Bordetella pertussis (Pertussis)

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Education Gaps

1. Clinicians must understand the changing epidemiology of pertussis and the reasons for the endemic and epidemic nature of infection despite widespread vaccination.
2. Clinicians must understand the strategies developed to prevent pertussis in those who are at high risk for complications.

Objectives

After completing this article, readers should be able to:

1. Recognize the antigenic components of pertussis.
2. Understand the changing epidemiology of the disease and the major factors contributing to this change.
3. Describe the clinical features during the natural progression of pertussis and the complications of infection.
4. List the options for laboratory testing of pertussis and their respective limitations.
5. List the recommended agents for antimicrobial treatment and postexposure chemoprophylaxis of pertussis.
6. Understand the rationale for the current pertussis vaccine recommendations.

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ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
DTaP	diphtheria, tetanus, and acellular pertussis vaccine
DTwP	diphtheria, tetanus, and whole cell pertussis vaccine
IHPS	infantile hypertrophic pyloric stenosis
PCR	polymerase chain reaction
Tdap	tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine
Th	T-helper

INTRODUCTION

Bordetella pertussis is a fastidious gram-negative coccobacillus responsible for the respiratory infection commonly known as "whooping cough." The organism is spread by respiratory droplets and is highly contagious among close contacts. The typical incubation period is 7 to 10 days, but it may be as long as 21 days. Neither natural infection nor pertussis vaccination results in long-lasting immunity, contributing to endemic infection and 3- to 5-year cycles of pertussis epidemics.

PATHOGENESIS

Several active components, which play a role in immunity and are responsible for the organism's ability to cause disease, are produced by *B pertussis*. (1) Pertussis toxin, filamentous hemagglutinin, pertactin, and agglutinogen allow the organism to adhere to ciliated epithelium of the respiratory tract, where it exerts its effects.

Pertussis toxin also induces cell cytoxicity, inhibits neutrophilic and monocytic responses, and delays induction of specific immune responses. Pertussis toxin is postulated to be responsible for the systemic manifestations of pertussis, including the leukocytosis and lymphocytosis evident in young infants. This virulence factor is also thought to sensitize β-islet cells in the pancreas, which may lead to hyperinsulinism, which rarely manifests as hypoglycemia in young infants. Other substances elaborated by the organism include adenylate cyclase and tracheal cytotoxin, which allow the bacteria to cause damage to the respiratory epithelium and evade the host immune system by altering leukocyte function. Pertussis vaccines contain these various antigenic components. Central nervous system complications of pertussis are thought to be secondary to hypoxemia induced by coughing and apnea associated with infection rather than to a direct effect on the central nervous system by the organism. (2)

EPIDEMIOLOGY

In the 1940s, before the introduction of pertussis vaccine in the United States, there were 100,000 to 200,000 cases of whooping cough and thousands of deaths annually. After the introduction of pertussis vaccine, there was a 99% decrease in the number of cases; the lowest number of cases was in 1976, with only 1,010 cases reported. Over the past few decades there has been an increasing incidence of pertussis (Fig 1). According to the Centers for Disease Control and Prevention (CDC), there were 48,277 cases reported in the United States in 2012, the highest number of cases since 1955. (3) Worldwide, pertussis is responsible for 16 million cases and approximately 195,000 deaths annually. (4)

Historically, the incidence of pertussis peaked in children 1 to 5 years of age and was less common in those younger than 1 year and older than 10 years. There has been a shift in recent decades with an increase in the incidence among infants younger than 1 year, adolescents, and adults (Fig 2). In 2015, 55% of reported pertussis cases in the United States were in individuals older than 10 years, and children younger than 1 year accounted for 13% of cases. (5)

There are multiple factors that seem to be responsible for the change in epidemiology of pertussis: the switch from whole cell pertussis vaccine to acellular pertussis vaccine, waning immunity, change in the organism, vaccine refusal, lack of natural disease to boost immune response, and undiagnosed individuals serving as reservoirs.

Switch from Whole Cell Pertussis Vaccine to Acellular Pertussis Vaccine

Concerns about the reactogenicity of the diphtheria and tetanus toxoids and whole cell pertussis vaccine (DTwP) lead to the development and introduction of the diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP). The DTaP was incrementally introduced into the US pediatric immunization schedule starting in 1992, with all children receiving only the DTaP by 1997. (6) Acellular pertussis vaccines are significantly less reactogenic than whole cell vaccines.

