Pertussis and Pertussis Vaccines
Updates

Karen Lewis, M.D.
Medical Director
Arizona Immunization Program Office
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Lecture Objectives

• Review the transition from whole cell to acellular pertussis vaccines.
• Describe the changes in pertussis epidemiology over the last seventy years.
• Explain immunologic responses to acellular vaccines that may be contributing to increases in pertussis.
## Impact of Vaccines in the 20th & 21st Centuries

### Comparison of 20th Century Annual Morbidity & Current Morbidity

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Morbidity*</th>
<th>2010 Reported Cases †</th>
<th>% Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,005</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>21,291</td>
<td>89%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>8</td>
<td>99%</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,316</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>61</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>2,528</td>
<td>98%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>6</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>CRS</td>
<td>152</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> (&lt;5 years of age)</td>
<td>20,000 (est.)</td>
<td>270 (16 serotype b and 254 unknown serotype)</td>
<td>99%</td>
</tr>
</tbody>
</table>

**Sources:**

* JAMA. 2007;298(18):2155-2163
† CDC. MMWR January 7, 2011;59(52);1704-1716. (Provisional MMWR week 52 data)
Whole Cell Pertussis Vaccines

- *Bordetella pertussis* first isolated in 1906
- Formalin inactivated *B. pertussis* vaccines
  - Developed 1930’s
  - Clinical use 1940’s

- 70-90% effective
- Duration: 5-10 years
- Local reactions
WHOLE CELL PERTUSSIS VACCINE WEARS OFF WITH TIME

<table>
<thead>
<tr>
<th>Years since vaccine</th>
<th>Total # Exposed</th>
<th>Attacks</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td># infected</td>
<td>Percent</td>
<td></td>
</tr>
<tr>
<td>0-3 years</td>
<td>85</td>
<td>18</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>4-7 years</td>
<td>61</td>
<td>29</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>8-11 years</td>
<td>43</td>
<td>28</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td>&gt; 12 years</td>
<td>21</td>
<td>20</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>210</td>
<td>95</td>
<td>45%</td>
<td></td>
</tr>
</tbody>
</table>

Kent County, Michigan outbreak 1960
UCLA Study of Side Effects Following 15,752 DTwP

- Fever $\geq 38^\circ$C. (37.4%)
- Persistent crying (3.1%)
- Febrile seizures (9)
- Hypotonic hyporesponsive episodes (9)

- Reports of development delay and chronic seizures after DTwP

Claims Filed VICP 1989-2007

Sugarman SD. NEJM Sept. 27, 2007
Dravet Syndrome

• Severe myoclonic epilepsy and developmental delay appearing in infancy
• 1:20,000
• Genetic mutations in SCN1A (neuronal sodium channel α1 subunit)

• *Pediatrics*, Sept 2011
  – 5/5 “pertussis vaccine encephalopathy” → Dravet
Pertussis in Japan, 1945-1995

Figure 1. Reported cases of and deaths from pertussis in Japan, 1947-1995

Cases: Statistics on Communicable Diseases in Japan
Deaths: Vital Statistics of Japan
( Ministry of Health and Welfare )
Whooping Cough or Pertussis  
\((Bordetella pertussis)\)

- Spread by respiratory droplets
- Incubation period of 5-21 days
- Immunity not life-long
Antigenic and Biologically Active Components of *B. pertussis*

- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- pertactin
- fimbriae
- agglutinogens
- adenylate cyclase
- tracheal cytotoxin
- dermonecrotic toxin
<table>
<thead>
<tr>
<th><strong>PERTUSSIS VACCINE ANTIGENS</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis toxin (PT)</td>
<td>“Lymphocytosis promoting factor”</td>
</tr>
<tr>
<td>Filamentous Hemagglutinin (FHA)</td>
<td>Mediates adherence</td>
</tr>
<tr>
<td>Pertactin (PRN)</td>
<td>Promotes cell binding</td>
</tr>
<tr>
<td>Fimbriae (FIM)</td>
<td>Attachment</td>
</tr>
</tbody>
</table>
## Components of Acellular Pertussis Vaccines

<table>
<thead>
<tr>
<th>Product</th>
<th>Type</th>
<th>PT µg</th>
<th>FHA µg</th>
<th>PERT µg</th>
<th>FIM µg</th>
<th>DIPH Lf</th>
<th>TET Lf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptacel</td>
<td>DTaP</td>
<td>10</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Tripedia</td>
<td>DTaP</td>
<td>23</td>
<td>23</td>
<td>--</td>
<td>--</td>
<td>6.7</td>
<td>5</td>
</tr>
<tr>
<td>Infanrix</td>
<td>DTaP</td>
<td>25</td>
<td>25</td>
<td>8</td>
<td>--</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Pediarix</td>
<td>DTaP+</td>
<td>25</td>
<td>25</td>
<td>8</td>
<td>--</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Pentacel</td>
<td>DTaP+</td>
<td>20</td>
<td>20</td>
<td>3</td>
<td>5</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Adacel</td>
<td>Tdap</td>
<td>2.5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Boostrix</td>
<td>Tdap</td>
<td>8</td>
<td>8</td>
<td>2.5</td>
<td>--</td>
<td>2.5</td>
<td>5</td>
</tr>
</tbody>
</table>
Whole cell pertussis vaccine

1997 DTaP used for all 5 childhood pertussis doses

2005 Tdap licensed for adults and adolescents

DTaP used for 4th and 5th doses

Graph from CDC Pink Book, 12th edition
Reported NNDSS pertussis cases: 1922-2011*

*2011 data have not been finalized and are subject to change. 2011 data were accessed on July 5, 2012.

