Chapter 4: A Review of Tetanus, Diphtheria, and Pertussis for Pharmacists and Pharmacy Technicians

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Learning objectives

After completion of this course, pharmacists and pharmacy technicians will be able to:

- Discuss the history and epidemiology of tetanus, diphtheria, and pertussis.
- Describe the pathogenesis of tetanus, diphtheria, and pertussis.
- List the symptoms and complications of tetanus, diphtheria, and pertussis.
- Describe the methods for diagnosing tetanus, diphtheria, and pertussis.
- Discuss the treatment of tetanus, diphtheria, and pertussis.
- Discuss the immunization schedule for vaccination against tetanus, diphtheria, and pertussis.

- List the contraindications and precautions for vaccination against tetanus, diphtheria, and pertussis.
- Discuss the efficacy of vaccination against tetanus, diphtheria, and pertussis, and describe adverse reactions associated with immunization.
- Discuss the use of Tdap in pregnant women and when it is appropriate to vaccinate pregnant women.
- Discuss strategies that can be used to improve immunization rates, including maintaining adequate records, reminding patients to vaccinate, and collaboration between the patient and provider.

Introduction

Tetanus, diphtheria, and pertussis are vaccine-preventable illnesses that can cause significant morbidity and mortality in patients who contract these diseases. Despite the medical advances of the 20th and 21st centuries, these diseases have yet to be eradicated and outbreaks still occur. Pertussis, for example, is a highly communicable disease that reached relatively low levels in the 1980s, but has been increasing in incidence, reaching nearly 50,000 cases reported in 2012. Outbreaks continue to occur in the United States, putting pregnant women, infants, and patients with comorbidities at a high risk of developing severe pertussis.

The most important tool available to health care providers in the United States to maintain low levels of these conditions is the use of vaccinations. Immunization rates in the United States are high, but gaps in care exist throughout the country. Economic and racial disparities exist, leaving vulnerable populations at a higher risk for contracting and transmitting contagious diseases.

Maintaining high immunization rates, especially in vulnerable populations, is critical to sustaining low levels of vaccine-preventable illnesses, and immunization providers are perfectly poised to ensure vaccinations are administered in a timely manner to everyone who needs them. Strict adherence to vaccination schedules, patient education on the safety of vaccinations, and the importance of immunization are essential to maintaining high immunization levels.

Tetanus, diphtheria, and pertussis can be prevented through the appropriate use of vaccinations. This course serves as a review of the history, epidemiology, symptoms, treatment, and prevention of these three illnesses[1,2].

TETANUS

Definition

Tetanus is an acute condition caused by an exotoxin produced by the bacteria Clostridium tetani. It is characterized by painful muscle contractions, often located in the jaw and neck, which is commonly referred to as lockjaw. Muscle spasms and stiffness can become generalized and affect alternate sites in the body as well. It is often transmitted through wounds contaminated with Clostridium tetani, which can be found in soil and animal feces. Tetanus is not contagious; it is the only vaccine-preventable illness that can cause infections but is not contagious[3,4].
**History**

Tetanus has been described in clinical literature since the 5th century BC. In 1889, Kitasato isolated the bacteria Clostridium tetani from a human source, showed that the bacteria can cause disease when injected into animals, and described the ability of the toxin to be neutralized by certain antibodies. In 1897, the protective effects of antitoxins transferred passively were demonstrated by Nocard, and antitoxins were used to treat and prevent tetanus through passive immunity during World War I. The early 1920s brought a method to inactivate tetanus toxin with formaldehyde, which allowed for the development of tetanus toxoid in 1924. Widespread use of tetanus toxoid to provide active immunization began during World War II.

**Epidemiology**

Tetanus toxoid was first introduced to the childhood vaccination schedule in the late 1940s, creating a significant decrease in mortality from tetanus compared to the early 1900s. Tetanus also became a nationally reportable disease in the 1940s: between 500 and 600 cases were reported per year during the first years of reporting.

Incidence rates steadily declined after the introduction of the tetanus toxoid vaccination. Approximately 50 to 100 cases per year have been reported from the 1970s to the 1990s, and an average of 31 cases per year was reported from 2000 to 2007. Incidence rates reached an all-time low in 2009, with 18 cases reported.

A total of 233 cases were reported from 2001 to 2008, indicating a 95% decrease in tetanus since 1947. Of these patients, 195 had a medical history available that showed 15% were intravenous (IV) drug users, and 79% had an acute wound that occurred before the development of tetanus.

Most reported cases occurred in people who have either never been vaccinated or had not received a booster in the previous 10 years. Heroin users have been found to be at a high risk of tetanus.

Newborns are also at a high risk of developing tetanus through the trauma of birth. Infants born to unvaccinated mothers, those whose umbilical cords are not cut hygienically, and those born to mothers with a history of neonatal tetanus in previous children are at a particularly high risk. Birth in underdeveloped countries can also be a risk factor, especially if unhygienic practices are followed such as applying mud to the umbilical stump or home deliveries in unhygienic areas. Only two cases of neonatal tetanus have been reported in the United States since 2009, and both infants were born to mothers who never received tetanus toxoid vaccination.

On an international level, tetanus occurs at a rate of between 500,000 and 1,000,000 cases per year. It occurs more commonly in underdeveloped countries without a widespread immunization program, and frequently affects neonates and young children.

Tetanus cases in the United States were studied between 1998 and 2000, and only 12% to 14% of the studied tetanus patients received a primary series of tetanus vaccination. In this study, 73% of patients developed tetanus after an acute injury, with half of these injuries being puncture wounds—32% of puncture wounds were caused by stepping on a nail.

Immunity against tetanus tends to decrease with age. Roughly half of adults over 50 years do not have adequate immunity against tetanus, either because they never received a primary series of vaccination, or did not receive periodic boosters at appropriate intervals.

**Pathogenesis**

Clostridium tetani is an anaerobic bacteria, a type of bacteria that grows in the absence of oxygen, and is involved in the development of tetanus. Clostridium tetani can develop spores that are incredibly resilient. Spores can survive for years in certain environments, and can survive treatment with disinfections, boiling for 20 minutes, and autoclaving at 249.8 °F (121 °C) for 10 to 15 minutes. Spores are commonly found in soil and animal feces. Human adults have been found to be carriers of spores in agricultural areas.

Clostridium tetani produces two types of exotoxins, tetanospasmin and tetanolysin. Tetanospasmin has been found to cause the clinical symptoms of tetanus, and is considered to be a potent neurotoxin.

Clostridium tetani enters the body through a wound in 65% of tetanus cases. The wound can be any size; only 5% of tetanus cases occur by transmission through a chronic skin ulcer. Complications from chronic conditions can also lead to tetanus, such as diabetic ulcers, tissue damage from childbirth, middle ear infections, burns, IV drug use, or surgical procedures. This puts patients with diabetes, IV drug users, and recent surgical patients at a higher risk of developing tetanus.

Once in the body, spores of Clostridium tetani germinate in anaerobic conditions, allowing for the release of bacteria that create tetanospasmin and tetanolysin. The toxins can spread to the rest of the body through the blood and lymphatic systems to cause generalized tetanus, or affect nerves that target only a specific muscle group to cause local tetanus. The toxins affect various sites of the central nervous system (CNS), such as the autonomic nervous system (ANS) that controls automatic bodily functions, the spinal cord, and the brain.

Symptoms of tetanus are caused by toxins binding to neurons to interfere with neurotransmitter release, blocking inhibitory actions in motor and autonomic neurons. This leads to uncontrolled muscle contractions and spasms that do not have an inhibitor impulse to stop the contraction. Once the toxins are bound to neurons, they cannot be neutralized. Recovery requires the development of new nerve terminals and synapses.

**Symptoms**

Tetanus has an incubation period between exposure and symptom onset that can range from 3 to 21 days, and averages around 8 to 10 days. Correlations have been found between the distance from the injury site to the CNS and length of incubation period; the farther the injury is from the CNS, the longer the incubation period. Shorter incubation periods have been associated with a higher risk of death.

Some patients can present without an apparent wound or entry site for tetanus to enter the body, since even very small wounds can introduce Clostridium tetani to the body, and the bacteria may have been introduced through another route.

There are four main types of tetanus. Generalized tetanus is the most common type, affecting between 80% and 90% of tetanus patients. It generally presents with symptoms that start at the head and progress downward. Between 50% and 75% of patients present with trismus (lockjaw) as their first symptom. Lockjaw renders the patient unable to open the mouth due to muscle spasms in the jaw muscles. Dysphagia, or difficulty swallowing, can be an early sign of tetanus as well, caused by spasms of the muscles in the throat. During the following 24 to 48 hours, muscle rigidity progresses downward from the face and jaw to affect the neck and abdominal muscles.
During disease progression, generalized muscle rigidity is a common manifestation of tetanus, with frequent widespread muscle spasms induced by sensory stimuli such as touch or light. Severe cases of tetanus may cause generalized, seizure-like convulsions. Spasms become more intense and frequency as the disease progresses. They can last from a few seconds to several minutes each time, and can continue for 3 to 4 weeks, though complete recovery can take months.

Severe spasms of tetanus can cause opisthotonos, a condition in which a patient’s head, neck, and spine are arched backward, so that if the patient is trying to lie on the back, only the head and feet touch the bed. Opisthotonos commonly occurs in waves, and can be severely painful. It can lead to bone fractures, tendon rupture, and respiratory failure.

Sustained contraction of the facial muscles can lead to risus sardonicus, a facial expression characterized by a sneering grin. As the disease progresses, the extremities become affected with muscle spasms, causing clenched fists and painfully flexed arms and legs. Severe muscle spasms can also lead to apnea, or periods when breathing stops temporarily, due to spasms of the diaphragm and muscles between the ribs. Dislocations can also occur due to muscle spasms at the joints.

