepatitis requiring a liver transplant. Of the ten cases, 50% (5/10) had HSV-1 serotype and 50% (5/10) had HSV-2 serotype. All children received antiviral therapy (acyclovir) except one child with disseminated disease who died on the day they presented to hospital. A second case, who also had disseminated disease, received aciclovir treatment but died before completing treatment. No neurological sequelae were recorded at discharge for any of the cases with CNS disease.

Analysis of 87 confirmed cases of neonatal HSV with neurological disease reported to the APSU between 1997 and 2020, out of a total of 195 cases of neonatal HSV reported during this period (45%), showed that male neonates were significantly more likely to have HSV CNS disease than those with other forms of HSV, and had higher frequencies of mortality and of neurodevelopmental sequelae in survivors.[23]

In 2022, data from APSU neonatal HSV surveillance[21] were included in a background comment on neonatal HSV incidence in Australia in updated Australian clinical guidelines for the management of HSV infection in infants.[24]

Perinatal exposure to HIV and paediatric HIV infection

APSU surveillance of perinatal exposure to human immunodeficiency virus (HIV) in infants and paediatric HIV infection has been conducted since 1993 in collaboration with the Kirby Institute.[2,3,25]

Perinatal exposure to HIV in infants

In 2022, there were 27 notifications of infants with perinatal exposure to HIV reported to the APSU. Of these, 20 were confirmed as incident cases; six were prevalent cases born in 2020 and 2021 and not previously reported; and one was a duplicate of a confirmed case reported in 2021 (Table 1). Confirmed cases were born to women with HIV infection and exposed perinatally by *in utero* exposure. In comparison, 43 confirmed cases of infants with perinatal exposure to HIV were reported each year in 2021 and 2020,[2,3] and 59 confirmed cases were reported in 2019.[26] Prior to 2019, an average of 30 infants with perinatal exposure were reported each year since surveillance commenced in 1993.[27] Of the 43 perinatal exposure cases reported in 2021, two cases were subsequently found to have mother-to-child transmission (MTCT) of HIV; previously, two cases of the 59 perinatal exposure cases reported in 2019 were subsequently found to have MTCT of HIV.[26]

Of the 20 infants confirmed in 2022 with perinatal HIV exposure, 19 were born in Australia and one in a country with a high prevalence of HIV. HIV test results were only provided for seventeen infants, of whom seven tested negative at their most recent test and ten did not have a result recorded at the time of reporting. Follow-up of these infants at 18 months will be conducted to obtain further HIV test results, in accordance with clinical recommendations.[28] Eight of the 20 infants were reported to have been treated with antiretroviral therapy and nine with prophylactic antiviral treatment after birth.

A separate CRF was used to record data for mothers of perinatally-exposed children; in 2022, CRFs were only completed for five mothers of the 20 infants confirmed as cases. All mothers were born outside of Australia and were diagnosed with HIV antenatally, receiving antiretroviral therapy during pregnancy. Three infants were delivered by elective and one infant by emergency caesarean section; however, one

infant was delivered vaginally. Breastfeeding was avoided for four infants; one infant was breastfed for four weeks.

Paediatric HIV

There were three cases of paediatric HIV notified in 2022. All were historic prevalent cases (Table 1) born in 2007, 2008 and 2013 outside of Australia in countries with a high prevalence of HIV. Two children had acquired HIV by MTCT, with HIV-1 as the identified sub-type. Both children were reported to be asymptomatic at the time of HIV testing in 2022. The exposure for the third child was unknown but presumed to be MTCT and the HIV subtype and clinical status were not recorded. One imported case of paediatric HIV (acquired overseas) was reported to the APSU in 2021,[2] and three imported cases were reported in 2014.[29]

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.[30]

Severe complications of influenza

APSU surveillance of severe complications of influenza has been conducted since 2008.[2,3,9] In 2020, the APSU added questions about co-infection with SARS-CoV-2[2,3] and in 2022 added questions about COVID-19 vaccination uptake.