Recent studies during epidemic outbreaks in Australia demonstrated that children who received the DTwP series

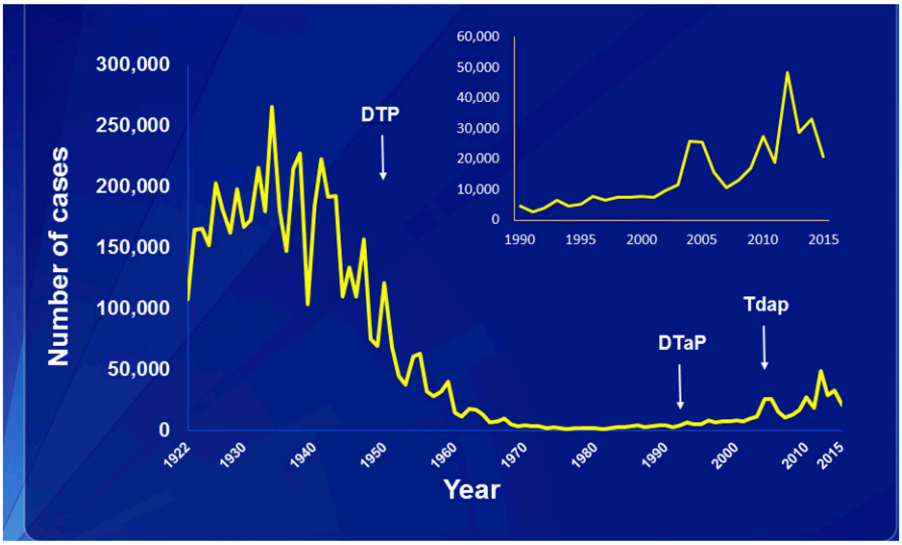

Figure 1. Reported pertussis cases, 1922-2015. From the Centers for Disease Control and Prevention National Notifiable Diseases Surveillance System for 1950 through 2015 and from passive reports to the Public Health Service from 1922 through 1949.
DTP=diphtheria, tetanus toxoids, and pertussis vaccine, DTaP=diphtheria, tetanus, and acellular pertussis vaccine, Tdap=tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine.

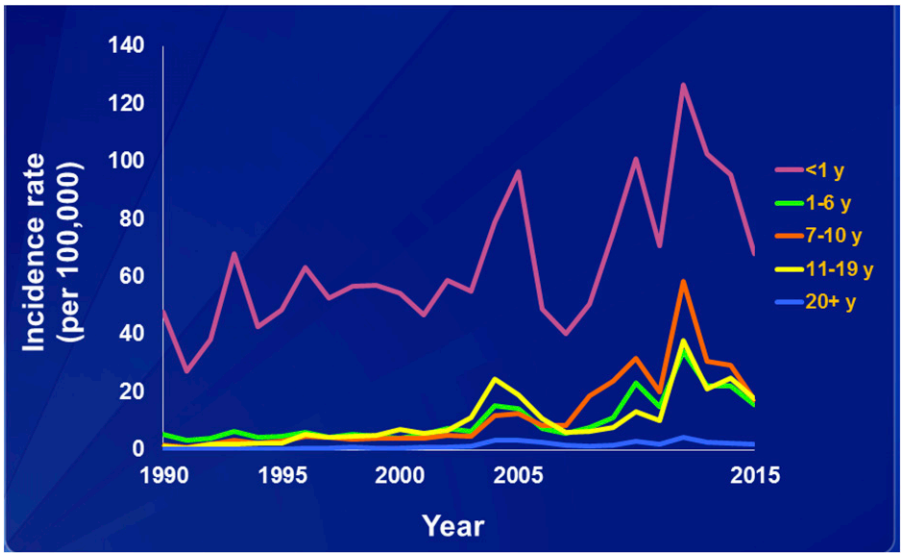

Figure 2. Pertussis incidence by age group, 1990-2015. From the Centers for Diseases Control and Prevention National Notifiable Diseases Surveillance System.

had lower rates of pertussis than those who received the DTaP series. (7) This effect may be related to the different responses elicited by the 2 types of vaccines: the whole cell pertussis vaccine activates T-helper (Th) type 1 cells, and the acellular pertussis vaccine elicits a Th2 response. The Th1 responses result in robust interferon-γ production, which is required for cell-mediated immunity and rapid clearance of the organism on repeated exposure, whereas Th2 responses do not seem to have the same effect on interferon-γ, resulting in less effective clearing of the organism from the respiratory tract after infection. Thus, humoral immunity provided by acellular pertussis vaccines seems to be effective at preventing severe disease but may lack the cellular responses needed to effectively eradicate the infection from the respiratory tract. (7)(8)(9)(10)(11)(12)(13)(14)

