Pertussis – A Big Whoop

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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
  - Incidence increasing in United States
- First U.S. pertussis vaccines for adolescents and adults (Tdap)† licensed in 2005

†Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine
## Impact of Vaccines in the United States

<table>
<thead>
<tr>
<th>Vaccine-Preventable Disease</th>
<th>Number of Reported Cases</th>
<th>20th Century Annual Morbidity*</th>
<th>2005**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>48,164</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175,885</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Pertussis</strong></td>
<td><strong>147,271</strong></td>
<td><strong>25,616</strong></td>
<td></td>
</tr>
<tr>
<td>Tetanus</td>
<td>1,314</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,316</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>503,282</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209</td>
<td>314</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Congenital rubella</td>
<td>823</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><em>H. influenza</em> (invasive &lt;5 yrs)</td>
<td>20,000</td>
<td>226</td>
<td></td>
</tr>
</tbody>
</table>

* Source: CDC, MMWR, April 2, 1999. 48:242-264

** Source: CDC, MMWR, August 18, 2006. 55(32); 880-893
Presentation Outline

• Pertussis pathogenesis
• Laboratory diagnostics
• Clinical characteristics
• Epidemiology
• Control
• Prevention (vaccines)
• Outbreaks first described in 16th century
• *Bordetella pertussis* isolated in 1906
**Bordetella pertussis**

Fastidious gram negative coccobacillus

Antigenic and biologically active components:
- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- agglutinogens
- adenylate cyclase
- pertactin
- tracheal cytotoxin
- fimbriae
Pathogenesis of *B. pertussis*

- Attachment to cilia of ciliated epithelial cells in respiratory tract
- Pertussis antigens allow evasion of host defenses (lymphocytosis but impaired chemotaxis)
- Local tissue damage in respiratory tract
- Systemic disease may be toxin mediated
Laboratory Tests for Pertussis

- Nasopharyngeal collection technique very important
- **Culture**
  - “Gold standard” because 100% specific, but low sensitivity (30-60%)
  - Highest yield in young patients, unvaccinated patients, patients early in cough illness prior to antimicrobials
  - Slow turnaround (up to 2 weeks)
- **PCR**
  - More sensitive than culture (50-80%), but possibility of false positives
  - No clinically validated, standard FDA approved test available
  - Rapid (clinical relevance)
- **Serology (IgG anti-pertussis toxin)**
  - Not yet standardized (except in MA)
CSTE Case Definition

• Clinical case definition:
  – Cough > 2 weeks AND
  – paroxysms, inspiratory whoop, or posttussive vomiting

Case Classification

<table>
<thead>
<tr>
<th>Probable</th>
<th>Confirmed</th>
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<tbody>
<tr>
<td>- Meets clinical case definition</td>
<td>- Culture positive</td>
</tr>
<tr>
<td></td>
<td>- PCR + clinical case definition</td>
</tr>
<tr>
<td></td>
<td>- Epi link + clinical case definition</td>
</tr>
</tbody>
</table>
Number of Pertussis Reports by Diagnostic Criteria, 1990 – 2004

- PCR and epi-link accepted since 1995.
- +2004 provisional
- * Other = Clinical & N/A
Clinical Course (in weeks)

Communicable period (onset to 3 weeks after start of paroxysmal cough)

Incubation period (typically 5-10 days; max 21 days)

Catarrhal stage (1-2 weeks)

Convalescent stage (weeks to months)

Paroxysmal stage (1-6 weeks)

Onset
Pertussis Clinical Stages

• Catarrhal (1-2 weeks)
  – Congestion, rhinorrhea, sneezing, lacrimation followed by onset of dry, intermittent cough
  – Presentation similar to many URIs

• Paroxysmal (2-5 weeks)
  – Spasms may occur hourly or more frequently
  – Classic symptoms: paroxysms, post-tussive vomiting, inspiratory whoop
  – Post-tussive exhaustion in all ages
  – Patients usually well appearing between episodes

• Convalescent (2-6 weeks)
  – Paroxysmal cough may recur
Pertussis Clinical Features

