

Diphtheria

DIPHThERIA IS AN ACUTE, TOXIN-MEDIATED DISEASE caused by *Corynebacterium diphtheriae*. The name of the disease is derived from the Greek *diphthera*, meaning leather hide. The disease was described in the 5th Century B.C. by Hippocrates, and epidemics were described in the 6th Century A.D. by Aetius. The bacterium was first observed in diphtheritic membranes by Klebs in 1883 and cultivated by Löffler in 1884. Antitoxin was invented in late 19th century, and toxoid was developed in the 1920s.

Corynebacterium diphtheriae

C. diphtheriae is an aerobic gram-positive bacillus. Toxin-production (toxigenicity) occurs only when the bacillus is itself infected (lysogenized) by a specific virus (bacteriophage) carrying the genetic information for the toxin (tox gene). Only toxigenic strains can cause severe disease.

Culture of the organism requires selective media containing tellurite. If isolated, the organism must be distinguished in the laboratory from other *Corynebacterium* species that normally inhabit the nasopharynx and skin (e.g., diphtheroids).

There are three biotypes — *gravis*, *intermedius*, and *mitis*. The most severe disease is associated with the *gravis* biotype, but any strain may produce toxin. All isolates of *C. diphtheriae* should be tested by the laboratory for toxigenicity.

Pathogenesis

Susceptible persons may acquire toxigenic diphtheria bacilli in the nasopharynx. The organism produces a toxin that inhibits cellular protein synthesis and is responsible for local tissue destruction and membrane formation. The toxin produced at the site of the membrane is absorbed into the bloodstream and then distributed to the tissues of

Diphtheria

- Greek *diphtheria* (leather hide)
- Recognized by Hippocrates in 5th century B.C.
- Epidemics described in 6th century
- *C. diphtheriae* described by Klebs in 1883
- Toxoid developed in 1920s

Corynebacterium diphtheriae

- Aerobic gram-positive bacillus
- Toxin production occurs only when *C. diphtheriae* infected by virus (phage) carrying tox gene
- If isolated, must be distinguished from normal diphtheroid

The patient may recover at this point; or if enough toxin is absorbed, develop severe prostration, striking pallor, rapid pulse, stupor, coma, and may even die within 6 to 10 days. Fever is usually not high, even though the patient may appear quite toxic. Patients with severe disease may develop marked edema of the submandibular areas and the anterior neck along with lymphadenopathy, giving a characteristic “bullneck” appearance.

Laryngeal diphtheria

Laryngeal diphtheria can be either an extension of the pharyngeal form or the only site involved. Symptoms include fever, hoarseness, and a barking cough. The membrane can lead to airway obstruction, coma, and death.

Cutaneous (skin) diphtheria

In the United States, cutaneous diphtheria has been most often associated with homeless persons. Skin infections are quite common in the tropics and are probably responsible for the high levels of natural immunity found in these populations. Skin infections may be manifested by a scaling rash or by ulcers with clearly demarcated edges and membrane, but any chronic skin lesion may harbor *C. diphtheriae*, along with other organisms. Generally, the organisms isolated from recent cases in the United States were non-toxigenic. In general, the severity of the skin disease with toxigenic strains appears to be less than in other forms of infection with toxigenic strains. Skin diseases associated with nontoxigenic strains are no longer reported to the National Notifiable Diseases Surveillance System in the United States.

Other sites of involvement include the mucous membranes of the conjunctiva and vulvo-vaginal area, as well as the external auditory canal.

Complications

Most complications of diphtheria, including death, are attributable to effects of the toxin. The severity of the disease and complications are generally related to the extent of local disease. The toxin, when absorbed, affects organs and tissues distant from the site of invasion. The most frequent complications of diphtheria are:

Myocarditis

Abnormal cardiac rhythms can occur early in the course of the illness or weeks later, and can lead to heart failure. If myocarditis occurs early, it is often fatal.

Diphtheria Complications

- Most complications and death attributable to toxin
- Severity of complications generally related to extent of local disease
- Most common complications are myocarditis and neuritis
- Death occurs in 5%-10% for respiratory disease, higher in <5 and >40 years

To isolate *C. diphtheriae* from carriers, it is best to inoculate a Löffler's or Pai's slant with the throat swab. After an incubation period of 18-24 hours, growth from the slant is used to inoculate a medium containing tellurite.