Waning Immunity

Neither natural infection nor vaccination induces lifelong immunity. Recent studies demonstrate that immunity wanes 4 to 20 years after natural infection and 4 to 12 years after vaccination. (15) After pertussis outbreaks in California in 2010 and 2014, it was determined that patients who developed pertussis were more likely to have had a longer period of time since their last DTaP or tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap). (16)(17) More specifically, immunity began to wane 5 years after the last DTaP, with a 42% increase in the odds of developing pertussis each year thereafter. (16) These studies also determined that immunity began to wane 2 to 3 years after Tdap vaccination. (17) Another study showed that the odds of pertussis increased 1.33 times per year after the last DTaP, with only an estimated 10% of children retaining immunity 8.5 years after the last immunization. (18)

Change in the Organism

Current vaccines contain various antigens to components of *B pertussis,* such as pertussis toxin, fimbriae, pertactin, and filamentous hemagglutinin. Since the introduction of the whole cell and acellular vaccines there have been genetic changes of *B pertussis*. Variants that are emerging include allele changes to the genes that code for pertactin (*prn2*), pertussis toxin promoter (*ptxP3*), and fimbriae (*Fim3*). (6)(19)(20)(21) Studies in Europe and Asia have demonstrated that current pertussis strains are different from when the vaccines were developed, which may be limiting the memory provided by vaccination. (20)(21) In addition, the adaptation of these components may make the organism more virulent and adept to evade the immune response. (19)

Vaccine Refusal

There is concern that vaccine hesitancy or refusal has contributed to the resurgence of preventable diseases, especially measles and pertussis. Phadke et al (22) reviewed the analysis of 32 pertussis outbreaks and found high percentages of unvaccinated individuals (24%–45%) in the states with the largest outbreaks, with a significant proportion of individuals (59%–93%) unvaccinated by choice.

Lack of Natural Disease to Boost Immune Response

Some have proposed that with decreased rates of pertussis since vaccine development there are fewer cases of pertussis to which an individual is exposed during their life, thereby limiting the chance to naturally boost the immune memory

to the infection. Without these exposures to less severe cases, an individual's immunity continues to wane without a boosted response. (15)

Undiagnosed Individuals Serving as Reservoirs

Last, adolescents and adults with pertussis may not manifest classic or severe symptoms of pertussis, resulting in underreporting of infection in these age groups. These individuals, however, serve as important reservoirs of infection and commonly transmit pertussis to infants and younger children who are unvaccinated or have been incompletely vaccinated or who may have waning immunity after vaccination. (23) Several studies have documented that adolescents and adults have an important role in transmission of the organism and that pertussis is a common cause of prolonged cough illness in these individuals. (24)(25)

CLINICAL PRESENTATION

Pertussis is typically divided into 3 stages: catarrhal, paroxysmal, and convalescent. Progression through these stages and symptoms varies among individuals, especially based on the patient's age.

Catarrhal Stage

The catarrhal stage typically begins 1 to 2 weeks after exposure to *B pertussis*. Symptoms at this time are nonspecific (cough, coryza, and low-grade fever) and may be confused with an upper respiratory tract infection. During this 1- to 2-week phase, individuals are contagious without realizing that they have pertussis. Infants may have a very short catarrhal phase before progressing to the next stage.

Paroxysmal Stage

Classical symptoms of whooping cough begin to be evident during this stage, which can last approximately 1 month. Children develop paroxysmal episodes of cough followed by an inspiratory "whoop" sound at the end of the episode. This high-pitched whoop sound is caused by rapid airflow during a forced inhalation after a repetitive coughing episode during which the lung is devoid of air and the glottis is partially closed. During the coughing episodes, cyanosis, especially perioral cyanosis in young children, and posttussive emesis are common; however, between episodes infants and children generally appear well. Individuals with pertussis may experience fatigue and exhaustion from lack of sleep and decreased appetite caused by persistent coughing. Fever is characteristically absent during pertussis infection; its presence should prompt a search for secondary bacterial infection.