- Fever usually minimal throughout course
- Characteristic lymphocytosis
- Antimicrobials do not modify the course of illness after cough established
  - Will decrease infectivity of patients if given early
- High risk groups for pertussis not well defined
Infant Pertussis

- Young infants
  - Highest rates of disease and pertussis-related complications
- Atypical symptoms: Catarrhal stage and cough may be minimal or absent at presentation
  - Apnea (sometimes with seizures)
  - Sneezing
  - Gagging, choking, vomiting
  - Whoop infrequent in young infants
- Cough illness among close contacts

Source: World Health Organization
Reported Pertussis-Related Deaths
United States, 1990-2004

Source: National Notifiable Diseases Surveillance System
Pertussis Complications and Hospitalizations, by Age

Pneumonia Hospitalization

*Percent of cases reported to CDC 1997-2000 (N=28,187) with pneumonia or hospitalized

*Percent of cases reported to CDC 1997-2000 (N=28,187) with pneumonia or hospitalized.
Reported Complications in 18,500 Infants with Pertussis, United States, 1990-1999*

<table>
<thead>
<tr>
<th>Complication</th>
<th>%</th>
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<tbody>
<tr>
<td>Hospitalized</td>
<td>67%</td>
</tr>
<tr>
<td>Pneumonia (CXR confirmed)**</td>
<td>22%</td>
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<tr>
<td>Seizure</td>
<td>2%</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>0.3%</td>
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<tr>
<td>Death</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

*Proportion of cases with information

**Denominator excluded cases in which CXR not done; if CXR not done included in denominator then 16% of cases had pneumonia, CDC unpublished data

Tanaka M et al. *JAMA* 2003
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
Clinical Manifestations: Adolescents and Adults

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Adolescents (N=314)</th>
<th>Adults (N=203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysms</td>
<td>74%</td>
<td>84%</td>
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<tr>
<td>Vomiting</td>
<td>56%</td>
<td>54%</td>
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<tr>
<td>Shortness of breath</td>
<td>72%</td>
<td>86%</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>3%</td>
<td>28%</td>
</tr>
<tr>
<td>Rib fracture</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>1%</td>
<td>6%</td>
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</tbody>
</table>
Cough Duration

- Adolescents:
  - 38% still coughing at 106 days
  - 83% missed school for 5.5 [0.4-32] days
  - 43% parents missed work for 2.4 [0.1-25] days

- Adults:
  - 61% still coughing at 94 days
  - 61% missed work for 9.8 [0.1-180] days

Lee et al., CID 2004
## Pertussis Epidemiology

<table>
<thead>
<tr>
<th>Reservoir</th>
<th>Human</th>
<th>Adolescents and adults</th>
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<tbody>
<tr>
<td>Transmission</td>
<td>Respiratory droplets</td>
<td>Airborne transmission rare</td>
</tr>
<tr>
<td>Communicability</td>
<td>Catarrhal stage - 3 weeks after cough onset</td>
<td>Duration depends on age, immunization status or previous pertussis, and antibiotic therapy</td>
</tr>
<tr>
<td></td>
<td>Duration typically longer in infants</td>
<td>Maximum in catarrhal stage</td>
</tr>
<tr>
<td></td>
<td>Secondary attack rate up to 80%</td>
<td></td>
</tr>
</tbody>
</table>
Reported Pertussis Cases – United States, 1922-2005*

Pertussis Incidence in Infants by Age in Months, 1984-2004

Source: National Notifiable Diseases Surveillance System
U.S. Reported Pertussis Deaths among Young Children by Age and Time Period

<table>
<thead>
<tr>
<th>Age</th>
<th>1980-9</th>
<th>1990-9</th>
<th>2000-4</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>0+1 mo</td>
<td>54</td>
<td>89</td>
<td>92</td>
<td>235</td>
</tr>
<tr>
<td>2+3 mo</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4+5 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-11 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1-4 yr</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

CDC, unpublished data
Distribution of Reported Pertussis Cases by Age, U.S., 2003