Between 1 June and 30 September 2022, there were 36 notifications of children with severe complications of influenza reported to the APSU: 27 were confirmed cases; one was a duplicate; six were errors (five were diagnosed outside the surveillance period and one was outside the age range); and a CRF was not returned for two (Table 1). No cases of severe influenza were reported in 2020 and 2021 COVID-19 pandemic years. In 2019, 62 confirmed cases were reported;[26] prior to 2019, cases had been reported each year since surveillance commenced in 2008.[31]

All 27 confirmed cases in 2022 had laboratory confirmed influenza A. The influenza A virus was subtyped in five: three had H1(09) and two had H3 subtypes. Fifteen children (56%) were aged 5–9 years and twelve children (44%) were aged < 5 years. Five children were admitted to intensive care units. Pneumonia was the most common complication, reported in fifteen children (56%). Laboratory proven bacterial co-infection was reported in six children (22%, and due to *Streptococcus pneumoniae* in four) and laboratory proven viral co-infection in six children, two of whom had laboratory proven co-infection with SARS-CoV-2.

Of the 27 children who were confirmed as cases, two had influenza complicated by shock (requiring resuscitation with > 40 ml/kg of intravenous fluids), one had seizures and one developed myocarditis. Fifteen children required supplemental oxygen, three required invasive ventilation and one required extracorporeal membrane oxygenation. Only five children were treated with oseltamivir and 15 received antibiotics. Two children died and three children were still hospitalised at the time of reporting. Only one child had received a seasonal influenza vaccine; 13 were not vaccinated and vaccination data were unavailable for another thirteen children. Only four children had an underlying medical condition that likely predisposed them to severe influenza complications (two with asthma and two with genetic disorders and neurodevelopmental delay) and 23/27 children (85%) were previously healthy. Six children had previously contracted COVID-19; only one had been hospitalised and hospitalisation data were unavailable for one child. The COVID-19 vaccination status was not reported for any child.

In 2022, data on neurological complications in children aged <15 years with severe influenza and reported to the APSU between 2008 and 2018 were published in the *Journal of the Pediatric Infectious Disease Society.*[32] More than a quarter of all children with severe influenza (165/633, 26%) had neurological complications, and neurological complications accounted for almost half of all deaths (15/32, 47%).

Juvenile-onset recurrent respiratory papillomatosis

APSU surveillance of juvenile-onset recurrent respiratory papillomatosis (JoRRP) has been conducted since 2011.[2,3,33]

In 2022, there was one confirmed case of JoRRP reported to the APSU (Table 1). The child was born in Vietnam, where there is a high prevalence of human papillomavirus (HPV) infection and no universal HPV vaccination program. Diagnosis of JoRRP was confirmed by histology. HPV genotyping identified HPV 6, which is strongly implicated in the development of JoRRP,[34] and is targeted by HPV vaccines.[35] HPV vaccination status was not recorded for the mother. The child was treated with debulking surgery.

Prior to 2021, the last case of JoRRP was reported in 2017.[27] The variable annual incidence estimate for JoRRP (Table 2)[2] is expected with very rare conditions.

Congenital rubella infection and syndrome

APSU surveillance of congenital rubella (infection and syndrome) has been conducted since 1993.[2,3,36]

In 2022, no notifications were received by the APSU (Table 1). This is the seventh consecutive year without a case and is consistent with the absence of congenital rubella notifications to the National Notifiable Diseases Surveillance System (NNDSS) for the same period. The last reports to the APSU were in 2015, with one case of congenital infection and one case of congenital rubella syndrome (CRS).[37] The incidence (Table 2) has steadily declined since the study commenced, when case numbers peaked at 24 per annum between 1993 and 1996.[38]

Congenital varicella syndrome and neonatal varicella infection

APSU surveillance of congenital varicella syndrome (CVS) and neonatal varicella infection (NVI) has been conducted since 2006. [2,3,39]

In 2022, no cases of CVS were reported to the APSU (Table 1) for the second consecutive year, with one case reported previously in 2020.[2]

However, one case of NVI was reported to the APSU (Table 1) for the first time since 2019, when three cases were reported.[26] Data for this case are pending.

APSU incidence estimates of CVS and NVI (Table 2) have been steadily declining since surveillance commenced, following the introduction of Australian Government funded varicella zoster virus vaccination for all children aged 18 months.[39]

In 2022, data comparing CVS and NVI incidence estimates obtained by APSU surveillance in the pre-vaccination era (1995–1997)[40] with the post-vaccination period (2006–2020) showed a sustained decline in both diseases, which was significant for NVI. These data were presented at the Royal Australasian College of Physicians Annual Congress[41] and subsequently published in an article.[42]

New communicable disease surveillance studies in 2022

APSU surveillance of dengue, Q fever, and severe acute hepatitis commenced in 2022 and the background and aims of each study and preliminary findings are described below.

