

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 bacteria
- Antigenic and biologically active components:
 - pertussis toxin (PT)
 - filamentous hemagglutinin (FHA)
 - agglutinogens
 - adenylate cyclase
 - pertactin
 - tracheal cytotoxin

Pertussis Pathogenesis

- Attachment to cilia of ciliated epithelial cells in respiratory tract
- Pertussis antigens allow evasion of host defenses (lymphocytosis but impaired chemotaxis)
- Local tissue damage in respiratory tract
- Systemic disease may be toxin mediated

Pertussis Clinical Features

- Incubation period 7-10 days (up to 21 days)
- Insidious onset, similar to minor upper respiratory infection with nonspecific cough
- Fever usually minimal throughout course

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 4,400 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.

PATHOGENESIS

Pertussis is primarily a toxin-mediated disease. The bacteria attach to the respiratory cilia, produce toxins that paralyze the cilia, and cause inflammation of the respiratory tract, thus interfering with the clearing of pulmonary secretions and potentially causing pneumonia. Pertussis antigens appear to allow the organism to evade host defenses, in that lymphocytosis is promoted, but chemotaxis is impaired. Until recently it was thought that *B. pertussis* did not invade the tissues. However, recent work has shown the bacteria in alveolar macrophages.

CLINICAL FEATURES

The **incubation period** of pertussis is commonly 7 to 10 days, with a range of 4 to 21 days, and rarely may be as long as 42 days. The clinical course of the illness is divided into three stages.

The first stage, the **catarrhal stage**, is characterized by the insidious onset of coryza (runny nose), sneezing, low-grade fever, and a mild, occasional cough, similar to the common cold. The cough gradually becomes more severe, and after 1-2 weeks, the second, or paroxysmal stage, begins.

It is during the **paroxysmal stage** that the diagnosis of pertussis is usually suspected. Characteristically, the patient has bursts, or paroxysms of numerous, rapid coughs, apparently due to difficulty expelling thick mucus from the tracheobronchial tree. At the end of the paroxysm, a long inspiratory effort is usually accompanied by a characteristic high-pitched whoop. During such an attack, the patient may become cyanotic (turn blue). Children and young infants, especially, appear very ill and distressed. Vomiting and exhaustion commonly follow the episode. The patient usually appears normal between attacks.

Paroxysmal attacks occur more frequently at night, with an average of 15 attacks per 24 hours. During the first 1 or 2 weeks of this stage the attacks increase in frequency, remain at the same level for 2 to 3 weeks, and then gradually decrease. The paroxysmal stage usually lasts 1 to 6 weeks, but may persist for up to 10 weeks. Infants under 6 months of age may not have the strength to have a whoop, but they do have paroxysms of coughing.

In the **convalescent stage**, recovery is gradual. The cough becomes less paroxysmal and disappears over 2 to 3 weeks. However, paroxysms often recur with subsequent respiratory infections for many 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. *B. pertussis* is estimated to account for up to 7% of cough illnesses per year in older persons.

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 1997-2000 indicate that pneumonia occurred among 5.2% of all reported pertussis cases, and among 11.8% 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 1997-2000, seizures and encephalopathy were reported among 0.8% and 0.1%, respectively, of all cases, and among 1.4%

Pertussis Clinical Features

- **Catarrhal stage** 1-2 weeks
- **Paroxysmal cough stage** 1-6 weeks
- **Convalescence** Weeks to months

Pertussis in Adults

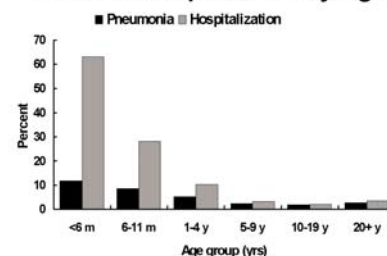
- Accounts for up to 7% of cough illnesses per year
- Disease often milder than in infants and children
- Adults often source of infection for children

Pertussis Complications*

Condition	Percent reported
Pneumonia	5.2
Seizures	0.8
Encephalopathy	0.1
Death	0.2
Hospitalization	20

*Cases reported to CDC 1997-2000 (N=28,187)

Pertussis Complications by Age



*Cases reported to CDC 1997-2000 (N=28,187)

and 0.2%, 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 1997-2000, 20% of all reported pertussis cases required hospitalization, including 63% of all infants <6 months of age. In this 4 year period, 62 deaths were due to pertussis (case-fatality rate 0.2%). Fifty-six (90%) of these deaths occurred in children <6 months of age.

LABORATORY DIAGNOSIS

The diagnosis of pertussis is usually based upon a characteristic history and physical examination. However, laboratory tests may be useful in young infants, atypical cases, and cases modified by vaccine.

The standard and preferred laboratory test for diagnosis of pertussis is **isolation of *B. pertussis* by culture**. Fastidious growth requirements make *B. pertussis* difficult to isolate. Isolation of the organism using direct plating is most successful during the catarrhal stage. Specimens from the posterior nasopharynx, not the throat, should be obtained using Dacron™ or calcium alginate (not cotton) swabs and should be plated directly onto selective media. Regan-Lowe agar or freshly prepared Bordet-Gengou medium is generally used. Success in isolating the organism declines with prior antibiotic therapy effective against pertussis (erythromycin or trimethoprim-sulfamethoxazole) or delay in specimen collection beyond the first 3 weeks of illness.

A second method of *B. pertussis* identification in nasopharyngeal specimens is the **direct fluorescent antibody (DFA)** technique. 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.

Serological testing has proven useful in clinical studies, but is not yet standardized. Due to lack of association between antibody levels and immunity to pertussis, results of serologic testing are difficult to interpret. For these reasons, serologic testing is not widely available. In some areas it is used for clinical diagnosis and reporting, but in the absence of standardization, serologic test results should not be relied upon for case confirmation for the purpose of national reporting. Cases meeting the clinical case definition that are serologically positive, but **not** culture positive or PCR positive, should be reported as probable cases.

