Diphtheria, Tetanus, and Pertussis

DTaP/DT and Tdap/Td Vaccines

Chapters 7, 21, and 16

1

Diphtheria Disease

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

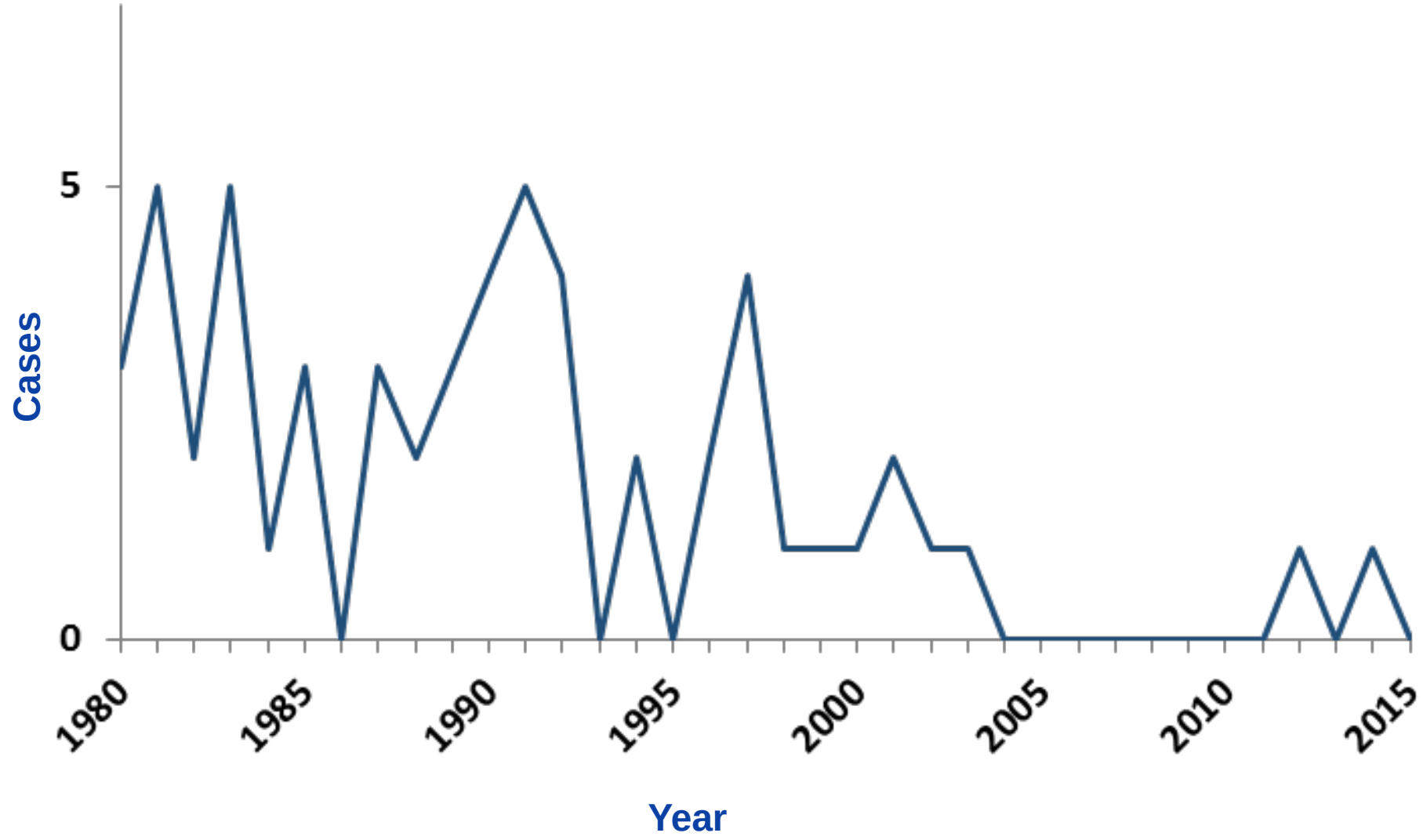
Tonsillar diphtheria

Diphtheria Clinical Features

- **Incubation period 2–5 days (range: 1–10 days)**
- **May involve any mucous membrane**
- **Classified based on site of disease**
  - Anterior nasal
  - Pharyngeal and tonsillar
  - Laryngeal
  - Cutaneous
  - Ocular
  - Genital

