Pertussis Epidemiology and Vaccine Impact in the United States

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Presented at Fondation Mérieux Conference - Pertussis: biology, epidemiology and prevention
11-13 November 2015
Reported NNDSS pertussis cases: 1922-2014

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
DTaP Coverage Among Children and Tdap Coverage Among Adolescents and Adults

*CDC National Immunization Survey: DTaP among children aged 19 through 35 months, Tdap coverage among adolescents aged 13 through 17 years. Coverage among adults aged 19 through 64 years from National Health Information Survey.*
Reported pertussis incidence by age group: 1990-2014

Incidence rate (per 100,000)

Year


SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System
Pertussis cases by age — United States, 2004
n=25,827

Vaccine Type Received*

- Acellular Only
- Whole Cell and Acellular
- Transition Period

Cases

Age (years)
Pertussis cases by age — United States, 2010
n=27,550

Cases

Age (years)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

Vaccine Type Received*

Acellular Only

Whole Cell and Acellular

Transition Period
### DTaP VE and Duration of Protection Estimates—California, 2010

<table>
<thead>
<tr>
<th>Model *</th>
<th>Case (n)</th>
<th>Control (n)</th>
<th>VE, %</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall VE, All Ages</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 dose</td>
<td>53</td>
<td>19</td>
<td>Ref</td>
<td>--</td>
</tr>
<tr>
<td>5 doses</td>
<td>629</td>
<td>1,997</td>
<td>88.7</td>
<td>79.4 – 93.8</td>
</tr>
<tr>
<td>Time since 5th dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>53</td>
<td>19</td>
<td>Ref</td>
<td>--</td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>19</td>
<td>354</td>
<td>98.1</td>
<td>96.1 – 99.1</td>
</tr>
<tr>
<td>12 – 23 months</td>
<td>51</td>
<td>391</td>
<td>95.3</td>
<td>91.2 – 97.5</td>
</tr>
<tr>
<td>24 – 35 months</td>
<td>79</td>
<td>366</td>
<td>92.3</td>
<td>86.6 – 95.5</td>
</tr>
<tr>
<td>36 – 47 months</td>
<td>108</td>
<td>304</td>
<td>87.3</td>
<td>76.2 – 93.2</td>
</tr>
<tr>
<td>48 – 59 months</td>
<td>141</td>
<td>294</td>
<td>82.8</td>
<td>68.7 – 90.6</td>
</tr>
<tr>
<td>60+ months</td>
<td>231</td>
<td>288</td>
<td>71.2</td>
<td>45.8 – 84.8</td>
</tr>
</tbody>
</table>

*Accounting for clustering by county and provider*
Pertussis cases by age — United States, 2012
n=48,277

Vaccine Type Received:
- Whole Cell and Acellular
- Acellular Only
- Transition Period

Cases

Age (years)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
# Tdap duration of protection among populations born during 1998-2000, that only received acellular vaccines, Washington and Wisconsin, 2012

<table>
<thead>
<tr>
<th>Time since Tdap</th>
<th>VE, % (95% CI)</th>
<th>Year of Tdap Receipt</th>
<th>VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Tdap</td>
<td>Reference</td>
<td>No Tdap</td>
<td>Reference</td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>73.1 (60.3-81.8)</td>
<td>2012</td>
<td>75.3 (55.2-86.5)</td>
</tr>
<tr>
<td>1 - &lt; 2 years</td>
<td>54.9 (32.4-70.0)</td>
<td>2011</td>
<td>68.2 (60.9-74.1)</td>
</tr>
<tr>
<td>2 - &lt; 4 years</td>
<td>34.2 (-0.03-58.0)</td>
<td>2010</td>
<td>34.5 (19.9-46.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2009/2008</td>
<td>11.9 (-11.1-30.1)</td>
</tr>
</tbody>
</table>


U.S. Pertussis Cases by Age — 2014

n = 32,971

Source: CDC National Notifiable Disease Surveillance System, 2014
Antigenic and Biologically Active Components

- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- pertactin
- fimbriae
- agglutinogens
- adenylate cyclase
- tracheal cytotoxin
Proportion of *B. pertussis* Isolates from the United States Lacking Prn

Martin SW et al. Clin Infect Dis. 2015; 60:223-7
Mutations Causing Lack of Prn

Deletions, multiple sizes
Promoter disruption

prn gene deletion
Clinical and Epidemiological Significance of Pertactin-Deficient *B. pertussis*

- Epi-Analysis of 753 isolates and corresponding case data
  - Isolates from 2012
    - 6 Enhanced Pertussis Surveillance (EPS) sites plus epidemics in WA and VT
  - Pertactin-deficiency (PRN-) fully assessed
  - 85% were PRN-
    - All states had a high proportion of PRN- isolates
  - Proportion of patients reporting pertussis symptoms similar by pertactin status
    - Except more without the deficiency reported apnea (p-value=0.005)
  - Vaccinated patients had a higher odds of having PRN- *B. pertussis* as compared to unvaccinated (OR=3.2; 95% CI= 1.9-5.3)
    - When vaccinated patients were restricted to those up-to-date with vaccinations the OR increased to 3.7 (95% CI=1.9-7.0).
Summary: Pertactin-Deficient *B. pertussis*