Medical Management

Diphtheria antitoxin

Diphtheria antitoxin, produced in horses, was first used in the United States in 1891. It is no longer indicated for prophylaxis of contacts of diphtheria cases, only for the treatment of diphtheria.

Antitoxin will not neutralize toxin that is already fixed to tissues, but will neutralize circulating (unbound) toxin and will prevent progression of disease. The patient must be tested for sensitivity before antitoxin is given. Consultation on the use of diphtheria antitoxin is available at all times through the CDC operator at (404) 639-2889 or 2888. During office hours, 8:00 am - 4:30 pm EST, contact staff at the Child Vaccine Preventable Diseases Branch, National Immunization Program, (404) 639-8255.

Persons with suspected diphtheria should be given antibiotics and antitoxin in adequate dosage and placed in isolation after the provisional clinical diagnosis is made and appropriate cultures are obtained. Respiratory support and airway maintenance should also be administered as needed.

Antibiotics

Treatment with erythromycin orally or by injection (40 mg/kg/day; maximum, 2 gm/day) for 14 days, or procaine penicillin G daily, intramuscularly (300,000 U/day for those weighing 10 kg or less and 600,000 U/day for those weighing more than 10 kg) for 14 days. The disease is usually not contagious 48 hours after antibiotics are instituted. Elimination of the organism should be documented by two consecutive negative cultures after therapy is completed.

Preventive measures

For close contacts, especially household contacts, a diphtheria booster, appropriate for age, should be given. Contacts should also receive antibiotics—benzathine penicillin G (600,000 units for persons less than 6 years old and 1,200,000 units for those 6 years old and older) or a 7- to 10-day course of oral erythromycin,

Diphtheria Antitoxin

- First used in 1891
- Produced in horses
- Used only for treatment of diphtheria
- Neutralizes only unbound toxin

Secular Trends in the United States

Diphtheria was once a major cause of morbidity and mortality among children. In England and Wales during the 1930s, diphtheria was among the top three causes of death for children <15 years of age.

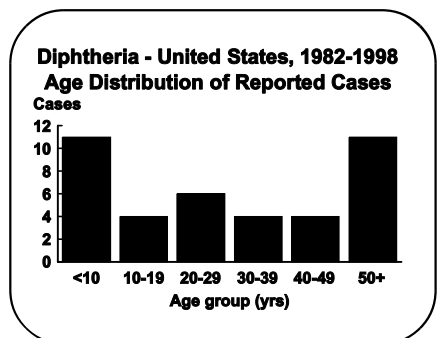
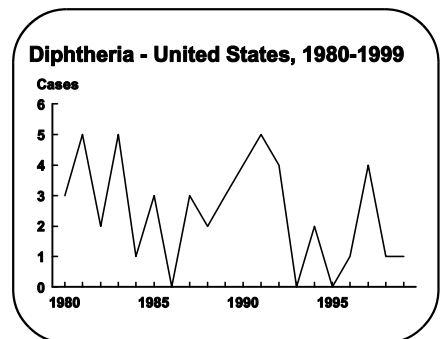
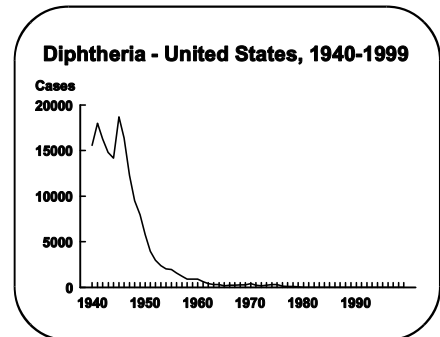
In the 1920s in the United States, 100,000-200,000 cases of diphtheria (140-150 cases per 100,000 population) and 13,000-15,000 deaths were reported each year. In 1921, a total of 206,000 cases and 15,520 deaths were reported. The number of cases gradually fell to about 19,000 cases in 1945 (15 per 100,000 population). A more rapid decrease began with the widespread use of toxoid in the late 1940s.

From 1970 to 1979, an average of 196 cases per year were reported. This included a high proportion of cutaneous cases from an outbreak in Washington state. Beginning in 1980, all cases with non-toxicogenic cutaneous isolates were excluded from reporting. Diphtheria was seen most frequently in Native Americans and persons in lower socioeconomic strata.

