Pertussis Control in New Zealand
How can we do better?
Conflict of interest

• In the past I have received support for vaccine work, clinical trials, presentation of papers and conference attendance from NZ Ministry of Health, US Government, Foundation Merieux, International Vaccine Institute, CSL, GSK, MSD, Novartis and Pfizer.
Pertussis Control in New Zealand

• The vaccination schedule
  – How we got there. Is it ideal?

• How we are performing?
  – What do we need to do to improve?

• What new strategies exist to better control pertussis?
But First Jim Aubrey’s Story
Two issues of Importance

• Pertussis immunity is not life long

• High vaccination coverage alone will not protect infants.
## Symptoms differ according to age

<table>
<thead>
<tr>
<th>Children</th>
<th>Adolescents/Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Typical symptoms:**¹,³</td>
<td>**Atypical symptoms:**²</td>
</tr>
<tr>
<td>Paroxysmal cough</td>
<td>Sneezing</td>
</tr>
<tr>
<td>Post-tussive vomiting</td>
<td>Coryza</td>
</tr>
<tr>
<td>Inspiratory whoop</td>
<td>Low grade fever</td>
</tr>
<tr>
<td><strong>Cough duration: 36–48 days</strong>⁴</td>
<td>Non-specific cough: duration 54 days⁴</td>
</tr>
</tbody>
</table>

Adolescents and adults have asymptomatic, mild or atypical disease

Usually unsuspected, undiagnosed, untreated and not reported, especially in older individuals

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Global pertussis disease burden

1. 300,000 deaths per year
2. 50 million cases in children worldwide each year
3. Disability-adjusted life years in 2000
   - Pertussis 12.7 million
   - Lung cancer 11.4 million
   - Meningitis 5.8 million

Disability adjusted life years = years of life lost + years lived with disability

But pertussis still causes significant global mortality...

Deaths in children younger than 5 years from vaccine-preventable diseases in 2008

Pertussis: 195,000 deaths per year (20%)

Immunisation programmes have decreased the incidence of pertussis

1980:
- almost 2 million reported cases
- low (~20%) vaccination coverage

2010:
- ~91,000 reported cases
- High (~80%) vaccination coverage

CAVEAT = under-reporting
- WHO estimated 195,000 deaths in 2008

Immunisation history of pertussis vaccination in hospitalised patients

Pertussis Vaccination History in New Zealand-1

• 1960 - 3 doses un-adjuvanted vaccine as DTPw at 3, 4 and 5 months of age

• 1971 - changed to two doses of alum adjuvanted vaccine at 3 and 5 months

• 1982 large pertussis epidemic with several deaths
Pertussis Vaccination History in New Zealand-2

• 1984 - Increase from two to three doses
  - because the two dose schedule at 3 and 5 months was inadequate
  - Two decisions - extra dose and when to be administered

• NZ unique primary immunisation schedule
  - 6 weeks 3 months 5 months
Pertussis Vaccination History in New Zealand -3

• Three to four doses - 1996

• Change to acellular pertussis vaccine - 2000

• Four to five doses - 2002

• Adolescent dose - 2006

NZ Immunisation Handbook 2011
# 2011 NZ Childhood Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Conjugate Pneumo</th>
<th>Hexavalent DTaP-IPV-Hib HepB</th>
<th>MMR</th>
<th>Hib</th>
<th>DTaP-IPV</th>
<th>Tdap</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 months</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 months</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

- HPV 3 doses
Vaccine Schedule

• Is this schedule ideal?

• Can it be started earlier?

  Possibly with a monovalent pertussis dose at birth.

Knuf et al J Ped 2008 and 2010
How are we performing?

