Pertussis modelling

Contributions of natural, vaccine immunity to epidemiology

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Pertussis: biology, epidemiology and prevention
Les Pensieres, Fondation Merieux Conference Centre, 11-13 November 2015
Overview

- Pertussis resurgence – Australia as a case study
- Modelling Australian pertussis trends
- Understanding the past, predicting the future
- Conclusions, context and next steps
Pertussis resurgence - background

- Resurgence of pertussis (whooping cough) observed recently in a number of developed countries
- Initial uncertainty re: ascertainment bias
- Associated infant deaths in US, UK indicate true increase

How might vaccination have contributed to rising disease?
- Waning immunity, loss of boosting
- Lower effectiveness of new vaccines
- Changes in bacterial population
Reported NNDSS pertussis cases: 1922-2013*

Number of cases

Year

*2013 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Australia as a case study – in context

Fig. 1 [colour online]. Boxplot of annual rates of change of pertussis incidence between 1990 and 2010 for countries that met our inclusion criteria: mean DTP3 vaccine uptake of > 80% between 1990 and 2010; populations of > 5 million individuals; and > 80% complete case count records for this time period. The pink area indicates countries with significantly positive trends in incidence based on Kendall’s tau rank correlation ($P < 0.05$), white indicates countries for which trends were not significant, and blue indicates countries with significantly decreasing trends. Note that rates of change are plotted on a log scale. Representative time-series of countries with increasing (Australia), stationary (Argentina), and decreasing (Spain) trends are shown on the right.
Use of pertussis vaccines in Australia

- 1953: DTPw commences Various schedules
- 1975: 3, 4, 5 & 15-18 mths
- 1978: 15-18 mths removed
- 1980: 18 mth added
- 1982: 2, 4, 6 mths
- 1990: Mandatory notification
- 1991: DTPa boosters
- 1994: 4-5 yr added
- 1997: DTPa all doses
- 1999: 18 mth removed
- 2000: 15-17 yr added
- 2003: 18 mth removed

Campbell et al PLoS ONE 2012
Pertussis resurgence in Australia
Australian pertussis seroepidemiology

Collected during and shortly after epidemic

Collected in trough before large epidemic

Campbell et al PLoS ONE 2012
Modelling Australian pertussis trends

“All I’m saying is we plug these into Excel, let it do its thing, and then we can all play until lunch!”
Vaccine/natural immunity interaction

Campbell et al Vaccine 2015
Pertussis model attributes

- Compartmental - susceptible, infected, recovered
- Age-structured – relates to disease risk, vaccine timing
- Dynamic – prevalence drives incidence in susceptibles
- Model of \textit{infection}, as opposed to symptoms or disease
- Model states are associated with pertussis AB levels: used as a marker of infection, vaccination and waning
Model simulation and selection

- Model parameters varied simultaneously
  - Plausible parameter distributions based on local data, literature review
  - 200,000 parameter combinations tested
  - Qualitative match to 3 criteria and large epidemic post removing toddler dose

- Large reduction in infant incidence
- 2–5 year epidemic cycles
- Highly seropositive adults

Large reduction in infant incidence
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Highly seropositive adults
Selected simulations (n=2,321)

*Naïve and low immune infections

Campbell et al Vaccine 2015
Understanding the past

- Natural immunity duration is far longer than either vaccine
- Coverage fluctuations open up opportunity for outbreaks
- Cycles of immunity and waning post outbreak have implications decades later
- Schedule change has opened up susceptible ‘pockets’ to fuel the most recent epidemic

Campbell et al. Vaccine 2015
Looking backwards and forwards

Australian Immunisation Schedule

1953: DTPw commences various schedules
1978: 3, 4, 5 mths
1985: 2, 4, 6 & 18 mths
1997: DTPa boosters

Scenario 2: 2, 4, 6, 18 mths, 4 yr

Scenario 3: 2, 4, 6, 18 mths, 4 yr, 15 yr

Scenario 4: 2, 4, 6, 18 mths, 4 yr

Scenario 5: 2, 4, 12 mths 4 yr, 15 yr


Campbell et al Vaccine 2015
### Impact of schedule changes

<table>
<thead>
<tr>
<th></th>
<th>Historical 2003-2013</th>
<th>Future 2014-2020</th>
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<tbody>
<tr>
<td></td>
<td>With 18mth dose/</td>
<td>Addition of 18mth dose</td>
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<tr>
<td></td>
<td>Without 15yr dose</td>
<td></td>
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<tr>
<td><strong>age</strong></td>
<td><strong>median incidence difference per year per 100,000 (99% CI)</strong></td>
<td><strong>median incidence difference per year per 100,000 (99% CI)</strong></td>
</tr>
<tr>
<td>&lt; 8 wks</td>
<td>62</td>
<td>-253 (-278, -223)</td>
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<tr>
<td></td>
<td>(28, 86)</td>
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<tr>
<td>8 wks to &lt; 1yr</td>
<td>9</td>
<td>-37 (-43, -33)</td>
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<tr>
<td></td>
<td>(5,13)</td>
<td></td>
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<tr>
<td>18mth to &lt;4yr</td>
<td>-282 (-313, -247)</td>
<td>-337 (-366, -311)</td>
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<tr>
<td>15yr to &lt;30yr</td>
<td>98</td>
<td>-21 (-23, -19)</td>
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<td>(91, 103)</td>
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*Best strategy: 43% reduction toddlers, 8% reduction infants*  

Campbell et al Vaccine 2015
Conclusions

- Multiple factors have contributed to pertussis resurgence in Australia and elsewhere
- Ongoing transmission of pertussis seems inevitable
- A six-dose vaccine schedule (reintroducing the toddler booster) is expected to have some impact on transmission, and hence disease
- Additional mitigation strategies are needed to protect infants at highest risk of severe outcomes
Context and next steps

- Other groups have used models to consider the drivers of pertussis resurgence in their own context
  - Yoon Choi, Public Health England, UK
  - Manoj Gambhir, Centers for Disease Control, US

- WHO-supported model comparison exercise underway to assess model applicability to other data and settings

- Development of models of maternal immunisation approaches in household structured populations
Acknowledgements

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**NCIRS**
- Peter McIntyre
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- Rob Menzies
- Lyn Gilbert
Thank you!

Any questions?

“I think you should be more explicit here in step two.”