From 1980 through 1999, only 49 cases of diphtheria were reported in the United States, an average of 3 per year (range, 0-5 cases per year). No cases were reported in 1993 and 1995. Only one case was reported each year in 1998 and 1999.

Of 40 reported cases with known age, in 1982-1998, twenty-five (63%) cases were in persons >20 years of age; 38% of cases were among persons >40 years of age. Most cases have occurred in unimmunized or inadequately immunized persons. The current age distribution of cases corroborates the finding of inadequate levels of circulating antitoxin in many adults (up to 60% with less than protective levels).

Although diphtheria disease is rare in the United States, it appears that *Corynebacterium diphtheriae* continues to circulate in areas of the country with previously endemic diphtheria. In 1996, 10 isolates of *C. diphtheriae* were obtained from persons in an American Indian community in South Dakota. Eight of these isolates were toxigenic. None of the infected persons had classic diphtheria disease, although 5 had either pharyngitis or tonsillitis. The presence of toxigenic *C. diphtheriae* in this community is a good reminder for providers not to let down their guard against this organism.



Vaccination Schedule and Use

DTaP (diphtheria and tetanus toxoids and acellular pertussis vaccine) is the vaccine of choice for children 6 weeks through 6 years of age. The usual schedule is a primary series of 4 doses at 2,4,6, and 15-18 months of age. The first, second, and third doses of DTaP should be separated by a minimum of 4 weeks. The fourth dose should follow the third dose by no less than 6 months.

If a child has a valid contraindication to pertussis vaccine, pediatric DT should be used to complete the vaccination series. If the child is less than 12 months old when the first dose of DT is administered (as DTP, DTaP, or DT), the child should receive a total of four primary DT doses. If the child is 12 months of age or older at the time that the first dose of DT is administered, a third dose 6-12 months after the second completes the primary DT series.

If the fourth dose of DT, DTP or DTaP is administered before the fourth birthday, a booster (fifth) dose is recommended at 4-6 years of age. The fifth dose is not required if the fourth dose was given on or after the fourth birthday.

Because of waning antitoxin titers, most individuals have antitoxin levels below optimal levels 10 years after the last dose. Tetanus toxoid should be given with diphtheria toxoid as Td every 10 years. The first booster dose may be given at 11-12 years of age, if at least 5 years have elapsed since the last dose of DTP, DTaP, or DT. If a dose is given sooner as part of wound management, the next booster is not needed for 10 years thereafter. More frequent boosters are not indicated and have been reported to result in an increased incidence and severity of local adverse reactions.

Td is the vaccine of choice for children 7 years old and older, and for adults. A primary series is three doses. The first two doses should be separated by at least 4 weeks, and the third dose given 6-12 months after the second. A booster dose of Td should be given every 10 years.

Interrupting the recommended schedule or delaying subsequent doses does not reduce the ultimate immunity. There is no need to restart a series regardless of the time elapsed between doses.

Diphtheria disease may not confer immunity. Individuals recovering from diphtheria should begin or complete active immunization with diphtheria toxoid during convalescence. This is less of a concern than with tetanus.

Routine DTaP Primary Vaccination Schedule

Dose	Age	Interval
Primary 1	2 months	—
Primary 2	4 months	4 wks
Primary 3	6 months	4 wks
Primary 4	15-18 months	6 mos

Routine DTaP Schedule Children <7 years of age

Booster Doses

- 4-6 years, before entering school
- 11-12 years of age if >5 years since last dose (Td)
- Every 10 years thereafter (Td)

Routine Td Schedule Persons >7 years of age

Dose	Interval
Primary 1	—
Primary 2	4 wks
Primary 3	6-12 mos
Booster dose every 10 years	