Infants and older individuals may have less classic symptoms during this stage. Infants may present with apnea, cyanosis, and gagging during the coughing spell without the classical whoop sound. Adolescents and adults also may lack the typical whoop sound at the end of coughing spells; however, the presence of a whoop sound or posttussive emesis in adults should raise suspicion for pertussis. (26)

Convalescent Stage

Diminished severity and frequency of cough paroxysms characterize this stage, which signify recovery from pertussis. However, because pertussis is also known as "the 100-day cough," this stage can last from weeks to months and is often exacerbated by intercurrent respiratory illness, especially in infants.

DIFFERENTIAL DIAGNOSIS

Adenovirus

Adenovirus can cause an illness of severe prolonged paroxysmal cough associated with an inspiratory whoop and posttussive emesis. The presence of pharyngitis, conjunctivitis, gastrointestinal symptoms and fever commonly associated with adenovirus infection can help distinguish this from pertussis.

Mycoplasma pneumoniae

Mycoplasma pneumoniae is a common cause of prolonged cough and pneumonia in school-aged children. The presence of other systemic symptoms, such as fever and pharyngitis, along with auscultatory (crackles) and chest radiographic findings can help differentiate this from pertussis.

Chlamydia trachomatis

Infants with *Chlamydia trachomatis* pneumonia may have a cough illness that may be difficult to distinguish from pertussis. The cough is more commonly described as a staccato cough, with inspiration between each cough. These infants may also have tachypnea and crackles, and 50% of them have a history of conjunctivitis. On laboratory evaluation they commonly have a normal white blood cell count and an elevated eosinophil count.

Respiratory Syncytial Virus

Respiratory syncytial virus is a common cause of respiratory infection in infants and may present with cough and apnea. Wheezing, fever, and significant rhinorrhea or congestion may help differentiate this from pertussis. Coinfection with pertussis and respiratory syncytial virus is well described.

Other *Bordetella* Species

Bordetella parapertussis causes a pertussis-like syndrome and accounts for approximately 5% of *Bordetella* isolates in the United States. Compared with *B pertussis*, the paroxysms and whoop are less severe, the posttussive emesis is less frequent, and the total duration of cough is shorter. (27)

COMPLICATIONS AND OUTCOMES

Young infants (<6 months old) with pertussis have the highest rates of morbidity and mortality compared with older infants, children, and adolescents. Complications in these young infants include secondary bacterial pneumonia, apnea, bradycardia, and pulmonary hypertension. Bacterial pneumonia is the most common complication of pertussis, occurring in approximately 5% of all cases and in approximately 10% to 25% of infants younger than 6 months. During coughing spells, infants may become hypoxic, leading to central nervous system complications, including seizures and encephalopathy. (2) Because of its propensity to cause apnea in young infants, pertussis has been proposed as a cause of sudden infant death syndrome. (28)

Additional complications include otitis media, dehydration, conjunctival/scleral hemorrhages, petechiae, rib fractures, subcutaneous emphysema, and pneumothorax.

DIAGNOSIS (TABLE 1)

Culture

Until recently, the gold standard for diagnosing pertussis was a positive respiratory culture for *B pertussis*. Culture also allows for strain typing and antimicrobial testing, which is useful for public health tracking. Culturing for the organism, however, is fraught with difficulty because it requires obtaining a sample within the first 2 weeks of illness, using a specific swab (calcium alginate or Dacron-tipped swab) for collection, immediate inoculation on solid media or transport in special media (Stainer-Scholte broth with cyclodextrin or Regan-Lowe semisolid transport media), and incubation at 95°F to 98.6°F (35°C–37°C) for 7 days, to maximize the yield for isolating the organism. Previous immunization or recent antimicrobial treatment can lower the yield of the culture.

Polymerase Chain Reaction

Polymerase chain reaction (PCR) testing is the "new" gold standard and is now more commonly used to diagnose pertussis because it allows for a more rapid result and seems to be more sensitive than culture, especially in individuals who are mildly symptomatic and in those who received antibiotics. It requires collection of a nasopharyngeal specimen using a Dacron swab or nasopharyngeal aspirate. The PCR test is most sensitive if obtained within the first 3 to 4 weeks of illness. (29) Overall sensitivity and specificity vary based on the performing laboratory, and it is important to note that there is no standard PCR assay. False-positives may occur due to contamination from other samples.

Serology

Serologic testing is helpful in epidemiologic studies of pertussis but have a limited role in the clinical setting.

