The Re-Emergence of Pertussis

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Presentation Outline

- Background and Clinical Characteristics
- Epidemiology and Vaccination
- Maximizing Current Vaccination Strategies
- Current and Future Activities
- Enhanced Pertussis Surveillance (EIP)
BACKGROUND & CLINICAL CHARACTERSISTICS
Pertussis (Whooping Cough)

- Highly contagious respiratory disease
- Severe, debilitating cough illness (“100 day cough”) in persons of all ages
- Highest morbidity and mortality among infants
- Estimated worldwide deaths > 300,000/yr
- Vaccine-preventable
- Poorly controlled, despite high vaccine coverage
Clinical Course (in weeks)

- **Incubation Period**
  - typically 5-10 days; max 21 days

- **Catarrhal Stage (1-2 wks)**
  - watery eyes, malaise, runny nose, mild eye inflammation, low-grade fever, late-phase non-productive cough

- **Paroxysmal Stage (1-6 wks)**
  - paroxysms followed by inspiratory whooping sound, post-tussive cyanosis, vomiting
  - infants <6 m: apnea, bradycardia, poor feeding, Prolonged cough, no paroxysms

- **Convalescent Stage**
  - weeks to months
  - paroxysms gradually improve but can recur w/ respiratory infections

- **Communicable Period**
  - (onset to 3 weeks after start of paroxysmal cough)

- **ONSET**
Infant Pertussis

- Young infants at highest risk of disease and complications
- Atypical symptoms:
  - Catarrhal stage and cough may be minimal or absent
  - Apnea (sometimes with seizures)
  - Sneezing, gagging, choking, vomiting
  - Whoop infrequent
- Cough illness among close contacts
- Presumptive treatment should begin immediately

Source: Shot of Prevention, Brady passed away at just 2 months from pertussis
Pertussis among Adolescents and Adults

- **Wide spectrum of presentation**
  - Disease often milder than in infants and children
  - May be asymptomatic
  - Can be quite severe and with classic presentation

- **Clinically difficult to distinguish from other causes of cough illness**

- **Persons with mild disease can transmit infection**
EPIDEMIOLOGY AND VACCINATION
Pertussis Surveillance and Reporting

- Nationally notifiable

- Clinical (Probable) case
  - Cough ≥2 weeks AND
  - One among paroxysms, whoop, post-tussive vomiting

- Confirmed case
  - Culture with cough of any duration OR
  - Clinical case and PCR positive OR
  - Clinical case and epi-linked to a laboratory-confirmed case

- Revisions to infant (<1yr) definition for 2014
  - Add apnea to list of case-defining clinical symptoms
  - Classify PCR positive or epi-linked cases occurring among infants with cough of any duration and one other clinical symptom as “probable”
Proportion of All Reported Pertussis Tests by Type, 1990-2012

- DFA only
- Serology only
- PCR only
- Culture only
- Multiple Test Types

Year:
- 1990
- 1992
- 1994
- 1996
- 1998
- 2000
- 2002
- 2004
- 2006
- 2008
- 2010
- 2012

Proportion of Reported Tests:
- 0.00%
- 10.00%
- 20.00%
- 30.00%
- 40.00%
- 50.00%
- 60.00%
- 70.00%
- 80.00%
- 90.00%
- 100.00%
Pertussis Immunization in the US

- **Infants/children**
  - Widely used since 1940s
  - Transitioned from DTP to DTaP throughout the 1990s
  - DTaP at 2, 4, 6 months (1997); 15-18 months (1992); 4-6 years (1992)
  - Children 7 through 10 years not fully immunized against pertussis should receive a single dose of Tdap

- **Adolescents/adults**
  - Licensed in 2005, recommended in 2006
  - Single Tdap, preferred at 11-12 years
  - All adolescents/adults who did not receive at 11-12 years should receive a single dose as soon as feasible (includes those 65 yr and older)
    - Tdap can be administered regardless of interval since the previous Td dose
Reported NNDSS Pertussis Cases: 1922-2013*

*2013 data are provisional.

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: 1990-2013*

*2013 data are provisional and subject to change.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Pertussis Incidence by Race/Ethnicity and Age Group, 2013*

*2013 data are provisional
Source: CDC, Unpublished data.
Infant Pertussis Hospitalizations by Age Group, 2000 to 2013*

*2013 data are provisional
Source: CDC, Unpublished data.
Pertussis Deaths by Age Group, 2000-2013*

*2013 data are provisional and subject to change.
Annual Incidence, by State, 2012

2012 Incidence = 15.4
(n=48,277)

Source: CDC National Notifiable Disease Surveillance System, 2012
2012 Census projections used for population estimates; Incidence is per 100,000 population
Changes in Pertussis Reporting by State from 2011 to 2012 †

†Cases reported through Week 52 in 2011 were compared with cases reported through Week 52 in 2012; fold-changes were calculated for each state.
Annual Incidence by State, 2013*

2013 Incidence = 7.7
(n=24,231)

*2013 Provisional and subject to change.