1. Contact state health department or CDC.
2. Obtain appropriate cultures and preliminary clinical and epidemiological information (including vaccine history).
3. Begin early presumptive treatment with antibiotics and antitoxin. Start antibiotics and antitoxin. Impose strict isolation until at least two cultures are negative 24 hours after antibiotics were stopped.
4. Identify close contacts, especially household members and other persons directly exposed to oral secretions of the patient. Culture all close contacts, regardless of their immunization status. Ideally, culture should be from both throat and nasal swabs. After culture, all contacts should receive antibiotic prophylaxis. Inadequately immunized contacts should receive DTaP/DT/Td boosters. If less than three doses diphtheria toxoid have been given, or vaccination history is unknown, an immediate dose of diphtheria toxoid should be given and the primary series completed according to the current schedule. If >5 years have elapsed since administration of diphtheria toxoid-containing vaccine, a booster dose should be given. If the most recent dose was within 5 years, no booster is required (see the ACIP's 1991 *Diphtheria, Tetanus, and Pertussis: Recommendations for Vaccine Use and Other Preventive Measures* for schedule for children <7 years of age.)

Unimmunized contacts should start a course of DTaP/DT/Td vaccine and be monitored closely for symptoms of diphtheria for 7 days.
5. Treat any confirmed carrier with adequate course of antibiotic, and repeat cultures at a minimum of 2 weeks to assure eradication of the organism. Persons who continue to harbor the organism after treatment with either penicillin or erythromycin should receive an additional 10-day course of erythromycin and should submit samples for follow-up cultures.
6. Treat any contact with antitoxin at the first sign of illness.

**Diphtheria
Summary**

- Toxin mediated
- Fewer than 5 reported cases per year
- Most cases in older persons
- Need for adult immunization

6

Chapter

Pertussis

PERTUSSIS, OR WHOOPING COUGH, IS AN ACUTE INFECTIOUS disease caused by the bacterium *Bordetella pertussis*. Outbreaks of pertussis were first described in the 16th century, and the organism was first isolated in 1906.

In the 20th century pertussis has been one of the most common childhood diseases and a major cause of childhood mortality in the United States. Prior to the availability of pertussis vaccine in the 1940s, over 200,000 cases of pertussis were reported annually. Since widespread use of the vaccine began, incidence has decreased more than 98%, to an average of about 3,700 cases per year since 1980.

In unimmunized populations in the world, pertussis remains a major health problem among children, with an estimated 300,000 deaths per year due to the disease.

Bordetella pertussis

B. pertussis is a small aerobic gram-negative rod. It is fastidious, and requires special media for isolation (see section on Laboratory Diagnosis).

B. pertussis produces multiple antigenic and biologically active products, including pertussis toxin, filamentous hemagglutinin, agglutinogens, adenylate cyclase, pertactin, and tracheal cytotoxin. These products are responsible for the clinical features of pertussis disease, and an immune response to one or more produces immunity to subsequent clinical illness. Recent evidence suggests that immunity from *B. pertussis* infection may not be permanent.

Pertussis

- Highly contagious respiratory infection caused by *Bordetella pertussis*
- Outbreaks first described in 16th century
- *Bordetella pertussis* isolated in 1906
- Estimated >300,000 deaths annually worldwide

Bordetella pertussis

- Fastidious gram-negative bacillus
- Multiple antigenic and biologically active components:
 - pertussis toxin (PT)
 - filamentous hemagglutinin (FHA)
 - agglutinogens
 - adenylate cyclase
 - pertactin
 - tracheal cytotoxin

months after the onset of pertussis. Fever is generally minimal throughout the course of pertussis.

Older persons (*i.e.*, **adolescents and adults**), and those partially protected by the vaccine may become infected with *B. pertussis*, but usually have milder disease. Pertussis in these persons may present as a persistent (>7 days) cough, and may be indistinguishable from other upper respiratory infections. Inspiratory whoop is uncommon. In some studies, *B. pertussis* has been isolated from 25% or more of adults with cough illness lasting >7 days.

Even though the disease may be milder in older persons, these infected persons may transmit the disease to other susceptible persons, including unimmunized or underimmunized infants. Adults are often found to be the first case in a household with multiple pertussis cases.

Complications

Young infants are at highest risk for acquiring clinical pertussis, and for pertussis-associated complications. The most common complication, and the cause of most pertussis-related deaths, is secondary bacterial pneumonia. Data from 1990-1996 indicate that pneumonia occurred among 9.5% of all reported pertussis cases, and among 17% of infants <6 months of age.

