Influenza Related Complications and Deaths in Australian Children: Seasonal Surveillance 2008 -2015

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• Influenza is a common *usually mild* disease

• Highest burden:
  – frail elderly
  – very young <2 yrs
  – people with predisposing chronic conditions

• Children are excellent virus reservoirs and efficient virus transmitters

• Severe complications and death occur

• Little data on severe complications and deaths
National Immunization Program

• **Children considered at risk** (recommended and funded):
  – 6mo to <5yrs ATSI
  – 6mo to < 5yrs Chronic Medical Conditions

• **Other healthy children** (recommended, not funded):
  “Annual influenza vaccination is recommended for any person ≥ 6mo of age for whom it is desired to reduce the likelihood of becoming ill with influenza”
Flu Vaccines for children

- Sanofi’s *FluQuadri® Junior* < 3yrs.
- GlaxoSmithKline *Fluarix Tetra®* >3yrs.
- Seqirus (formerly bioCSL) flu vaccine *Fluvax®* is not registered for use in children less than five years of age
Aim:
To describe:
• Influenza related complications and deaths in Australian children 2008 -2015
• Predisposing conditions
• Vaccination
• Treatment with flu specific antivirals
Methods

APSU: ~1500 paediatricians

- Monthly reporting
  - 90% report by e-mail
  - Response rates to card >90%

Each year July-September

Clinicians are asked to reports cases as they see them

Weekly reporting to the Department of Health and Ageing Surveillance Section
Case definition

Any child aged < 15 years with laboratory confirmed influenza AND admitted to hospital AND who have at least one of the following complications:

- Pneumonia (Confirmed on X-ray or microbiology) and Oxygen requirement
- Mechanical ventilation
- 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
- Guillain-Barré syndrome
- 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
Data collection: paper/fax 2008-13; on-line via REDCap from 2014
Results:

N = 474  Male: 252 (54%)  Female: 210 (46%)

Median Age: 3.5 (0.12 - 14.4) years

Flu A – 329;  Flu B – 154
Results:

- Pre-existing chronic conditions – 174 (36.7%)
  Vaccinated: 18 (10%)

- Previously healthy – 300 (63.3%)
  Vaccinated: 3 (1%)

Vaccination status unknown in ~ 75%

Suggests that clinicians don’t ask
Complications:

283 (59.7%) Pneumonia
86 (18.0%) Co-infection (laboratory proven)
71 (15.0%) Encephalitis/encephalopathy
19 (4.0%) Rhabdomyolysis
19 (4.0%) Myocarditis/ cardiomyopathy

~35% had more than one complication
Total treated 2008-2015:(185)39%

Given after 48 hours in 90%
2008-2015
474 cases; 191 ICU admissions; 25 deaths

Severe influenza cases reported
Severe influenza cases <16yrs reported

APSU cases

CDNA – Lab confirmed cases
## Deaths: N=25

<table>
<thead>
<tr>
<th>State</th>
<th>N (%)</th>
<th>Hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSW</td>
<td>9 (40)</td>
<td>Westmead - 3; Randwick - 1; Bankstown - 3; Lismore Base – 1; Albury Base – 1</td>
</tr>
<tr>
<td>Vic</td>
<td>4 (16)</td>
<td>RCH – 2; Gippsland -1; Ballarat Base-1;</td>
</tr>
<tr>
<td>Qld</td>
<td>4 (16)</td>
<td>Mater-1; RCH-1; Gold Coast – 1; Nambour- 1; Rockhampton - 1</td>
</tr>
<tr>
<td>SA</td>
<td>2 (8)</td>
<td>Women’s and Children’s -1; Flinders Medical Centre -1</td>
</tr>
<tr>
<td>WA</td>
<td>2 (8)</td>
<td>Princess Margaret - 2</td>
</tr>
<tr>
<td>Tas</td>
<td>2 (8)</td>
<td>Launceston General - 1; Mersey Community Hospital -1</td>
</tr>
<tr>
<td>NT</td>
<td>1 (4)</td>
<td>Royal Darwin - 1</td>
</tr>
</tbody>
</table>

- Tertiary paediatric referral centres: 11 (44%)
- Other Hospitals: 14 (56%)
Complications Before Death

7 pneumonia
7 mechanical ventilation
  1 ECMO

5 Encephalitis/encephalopathy
1 acute necrotising encephalopathy
4 Seizures
1 intracranial haemorrhage

5 Shock requiring fluid resuscitation

4 Proven Co-infection
1 Disseminated Intravascular Coagulation
1 Rhabdomyolysis
1 metabolic acidosis
1 myositis
4 cardiomyopathy/myocarditis

Most had multiple complications

ICU: 15 (60%)

3 dead on arrival in ED
Deaths by age group

- **<5 yrs old**: 6 (2.1%) died
- **5-14 yrs old**: 19 (11.3%) died

P < 0.01
Underlying condition

15 (60%) had a chronic condition

- 3 Neuromuscular disorders
- 2 Cerebral Palsy
- 2 Malignancy or other immunodeficiency
- 1 Gastrointestinal disorders (GORD, fundoplication)
- 2 Congenital heart disease
- 1 CHARGE syndrome
- 1 Panhypopituitarism
- 3 Undiagnosed rare genetic syndrome

2 vaccinated for flu

10 (40%) were healthy

None vaccinated for flu
Previously Healthy Children – Examples

2009

• 12 yo, fever, cough, headache, malaise, sore throat, myalgia

• Admitted to hospital

• Not tested for influenza

• No Oseltamivir

• Discharged home after 2 days in hospital

• Developed serious pneumonia – dead on arrival at hospital 2 days later

• Flu A H1N1 2009 confirmed on autopsy
Previously Healthy Children - Examples

2015

- 4.3yo; Flu B
- Usual flu symptoms (fever, malaise, cough etc.)
- Deteriorated quickly in hospital
- Seizure
- Encephalitis / encephalopathy, acute necrotising encephalopathy
- Shock (requiring >40ml/kg fluid resuscitation)
- Persistent metabolic acidosis,
- ? Secondary infection
- Cefotaxime, IV aciclovir, Vancomycin, Gentamicin

- Died 2 days later
Summary

Severe complications:
• Only 39% were treated with flu specific antivirals
• Of the treated 90% were treated late (>48hrs)

Vaccination:
• 10% children with chronic disorders

Deaths:
• every year 2008-2015 (total 25)
  • more common among older children ≥ 5 years
  • ~ 60% chronic conditions and 40% previously healthy
• general hospitals (66%) rather than paediatric referral centres
Conclusions

- Better awareness among clinicians
- Earlier detection
- Earlier treatment and referral to paediatric centre
- Vaccination
- Ongoing surveillance to monitor the effectiveness of any prevention and intervention strategies

CDC:

the benefits of flu vaccination 2014-2015

The estimated number of influenza-associated illnesses prevented by flu vaccination during the 2014-2015 season: 1.9 million

The estimated number of flu-associated medical visits prevented by vaccination during the 2014-2015 season: 966,000

The estimated number of flu hospitalizations prevented during the 2014-2015 season: 67,000
Thank You

• Co-Authors

• Australian Department of Health and Ageing

• all APSU clinicians for reporting cases

Questions?