Diphtheria in the Late 19th–Early 20th Century

Number of reported diphtheria cases -- United States, 1980-2015



Source: National Notifiable Diseases Surveillance System

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Tetanus Disease

Tetanus

- **A toxin-mediated disease caused by *Clostridium tetani***
- **Anaerobic gram-positive, spore-forming bacteria**
- **Spores found in soil, animal feces**
- **Two exotoxins produced with growth of bacteria**
  - Tetanospasmin responsible for clinical manifestations of tetanus

Tetanus Clinical Features

- **Incubation period: 8 days (range: 3–21 days)**
- **Three clinical forms: local (uncommon), cephalic (rare), generalized (most common)**
- **Generalized tetanus: descending pattern of trismus (lockjaw), stiffness of the neck, difficulty swallowing, rigidity of abdominal muscles**
  - Spasms continue for 3–4 weeks
  - Complete recovery may take months
- **Neonatal tetanus**
  - Generalized tetanus in newborn infant
  - Infant born without protective passive immunity
  - 58,000 neonates died in 2010 worldwide

Morbidity and Mortality Weekly Report (*MMWR*)

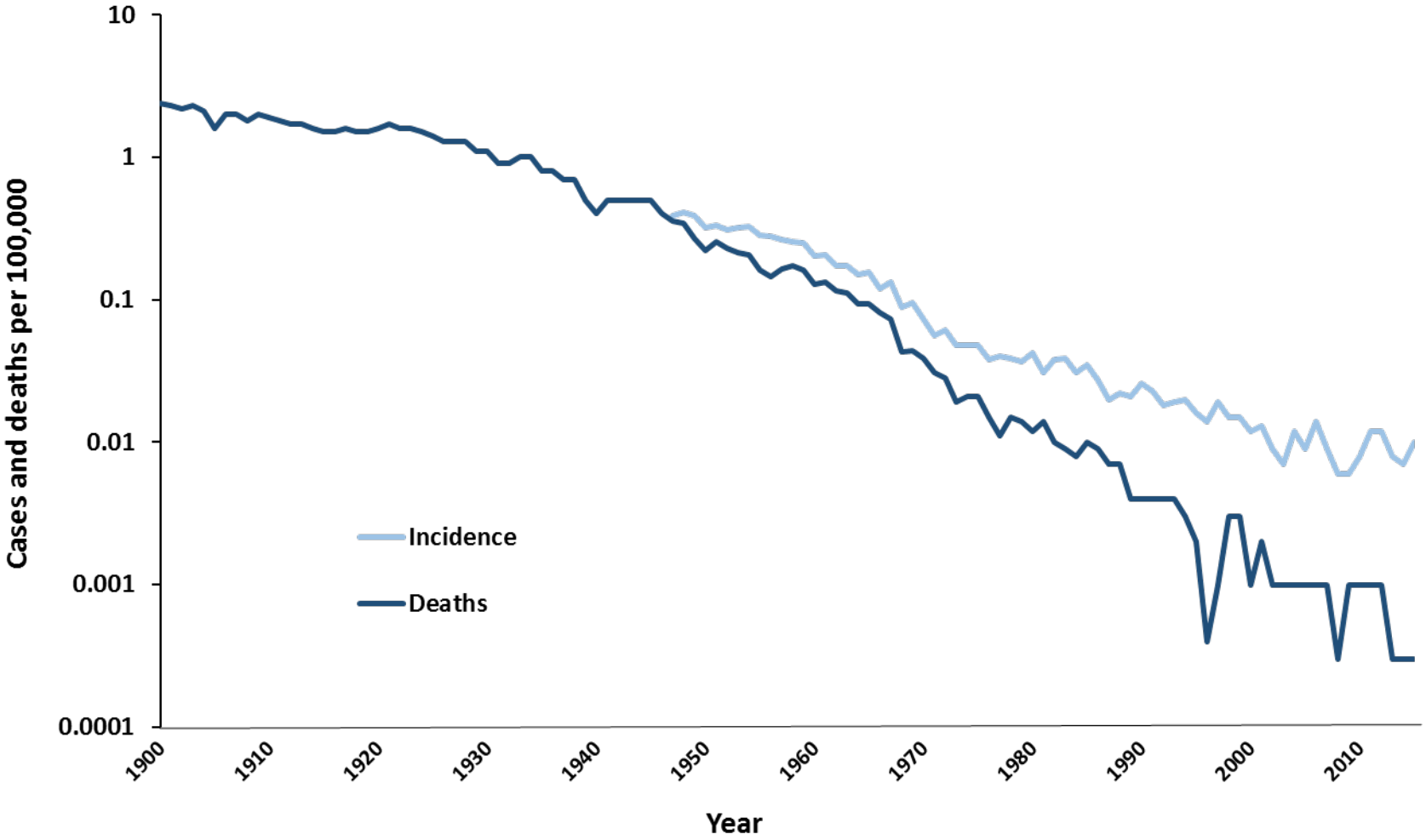
CDC > MMWR

Notes from the Field: Tetanus in an Unvaccinated Child — Oregon, 2017

Weekly / March 8, 2019 / 68(9);231–232

- **Required 57 days of inpatient acute care, including 47 days in the intensive care unit**
- **The inpatient charges totaled $811,929 (excluding air transportation, inpatient rehabilitation, and ambulatory follow-up costs)**