As the levels of tetanus toxins accumulate in the CNS, the ANS, which is responsible for controlling automatic bodily functions such as heart function, breathing, and digestion, becomes affected more severely. The ANS becomes unstable and increases sweat production, blood pressure, heart rate, and body temperature. ANS dysfunction can also lead to abnormal heart rhythms and rhabdomyolysis, a condition in which muscle tissue breaks down and releases proteins into the bloodstream that can damage other organs such as the kidneys.

Generalized tetanus can have a variable clinical course, depending on the levels of prior immunity, concentration of toxins in the body, and the patient’s age and comorbid conditions.

Complications

Spasms in the muscles of the vocal cords or throat can interfere with breathing. These spasms can cause significant pain and potentially obstruct the upper airways, causing asphyxia, or suffocation. Asphyxia was the leading cause of death from tetanus before 1954, but advances in mechanical ventilation and the development of medications to control spasms have decreased the risk of death from asphyxia.

Bone fractures throughout the body can be caused by tetanus, due to extended severe contraction of muscles around the bones. Joint dislocations can also be caused by tetanic spasms.

Patients with tetanus are often in the hospital for longer periods of time, increasing the risk of hospital-acquired infections such as pneumonia, bedsores, and infections or sepsis from the use of catheters. Aspiration pneumonia is a common complication of tetanus, found in 50% to 70% of autopsied tetanus patients, as patients with difficulty swallowing are at a higher risk of inhaling foreign materials.

The alterations in activity of the ANS during tetanus can lead to high blood pressure or arrhythmias. Patients with underlying heart conditions may be affected more severely by ANS complications. Sudden cardiac death is the leading cause of death from tetanus, and can be related to ANS dysfunction, increases in production of naturally stimulating substances, or the direct action of tetanus toxins on the heart wall.

Pulmonary embolism, or a blood clot in the lungs that travelled from elsewhere in the body, is a possible complication of tetanus. It more commonly affects elderly patients and IV drug users.

Seizures related to tetanus, also known as tetanic seizures, can occur, and often represent a poor prognosis. They are similar to epileptic seizures, in that sudden muscle contractions occur, but the patient generally does not lose consciousness and can experience severe pain. The severity of tetanic seizures is often related to the severity of tetanus.

Tetanus is fatal in approximately 11% of cases. Infants, patients over 60 years of age, and those who have never received a tetanus vaccination, are at a higher risk of death.

Diagnosis and laboratory testing

The diagnosis of tetanus is entirely based on clinical findings, as there are no laboratory tests that are specific for tetanus. Testing for the bacteria that causes tetanus, Clostridium tetani, is highly variable. It is found in wounds of only 30% of tetanus patients, and can be found in patients who do not have tetanus. Laboratory tests may be useful in excluding strychnine poisoning, which can have a similar clinical presentation to tetanus.

Local tetanus, an uncommon manifestation of the disease, only produces muscle contractions in the same anatomic area as the wound that introduced tetanus to the body. Muscle contractions can range from mild to severe and last for several weeks before diminishing. Mild symptoms may be related to partial immunity in the patient. Symptoms of local tetanus may present before the onset of generalized tetanus.

Cephalic tetanus, or tetanus affecting the head, is a rare manifestation of tetanus that can occur during ear infections when the patient has Clostridium tetani in the flora of the middle ear. Cephalic tetanus has also developed following traumatic injuries to the head or face. Cranial nerve palsies often occur, in which the nerves originating from the brain that control sensory functions in the face function improperly or not at all, creating weakness or paralysis of muscles affected by these nerves. Cranial nerve palsies are more common than muscle spasms in cephalic tetanus, particularly those found in the facial area, though jaw muscle spasms can occur simultaneously with cranial nerve palsies.

Cephalic tetanus is often associated with a short incubation period, often around 1 to 2 days, indicating a poor prognosis. Similar to local tetanus, cephalic tetanus can also progress to generalized tetanus.

Neonatal tetanus is a variation of generalized tetanus that affects newborns. It occurs in infants born to mothers without immunity to tetanus. It commonly occurs when the umbilical cord is cut with instruments that are not sterile, or when the umbilical stump becomes infected. Infants with neonatal tetanus often develop symptoms between 4 and 14 days after birth, with an average onset of 7 days. Infants with neonatal tetanus often present with an inability to suck, as the first symptom; grimacing, muscle rigidity, opisthotonos, and irritability can also be presenting symptoms. Neonatal tetanus is rare in the United States, but is more common in underdeveloped countries, causing more than 257,000 deaths per year between 2000 and 2003. The prognosis is poor for patients with neonatal tetanus, with mortality between 70% and 90%. Survivors of neonatal tetanus commonly experience developmental delays.

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**Treatment**

The treatments chosen for a particular tetanus patient will depend on the severity of the disease. Admission to the intensive care unit (ICU) is necessary for most tetanus patients. Patients should be placed in a dark and quiet room to minimize the risk of inducing reflex spasms, and unnecessary procedures should be minimized.

**Maintain airways**

Patients with compromised airways may need intubation, mechanical ventilation, or tracheostomy (a surgical opening of the airway at the throat) to ensure the airways remain open. Prophylactic intubation may be considered in all patients with moderate to severe symptoms, as intubation or ventilation is necessary in approximately 2/3 of tetanus patients. Intubation can cause reflex spasms of the airways, so rapid intubation techniques should be used in tetanus patients, and emergency preparations for surgical airway opening should be made before attempting intubation. Tracheostomy should be used for patients who require intubation for more than 10 days, and may be considered if the patient experiences a tetanic seizure, due to the poor prognosis associated with this symptom.

**Neutralize unbound toxins**

Tetanus immune globulin (TIG) is used to provide passive immunity to tetanus patients. It should be used in all patients with active tetanus, and should be administered as soon as a diagnosis is made. TIG helps remove unbound tetanus toxins from the body, though it cannot remove toxins that are already bound to nerve endings. Therefore, rapid administration of TIG after diagnosis is crucial to minimize the severe symptoms of tetanus. It is recommended to use a single dose of 3,000 to 5,000 units administered intramuscularly (IM) for adults and children. A portion of the dose can be infiltrated around the wound that introduced tetanus, if the wound has been identified.

**Prevent further toxin production**

Antimicrobials have been used for years to decrease the amount of Clostridium tetani in the wound to prevent further toxin production. Penicillin G was used for many years for this purpose, but has been largely replaced by metronidazole as the drug of choice. Metronidazole penetrates wounds and abscesses effectively and creates minimal excitation of the CNS, minimizing side effects in tetanus patients. Metronidazole is commonly used in doses of 500 mg every 6 hours for 10 to 14 days in adults with tetanus. Penicillin G may still be used in patients allergic to metronidazole. High doses of penicillin G should be avoided in patients with severe kidney disease due to the risk of accumulation and toxicity to the nervous system, as well as the risk of hemolytic anemia, a form of anemia caused by the breakdown of red blood cells (RBCs). If used, a 10- to 14-day course of penicillin G, given at 100,000 units/kg/day divided every 4 to 6 hours is recommended for tetanus patients. Other antimicrobials can be used as well, such as vancomycin, clindamycin, erythromycin, and tetracycline, but their use is not well established and they should only be used if metronidazole and penicillin are contraindicated.

**Control muscle spasms**

Benzodiazepines are the first line of treatment for muscle spasms caused by tetanus. They can help prevent spasms that last longer than 5 to 10 seconds, induce sedation, and prevent seizures. Diazepam is the most commonly used medication for this purpose, as it has been shown to decrease anxiety, produce muscle relaxation, and sedate patients. Diazepam is typically administered in IV doses of 10 to 40 mg every 1 to 8 hours, though dosages should be monitored and titrated based on the patient’s response to minimize over-sedation. Respiratory depression, low blood pressure, low heart rate, and sedation are possible side effects, and diazepam should be used cautiously in tetanus patients with severe cardiac symptoms.

The effects of diazepam can be prolonged when adding the anticonvulsant phenobarbital. Additionally, phenobarbital can help treat severe muscle spasms and contribute to sedation. Low dosages should be used in patients who are not on ventilators to prevent respiratory depression, though patients already on ventilators may use higher doses since this effect is less of a concern. Dosages should be considered on a case-by-case basis and patients should be monitored for over-sedation.

Midazolam is a shorter-acting benzodiazepine that can be used in patients who require acute sedation, and may be more beneficial than diazepam in patients requiring long-term sedation since it carries less of a risk of accumulating long-acting metabolites. It can be administered IV at a rate of 5 to 15 mg/hr, though dosages should be titrated based on the patient’s response.

Baclofen, a skeletal muscle relaxer, can also be used in tetanus patients to help control muscle spasms. It can be used orally or injected into the spinal canal through the intrathecal route to introduce the medication directly into the cerebrospinal fluid. When administered through the intrathecal route, baclofen is 600 times more potent than baclofen administered orally, so lower doses may be used, decreasing side effects. Effects begin within 1 to 2 hours of intrathecal administration and last between 12 and 48 hours. Adverse effects associated with baclofen include decreased consciousness and respiratory rate. Dantrolene, another skeletal muscle relaxer, has been used off-label in tetanus patients to decrease painful muscle cramps and muscle tightening. It is preferred in cerebral tetanus, as it causes less cognitive dysfunction than baclofen or benzodiazepines. Dantrolene can be administered orally or IV, in dosages of 400 mg/day or less. The risk of liver toxicity limits its use.

Patients whose reflex muscle spasms do not respond to benzodiazepines, and those with severe muscle spasms preventing adequate breathing, may need treatment with neuromuscular blockers. Neuromuscular blocking agents can be used to prevent nerve impulses from reaching skeletal muscles, preventing muscle contraction and inducing paralysis. Vecuronium is the most common neuromuscular blocker used in tetanus patients because it does not cause adverse effects on the cardiovascular system. Vecuronium can be administered via continuous infusion to maintain paralysis, though this medication should not be used in infants due to increased sensitivity and prolonged recovery times. Mechanical ventilation is necessary in patients receiving neuromuscular blockers to control muscle spasms that impair breathing.
Manage ANS dysfunction

Magnesium sulfate can be used to help manage symptoms associated with ANS dysfunction. It can be administered through the IV route with an initial loading dose of 5 g, then a continuous infusion of 2 to 3 g/hr until the patient’s spasms are under control.

