National incidence of viral disease in children

Yvonne Zurynski
• National – began in 1993
• Rare childhood conditions
• Infectious, genetic, mental health conditions, rare injuries (~ 55 conditions studied)
• Standardised case definitions
• Demographics, diagnosis, treatment, complications, outcomes
• Translation into policy and practice

Surveillance activities funded by DoHA Office of Health Protection and DoHA Chronic Disease Branch
Supported by RACP, University of Sydney, competitive grants (NHMRC Enabling grant, ARC Linkage, other grants)
The APSU Mechanism

** De-identified data

Multiple conditions studied simultaneously

- Case to report
- Nothing to report

Card Returned

Child health clinicians ~1390

Children < 15 years

87% email
13% yellow card
Clinicians Reporting to APSU

Number of Reporting Clinicians

Year

Response rate to APSU report card

≥ 90% since 1994
## APSU surveillance for viral disease

<table>
<thead>
<tr>
<th>Surveillance</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital rubella</td>
<td>1993 - ongoing</td>
</tr>
<tr>
<td>Perinatal exposure to HIV</td>
<td>1993 - ongoing</td>
</tr>
<tr>
<td>Acute flaccid paralysis</td>
<td>1995 - ongoing</td>
</tr>
<tr>
<td>Congenital cytomegalovirus</td>
<td>1999 - ongoing</td>
</tr>
<tr>
<td>Neonatal herpes simplex virus infection</td>
<td>1997 – ongoing 2012-ongoing</td>
</tr>
<tr>
<td>Neonatal and Infant HSV</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C virus infection</td>
<td>2003 - 2008</td>
</tr>
<tr>
<td>Severe complications of varicella infection</td>
<td>2006 – ongoing</td>
</tr>
<tr>
<td>Severe complications of influenza</td>
<td>July-Sept since 2007</td>
</tr>
<tr>
<td>Juvenile onset recurrent respiratory papillomatosis</td>
<td>Oct 2011 - ongoing</td>
</tr>
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<pre><code>                                                   | 2006 – ongoing         |
</code></pre>
<p>| Congenital cytomegalovirus                             | 1999 - ongoing         |
| Neonatal herpes simplex virus infection                | 1997 – ongoing         |
|                                                       | 2012-ongoing           |
| Neonatal and Infant HSV                                |                        |
| Hepatitis C virus infection                            | 2003 - 2008            |
| Severe complications of varicella infection            | 2006 – ongoing         |
| Severe complications of influenza                      | July-Sept since 2007   |
| Juvenile onset recurrent respiratory papillomatosis    | Oct 2011 - ongoing     |</p>
Acute flaccid paralysis
Bruce Thorley
Elizabeth Elliott
Monique Ryan
Linda Hobday
PEP

Paediatric HIV infection OR perinatal exposure to HIV
Ann McDonald,
David Wilson,
John Kaldor,
John Ziegler,
Elizabeth Elliott

Severe Complications of Influenza
Robert Booy,
Elizabeth Elliott,
Yvonne Zurynski
Marion Festa
Alisson Kesson

Congenital cytomegalovirus infection
William Rawlinson
Daniel Trincado
Gillian Scott
Sian Munro
Cristina Baleriola
Pamela Palasanthiran,
Professor Mark Ferson
David Smith,
Geoff Higgins
Micheal Catton
Alistair McGregor
Dominic Dwyer,
Alisson Kesson
Beverley Hall

Varicella
Robert Booy,
David Burgner,
Michael Nissen,
Jim Buttery,
Yvonne Zurynski,
Elizabeth Elliott,
Michael Gold,
Elizabeth Peadon

Juvenile onset Recurrent Respiratory Papillomatosis
Daniel Novakovic
Alan Cheng,
Julia Brotherton
Yvonne Zurynski
Robert Booy
Elizabeth Elliott
Paul Walker
Robert Berkowitz
Henley Harrison
Robert Black
Chris Perry
Shyan Vijayasekaran
David Wabnitz

Congenital Rubella
Cheryl Jones
Gulam Khandakar
Camille Raynes-Greenow
Margaret Burgess
Jill Forrest
AFP case definition criteria

Any child less than 15 years of age with:

Acute Flaccid Paralysis i.e. onset of flaccid paralysis in one or more limbs (ataxia, unsteady gait, GBS, TM and ADEM), OR
Acute onset of bulbar paralysis.

