Review of Proposed Recommendations of Pertussis Working Group

C. A. Siegrist, SAGE Pertussis Working Group Chair

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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

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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

Vaccinate on time, every time.

MDH

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General Recommendations (2)

- **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)

General Recommendations (3)

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