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

3

Pertussis Disease

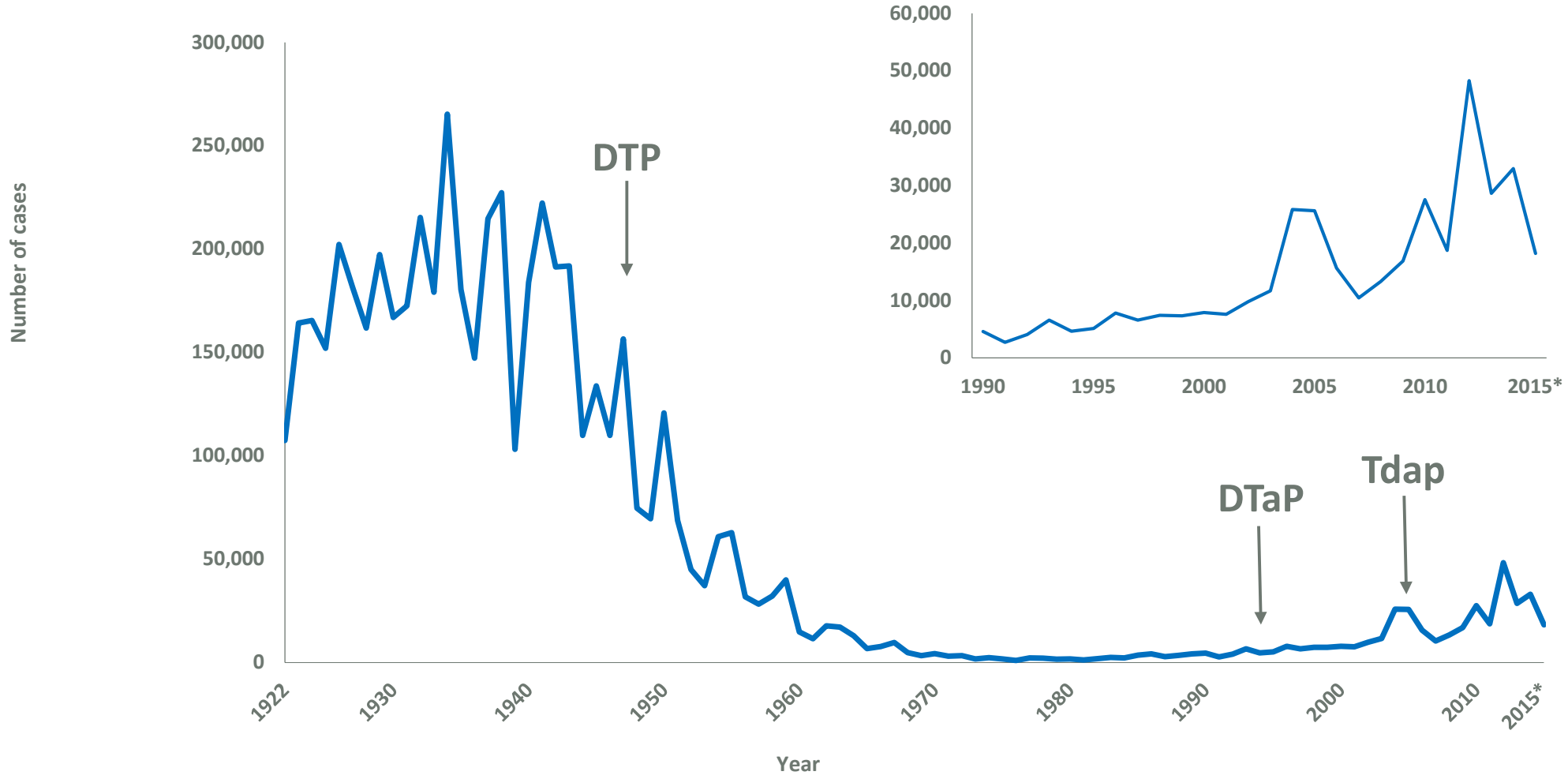
Pertussis

- Acute infectious disease caused by *Bordetella pertussis*
- Outbreaks first described in 16th century
- *Bordetella pertussis* isolated in 1906
- Estimated 195,000 deaths worldwide in 2008

Pertussis Clinical Features