Neurologic complications such as seizures and encephalopathy (a diffuse disorder of the brain) may occur as a result of hypoxia (reduction of oxygen supply) from coughing, or possibly from toxin. Neurologic complications of pertussis are more common among infants. In 1990-1996, seizures and encephalopathy were reported among 1.4% and 0.2%, respectively, of all cases, and among 2.1% and 0.4%, respectively, of infants <6 months of age.

Other less serious complications of pertussis include otitis media, anorexia, and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax, epistaxis, subdural hematomas, hernias, and rectal prolapse.

In 1990-1996, 32% of all reported pertussis cases required hospitalization, including 72% of all infants <6 months of age. In this 7 year period, 57 deaths were due to pertussis (case-fatality rate 0.2%). Forty-eight (84%) of these deaths occurred in children <6 months of age.

Pertussis in Adults

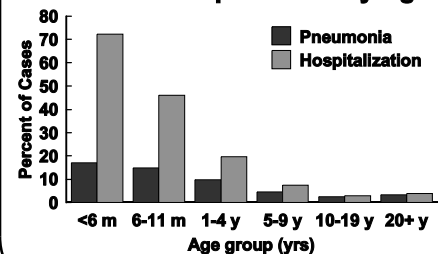
- May account for ~25% of cough illness lasting ≥ 7 days
- Disease often milder than in infants and children
- Adult often source of infection for children

Pertussis Complications*

Condition	Percent reported
Pneumonia	9.5
Seizures	1.4
Encephalopathy	0.2
Death	0.2
Hospitalization	32

*Reported cases 1990-1996 (N=35,508)

Pertussis Complications by Age



An elevated white blood cell count with a lymphocytosis is usually present in classical disease. The absolute lymphocyte count often reaches 20,000 or greater. However, there may be no lymphocytosis in infants and children or in mild or modified cases of pertussis.

Medical Management

The medical management of pertussis cases is primarily supportive, although antibiotics are of some value. Erythromycin is the drug of choice. This therapy eradicates the organism from secretions, thereby decreasing communicability and, if initiated early, may modify the course of the illness.

Erythromycin or trimethoprim-sulfamethoxazole prophylaxis should be administered for 14 days to all household and other close contacts of persons with pertussis, **regardless of age and vaccination status**. Although data from controlled clinical trials are lacking, prophylaxis of all household members and other close contacts may prevent or minimize transmission. All close contacts <7 years of age who have not completed the four-dose primary series should complete the series with the minimal intervals. Close contacts <7 years of age who have completed a primary series but have not received a dose of DTP or DTaP within 3 year's of exposure, should be given a booster dose.

Epidemiology

Occurrence

Pertussis occurs worldwide.

Reservoir

Pertussis is a human disease. No animal or insect source or vector is known to exist. Adolescents and adults are an important reservoir for *B. pertussis* and are often the source of infection for infants.

Transmission

Transmission most commonly occurs by the respiratory route through contact with respiratory droplets, or by contact with airborne droplets of respiratory secretions. Transmission occurs less frequently by contact with freshly contaminated articles of an infected person.

A silent carrier state is thought to exist, but is infrequent, transient in duration, and probably of little importance in maintaining pertussis organisms in the community.

Pertussis Epidemiology

- | | |
|-------------------|---|
| • Reservoir | Human
Adolescents and adults |
| • Transmission | Respiratory droplets
Airborne rare |
| • Communicability | Maximum in catarrhal
stage
Secondary attack rate
up to 90% |

Of the 10,650 children 3 months to 4 years of age with reported pertussis during 1990-1996 and known vaccination status, 54% were not age-appropriately vaccinated with DTP.

Case Definition

The current case definition for pertussis was developed and adopted by the Council of State and Territorial Epidemiologists (CSTE) and the Centers for Disease Control and Prevention (CDC). It defines a clinical case of pertussis as a cough illness lasting at least 2 weeks with either paroxysms of coughing, inspiratory “whoop,” or post-tussive vomiting without other apparent cause (as reported by a health professional).

Case Classification

Probable - Meets the clinical case definition, but is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case.

Confirmed - A clinically compatible case that is laboratory-confirmed or epidemiologically linked to a laboratory-confirmed case.

The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least 2 weeks (as reported by a health professional). Because direct fluorescent antibody testing of nasopharyngeal secretions has been shown in some studies to have low sensitivity and variable specificity, it should not be relied on as a criterion for laboratory confirmation.