Patients receiving magnesium sulfate should have their patellar reflex monitored; those that do not have a reflex response to striking the area just below the patella of the knee with a reflex hammer may be receiving too much magnesium and may require a dosage reduction.

Morphine may be used to help manage pain and can also help manage cardiovascular effects of nervous system dysfunction such as increased heart rate. It can be given every 4 to 6 hours, for a total daily dose of 20 to 180 mg. Dosages should be titrated based on the patient’s response to prevent over-sedation and respiratory depression.

Patients experiencing increased heart rate or high blood pressure may need treatment with antihypertensive medications. Most beta-blockers are not recommended because of the risk of low blood pressure and sudden cardiac death, with the exception of esmolol, a short-acting beta-blocker. Esmolol can be administered through continuous infusion to control cardiac effects associated with tetanus. Clonidine, an alpha-agonist, may also be used to manage blood pressure in tetanus patients, and can be administered IV or intrathecally.

Atropine, an anticholinergic medication that decreases secretions throughout the body, can be used to reduce excessive sweating and respiratory secretions. This prevents excessive secretions from interfering with breathing.

Patients experiencing low blood pressure will need fluid replacement to increase blood pressure. Dopamine or norepinephrine may be used as well to increase significantly low blood pressure to maintain blood flow throughout the body.

General anesthetics may be used to block nerve impulses to produce anesthetic effects. Propofol may be used to induce anesthesia in severe cases of tetanus, and also has anticonvulsant properties. Propofol should be used cautiously in combination with benzodiazepines due to the risk of significant respiratory depression, and should not be used long-term.[3,8,11]

Wound care

After ensuring the patient’s airways are open and stabilizing the patient, aggressive wound care should begin, starting with cleaning the wound to remove foreign material and necrotic tissue. Surgical debridement may be necessary in severely contaminated wounds, but should not be completed until after active tetanus patients have been stabilized.

Not all tetanus-inducing wounds are contaminated, and clean wounds do not benefit significantly from surgical debridement, so wound care should be patient-specific. Wounds should not be manipulated until several hours after the administration of TIG to prevent the release of tetanus toxins into the bloodstream.[8,9]

Nutrition

Since tetanus patients have a high risk of aspiration, food and other forms of nutrition should not be given orally. Patients may require nutrition through nasogastric tubes or parenteral nutrition.

Consultation with a nutritionist will help ensure the patient receives appropriate nourishment.[9]

Immunization

Due to the high potency of tetanus toxin, immunity does not develop as a result of tetanus. As soon as the patient’s condition has become stable, he or she should be immunized with tetanus toxoid to prevent recurrences[9].

PREVENTION OF TETANUS

Wound care

Wound characteristics are directly correlated with the risk of developing tetanus. The wounds that are least likely to develop tetanus are recently acquired, with sharp edges, and not contaminated. Essentially, all other wounds are at risk for tetanus, especially those that have been present for more than 6 hours, those deeper than 1 cm, those that are infected or have been exposed to saliva or feces, and puncture wounds.

The wounds at highest risk of developing tetanus are severely contaminated with foreign materials, and those caused by bites or blunt trauma. All wounds should be evaluated and properly cleaned as soon as possible after they develop to prevent the development of tetanus[8].

Tetanus immune globulin (TIG)

TIG should be used to provide passive immunity to patients with inadequate or unknown vaccination status who present with a wound that may be contaminated with Clostridium tetani. Patients with wounds at moderate to high risk of developing tetanus should receive TIG in addition to tetanus toxoid vaccine, as well as patients who have received less than three doses of tetanus toxoid. A dosage of 250 to 500 units should be administered IM in the opposite extremity of the wound[8,9].

Immunization

Patients presenting with wounds at risk of developing tetanus should receive a tetanus toxoid-containing booster vaccine if it has been more than 5 years since their last dose of tetanus toxoid or if they did not complete a primary vaccination series[9].

Vaccination

The tetanus vaccination was first developed in 1924, and began to be used widely during World War II. The widespread use of tetanus toxoid vaccinations has significantly decreased the occurrence of tetanus in the United States, and continued vaccination will help maintain low rates of tetanus.
The tetanus toxoid is available in several forms. The combination of tetanus toxoid with diphtheria toxoid is available in pediatric (DT) and adult forms (Td). DT is available with no brand name, and is recommended for children up to age 6. Td is available under the brand names Decavac and Tenivac, in addition to a generic form, for use in people aged 7 and older.

The combination of tetanus, diphtheria, and pertussis is available in pediatric (DTaP) and adult (Tdap) forms. Two brands of DTaP are available: Daptacel, which is approved by the U.S. Food and Drug Administration (FDA) for use in children 6 months to 6 years old, and Infanrix, approved for use in children aged 6 months to 7 years. There are also two brands of Tdap available: Adacel, approved for use in ages 10 to 64, and Boostrix, approved for use in ages 11 to 64.

The vaccine abbreviations should be acknowledged to assess the different levels of diphtheria and pertussis in each product. The amount of tetanus toxoid in all forms of tetanus-containing vaccine for children and adults is similar; however, the quantities of diphtheria toxoid and pertussis are different for adults and children. Children require higher levels of diphtheria and pertussis than adults, which are indicated by capital letters in the pediatric vaccines. For example, DTaP has higher levels of diphtheria and pertussis than the adult vaccine Tdap.

Tetanus toxoid is also available in combination with other vaccinations. Tetanus, diphtheria, pertussis, hepatitis B, and inactivated poliovirus are available in the combination product Pediarix. Pediarix is licensed for use up to age 6, and can be used for the primary series but not booster doses. Tetanus, diphtheria, pertussis, Haemophilus influenza type B, and inactivated poliovirus are available in the combination product Pentacel, which can also be used in the primary vaccination series, and is licensed for use in children between 6 weeks and 4 years of age.

Single-antigen tetanus toxoid is not recommended, and is now no longer available. Since diphtheria toxoid requires booster doses at the same intervals as tetanus toxoid, it is recommended to use combination agents including both toxoids to ensure immunity against both diseases[3,12].

**Efficacy of tetanus vaccination**

Following a primary series of tetanus toxoid vaccinations, recipients produce antitoxin levels significantly higher than the known minimal protective levels of 0.1 IU/mL. While tetanus toxoid efficacy has not been formally evaluated in a clinical trial, protective antitoxin levels from a complete primary series and regular booster doses are assumed to be effective in nearly 100% of cases since cases of tetanus in completely immunized people are extremely rare.

Antitoxin levels are known to decrease over time. Approximately 10 years after the last dose of tetanus toxoid, antitoxin levels decrease to the minimally protective levels. Therefore, booster doses are recommended every 10 years to maintain adequate antitoxin levels and ensure protective immunity.

In a small fraction of the population, antitoxin levels decrease below minimally protective levels in less than 10 years after the last booster dose. Patients who develop wounds that are not clean or minor should receive a booster dose of tetanus if more than 5 years have passed since their last dose of tetanus toxoid, to increase protection in this fraction of the population[10].

**Vaccination schedule**

The vaccine of choice in children aged 6 weeks to 6 years is the DTaP vaccine, containing tetanus and diphtheria toxoids in addition to acellular pertussis. The standard primary series in this age group is four doses of the vaccine at 2, 4, 6, and 15 to 18 months of age. The first three doses should be separated by at least 4 weeks. The fourth dose should be given at least 6 months after the third, and should not be given before 12 months of age.

Children who have contraindications to the pertussis vaccine should be given the DT vaccine, containing only diphtheria and tetanus. Children who receive the first dose of DT at an age younger than 12 months should receive four doses to complete the primary series, ideally given at 2, 4, 6, and 15 to 18 months of age. Children who are older than 12 months at the first dose of DT should receive three doses in their primary series, with the third dose administered 6 to 12 months after the second dose.

Regardless of the vaccine used, if a child receives the fourth dose of DTaP or DT before age 4, a fifth booster dose should be given between 4 and 6 years of age, before the child enters school. If the child receives the fourth dose at or after age 4, a fifth dose is not required. Since tetanus antitoxin levels decrease with time, booster doses should be given every 10 years to maintain adequate protection. The first booster dose should be given at 11 to 12 years of age, if 5 years have passed since the last dose of tetanus toxoid vaccination. The Advisory Committee on Immunization Practices (ACIP) recommends the use of Tdap for this dose to ensure adequate protection against pertussis.

If less than 5 years has passed since the last tetanus toxoid-containing dose, due to late completion of a primary series or a booster dose administered following a wound, another dose is not necessary for 10 years. Booster doses are not recommended to be administered more frequently than every 10 years due to the higher risk of developing local reactions to the vaccine.

The recommended booster vaccine for people 7 years of age and older is Td, with Tdap administered in place of one dose of Td. Unvaccinated people, and those with inadequate documentation, should receive a primary series of three doses, with the first two doses separated by at least 4 weeks, and the third dose administered 6 to 12 months after the second. The ACIP recommends that the first booster dose be administered as Tdap, to ensure adequate protection against pertussis; the second and third dose should be administered as Td.

If the vaccination schedule has been interrupted or delayed, the series does not need to be restarted, regardless of the amount of time that has passed between doses. Interruptions in the primary series do not decrease the vaccine response. Children under age 7 should complete their series with DTaP or DT, and anyone over age 7 should complete their series with Td or Tdap, even if a pediatric series with DTaP or DT was not completed.

Patients who have experienced tetanus do not develop immunity to it. They should receive vaccination with Td to begin or complete their primary series as part of their treatment[3].