Possible causes of AFP

**Peripheral neuropathy**
- Guillain-Barre syndrome
- Acute axonal neuropathy
- Neuropathies of infectious diseases

**Acute myelopathy**
- Demyelinating diseases
- Transverse myelitis
- Acute Disseminated Encephalomyelitis (ADEM)
- Spinal cord ischaemia
- Peri-operative complication

**Systemic disease**
- Acute porphyria
- Critical illness neuropathy/myopathy
- Conversion disorder

**Disorders of neuromuscular transmission**
- Botulism
- Insecticide (organophosphate poisoning)
- Tick bite paralysis
- Snake bite

**Anterior horn cell disease**
- Acute poliomyelitis
- Vaccine associated poliomyelitis
- Other neurotropic viruses

**Muscle disorders**
- Polymyositis, dermatomyositis
- Trichinosis
- Periodic paralyses
- Corticosteroids and blocking agents
- Mitochondrial diseases (infantile type)
- Post viral myositis

**Other** (please specify)

Exclude Trauma

Bruce Thorley
Elizabeth Elliott
Monique Ryan
Linda Hobday
PEP
- Acute Flaccid Paralysis (AFP) started 1995
- Coordinated by VIDRL since 2000 in collaboration with APSU

WHO surveillance targets:

1/100,000 children <15y

80% stool collection rate
(2 stool samples within 14 days)

All case reports are reviewed by the PEP

• Targets difficult to reach
Jointly developed and managed by APSU and NCIRS

- Hospital based system
- Started active surveillance end of 2007
- Active case ascertainment – specialist surveillance nurses
- Timely
- Detailed data (clinical, management, outcome)
- Biological samples and clinical data on the same child
- Severe vaccine preventable diseases or AEFI
- Funded by DoHA and State Health
PAEDS

Hospitals involved in PAEDS

➢ Children’s Hospital at Westmead, Sydney
   APSU Elizabeth Elliott, Yvonne Zurynski
   NCIRS Kristine Macartney, Peter McIntyre, Robert Booy, Nick Wood

➢ Royal Children’s Hospital Melbourne
   Jim Buttery
   Jenny Royle
   Nigel Crawford

➢ Women’s and Children’s Hospital Adelaide
   Helen Marshall
   Mike Gold

➢ Princess Margaret Hospital, Perth
   Peter Richmond
   Christopher Blyth

➢ Royal Children's Hospital, Brisbane (2013)
   Michael Nissen
Non-polio AFP Australia 1995-2012

WHO AFP surveillance performance indicator: 1.0 non-polio AFP case per 100,000 children <15 years

PAEDS begins surveillance
Stool Collection Rate Australia 1995-2012

WHO AFP surveillance performance indicator: **two stools collected** <14 days of onset of paralysis from 80% non-polio AFP cases

PAEDS begins surveillance
At least one stool ~74%
• Guillain-Barre Syndrome
• Acute disseminated encephalomyelitis
• Transverse Myelitis

APSU and PAEDS Cases

- APSU
- PAEDS
- APSU/PAEDS

PAEDS begins surveillance
Congenital Rubella Syndrome

Diagnosis of congenital rubella confirmed by:
- IgM antibodies detected in the 1st months of life
- IgG antibodies in children 6-12 mo or a child < 2 years who has not been vaccinated
- Isolation of the virus from throat, urine