Both probable and confirmed cases should be reported to the National Notifiable Disease Surveillance System (NNDSS).

Pertussis Vaccines

Whole-cell pertussis vaccine

Whole-cell pertussis vaccine is composed of a suspension of formalin-inactivated *B. pertussis* cells. It was developed in the 1930s, and used widely in clinical practice by the mid-1940s.

Whole Cell Pertussis Vaccine

- Developed in mid-1930s and combined as DTP in mid-1940s
- 70%-90% efficacy after 3 doses
- Protection for 5-10 years
- Local adverse reactions common

Confidence intervals for vaccine efficacy overlap, suggesting that none of the vaccines is significantly more effective than the others. When studied, the acellular pertussis vaccine was significantly more effective than whole-cell DTP. Mild local and systemic adverse events and more serious adverse events (such as high fever, persistent crying, hypotonic hyporesponsive episodes, and seizures) occurred less frequently among infants vaccinated with acellular pertussis vaccines than among those vaccinated with whole-cell DTP.

Vaccination Schedule and Use

Acellular pertussis vaccine (DTaP) is recommended for all doses of the pertussis schedule. Whole-cell vaccine (DTP) is no longer recommended for use in the U.S. The primary series of DTaP consists of four doses of vaccine, the first three doses given at 4-to 8-week intervals (minimum of 4 weeks), beginning at 6 weeks to 2 months of age. The fourth dose is given 6-12 months after the third to maintain adequate immunity for the ensuing preschool years. DTaP should be administered simultaneously with all other indicated vaccines.

The **fourth dose** of all brands of DTaP are licensed, and recommended by ACIP, to be administered at 15 to 18 months of age. However, ACIP also recommends that under certain circumstances the fourth dose be given earlier than 15 months of age. ACIP recommends that the fourth dose of DTaP be given if the child is *at least 12 months of age, and at least 6 months have elapsed since the third dose of pertussis vaccine was given, and, in the opinion of the immunization provider, the child is unlikely to return for an additional visit at 15 to 18 months of age.* All three of these criteria should be met in order to administer the fourth dose of DTaP at 12-14 months of age.

Children who received all four primary doses before the 4th birthday should receive a **fifth (booster) dose of DTaP** before entering school. This booster dose is not necessary if the fourth dose in the primary series was given on or after the 4th birthday. The booster dose increases protective antibody levels and may decrease the risk of school-age children transmitting the disease to younger siblings who are not fully vaccinated. As of January 2000, only Acel-Imune is approved for the fifth dose following a series of 4 doses of DTaP. However, if any of the first 4 doses were whole cell vaccine, any licensed DTaP vaccine may be used for the 5th dose.

Most children who have received DTaP for all doses of the

Routine DTaP Primary Vaccination Schedule

Dose	Age	Interval
Primary 1	2 months	---
Primary 2	4 months	4 wks
Primary 3	6 months	4 wks
Primary 4	15-18 months	6 mos

DTaP Fourth Dose

- Recommended at 15-18 months
- May be given at 12 months of age if:
 - child is ≥ 12 months of age, and
 - ≥ 6 months since DTaP3, and
 - unlikely to return at 15-18 months

DTaP Fifth Dose

- Fifth dose recommended when 4th dose given before age 4 years
- Only Acel-Imune licensed for 5th dose following acellular pertussis series
- All DTaP vaccines interchangeable for 5th dose following whole cell series

any licensed DTaP vaccine may be used to continue or complete the vaccination series. **Vaccination should NOT be deferred because the type of DTaP used for earlier doses is not available.**

Three vaccines containing either whole-cell DTP or DTaP combined with Hib vaccine are available in the United States. The combinations containing whole cell DTP (Tetramune, ActHib/DTP) are not recommended because of the whole-cell pertussis component. As of January 2000, the only available DTaP-Hib combination (TriHIBit) is approved only for the fourth dose of the DTaP and Hib series. DTaP-Hib combination vaccines may be licensed for the first three doses of the DTaP and Hib series in the future.

