Cocooning: The US Experience and Current Strategies

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Centers for Disease Control and Prevention

NCIRS Pertussis Meeting
August 26, 2011
BACKGROUND
Reported pertussis-related deaths by age-groups - 1980-2009*

<table>
<thead>
<tr>
<th>Age-Group</th>
<th>1980-1989¹</th>
<th>1990-1999¹</th>
<th>2000-2009²</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 month</td>
<td>38</td>
<td>68</td>
<td>119</td>
</tr>
<tr>
<td>2-3 month</td>
<td>11</td>
<td>16</td>
<td>56</td>
</tr>
<tr>
<td>4-5 month</td>
<td>5</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>6-11 month</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>1-4 years</td>
<td>13</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5-10 years</td>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>11-18 years</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>77†</td>
<td>103</td>
<td>195*</td>
</tr>
</tbody>
</table>

*2009 Data are provisional
² National Notifiable Diseases Surveillance System, CDC, 2009*
† Includes one case with unknown age
Average Pertussis Case Fatality Rate, by State 2000 - 2010

Source: CDC National Notifiable Disease Surveillance System, through 2010 provisional data.
Pertussis Incidence among Infants 2001-2009

Hospitalizations and Deaths
% Total Cases, 2001-2009

Source of Infant Pertussis

- Household members 75%–83%
- Parents and siblings most common sources
  - Parents (55%)
  - Siblings (16%–20%)
  - Aunts/uncles (10%)
  - Friends/cousins/others (10%–24%)
  - Grandparents (6%)
  - Caretakers (2%)

Tdap coverage among adolescents aged 13-17 years – 2006-2009

- 2006: 10.8%
- 2007: 30.4%
- 2008: 40.8%
- 2009: 55.6%

CDC. National, State, and Local Area Vaccination Coverage among Adolescents Aged 13-17 Years - United States, 2009 MMWR 2010 ;59(32);1018-1023.
Tdap Vaccine Effectiveness

- Bridging studies of ADACEL and BOOSTRIX\(^1\)
  - 85-89%
- APERT study\(^2\)
  - 92% (95% CI: 32.0-99.0)
- Australia\(^3\) – screening method
  - 78.0% (95% CI: 60.7-87.6)
- St. Croix outbreak\(^4\) – case-control study
  - 65.6% (95% CI: 35.8-91.3)
- MN case-control study (poster #80)
  - 72.3% (95% CI: 38.8-87.4)

\(^1\) Schmitt HJ et al. JAMA 1996;275:37-41; Gustafsson LH et al. NEJM 1996;334:349-355
IMPLEMENTATION AND EVALUATION
Cocooning Can Be Successful

- **Demonstration projects**
  - Houston, TX – Ben Taub General Hospital
  - Nevada - 18 birthing hospitals

- **Important success factors**
  - “Champion” for the cause
  - Donated healthcare provider time
  - Free Tdap
Challenges to implementation of postpartum immunization

- New immunization platform
- Pertussis awareness
- Two populations
  - Postpartum women
  - Other family members
- Vaccine history
- New immunization providers
- Reimbursement issues

Five years later, is cocooning working?

- **No, not at a national level**
  - Very limited success of vaccinating fathers or other family members
  - Poor uptake of Tdap when made available at birthing hospitals
  - No demonstration of program sustainability or scale-up
  - No program of support at Federal level

- **Not fully successful examples**
  - Jefferson County, NY: free Tdap
  - California: during an epidemic, free Tdap
Effectiveness of cocooning
Limited data available

- One ecological study found no impact of only maternal postpartum Tdap on infant disease.\(^1\)

- Pertussis incidence in infants born at CA hospitals with a postpartum Tdap policy was lower compared to hospitals without a postpartum Tdap policy\(^2\)

- No system to measure coverage

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\(^1\) Castagnini L, et al. Impact of maternal post-partum Tdap vaccination on pertussis illness in young infants. IDSA, Vancouver Canada. Presented on October 23, 2010

ACIP Conclusions about Cocooning

- Recommend vaccination of all contacts of infants
- Cocooning is an insufficient national strategy to prevent pertussis morbidity and mortality in newborn infants
- Consideration of pregnancy immunization at June ACIP meeting
A NEW STRATEGY
Overview of ACIP Workgroup Considerations

- **Safety in mothers and newborns**
  - Vaccine Adverse Event Reporting System (VAERS)
  - Pregnancy registry data (GSK and sanofi pasteur)
  - Recent studies

- **Immunogenicity of Tdap use in pregnancy**
  - Recent studies

- **Interference by maternal antibodies**
  - Recent studies
  - Currently registered trials

- **Programmatic considerations**
# Evaluation of Tdap use in pregnant women

<table>
<thead>
<tr>
<th></th>
<th>Favorable to maternal vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe to pregnant women</td>
<td>Yes</td>
</tr>
<tr>
<td>Safe to newborn</td>
<td>Yes</td>
</tr>
<tr>
<td>Transplacental transfer of pertussis antibodies to neonates</td>
<td>Yes</td>
</tr>
<tr>
<td>Adverse impact on primary DTaP response</td>
<td>?</td>
</tr>
<tr>
<td>Programmatic considerations</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Tdap during pregnancy?