What can we do to improve?
Pertussis hospital discharge rate in New Zealand

1945 pertussis vaccine available
Annual pertussis hospital discharge rate per decade per 100,000 person years 1873 to 2004

- Pertussis vaccine available 1945
- 3 doses 1958
- 2 doses 1971
- 3 doses 1984
- 4 doses 1996
- 5 doses 2002
Pertussis notifications and hospitalisations by calendar month-year since 1997 up to 31 July 2012

Figure 1: Number of pertussis notifications by week reported 2010 - 2012

Age distribution by ethnicity

Figure 1: Pertussis rates per 100 000 populations by age group and ethnicity, in 2012

Note: Rate of pertussis cases per 100 000 population calculated using Census 2006 usually resident populations.
To control pertussis you have to do immunisation well
New Zealand Coverage

• At age 2 years
• 60% in 1992 –
• 77% in 2005 –
• 85% in 2009
• Now 92%

• Significant ethnic differences and large variability between DHBs
• 82% - 95% at 24 months
  (NIR data for year ending June 2012)

MoH Data
Why pertussis is still a problem?

• Timeliness
  – Timeliness
    • Timeliness
      – Timeliness
        » Timeliness
          • Timeliness
            • Timeliness
              • Timeliness
NZ Immunisation coverage and timeliness at age 1 year

Ministry of Health National Immunisation Coverage Survey 2005
Reinforce current infant and toddler immunisation strategies

Coverage of immunisation programmes and timeliness of vaccine delivery are crucial

Only 72% of children aged 6 months had completed their age-appropriate immunisations in June 2012

78% European, 58% Māori, 70% Pacific,

MoH data
5 fold increased risk of an infant being hospitalised with pertussis if any of the three doses of the primary infant immunisation series are delayed

Immunisation Timeliness

• For Pertussis the Target must be -

• “three doses of pertussis containing vaccine by 6 months of age”

NZMJ 2010:123 No1313
What do we have to do?

- Improve coverage to 95%
- Give the (particularly infant schedule) vaccines on time.
- Consider supplementary strategies
Global pertussis initiative:
Pertussis control strategies

1. Reinforce and/or improve current infant and toddler immunisation strategies
   – Direct protection

2. Create a cocoon of contacts who are immunised and hence less able to spread pertussis to infants
   – Indirect protection

Global pertussis initiative:
Seven pertussis control strategies

1. Reinforce and/or improve current infant and toddler immunisation strategies
2. Universal preschool booster doses at age 4-6 years
3. Universal adolescent immunisation
4. Universal adult immunisation
5. Selective immunisation of new mothers, family, and close contacts of newborns
6. Selective immunisation of health care workers
7. Selective immunisation of child care workers

Cocoon Immunisation

- Families of newborns
- Health care workers
- Childcare workers
Transmission from older adults to unvaccinated infants

Potential source of transmission

3. McIntyre et al Vaccine 2009 27:1062
How frequent is pertussis in adults?

Relative proportion of pertussis in adults -cough >7days

- USA (Strebel et al 2001) 10%
- USA (Nennig et al 1996) 12%
- USA (Wright et all 1998) 16%
- USA (Mink et al 1992) 13%
- Can (Senzilet et all 2001) 20%
- DK (Birkebaek et al 1999) 17%
- F (Gilberg et al 2002) 32%
- UK (Miller et al 2001) 28%
- D (Riffelmann et al 2006) 10%
Pertussis – Who infects infants?

~50% source not identified – all studies

- F Baron et al 1998 Hospitalised infants – 34% parents, 46% sibs
- D Kowalzik et al 2003 Infants in ICU – 46% adults mostly mothers
- GB Crowcroft et al Infants mostly in ICU – 43% parents 27% vaccinated sibs
- USA Bisgard et al 2004 Infants <4 months notified cases 35% mothers, 14% fathers, 8% grandparents
- Can, D, F, USA Wendelbore et al 2007 Hospitalised infants 55% parents mostly mothers, 16% siblings, 28% other adults in household
Pertussis - Sources of infection in infants

- Parents (Mothers particularly)
- Siblings
- Other adults in household
Selective immunisation of new mothers, family, and close contacts of newborns

Birth of a child should be the trigger for ensuring all children and adolescents have received scheduled immunisations and boosters are offered to all other household members
ACIP Provisional Recommendations for Pregnant Women on Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (Tdap)

Date of ACIP vote: June 22, 2011 Date of posting of provisional recommendations: August 5, 2011

“Summary of new recommendations: **Use of Tdap in pregnant women**

- Women’s health care providers should implement a Tdap vaccination program for pregnant women who previously have not received Tdap. Health care providers should administer Tdap during pregnancy, preferably during the third or late second trimester. Alternatively, if not administered during pregnancy, Tdap should be administered immediately postpartum.”

