Diphtheria, Tetanus, and Pertussis

DTaP/DT and Tdap/Td Vaccines

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Diphtheria

- A toxin-mediated disease caused by *Corynebacterium diphtheriae*

- Usually produces exudate and membrane involving pharynx and tonsils

- Complications attributable to toxin – severity generally related to extent of local disease

- Most complications are myocarditis and neuritis

- Death in 5% to 10% of cases
Tonsillar diphtheria
Number of reported diphtheria cases -- United States, 1980-2015

Source: National Notifiable Diseases Surveillance System
Diphtheria in the late 19th - early 20th century
Tetanus

- A toxin-mediated disease caused by *Clostridium tetani*

- Infectious from environment, not contagious

- Most common form is generalized tetanus: descending symptoms of trismus (lockjaw), difficulty swallowing, muscle rigidity, spasms

- Complications caused by spasms, asphyxia, or nosocomial infection
Annual incidence* of and deaths due to tetanus -- United States, 1900-2015

Sources: National Notifiable Diseases Surveillance System and passive reports to the Public Health Service
* Per 100,000 population
Tetanus 2001-2008

- 233 cases reported (29 cases per year)
- Case-fatality rate 13%
- Median age 49 years (range 5 to 94 years)
  - 49% were among persons 50 years of age or older
- Among the reported tetanus cases
  - 72% reported an acute wound (puncture or contaminated wound)
  - 13% reported a chronic wound (a diabetic ulcer or dental abscess)
Generalized tetanus (opisthotonos)
Pertussis

- Highly contagious respiratory infection caused by *Bordetella pertussis*
- Insidious onset, similar to minor upper respiratory infection with nonspecific cough
- Fever usually minimal throughout course
- Catarrhal stage 1-2 weeks
- Paroxysmal cough stage 1-6 weeks
- Convalescence weeks to months
Reported NNDSS pertussis cases: 1922-2015*

*2015 data are provisional
* 2010 NNDSS 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
Reported Pertussis Incidence by Age Group: 1990-2016*

*2016 data are provisional.

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System
Pertussis Deaths in the United States, 2008-2014

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>Less than 3 months</th>
<th>3 months and older</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 3 months</td>
<td>95 (81%)</td>
<td>23 (19%)</td>
<td>118</td>
</tr>
</tbody>
</table>

Why Adolescents and Adults Need Pertussis Vaccine

- 20,762 pertussis cases reported in the U.S. in 2015, 15,737 cases in 2016
  - >50% of cases in those 11 years and older

- Infection may be asymptomatic, or may present as classic pertussis

- Disease often milder than in infants and children
  - Persons with mild disease may transmit the infection

- Older persons and household contacts often source of infection for infants and children

* Provisional data www.cdc.gov/pertussis
Pertussis Complications Among Adolescents and Adults

- Difficulty sleeping
- Urinary incontinence
- Pneumonia
- Rib fracture

Plus:
- Medical costs
- Missed school and work
- Impact on public health system
Vaccinate Throughout a Lifetime!

DTaP  Tdap  Td

Birth
DTaP-containing Vaccines

- **DTaP (pediatric)**
  - Approved for children 6 weeks through 6 years (to age 7 years)
  - Contains same amount of diphtheria and tetanus toxoid as pediatric DT

- **Multiple manufacturers and brands**
  - 2 DTaP only vaccine products
  - 3 combination products contain DTaP

- **Indications can vary by product**
DTaP–HepB–IPV (Pediarix)

- Components: DTaP, HepB, and IPV

- Licensed for:
  - Children 6 weeks through 6 years of age
  - Doses 1 through 3

- Not approved for doses 4 or 5

- Can be given to infants who received a birth dose of hepatitis B vaccine
  - Total of 4 doses of HepB vaccine
DTaP-IPV/Hib (Pentacel)

- Components: DTaP, IPV, and Hib

- Licensed for:
  - Children 6 weeks through 4 years of age
  - Doses 1 through 4

- Not approved for the 5th dose of DTaP series, or for children older than 5 years
DTaP-IPV/Hib (Pentacel)

- Must be reconstituted (mixed) prior to administration
- ONLY use the manufacturer-supplied vaccine diluent (DTaP-IPV)

Hib vaccine + DTaP-IPV diluent = Pentacel vaccine
DTaP-IPV (Kinrix and Quadracel)

- **Components:** DTaP and IPV
- **Licensed for:**
  - Children 4 through 6 years of age
  - Dose 5 only

*Do NOT use for doses 1 through 4 or for children younger than 4 years of age*
Administer the Correct Vaccine!