Dengue

APSU surveillance of dengue virus infection commenced in February 2022. Dengue virus infection is caused via mosquito-borne transmission of the dengue virus (DENV).[43,44] Infection mainly occurs in tropical and subtropical regions.[43,44] In Australia, outbreaks of

dengue have been documented in Far North Queensland, however local transmission of DENV has been reported further south in Central Queensland.[45,46] Four serotypes of DENV are known to cause human disease (DENV-1, DENV-2, DENV-3, and DENV-4).[43,44] The spectrum of symptoms associated with DENV infection range from a mild febrile illness usually mistaken for the flu to severe dengue, which is a life-threatening emergency and includes dengue haemorrhagic fever and dengue shock syndrome.[43,44] Children have a greater risk of severe disease and death.[47] Presently, there is no specific treatment for dengue and care is supportive.[42,43] In 2015, the world's first dengue vaccine was developed by Sanofi Pasteur (CYD-TDV or Dengvaxia);[48] however it is only for use in individuals aged 9–45 years who have had previous dengue infection.[44] Two candidate dengue vaccines have since been developed for use in dengue-seronegative individuals, and phase 3 clinical trials are currently underway.[49]

The prevalence and characteristics of this emerging condition have not been well studied in children in Australia. APSU is conducting surveillance of dengue to document the geographic distribution of dengue in children and describe the demographics, clinical features and severity, treatment and short-term outcomes prior to the availability of vaccination. In addition, the APSU study aims to document serotype trends of DENV paediatric infections in Australia.

The case definition for APSU surveillance of dengue is: Any child aged < 16 years with either a confirmed or probable infection.

A confirmed case requires laboratory-confirmed Dengue infection as determined by:

- Isolation of dengue virus or detection of dengue virus by nucleic acid testing; or
- Detection of dengue non-structural protein 1 (NS 1) antigen in blood by enzyme immunoassay; or
- IgG seroconversion, a significant increase in antibody level, or a fourfold or greater rise in titre to dengue virus, proven by neutralisation or another specific test; or
- Detection of dengue virus-specific IgM in cerebrospinal fluid, in the absence of IgM to Murray Valley encephalitis, West Nile virus/Kunjin or Japanese encephalitis viruses; and
- A clinically compatible illness (includes fever, headache, arthralgia, myalgia, rash, nausea, and vomiting, with possible progression to severe plasma leakage, severe haemorrhage, or severe organ impairment – CNS, liver, heart or other).

A probable case requires laboratory suggestive evidence, which is:

- Detection of NS1 antigen in blood by a rapid antigen test, or detection of dengue virus-specific IgM in blood; and
- A clinically compatible illness and epidemiological evidence; or
- A clinical compatible illness and household epidemiological evidence.

In 2022, two cases of dengue were notified to the APSU, one confirmed and one probable (Table 1), and the incidence estimate for the surveillance period (1 February – 31 December 2022) is shown in Table 2. Neither child had a prior history of dengue or had recently travelled to an endemic country. One had DENV2 serotype and the serotype was not recorded for the second child. Both children were hospitalised and symptoms included fever, rash, cough, severe abdominal pain, diarrhoea, fatigue, retro-orbital pain and myalgia/arthralagia joint pains. One child had respiratory co-infection with human metapneumovirus. Both children received supportive therapies (intravenous fluids, pain relief) and one child received ceftriaxone. On discharge, one child had ongoing problems including arthralgia, fatigue, thrombocytopaenia and hepatitis.