Number of cases

Age group (yrs)

Number of cases

Incidence rate

Incidence per 100,000

<6m  6-11m  1-4  5-9  10-14  15-19  20-29  30-39  40-49  50+

0  500  1000  1500  2000  2500  3000

National Notifiable Diseases Surveillance System
Adolescent Pertussis – Waning Immunity from Childhood Pertussis Vaccines

Average Annual Incidence of Reported Pertussis Cases in Massachusetts Adolescents by Age, 1996–2004*

Adult Pertussis

- Adults vulnerable to pertussis
  - Pertussis immunity wanes 5-10 years after childhood series

- Underreported among adults
  - Often considered a childhood disease and not recognized by clinicians
  - Difficult to diagnose

- Significant burden of illness
  - Almost 8,000 cases of adult pertussis reported in 2005 in United States (27% of reported cases)
  - Estimate of true disease ~ 600,000 cases / year among adults aged 19-64 years

- Pertussis is costly
  - Societal cost / adult pertussis case ~$773
  - Outbreaks burden public health system (controlled by contact tracing and prophylactic antimicrobials)
Adults Transmit Pertussis to Infants

Reported Relationship of Source Case 494 Pertussis Cases Aged <4 Months 1999-2002

<table>
<thead>
<tr>
<th>Source Relationship</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>282 (57)</td>
</tr>
<tr>
<td>Mother</td>
<td>75 (15)</td>
</tr>
<tr>
<td>Sibling</td>
<td>38 (8)</td>
</tr>
<tr>
<td>Father</td>
<td>29 (6)</td>
</tr>
<tr>
<td>Grandparent</td>
<td>17 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>53 (11)</td>
</tr>
</tbody>
</table>

Among 264 known source-cases of infants <1 year
55% identified as mother, father or grandparent
51% were adults >19 years of age

Pertussis in Health-Care Settings

- Health-care personnel (HCP) at increased risk of pertussis exposure and infection
- HCP can transmit to vulnerable patients, including infants
- Pertussis outbreaks reported in pediatric and adult inpatient wards, maternity units and obstetric units
- Infection control activities are resource-intensive, disruptive and costly
Pertussis Treatment

• When to treat
  – Adults, adolescents, children
    • Antimicrobials may modify course if given early
    • Treatment ≥3 weeks after cough onset limited benefit
  – Infants and pregnant women near term
    • Treatment up to 6 weeks after cough onset should be considered

• Recommended treatment
  – Macrolide / azolide antimicrobial
    • 5 day course azithromycin
    • 7 day course clarithromycin
    • 14 day course erythromycin
  – Alternative agent:
    • 14 day course trimethoprim-sulfamethoxazole
Prophylaxis

• Rationale
  – Patients most infectious first 1-2 weeks of cough
  – For symptomatic patients: prevent secondary spread
  – For asymptomatic contacts: kill bacteria that may have been transmitted, prevent disease

• Prophylaxis
  – Administer to close contacts within 3 weeks of exposure
  – Same doses as treatment

• Priorities
  – Infants age <6 months or who received <3 DTaP vaccine doses
  – Persons who may expose infants
  – Persons of any age to decrease morbidity
# Pertussis Vaccines

## Appendix A

**Composition of selected vaccines with tetanus toxoid, diphtheria toxoid, and acellular pertussis components licensed in the United States, 2006**