<table>
<thead>
<tr>
<th>Product (mfr)</th>
<th>Component(s)</th>
<th>Use for Ages</th>
<th>Use for DTaP doses</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptacel (SP)</td>
<td>DTaP</td>
<td>6 wks thru 6 yrs</td>
<td>1 thru 5</td>
<td>IM</td>
</tr>
<tr>
<td>Infanrix (GSK)</td>
<td>DTaP</td>
<td>6 wks thru 6 yrs</td>
<td>1 thru 5</td>
<td>IM</td>
</tr>
<tr>
<td>Pediarix (GSK)</td>
<td>DTaP-HepB-IPV</td>
<td>6 wks thru 6 yrs</td>
<td>1 thru 3</td>
<td>IM</td>
</tr>
<tr>
<td>Pentacel (SP)</td>
<td>DTaP-IPV/Hib</td>
<td>6 wks thru 4 yrs</td>
<td>1 thru 4</td>
<td>IM</td>
</tr>
<tr>
<td>Kinrix (GSK), Quadracel (SP)</td>
<td>DTaP-IPV</td>
<td>4 thru 6 yrs</td>
<td>Dose 5</td>
<td>IM</td>
</tr>
</tbody>
</table>

Order, administer, and document the correct vaccine!
Interchangeability of Different Brands of DTaP Vaccine

- Whenever feasible, the same DTaP vaccine should be used for all doses of the series

- Limited data suggest that “mix and match” DTaP schedules do not adversely affect safety and immunogenicity

- If vaccine used for earlier doses is not known or not available, any brand may be used to complete the series
# Primary DTaP Schedule

<table>
<thead>
<tr>
<th>Dose</th>
<th>Routine Age</th>
<th>Minimum Interval to Next Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary 1</td>
<td>2 months</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Primary 2</td>
<td>4 months</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Primary 3</td>
<td>6 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Primary 4</td>
<td>15-18 months</td>
<td></td>
</tr>
</tbody>
</table>
DTaP Fourth Dose

- Routinely recommended at 15 through 18 months

- May be given earlier if:
  - Child is at least 12 months of age and
  - At least 6 months since DTaP dose 3 and
  - Child is unlikely to return at 15 through 18 months of age
Administer a 5th dose of DTaP when the 4th dose was given before age 4 years

All DTaP products are approved for use for the 5th dose except:
- Pediariix (DTaP-HepB-IPV)
- Pentacel (DTaP-IPV/Hib)
Diphtheria and Tetanus Toxoid
DT Vaccine

- Given as a 3- or 4-dose series
- DT should only be used for children with a true contraindication to pertussis vaccine

Primary series doses
Use for children 6 weeks through 6 years of age
Pediatric DT Schedule

- First dose of DT at younger than one year of age
  - Total of 4 doses

- First dose of DT at one year of age or older
  - Total of 3 doses

- Fourth or fifth dose at school entry not needed if pertussis vaccine is not being administered
DTaP Contraindications

- Severe allergic reaction to vaccine component or following a prior dose

- Encephalopathy not due to another identifiable cause occurring within 7 days after vaccination
DTaP Precautions

- Moderate or severe acute illness
DTaP Precautions*
(Relevant to pertussis only)

- Temperature of 105° F (40.5° C) or higher within 48 hours with no other identifiable cause
- Collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours
- Persistent, inconsolable crying lasting 3 hours or more, occurring within 48 hours
- Convulsions with or without fever occurring within 3 days

*May consider use in outbreaks
DTaP Adverse Reactions

- Local reactions (pain, redness, swelling) 20%-40%
- Temperature of 101° or higher 3%-5%
- More severe adverse reactions Not common
Adverse Reactions Following the Fourth and Fifth DTaP Doses

- Local adverse reactions and fever increased

- Reports of swelling of entire limb
  - Self-limited and resolves without sequelae

- Limb swelling after 4th dose NOT a contraindication to 5th dose
Tdap and Td Vaccines
Tdap Vaccines

- 2 products available licensed for single use with different age indications
  - Less diphtheria toxoid and acellular pertussis antigen than DTaP
  - Lowercase letters = less antigen!