Q fever

APSU surveillance of Q fever commenced in February 2022. Q fever is caused by *Coxiella burnetii*, which is a zoonotic bacterial infection mainly carried by large domestic animals such as cattle and sheep but also found in wild mammals and domestic pets.[50] Transmission of *C. burnetii* from animals to humans is by inhalation of dust particles containing aerosolised spores of the bacterium.[50] *C. burnetii* infection can also be acquired from contaminated animal products such as meat, milk, wool, placenta and other birth products.[51] In Australia, Q fever is a nationally notifiable disease. Cases have been observed in all states and territories, but over 80% of all notified cases are residents of Queensland and New South Wales.[52] Although Q fever has mostly been observed in rural areas, cases have also been observed in urban areas.[53]

Q fever may manifest as asymptomatic, mild, or severe disease that results in hospitalisation and death.[54] Clinical symptoms of acute Q fever from primary *C. burnetii* infection include: an influenza-like illness with fever, sweats, muscle aches and headaches, and less commonly pneumonia and hepatitis.[54] Approximately 5% of individuals with acute Q fever will develop chronic Q fever, which can present as endocarditis, bone and joint infections or chronic fatigue syndrome.[55] Treatment of acute and chronic Q fever is primarily with the antibiotic doxycycline.[54]

Q fever is reported less often in children than adults and the symptoms are less specific,[56]so there is a concern that the disease may be under-recognised in children and that the true burden of disease is unknown.[56] A Q fever vaccine, developed in Australia, has been available for human use since 1989; however, it can only be administered to individuals aged ≥ 15 years with no previous exposure to *C. burnetii*.[57] Plans to commence an Australian clinical trial of Q fever vaccination in children aged 10–15 years were announced in 2020.[58] It is envisaged that APSU surveillance will provide epidemiological and clinical data on the burden of Q fever among Australian children prior to the availability of vaccination.

The case definition for APSU surveillance of Q fever is: Any child aged < 15 years who has either: laboratory-confirmed acute Q fever as determined by:

- Laboratory detection of *Coxiella burnetii* by polymerase chain reaction (PCR) testing of unclotted blood or serum; or
- Laboratory detection of a ≥ four-fold increase in IgG antibody titres to phase II *C. burnetii* antigen by indirect immunofluorescence antibody (IFA) in a serum sample collected 2–3 weeks after onset (convalescent), when compared with a serum sample collected at onset, in the absence of recent vaccination; or

probable acute Q fever as determined by:

- A clinical presentation compatible with acute Q fever disease (fatigue, cough, headache and fever) and laboratory detection of IgM antibody to phase II *C. burnetii* antigen in serum in the absence of recent vaccination; or

chronic Q fever as

- A clinical presentation consistent with chronic Q fever disease (e.g. endocarditis, osteomyelitis, hepatitis, encephalitis or other); and
- Laboratory detection by IFA of elevated IgG antibody titres to phase I *C. burnetii* antigen, with or without detection of IgA in serum or laboratory detection of *C. burnetii* by PCR in blood or tissue at infection site (e.g. bone).

Between 1 February and 31 December 2022, there were seven notifications of Q fever to the APSU, of which one was classified as a probable case and one was a laboratory-confirmed case diagnosed in 2012. Information is not yet available for five cases (Table 1). Confirmed

and probable cases were aggregated to calculate incidence estimates (Table 2). The probable case had laboratory detection of IgM antibody to phase II *C. burnetii* antigen in serum, which was indicative of probable infection and had multiple symptoms at presentation, including fever, sweats, cough, diarrhoea, chills/rigors, weight-loss and loss of appetite. The child was not hospitalised and remained unwell at the time of reporting. The laboratory-confirmed case was diagnosed in 2012 and had laboratory detection of chronic *C. burnetii* infection with osteomyelitis of the leg, requiring multiple surgeries. The child remained unwell at the time of APSU reporting. Both children had reportedly visited/lived on farms/rural properties and had exposure to large domestic animals (cattle and sheep).

Severe acute hepatitis

APSU surveillance of severe acute hepatitis commenced in September 2022. In early April 2022, the World Health Organization (WHO) released an emergency outbreak notice for severe acute hepatitis *of unknown origin* in the United Kingdom and Northern Ireland that affected young children in whom hepatitis viruses (A–E) were not detected.[59–61] This severe hepatitis was characterised by acute onset of symptoms including jaundice, abdominal pain, nausea and vomiting, which, in rare instances, progressed to fulminant hepatic failure and the need for liver transplantation in children who had been previously healthy.[59] Adenovirus (Type 41 and 44) was identified in up to one-third of the cases. [59–61] Since then, cases have been identified in 35 countries with 2% of children dying and 5% requiring a liver transplant.[61] Most cases (76%) were aged < 6 years.[61] In response to the emergence of severe acute hepatitis of unknown origin internationally, members of the International Network of Paediatric Surveillance Units (of which APSU is a member) initiated a collaborative surveillance study to determine the distribution and characteristics of severe acute hepatitis of unknown cause in children.