<table>
<thead>
<tr>
<th>Vaccines for persons aged &lt;7 years</th>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Pertussis antigens (μg)</th>
<th>Diphtheria toxoid</th>
<th>Tetanus toxoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTap</td>
<td>INFANRIX®</td>
<td>GlaxoSmithKline Biologics (GSK)</td>
<td>25 25 8 —</td>
<td>25 L U</td>
<td>10 L U</td>
</tr>
<tr>
<td>DTap</td>
<td>DAPTACE®</td>
<td>sanofi pasteur</td>
<td>10 5 3 5†</td>
<td>15 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>DTaP</td>
<td>Tripedia®</td>
<td>sanofi pasteur</td>
<td>23.4 23.4 — —</td>
<td>6.7 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>DTaP+HIB (Tripedia + Act-HIB)™**</td>
<td>TriHIB®</td>
<td>sanofi pasteur</td>
<td>23.4 23.4 — —</td>
<td>6.7 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>DT</td>
<td>No trade name</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>6.7 L U</td>
<td>5 L U</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vaccines for persons aged ≥7 years</th>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Pertussis antigens (μg)</th>
<th>Diphtheria toxoid</th>
<th>Tetanus toxoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tdap</td>
<td>BOOSTRIX™††</td>
<td>GSK</td>
<td>8 8 2.5 —</td>
<td>2.5 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>Tdap</td>
<td>ADACEL™††</td>
<td>sanofi pasteur</td>
<td>2.5 5 3 5†</td>
<td>2 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>Td</td>
<td>No trade name</td>
<td>Massachusetts Public Health Biologies Laboratory</td>
<td>— — — —</td>
<td>2 L U</td>
<td>2 L U</td>
</tr>
<tr>
<td>Td</td>
<td>DECAYAC™</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>2 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>Td</td>
<td>TENVAC™</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>2 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>Td</td>
<td>No trade name</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>2 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>TT (adsorbed)</td>
<td>No trade name</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>5 L U</td>
<td>5 L U</td>
</tr>
<tr>
<td>TT (booster) (fluid)</td>
<td>No trade name</td>
<td>sanofi pasteur</td>
<td>— — — —</td>
<td>4 L U</td>
<td>5 L U</td>
</tr>
</tbody>
</table>

* Consult package inserts for prescribing information, age indication, and additional product information; package inserts are routinely updated. Some vaccines are licensed but no longer available in the United States. See Appendix F for a complete list of abbreviations.

† Per recommended dose of 0.5 mL. PT-pertussis toxin (vaccine component is inactivated/denatured), FHA=filamentous hemagglutinin, PRN=pertactin, FIM=fimbriae.

†† The tetanus, diphtheria, and pertussis components are the same as those in INFANRIX®.† but contains hepatitis B surface antigen, plus polysaccharide Type 1 (Menatone), Type 2 (MEF-1), and Type 5 (Saukett).

†† The tetanus, diphtheria, and pertussis components are the same as those in Tripedia®, but contains Haemophilus influenzae type b (Tetanus Toxoid Conjugate).

†† BOOSTRIX®—indicated as a single dose for persons aged 10–18 years.

††† ADACEL™—indicated as a single dose for persons aged 11–64 years.
Timeline: Childhood Pertussis Vaccination Policy in the United States

• 1940 and 50s: Whole cell pertussis vaccines (DTP) recommended

• 1992: Advisory Committee on Immunization Practices (ACIP) published recommendations for use of acellular pertussis vaccines (DTaP) for 4th and 5th doses

• 1997: ACIP published recommendations for use of DTaP for all 5 doses from 2 months to 6 years of age*

• 1994-2003: Coverage 3+ doses DTP/DTaP: >90%

Pediatric Pertussis Vaccine Formulations: Children Aged <7 years

Licensed
- DTaP (diphtheria, tetanus and acellular pertussis)
  - DAPTACEL™, sanofi pasteur
  - Tripedia®, sanofi pasteur
  - Infanrix™, GlaxoSmithKline Biologicals
- DTaP-IPV-Hep B (DTaP and inactivated polio and hepatitis B)
  - Pediarix™, GlaxoSmithKline
- DTaP-Hib (DTaP and Haemophilus influenzae type b)
  - TriHIBiT®, sanofi pasteur
- DT (pediatric diphtheria and tetanus toxoid)
  - (No trade name, sanofi pasteur)

Under consideration for licensure
- DTaP-IPV-Hib
  - Pentacel™, sanofi pasteur

No longer distributed in the United States
- *DTP (whole cell pertussis) not distributed in US since 2002
# Pertussis Vaccines: DTaP