- Boostrix (GlaxoSmithKline)
  - FDA approved for persons 10 years of age and older

- Adacel (Sanofi Pasteur)
  - FDA approved for persons 10 through 64 years of age
Tdap Vaccination Recommendations

- **Adolescents 11 through 18 years of age**
  - Preferred administration at 11-12 years

- **Adults 19 years of age and older**

- **Women during every pregnancy***

*Off-label recommendation  *MMWR* 2013;62(No. 7):131-5
Use of Tdap Among Children 7 through 10 Years of Age*

- Persons 7 through 10 years of age who are *not fully immunized* against pertussis (including those never vaccinated or with unknown pertussis vaccination status) should receive a single dose of Tdap.

- For those who received Tdap at ages 7 through 10 years as part of the catch-up schedule, they may receive Tdap at age 11-12 years old.

*Off-label recommendation. MMWR 2011; 60 (No. 1):13-5*
“Not Fully Immunized”

- Children 7 through 10 years of age are not fully immunized against pertussis if they have received:
  - Fewer than 4 doses of DTaP OR
  - Four doses of DTaP and last dose before 4 years of age

*MMWR 2011; 60 (No. 1):13-5*
Use of Tdap Among Adults

- Administer Tdap vaccine to adults $\geq 19$ years who have not received Tdap, or with unknown vaccination status

- When feasible, Boostrix should be used for adults $\geq 65$ years
  - If Boostrix is not available, administer Adacel*
  - Either Tdap vaccine administered to persons $\geq 65$ years provides protection

*Off-label recommendation: Adacel
Adults and Td Vaccine

- Routinely recommended every 10 years following Tdap vaccine
- Also approved for primary series doses
Tdap For Persons Without History of DTP or DTaP

- All adolescents and adults should have documentation of having received a series of DTaP, DTP, DT, or Td

- Persons without documentation should receive a series of 3 vaccinations

- One dose should be Tdap, preferably the first
Tdap For Persons Without History of DTP or DTaP

Preferred schedule:
- Dose 1  Tdap
- Dose 2  Td at least 4 weeks after dose 1
- Dose 3  Td at least 6 months after dose 2
- Booster Td every 10 years
You can start protecting your baby from whooping cough before birth

Whooping cough is serious and causes coughing spasms that can be frightening to parents. Newborn babies can get whooping cough without getting the whooping cough vaccine. If you get whooping cough while you are pregnant, your baby may get it from you before birth. Your baby can get whooping cough very early in life, before you can give your baby the whooping cough vaccine. Early infections can be dangerous for your baby, and you can get whooping cough even before you have symptoms. The whooping cough vaccine is not recommended for pregnant women. The whooping cough vaccine is safe and important for babies. It helps protect your baby from whooping cough.

Getting your whooping cough vaccine in your 3rd trimester...

Talk to your doctor or nurse about the whooping cough vaccine.

The whooping cough vaccine I got during my 3rd trimester will help protect my baby starting at her first breath.

You can start protecting your baby from whooping cough before birth.

Whooping cough is serious and causes coughing spasms that can be frightening to parents. Newborn babies can get whooping cough without getting the whooping cough vaccine. If you get whooping cough while you are pregnant, your baby may get it from you before birth. Your baby can get whooping cough very early in life, before you can give your baby the whooping cough vaccine. Early infections can be dangerous for your baby, and you can get whooping cough even before you have symptoms. The whooping cough vaccine is not recommended for pregnant women. The whooping cough vaccine is safe and important for babies. It helps protect your baby from whooping cough.

Getting your whooping cough vaccine in your 3rd trimester...

Talk to your doctor or nurse about the whooping cough vaccine.
Tdap Recommendations and Pregnant Women

- Health care personnel should administer a dose of Tdap during each pregnancy, irrespective of the patient's prior history of receiving the vaccine.