• Move mother’s dose to the 3rd trimester
  – Protect infant against transmission from mother (similar to postpartum)
  – Likely benefit -- direct immunity to infant through maternal antibodies¹

Methods

Pregnancy
• Mothers vaccinated in 3\textsuperscript{rd} trimester of pregnancy
• Increase in risk of disease during 2\textsuperscript{nd} and 3\textsuperscript{rd} month to model “blunting”

Postpartum dose
• 2 week delay in booster immune response
• Additional cocooning doses given before birth of infant

• Vaccine cost same for all Tdap doses: $37.55 dose cost\textsuperscript{1} + $20 administrative cost\textsuperscript{2}

\textsuperscript{1} CDC 2011a.
\textsuperscript{2} Caro 2005.
Model

- A simulated birth cohort
  - 4,131,019 (2009 birth cohort size) infants followed for one year\(^1\)
- Monthly incidence, hospitalization, and death rate
- Societal costs perspective for infants only
- Analytic horizon
  - Direct disease costs totaled over first year of life
  - Life years lost, 2009 average life expectancy (77.9 years\(^2\))

Note:
- This tree is repeated each month of the cohort, for a total of 12 months (incidence varies by age)
- Outcomes repeated for cocooning and base case
Results
Pregnancy vs. Postpartum + Father + Grandparent

- Base Case (DTaP series)
- Postpartum
- Postpartum + father
- Postpartum + father + grandparent
- Pregnancy

Chart showing the number of cases over different months for each scenario.
## Mean % Reductions from Base Case (all interventions)

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy</th>
<th>Postpartum</th>
<th>+ father</th>
<th>+grandparent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>33%</td>
<td>20%</td>
<td>29%</td>
<td>32%</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>38%</td>
<td>18%</td>
<td>28%</td>
<td>32%</td>
</tr>
<tr>
<td>Deaths</td>
<td>49%</td>
<td>16%</td>
<td>25%</td>
<td>29%</td>
</tr>
<tr>
<td>Program cost (72% coverage)</td>
<td>171 million</td>
<td>171 million</td>
<td>342 million</td>
<td>513 million</td>
</tr>
</tbody>
</table>
## Cost Effectiveness Summary

<table>
<thead>
<tr>
<th>Incremental Cost Effectiveness Ratio</th>
<th>Pregnancy*</th>
<th>Postpartum*</th>
<th>+ father**</th>
<th>+ grandparent***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per case averted</td>
<td>162,298</td>
<td>280,947</td>
<td>606,966</td>
<td>1,526,713</td>
</tr>
<tr>
<td>Cost per hospitalization averted</td>
<td>294,114</td>
<td>606,179</td>
<td>1,261,757</td>
<td>3,173,722</td>
</tr>
<tr>
<td>Cost per QALY saved</td>
<td>415,442</td>
<td>1,174,143</td>
<td>2,154,170</td>
<td>5,418,427</td>
</tr>
<tr>
<td>Cost per life year saved</td>
<td>498,960</td>
<td>1,569,926</td>
<td>2,753,358</td>
<td>6,925,576</td>
</tr>
</tbody>
</table>

*Relative to base case, **Relative to postpartum, ***Relative to postpartum + father
Conclusions

• Two factors drive pregnancy cost effectiveness
  – Mother fully protected at birth (for a given vaccine efficacy)
  – Maternal antibody transfer to infant
• Additional cocooning doses are predicted to be less cost effective

During pregnancy  
Postpartum
3rd trimester
Next Steps

- Planned case-control study evaluating cocooning and post-partum vaccination effectiveness
- Building on success of H1N1 campaign to achieve coverage
- Addressing revaccination with Tdap
Thank You

For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

- 129 (1.2%) of 10,350 (US) reports after Tdap vaccines involved pregnant women
  - 3.1% (4) of 129 reports classified as “serious”†
  - No maternal deaths

- Most commonly reported pregnancy-related AEs:
  - Spontaneous abortion (N=20; 15.5% of all Tdap pregnancy reports)
  - Six (4.7%) gestational diabetes
  - 3 each (2.3%) of oligohydramnios and pregnancy toxemia (nausea and vomiting)
  - Two (1.6%) each of stillbirths and congenital anomalies (gastroschisis, patent foramen ovale and peripheral pulmonic stenosis)