Source: CDC National Notifiable Disease Surveillance System, 2013

2012 Census projections used for population estimates; Incidence is per 100,000 population
Changes in Pertussis Reporting by State from 2012 to 2013* †

*Data for 2013 are provisional and subject to change. †Cases reported through Week 52 in 2012 were compared with cases reported through Week 52 in 2013.
U.S. Pertussis Cases by Age — 2004
n=25,827

Cases

Age (years)

Vaccine Type Received*

Acellular Only

Whole Cell and Acellular

Transition Period
U.S. Pertussis Cases by Age –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

Tdap
## Overall DTaP VE & 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 5(^{th}) 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
U.S. Pertussis Cases by Age — 2012


Aging of acellular cohorts (born ≥ 1998)

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
U.S. Pertussis Cases by Age, 2012 and 2013*

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Hypotheses/Contributing Factors

- **Rapid waning of aP-induced immunity after vaccination**
- **Surveillance bias**
  - Improved diagnosis and reporting likely contributing to increasing incidence
  - *However,* changes in risk by age strongly suggests cohort effect
- **Vaccine refusal or under-vaccination**
  - *However,* coverage is high/increasing; majority of cases vaccinated and outbreaks are widespread
- **Selective pressure of vaccination on circulating strains**
  - Allelic polymorphisms exist; predominant strains differ from vaccine strains
  - Recent emergence of pertactin-deficient strains, a key pertussis acellular vaccine antigen that mediates adherence to upper respiratory epithelium
  - *However,* conflicting evidence for strain change correlating with changes in epidemiology or vaccination
MAXIMIZING CURRENT PERTUSSIS VACCINATION STRATEGIES
ACIP Conclusions for Not Recommending a Second Tdap, June 2013

- Data do not support recommendation for second Tdap in general population
  - No change to current Tdap recommendation
  - Focus on preventing pertussis in infants
    - Pregnant women receive Tdap during each pregnancy

- Universal recommendation for second Tdap not favored but willing to consider revaccination of “at risk” populations
  - Anticipates limited impact on overall disease burden
Vaccination During Pregnancy

- Believed to be the most effective means of protecting young infants

- Provides earlier benefit to mother, thereby protecting infant at birth

- High levels of transplacental maternal antibodies in infants of mothers vaccinated during pregnancy
  - Likely provides direct immunity to infant

- Women should receive a dose of Tdap with every pregnancy
  - Optimal timing between 27 and 36 weeks gestation to maximize maternal antibody response and passive antibody transfer to infant
Projected Number of Infant Cases Under a Postpartum versus Pregnancy Tdap Program Relative to No Maternal Vaccination

Terranella et al Peds 2013.
Tdap Vaccination Coverage Among Pregnant Women, By Stage of Pregnancy, 2011-12 and 2012-13 Influenza Seasons—Preliminary Results

- After most recent pregnancy
- During most recent pregnancy
- Before most recent pregnancy

2012 VSD Coverage
Overall: 18.7%
CA only: 19.5%
Overall (w/o CA): 16.1%

Source: Internet Panel Survey. Women aged 18–49 years who were pregnant at any time since August of the prior year (e.g. 2012 for the April 2013 survey) were recruited in a general population internet panel operated by Survey Sampling International.
Effectiveness of Vaccination During Pregnancy

- Early evaluation of the maternal pertussis vaccination program in the UK is encouraging
  - High vaccine coverage during pregnancy
  - High vaccine effectiveness when it was administered a month prior to baby’s birth
  - No evidence of safety risks to mother or baby

- EIP case-control evaluation of the effectiveness of maternal vaccination during pregnancy
Current and Future CDC Activities

- Increasing evidence base for new vaccines or strategies
  - Clinical/epi relevance of strain changes - molecular characterization of isolates
  - DTaP and Tdap VE against pertactin-deficient pertussis
  - Immunology studies

- Evaluation of maternal vaccination recommendation
  - Maternal Tdap vaccination effectiveness
  - Blood spot study
  - Formative research (KAP survey of OB/GYNs and pregnant women)

- Treatment and chemoprophylaxis studies
  - 3 vs. 5 day Azithromycin
  - $2^0$ transmission following PEP
Current and Future CDC Activities, cont.

- **Economic Analyses**
  - Cost-effectiveness of vaccination
  - Cost of pertussis

- **Assessing temporal trends in susceptibility/infection**
  - Serosurvey and mathematical modeling

- **Additional changes to CSTE case definition (serology/PCR)**

- **Enhanced Pertussis Surveillance/Emerging Infection Program Network (EIP)**
ENHANCED PERTUSSIS SURVEILLANCE (EPS)
Enhanced Pertussis Surveillance (EPS)

- Established within EIP in 2011

- Builds upon existing pertussis surveillance infrastructure
  - Improved completeness and quality of data
  - Augmented data collection
  - Routine isolate collection

- Objectives
  - Describe the epidemiology and molecular characteristics of *B. pertussis*
  - Describe the epidemiology and molecular characteristics of other *Bordetella* species
  - Provide an infrastructure for special studies
Enhanced Pertussis Surveillance (EPS): Sites