In contrast, the case definition for APSU surveillance of severe acute hepatitis is any newly diagnosed case of severe acute hepatitis of *any aetiology* in any child aged < 17 years with: acute onset of symptoms consistent with hepatitis (e.g. fever, jaundice, abdominal pain, fatigue, loss of appetite, rash, itch, joint or muscle ache, dark urine, pale coloured stools, nausea or vomiting); and elevated serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels (> 500 international units per litre [IU/L]). The cause of the hepatitis may unknown or due to infections, drugs, metabolic or auto-immune causes.

Between 1 September and 31 December 2022, there were ten notifications of severe acute hepatitis reported to the APSU, of which nine were confirmed as cases and one was a duplicate report (Table 1). Incidence estimates were calculated for the surveillance period (Table 2). Six of the nine confirmed cases were aged < 6 years. Only one child had travelled overseas in the previous six months. Five children were given a final diagnosis of viral hepatitis and one child had autoimmune hepatitis. Two children were not given a final diagnosis, with one child reported to have suspected viral hepatitis. Both children tested positive for adenovirus. Of the nine children, one child was still hospitalised with ongoing hepatitis and liver failure and one child had liver dysfunction at the time of reporting; five children had recovered; and the outcome was not stated in two children.

Discussion and conclusions

For the past 30 years, the APSU has collected national prospective data on a range of rare communicable diseases and complications of communicable diseases in the Australian paediatric population. APSU data have often provided the first national incidence estimates of these diseases (e.g. microcephaly)[62] as well as data on epidemiology, clinical features, treatment, risk factors, vaccination and outcomes; these data have helped inform public policy, management and education. For example, the publication of APSU data on haemolytic uraemic syndrome,[63]

which has been cited 266 times in the research literature, influenced changes in government regulations regarding production of uncooked fermented meat products. The publication of APSU study data on JoRRP[33] has been cited 140 times and emphasises the importance of prospective data collection for assessing impacts of HPV vaccination. Other publications of APSU data, including on severe complications of influenza,[64] congenital rubella,[36] CVS and NVI,[39] HSV[21] and CMV,[19] have been frequently cited and included in evidence-based systematic reviews,[65–67] articles on policy,[68–71] and clinical management guidelines.[20,24]

The response rate to the monthly report card from APSU Contributors was the same as for 2021 at 81%, but lower than in the previous 29 years of ≥ 90%.[2] Although the 81% result represents good engagement by clinicians reporting to the APSU, we speculate that the reduction in response rate may have been due in part to ongoing workload fatigue experienced by Contributors during the COVID-19 pandemic. Additionally, the implementation in 2022 of tighter security restrictions for email distribution of electronic report cards through public health email systems resulted in many Contributors not receiving APSU emails. The APSU is investigating ways of maintaining the email distribution system and ensuring that all emails are received by Contributors in a timely manner.

Key findings from APSU surveillance of thirteen communicable diseases and complications of communicable diseases in 2022 were as follows:

Cases of severe complications of seasonal influenza were reported to the APSU for the first time since 2019 (i.e. prior to the COVID-19 pandemic),[26] with two deaths recorded. Our data are consistent with an increase of influenza notifications in 2022 in Australia to other surveillance systems.[72] Other surveillance systems reported an earlier occurrence of influenza in the season,[72] which we also observed, with six children reported before the 1 June commencement of APSU surveillance. Consistent with other systems, we also identified a high number children aged 5–9 years with influenza.[72] It is concerning that only one child with severe influenza reported to the APSU in 2022 was documented to have received an influenza vaccine, despite the availability of free influenza vaccination for children ≥ 6 months with underlying medical conditions since 2010, and for all children aged ≥ 6 months to < 5 years since 2020, under the National Immunisation Program (NIP).[73] The appearance of severe influenza in children in 2022, as well as other viral and bacterial co-infections, including COVID-19, could be attributed to relaxation in early 2022 of government-mandated public health measures imposed during the 2020 and 2021 COVID-19 pandemic years, such as the closure of international and interstate borders, stay-at-home orders, physical distancing and mask wearing and high uptake of COVID-19 vaccination. Moreover, in 2021, the uptake of free influenza vaccination under the NIP was 20% lower than in 2020 in children aged ≥ 6 months to < 5 years and almost 50% lower in children aged 5–15 years.[74] Influenza vaccination rates increased slightly in 2022 but were still nearly 15% lower in children aged ≥ 6 months to < 5 years and nearly 5% lower in children aged 5–15 years, compared to 2020.[75] Influenza infection was greatly reduced in the Australian community in 2020–2021, which may have introduced a complacency for getting influenza vaccination during these years.[75] It will therefore be important to continue surveillance of severe influenza in children in the 2023 winter season to assess influenza infection rates and influenza vaccine uptake in this population.