- The ~3-fold greater odds of having PRN- *B. pertussis* when up-to-date with vaccinations compared to unvaccinated
  - First evidence for a possible selective advantage of PRN- strains

- The large number of mutations (>16)
  - Vaccine pressure may have played a significant role in the emergence of PRN- strains

- Next step: vaccine effectiveness in pertactin-deficient strains
  - Case-control evaluation in Vermont
Impact of Pertactin-deficiency on Vaccine Effectiveness: Vermont VE Evaluation

- Vermont reported 645 cases in 2012
  - (103/100,000 population)
- Centralized testing at the VT SPHL
  - All PCR+ specimens are cultured
  - 94% of tested isolate are Prn-deficient

Objective:
- Estimate VE and duration of protection
  - 5-dose DTaP series among 4-10 year olds
  - Tdap dose among 11-19 year olds

*slide provided by Anna Acosta, MD (MVPDB/CDC)
### DTaP Duration of Protection

**Do not distribute – pending publication**

<table>
<thead>
<tr>
<th>Vaccine Status</th>
<th>Case (n)</th>
<th>Control (n)</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DTaP doses</td>
<td>19</td>
<td>11</td>
<td>84 (58-94)</td>
</tr>
<tr>
<td>5 on-schedule DTaP doses</td>
<td>244</td>
<td>715</td>
<td></td>
</tr>
</tbody>
</table>

#### Duration of Protection

<table>
<thead>
<tr>
<th>Time since 5th DTaP (years)</th>
<th>Case (n)</th>
<th>Control (n)</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DTaP doses</td>
<td>19</td>
<td>11</td>
<td>Ref</td>
</tr>
<tr>
<td>&lt;1</td>
<td>19</td>
<td>95</td>
<td>90 (71-97)</td>
</tr>
<tr>
<td>1 – 2</td>
<td>21</td>
<td>144</td>
<td>93 (79-98)</td>
</tr>
<tr>
<td>2 – 3</td>
<td>28</td>
<td>119</td>
<td>89 (69-96)</td>
</tr>
<tr>
<td>3 – 4</td>
<td>33</td>
<td>120</td>
<td>87 (63-95)</td>
</tr>
<tr>
<td>4 – 5</td>
<td>60</td>
<td>113</td>
<td>76 (33-91)</td>
</tr>
<tr>
<td>5 – 7</td>
<td>83</td>
<td>124</td>
<td>68 (10-88)</td>
</tr>
</tbody>
</table>

*slide provided by Anna Acosta, MD (MVPDB/CDC)*
# Tdap Duration of Protection

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<table>
<thead>
<tr>
<th>Vaccine status</th>
<th>Case</th>
<th>Control</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Tdap dose</td>
<td>103</td>
<td>163</td>
<td>70 (54-81)</td>
</tr>
<tr>
<td>1 on-schedule Tdap</td>
<td>141</td>
<td>551</td>
<td></td>
</tr>
</tbody>
</table>

## Duration of Protection

<table>
<thead>
<tr>
<th>Time since Tdap (years)</th>
<th>Case</th>
<th>Control</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Tdap dose</td>
<td>103</td>
<td>163</td>
<td>Ref</td>
</tr>
<tr>
<td>&lt;1</td>
<td>35</td>
<td>202</td>
<td>76 (60-85)</td>
</tr>
<tr>
<td>1 – 2</td>
<td>51</td>
<td>180</td>
<td>63 (37-78)</td>
</tr>
<tr>
<td>2 – 4</td>
<td>55</td>
<td>169</td>
<td>56 (16-77)</td>
</tr>
</tbody>
</table>

*slide provided by Anna Acosta, MD (MVPDB/CDC)*
Vaccine Effectiveness among Pertactin-Deficient Strains – Tdap

**Do not distribute – pending publication**

<table>
<thead>
<tr>
<th>Tdap</th>
<th>No. of doses</th>
<th>Case</th>
<th>Control</th>
<th>VE % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>0</td>
<td>103</td>
<td>163</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>141</td>
<td>551</td>
<td>70 (54-81)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>244</td>
<td>714</td>
<td></td>
</tr>
</tbody>
</table>

| Pertactin-deficient strains only | 0 | 33  | 62 |               |
| Total                          | 1 | 71  | 246| 51 (5-75)     |

| Total                          | 104 | 308 |

*slide provided by Anna Acosta, MD (MVPDB/CDC)*
CDC’S ADVANCED MOLECULAR DETECTION INITIATIVE
### B. pertussis Genome Sequencing

<table>
<thead>
<tr>
<th>Year</th>
<th>Selected</th>
<th>Sequenced</th>
<th>CLOSED Assembly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geographic Diversity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000 – 2013</td>
<td>175</td>
<td>101</td>
<td>81</td>
</tr>
<tr>
<td>Enhanced Pertussis Surveillance</td>
<td>117</td>
<td>92</td>
<td>82</td>
</tr>
<tr>
<td>California Epidemic</td>
<td>2010</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>Vermont Epidemic</td>
<td>2012</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Prospective, Non-EPS</td>
<td>2014</td>
<td>88</td>
<td>48</td>
</tr>
<tr>
<td>Other*</td>
<td>20</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>433</td>
<td>288</td>
<td>215</td>
</tr>
</tbody>
</table>

* Other
Vaccine strains (Tohama I, CS, Sanofi-Pastuer)
Pertussis toxin-negative (2)
Filamentous hemagglutinin-negative (2)

All assemblies yield closed genomes that will be publically-available via NCBI.