Areas
- CO (5 counties)
- CT (state)
- GA (8 counties)
- MN (state)
- NM (state)
- NY (15 counties)
- OR (3 counties)

Covers 6.8% of US population
Enhanced Pertussis Surveillance (EPS): Data Collection

- **Case Report Form**
  - NNDSS form as foundation
    - Source of infant infection (relationship)
    - Pregnancy status
    - # of physician visits prior to diagnosis
    - # of residents in household
    - Date of death
    - Coinfection with another *Bordetella* species
    - Maternal Tdap vaccination history
    - Reason for insufficient infant cough
    - Healthcare personnel
    - Cyanosis
  - Annual review of form; flexibility to add new questions
Enhanced Pertussis Surveillance (EPS): 2012-2013* Data Completeness

<table>
<thead>
<tr>
<th>Condition</th>
<th>NNDSS % Complete</th>
<th>EPS % Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough Present</td>
<td>84.1</td>
<td>100</td>
</tr>
<tr>
<td>Paroxysmal Cough</td>
<td>82</td>
<td>99.6</td>
</tr>
<tr>
<td>Whoop</td>
<td>78.4</td>
<td>97.6</td>
</tr>
<tr>
<td>Posttussive Vomiting</td>
<td>79.8</td>
<td>98.7</td>
</tr>
<tr>
<td>Cough onset date</td>
<td>74.5</td>
<td>100</td>
</tr>
<tr>
<td>Duration of cough</td>
<td>76.9</td>
<td>99.9</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>72.9</td>
<td>99</td>
</tr>
<tr>
<td>Outcome</td>
<td>69.4</td>
<td>100</td>
</tr>
<tr>
<td>Vaccinated cases with &gt;=1 known vaccine date, aged 3 mos to 7 yrs</td>
<td>70.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Race</td>
<td>78.6</td>
<td>92.1</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>75</td>
<td>92.9</td>
</tr>
</tbody>
</table>

*2013 NNDSS pertussis data are provisional. 2012 and 2013 EPS data are not closed out and are subject to change.
†Unknown and missing responses are considered incomplete.
Enhanced Pertussis Surveillance (EPS):
EPS Isolate Collection

- Isolates are collected, when available, and sent to CDC
  - Challenging given increasing reliance on PCR for dx of pertussis

- CDC testing
  - PFGE testing
  - Susceptibility testing
  - Molecular characterization (MLVA, MLST)
  - Assessment of pertactin-deficiency (PCR screening, expression, sequencing)

- Expanding to specimen collection in 2014
  - CDC lab establishing methods to type *B. pertussis* directly from clinical specimens
**EPS *B. pertussis* Isolates 2012-2013**

- EPS isolates represent > 50% of all *B. pertussis* isolates received at CDC
- >85% of isolates from cases >1 year of age

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>7</td>
<td>29</td>
<td>14</td>
<td>50 (14)</td>
</tr>
<tr>
<td>1-6 years</td>
<td>5</td>
<td>39</td>
<td>10</td>
<td>54 (15)</td>
</tr>
<tr>
<td>7-10 years</td>
<td>13</td>
<td>63</td>
<td>3</td>
<td>79 (22)</td>
</tr>
<tr>
<td>11-14 years</td>
<td>8</td>
<td>63</td>
<td>14</td>
<td>85 (24)</td>
</tr>
<tr>
<td>15-19 years</td>
<td>2</td>
<td>40</td>
<td>7</td>
<td>49 (14)</td>
</tr>
<tr>
<td>20+ years</td>
<td>3</td>
<td>29</td>
<td>9</td>
<td>41 (11)</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>263</td>
<td>57</td>
<td>358</td>
</tr>
</tbody>
</table>

*This analysis is limited to isolates currently matched with available EPS case-data; matched isolates will increase as case-data are closed and transmitted to CDC.*
EPS Key Accomplishments & Policy Implications

- EPS data are of higher quality and completeness than NNDSS
  - Assess pertussis trends and characterize epidemiology of disease

- Source of isolates linked to clinical and epidemiologic information
  - Critical to understanding the evolving molecular epidemiology, including the emergence & relevance of pertactin-deficient strains

- EPS platform valuable for assessing national pertussis surveillance practices
  - Informed revisions to CSTE case definition for infants; piloting of future case definition changes being planned

- Filled data “gaps” that will inform ACIP policy decisions
  - Maternal Tdap vaccination for infant cases
  - Health care occupation
Summary

- **Pertussis resurgence is real and probably here to stay**
  - Waning immunity from acellular vaccines a likely contributor but probably not the whole story

- **Vaccination is our best prevention tool**
  - Maintain high level of DTaP coverage
  - Sustain Tdap coverage in adolescents

- **Goal is no infant deaths**
  - Remove barriers to vaccination of pregnant women
  - A baby’s first dose of pertussis vaccine should be the one its mother gets
  - Make sure infant caregivers are up-to-date with pertussis vaccinations

- **Continue to evaluate and refine vaccination policy and prevention and control recommendations**
Thank you

- Questions?