

**Vaccination Overview:  
Diphtheria and Pertussis**

0.25 CREDIT HOURS



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## PHARMACIST OBJECTIVES

1. Select appropriate vaccination recommendations for diphtheria and pertussis

## PHARMACY TECHNICIAN OBJECTIVES

1. Select appropriate vaccination recommendations for diphtheria and pertussis

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## OVERVIEW

Micro-learning opportunities were created in response to evidence that learning is maximized when delivered in short and focused 'bursts.' In this session, common childhood vaccines are examined, including vaccines for diphtheria and pertussis.

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## TARGET AUDIENCE

Pharmacist, Pharmacy Technician

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One of the most significant demonstrations of the importance of diphtheria antitoxin was its use in the 1925 diphtheria epidemic in Nome, Alaska. Coordinated emergency delivery of this life-saving antitoxin by the dog-sled relay in the harshest of conditions has left a profound legacy in the annals of vaccinology and public health.

This adventure crossed 674 miles, using 20 mushers and 150 sled dogs, and ran from January 27 to February 1. Airplanes were not reliable at that time, and the nearest port to Nome was frozen shut. Lead dogs Balto and Togo, and the dog-led antitoxin run of 1925 represent a dynamic illustration of the contribution made by non-human species towards mass immunization in the history of vaccinology. This unique example of cooperative interspecies fellowship and collaboration highlights the importance of the human-animal bond in the one-health initiative.

- [The 1925 Diphtheria Antitoxin Run to Nome - Alaska: A Public Health Illustration of Human-Animal Collaboration - PubMed \(nih.gov\)](#)

You can meet the mushers and sled dogs on Wikipedia. Look up “1925 Serum Run to Nome.” Better yet, there are some short YouTube videos that are enlightening... especially for you dog lovers!

## Diphtheria

- Diphtheria is another communicable disease that has been virtually eliminated, thanks to vaccination
- First described by Hippocrates in the 5th century BC
- December 2022: 154 cases of diphtheria reported by eight EU/EEA countries:
  - Germany (64)
  - Austria (42)
  - Belgium (18)
  - France (14)
  - Norway (7)
  - Netherlands (5)
  - Italy (3)
  - Spain (1)
  - Most of these cases were brought in by refugees
- From 1996 to 2018, the United States averaged less than one case per year, due to consistently high vaccination rates (over 93%)
- The causative agent for diphtheria is *Corynebacterium diphtheriae* or *C. diphtheriae*
  - Gram-positive aerobic bacillus
- The primary mechanisms of transmission are close contact with respiratory secretions (direct or via airborne droplets) or skin lesions
- Can also be spread from human to human by fomites such as towels, handkerchiefs, and used tissues
- Humans are believed to be the only known reservoir for *C. Diphtheriae*
- Diphtheria has an  $R_0$  value of 2.6 and is highly contagious

## Typical course

- Normal incubation period is 2-5 days
- *C. diphtheriae* has four biotypes:
  - *Gravis*
  - *Intermedius*
  - *Mitis*
  - *Belfanti*
  - All biotypes can become toxigenic and cause severe disease
- Toxigenic diphtheria bacilli acquired in the nasopharynx produce an exotoxin that inhibits cellular protein synthesis, destroys local tissue, and forms a pseudo membrane
- Four major complications:
  - Myocarditis
  - Polyneuropathies
  - Nephritis
  - Thrombocytopenia
- Non-toxin-producing *C. diphtheriae* strains cause mild to severe exudative pharyngitis and sometimes lesions, endocarditis, bacteremia, and septic arthritis
- Before vaccines, diphtheria was a major cause of morbidity and mortality worldwide, primarily affecting children under the age of 15
- Until the beginning of the 20th century, as many as 10% of American children developed diphtheria
  - 5-10% died from its complications
- By adolescence, so many kids were exposed to diphtheria that 70-80% percent of the urban population was immune from natural infection
- 100,000-200,000 cases and 13,000-15,000 deaths were reported annually in the 1920s, before vaccines were available

## Major types of diphtheria:

- Pharyngeal and Tonsillar Diphtheria
  - Most common sites of diphtheria are the pharynx and the tonsils
  - A thick gray membrane covers the throat and tonsils
  - Infection at these sites is usually associated with substantial systemic absorption of the toxin
- Anterior Nasal Diphtheria:
  - Looks like the common cold, due to low absorption of the toxin
- Cutaneous Diphtheria:
  - May be manifested by a scaling rash or by ulcers with clearly demarcated edges
  - Mostly seen in the tropics.
- Other sites:
  - Mucous membranes of the conjunctiva and vulvovaginal area, as well as the external auditory canal

## Treatment

- Antitoxin:
  - A hyperimmune antiserum produced in horses that binds to and inactivates the diphtheria toxin
  - In 1898, a trial showed that the antitoxin reduced mortality from 7% to 2.5%
  - Must be administered early because it is only effective when the toxin has not yet entered the cells
  - The antitoxin is only available through the CDC and it is only used for respiratory and cutaneous diphtheria
- Antibiotics:
  - All of the following are effective treatments for diphtheria must be administered for 14 days:
    - Erythromycin (Ery-Tab®)
    - Procaine penicillin-G (Wycillin®)
    - Oral penicillin VK (Veetids®)
  - By killing off the bacteria, toxin release is attenuated