TABLE 1. **Diagnostic Testing for Pertussis**

TEST	TIMING	ADVANTAGES	DISADVANTAGES	COMMENTS
Culture	First 2 wk of illness	100% specific; allows for strain typing for public health tracking	Difficult to grow, especially with history of treatment or vaccination; results delayed (~1 wk)	Must be collected on Dacron or calcium alginate swab with immediate plating on appropriate media or transport media
Polymerase chain reaction (PCR)	Within the first 3–4 wk of illness	More rapid results, does not require live bacteria	False-positives and false-negatives; no standard PCR assay; laboratory dependent	Cannot use calcium alginate swab to collect
Serology	After 2 wk of symptoms	May be helpful later in the course of the illness if rising titer or seroconversion	Not sensitive or specific; no defined cutoff values for positive tests	Not used for diagnostic purposes; used for epidemiologic studies
Direct fluorescent antibody	No longer recommended			

Adapted with permission from Centers for Disease Control and Prevention Pertussis Laboratory Testing.

Acute and convalescent titers against pertussis antigens are generally required for serologic diagnosis. However, such testing is difficult to interpret in immunized individuals, specific cutoff data are not available, and these tests are not licensed for commercial use.

Direct Fluorescent Antibody Testing

Direct fluorescent antibody testing of nasopharyngeal specimens for pertussis antigens is no longer recommended. These tests have poor sensitivity compared with culture and PCR and require experienced laboratory personnel.

Supporting Laboratory Testing and Imaging

Leukocytosis, specifically absolute lymphocytosis, is common in infants and young children with pertussis, especially in the late catarrhal and paroxysmal stages. The degree of lymphocytosis correlates with the severity of disease. (30)(31)(32) The presence of absolute lymphocytosis in the setting of an appropriate clinical scenario should raise suspicion for the possibility of pertussis, keeping in mind that normal lymphocyte counts vary with age. Thrombocytosis is common and correlates with a poorer prognosis in infants. Chest radiography may reveal nonspecific findings, such as hyperinflation and perihilar infiltrates, but most often is normal.

MANAGEMENT

Antimicrobials

Antimicrobial therapy (Table 2) is recommended to eliminate the organism from the nasopharynx and, thus, reduce transmission of the organism. In general, antimicrobial therapy does not influence the clinical course of pertussis, although it may reduce the duration and severity of symptoms if administered before the paroxysmal stage. A recent case-control study of infant deaths from pertussis concluded that early recognition and appropriate antibiotic therapy are important in preventing death. (33) Therapy should be given to any infant younger than 1 year within the first 6 weeks of symptoms and anyone older than 1 year within the first 3 weeks if pertussis is suspected. (34)

Macrolides (azithromycin, clarithromycin, and erythromycin) are the preferred class of antibiotics to treat pertussis. Azithromycin is most commonly used because it has less adverse effects and is easier to administer. When

TABLE 2. **Therapeutic and Chemoprophylactic Options for Pertussis**

AGENT	INFANTS (<1 MO)	INFANTS (1–5 MO)	CHILDREN (>6 MO)	ADULTS	NOTES
Primary Therapy					
Azithromycin (first line, drug of choice)	10 mg/kg once daily × 5 d	10 mg/kg once daily × 5 d	Day 1: 10 mg/kg (max, 500 mg) once; days 2–5: 5 mg/kg (max, 250 mg) once daily	Day 1: 500 mg Days 2–5: 250 mg	Preferred agent. Caution in patients with underlying cardiac disease (can prolong QTc)
Erythromycin	Not recommended	40–50 mg/kg per day (max, 2 g/d) divided 4 times daily × 14 d	40–50 mg/kg per day (max, 2 g/d) divided 4 times daily × 14 d	2 g/d divided 4 times daily × 14 d	Gastrointestinal adverse effects
Clarithromycin	Not recommended	15 mg/kg per day (max, 1 g/d) divided twice a day × 7 d	15 mg/kg per day (max, 1 g/d) divided twice a day × 7 d	1 g/d divided twice a day × 7 d	Not palatable
Alternative Agent					
TMP-SMX	Contraindicated in infants <2 mo of age	TMP 8 mg/kg per day (max, 320 mg/d); SMX 40 mg/kg per day divided twice a day × 14 d **Contraindicated in infants <2 mo of age*	TMP 8 mg/kg per day (max, 320 mg/d); SMX 40 mg/kg per day divided twice a day × 14 d	TMP 320 mg; SMX 1,600 mg/d divided twice a day × 14 d	Contraindicated in infants <2 mo old