## Recommended Immunization Schedule for Persons Aged 0–6 Years — United States, 2007

<table>
<thead>
<tr>
<th>Vaccine ▼</th>
<th>Age ▼</th>
<th>Birth</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>19–23 months</th>
<th>2–3 years</th>
<th>4–6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B¹</td>
<td></td>
<td>HepB</td>
<td>HepB</td>
<td>HepB</td>
<td>HepB</td>
<td>HepB</td>
<td>HepB Series</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Rotavirus²</td>
<td></td>
<td>Rota</td>
<td>Rota</td>
<td>Rota</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis³</td>
<td></td>
<td>DTaP</td>
<td>DTaP</td>
<td>DTaP</td>
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<td>DTaP</td>
<td>DTaP</td>
<td>DTaP</td>
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<tr>
<td><em>Haemophilus influenzae type b</em>⁴</td>
<td></td>
<td>Hib</td>
<td>Hib</td>
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<td>Hib</td>
<td>Hib</td>
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<tr>
<td>Pneumococcal⁵</td>
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<td>PPV</td>
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<td>Inactivated Poliovirus</td>
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<td>Influenza⁶</td>
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<tr>
<td>Measles, Mumps, Rubella⁷</td>
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<td>MMR</td>
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<tr>
<td>Varicella⁸</td>
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<td>Varicella</td>
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<tr>
<td>Hepatitis A⁹</td>
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<td>HepA (2 doses)</td>
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<td>HepA Series</td>
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<tr>
<td>Meningococcal¹⁰</td>
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<td>MPSV4</td>
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</tbody>
</table>

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 0–6 years. Additional information is available at [http://www.cdc.gov/nip/recs/child-schedule.htm](http://www.cdc.gov/nip/recs/child-schedule.htm). Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at [http://www.vaers.hhs.gov](http://www.vaers.hhs.gov) or by telephone, 800-822-7967.
# Licensed Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccines

<table>
<thead>
<tr>
<th></th>
<th>BOOSTRIX® (GlaxoSmithKline Biologicals)*</th>
<th>ADACEL® (sanofi pasteur)†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date of FDA licensure</strong></td>
<td>May 3, 2005</td>
<td>June 10, 2005</td>
</tr>
<tr>
<td><strong>Age Indication (years)</strong></td>
<td>10–18</td>
<td>11–64</td>
</tr>
<tr>
<td><strong>Usage</strong></td>
<td>Active booster immunization for prevention of tetanus, diphtheria, and pertussis as a single dose</td>
<td></td>
</tr>
</tbody>
</table>

Tdap Vaccines

• Vaccines combined with tetanus, diphtheria
  – No pertussis-only vaccines licensed

• Tetanus and diphtheria toxoids similar to Td

• Acellular pertussis antigens same as DTaP except some antigens present in lower quantity
  – BOOSTRIX® ~ INFANRIX®*
  – ADACEL® ~ DAPTACEL®†

• Safe and immunogenic

• Efficacy for licensure based, in part, on “serologic bridge” from adolescents to infants
  – Compared immune responses in adolescents after 1 dose Tdap with immune responses in infants who received 3 doses DTaP with same pertussis components in clinical efficacy study

*BOOSTRIX® and INFANRIX®: pertussis toxin (PT); filamentous haemagglutinin (FHA); pertactin (PRN)
†ADACEL® and DAPTACEL®: PT, FHA, PRN and Fimbrae 2/3
Routine Adolescent Tdap Use

• Adolescents aged 11–18 years should receive Tdap instead of Td if they have not received Td or Tdap. The preferred age for Tdap vaccination is 11–12 years.