## Vaccination

- Diphtheria toxoid was developed in the early 1920s, but was not widely used until the early 1930s
  - Incorporated with the tetanus toxoid and pertussis vaccine and became routinely used in the 1940s
  - Vaccination does not prevent colonization, but reduces transmission by 60%, likely through reduced symptomatic shedding
- Diphtheria toxoid produced by growing toxigenic *C. diphtheriae* in a liquid medium
  - Combined with tetanus toxoid as diphtheria and tetanus toxoid (DT) vaccine or tetanus and diphtheria toxoid: Td (Tenivac®) and (Tdvax®) vaccine
  - Also combined with both tetanus toxoid and acellular pertussis vaccine as DTaP (Infanrix®) and (Daptacel®) or Tdap (Boostrix®) and (Adacel®) vaccines
  - Td contains reduced amounts of diphtheria toxoid compared with DT
  - More than 95% of recipients develop protective antibody levels after 3 doses and booster for infants or 3 doses for adults

I have had quite a few older patients come into the pharmacy and say “hey doc, what vaccine am I supposed to get now that my daughter is going to have a baby next month?”

First, I congratulate them on the new bundle of joy, then I give them information about TDaP. EVERYONE who gets to have direct contact with a newborn SHOULD (OK, MUST) have an up-to-date Tdap!

## Pertussis

- *Bordetella pertussis* is a small, aerobic gram-negative rod
- A toxin produced by the bacteria causes most of the pathogenesis of the disease
  - Bacteria attached to the cilia of the respiratory epithelial cells produce toxins that paralyze the cilia and cause inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions

- Incubation period is quite long and starts with symptoms similar to the common cold
  - Ranges from 4-21 days
- Once the disease enters the paroxysmal stage, it becomes evident that the patient is infected with pertussis
- The patient might have bursts of numerous, rapid coughs due to difficulty expelling thick mucus from the tracheobronchial tree
- At the end of the paroxysms, a long inspiratory effort is usually accompanied by a characteristic high-pitched whoop or barking sound
  - Between these attacks, the patient usually does not appear to be very ill
  - When an attack occurs, the patient can become distressed, turn cyanotic, and possibly, vomit
  - These attacks are more frequent at night, with up to fifteen attacks in 24 hours
  - Seizures and encephalopathy, which are more commonly seen in infants, may occur as a result of hypoxia from coughing, or possibly from pertussis toxin

## **Treatment**

- Pediatrics:
  - azithromycin (Z-pak®),
  - clarithromycin (Biaxin®) or
  - trimethoprim-sulfamethoxazole (Bactrim®)
- Adults:
  - azithromycin (Z-pak®)
    - Day 1: 500 mg
    - Days 2-5: 250 mg
  - trimethoprim-sulfamethoxazole DS (Bactrim DS®)
    - twice daily
  - clarithromycin (Biaxin®)
    - 500 mg twice daily

## **Vaccination**

- 1914: Whole-cell pertussis vaccines were first licensed in the United States
- 1948: Available as a combined vaccine with diphtheria and tetanus toxoids (as DTP)
- In the 20th century, pertussis was one of the most common childhood diseases and a major cause of childhood mortality in the United States, primarily due to secondary bacterial pneumonia
- Prior to the 1940 pertussis vaccine, more than 200,000 cases of pertussis were reported annually
  - Since the widespread use of the vaccine began, the incidence has decreased by more than 75%
- However, between 2000 and 2017, there were 307 deaths from pertussis reported to the CDC
  - Children younger than age 2 months accounted for 84.0% of these deaths

## **DTwP versus DTaP: What is acellular pertussis?**

- The acellular pertussis vaccine (aP) has three or more antigens which provided around 85% efficacy
  - Efficacy is similar to the whole-cell pertussis vaccine
  - Declines faster compared to the whole-cell pertussis vaccine
  - Fewer side effects compared to whole-cell vaccines

### **Tdap products**

- Boostrix®:
  - Approved in 2005.
  - Indications
    - One dose in adults, then use Td for subsequent doses
    - May be used if over age 65
- Adacel®:
  - Its safety and efficacy have not been established for geriatrics (65+), however, do not hesitate to use it if only Adacel® is available.

### **Tdap**

- Recommended once after the age of 19
  - Then Td is recommended every 10 years
- Tdap vaccine can protect adolescents and adults from tetanus, diphtheria, and pertussis
  - One dose of Tdap is routinely given at age 11 or 12
  - People who did not get Tdap at that age should get it as soon as possible
- Especially important for healthcare professionals and anyone having close contact with a baby younger than 12 months
- Pregnant women should get a dose of Tdap during every pregnancy, during the third trimester, to protect the newborn from pertussis
  - Infants are most at risk for severe, life-threatening complications from pertussis

*--Have a great day on the bench!!*

# Activity Test

## Vaccination Overview: Diphtheria and Pertussis

Activity tests must be completed online at [www.freeCE.com](http://www.freeCE.com).

A passing grade of 70 or higher and completion of an online activity evaluation are required to earn credit.

- 1. Jimmy is picking up some medications for his wife at your local pharmacy. Jimmy's wife is pregnant and currently in her third trimester. He is wondering what vaccination his wife should get to protect their newborn from pertussis. What would you recommend?**
  - A. Tenivac®
  - B. Tdvax®
  - C. Boostrix®
  - D. Diphtheria antitoxin
- 2. Mr. Myers is a 70-year-old patient who came into a primary care clinic for his 6-month follow-up. His doctor just noticed that he never got his Tdap vaccine. This patient has no known allergies. What is the best recommendation for this patient?**
  - A. Because he is over 65 years old, he can now get the Td every 10 years.
  - B. He should get Boostrix® as soon as possible.
  - C. Because he is over 65 years old, he has gained immunity against diphtheria and pertussis.
  - D. He should get Adacel® as soon as possible.