In 2022, the minimum surveillance target of ≥ 1 non-polio AFP case per 100,000 children aged < 15 years was achieved for the fifteenth consecutive year, contributing to the retention of Australia's polio-free status. Maintaining ongoing surveillance of AFP in Australia is required, as Australia remains at risk of imported wild-type or vaccine-derived poliovirus from countries reporting poliomyelitis.[76]

Under the NIP, there was good coverage of measles-mumps-rubella-varicella vaccination in Australian children by age 60 months, at 96.6% in 2021;[74] however, there was a 15% reduction in the number of HPV vaccination courses started and completed in 2021, due to school closures during the COVID-19 pandemic.[73] The persistence of NVI and JoRRP cases reported to the APSU in 2022 indicates gaps in vaccination coverage, especially in young migrant and refugee women of child-bearing age from countries without universal vaccination programs, who need to be prioritised for vaccination. As of 2023, HPV vaccine is provided free under the NIP as a single catch-up dose for females and males up to age 26 years.[77] Ongoing surveillance of NVI and JoRRP will be important to identify further cases and potential gaps in vaccination uptake.

Cases of cCMV and HSV continue to be reported in infants, at similar rates to previous years. Despite awareness and education programs to prevent CMV infection in newborns,[20] many women are unaware they are infected with CMV during pregnancy if symptoms are lacking.[24] Our data suggest that vaccination of women of child-bearing age will be key to preventing these diseases in infants once suitable vaccines become available. In the meantime, early diagnosis and treatment of CMV and HSV infection in newborns is critical for reducing the mortality and significant morbidity caused by these infections, which include neurological and developmental sequelae[78–80] and sensorineural deafness associated with cCMV.[15]

Cases of perinatal exposure to HIV were fewer in 2022 than in previous years, but case numbers have been increasing since the study's commencement, as more women of childbearing age are now living with HIV due to effective antiretroviral treatments.[81] No maternal transmissions of HIV infection were recorded in 2022; however, follow-up HIV testing of infants at 18 months after birth will be required to confirm this. Most paediatric HIV cases reported to the APSU since 1993 have resulted from MTCT. Maternal transmission of HIV infection in infants within Australia continues to decrease, due to prevention strategies such as antiretroviral therapy during pregnancy, and prophylactic treatment of the child, elective caesarean section as the mode of delivery, and avoiding breastfeeding.[i] Imported cases of HIV infection from high prevalence countries were reported to the APSU in 2022, indicating the need for ongoing surveillance to inform clinical care and management. Also, as Australia is committed to meeting the World Health Organization goal for the elimination of MTCT of HIV by 2030,[82] continued surveillance of infants with perinatal exposure to HIV, and of their definitive HIV status at 18 months of age, is required.

Three new prospective national surveillance studies of rare and emerging communicable diseases (dengue, Q fever and severe acute hepatitis) were implemented using APSU methodology in 2022. None of the dengue cases reported were likely to have acquired the infection in Australia, based on their recent overseas travel to endemic countries. Q fever cases were all exposed to large domestic animals in rural areas. Most children with severe acute hepatitis had viral infection; however, the cause of acute hepatitis could not be determined in two of the children at the time of reporting. Future APSU reports will describe the distribution of these communicable diseases within Australia, relevant exposures, clinical features, management and outcomes.