- Most commonly reported non-pregnancy-related AEs:
  - Six (4.7%) each of injection site reactions and acute respiratory infections

- Summary: no unexpected patterns or unusual events

*CDC/ISO unpublished data
† Serious reports are coded as such based on Code of Federal Regulations if they result in: death, life-threatening illness, hospitalization, prolongation of hospitalization, persistent or significant disability, congenital anomaly
# General Model Inputs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case (Min, Max)</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coverage for all doses</td>
<td>72% (25, 85) (min father 6%)</td>
<td>Healy (2009)</td>
</tr>
<tr>
<td>Tdap efficacy</td>
<td>85% (50, 92)</td>
<td>Schmitt (1996); Skoff (2011); Ward (2005)</td>
</tr>
<tr>
<td>Incidence infants &lt; 1 yr</td>
<td>Mean 2000-2007 incidence</td>
<td>CDC (2010)</td>
</tr>
<tr>
<td>Hospitalization probability</td>
<td>Mean 2000-2007 hospitalizations % total cases</td>
<td>CDC (2010)</td>
</tr>
<tr>
<td>Death probability</td>
<td>Mean 2000-2007 deaths by month % total cases</td>
<td>CDC (2010)</td>
</tr>
<tr>
<td>Underreporting</td>
<td>15% (0, 30)</td>
<td>Cortese (2008); Sutter (1992)</td>
</tr>
<tr>
<td>Discount rate</td>
<td>3% (0, 5)</td>
<td></td>
</tr>
</tbody>
</table>
## Intervention Model Inputs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case (Min, Max)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy maternal antibodies</td>
<td>60% (15, 85)</td>
<td>Authors’ Assumption; Gall (2011)</td>
</tr>
<tr>
<td>Duration antibody effectiveness</td>
<td>2 months (1, 3)</td>
<td>Van Savage (1990); Healy (2009); Shakib (2010)</td>
</tr>
<tr>
<td>Blunting (months 2 and 3)</td>
<td>10% (0, 20)</td>
<td>Van Savage (1990)</td>
</tr>
<tr>
<td>Transmission mother</td>
<td>35% (30, 40)</td>
<td>Bisgard (2004); Wendelboe (2007); Westra (2010)</td>
</tr>
<tr>
<td>Transmission father</td>
<td>15% (10, 20)</td>
<td>Bisgard (2004); Wendelboe (2007)</td>
</tr>
<tr>
<td>Transmission grandparent</td>
<td>6% (0, 10)</td>
<td>Wendelboe (2007)</td>
</tr>
<tr>
<td>Cost Category</td>
<td>Medical</td>
<td>Non-medical**</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>---------</td>
<td>---------------</td>
</tr>
<tr>
<td>Outpatient visit(^1)</td>
<td>110</td>
<td>47</td>
</tr>
<tr>
<td>Inpatient respiratory illness(^1)</td>
<td>7,323</td>
<td>487</td>
</tr>
<tr>
<td>Inpatient neurologic illness(^1)</td>
<td>7,032</td>
<td>745</td>
</tr>
<tr>
<td>Death (medical cost)(^1)</td>
<td>15,808</td>
<td>735</td>
</tr>
<tr>
<td>Public health response(^2,***)</td>
<td>$2,162 (min 1,081; max 3,243)</td>
<td></td>
</tr>
</tbody>
</table>

*Quality Adjusted Life Year (QALY).

** Parent’s lost work, transportation, over-the-counter medications

*** Public health labor time spent tracing contacts, reporting cases, etc.

\(^1\)Lee et al. 2007 and Lee et al. 2005.

\(^2\)CDC 2011b.
Postpartum + Father

Base Case (DTaP series)

Postpartum

Postpartum + father

# Cases

Month
Postpartum + Father + Grandparent

Base Case (DTaP series)

Postpartum

Postpartum + father

Postpartum + father + grandparent

# Cases

Month

<1 1 2 3 4 5 6 7 8 9 10 11
Sensitivity Analyses
Worst Case Scenario

• 50% increase in risk of disease in months 2 and 3
• 20% efficacy of maternal antibodies
Worst Case Scenario

50% increase in risk of disease (months 3,4) & 20% maternal antibody effectiveness

Base Case (DTaP series)

### % reduction (base case)

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy</th>
<th>Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>26%</td>
<td>16%</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>15%</td>
<td>19%</td>
</tr>
<tr>
<td>Cases</td>
<td>13%</td>
<td>20%</td>
</tr>
<tr>
<td>Cost/ QALY saved($)</td>
<td>849,474</td>
<td>1,183,187</td>
</tr>
</tbody>
</table>
Varying the efficacy of transplacental maternal antibody*

*Efficacy in mother held constant, 10% blunting