- **Incubation period: 7–10 days (range: 4–21 days)**
- **Insidious onset, similar to the common cold with nonspecific cough**
- **Fever usually minimal throughout course of illness**
- **Catarrhal stage**
  - 1–2 weeks
- **Paroxysmal cough stage**
  - 1–6 weeks
- **Convalescence**
  - Weeks to months

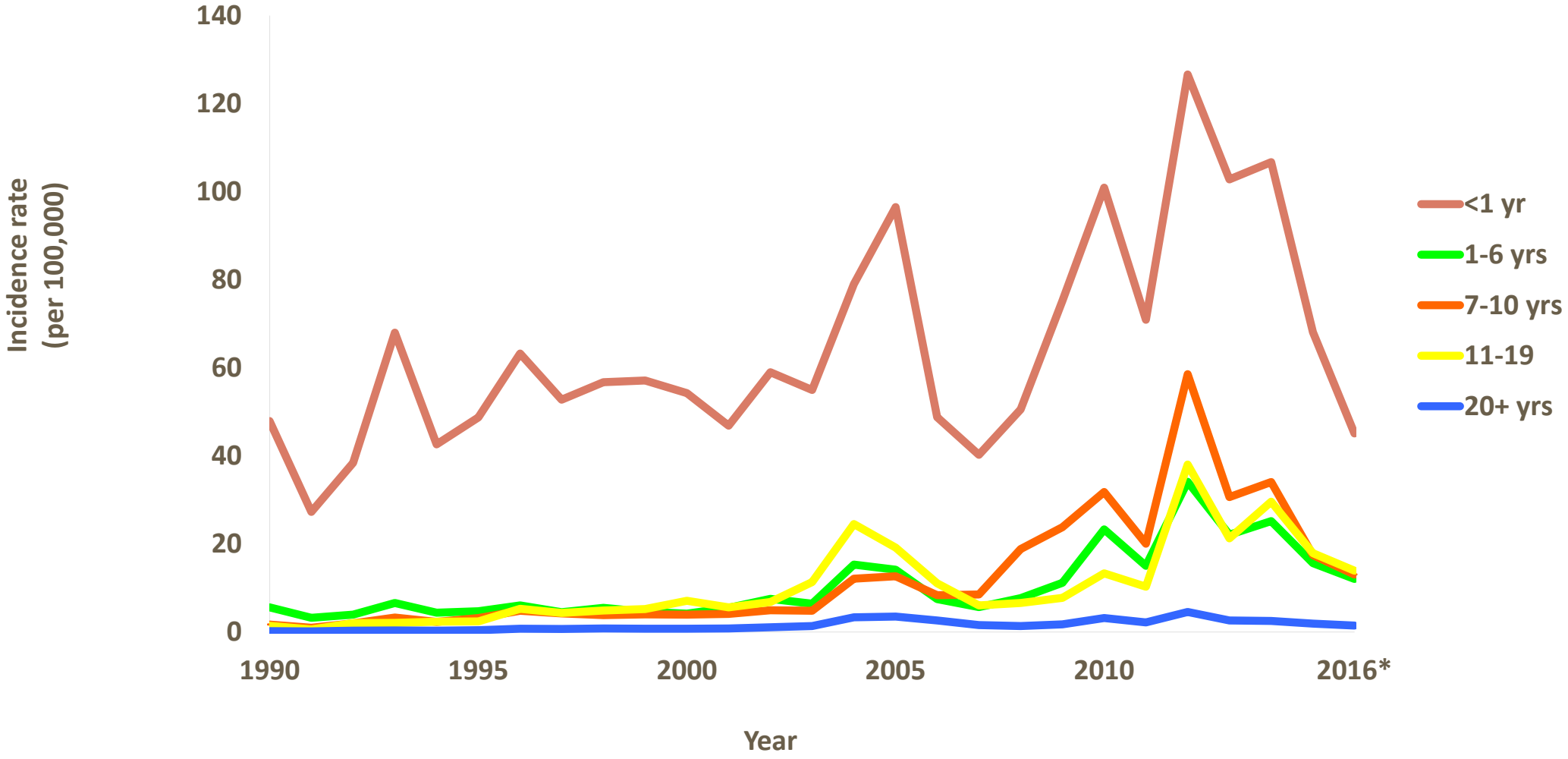
Reported NNDSS pertussis cases: 1922-2015*