*slide provided by Michael Weigand, PhD (MVPDB/CDC)
**B. pertussis** Comparative Genomics, mid-2014

- Limited ability to detect variation with short-read technologies, challenged by:
  - High G+C content
  - Repeat regions
  - High copy number of insertion sequence elements (IS481)
- Genomics based on reference sequence of Tohama I through resequencing efforts

**Sequence (SNPs)**

- Very few nucleotide differences in most genes

**IS481**

- Occasional gene disruption (e.g. prn)

**RESULT:** Global population appeared **CLONAL and MONOMORPHIC**

*(despite unexplained variation in PFGE)*

*slide provided by Michael Weigand, PhD (MVPDB/CDC)*
Reference-free, comprehensive detection of all variation:

- **Sequence**
  - SNPs, insertions/deletions

- **Structural/Organization**
  - IS-element stability
  - Genome architecture

Rearrangements

Genome structure varies between *B. pertussis* strains:

Only resolvable with CLOSED (complete) assemblies

*slide provided by Michael Weigand, PhD (MVPDB/CDC)
Genome Structural Diversity Within an Epidemic

Example: CA 2010

*slide provided by Michael Weigand, PhD (MVPDB/CDC)
VACCINATION STRATEGIES TO PROTECT INFANTS
Changing pertussis epidemiology – shift in source of transmission to infants

- Previously, parents commonly identified as source
  - Mothers most often

- More recently, siblings identified as most common source
  - Having a sibling was a risk factor for infant pertussis
  - Source of infection study
    - 2006-2013 a source of infection for 44% of identified infant pertussis cases
    - 85% of identified sources were classified as family members
      - Siblings most commonly identified (35.5%)


Tdap coverage among pregnant women from various sources, United States

- **Vaccine Safety Datalink sites**
  - 13.7% (2012)

- **Michigan Medicaid**
  - 14.3% (2011-2013)

- **2014-2015 Internet Panel Survey of pregnant women, during flu season**
  - 23.5% (2014-2015 flu season)


CDC. Internet Panel Survey. Women aged 18–49 years pregnant at any time since August of prior year (e.g. 2014 for the April 2015 survey) were recruited in a general population internet panel operated by Survey Sampling International.
Effectiveness of Maternal Tdap Vaccination Strategies at Preventing Infant Pertussis

- **Objective:** Measure effectiveness of vaccination during pregnancy at preventing pertussis among infants <6 months of age (<2 months, 2-<6 months groups)
- **CA, CT, MN, NM, NY, OR**
- **Case-control evaluation; 1:3**
  - Cases: Confirmed and probable pertussis cases, also PCR+ cases with cough of any duration; cough onset 1/1/11 – 12/31/14
  - Controls: birth certificates; selected by age group & birth hospital
- **Provider-verified vaccination status:**
  - Case/control infants and mothers

*slide provided by Tami Skoff, MS (MVPDB/CDC)
Effectiveness of Maternal Tdap Vaccination Strategies at Preventing Infant Pertussis

- Exclude cases and controls <2 weeks
  - Disproportionate number of controls <2 weeks

- Multivariate models control for:
  - Infant age in weeks
  - More than 2 family members in the household
  - Hispanic ethnicity
  - Income less than $75,000/year
  - Mother did not attend any college
  - Infant was breastfed at any time (for any length of time)
  - Someone in the home diagnosed with pertussis

*slide provided by Tami Skoff, MS (MVPDB/CDC)
PRELIMINARY VE of Tdap During Pregnancy at Preventing Pertussis in Infants <2 Months
PRELIMINARY VE of Tdap During Pregnancy at Preventing Pertussis in Infants <2 Months, Stratified by Trimester

*slide provided by Tami Skoff, MS (MVPDB/CDC)
Possible Contributing Factors

- Surveillance bias
  - *However*, changes in risk by age strongly suggest a cohort effect

- Vaccine refusal or under-vaccination
  - *However*, coverage is excellent and majority of cases are vaccinated and outbreaks are widespread

- Waning of immunity after vaccination
  - Studies provide strong evidence of waning of protection

- Type of immune response
  - Animal models suggest aP vaccines may not prevent infection and transmission

- Molecular changes in the population of *B. pertussis*
  - Yes, *but* impact on disease and transmission is still uncertain
Thank You

www.cdc.gov/pertussis
www.cdc.gov/pregnant

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.