Review of Proposed Recommendations of Pertussis Working Group

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Evidence Reviewed

- Country-specific data
- Baboon experimental model
- Historical randomized trials
- Mathematical modelling
Summary

• Pertussis epidemiology
  • *B. pertussis* strains have evolved over time
    • Inconsistent correlation with vaccine programs and epidemiology
    • No evidence to date for diminished effectiveness of vaccines against different allelic variants
    • No evidence of emergence of *B. parapertussis* in aP or wP using countries

• Pertussis vaccination
  • Main objective of pertussis vaccination is to reduce risk of severe pertussis in infants
  • wP and aP very effective in reducing disease with high coverage
    • Drastic decline in global incidence *and* mortality in post-vaccine era
Acellular (aP) vs Whole cell (wP) Vaccines

- Acellular vaccines
  - Lower initial efficacy
  - Faster waning of immunity
  - Possible reduced impact on transmission
  - Likely to result in resurgence
    - Magnitude and timing of resurgence difficult to predict
    - Potential increased risk of death in those too young to be vaccinated

Not Vaccinated? No Kisses!

Get the adult whooping cough vaccine.

www.VaccinateYourFamily.org
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- Proposed mechanism
  - aP vaccines induce different type of immune response
    - Higher Th2-promoting antibody responses
    - Lower Th1 and Th17 responses
  - Less effective at limiting and clearing mucosal infections
Acellular (aP) vs Whole cell (wP) Vaccines

Transition from wP to aP vaccines?

- Must consider overall goal of national immunization program

  1. Protection of infants? No benefit of aP over wP vaccines
     - disease-related mortality significantly reduced with either wP or aP vaccination

  2. Protection of older children or adults? Multiple doses of aP required
     - Only possible with aP vaccines (less reactogenic)
     - Requires repeat boosting (limited duration of efficacy) to limit/prevent resurgence and increased risks to infants
     - Increased program cost
Supplemental Strategies may be considered to Prevent Infant Mortality

• **Maternal immunization**
  • aP vaccines safe & effective (via transfer of maternal antibodies)

• **Immunization of newborns**
  • Limited safety and effectiveness data; no standalone aP vaccine

• **Cocooning**
  • Potential reduction in severe morbidity; timing crucial; requires high coverage

• **Adolescent/adult booster**
  • Health care workers should be priority group
Supplemental Strategies: Maternal Immunization

• Likely most cost-effective supplemental strategy
  • Consideration when residual pertussis infant mortality is high
    <-> Priority should remain on early infant vaccination
    <-> Requires surveillance of infant disease burden
  • TdaP recommended (not DTwP)
    • 1 dose in 2nd or 3rd trimester; >1 week prior to delivery
    • More cost-effective than cocooning or neonatal immunization

• Further evaluation required to determine utility in women primed with aP vaccines
  • Potential reduced immune response in aP primed adolescents
Supplemental Strategies: Neonatal Immunization

- Neonatal immunization not recommended at this time
  - Limited data on impact and safety
  - Lack of availability of an aP alone vaccine
  - Window period of susceptibility

- Continued evaluation recommended
  - Data from human and baboon infants receiving a single vaccine dose demonstrate protection against severe pertussis disease
  - If data supporting immunogenicity, presumptive protection, and safety become available, it may have supplementary role along with maternal vaccination
Supplemental Strategies: Cocooning Immunization

• May reduce severe infant morbidity
  • Timing is crucial – as well as coverage
  • Cost-effectiveness varies (lower due to required multiple vaccine doses)

• Advantages
  • Better acceptability of vaccination post-partum than during pregnancy
  • Accessibility to whole family and opportunity to educate

• Disadvantages
  • Delay in protection, parental refusal, logistic, political, & economic issues
Supplemental Strategies: Adult Booster

- Adolescence or adult boosters
  - Not generally recommended to control infant disease
    - No evidence of impact on infant disease
    - Does reduce disease in adolescents

- Requirements prior to country introduction
  - Careful assessment of local epidemiology
    - Estimate adolescent contribution to infant disease
  - Selection of adolescent and/or adult target groups
Supplemental Strategies: Adult Booster

• Health Care Workers (HCW)
  • Should be a prioritized adult group
    • Focus on those with direct contact with pregnant mothers and infants
  • Prevention of nosocomial transmission to infants in health care settings
    • Requires high coverage rates
    • No evidence that strategy prevents acquisition and transmission
    • Some evidence of transmission after Tdap in hospital settings
  • Strategy to be revisited to assess impact in those primed with aP only
Surveillance

• Careful epidemiological surveillance is key
  • Monitoring of disease burden and immunization impact
    • Influence of differing vaccine booster doses on disease incidence
    • Focus on infants <1 year of age (investigation of infant fatalities)
  • Hospital surveillance should be a priority
  • Outbreak epidemiology has important role

• Laboratory data
  • Focus on enhancing specificity
  • Retention of cultures for assessment of molecular characteristics
    • Samples may be frozen and sent for assessment reference laboratories
Modelling: Research Questions

• Methodology
  • Application of country-specific data to models to:
    • Validate models
    • Evaluate strategies
    • Understand program impacts

• Priority research questions
  1. What are the circumstances under which a resurgence should be expected?
  2. What is the impact of different boosting strategies on disease incidence and resurgence?
General Recommendations (1)

• All children should be immunized against pertussis
  • Maintain high levels of coverage (≥90%)
    • Minor reductions can lead to an increase in incidence

• Goal is early and timely vaccination in all countries
  • As soon as possible ≥ 6 weeks of age
  • ≥ 3 doses of assured quality vaccine
    • 1 dose (~50%+) 2 doses (~ 80%+) effective against severe disease
• **wP vaccines preferred when:**
  - Program target is prevention of infant disease
  - Limited number of pertussis doses delivered / affordable

• **aP vaccines should only be considered when:**
  - Program objectives include older children and adults
  - Large numbers of doses may be included in a national immunization schedule
    - Cost implications (higher unit cost & number of required doses)
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