Max=maximum, TMP-SMX=trimethoprim-sulfamethoxazole.
Adapted with permission from Tiwari T, Murphy TV, Moran J, et al; National Immunization Program, CDC. Recommended antimicrobial agents for treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. *MMWR Recomm Rep* 2005;54(RR-14):10.

erythromycin is used, the estolate form is preferred because of its superior serum and respiratory tissue concentrations compared with the ethylsuccinate and stearate forms. Trimethoprim-sulfamethoxazole may be used as an alternative agent in rare clinical situations when macrolides are not tolerated, there is clear severe allergy to macrolides, or in cases of macrolide-resistant strains.

Treatment of infants with pertussis requires specific considerations. Infants younger than 6 weeks must be monitored for infantile hypertrophic pyloric stenosis (IHPS), which is associated with macrolide therapy, for 1 to 2 months after treatment. (35) Azithromycin is the preferred treatment because it seems to be less associated with IHPS than is erythromycin, although cases of IHPS have also been associated with azithromycin. (35)(36)(37) It must be stressed that the benefit of macrolide therapy outweighs the risk of IHPS, and such therapy should not be withheld for a young infant with pertussis. Trimethoprim-sulfamethoxazole is contraindicated in children younger than 2 months.

Supportive Care

Because antimicrobial therapy for pertussis may not be effective at the time of diagnosis, supportive care is the mainstay of management. Any infant younger than 6 months with suspected pertussis should be admitted to the hospital to monitor for progression of the illness and associated complications and to educate family members before discharge. (38) The duration of hospitalization depends on the clinical course, including the severity of cough episodes, ability to tolerate feeds, presence of apnea and bradycardia, and presence of other complications, such as pneumonia. Although cough may persist for weeks to months, the severity and frequency of these wane with time. Infants have an increased risk of mortality from pertussis, with 1 in 100 infants hospitalized for pertussis succumbing to the infection. (23)

Episodes of apnea may require mechanical ventilation. Infants with severe disease should be monitored for the development of pulmonary hypertension. (38) Patients with extreme leukocytosis may require exchange transfusion.

CONTROL MEASURES

Chemoprophylaxis

Postexposure chemoprophylaxis is recommended for asymptomatic close contacts and high-risk individuals. The CDC defines a close contact as "a person who had face-to-face exposure within 3 feet of a symptomatic patient; direct contact with respiratory, oral or nasal secretions; or shared the same confined space in close proximity with a symptomatic patient for ≥ 1 hour."(34) Chemoprophylaxis for high-risk individuals should be determined on a case-by-case basis. High-risk individuals include infants younger than 12 months, pregnant women in their third trimester, immunocompromised individuals, those with preexisting health conditions that may be worsened by pertussis, and individuals with close contact with high-risk individuals.

Chemoprophylaxis is most effective if given within the first 3 weeks after exposure and is recommended for all close contacts regardless of age or immunization status because previous immunization may not always prevent infection. Chemoprophylactic agents to be used, dosages, and duration of chemoprophylaxis are identical to the treatment regimens shown in Table 2. Any household contact of a patient with pertussis who is symptomatic should be treated as having pertussis.

Immunization

Immunization with a pertussis vaccine (DTaP or Tdap) is recommended for all exposed individuals who do not have an age-appropriate complete immunization history for pertussis.

Infection Prevention Measures

Droplet precautions are recommended for hospitalized patients with suspected or proven pertussis for 5 days after beginning therapy or for 21 days from initial coughing illness if no treatment was given.

Transporting of patients with proven or suspected pertussis in the ambulatory setting, such as from a pediatrician's office to a laboratory or radiology suite, should include communication among health-care workers regarding the appropriate use of droplet precautions.

Individuals exposed to a person with pertussis should be monitored for symptoms for up to 21 days. They should be excluded from child care facilities, school, and visitation at the hospital for 5 days after starting chemoprophylaxis or for 21 days if no treatment was given and they are not symptomatic.

PREVENTION

Vaccination is the primary method to prevent pertussis infections (Table 3). The specific composition of pertussis vaccines varies around the world, with some countries still using whole cell vaccines. In the United States, whole cell pertussis vaccine was initially introduced in the 1940s and was transitioned to only acellular vaccines for all recommended pertussis immunizations by 1997.