**Contraindications and precautions**

Severe allergic reactions, such as anaphylaxis, to vaccine components are considered to be contraindications to the tetanus toxoid vaccine. Generalized allergic reactions should be referred to allergy specialists before discontinuing the immunization series.

Patients with moderate to severe illnesses should wait until their illness is resolved before receiving routine vaccinations, but patients with mild illnesses such as ear infections may still receive vaccinations[3].

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Diphtheria is a contagious, acute disease caused by a toxin produced by the bacteria Corynebacterium diphtheriae. It is spread from person to person through the respiratory tract and is characterized by inflammation of the mucous membranes. Diphtheria can create false membranes at mucosal membranes in the body, such as at the back of the throat, which can inhibit breathing and swallowing. The toxins produced by Corynebacterium diphtheriae can also damage the heart and nervous systems. Rapid treatment with antibiotics can prevent some of the more severe clinical manifestations of diphtheria⁴⁻⁵.

Vaccine components, storage and administration

DTaP and Tdap vaccinations do not contain thimerosal as a preservative. Vaccines containing tetanus toxoids should be stored in the refrigerator at 35 °F to 46 °F (2 °C to 8 °C). They should never be stored in the freezer because exposure to freezing temperatures decreases the potency of the tetanus component of the vaccination. Vaccines that have been exposed to freezing temperatures should not be administered.

Tetanus toxoid-containing vaccines should be administered IM. The deltoid muscle of the upper arm is preferred for adults and older children, and the midlateral thigh muscles are preferred for infants³⁹.

Adverse reactions

Local adverse reactions at the injection site are common and include redness, swelling, and pain. They are generally self-limiting and do not require treatment. Abscesses and nodules at the injection site have been reported. Exaggerated local reactions occur most often in adults who have very high antitoxin levels due to frequent immunization with tetanus or diphtheria toxoids. These patients should not receive another immunization with tetanus or diphtheria toxoid for 10 years.

Systemic reactions such as fever are not common. Hives, anaphylaxis, and neurological complications have been reported. Peripheral neuropathy and Guillain-Barré syndrome have been reported rarely³¹.

DIPHTHERIA

Definition

Diphtheria is a contagious, acute disease caused by a toxin produced by the bacteria Corynebacterium diphtheriae. It is spread from person to person through the respiratory tract and is characterized by inflammation of the mucous membranes. Diphtheria can create false membranes at mucosal membranes in the body, such as at the back of the throat, which can inhibit breathing and swallowing. The toxins produced by Corynebacterium diphtheriae can also damage the heart and nervous systems. Rapid treatment with antibiotics can prevent some of the more severe clinical manifestations of diphtheria⁴⁻⁵.

History

Diphtheria was first described by Hippocrates in the 5th century BC, and epidemics have been recorded since the 6th century AD. In the late 1880s, Corynebacterium diphtheriae was observed in mucous membranes of diphtheria patients, and the antitoxin was first developed. The 1920s brought the development of the diphtheria toxoid, which was developed into the diphtheria toxoid vaccination that was widely used beginning in the 1940s.

Historically, diphtheria was a childhood illness, commonly affecting children under 12 after maternally acquired immunity waned between 6 and 12 months of age. Once the widespread use of the diphtheria toxoid vaccination began, cases of diphtheria in children declined significantly, and a higher proportion of adolescents and adults became affected due to waning immunity and inadequate boosting¹³.

Epidemiology

In the United States in the 1920s, between 100,000 and 200,000 cases of diphtheria occurred per year, causing an average of 14,000 deaths per year. Outbreaks were common, and diphtheria was one of the top three causes of death in children under 15 years old in England and Wales in the early 1930s. The diphtheria toxoid vaccination was made available in the 1930s, and was used widely starting in the late 1940s. Widespread vaccine use resulted in a sharp decrease in the number of cases of diphtheria. In the 1970s, an average of 196 cases was reported per year, including an outbreak of cutaneous diphtheria in Washington State. Most of the cases reported during this time were seen in people of low socioeconomic status, including Native Americans.

Cases of diphtheria continued to decline, with only 57 cases reported in the United States between 1980 and 2004. Most of these cases developed in people who were unimmunized or underimmunized, and continued to affect people of low socioeconomic status, with a significant portion of cases reported in homeless people. Of the 57 cases, 58% were 20 years of age or older, and many adults were found to have low levels of antitoxins, confirming beliefs that vaccine-induced immunity wanes over time.

On an international level, diphtheria remains a health threat in developing countries. A major outbreak occurred in 1990 in 15 countries that were part of the former Soviet Union, affecting more than 157,000 people and causing more than 5,000 deaths. The outbreak in these 15 countries accounted for over 90% of all diphtheria cases reported worldwide in 1995, and disproportionately affected adults over age 40, reiterating a need for booster vaccinations in adults. Outbreaks continue to occur worldwide; 7,088 cases were reported in 2008¹¹⁻¹⁴.

Pathogenesis

Corynebacterium diphtheriae is spread from person to person through respiratory droplets and nasal secretions, and can spread through wound secretions in cases of cutaneous diphtheria.

People living in close quarters in substandard living conditions are at a higher risk of acquiring diphtheria, as are those who are immunocompromised or lacking adequate immunization.

Once acquired, Corynebacterium diphtheriae adheres to cells in mucous membranes and produces a toxin that causes inflammation, builds false membranes, and damages local tissue. Tissue damage allows the toxins to enter the bloodstream and lymphatic system for distribution to other parts of the body. The toxin is known to spread to the kidneys, nervous system, and the myocardial layer of the heart, causing complications.

Patients with diphtheria can transmit the bacteria for an average of 2 weeks without antibiotic treatment, though chronic carriers of the bacteria could transmit the organism for 6 months or more. Appropriate treatment with antibiotics terminates bacterial transmission.

Not all strains of Corynebacterium diphtheriae produce toxins, and strains that do not produce toxins create much more mild forms of diphtheria.

The average mortality rate of diphtheria is around 5% to 10%. Death from diphtheria commonly occurs 3 to 4 days into the course of diphtheria,
Low herd immunity, or low levels of immunization among a population, increasing disease prevalence.

Risk factors for developing diphtheria include:
- Lack of immunization or inadequate boosting, especially in adults.
- Low herd immunity, or low levels of immunization among a population.
- International travel in endemic areas.
- Immunocompromised status, such as HIV or cancer.
- Low socioeconomic status.
- Large-scale movements of populations, such as during the collapse of the former Soviet Union.
- Overcrowding, such as in homeless shelters or military housing.

**Symptoms**

Once C. diphtheriae is transmitted to a new person, it undergoes an incubation period that averages between 2 and 5 days. After the incubation period, diphtheria can affect nearly any mucous membrane in the body, though some are more commonly affected than others.

**Anterior nasal diphtheria**

Anterior nasal diphtheria is initially indistinguishable from the common cold, with nasal discharge being a common initial symptom. A white membrane can form on the nasal septum, the tissue in the nose separating the left and right nostril. This form of diphtheria is often mild, since the toxin is poorly absorbed into the bloodstream and lymphatic system from this area. Anterior nasal diphtheria can be rapidly resolved with antibiotic and antitoxin treatment.[13]

**Pharyngeal and tonsillar diphtheria**

The pharynx and tonsils comprise the most common mucous membrane to be affected by diphtheria. Initial symptoms are commonly sore throat, low-grade fever, malaise, difficulty swallowing, and decreased appetite.

Within 2 to 3 days of symptom onset, a thick, leathery, blue-white membrane forms at the back of the mouth, and can range in size from a small patch to a large membrane covering most of the soft palate.

The membrane adheres to the tissue, and attempts at removal cause bleeding. Large membranes can obstruct breathing.

Since absorption of the toxin into the bloodstream and lymphatic system is high in this form of diphtheria, patients can develop systemic symptoms, such as rapid pulse or coma. Severe cases can develop swelling under the jaw and at the front of the neck, creating the characteristic “bull neck” appearance.[13,15]

**Laryngeal diphtheria**

Diphtheria of the larynx, the portion of the respiratory system above the trachea that contains the vocal folds, can develop as an extension of pharyngeal diphtheria, or on its own. Symptoms include low-grade fever, malaise, and sore throat. Membrane formation in this type of diphtheria can interfere with breathing to cause hoarseness or a barking cough, initially resembling an upper respiratory infection.

Diphtheria patients can initially present with severe acute heart failure, which can lead to heart failure. The limbs, eye muscles, and diaphragm can also be paralyzed, which occurs most often during the third week after the onset of diphtheria. The heart valves, can also occur, especially in patients with artificial heart valves.[13,15]

**Cutaneous diphtheria**

Cutaneous diphtheria, or diphtheria of the skin, commonly appears as ulcers with clear edges, covered with a gray membrane. Ulcers can be co-infected with variations of *Staphylococcus* bacteria. The ulcers are infectious, and the bacteria can be spread from the skin to the respiratory passages. Many cases of cutaneous diphtheria in the United States are infected with nontoxin-producing bacteria, which results in a less severe disease.[13]

**Other sites of infection**

Diphtheria can affect any mucous membrane, and rarely affects the conjunctiva of the eye, the vaginal area, and the external ear canal.[13]

**Complications**

The complications of diphtheria can be attributed to the effects of the diphtheria toxin.

**Cardiac toxicity**

Toxicity to the heart commonly occurs 1 to 2 weeks after the onset of illness, after the pharyngeal phase begins to improve. Up to 60% of diphtheria patients can develop myocarditis, or inflammation of the wall of the heart, especially if they have not been properly immunized. The presentation of myocarditis often begins with abnormal heart rhythms. The onset of arrhythmias is variable, and can occur early in the course of diphtheria or weeks after, though early onset is correlated with a poor outcome. Arrhythmias can prevent the heart from pumping adequate amounts of blood to the rest of the body, leading to heart failure.