• Adolescents aged 11–18 years who received Td, but not Tdap, are encouraged to receive a single dose of Tdap. A 5 year interval between Td and Tdap is encouraged to reduce risk for local and systemic reactions.
New Pertussis Vaccines:
Tdap for Adolescents

<table>
<thead>
<tr>
<th>Vaccine ▼</th>
<th>Age ▶</th>
<th>7–10 years</th>
<th>11–12 YEARS</th>
<th>13–14 years</th>
<th>15 years</th>
<th>16–18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus, Diphtheria, Pertussis¹</td>
<td></td>
<td></td>
<td>Tdap</td>
<td></td>
<td></td>
<td>Tdap</td>
</tr>
<tr>
<td>Human Papillomavirus²</td>
<td></td>
<td></td>
<td>HPV (3 doses)</td>
<td></td>
<td>HPV Series</td>
<td></td>
</tr>
<tr>
<td>Meningococcal³</td>
<td>MPSV4</td>
<td></td>
<td>MCV4</td>
<td></td>
<td>MCV4³</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal⁴</td>
<td></td>
<td></td>
<td>PPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza²</td>
<td></td>
<td></td>
<td>Influenza (Yearly)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A⁶</td>
<td></td>
<td></td>
<td>HepA Series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B⁷</td>
<td></td>
<td></td>
<td>HepB Series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated Poliovirus⁸</td>
<td></td>
<td></td>
<td>IPV Series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, Mumps, Rubella⁹</td>
<td></td>
<td></td>
<td>MMR Series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella¹⁰</td>
<td></td>
<td></td>
<td>Varicella Series</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2006, for children aged 7–18 years. Additional information is available at http://www.cdc.gov/vaccines/recs/child-schedule.htm. Any dose not administered at the recommended age should be administered at any subsequent visit, when indicated and feasible. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and other components of the vaccine are not contraindicated and if approved by the Food and Drug Administration for that dose of the series. Providers should consult the respective Advisory Committee on Immunization Practices statement for detailed recommendations. Clinically significant adverse events that follow immunization should be reported to the Vaccine Adverse Event Reporting System (VAERS). Guidance about how to obtain and complete a VAERS form is available at http://www.vaers.hhs.gov or by telephone, 800-822-7967.
Routine Adult Tdap Use

• Routine recommendations apply to adults who
  – Are aged 19-64 years
  – Have not previously received a dose of Tdap

• Licensed for single use only
  – After receipt of Tdap, subsequent doses of boosters should be with Td according to previously published guidance

• ADACEL® only Tdap licensed for adults
Routine Adult Tdap Use
General Use

• Adults should receive a single dose of Tdap to replace a single dose of Td if they received their last dose of Td ≥10 years earlier.

• If Tdap and another vaccine is indicated, they should be administered during the same visit (i.e., simultaneous vaccination).
Interval Between Td and Tdap

- Intervals <10 years since the last Td may be used to protect against pertussis. Particularly in settings with increased risk for pertussis, the benefit of using a single dose of Tdap at an interval <10 years to protect against pertussis generally outweighs the risk for local and systemic reactions after vaccination.

- The safety of intervals as short as ~2 years is supported by data from a Canadian study*; shorter intervals may be used.

Routine Adult Tdap Use
Adults in Contact With Infants

- Adults who have or who anticipate having close contact with an infant aged <12 months should receive a single dose of Tdap
  - An interval as short as 2 years from last Td suggested
  - Ideally at least 2 weeks before contact with the infant.
- Infants should receive DTaP on schedule
- When possible, women should receive Tdap before conception.
- Pregnant women should receive Tdap in the immediate post-partum period.
Routine Adult Tdap Use
Health-Care Personnel

• Recommendations supported by HICPAC

• Health-care personnel (HCP) in hospitals* or ambulatory care settings who have direct patient contact should receive Tdap as soon as feasible at an interval as short as 2 years from the last Td.

• Priority to HCP in contact with infants

• Hospitals and ambulatory care facilities should provide Tdap for HCP and use approaches that maximize vaccination rates.

