Pertussis Vaccine Schedules: 
What can serosurveillance and modelling tell us?

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Overview

• Rationale for pertussis serosurveys
• Findings of the Australian pertussis serosurveys
• How can models help?
• What are the key features of a model to explore drivers of pertussis trends in Australia?
• Summary and conclusions
Rationale for pertussis serosurveys

- Clinical case finding subject to multiple sources of bias
- Objective assessment of recent exposure
- Antibody concentration thresholds deemed as evidence of recent exposure from studies of natural infection
- While correlates of protection may be complex, do undetectable antibody levels correlate with population susceptibility?
The Australian pertussis serosurveys

• Specimens collected through national serosurveillance program
• Residual diagnostic sera from nationally representative laboratories
• Immunosuppression (incl HIV), transfusion excluded
• Identifiers: sex, age, location, unique ID
• Anti PT IgG ELISA – 1997/8 Italy (ESEN), 2002, 2007 Australia (CIDM)
Timing of collections & the epidemic cycle

Notification rate for pertussis in Australia 1991-2011

- 4-5yr DTP booster
- DTaP 4th/5th doses
- DTaP all doses
- 18mth DTaP
- +12-17yr dTap

1997

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 EU/ml</td>
<td>100%</td>
</tr>
<tr>
<td>5 to &lt; 62.5 EU/ml</td>
<td>90%</td>
</tr>
<tr>
<td>62.5 to &lt; 125 EU/ml</td>
<td>70%</td>
</tr>
<tr>
<td>≥ 125 EU/ml</td>
<td>50%</td>
</tr>
</tbody>
</table>
Cross sectional survey - 2002

Age group (years)

Percentage

0%
20%
40%
60%
80%
100%

1 2 3 4 5 6 7 8 9 10-14 15-19 20-24 25-34 35-44 45-59

< 5 EU/ml  5 to < 62.5 EU/ml  62.5 to < 125 EU/ml  ≥ 125 EU/ml
Cross sectional survey - 2007

Age group (years)

Percentage

2007

< 5 EU/ml
5 to < 62.5 EU/ml
62.5 to < 125 EU/ml
≥ 125 EU/ml
Change in proportions with undetectable anti-PT IgG levels

anti-PT IgG level below detection threshold (< 5 EU/ml)

Percent with anti-PT IgG level < 5 EU/ml

Age group (years)

1997/98
Change in proportions with undetectable anti-PT IgG levels

anti-PT IgG level below detection threshold (< 5 EU/ml)

* Significantly higher than previous collection
Change in proportions with undetectable anti-PT IgG levels

anti-PT IgG level below detection threshold (< 5 EU/ml)

* Significantly higher than previous collection
† Significantly lower than previous collection
How can models help?

• Using mathematical transmission models, we can:
  – Simulate how pertussis spreads through populations under different assumptions
  – Isolate the effect of previous changes on observed disease experience, such as vaccination schedule changes
  – Simulate situations where exact information is not readily obtained, such as duration of immunity, to determine most likely values
  – Introduce different interventions to compare the likely outcomes

• We hypothesize that pertussis toxin antibodies correlate with protection and this forms the basis for our model
The SIRS model framework

- **Susceptible**
- **Infected**
- **Removed**

**Processes:**
- Vaccination
- Infection
- Recovery
- Waning immunity
Key questions to be posed of the model

- How have changes to the vaccine schedule impacted on protection?
  - Age at administration
  - Vaccine formulations
- How have changes in pathogen circulation impacted on duration of protection?
- Has widespread immunisation selected for vaccine-escape mutants?
Pertussis transmission model

Vaccine cycle

Natural immunity cycle

births

\( \nu \)

\( \lambda \)

\( \theta \)

\( \phi \)

QSS

\( f_1 \)

\( f_2 \)

\( (1-f_1-f_2) \)

\( e \)

\( (1-e) \)

\( a_1 \)

\( a_2 \)

\( (1-a_1-a_2) \)

\( v \)

\( c_1 \)

\( c_2 \)

\( (1-c_1-c_2) \)

\( b \)

\( (1-b) \)

\( \mu \)

\( \omega \)

\( \alpha \)

\( \beta \)

\( \gamma \)

\( \delta \)

\( \epsilon \)

\( \zeta \)

\( \eta \)

\( \chi \)

\( \theta \)

\( \varphi \)

\( \psi \)

\( \omega \)

\( \nu \)

\( \lambda \)
Summary and conclusions

• There have been marked shifts in immunity to pertussis in Australia in recent decades
• The ‘epidemic signature’ dominates over vaccine derived immunity
• Non-linear dynamic models can be used to analyse multiple data sources, and test alternative hypotheses regarding causal pathways
• Data-driven predictive models may provide helpful insights for decision support by comparing likely relative benefits of alternative interventions
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