Primary Series

The current recommended schedule in the United States for pertussis vaccination is DTaP at 2, 4, and 6 months; 15 to 18 months; and 4 to 6 years of age; the fifth and final dose need not

TABLE 3. **Recommended Pertussis Vaccines**

PERTUSSIS-CONTAINING VACCINE RECOMMENDED	AGE
DTaP	2, 4, and 6 mo 15–18 mo 4–6 y
Tdap	7–10 y *(if incomplete vaccination prior)* 11–12 y Adults age ≥18 y *(once in place of tetanus booster)* Pregnant women *(once with each pregnancy)*

DTaP=diphtheria, tetanus, and acellular pertussis vaccine, Tdap=tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine. Based on Centers for Disease Control and Prevention Pertussis Vaccine Recommendations. Combination vaccines may be used for appropriate ages.

be given if the fourth dose was given at 4 years or older. Vaccine effectiveness after the primary series is 80% to 90%. (39)

Booster Doses

After the transition to DTaP, there was an increase in pertussis cases noted in 2005, especially in the cohort that received only DTaP and were approximately 5 years from their last dose (Fig 1). Findings in the US data mirrored findings in Australia after their transition to the acellular pertussis vaccine. (7) Based on these data, Tdap booster was recommended for 11- to 12-year-olds starting in 2005. Also, Tdap is recommended for any individual aged 7 to 10 years who has not previously been vaccinated or has been incompletely vaccinated with pertussis vaccine. (40)

Recommendations for Tdap vaccination have been expanded over the past several years based on changing epidemiologic data, including increased cases in infants younger than 12 months, which is associated with high mortality. Recommendations for booster doses for adults and pregnant women were made to address the issue of undiagnosed adult cases serving as a reservoir leading to severe infection in infants. In addition to the Tdap booster doses at 11 to 12 years old, all adults who have not previously received a Tdap should receive 1 dose of Tdap in place of routine tetanus vaccination. It is also recommended that pregnant women receive Tdap with each pregnancy at 26 to 37 weeks' gestation, ideally earlier during this period to allow for transfer of antibodies to the infant. (41) These recommendations are part of a cocooning strategy to prevent severe disease in young infants. This strategy uses vaccination of close contacts, such as parents, grandparents, and other caregivers, to help protect high-risk individuals. Although the cocooning strategy has been challenging, it is currently the best method available to protect infants who are too young to be vaccinated. (23)

Adverse Events and Contraindications

Local reactions to pertussis vaccines are the most common adverse events in infants after pertussis immunization and include erythema, swelling, and tenderness at the site of injection, and they are often accompanied by sleepiness, restlessness, vomiting, and low-grade fever. Entire limb swelling involving the thigh or the arm occurs in 2% to 3% of vaccines after the fourth or fifth dose of pertussis vaccine. Erythema, pain, and fever often occur in conjunction with the limb swelling, which resolves spontaneously and rarely limits a child's activity.

Systemic reactions to pertussis vaccination occur much less frequently after DTaP than after DTwP and include:

- Prolonged severe crying for 3 or more hours occurring within 48 hours of vaccination
- Seizures, most of which are febrile seizures
- Hypotonic-hyporesponsive episodes
- High fever (temperature ≥104.9°F [≥40.5°C])

Because these reactions do not result in any long-term sequelae, they are not contraindications to subsequent pertussis vaccination. (29)

According to the American Academy of Pediatrics Committee on Infectious Diseases, the only true contraindications to pertussis vaccination include a previous anaphylactic reaction to a previous dose or a vaccine component, and an encephalopathy occurring within 7 days of a previous dose of pertussis-containing vaccine that is not attributable to another cause. (29)

Local events after pertussis vaccination in adolescents are common and include redness, swelling, and pain at the injection site. Severe arm swelling in this population is rare and self-limited. Systemic signs of illness, such as fever, headache, and fatigue, are common. Syncope is more common in adolescents than in infants and young children.

Summary

- Based on strong research evidence, the epidemiology of whooping cough is changing. (3)(5)
- Based on strong research evidence, many factors seem to be contributing to the changing epidemiology of pertussis, including the exclusive use of acellular pertussis vaccines, waning immunity, changes to the organism, vaccine refusal, and undiagnosed cases. (7)(16)(17)(18)(19)(20)(21)(22)(23)(24)(25)
- Symptoms of perioral cyanosis during coughing spells, posttussive emesis, and prolonged coughing illness all should raise concern for pertussis.
- Based on strong research evidence, although there has been an increase in incidence among children younger than 1 year and older than 10 years, the more severe complications are seen in infants younger than 6 months. (4)
- Based on some research evidence, early recognition of pertussis and appropriate antimicrobial therapy in infants may be associated with lower mortality. (33)
- Vaccination is the primary method to prevent pertussis; current immunization recommendations are based on changing epidemiology.