- Tdap should be administered between 27 and 36 weeks gestation, although it may be given at any time during pregnancy.
  - Currently available data suggest that vaccinating earlier in the 27 through 36 week time period will maximize passive antibody transfer to the infant.

- If not administered during pregnancy, for women not previously vaccinated with Tdap, Tdap should be administered immediately postpartum

*Off-label recommendation  MMWR 2013;62(No. 7):131-5
Studies show maternal Tdap vaccination very effective in prevention of infant pertussis infection

<table>
<thead>
<tr>
<th>Definitions</th>
<th>Vaccine effectiveness (95% confidence intervals)</th>
<th>Infant age at pertussis onset</th>
<th>Mother gestational age received Tdap</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observational 1, screening method</td>
<td>91% (83%-95%)</td>
<td>&lt;3 mths</td>
<td>at least 28 days before birth*</td>
</tr>
<tr>
<td>Case-Control 2, retrospective</td>
<td>91% (77%-97%), unadjusted</td>
<td>&lt;2 mths</td>
<td>Cases: 31.5 wks (range, 28-38)</td>
</tr>
<tr>
<td></td>
<td>93% (81%-97%), adjusted¶</td>
<td></td>
<td>Controls: 33 wks (range, 26-38)</td>
</tr>
<tr>
<td>United States</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort 3, retrospective</td>
<td>85% (33%-98%)</td>
<td>&lt;2 mths</td>
<td>27-36 wks</td>
</tr>
<tr>
<td>Case-Control 4, retrospective</td>
<td>78% (44%-91%)</td>
<td>&lt;2 mths</td>
<td>27-36 wks</td>
</tr>
</tbody>
</table>

*2012 UK recommendation: Tdap between 28 and 38 weeks
¶Adjusted for sex, geographical area, and birth period

ACIP Conclusions
Safety of Tdap for Every Pregnancy

- Data reassuring on 2 doses of Tdap

- Data and experience with tetanus toxoid vaccine suggest no excess risk of adverse events
  - ~5% of women would receive 4 or more doses

- CDC provides ongoing monitoring to address concerns about the safety of Tdap given during subsequent pregnancies
Tdap AND HEALTHCARE PERSONNEL
Tdap and Healthcare Personnel (HCP)

- Previously unvaccinated HCP who have direct patient contact should receive a single dose of Tdap as soon as feasible, regardless of time since last Td dose

- Prioritize vaccination of HCP who have direct contact with infants ≤12 months of age

MMWR 2006;55(RR-17):1-37
Tdap Contraindications

- Severe allergic reaction to vaccine component or following a prior dose
- Encephalopathy not due to another identifiable cause within 7 days of administration of a pertussis-containing vaccine
Tdap Precautions

- History of Guillain-Barré syndrome within 6 weeks after a prior dose of tetanus toxoid-containing vaccine
- Progressive neurologic disorder until the condition has stabilized
- History of a severe local reaction (Arthus reaction) following a prior dose of a tetanus and/or diphtheria toxoid-containing vaccine
- Moderate or severe acute illness
Conditions NOT Precautions for Tdap

- Following a dose of DTaP/DTP:
  - Temperature 105°F (40.5°C) or higher
  - Collapse or shock-like state
  - Persistent crying lasting 3 hours or longer
  - Convulsions with or without fever
  - History of an extensive limb swelling reaction
Tdap/Td Adverse Reactions

- Local reactions (pain, redness, swelling)
  - 21%-66%
- Temp of 100.4°F or higher
  - 1.4%
- Adverse reactions occur at approximately the same rate as Td alone (without acellular pertussis vaccine)
Diphtheria, Tetanus, and Pertussis Resources

- ACIP’s DTaP/DT and Tdap/Td Recommendations web page
  www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/dtap.html
  www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/tdap-td.html

- CDC’s Diphtheria, Tetanus, and Pertussis Infection web pages
  www.cdc.gov/diphtheria/clinicians.html
  www.cdc.gov/tetanus/index.html
  www.cdc.gov/pertussis/

- CDC’s Pertussis and Pregnancy web page
  www.cdc.gov/pertussis/pregnant