Infants and children with recognized, possible, or potential **underlying neurologic conditions** present a unique problem. They seem to be at increased risk for manifesting the underlying neurologic disorder within 2-3 days after vaccination. However, more prolonged manifestations or increased progression of the disorder, or exacerbation of the disorder have not been recognized.

Under certain circumstances, vaccination with DTaP vaccine should be delayed until the child has been evaluated, treatment initiated, and the condition stabilized. These conditions include the presence of an evolving neurologic disorder (*e.g.*, uncontrolled epilepsy, infantile spasms, and progressive encephalopathy), a history of seizures which has not been evaluated, or a neurologic event which occurs between doses of pertussis vaccine.

A family history of seizures or other neurologic diseases, or stable or resolved neurologic conditions (*e.g.*, controlled idiopathic epilepsy, cerebral palsy, developmental delay) are not contraindications to pertussis vaccination. Acetaminophen or ibuprofen may be administered to these children at the time of DTaP vaccination, and for 24 hours thereafter, to reduce the possibility of postvaccination fever.

Reducing the dose of whole-cell DTP or DTaP vaccine, or giving the full dose in multiple smaller doses may result in an altered immune response and inadequate protection. Furthermore, there is no evidence that the frequency of significant vaccine reactions is likely to be reduced by this practice. The use of multiple reduced doses that together equal a full immunizing dose or the use of smaller divided doses is not endorsed or recommended. Any vaccination using less than the standard dose or a nonstandard route or site of administration should not be counted, and the person should be revaccinated according to

DTP/DTaP-Hib Combinations

- Whole cell DTP-Hib combinations
 - Tetramune, ActHib/DTP
 - Not recommended because of whole cell pertussis
- DTaP-Hib combination
 - TriHIBit
 - Licensed only for 4th dose of DTaP and Hib series

Pertussis Vaccine Use in Children with Underlying Neurologic Disorders

Underlying Condition	Recommendation
Prior seizure	Delay and assess*
Suspected neurologic disorder	Delay and assess*
Neurologic event between doses	Delay and assess*
Stable/resolved neurologic condition	Vaccinate

*Vaccinate after treatment initiated and condition stabilized

encephalopathy except in children who developed acute encephalopathy.

Contraindications and Precautions to Vaccination

Contraindications to further vaccination with DTP or DTaP are **severe allergic reaction** to a prior dose of vaccine or vaccine component and **encephalopathy** not due to another identifiable cause within 7 days of vaccination.

Moderate or severe acute illness is a precaution to vaccination. Children with mild illness, such as otitis media or upper respiratory infection, should be vaccinated. Children for whom vaccination is deferred due to moderate or severe acute illness should be vaccinated when their condition improves.

Certain infrequent adverse events following pertussis vaccination will generally contraindicate subsequent doses of pertussis vaccine. These adverse events are:

Temperature of $\geq 40.5^{\circ}\text{C}$ (105°F) within 48 hours not due to another identifiable cause.

Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.

Persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours.

Convulsions with or without fever occurring within 3 days.

There may be circumstances (*e.g.*, during a community-wide outbreak of pertussis) in which the benefit of vaccination outweighs the risk, even if one of the four precautionary adverse events occurred following a previous dose. Under these circumstances, one or more additional doses of pertussis vaccine may be considered. DTaP should be used in these circumstances.

Acellular pertussis vaccine should **NOT** be substituted in children who have a valid contraindication to whole cell pertussis vaccine. If a valid contraindication or precaution exists, DT should be used for the remaining doses in the schedule.

DTaP/DTP Contraindications

- **Serious allergic reaction to component or following prior dose**
- **Encephalopathy, not due to another identifiable cause, occurring within 7 days after vaccination**

DTaP/DTP Precautions (Warnings)*

- **Moderate or severe acute illness**
 - **Temperature of 105 F (40.5 C) or higher within 48 hours with no other identifiable cause**
 - **Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours**
 - **Persistent, inconsolable crying lasting 3 hours or more, occurring within 48 hours**
 - **Convulsions with or without fever occurring within 3 days.**
- *May consider use in outbreaks

DTaP Substitution

- **DTaP should not be substituted in children who have a valid contraindication to whole cell pertussis vaccine**
- **DT should be used to complete the series**

The onset of infantile spasms has occurred among infants who had recently received DTP or DT. A case-control study of infantile spasms in England showed that receipt of DTP or DT was not causally related to infantile spasms, but that receipt of DTP may trigger onset in children in whom the disorder is destined to develop. By chance alone, some cases of SIDS and infantile spasms can be expected to be temporally related to the recent receipt of DTP or DT.