Diphtheria patients can initially present with severe acute heart failure or other cardiac symptoms such as progressive shortness of breath, decreased heart sounds, and weakness. Endocarditis, or inflammation of the heart valves, can also occur, especially in patients with artificial heart valves.[13,15]

**Nerve toxicity**

Neuritis, or inflammation of the nerves, is caused by the diphtheria toxin spreading through the bloodstream to the nerves and is more common in patients with severe, prolonged diphtheria. Neuritis can lead to paralysis of various areas of the body. The soft palate can become paralyzed, which occurs most often during the third week after the onset of diphtheria. The limbs, eye muscles, and diaphragm can also become paralyzed, often during or after the fifth week after diphtheria onset. Neuritis leading to paralysis of the diaphragm can inhibit breathing and
lead to pneumonia and respiratory failure. Urinary incontinence can also affect nerves leading to the bladder, causing urinary incontinence.

Nerve toxicity can also cause dysfunction of the facial and peripheral nerves. Peripheral neuropathy can begin from 10 to 90 days after contact with diphtheria. Approximately 5% to 10% of diphtheria cases are fatal, though death rates can reach 20% in children under 5 and adults over 40. Death caused by diphtheria is often related to myocarditis, false membranes blocking the airways, or aspiration pneumonia.[13]

Other complications

Respiratory issues caused by membranes obstructing the airways are possible, and can be severe. Membranes located in or near the airways can cause difficulty swallowing and increase the risk of aspiration of foreign materials, putting patients at risk of aspiration pneumonia. Membranes that completely block airways may require airway or surgical interventions to maintain airflow in affected patients.

Diagnosis and laboratory testing

Diphtheria is generally diagnosed based on clinical findings since patients often need rapid treatment to maintain airflow. A culture of the membrane or wound may be done to confirm the diagnosis. If diphtheria bacteria are found, they should be tested to see if they produce toxins. Antibody titers can also be useful in determining if a patient has immunity to diphtheria, especially if antibiotic use prevents development of a positive culture.[13]

Treatment

Suspected and confirmed diphtheria patients should be isolated from other patients upon diagnosis, and universal, as well as droplet, precautions should be followed to limit the spread of disease. All cases may require intubation or surgical airway management, depending on the location of false membranes and the severity of disease.[16]

Maintain airways

Patients with laryngeal or pharyngeal membranes should have their airways monitored beginning at diagnosis to prevent aspiration. Early airway management also prevents aspiration of foreign materials. Patients may require intubation or surgical airway management, depending on the location of false membranes and the severity of disease.[16]

Diphtheria antitoxin

Patients who are suspected to have diphtheria should be tested for sensitivity to the antitoxin before it is administered. Health care professionals who are caring for patients who are suspected to have respiratory forms of diphtheria can contact the CDC’s Emergency Operations Center by phone at 770-488-7100 to attempt to procure diphtheria antitoxin. The diphtheria duty officer at the CDC’s Meningitis and Vaccine Preventable Diseases Branch in the Division of Bacterial Diseases of the National Center for Immunization and Respiratory Diseases is available to discuss the suspected patient’s case and protocol for diphtheria antitoxin use with the physician treating the patient. If the use of diphtheria antitoxin is indicated, the product will be released from a U.S. Public Health Service quarantine station to get to the patient as soon as possible.[13,16,17,18]

Antibiotics

Antibiotics are used in diphtheria patients to eliminate C. diphtheriae from the body. Starting treatment with antibiotics as early as possible will prevent the further production of diphtheria toxins. First-line treatment is a 14-day course of erythromycin, which can be administered orally or IV, in doses of 40 mg/kg/day, with a maximum dose of 2 g/day. Children under 6 months of age should not receive erythromycin, due to the risk of pyloric stenosis, or narrowing of the opening between the stomach and small intestine that can lead to blockage.

Penicillin G procaine is also effective against C. diphtheriae, and can be administered IM at doses of 300,000 units/day for patients that weigh less than 10 kg, or 600,000 units/day for patients that weigh more than 10 kg. A 14-day course is recommended for diphtheria treatment. Patients are generally not contagious after they have been taking antibiotics for 48 hours. After antibiotic therapy is complete, two consecutive cultures should be completed to ensure the bacteria has been eradicated.[13,16,17]

Manage complications

Diphtheria patients should be monitored for abnormal cardiac activity from their initial diagnosis to attempt to detect abnormal rhythms early. Cardiac medications may be necessary for abnormal heart rhythms or heart failure. Consultation with a cardiologist may be necessary to manage cardiac complications of diphtheria.

Neuritis leading to paralysis of the diaphragm may need mechanical ventilation to maintain adequate breathing rates. Those with urinary symptoms caused by neuritis in nerves affecting the bladder may need incontinent pads to manage urinary incontinence.[13,16]
### Prevention
Caregivers, family members, and household contacts of diphtheria patients should receive an age-appropriate booster dose of diphtheria toxoid vaccination. Close contacts should also be treated with antibiotics, regardless of their immunization status or age, to prevent the development of diphtheria and halt the spread of disease. Penicillin G procaine or erythromycin can be used in the same doses used to treat diphtheria patients[13,17].

### Vaccination
The diphtheria toxoid was first developed in the early 1920s, but use of the diphtheria toxoid vaccination did not begin until the 1930s. In the 1940s, the diphtheria toxoid was combined with the tetanus toxoid and pertussis vaccine for routine use. Single-antigen diphtheria vaccinations are no longer available; the diphtheria vaccination is available in combination with the tetanus toxoid, with tetanus and pertussis, with Tetanus, pertussis, hepatitis B, and inactivated poliovirus, and with tetanus, pertussis, Haemophilus influenza type B, and inactivated poliovirus, as discussed in the tetanus section.

Pediatric formulations of DT and DTaP contain 3 to 4 times as much diphtheria toxoid as the adult products. Children under 7 years of age should receive the higher dosage of diphtheria toxoid; children over 7 years should receive the lower adult dosing, even if they never finished a course with the childhood formulation.

Immunity does not develop in patients who have had diphtheria; these patients should complete or begin an initial course of diphtheria toxoid to prevent future occurrence[13,16].

### Efficacy of diphtheria vaccination
Following a primary series of diphtheria toxoid, more than 95% of patients develop protective levels of antitoxin, which can be defined as more than 0.1 units/mL. Clinical efficacy is estimated to be around 97%.

Antitoxin levels are known to decrease over time. Booster doses are recommended every 10 years to maintain adequate immunity against diphtheria[13].

### Vaccination schedule
Children and adults should be immunized against diphtheria following the same guidelines discussed in the section on tetanus. Since antitoxin levels can decrease with both tetanus and diphtheria vaccinations, they should both be administered using a combination vaccine every 10 years to maintain adequate levels of antitoxins[13].

### Contraindications and precautions
Severe allergic reactions, such as anaphylaxis, to vaccine components are considered to be contraindications to the use of the diphtheria toxoid vaccine. Generalized allergic reactions should be referred to allergy specialists before discontinuing the immunization series.

People with moderate to severe acute illnesses should wait until their illness is resolved before receiving routine vaccinations, but patients with mild illnesses may still receive vaccinations as appropriate[13].

### Adverse reactions
Local reactions, such as itching, hardening, or tenderness at the injection site are common after receiving diphtheria toxoid-containing vaccinations. Fever and abscesses can occur, but are not common. Rarely, severe systemic reactions such as anaphylaxis or neurological complications have been reported.

Exaggerated local reactions have been reported, such as swelling of the arm from the shoulder to elbow, and often begin within 2 to 8 hours after administration. Exaggerated local reactions are more common in adults who have received frequent doses of tetanus or diphtheria toxoid. These patients may have high antitoxin levels, and should be recommended to receive booster doses ofTd no more frequently than every 10 years[13].

### PERTUSSIS

#### Definition
Pertussis, also known as whooping cough, is a contagious acute illness caused by the bacteria *Bordatella pertussis*. It is an infection spread through respiratory droplets or secretions and affects the respiratory tract. It causes a characteristic cough, in which the patient experiences violent coughing attacks that cause the patient to gasp for breath, creating a “whooping” sound.

Pertussis can cause significant morbidity and mortality in children under 2 years of age, as well as the elderly. Pertussis is the most commonly reported vaccine-preventable disease in the United States in children under 5 years of age, indicating a need for reinforcement of adequate immunization[19,20].

#### History
Pertussis was first described in the 16th century. The bacteria that causes whooping cough was isolated in 1906, but the vaccination did not become available until the 1930s. Before the release of the vaccine, pertussis was a common childhood illness and caused significant morbidity and mortality in children, with over 200,000 cases reported per year. Once the use of the vaccine became widespread in the 1940s, incidence of whooping cough decreased more than 99%.

The number of outbreaks has been rising since the 1980s, and outbreaks continue to occur in the United States and worldwide. Pertussis remains a major world health issue, especially among children in developing countries. An estimated 195,000 deaths from pertussis occurred worldwide in 2008. The United States experiences outbreaks of pertussis as well; over 28,000 cases were reported in 2014[12,19,20].

#### Epidemiology
Prior to the widespread use of the pertussis vaccine, whooping cough was a common ailment among children. More than 1 million cases were reported between 1940 and 1945, with an average of 175,000 cases per year. After the first pertussis vaccine was introduced in the
In 1940s, the incidence of whooping cough declined to 15,000 cases reported in 1960. Less than 5,000 cases per year were reported by 1970, and the 1980s saw an average of 2,900 cases per year. The incidence of pertussis has been increasing since the 1980s. In 2004, over 25,000 cases were reported, which is the largest number of cases reported since 1959. In 2010, over 27,000 cases were reported. The CDC estimates that only 5% to 10% of all pertussis cases are actually diagnosed and reported. Studies have shown that between 12% and 32% of adults with a cough that between 1 and 4 weeks have been found to have pertussis. Adolescents and adults comprise a larger portion of cases reported in the 21st century than the 20th century. This could be because of increased recognition of pertussis in adult and adolescent patients, or waning immunity from childhood vaccinations. People can be carriers of *Bordetella pertussis*, and adolescents and adults are a common source of infection of infants.