*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

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, 2012–2018

Age at onset		
Less than 12 months	12 months and older	Total
59 (72%)	23 (28%)	82

https://www.cdc.gov/pertussis/surv-reporting.html

Why Adolescents and Adults Need Pertussis Vaccine

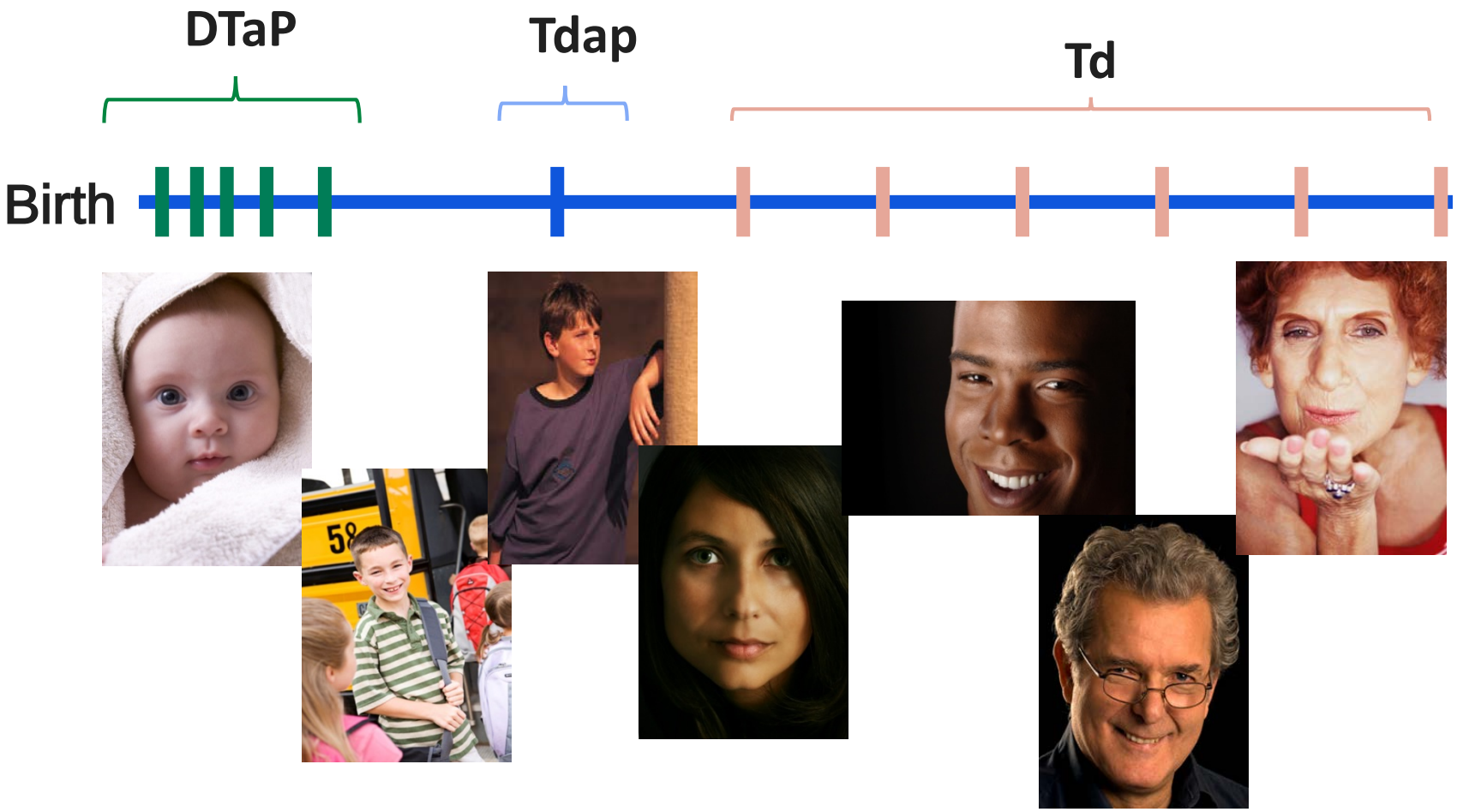
- 20,762 pertussis cases reported in the U.S. in 2015, 15,737 cases in 2016
  - >50% of cases in those 11 years and older
- Infection may be asymptomatic, or may present as classic pertussis
- Disease often milder than in infants and children
  - Persons with mild disease may transmit the infection
- Older persons and household contacts often source of infection for infants and children