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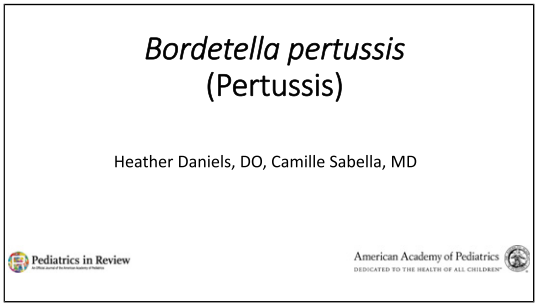

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1. A 7-week-old infant presents to your office with a history of cough for 4 days. The baby was born full term and without complications. There is no other significant medical history. The mother reports that overnight she noted several short episodes of apnea and is concerned that the baby has been feeding poorly. The baby is afebrile. There is a 5-year-old sibling in the home who has been healthy and has had all regularly recommended vaccinations. On further interview, the mother tells you that the maternal grandmother, who has been helping care for the infant, has had a "terrible" cough for the past 2 weeks with some posttussive emesis. The grandmother had received whole cell pertussis vaccine many years ago. What is the most likely epidemiologic factor leading to the transmission of pertussis to the infant in this scenario?
   A. Children aged 1 to 5 years are an important reservoir of pertussis infection.
   B. The acellular pertussis vaccine that is used now seems to be more effective than whole cell pertussis vaccine.
   C. There has been consistency in the *Bordetella pertussis* organism over time, leading to poor vaccine efficacy.
   D. There is waning immunity, leading to more transmission from adolescents and adults.
   E. Vaccine refusal has most likely contributed to the infant contracting pertussis.
2. A 3-month-old infant is brought to the emergency department after 6 days of cough, poor sleep, and some gagging with feeds. The parents also report some mild nasal congestion and coryza the week before development of the cough. The child has not yet received his 2-month vaccines. While being examined in the emergency department, the baby has a violent coughing episode and briefly becomes apneic, cyanotic, and limp but quickly recovers after approximately 20 seconds and begins to cry. You decide to admit the infant to the hospital for further evaluation and monitoring. What is the most common complication of this illness that you would be concerned about in this child?
   A. Encephalitis.
   B. Otitis media.
   C. Pneumonia.
   D. Pneumothorax.
   E. Rib fractures.
3. A 2-month-old infant presents to your office with a cough. The mother describes a recent upper respiratory tract illness without fever. She says that the cough started 4 days earlier, is paroxysmal in nature, with posttussive emesis and brief periods of apnea. You are concerned for pertussis infection. What is the best method of diagnosis of *B pertussis*?
   A. Direct fluorescent antibody testing.
   B. Rapid antigen testing.
   C. Respiratory culture.
   D. Polymerase chain reaction testing.
   E. Serologic testing.
4. An infant is hospitalized with confirmed pertussis infection, and macrolide therapy is initiated. There are 2 other siblings in the home, ages 3 and 6 years, who are both up to date with their vaccinations, including pertussis. The parents are concerned about the other children in the home becoming ill. What would you recommend for the siblings at this time?
   A. An immediate booster vaccine with diphtheria, tetanus, and acellular pertussis vaccine (DTaP) is recommended for both siblings.
   B. Begin macrolide therapy for both siblings and any other household contacts.

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C. No chemoprophylaxis treatment is necessary because the siblings have both been vaccinated.
D. Test both siblings for *B pertussis* infection, and if the test result is positive, begin chemoprophylaxis.
E. Vaccination with DTaP is recommended for the siblings if they are considered high risk.

5. An 8-year-old who recently immigrated to the United States from Guatemala has not received all the recommended US vaccinations. In addition to other catch-up vaccines, what is the current recommendation for the child in terms of pertussis vaccination?
   A. A DTaP is indicated at this time.
   B. A tetanus and diphtheria (Td) vaccine is indicated at this time.
   C. A tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine is indicated at this time.
   D. Both a Td and a DTaP are indicated at this time.
   E. Pertussis vaccine alone is indicated.

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