### Current outbreaks

Outbreaks of pertussis continue to occur throughout the United States. As of December 2014, over 28,000 cases of pertussis were reported to the CDC. This represents an 18% increase over the number of cases reported in 2013. Incidence rates in 2014 were highest in infants, with the number of cases reported in infants exceeding that of any other age group. Children 7 to 10 years of age represented the second highest rate of pertussis, and incidence rates in adolescents aged 13 to 14 increased in 2014 as well. Although incidence rates in 2014 were high, the CDC estimates that only 5% to 10% of pertussis cases are actually reported, indicating that pertussis is much more widespread than incidence rates may suggest. People can be carriers of *Bordetella pertussis*, and adolescents and adults are a common source of infection of infants.

### Pathogenesis

Pertussis is transmitted through the respiratory droplets or secretions of an infected patient. Once the bacteria *Bordetella pertussis* is inhaled, it attaches to the respiratory cilia, or tiny hair-like cellular extensions that line the respiratory tract. After attachment, the bacteria produces toxins that paralyze the cilia, which leads to inflammation in the respiratory tract. This inflammation encourages the production and build-up of respiratory secretions, which can interfere with airflow in the small airways, especially in infants. Decreased function of the small airways can lead to lung collapse, cough, pneumonia, and blue or purple skin discoloration caused by a lack of oxygen. Patients with pertussis are the most contagious once respiratory secretions are produced until approximately 2 weeks after the onset of cough.

Pertussis is highly contagious; over 80% of susceptible people exposed to the bacteria will develop pertussis. Infants, especially premature infants, and older patients with heart, lung, or neurological comorbidities are at a high risk of contracting pertussis and developing severe complications. Other risk factors for contracting pertussis include underimmunization, close contact with infected patients, and pregnancy.

### Symptoms

Once *Bordetella pertussis* enters the body, it typically replicates during an incubation period lasting an average of 7 to 10 days, though it can range from 4 to 21 days. The clinical course of whooping cough often lasts around 6 weeks and can be divided into three stages, each of which lasts an average of 1 to 2 weeks. The first stage is known as the catarrhal stage, during which mucous membranes of the respiratory passages become inflamed and create a thick mucus. Other symptoms in this stage include sneezing, runny nose, mild cough, and low-grade fever. Pertussis is the most communicable during the catarrhal stage, though it can remain contagious throughout the second phase as well.

The cough that begins in the catarrhal stage gradually becomes more severe, and after 7 to 14 days in the catarrhal stage, the second stage, known as the paroxysmal stage, begins. Paroxysms, or sudden attacks, of frequent, rapid coughs occur and are caused by thick mucus in the airways that is difficult to move. Coughing attacks can last up to several minutes, and patients can feel like they are suffocating. Patients can have difficulty breathing in enough oxygen during paroxysms of coughing, which can cause cyanosis, or the skin turning blue. After a paroxysm of coughing, the patient often tries to take in a long breath, sometimes accompanied by a high-pitched “whoop” sound, which is most common in patients 6 months to 5 years old. Infants under 6 months old may not have enough strength to take in a long, sharp breath after a paroxysm of coughing, and may not produce the characteristic whooping sound. Vomiting can occur following coughing attacks.

Paroxysmal coughing tends to occur more often at night, and patients experience an average of 15 attacks every 24 hours. Coughing attacks generally increase in frequency over the first 1 to 2 weeks of illness, remain steady for 2 to 3 weeks, then gradually decline. The paroxysmal stage often lasts from 1 to 6 weeks, but can continue for up to 10 weeks.

The patient begins to gradually recover in the third stage, also known as the convalescent stage. During the next 2 to 3 weeks, the cough becomes less paroxysmal and gradually disappears. Recurrences of paroxysmal cough can occur during the convalescent stage. Chronic cough can last for weeks for some patients, potentially leading to the development of respiratory infections, even months after the initial infection.

Patients with partial immunity from previous vaccinations can become infected with *Bordetella pertussis* but develop more mild symptoms than unimmunized individuals. These patients may experience symptoms ranging from a mild cough to classic pertussis, though whooping is not common in partially immunized patients. Infected adults and adolescents with mild disease may not know they have pertussis, but can carry the bacteria and pass it on to unimmunized or underimmunized people, such as infants.

The prognosis for full recovery is generally good in children over 6 months of age. Infants under 6 months are more likely to have severe cases of pertussis that require hospitalization and develop complications; 69% of infants under 6 months of age with pertussis between 2001 and 2003 required hospitalization. Infants under 3 months experienced a mortality rate of 1% to 3%. Immunity to pertussis does not develop in response to natural disease. Immunity in response to vaccination typically wears off 3 to 5 years after vaccination, and is not detectable in the bloodstream after 12 years, indicating a need for reimmunization. During 2001 to 2003, 23% of pertussis patients were under 1 year old, 12% were between 1 and 4 years old, 9% were 5 to 9 years old, 33% were 10 to 19 years old, and 23% were 20 years and older. The higher incidence in infants can be attributed to the lack of transfer of maternal immunity to the infant before birth, and the inability to vaccinate infants under 6 weeks of age against pertussis. Infants are at the highest risk of death from pertussis.

On an international level, the incidence rate of pertussis is estimated to be approximately 48.5 million cases per year, with approximately 295,000 deaths per year. Worldwide pertussis vaccination rates are low, even in established countries, contributing to the continued spread of pertussis. Less than 30% of people in England have been vaccinated against pertussis during the last 40 years.
Control measures to prevent the spread of pertussis should be implemented immediately upon the diagnosis of one or more cases of pertussis in the health care setting. Droplet and standard precautions should be followed, and patients should be isolated to prevent the spread of pertussis. Both confirmed and suspected cases of pertussis should be reported to the local health department for monitoring of this communicable disease[19,20,21].

Complications

Infants (especially those born prematurely) and elderly patients (especially those with underlying heart or lung disease) are at a particularly high risk of developing complications from pertussis. The most common complication associated with pertussis is bacterial pneumonia. Patients with pertussis have a compromised immune system and are more susceptible to infections with other bacteria, allowing for secondary pneumonia to develop. Pneumonia occurred in 5.2% of all pertussis cases reported from 1997 to 2000, and in 11.8% of infants under 6 months of age. Pneumonia is the most common cause of death related to pertussis.

Neurological complications can occur as a complication of infection with pertussis. They are thought to be caused by a decrease in oxygen supply from paroxysms of coughing, or due to the direct effect of pertussis toxins on the CNS. Seizures occur in approximately 1% to 2% of infants with pertussis. Brain dysfunction, known as encephalopathy, is also more common in infants. Complications can also occur because of changes in pressure caused by severe coughing attacks, such as a collapsed lung, nosebleed, and hernias. Other complications of pertussis can include ear infections, loss of appetite, rib fractures, difficulty sleeping, urinary incontinence, and dehydration[19,20].

Diagnosis and laboratory testing

Pertussis is commonly diagnosed based on symptoms as well as a variety of lab tests. Since laboratory confirmation of pertussis can be delayed, health care providers often need to make a presumptive diagnosis of pertussis based on the patient’s symptoms to begin treatment, and confirm the presumptive diagnosis with lab testing. Cultures are considered the most specific lab test for pertussis, even though Bordatella pertussis requires particular collection and isolation techniques for accurate growth. Specimens should be collected from deep in the nasopharynx, at the back of the sinuses where the sinuses and pharynx meet, using a swab entered through the nostril, not the throat. A particular type of swab must be used, one which is composed of calcium alginate, not cotton. Cultures can take up to 14 days to grow, which can minimize their clinical practicality. Isolation of the bacteria is highest during the catarrhal stage and the beginning of the paroxysmal stage, and lowest in late stages, vaccinated patients, or those who have received antibiotics. A negative culture should not exclude the diagnosis of pertussis.

The polymerase chain reaction (PCR) assay does not require live bacteria to produce accurate results, allowing it to be more sensitive and produce faster results than cultures. It is commonly used in addition to cultures for diagnosis of pertussis. Similar to cultures, a PCR assay can be affected by the collection of specimens, and requires a swab of the nasopharynx obtained through the nostril. Inappropriately collected swabs can result in false-negative results. PCR assays are not affected by antibiotic treatment, since the bacteria does not need to be alive to create results. The CDC recommends the use of both cultures and a PCR assay to assess for pertussis in patients with a cough lasting more than 3 weeks.

Rapid elevations of WBC counts can also indicate severe disease. Chest x-rays can be performed, though they are generally not diagnostic. They can be helpful in diagnosing pneumonia or lung collapse[19,20,21].

Treatment

When treating pertussis patients, limiting the number of cough paroxysms, providing support during paroxysms, and maximizing rest, nutrition, and recovery are the goals of treatment. Oxygen and breathing treatments may be necessary to improve airflow in pertussis patients, and patients should be monitored for signs they are not getting enough oxygen, such as cyanosis.

Hospitalization is necessary in patients with failure to thrive, seizures, encephalopathy, intractable nausea or vomiting, severe dehydration, pneumonia, and in those patients requiring oxygen. Inpatient treatment should be considered in patients at risk for severe pertussis, such as infants under 6 months of age, premature infants, and infants and children with underlying heart, lung, or neurological disease. Adults over 65 years of age with underlying heart, lung, or neurological conditions may also require hospitalization.

Hospitalized patients should have their heart rates, respiratory rates, and oxygen saturation monitored, especially during coughing attacks, to ensure they are getting enough oxygen and the heart is functioning appropriately. Feeding, hydration, and weight changes should also be monitored, especially in infants. Droplet and standard precautions should be utilized for all hospitalized pertussis patients, and are recommended for 5 days after starting antibiotics, or until 3 weeks after the onset of paroxysmal cough if antibiotics are not used[19,20,21,24].