*Hospitals, as defined by the Joint Commission on Accreditation of Healthcare Organizations, do not include long term care facilities such as nursing homes, skilled nursing facilities, rehabilitation and convalescent facilities. Ambulatory care settings include all outpatient and walk-in facilities.
### Selected Contraindications and Precautions for Tdap and DTaP

<table>
<thead>
<tr>
<th>Event</th>
<th>DTaP (infant/child)</th>
<th>Tdap (adolescent/adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious allergic reaction to vaccine component</td>
<td>Contraindication</td>
<td>Contraindication</td>
</tr>
<tr>
<td>Encephalopathy within 7 days of DTP/DTaP</td>
<td>Contraindication</td>
<td>Contraindication</td>
</tr>
<tr>
<td>Neurologic conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive Unstable</td>
<td>Contraindication</td>
<td>Precaution (adolescent)</td>
</tr>
<tr>
<td>Guillain-Barré syndrome ≤6 weeks after tetanus toxoid-containing vaccine</td>
<td>Precaution</td>
<td>Precaution</td>
</tr>
<tr>
<td>Certain adverse events after DTP/DTaP*</td>
<td>Precaution</td>
<td>None</td>
</tr>
</tbody>
</table>

*Temperature ≥105°F (≥40.5°C) within 48 hours after DTP/DTaP; collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours; persistent crying lasting ≥3 hours, within 48 hours; convulsions with or without fever, within 3 days
## Selected Special Situations

<table>
<thead>
<tr>
<th>Situation</th>
<th>Recommendations for adolescents who have not received Tdap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertussis outbreak</td>
<td>Tdap can be used at shorter intervals since most recent Td</td>
</tr>
<tr>
<td>History of Pertussis</td>
<td>Use Tdap</td>
</tr>
<tr>
<td>Wound management</td>
<td>Tdap preferred to Td if tetanus prophylaxis indicated; use standard algorithm</td>
</tr>
<tr>
<td>Incomplete schedule</td>
<td>Use Tdap as one of the doses for catch-up; use Td for other doses</td>
</tr>
</tbody>
</table>
Inadvertent Administration of Tdap (BOOSTRIX®) or Pediatric DTaP

• If BOOSTRIX® or pediatric DTaP is administered to an adolescent or adult, this dose should count as the Tdap dose and the patient should not receive an additional dose of Tdap (ADACEL®).

Source: www.vaccineshoppe.com
Adults Aged ≥65 Years

• Tdap is not licensed for use among adults aged ≥65 years.

• The safety and immunogenicity of Tdap among adults aged ≥65 years were not studied during U.S. pre-licensure trials.

• Adults ≥65 years of age should receive a dose of Td every 10 years for protection against tetanus and diphtheria, and as indicated for wound management.
Pertussis Vaccines: Tdap for Adults
Summary and Recommendations

• Pertussis continues to be a public health problem, despite well-implemented infant/child vaccination program
• Pertussis causes greatest morbidity and mortality among infants
• Adolescents / adults
  – Reported cases have increased
    • True increase in disease, and/or
    • Better recognition, diagnosis, reporting
  – Very underreported: only small fraction of cases are reported
• Case reporting important to monitor disease
  – Important to confirm cases by culture
• Tdap important new tool to reduce morbidity in all age groups
Issues

• ACIP to consider DTaP-IPV-Hib vaccine (Pentacel) at next meeting
• Need for post-exposure prophylaxis if vaccinated
• Diagnostic difficulties complicate epidemiology
• Need for improved, standardized pertussis diagnostics
Acknowledgements

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Christina Mijalski  Tej Tiwari
Thank you

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.
Back-up Slides
## Composition of DTaP, Td and Tdap Vaccines: Pertussis Antigen and Diphtheria & Tetanus Toxoid Content

<table>
<thead>
<tr>
<th>GlaxoSmithKline Biologicals</th>
<th>sanofi pasteur</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFANRIX™ (DTaP)</td>
<td>BOOSTRIX® (Tdap)</td>
</tr>
<tr>
<td>ug/dose</td>
<td>ug/dose</td>
</tr>
<tr>
<td>PT*</td>
<td>25</td>
</tr>
<tr>
<td>FHA*</td>
<td>25</td>
</tr>
<tr>
<td>PRN*</td>
<td>8</td>
</tr>
<tr>
<td>FIM* (2&amp;3)</td>
<td>---</td>
</tr>
<tr>
<td>Lf/dose</td>
<td>Lf/dose</td>
</tr>
<tr>
<td>Tetanus</td>
<td>10</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>25</td>
</tr>
</tbody>
</table>

