Centers for Disease Control and Prevention National Center for Immunization and Respiratory Diseases



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



Diphtheria in the late 19th - early 20th century





KERSHAW

· FRANCIS

· FREDERICK APR. 5, 1896 MAR 9, 1897

FERDINAND

FEB. 6, 1898 FEB. 6, 1898

JOHN

NOV. 18, 1900 SEPT. 10, 1902

LYDIA

HARRIET

JOSEPH

· WILLIAM



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 Surveillanc 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 11%

□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

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

Number of cases

Reported Pertussis Incidence by Age Group: 1990-2016*



*2016 data are provisional.

Incidence rate

(per 100,000)

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

Pertussis Deaths in the United States, 2008-2014

	Age at onset					
Less than 3 months	3 months and older	Total				
95 (81%)	23 (19%)	118				

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-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

- DTaP only vaccine products
- 4 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 though 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)



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!

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

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

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 VIS	16-18 vrs
Diphtheria, tetanus, & acel- Iular pertussis³ (DTaP: <7 yrs)			1ª dose	2 nd dose	3 rd dose			∢ 4 th	dose>			5 th dose				

Μ	in	im	um

Dose	Routine Age	Interval to Next Dose
Primary 1	2 months	4 weeks
Primary 2	4 months	4 weeks
Primary 3	6 months	6 months
Primary 4	15-18 months	

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

Fifth DTaP Dose

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16-18 yrs
Diphtheria, tetanus, & acel- Iular pertussis ³ (DTaP: <7 yrs)			1ªdose	2 nd dose	3 rd dose			∢ 4th	dose>			5 th dose				

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:
 - Pediarix (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



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

- Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized
- **GBS** <6 weeks after previous dose of tetanus-toxoid vaccine
- History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid or tetanus-toxoid vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid vaccine

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 should receive another dose of Tdap at age 11-12 years old **

*Off-label recommendation. MMWR 2011; 60 (No. 1):13-5

**Liang JL, Tiwari T, Moro P, et al. Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2018;67(No. RR-2):1-46.

"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
- Last dose before 4 years of age

Use of Tdap Among Adults

□Administer Tdap vaccine to adults ≥19 years who have not received Tdap, or with unknown vaccination status

□When feasible, Boostrix should be used for adults ≥65 years

- If Boostrix is not available, administer Adacel*
- Either Tdap vaccine administered to persons ≥65 years provides protection

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

Tdap AND PREGNANT WOMEN



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

Studies show maternal Tdap vaccination very effective in prevention of infant pertussis infection

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

*2012 UK recommendation: Tdap between 28 and 38 weeks

[¶]Adjusted for sex, geographical area, and birth period

¹Amirthalingam G, et al. 2014; ²Dabrera G, et al. 2015; ³Winter K, et al. 2016; ⁴Skoff T, Clin Inf Dis 2017

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

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

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

Other References

<u>Clin Infect Dis.</u> 2017 Nov 29;65(12):1977-1983. doi: 10.1093/cid/cix724.Impact of the US Maternal Tetanus, Diphtheria, and Acellular Pertussis Vaccination Program on Preventing Pertussis in Infants <2 Months of Age: A Case-Control Evaluation. <u>Skoff TH¹, Blain AE¹, Watt J², Scherzinger K³, McMahon M⁴, Zansky SM⁵, Kudish K⁶, Cieslak PR⁷, Lewis <u>M¹, Shang N¹, Martin SW¹</u>.
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