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!



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DTaP/DT Vaccine

DTaP-Containing Vaccine Products

Vaccine product	Age indications	Comments
Single component vaccines		
Daptcel	6 weeks - 6 years	Approved for doses 1-5
Infanrix	6 weeks - 6 years	Approved for doses 1-5
Combination vaccines		
Pediarix		
DTaP, HepB, and IPV	6 weeks-6 years	Not approved for doses 4 or 5
Pentacel		
DTaP, IPV, and Hib	6 weeks–4 years	Not approved for 5th dose
Kinrix and Quadracel		
DTaP and IPV	4-6 years	Not approved for doses 1-4
Vaxelis		
DTaP, IPV, Hib, and HepB	6 weeks–4 years	3-dose series
Vaccines without pertussis component		
No trade name	6 weeks–4 years	3- or 4-dose series

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

- Use ONLY the manufacturer-supplied vaccine diluent (DTaP-IPV)

Hib vaccine

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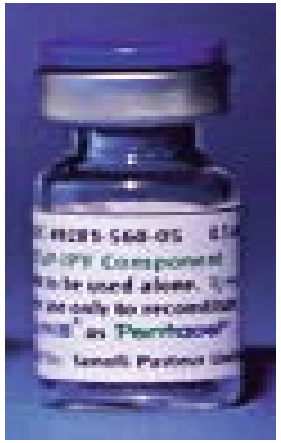

DTaP-IPV diluent

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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**

DTaP, IPV, Hib, HepB (Vaxelis)

- **Components: DTaP, IPV, Hib, HepB**

- **Licensed for:**
  - Children 6 weeks through 4 years
  - 3-dose series (2, 4, 6 months of age)

- **Do NOT use for 4th or 5th doses**

Administer the Right Vaccine!

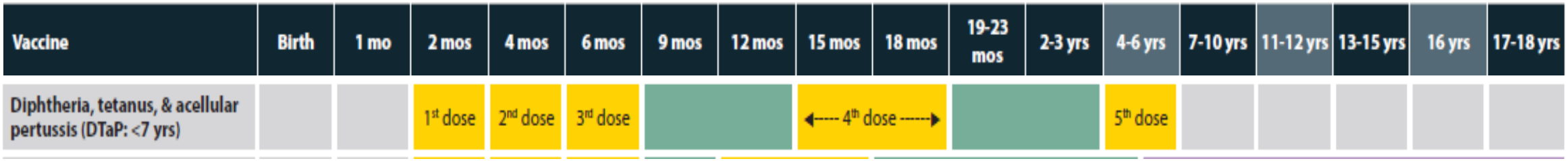
Product (mfr)	Component(s)	Use for ages	Use for DTaP doses	Route
Daptacel (SP)	DTaP	6 wks thru 6 yrs	1 thru 5	IM
Infanrix (GSK)	DTaP	6 wks thru 6 yrs	1 thru 5	IM
Pediarix (GSK)	DTaP-HepB-IPV	6 wks thru 6 yrs	1 thru 3	IM
Pentacel (SP)	DTaP-IPV/Hib	6 wks thru 4 yrs	1 thru 4	IM
Kinrix (GSK), Quadracel (SP)	DTaP-IPV	4 thru 6 yrs	5	IM
Vaxelis (Merck)	Dtap-IPV-Hib-HepB	6 wks thru 4 years	3-dose series	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 yrs	16 yrs	17-18 yrs
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			◄---- 4th dose ----►				5th dose					