Antibiotic therapy

Antibiotics can help eradicate Bordatella pertussis to decrease communicability, and can change the course of illness to prevent severe pertussis if administered before the onset of cough. The disease course is generally not changed if antibiotics are administered in the paroxysmal stage, though they can still reduce communicability and prevent pneumonia.

There are several antibiotics that are effective against pertussis. Azithromycin, a macrolide antibiotic, can be used to treat pertussis in patients of all ages, and is often preferred because of the shorter course needed to complete treatment. Azithromycin should be used cautiously in patients with underlying heart conditions or arrhythmias due to the risk of electrical changes in the heart that can lead to arrhythmias. Infants under 6 months of age should receive doses of 10 mg/kg for 5 days; patients over 6 months of age should receive 10 mg/kg (up to 500 mg) on the first day, and 5 mg/kg (up to 250 mg) on days 2 to 5. Azithromycin is in pregnancy category B, and may be considered necessary in pregnant women.

Other macrolide antibiotics such as erythromycin or clarithromycin are also effective against pertussis, though they should only be used in patients 1 month of age and older due to the risk of infantile hypertrophic pyloric stenosis (IHPS), enlargement of the sphincter muscles connecting the stomach to the small intestine, causing
narrowing of the sphincter. Potential drug interactions should be monitored when using erythromycin or clarithromycin, since they are both inhibitors of the 3A subclass of the cytochrome P450 enzyme system in the liver and are involved in many drug interactions.

Erythromycin can be administered to both pertussis patients and close contacts over 1 month old in doses of 40 to 50 mg/kg/day, up to 2,000 mg/day, divided into four evenly spaced doses, for a total of 14 days. Erythromycin estolate is the preferred form of erythromycin because of its enhanced absorption, especially in infants. Clarithromycin can be used in patients over 1 month old in doses of 15 mg/kg/day, up to 1,000 mg/day, divided into two doses given every 12 hours for 7 days. Adverse reactions associated with macrolide antibiotics include diarrhea, nausea, vomiting, and abdominal pain.

Trimethoprim-sulfamethoxazole can be used in patients 2 months of age or older who are allergic to macrolide antibiotics. Infants and children over 2 months old can receive 8 mg/kg/day of trimethoprim and 40 mg/kg/day of sulfamethoxazole, divided into two doses given every 12 hours for 14 days. Adults can receive 320 mg trimethoprim and 1,600 mg sulfamethoxazole per day, divided into two doses given every 12 hours for 14 days. Common adverse reactions to trimethoprim-sulfamethoxazole include nausea, diarrhea, upset stomach, and hypersensitivity reactions.[23,24,25].

Other treatments

The use of corticosteroids or albuterol in pertussis patients is not supported by controlled studies, though their use may be necessary depending on the patient’s underlying conditions. Corticosteroids and albuterol should only be used on a case-by-case basis.[23,24].

Post-exposure prophylaxis

Antibiotics can prevent pertussis if administered before the onset of symptoms, but antibiotics must be used responsibly. The CDC supports the use of antibiotics for post-exposure prophylaxis in patients at high risk of developing severe cases of pertussis, as well as people who are in close contact with these patients. There is no information indicating that the widespread use of antibiotics for post-exposure prophylaxis against pertussis effectively controls outbreaks, and widespread antibiotic use increases bacterial resistance, so everyone who may have been exposed to pertussis outside of the household does not need antibiotic treatment.

Household contacts of pertussis patients should receive post-exposure prophylaxis with antibiotics effective against pertussis, regardless of their immunization status or age. The likelihood of acquiring pertussis from a family member who has an active pertussis case is high, even in households with contacts who are appropriately immunized. Antibiotics should be administered to asymptomatic household contacts within 21 days of the onset of cough in the original pertussis patient to prevent the spread of infection.

Outside of the household, post-exposure prophylaxis should be provided to people at high risk of developing severe cases of pertussis, as well as people in close contact with them. People at high risk of developing pertussis include infants under 12 months of age, pregnant women in their third trimester, people with comorbid conditions that can be exacerbated by infection with pertussis, people in contact with the aforementioned individuals, childcare workers, and health care workers that deal with children or pregnant women. People who have been exposed to pertussis multiple times should not repeat a course of antibiotics, as its effectiveness has not been shown and this practice increases the risk of resistance. People exposed multiple times should be monitored for signs and symptoms of pertussis for 21 days after the most recent exposure.

A 5-day course of azithromycin is the preferred antibiotic course for post-exposure prophylaxis, though a 14-day course of erythromycin or clarithromycin can be used if necessary. The same dosages can be used for treatment and post-exposure prophylaxis.

Vaccination

Prevention of whooping cough through immunization is the best defense against pertussis. However, a significant portion of the patients who develop severe or fatal cases of pertussis are infants who are too young to receive pertussis immunizations, so unique approaches must be used to ensure protection in these patients.[19,23,24,26].

Whole-cell pertussis vaccination

The whole-cell pertussis vaccination was first developed in the 1930s, and was widely used starting in the mid-1940s. Studies conducted in the 1940s determined that a primary series of pertussis vaccination using four doses of whole-cell pertussis, tetanus, and diphtheria vaccine was 70% to 90% effective at preventing severe pertussis. Studies found that immunity against pertussis decreased over time, and patients had little to no immunity within 5 to 10 years after the last dose of pertussis vaccine. Adverse local reactions developed in nearly half of patients who received the whole-cell pertussis vaccine. Reactions include pain, redness, and swelling at the injection site, as well as fever and other systemic reactions such as seizure or encephalitis. In response to concerns about adverse events, an acellular pertussis vaccination was developed and led to a decrease in adverse reactions following vaccination. The whole-cell pertussis vaccination was commonly used from the mid-1940s until the 1990s, and is no longer available in the United States, though it is still used in other countries.[19,23,24].

Acellular pertussis vaccination

The acellular pertussis vaccination is available in combinations with tetanus and diphtheria toxoids as well as with tetanus, diphtheria, hepatitis B, and inactivated poliovirus, and with tetanus, diphtheria, Haemophilus influenza type B, and inactivated poliovirus. Dosing regimens for these products are discussed in the section on tetanus. A single-antigen pertussis vaccination is not available. Vaccines containing pertussis for children under 7 years of age contain a higher dosage of pertussis antigens than the vaccines used for people over age 7, to induce an appropriate immune response in children.[19,23,24].

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## Efficacy of pertussis vaccination

Several studies conducted since 1991 in Europe and Africa have assessed the efficacy of DTaP in infants. The vaccines currently available in the United States were found to be 80% to 85% effective, and no single vaccine was found to be more effective than the others. The acellular vaccines were found to be significantly more effective and caused fewer adverse reactions than whole-cell pertussis vaccines, though whole-cell pertussis vaccines are no longer available in the United States[19].

## Vaccination schedule

The childhood vaccination schedule for administering four doses of DTaP follows the recommendations discussed in the section on tetanus. Children with suspected neurological conditions such as infantile seizures or encephalopathy should wait until their condition has been treated and stabilized before initiating the DTaP series.

Adolescents who have completed their primary series of DTaP vaccinations as children should receive one dose of Tdap at the 11- to 12-year-old wellness doctor visit. Adolescents and adults unvaccinated against tetanus, diphtheria, and pertussis should receive a primary series of three doses of Td as discussed in the section on tetanus, with the first dose administered as Tdap, to ensure adequate protection against pertussis.

Adults should receive booster doses of tetanus and diphtheria with the Td vaccine once every 10 years, and one dose of Td should be replaced with Tdap to ensure immunity against pertussis. If the tetanus vaccination is needed for wound management, patients should receive Tdap instead of Td if they have never received a dose of Tdap. Tdap can be given regardless of the time since the last dose of tetanus- or diphtheria-containing vaccine.

Adolescents, adults, and health care personnel who plan to care for infants under 12 months of age should receive a single dose of Tdap if they have not previously received Tdap, to reduce the chance of transmitting Bordetella pertussis to infants. Ideally, Tdap should be administered at least 14 days before beginning close contact with infants.

### Protecting infants and children

There is overwhelming evidence that infants are primarily infected with pertussis from parents, siblings, or caregivers that are carriers of Bordetella pertussis. One study conducted in the Netherlands found that 35% to 55% of infant pertussis cases could be prevented if the infant’s parents maintained or boosted their immunity. Vaccinating the whole family and potential close contacts against pertussis when an infant is born is crucial to preventing the spread of pertussis to infants[19,23,24].

### Tdap during pregnancy

Pertussis-containing vaccines are approved by the FDA for use in children 6 weeks and older, putting infants under 6 weeks of age at a high risk of developing pertussis. In an attempt to provide greater protection to young infants, the ACIP and the CDC recommend that pregnant women receive a dose of Tdap during each pregnancy, ideally between weeks 27 and 36, regardless of the mother’s pre-pregnancy history of Td or Tdap. Mothers who receive a dose of Tdap before conception should receive another between weeks 27 and 36 of pregnancy. Women who received a dose earlier in the pregnancy as part of a wound care regimen or during a community outbreak do not need another dose between weeks 27 and 36 of pregnancy; only one dose of Tdap is recommended with each pregnancy.

One dose of Tdap during pregnancy provides protection to the mother. It prevents her from acquiring pertussis and passing it to the infant, and provides passive immunity to the infant. Administration of Tdap between 27 and 36 weeks helps maximize the mother’s antibody response and promote the transfer of antibodies to the infant. Since antibodies to pertussis decrease over time, women should receive a new dose of Tdap with each pregnancy, to maximize the transfer of antibodies to each infant.

Providing Tdap during pregnancy rather than postpartum provides greater protection to the infant. Postpartum doses provide protection to the mother, but do not allow for the passive immunization of the infant. The lack of passive immunization puts the infant at risk of contracting pertussis from family members, caregivers, and other people. Postpartum doses also take approximately 2 weeks to become effective, putting the infant at risk of acquiring pertussis from the mother during this time.