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

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>0-1 month</td>
<td>38</td>
<td>68</td>
<td>152</td>
</tr>
<tr>
<td>2-3 months</td>
<td>11</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>4-5 months</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6-11 months</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>3</td>
</tr>
<tr>
<td>11-18 years</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 18 years</td>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>77</strong>*</td>
<td><strong>103</strong></td>
<td><strong>194</strong></td>
</tr>
</tbody>
</table>

*One with age unknown

CDC National Notifiable Disease Surveillance System, 2009
Pertussis in California as of 7/8/2014

Figure 2. Number and incidence of reported pertussis cases by year of onset -- California, 1946-2014*
Pertussis Cases, Arizona, 1994–2013

Cases

Year

Total

Confirmed

As of 6/23/2014
Hospitalizations and Deaths
% Total Infant Cases, 2001-2011

Hospitalizations % of cases

Deaths % of cases

Acellular Pertussis Vaccines Protects Infants

Pertussis incidence among infants, 2001-2011

75% of suspected sources for infant pertussis cases were family members.

Mom or Dad: 47%
- Mom: 32%
- Dad: 15%
Sibling: 20%
Grandparent: 8%
Other: 25%

76% of suspected sources* for infant pertussis cases were adolescents or adults

- Young Children 0-4 years: 17%
- Children 5-9 years: 7%
- Adolescents: 20%
- Adults: 56%

CDC Emphasis on Tdap to All Contacts of Infants

- Family members are source in most of newborn cases

- **Cocooning**

- Everyone around infant needs Tdap

- 2012: Give Tdap to pregnant women if not already received
Reported pertussis incidence by age group: 1990-2012*

*2012 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System

- 3+ Childhood DTaP
- 4+ Childhood DTaP
- Adolescent Tdap
- Adult Tdap

Percent coverage

Tdap recommended

2004 2005 2006 2007 2008 2009 2010 2011

Acosta A. CDC. ACIP Presentation June 19, 2013. CDC NIS Surveys for 0-17 yo and and NHIS for adults.
Possible Reasons for More Pertussis

1. Waning immunity after acellular vaccines
2. Whole cell vaccines gave better immunity than acellular
3. *Bordetella* pertussis strain change
4. Local collections of unvaccinated and susceptible children and adults

Plotkin SA. Clinical Infectious Diseases. March 15, 2014
Pertussis Antigens GMC up to 10 Years After Tdap (Adacel)

Adults (n=644)

PT: pertussis toxin; FHA: filamentous hemagglutinin; PRN: pertactin; FIM: fimbriae types 2&3


Liang. ACIP June 2013
CDC: Tdap for Every Pregnancy

• Waning pertussis antibodies after Tdap
  – Rapid decrease over 1 year
  – Cord blood antibodies within 2 year Tdap not high
• Average 2 children per woman in US
  – Only 5% have ≥ 4 children
  – Only 2.5% have intervals between babies of ≤ 12 months
• Active transport of IgG starts about 30 weeks
• Safe
# Pertactin Negative *Bordetella pertussis* in the U.S.

<table>
<thead>
<tr>
<th></th>
<th>Total isolates</th>
<th>Pertactin negative</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical isolates, 1935-2009</td>
<td>666</td>
<td>1</td>
<td>0.0015%</td>
</tr>
<tr>
<td>2010 CA outbreak</td>
<td>33</td>
<td>4</td>
<td>12%</td>
</tr>
<tr>
<td>US 2010-2012</td>
<td>385</td>
<td>144</td>
<td>37%</td>
</tr>
<tr>
<td>2012 Washington state outbreak</td>
<td>216</td>
<td>157</td>
<td>73%</td>
</tr>
</tbody>
</table>

Pertactin Negative *B. pertussis* (BP) Does Not Change Disease Severity

- No difference in severity of illness between pertactin positive and negative infants
- Pertactin NEG infants more likely to be diagnosed later \((p=0.04)\)
  - Pertactin POS: 9.9 days
  - Pertactin NEG: 14.6 days
- Infants who had one or two DTaP vaccines had less severe illness and fewer complications
<table>
<thead>
<tr>
<th>Baboons</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uninfected</td>
<td>Sick and shed BP for 30 days</td>
</tr>
<tr>
<td>Previous BP infection</td>
<td>Not ill, did not shed BP</td>
</tr>
<tr>
<td>DTwP at 2, 4, 6 months</td>
<td>Not ill, shed BP for 18 days</td>
</tr>
<tr>
<td>DTaP at 2, 4, 6 months</td>
<td>Not ill, lower # of BP but shed BP for 35 days &amp; easily spread BP to unvaccinated baboons</td>
</tr>
</tbody>
</table>
Current Efforts to Control Pertussis

- Surveillance
- Diagnosis BP early, treat, prophylaxis
- Vaccinate
  - One Tdap for every teenager and adult.
  - Tdap for pregnant women in every pregnancy
  - Cocooning
  - Develop better pertussis vaccine.