Dose	Routine Age	Minimum 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	

https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

Fourth DTaP 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 yrs	17-18 yrs
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			◄---- 4th dose ----►				5th 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 1 year of age**
  - Total of 4 doses
- **First dose of DT at 1 year of age or older**
  - Total of 3 doses
- **4th or 5th 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 or unstable neurologic disorder, including infantile spasms, uncontrolled seizures, or progressive encephalopathy
- Guillain-Barré syndrome <6 weeks after previous dose of tetanus-toxoid-containing vaccine
- History of Arthus-type hypersensitivity reactions after a previous dose of tetanus- or diphtheria-toxoid-containing vaccines

DTaP Former Contraindications – No Longer Applicable

- 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
- Family history of seizures, SIDS, adverse event after pertussis vaccination
- Stable neurological condition(s)

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 4th and 5th 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**

2

Tdap/Td Vaccine

Tdap and Td Vaccines

Vaccine product	Age indications
Tdap vaccines	
Boostrix	10 years and older
Adacel	10–64 years
Td vaccines	
TDVAX	7 years and older
TENIVAC	7 years and older

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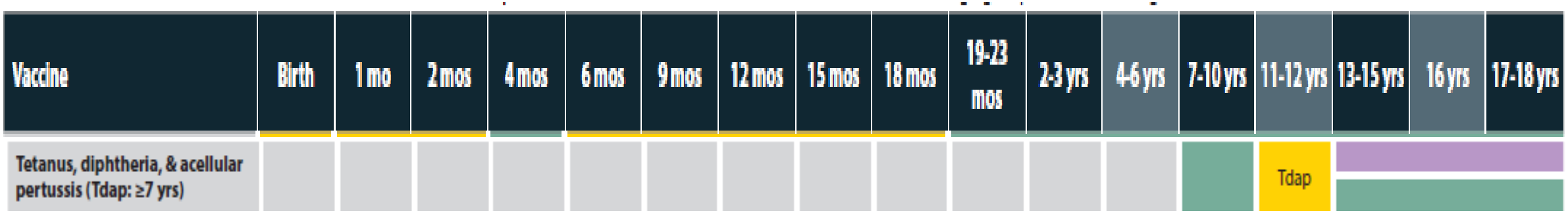
Clinical Considerations

ACIP Tdap/Td Vaccine Recommendations



Vaccine	19–21 years	22–26 years	27–49 years	50–64 years	≥65 years
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap, then Td booster every 10 yrs				

*Off-label recommendation: Adacel for persons 65 years of age and older

Tdap Recommendations: Adolescent

- Routinely recommended at 11–12 years of age
- Catch-up adolescents 13 years of age and older who were not vaccinated

MMWR 67(2):1–44

Tdap Recommendations: Adults

- **Administer Tdap vaccine to persons 19 years of age and older who were NOT *previously vaccinated* and to those with unknown vaccination status**
  - Persons who were vaccinated with Tdap during adolescence (or at another time) = *previously vaccinated*, including:
    - Health care personnel
    - New fathers
    - Close contacts of newborns
    - Day care workers or babysitters
  - No additional doses are recommended

MMWR 67(2):1–44

Tdap Recommendations: Children 7 through 10 Years of Age*

- **Children who have not completed a primary series**
  - Tdap should be administered first
  - If additional doses are needed, Td should be administered
- **Those who are not fully immunized against pertussis (i.e., did not complete a series of pertussis-containing vaccine before their 7th birthday) should receive a single dose of Tdap**
  - If additional doses are needed, Td should be administered
- **Adolescents who received Tdap inadvertently or as part of the catch-up series between 7–10 years of age should be given the routine adolescent Tdap dose at 11–12 years of age**

*Off-label ACIP recommendation

MMWR 67(2):1–44

Tdap Recommendations: Pregnant Women

- **Administer a dose of Tdap during each pregnancy, regardless 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

Off-label ACIP recommendation** ***MMWR **67(2):1–44**

Tdap and Pregnant Women

- **Vaccination coverage for pregnant women:**
  - 2010 and earlier <1%
  - 2013 28%
  - 2015 53%
- **96% of Tdap vaccinations were administered in physicians' offices or clinics**

Maternal Vaccination

Resources for healthcare professionals

Vaccines help keep your pregnant patients and their growing families healthy.