To maximize protection of the infant against pertussis, caregivers, family members, and other people who will be in close contact with the infant should receive a dose of Tdap at least 2 weeks before contact with the infant[27].

A study that assessed the safety of the pertussis vaccine administered during pregnancy in 123,494 women found that the pertussis vaccine did not increase the risk of adverse birth outcomes. Tdap was the vaccine administered to 26,229 women in this study. Preterm delivery rates were estimated to be 6.3% in vaccinated women and 7.8% in unvaccinated women.

A small but statistically significant increase in the risk of chorioamnionitis, an infection of the membranes surrounding the fetus, was found in women vaccinated against pertussis during pregnancy; 6.1% of vaccinated women developed chorioamnionitis, while 5.5% of unvaccinated women developed this condition. The benefits of administering Tdap during pregnancy far outweigh the risks, and Tdap should be recommended to all pregnant women to ensure protection of the infant[30].

### Contraindications and precautions

Contraindications to the use of DTaP in children include severe allergic reactions to vaccine components and encephalopathy that develops within 7 days after administration of a pertussis-containing vaccination. Moderate or severe illnesses are considered to be a precaution to vaccination with DTaP, though children with mild illnesses such as ear infections should not delay administration of DTaP. Other precautions to administration of additional doses of DTaP include fever of 105 °F or higher within 48 hours of a dose of DTaP that is not due to another cause; development of a hypotonic hyporesponsive episode in which the child loses consciousness, becomes limp, and experiences shallow breathing within 48 hours of a dose of DTaP; inconsolable crying that lasts 3 hours or longer within 48 hours of DTaP; or convulsions with or without fever that occur within 3 days of a dose of DTaP. These responses are thought to be related to the pertussis component of DTaP, and the benefits and risks...
of additional doses of DTaP in patients with these conditions should be assessed on a case-by-case basis.

DTaP may also need to be deferred in children with suspected or known neurological conditions that have not been stabilized, such as uncontrolled epilepsy, encephalopathy, a history of seizures that has not been evaluated, or neurological conditions that develop between doses of DTaP. Family history and stable neurological conditions should not be considered contraindications to vaccination with pertussis-containing vaccinations.

Contraindications to the use of Tdap include a history of severe allergic reactions to vaccine components and encephalopathy that develops within 7 days after administration of a pertussis-containing vaccination. Precautions include moderate to severe acute illness, progressive, unstable neurological conditions such as seizures or encephalopathy, and a history of Guillain-Barré syndrome within 6 weeks of receiving a tetanus-toxoid containing vaccine. Patients with a history of developing severe local reactions to the Tdap vaccine should not receive another dose of Td or Tdap for 10 years after the last dose of Td-containing vaccine[19].

### Adverse reactions

Adverse reactions following administration of DTaP include local pain, redness, or swelling at the injection site, which has been reported in 20% to 40% of children who have received three doses of DTaP. Local reactions are more common after the fourth and fifth doses of DTaP, and can include limb swelling and itching. Mild systemic reactions such as lethargy, low-grade fever, and agitation are possible. Approximately 3% to 5% of children administered DTaP develop a fever of 101°F or higher. Moderate to severe reactions are rare, occurring in less than one patient per 10,000 doses administered. Moderate to severe reactions can include fever of 105 °F or higher within 48 hours; development of a hypotonic hyporesponsive episode in which the child loses consciousness, becomes limp, and experiences shallow breathing; inconsolable crying that lasts 3 hours or longer; or convulsions with or without fever.

The most common adverse reaction to Tdap is pain at the injection site, which occurs in 66% of patients. Redness and swelling occur in up to 25% of patients. Approximately 1.4% of patients receiving Tdap develop a fever of 100.4 °F or higher. Other reactions can include fatigue, headache, and upset stomach. No severe adverse reactions have been attributed to Tdap[19].

### Strategies for improving vaccination rates

Despite generally high vaccination rates in the United States, gaps in care exist, and health care professionals must remain diligent in encouraging vaccinations to maintain population immunity against contagious diseases. Several strategies have been utilized to maximize immunization rates among the U.S. population. Maintaining adequate records of immunizations is critical to ensure patients receive vaccinations at appropriate intervals. Immunization records must be accurate and include all necessary information on the vaccine administered to comply with state and local laws. Records should be updated as new immunizations are administered.

The maintenance of adequate immunization records can be simplified by the use of immunization information systems, or immunization registries. These computerized databases have the ability to record all doses of vaccines administered by participating providers. Immunization information is collected from various providers to create a single official immunization record for each patient, allowing for consolidated records that can be used in patient care. Immunization information systems have the ability to exchange information with health care providers who administer immunizations to ensure vaccines are given in a timely manner, consolidate records, and increase efficiency of immunization programs.

The recommendations of a health care provider can be a powerful tool to help motivate patients to comply with immunization schedules. Some patients are simply unaware that they are missing vaccinations, or they may not understand that return visits to complete vaccination schedules are necessary. Patients are more likely to receive timely vaccinations if they are encouraged to do so by a health care professional.

Reminder messages to patients can help them comply with immunization schedules. Reminders that vaccines are due soon, or past due, can help improve adherence to recommended immunization schedules. Providers can utilize automatic systems to notify patients when they are due or past due for vaccinations, simplifying the process and increasing vaccination rates.

Reducing the number of missed opportunities to vaccinate patients is also critical to improving vaccine schedule adherence. There are several reasons why opportunities to vaccinate may be missed. Providers may be reluctant to administer several vaccinations in one visit, despite the lack of evidence that this is harmful. Inability to access immunization records during a patient’s visit has also been cited as a reason for missed opportunities to vaccinate. Policies can also create missed opportunities for immunizations, such as only providing vaccinations at annual well child visits. Ensuring immunization records are available during all patients’ visits and that recommendations are followed for administering multiple vaccinations or vaccinating during mild illness can help improve overall vaccination rates.

Reducing barriers to immunization for patients can also impact immunization rates across populations. Physical barriers to immunization, such as inconvenient office hours for working adults and long wait times, can prevent patients from seeing a health care professional for immunizations. Providers must assess the needs of their patient population and take steps to minimize the number of physical barriers to timely receipt of vaccination.

Cost can also be a significant barrier to vaccination for many patients. Health care providers should utilize federal resources such as the Vaccines for Children program, as well as state-funded resources, to minimize the cost of vaccinations to patients to maximize immunization rates.

Psychological barriers to immunization can also play a role in reducing adherence to vaccination schedules. Fears of immunizations, previously unpleasant immunization experiences, and reluctance to listen to criticism for missed appointments can cause patients to delay the administration of vaccinations. Concerns about the safety of vaccinations and potential adverse reactions can also be considered a barrier to immunization. Overcoming these barriers requires collaboration and an open line of communication between the health care provider and the patient. Health care professionals should be prepared to provide knowledge and resources on vaccine safety and recommendations in a supportive environment to ease patient concerns[11].

### Conclusion

Vaccination against tetanus, diphtheria, and pertussis is the best method for preventing these potentially serious conditions. Immunizations should be offered to all appropriate patients based on the discussed immunization schedules. Health care professionals who
administer vaccinations have a responsibility to consider a patient’s reservations when offering vaccines, and correct any misconceptions the patient or caregiver may have regarding the safety and efficacy of vaccinations. Utilizing strategies to improve immunization rates such as maintaining adequate records, reminding patients to vaccinate, and collaboration between the patient and provider can help minimize barriers to immunization and maximize immunization rates, which, in turn, will minimize the spread of contagious diseases.

References


A REVIEW OF TETANUS, DIPHTHERIA AND PERTUSSIS FOR PHARMACISTS AND PHARMACY TECHNICIANS

Final Examination Questions

Choose the best answer for questions 1 through 10 and mark your answers online at PharmacyTech.EliteCME.com

1. Tetanus is often transmitted through wounds contaminated with __________, which can be found in soil and animal feces.
   a. Clostridium tetani.
   b. Saccharomyces tetani.
   c. Bordetella tetani.
   d. Corynebacterium tetani.

2. __________ is used to provide passive immunity to tetanus patients.
   a. DTAp.
   b. Pediarix.
   c. Tetanus immune globulin (TIG).
   d. Boostrix.

3. __________ is/are the first line of treatment for muscle spasms caused by tetanus.
   a. Benzodiazepines.
   b. Baclofen.
   c. Dantrolene.
   d. Vecuronium.

4. The vaccine of choice in children aged 6 weeks to 6 years is the __________ vaccine.
   a. Tdap.
   b. DT.
   c. Td.
   d. DTAp.

5. The average mortality rate of diphtheria is around __________.
   a. 50% to 60%.
   b. 1% to 2%.
   c. 5% to 10%.
   d. 25%.

6. Diphtheria patients are generally not contagious after they have been taking antibiotics for __________.
   a. 24 hours.
   b. 48 hours.
   c. 7 days.
   d. 14 days.

7. The first stage of pertussis is known as the __________, during which mucous membranes of the respiratory passages become inflamed and create a thick mucus.
   a. Paroxysmal stage.
   b. Convalescent stage.
   c. Catarrhal stage.
   d. Postpartum stage.

8. __________, a macrolide antibiotic, can be used to treat pertussis in patients of all ages, and is often preferred because of the shorter course needed to complete treatment.
   a. Azithromycin.
   b. Penicillin.
   c. Amoxicillin.
   d. Trimethoprim-sulfamethoxazole.

9. A 5-day course of __________ is the preferred antibiotic course for post-exposure prophylaxis against pertussis.
   a. Clarithromycin.
   b. Clindamycin.
   c. Azithromycin.
   d. erythromycin.

10. The maintenance of adequate immunization records can be simplified by the use of __________.
    a. Paper records.
    b. Immunization information systems.
    c. Electronic prescribing systems.
    d. Bar code technology.