At least 20% of infants have severe birth defects
- Eyes: Cataract, microophthalmia, glaucoma, pigmentary retinopathy
- Ears: Bilateral or unilateral sensorineural deafness
- Heart: PDA, PA and valvular stenosis, VSD
- Triad: Abnormalities of the eyes, ears, and heart

- CNS: Microcephaly, psychomotor retardation, behavioral disorders
  - Persistent infection: Progressive rubella subacute sclerosing panencephalitis (SSPE)

Other symptoms associated with CRS
- Bone translucency and retarded growth
- Hepatosplenomegaly
- Intrauterine growth retardation
- 10 -20% of babies with CRS die within 1 year
Congenital Rubella

Year

Number of cases

Measles campaign

Forrest, Burgess, Donovan. CDI 2003
Congenital Rubella

Number of cases

Year


Congenital Rubella

Imported cases

Local cases

Measles campaign
Countries using rubella vaccine in their national immunization system

1996
12% of birth cohort

2011
41% of birth cohort

WHO 2011:

DRC (134,042 cases)
Nigeria (18,843 cases)
Somalia (17,298 cases)
Zambia (13,324 cases)
Chad (8,650 cases)
Sudan (5616 cases)
Ethiopia (3255 cases)
Afghanistan (3013 cases)
Uganda (3312 cases)

Indonesia (21,893 cases)
The Philippines (6,538 cases)

India (29,339 cases)
Pakistan (4386 cases)

France (14,949 cases)
Italy (5189 cases)
Romania (4189 cases)
Spain (3802 cases)
2012 Outbreaks recorded in NSW, Vic, Qld

NSW suffers worst measles epidemic in 14 years

SMH October 4, 2012

"It's easy to forget that in decades past, measles and its complications led to the deaths of hundreds of Australians, it was once more deadly than polio," Associate Professor Owler said.
Perinatal Exposure to HIV - Case definition

1993 start

- Any child < 16y diagnosed with HIV in Australia including children born to women with diagnosed HIV infection
- Any child known to have been exposed to HIV either perinatally or in utero or through breastfeeding even if they are eventually proved to be HIV –ve
- All cases identified via APSU are also enrolled in the national HIV register
Perinatal Exposure to HIV

Guidelines on prevention:
- Avoid breastfeeding
- C-section
- Antiretrovirals

Combination Highly active Anti-retroviral Therapies
Figure 32
Newly diagnosed HIV among women, 2002 – 2011, by year and HIV exposure category

Source: State and Territory health authorities
Perinatal Exposure to HIV

Incidence per 100,000 births
2.3 (1982–1986)
8.3 (2003–2006)

8.3 (2009)
9.2 (2010)
11.7 (2011)
13.7 (2012)

Prenatal diagnosis increasing (95% of mothers of reported infants)

Uptake of interventions increasing
Perinatal exposure to HIV

3 Number of Australian-born children reported with perinatal HIV exposure and number infected, by timing of the mother’s HIV diagnosis with respect to the child’s birth

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>Antenatal diagnosis</th>
<th>Postnatal diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. exposed</td>
<td>No. infected</td>
<td>No. exposed</td>
</tr>
<tr>
<td>1982–1986</td>
<td>3</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>1987–1990</td>
<td>16</td>
<td>4 (25%)</td>
<td>15</td>
</tr>
<tr>
<td>1991–1994</td>
<td>37</td>
<td>9 (24%)</td>
<td>18</td>
</tr>
<tr>
<td>1995–1998</td>
<td>36</td>
<td>4 (11%)</td>
<td>19</td>
</tr>
<tr>
<td>1999–2002</td>
<td>93</td>
<td>1 (1%)</td>
<td>7</td>
</tr>
<tr>
<td>2003–2006</td>
<td>82</td>
<td>4 (5%)</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>22 (8%)</td>
<td>86</td>
</tr>
</tbody>
</table>

* Includes one mother whose date of HIV diagnosis was not reported.