Cocoon Immunisation

- Families of newborns
- Health care workers
- Childcare workers
Selective immunisation of health care workers

- Health care workers are at increased risk of pertussis
- Outbreaks in maternity wards, neonatal units and in outpatient settings
- Fatalities occur as a result
- Benefit for the hospital is estimated to be 2.4 times the dollar amount spent on vaccinating health care workers

NZMJ 2010:123 No1313
Staff immunisation logistics

• Pertussis epidemics are long
  – Approx 18 months
  – Staff turnover

• Staff identification and capture!

• Priority is staff in neonatal and paediatric intensive care units, emergency department, general paediatric wards, paediatric cardiology, all those working in obstetrics.
  – Other relevant healthcare workers include
    • GP’s and practice nurses
    • Providers of well-child services
In my opinion all GPs and practice nurses should receive Tdap if they have not received it within last 10 years
Cocoon Immunisation

- Families of newborns
- Health care workers
- Childcare workers
Selective immunisation of child care workers

• How do we identify all of the child care workers
• The priority is to immunise all of the children in childcare first?
• But if asked by a childcare worker don’t hesitate to offer vaccination
Universal adult immunisation

Could change Td to Tdap
• Coverage not high enough
• Dose interval not frequent enough
  • 45 years and 65 years
• But policy could change back to decennial boosting
<table>
<thead>
<tr>
<th>Strategy</th>
<th>Do we have it?</th>
<th>How well do we do it?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary series</td>
<td>Yes</td>
<td>Not well enough on time</td>
</tr>
<tr>
<td>4 year booster</td>
<td>Yes</td>
<td>Not well enough 80%</td>
</tr>
<tr>
<td>Adolescent immunisation</td>
<td>Yes</td>
<td>Don't know</td>
</tr>
<tr>
<td>Universal adult immunisation</td>
<td>No</td>
<td>Possibly</td>
</tr>
<tr>
<td>Immunisation of new mothers, family, and close contacts of newborns</td>
<td>No</td>
<td>But we should</td>
</tr>
<tr>
<td>Selective immunisation of health care workers</td>
<td>Yes, some DHBs</td>
<td>Don’t know but all GPs and PNs should</td>
</tr>
<tr>
<td>Selective immunisation of child care workers</td>
<td>No</td>
<td>Possibly in the future - currently opportunistic.</td>
</tr>
</tbody>
</table>
How soon after Td can Tdap be given?

• The Immunisation Handbook 2006 stated - two years

• Derived from Canadian studies showing no increase in adverse event for those vaccinated 18-23 months after Td$^{1,2,3}$

• The Immunisation Handbook 2011 states

“When Tdap is given to protect infants there is no minimum dosage interval”

1. PIDJ 2006;25:195-200  
2. MMWR 2006:55:RR17  
6.5 Recommended immunisation schedule

• A primary course of pertussis vaccine is given as DTaP-IPV-HepB/Hib (*Infanrix-hexa*) at ages six weeks, three months and five months, followed by a dose of DTaP-IPV (*Infanrix-IPV*) at age four years, prior to school entry, to extend the duration of protection during the school years.
• A further booster is given at age 11 years (school Year 7) as Tdap (*Boostrix*).

**Recommended but not funded**

Tdap is recommended but not funded by the Ministry for:

• Lead maternity carers (LMCs) and other health care personnel who work in neonatal units and other clinical settings where they are exposed to infants, especially those with respiratory, cardiac, neurological or other co-morbid conditions (a booster dose at 10-yearly intervals)
• Household contacts of newborns, including update vaccination of older siblings (funded), adult household and other contacts during pregnancy, and maternal immunisation shortly after delivery
• Early childhood service personnel (a booster dose at 10-yearly intervals) although the priority is to ensure all children attending childcare have received age-appropriate vaccination.
Summary

