Modeling new vaccination strategies for pertussis control

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Background

- Pertussis is an endemic vaccine preventable disease
  - Estimated 50 million cases and 300,000 deaths worldwide each year
  - Childhood vaccination lead to a fall in pertussis incidence rates, but does not result in adequately control of pertussis, even with high coverage rates (95%)
  - Since 1976, the incidence of reported pertussis has been steadily increasing in all age groups in USA
  - Infant pertussis accounts for > 60% of pertussis related complications, 86% hospitalizations and 90% of deaths
  - Reported pertussis severely underestimates true incidence
Pertussis, United States, 1940-2005

Cases

Pertussis, United States, 1980-2005

The graph shows the number of pertussis cases in the United States from 1980 to 2005. The number of cases generally increased over time, with a sharp rise towards the end of the period.
Reported Pertussis by Age 1990-2005

Year


Cases

<11 11-18 >18

0 5000 10000 15000 20000 25000 30000
Is pertussis in adults a problem?

- Prolonged cough (3 months or longer), +/- post-tussive vomiting, +/- complications
- Medical costs - Multiple medical visits and extensive medical evaluations
- Missed work
- Transmission to young infants
  - parents accounted for 55% of source cases, followed by siblings (16%), aunts/uncles (10%), friends/cousins (10%), and grandparents (6%) (Wendelboe et al, 2007)
- “reservoir” of pertussis in community
Age specific pertussis incidence

Pertussis complications by age

- **Pneumonia**
- **Hospitalization**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Pneumonia</th>
<th>Hospitalization</th>
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<tr>
<td>&lt;6 m</td>
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<td>6-11 m</td>
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<td>1-4 y</td>
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<td>5-9 y</td>
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<td>10-19 y</td>
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<td>20+ y</td>
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Percent
Need to protect infants

1. Develop vaccines that are immunogenic at birth
   - Slow progress, still in the animal model, recent encouraging data in premature infants

2. Boost the immunity of adolescents and adults using new vaccination strategies
   - Safe and effective pertussis boosters now available for adolescents/adults
Adult and adolescent vaccination

- **Primary objective**
  - Direct protection of the vaccinated adolescent or adult

- **Secondary objective**
  - Reduction of the reservoir of *B. pertussis*
  - Reduce incidence of pertussis in infants

- Can the introduction of new vaccination strategies achieve this and will this be cost-effective?
1997: Age structured model for pertussis transmission (Hethcote)
1999: effects of adult booster vaccination (Hethcote)
2004: Five adolescent and adult pertussis strategies (Van Rie & Hethcote)
2006: Update of epidemiological model (Coudeville, Van Rie, Andre)

- Determine probability of developing pertussis after exposure to B. pertussis using recently published data of efficacy per dose of vaccine administered *
- Determine age-specific forces of infection based on recent US incidence data instead of pre-vaccine era seroprevalence data*
- Revise the role of asymptomatic infection in the transmission of B. pertussis*

* Simultaneous calibration based on an expectation-minimization algorithm

- Use recent data on sources of transmission of B. pertussis to young infants,
- Factor in US population growth over time.
Results: incidence by strategy
Results: Incidence by age group
Impact of age of single booster
Is adult vaccination economically viable?

- At current disease rates, the financial cost of adolescent pertussis in this decade is projected at $3.2 billion. (Judelsohn 2007)
- Nosocomial pertussis outbreaks result in substantial costs to hospitals, even when the number of pertussis cases is low. The prevention of nosocomial pertussis outbreaks by including vaccination of healthcare workers should be evaluated (Bagett 2007)
- Exposure of HCWs to pertussis during contact with children who have the disease is largely unavoidable, and management of this exposure is resource intensive. Universal pre-exposure vaccination of HCWs is a better utilization of resources than is case-based post-exposure management. (Daskalaki 2007)
Cost-effectiveness analyses

- Purdy 2004
  - A cost-benefit analysis evaluated the health and economic benefits of 7 strategies for pertussis booster to adolescents and adults.
  - The most economical: immunize adolescents 10-19 years of age.
  - Routine adult booster vaccinations every decade would be more expensive and more difficult to implement.
Cost effectiveness analyses

- Caro 2005
  - Epidemiologic model of routine pertussis immunization in adolescents in US, considering both direct and herd immunity.
  - Conditions required for adolescent immunization to be economically warranted are realistic
Cost effectiveness analyses

- Lee 2005
  - Markov model to examine: (1) no vaccination; (2) 1-time adolescent vaccination; (3) 1-time adult vaccination; (4) adult vaccination with boosters; (5) adolescent and adult vaccination with boosters; and (6) postpartum vaccination
  - Adult vaccination strategies were more costly and less effective than adolescent vaccination strategies.
  - Results were sensitive to assumptions about disease incidence, vaccine efficacy, frequency of vaccine adverse events, and vaccine costs
Cost-effectiveness analyses

Lee 2007:

- Markov model to calculate health benefits, risks, costs, and cost effectiveness of: (1) no adult pertussis vaccination, (2) one-time adult vaccination at 20-64 years, and (3) adult vaccination with decennial boosters.

- Routine vaccination of adults aged 20 to 64 years with combined TD is cost effective if pertussis incidence in this age group is greater than 120 per 100,000 population.
Limitations of prior studies

- None of the prior studies of adult vaccination fully included in depth assessment of:
  - herd immunity
  - benefits and costs over time

- Solution: cost-effectiveness analyses that builds upon on a compartmental age-structured transmission model of pertussis and looks at different timepoints (Coudeville et al)
Costs over time by strategy

- Current US vaccination schedule
- Current US + adolescent (vc 75%)
- Current US + adolescent (vc 75%) + Cocoon strategy (vc 65%)
- Current US + adolescent (vc 75%) + routine adult every 10 yrs (vc 40%)
- Current US + adolescent (vc 75%) + Cocoon strategy & 1 dose at 40 yrs (vc 65%)

Annual cost (2006 US$ - 1,000,000 people)
Sensitivity analysis

Parameters assessed in sensitivity analysis

- Vaccine efficacy
- Pertussis incidence
- Vaccine coverage
- Disease associated costs
- Discount rate
- Transmission to infants

Similar to study by Lee, results are sensitive to vaccine efficacy, pertussis incidence at baseline
Conclusion

- Pertussis remains endemic, even with high coverage rates of a highly effective vaccine in children
- Analysis of pertussis epidemiology is complicated by lack of diagnostic gold standard, wide range of disease presentation, and waning of immunity
- Changes in model structure and parameters have important impact on results
- Most recent models seem to indicate that pertussis could be eliminated as public health problem if both adolescent and adult vaccination is implemented
- This strategy may be economically viable
Acknowledgements

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