Last Updated September, 2016

Vaccine	Before pregnancy	During pregnancy	After pregnancy	Type of vaccine
Influenza	Yes	Yes, during flu season	Yes	Inactivated
Tdap	May be recommended; it is better to vaccinate during pregnancy when possible	Yes, during **each** pregnancy	Yes, immediately postpartum, if Tdap never received in lifetime; it is better to vaccinate during pregnancy	Toxoid/ Inactivated
Td	May be recommended	May be recommended, but Tdap is preferred	May be recommended	Toxoid
Hepatitis A	May be recommended	May be recommended	May be recommended	Inactivated
Hepatitis B	May be recommended	May be recommended	May be recommended	Inactivated
Meningococcal	May be recommended	Base decision on risk vs. benefit; inadequate data for specific recommendation	May be recommended	Inactivated
Pneumococcal	May be recommended	Base decision on risk vs. benefit; inadequate data for specific recommendation	May be recommended	Inactivated
HPV	May be recommended (through 26 years of age)	No	May be recommended (through 26 years of age)	Inactivated
MMR	May be recommended; once received, avoid conception for 4 weeks	No	May be recommended	Live
Varicella	May be recommended; once received, avoid conception for 4 weeks	No	May be recommended	Live

For more information, visit: www.cdc.gov/vaccines/pregnancy
Get an answer to your specific question by e-mailing cdcinfo@cdc.gov
or calling 800-CDC-INFO (232-4636)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

MMWR 66(41):1105–1108

Maternal Tdap Vaccination is 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%)	Younger than 3 months	At least 28 days before birth*
Case-Control,[2] retrospective	91% (77–97%), unadjusted 93% (81–97%), adjusted¶	Younger than months	Cases: 31.5 weeks (range, 28–38) Controls: 33 weeks (range, 26–38)
United States			
Cohort,[3] retrospective	85% (33–98%)	Younger than 2 months	27–36 weeks
Case-Control,[4] retrospective	78% (44–91%)	Younger than 2 months	27–36 weeks

*2012 UK recommendation: Tdap between 28 and 38 weeks

¶Adjusted for sex, geographical area, and birth period

[1]Amirthalingam G, et al. 2014; [2]Dabrera G, et al. 2015; [3]Winter K, et al. 2016; [4]CDC, unpublished

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**

Postpartum Women and Close Contacts of Infants

- **Previously unvaccinated EVER or vaccination status unknown– administer Tdap**

- **Previously vaccinated persons – Tdap is NOT indicated**
  - Including mothers, fathers, siblings, and grandparents
  - Any previous, documented dose counts

Tdap for Persons Without History of DTP or DTaP

- All adolescents and adults should have documentation of having received a primary series of DTaP, DTP, DT, Tdap, or Td
- Persons without documentation who have never been vaccinated or have unknown status should receive a 3-dose primary series
- 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**

No Additional Doses of Tdap for the General Population

- ACIP recognizes the increasing burden of pertussis and the need for an effective strategy to reduce this burden
- A study evaluating additional doses of Tdap administered at either a 5- or 10-year interval suggested that the reduction in pertussis disease burden would be limited
- ACIP concluded that the data do not support a general recommendation for a routine second dose of Tdap, and that the public health impact of routinely recommending a second dose of Tdap would be limited

MMWR 67(2):1–44

Tdap and Health Care Personnel

Tdap and Health Care Personnel (HCP)

- Previously unvaccinated HCP should receive a single dose of Tdap as soon as feasible, regardless of time since last Td dose
- After receipt of 1 dose of Tdap, health care personnel should receive routine Td booster immunizations according to the recommended schedule
- Additional doses of Tdap are not recommended for previously vaccinated HCP*

*Except pregnant women

MMWR 2006;55(RR-17):1–37

Tetanus Prophylaxis

TABLE 6. Guide to tetanus prophylaxis in routine wound management

No. doses of adsorbed tetanus toxoid–containing vaccines	Clean and minor wound		All other wounds*	
	DTaP, Tdap, or Td†§	TIG	DTaP, Tdap, or Td†	TIG§
Unknown or <3	Yes	No	Yes	Yes
≥3	No¶	No	No**	No

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; Td = tetanus and diphtheria toxoids; TIG = tetanus immune globulin.

* 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.

† DTaP is recommended for children aged <7 years. Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series.

§ Persons with HIV infection or severe immunodeficiency who have contaminated wounds should also receive TIG, regardless of their history of tetanus immunization.

¶ Yes, if >10 years since the last tetanus toxoid–containing vaccine dose.

** Yes, if ≥5 years since the last tetanus toxoid–containing vaccine dose.

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)**