• Achieve 95% coverage for all five schedule doses with on time coverage particularly for the first three doses

• Immunise family/household contacts of newborns, particularly mothers

• Immunise healthcare workers dealing with children particularly those who treat sick infants

• Opportunistically immunise childcare workers
Acellular vaccines

• Epidemic pertussis 2012
  NEJM 30 August 2012
• Lambert Article
  JAMA 1 August 2012
• Pertussis epidemic - Washington 2012
  MMWR 20 July 2012
Thank you for your attention

- Acknowledgments and thanks
- Cameron Grant,
- Diana Lennon
- Mark Thomas
- Elizabeth Wilson
Back up slides
Immunogenicity of decennial dose of Tdap in adults

- One month after the decennial dTpa booster dose, all subjects were seropositive for antibodies against PT, FHA and PRN.
- 100% of subjects in the dTpa group and at least 99.3% in the Td + pa group had antibody concentrations associated with seroprotection against diphtheria and tetanus.

GMC, geometric mean concentration; pa, reduced antigen content acellular pertussis; Td, tetanus & reduced antigen content diphtheria.

Booy et al. Vaccine 2011; 29: 45–50 (Figure reproduced with kind permission from Elsevier)
Pertussis notifications 2004 - present

Number

Month

Jan-04 Apr-04 Jul-04 Oct-04 Jan-05 Apr-05 Jul-05 Oct-05 Jan-06 Apr-06 Jul-06 Oct-06 Jan-07 Apr-07 Jul-07 Oct-07 Jan-08 Apr-08 Jul-08 Oct-08 Jan-09 Apr-09 Jul-09 Oct-09 Jan-10 Apr-10

- 15+
- 5 to 14
- 1 to 4
- <1
International comparison pertussis hospitalisation rates - infants < 1 year

Life for an infant in New Zealand is 6 times more dangerous than life for an infant in the USA

Elliot E. PIDJ 2004;23:246-52.
Van Buynder P. Epidemiol Infect 1999;123:403-11
Tanaka M. JAMA 2003;290:2968-75.
US recommendations for use of Tdap vaccines - Advisory Committee on Immunization Practices, 2010

• General Recommendations –
  – For routine use, **adolescents aged 11-18 yrs** who have completed the recommended childhood DTP / DTaP vaccination series, and **adults aged 19 – 64 yrs** and older should receive a single dose of Tdap. **Adolescents should preferably receive Tdap at the 11 to 12 year-old preventive health-care visit.**

• Timing of Tdap -
  – Can be administered **regardless of interval** since last T or Td vaccine.

• Adults Aged > 65 yrs –
  – Those with **close contact to an infant <12 m old** should receive a dose of Tdap.
  – Other adults ages **65 years and older** may also be given a single dose of Tdap.

• Children Aged 7 Through 10 Years -
  – Those not fully vaccinated against pertussis* and for whom no contraindication to pertussis vaccine exists should receive a single dose of Tdap.
  – Those never vaccinated against T, D or P or who have unknown vaccination status should receive a series of three vaccinations containing T & D. The first of these three doses should be Tdap.

• * Fully vaccinated is defined as 5 doses of DTaP or 4 doses of DTaP if 4\(^{th}\) dose administered on or after 4\(^{th}\) BD.
Conclusions: evolving epidemiology

• Pertussis is still endemic in many countries
• Periodic outbreaks across all age groups and high mortality in infants $^{1,2}$
• Newborns and partially vaccinated infants are most susceptible and at risk of severe disease $^{3}$
• Pertussis is under-diagnosed and under-reported, with a wide range of symptoms
• Older children and adults act as a reservoir for transmission to susceptible infants $^{4}$

Conclusions: evolving strategies for prevention

• Available vaccines are immunogenic and effective
• Timely childhood vaccination is important
• Immunity is not life-long – levels of antibody wane with all vaccines
• Cocooning strategies vaccinate parents and close contacts to protect vulnerable infants\textsuperscript{6,7,8}
• Decennial booster vaccination is well-tolerated and immunogenic
• Adult vaccination should protect the whole population via reduced circulation and herd immunity