Claims that DTP may be responsible for transverse myelitis, other more subtle neurological disorders (such as hyperactivity, learning disorders, and infantile autism), and progressive degenerative central-nervous-system conditions have no scientific basis.

Besides the evidence of vaccine efficacy of 70%-90% noted before, other data point to the effectiveness of pertussis vaccination. Mortimer studied the relative impact of vaccination versus improved living conditions on pertussis incidence. He reviewed deaths from pertussis in children less than 5 years of age from 1900 to 1974, and showed an acceleration of the decline in pertussis mortality beginning in 1940 when vaccine was first widely used. Only 52 deaths from pertussis occurred from 1970 until 1974, when 4,000-8,000 deaths would have been expected on the basis of the rate of decline before 1940.

Another way of studying the effectiveness of DTP vaccination is to examine the experience in nations where pertussis vaccine utilization declined. In Japan, for example, pertussis vaccination was used nationwide by 1950. By 1974, pertussis incidence had dropped from 100 cases to 1 case per 100,000 population. However, in the last half of the 1970s, vaccine use in Japan markedly decreased after two deaths occurred following pertussis vaccination. A major epidemic of pertussis ensued, with an increase in incidence rate to 11.5 per 100,000 in 1977. The annual number of deaths from pertussis increased from an average of less than 5 for the years 1970-1974 to an average of 32 during 1977-1979.

In the United Kingdom, an estimated 75% of children were fully vaccinated between 1958 and 1974. Following allegations of adverse reactions after pertussis immunization, the estimated coverage of children fell to 30% by 1978. A major epidemic occurred in 1978-1979, with an incidence rate as high as 200 per 100,000 for the period 1977-1979. More than 100,000 cases of pertussis and 36 deaths caused by pertussis were reported in the

Selected References

Birkebaek NH, Kristiansen M, Seefeldt T, et al. Bordetella pertussis and chronic cough in adults. *Clin Infect Dis* 1999;29:1239-42.

CDC. Pertussis vaccination: Use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1997;46(RR-7):1-25.

CDC. Pertussis—United States, January 1992-June 1995. *MMWR* 1995;44:525_9.

CDC. Transmission of pertussis from adult to infant—Michigan, 1993. *MMWR* 1995;44:74_6.

Decker MD, Edwards KM, Steinhoff MC, et al. Comparison of 13 acellular pertussis vaccines: adverse events. *Pediatrics* 1995;96(suppl):557-66.

Evans AS and Brachman PS, eds. *Bacterial Infections of Humans. Epidemiology and Control*. 3rd edition. New York, NY: Plenum Medical Book Company, 1998.

Gangarosa EJ, Galazka AM, Phillips LM, et al. Impact of anti-vaccine movements on pertussis control: the untold story. *Lancet* 1998;351:356-61.

Guris D, Strebel PM, Bardenheir B, et al. The changing epidemiology of pertussis in the United States: increasing reported incidence in adolescents and adults, 1990-1996. *Clin Infect Dis* 1999;28:1230-7.

Halperin SA, Schiefele D, Barreto L, et al. Comparison of a fifth dose of a five-component acellular or a whole cell pertussis vaccine in children four to six years of age. *Pediatr Infect Disease J* 1999;18:772-9.

Institute of Medicine. Adverse effects of pertussis and rubella vaccines. Washington D.C.: National Academy Press, 1991.

Institute of Medicine. Adverse events associated with childhood vaccines: evidence bearing on causality. Washington, D.C.: National Academy Press, 1994.

Orenstein WA, Hadler S, Wharton M. Trends in Vaccine-Preventable Diseases. *Semin Pediatr Infect Dis* 1997;8:23-33.

Plotkin SA, Orenstein WA, eds. *Vaccines*. 3rd edition. Philadelphia: W.B. Saunders Company, 1999.

Peter G, ed 1997 *Red Book: Report of the Committee on Infectious Diseases*. 24th ed. Elk Grove Village, IL: American Academy of Pediatrics, 1997.