In addition to conducting surveillance of the thirteen studies described in this report, the APSU developed studies of new and emerging communicable diseases and complications for implementation in 2023 in collaboration with the PAEDS network, namely paediatric inflammatory multisystem syndrome temporally associated with SARS-COV-2 (PIMS-TS) and Japanese encephalitis virus (JEV) infection. PIMS-TS has been identified internationally since late April 2020 in severely ill children and adolescents with COVID-19 who developed fever and shock frequently associated with abdominal pain and rash.[83–85] JEV infection

i Khawar et al, manuscript of APSU data in preparation.

is transmitted by mosquitos and a major outbreak occurred in Australia in early 2022 for the first time in 24 years,[86] with severe neurological disease and deaths occurring.[86] Neither PIMS-TS nor JEV have been well characterised in Australian children, so understanding the demographic and clinical characteristics will be important for identifying known risk factors, appropriate management and effectiveness of vaccines available for the infections causing these diseases.

Implications

Data obtained by APSU surveillance in 2022 have important implications:

- The need to promote influenza vaccination of children in 2023 and beyond is critical for reducing severe complications as influenza returns at high levels in the community.
- APSU surveillance will provide the first incidence estimates for dengue, Q fever and severe acute hepatitis in Australian children, and will improve knowledge of the distribution and key clinical features of these diseases to guide policy and management protocols.
- Rare vaccine-preventable diseases including NVI and JoRRP are still occurring despite high levels of free vaccination in the community through the NIP.

Current strategies aimed at preventing cCMV and HSV infection in newborns are ineffective in the absence of safe and effective vaccines. Efforts to diagnose and treat affected infants as early as possible are crucial for avoiding mortality and long-term neurological disability.

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Appendix A: Case definitions of APSU communicable diseases and complications under surveillance in 2022

Surveillance study – Case definition
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).
Congenital cytomegalovirus (cCMV) 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 *and/or* a positive serum IgM is found *and* 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, thrombocytopaenia, pneumonitis or myocarditis.
Neonatal and 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 *and* with either clinical evidence of HSV infection *or* laboratory confirmation of maternal perinatal HSV infection in an asymptomatic infant. Laboratory confirmation is by detection of HSV by PCR in a surface swab, respiratory specimen and/or sterile site (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 EEG). Laboratory evidence of maternal perinatal HSV infection is provided by detection of HSV in maternal genital swab and /or mother seroconverted to HSV or IgM positive in pregnancy or early postnatal period.

Surveillance study – Case definition

Perinatal exposure to HIV

Any infant 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 *in utero* exposure or through breastfeeding, should be notified, even if they are subsequently confirmed as HIV antibody negative.

Paediatric HIV infection

Any child aged less than 16 years at diagnosis of HIV infection in Australia

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 *and* by histology.

Probable case: as above but without histological confirmation

Severe complications of influenza in children <15 years

Any child aged less than 15 years with laboratory confirmed influenza admitted to hospital with at least one of the following complications:

Pneumonia (confirmed radiologically and/or microbiology)
Acute Respiratory Distress Syndrome (ARDS)
Laboratory proven viral co-infection including COVID-19
Laboratory proven bacterial co-infection; Bacteraemia; Septicaemia
Encephalitis / encephalopathy
Seizures (including simple febrile seizure, prolonged or focal seizure or status epilepticus)
Transverse myelitis
Polyneuritis / mononeuritis
Guillain-Barré syndrome
Reye Syndrome
Myocarditis; Pericarditis; Cardiomyopathy
Rhabdomyolysis
Purpura fulminans
Disseminated intravascular coagulopathy
Shock (requiring >40 ml/kg fluid resuscitation)
Acute renal failure
Death, including death at presentation to hospital
Requirement for supplementary oxygen, non-invasive ventilation, invasive ventilation or Extracorporeal Membrane Oxygenation (ECMO)

Surveillance study – Case definition

Congenital rubella infection/syndrome

Confirmed case

A confirmed case requires laboratory definitive evidence (fetal).

OR

Laboratory definitive evidence (infant) AND epidemiological evidence.

Laboratory definitive evidence

Fetal

Isolation or detection of rubella virus from an appropriate clinical sample (i.e. fetal blood or tissue, amniotic fluid, chorionic villus sample) by culture or nucleic acid testing.

Infant

Isolation or detection of rubella virus from an appropriate clinical sample in an infant, by culture or nucleic acid testing.