This trend has continued
Most women diagnosed antenatally
Most use interventions
No transmissions in 2011/2012 in antenatally diagnosed women
Varicella

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

**Neonatal**
- Any infant diagnosed with varicella in the first month of life according to history and/or laboratory findings without features of congenital varicella syndrome
- Pox-like rash (papulovesicular, vesiculopustular or haemorrhagic)
- Fever
- Complications may be present – superinfection, neurological or haematological problem

**Investigators**
Robert Booy,
David Burgner,
Michael Nissen,
Jim Buttery,
Yvonne Zurynski,
Elizabeth Elliott,
Michael Gold,
Elizabeth Peadon
Congenital and Neonatal Varicella

Varicella vaccine funded
<table>
<thead>
<tr>
<th>Year</th>
<th>Congenital varicella (n)</th>
<th>Incidence* (95% CI)</th>
<th>Neonatal varicella</th>
<th>Incidence* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>3</td>
<td>1.2 (0.3 to 3.7)</td>
<td>15</td>
<td>5.9 (3.4 to 9.9)</td>
</tr>
<tr>
<td>1996</td>
<td>1</td>
<td>0.4 (0.02 to 2.6)</td>
<td>16</td>
<td>6.3 (3.7 to 10.5)</td>
</tr>
<tr>
<td>1997</td>
<td>2</td>
<td>0.8 (0.3 to 1.8)</td>
<td>13</td>
<td>5.2 (2.9 to 9.1)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>6</td>
<td>0.8 (0.3 to 1.8)</td>
<td>44</td>
<td>5.8 (4.3 to 7.8)</td>
</tr>
<tr>
<td>2006†</td>
<td>1</td>
<td>0.7 (0.0 to 2.1)</td>
<td>7</td>
<td>5.0 (2.4 to 7.6)</td>
</tr>
<tr>
<td>2007</td>
<td>1</td>
<td>0.3 (0.0 to 1.0)</td>
<td>5</td>
<td>1.8 (0.2 to 3.3)</td>
</tr>
<tr>
<td>2008</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0.7 (0.0 to 1.6)</td>
</tr>
<tr>
<td>2009</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0.7 (0.0 to 1.6)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>2</td>
<td>0.19 (0.0 to 0.7)</td>
<td>16</td>
<td>2.05 (0.3 to 3.4)</td>
</tr>
</tbody>
</table>

*National incidence per 100,000 live births per year.
†Data from June 2006 so only 7 months follow-up in 2006.
Varicella hospitalisation pre and post varicella vaccine introduction in Australia

Zoster hospitalisation pre and post varicella vaccine introduction in Australia

Changes in Patterns of Hospitalized Children With Varicella and of Associated Varicella Genotypes After Introduction of Varicella Vaccine in Australia

Abstract

Background: Varicella in children, although usually mild, can cause hospitalization and rarely death. This study examined patterns of hospitalized children with varicella, and associated varicella genotypes, in 4 tertiary children's hospitals throughout Australia before and after varicella vaccine was introduced.

Methods: We obtained coded data on discharge diagnoses from each hospital before (1990 to 2001) and after (2007 to 2010) varicella vaccine introduction in 2005, adding active
Severe Complications of Influenza

Influenza is a common *usually mild* disease

**Recognised high risk:**
- frail elderly
- very young <2 yrs
- people with underlying chronic conditions
- Australian indigenous communities

Children are an efficient virus transmitter
Severe complications and deaths occur

**Surveillance for seasonal flu**
- 2007 feasibility study for one month
- 2008 - 2012 surveillance for seasonal flu (July-September)
Severe Complications of Influenza
Case definition

Any child aged < 15 years and admitted to hospital with laboratory confirmed influenza
and any of the following severe complications:

- Pneumonia (X-ray confirmed) and requiring oxygen
- Requirement for Ventilation
- Encephalitis / encephalopathy with or without seizures
- Myocarditis; Pericarditis; Cardiomyopathy
- Rhabdomyolysis
- Purpura fulminans
- Disseminated coagulopathy
- Transverse myelitis
- Polyneuritis
- Guillain-Barré Syndrome
- Shock (requiring >40 ml/kg fluid resuscitation)
- Acute renal failure
- Reye’s Syndrome
- Laboratory proven secondary bacterial infection; Bacteraemia, Septicaemia, Bacterial pneumonia
- Death

**Exclusion:** Simple febrile seizures
### Severe complications of Influenza

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>59</td>
<td>100</td>
<td>25</td>
<td>36</td>
<td>50</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>1.6(0.1-14.4)</td>
<td>3.2(0.1-14.9)</td>
<td>3.3(0.1-11)</td>
<td>4.8(0.2-14.8)</td>
<td>5.5 (0.2-14.8)</td>
</tr>
<tr>
<td>Flu A</td>
<td>11(19)</td>
<td>100(100)</td>
<td>23(92)</td>
<td>25(69)</td>
<td>35(70)</td>
</tr>
<tr>
<td>Flu B</td>
<td>48(81)</td>
<td>0</td>
<td>2(8)</td>
<td>9(25)</td>
<td>15(30)</td>
</tr>
</tbody>
</table>
Underlying chronic conditions ~40%

- Down Syndrome
- Interstitial lung disease
- Pre-term infant
- Chronic renal disease/failure
- Congenital heart disease
- Sickle-cell disease
- Clotting disorders
- Tracheomalacia
- Barnes Syndrome
- Wolf Hirschan Syndrome
- Congenital hydrocephalus/arachnoid cysts/shunt
- Autoimmune disease
- Developmental delay
- Panhypopituitarism
- Recurrent myositis
- Down Syndrome + epilepsy
- Cerebral Palsy
- Rett Syndrome

Only ~8% of those with underlying conditions vaccinated

~60% were previously healthy
Severe influenza 2008-2012

Total: 270
PICU: 110
Deaths: 18; 5 previously healthy; median age 7yrs
2012 APSU flu surveillance

- June – September
- Review of protocol and questionnaire

H7N9 Influenza
Important Information for Clinicians and Laboratories
10 April 2013

Summary: As of 10 April, 2013, 24 cases of H7N9 influenza have been reported in China, including 7 deaths. Although the environmental source has not yet been definitively determined, some of the confirmed cases have been associated with contact with chickens or poultry or an animal “wet market” environment.

In patients with acute pneumonia or pneumonitis with a history of travel to China within 7 days of illness onset, or contact with known confirmed or probable cases, the following is recommended:

1. Place the patient in a single room with negative pressure air-handling, or a single room from which the air does not circulate to other areas, and implement standard and transmission-based precautions (contact and airborne), including the use of personal protective equipment (PPE).
Acknowledgements

APSU

- 1390 APSU contributors
- APSU staff: Marie Deverell, Kirrilee Drew, Ingrid Charters, Jade Mangan
- APSU Investigators and study coordinators

PAEDS

- PAEDS Investigators: Elizabeth Elliott, Peter McIntyre, Robert Booy, Kristine Macartney, Yvonne Zurynski, Nicholas Wood, Peter Richmond, Christopher Blyth, Helen Marshall, Mike Gold, Jim Buttery, Nigel Crawford, Jenny Royle
- PAEDS Coordinator: Jocelynne McRea
- PAEDS surveillance nurses in all 5 states
The Australian Paediatric Surveillance Unit
at the Kids Research Institute

Current Studies

ACUTE FLACCID PARALYSIS (AFP)
- Protocol AFP
- Questionnaire AFP Initial

CONGENITAL CYTOMEGALOVIRUS INFECTION (CMV)
- Protocol CMV
- Questionnaire (NSW Participants)
- Questionnaire (Other States)

CONGENITAL RUBELLA (RUB)
- Protocol Rub
- Questionnaire Rub

CONGENITAL VARICELLA (VCON)

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