*Pertussis toxin (PT); filamentous haemagglutinin (FHA); pertactin (PRN); fimbriae (FIM)
Vaccination During Pregnancy

• Provisional recommendations
• Routine post-partum Tdap:
  – Pregnant women who have not received a dose of Tdap (including breastfeeding) should receive Tdap after delivery, before discharge from the hospital.
• Tetanus, diphtheria and neonatal tetanus protection:
  – Pregnant women for whom 10 years or more have elapsed since last Td booster may defer Td and use Tdap post-partum if tetanus protection is likely.
  – Td recommended if tetanus and diphtheria protection required during pregnancy
• Pregnancy not contraindication for Tdap
**Tetanus prophylaxis in routine wound management**

<table>
<thead>
<tr>
<th>Clean, minor wound</th>
<th>All other wounds*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus doses</td>
<td>Tdap or Td†</td>
</tr>
<tr>
<td>Unknown or &lt;3</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>≥3</td>
<td>No§</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

*Such as, but not limited to, wounds contaminated with dirt, feces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns and frostbite.
† Tdap is preferred to Td for adults who have never received Tdap. Td is preferred to TT for adults who received Tdap previously or when Tdap is not available. (If TT and TIG are both used, Tetanus Toxoid Adsorbed rather than Tetanus Toxoid for Booster Use Only [fluid vaccine] should be used).
§Yes, if >10 years since the last tetanus toxoid-containing vaccine dose.
¶ Yes, if >5 years since the last tetanus toxoid-containing vaccine dose (see text for discussion of Arthus reactions).
Where to Find Tdap Recommendations

• Adolescent Tdap recommendations:
  http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5503a1.htm

• Adult Tdap recommendations:
  http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5517a1.htm

• Prevention of tetanus, diphtheria and pertussis among pregnant women:
  http://www.cdc.gov/nip/recs/provisional_recs/tdap-preg.pdf
Reported Vaccination History in Infants Aged 3-11 Months with Pertussis, United States, 1990-1999*

<table>
<thead>
<tr>
<th>Age Group Months</th>
<th>No. of Cases</th>
<th>Percent of Cases Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 Dose</td>
</tr>
<tr>
<td>3-4</td>
<td>3577</td>
<td>23%</td>
</tr>
<tr>
<td>5-6</td>
<td>1744</td>
<td>22%</td>
</tr>
<tr>
<td>7-11</td>
<td>2066</td>
<td>27%</td>
</tr>
</tbody>
</table>

** minimum dose required for age by ACIP; permits a one-month grace period

* Tanaka M et al. JAMA 2003;290:2968-2975; proportion of cases with known age and vaccination status (7387 of 8116 infants)

Up-to-date
Tdap Immunogenicity for Tetanus and Diphtheria*

- Efficacy inferred from immunogenicity data for licensure
  - Accepted serologic correlate of protection ($\geq 0.1$ IU/ml)
- Adult immune responses after Tdap not inferior to Td (standard of care)
- Seroprotective rate
  - Tetanus: 100%
  - Diphtheria: 94%
- Booster responses acceptable

*Product label available at http://www.vaccineplace.com/products
Clinical Efficacy of Adult Acellular Pertussis Vaccine: US Adult Pertussis Trial (APERT)*

Vaccine efficacy: 92% (95% CI 32-99%)

Persons Aged 15 to 64 years (N=2781)

Acellular Pertussis Vaccine† N=1391

Hepatitis A Vaccine (control) N=1390

Pertussis Case‡ N=1

Pertussis Cases‡ N=9


†Three component acellular pertussis vaccine (PT, FHA, PRN) without tetanus and diphtheria toxoids (manufactured by GlaxoSmithKline biologicals; same pertussis components used in BOOSTRIX®)

‡Pertussis defined as a cough illness lasting ≥ 5 days with laboratory evidence of pertussis by culture, PCR, and/or serologic testing results