OR

Detection of rubella-specific IgM antibody in the serum of the infant.

Epidemiological evidence

The mother has confirmed rubella infection during pregnancy

Probable case

Epidemiological evidence (1st trimester infection).

OR

Epidemiological evidence (2nd and 3rd trimester infection) AND laboratory suggestive evidence (infant).

Laboratory suggestive evidence

Infant

High / rising rubella-specific IgG level in first year of life.

Congenital Rubella Syndrome

A confirmed case requires laboratory definitive evidence (fetal or infant), as described above AND clinical evidence.

Clinical evidence

A live or still born infant with ANY of the following compatible defects:

- Cataracts
- Congenital glaucoma
- Congenital heart disease
- Hearing defects
- Microcephaly
- Pigmentary retinopathy
- Development delay
- Purpura
- Hepatosplenomegaly
- Meninigoencephalitis
- Radioluscent bone disease
- Other defect not better explained by an alternative diagnosis

Surveillance study – Case definition

Congenital varicella syndrome (CVS)

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 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 CVS:
- 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.

Neonatal varicella infection (NVI)

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

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).

Dengue

Children aged <16 years who are either a:

Confirmed case

A confirmed case requires laboratory definitive evidence AND clinical evidence.

Laboratory definitive evidence

Isolation of dengue virus or detection of dengue virus by nucleic acid testing, detection of dengue non-structural protein 1 (NS1) antigen in blood by EIA, IgG seroconversion or a significant increase in antibody level or a fourfold or greater rise in titre to dengue virus, proven by neutralisation or another specific test or detection of dengue virus-specific IgM in cerebrospinal fluid, in the absence of IgM to Murray Valley encephalitis, West Nile virus/Kunjin or Japanese encephalitis viruses.

Clinical evidence

A clinically compatible illness includes fever, headache, arthralgia, myalgia, rash, nausea, and vomiting, with possible progression to severe plasma leakage, severe haemorrhage, or severe organ impairment – CNS, liver, heart or other.

OR a:

Probable case

Requires laboratory suggestive evidence AND clinical evidence AND epidemiological evidence OR clinical evidence AND household epidemiological evidence.

Laboratory suggestive evidence

Detection of NS1 antigen in blood by a rapid antigen test (unless dengue NS1 antigen by EIA is negative) or detection of dengue virus-specific IgM in blood.

Clinical evidence

A clinically compatible illness (e.g. fever, headache, arthralgia, myalgia, rash, nausea/vomiting).

Surveillance study – Case definition

Q fever

Children aged <15 years who have either:
Confirmed acute Q Fever as determined by:
Laboratory detection of *Coxiella burnetii* by PCR testing of unclotted blood or serum
OR
Laboratory detection of a ≥ four-fold increase in IgG antibody titres to phase II *C. burnetii* antigen by indirect immunofluorescence antibody (IFA) in a serum sample collected 2-3 weeks after onset (convalescent), when compared with a serum sample collected at onset, in the absence of recent vaccination
OR
Probable acute Q Fever as determined by:
Laboratory detection of IgM antibody to phase II *C. burnetii* antigen in serum in the absence of recent vaccination
AND
Clinical presentation compatible with acute Q Fever disease (fatigue, cough, headache and fever)
OR
Chronic Q Fever as determined by:
Clinical presentation consistent with chronic Q fever disease (e.g. endocarditis, osteomyelitis, hepatitis, encephalitis or other)
AND
Laboratory detection by IFA of elevated IgG antibody titres to phase I *C. burnetii* antigen, with or without detection of IgA in serum
OR
Laboratory detection of C. burnetii by PCR in blood or tissue at infection site (e.g. bone, joint)

Severe acute hepatitis

Any newly diagnosed case of severe acute hepatitis of any aetiology in any child aged <17 years with:
acute onset of symptoms consistent with hepatitis (e.g. fever, jaundice, abdominal pain, fatigue, loss of appetite, rash, itch, joint or muscle ache, dark urine, pale coloured stools, nausea or vomiting); AND
elevated serum alanine aminotransferase (ALT) OR aspartate aminotransferase (AST) levels (>500 IU/L); AND
hepatitis, of known or unknown cause, including infections, drugs, metabolic or auto-immune causes.