Polymerase chain reaction (PCR) testing of nasopharyngeal swabs or aspirates has been found to be a rapid, sensitive, and specific method for diagnosing pertussis. Currently, it is only available

in certain laboratories and direct comparison with culture and serology are necessary before it can be used for laboratory confirmation of *B. pertussis* infection. PCR, once validated, should be used in addition to culture, NOT as a replacement for culture, because bacterial isolates may be required for evaluation of antimicrobial resistance, or for molecular typing.

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.

More information on the laboratory diagnosis of pertussis is available on the National Immunization Program website at <<http://www.cdc.gov/nip/publications/pertussis/guide.htm>>.

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

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

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.

TEMPORAL PATTERN

Pertussis has no distinct seasonal pattern, but may increase in the summer and fall.

COMMUNICABILITY

Pertussis is highly communicable, as evidenced by secondary attack rates of 80% among susceptible household contacts.

Persons with pertussis are most infectious during the catarrhal period and the first 2 weeks after cough onset (*i.e.*, approximately 21 days).

SECULAR TRENDS IN THE UNITED STATES

Prior to the availability of vaccine, pertussis was a common cause of morbidity and mortality among children. During the six years of 1940-1945, over 1 million cases of pertussis were reported, an average of 175,000 cases per year (incidence of approximately 150 cases per 100,000 population).

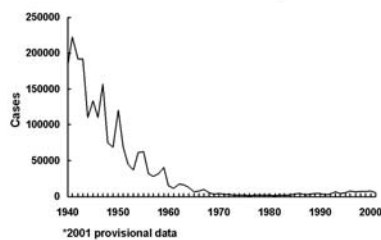
Following introduction of vaccine in the 1940s, pertussis incidence gradually fell, reaching 15,000 reported cases in 1960 (~8 per 100,000 population). By 1970, annual incidence was <5000 cases per year, and from 1980-1990, an average of 2,900 cases per year were reported (~1 per 100,000 population).

Pertussis incidence has been gradually increasing since the early 1980s. A total of 7,867 cases was reported in 2000, the largest number since 1967. A provisional total of 5,396 cases was reported in 2001. The reasons for the increase are not clear, but may be a reflection of the 3-5 year cyclicity observed with the disease.

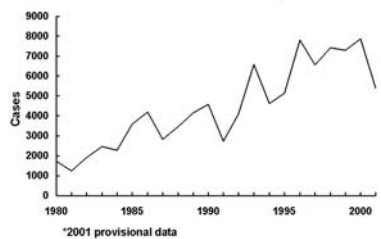
Children are the most frequent age group with reported pertussis. From 1985 through 2000, 39% of reported cases were among children aged <1 year, and 54% were among children aged <5 years. In 1997-2000, the highest annual pertussis incidence was among infants aged <1 year (55.5 cases per 100,000 population).

Compared with surveillance data for 1994-1996, the pertussis incidence rate among adolescents and adults increased 62% and 60%, respectively, in 1997-2000. These increases could reflect a change in reporting or a true increase in incidence. In 1995, criteria for reporting a pertussis case changed in two ways: polymerase chain reaction (PCR) became a method of confirmation, and data collection began for pertussis cases epidemiologically linked to another pertussis case. These changes primarily affected the reporting among persons aged ≥10 years. Increased recognition and diagnosis of pertussis among older age groups probably contributed to the

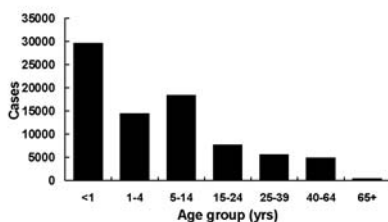
Pertussis – United States, 1940-2001*



Pertussis – United States, 1980-2001*



**Pertussis – United States, 1985-2000
Age Distribution of Reported Cases**



large recent increase of reported cases among adolescents and adults.

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 an acute 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 Diseases 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.

Based on controlled efficacy trials conducted in the 1940s and on subsequent observational efficacy studies, a primary series of four doses of whole-cell DTP vaccine was 70% to 90% effective in preventing serious pertussis disease. Protection from pertussis vaccine decreased over time, with little or no protection 5 to 10 years following the last dose. Local reactions such as redness, swelling, and pain at the injection site occurred following up to half of doses of whole-cell DTP vaccines. Fever, and other mild systemic events were also common. More severe systemic events, such as convulsions and

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

Acellular Pertussis Vaccine (DTaP)

- Purified "subunit" vaccines
- Intended to reduce adverse reactions
- Licensed for fourth and fifth doses in 1991
- Licensed for full series in 1996

Composition* of Acellular Pertussis Vaccines

Product	PT	FHA	PERT	FIM
DAPTACEL	10	5	3	5
Infanrix	25	25	8	--
Tripedia	23	23	--	--

*mcg per dose

DTaP Clinical Trials

Product	Location	VE (95% CI)
Infanrix	Italy	84% (76-89)
Tripedia	Germany	80% (59-90)
DAPTACEL	Sweden	85% (80-89)

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

hypotonic hyporesponsive episodes occurred less frequently (one case to 1,750 doses administered). Acute encephalopathy occurred even more rarely (0-10.5 cases per million doses administered). Experts disagreed on whether whole-cell pertussis vaccine caused lasting brain damage, but agreed that if the vaccine caused such damage it did so only rarely. Concerns about safety led to the development of more purified (acellular) pertussis vaccines that are associated with a lower frequency of adverse events.

ACELLULAR PERTUSSIS VACCINE

Acellular pertussis vaccine contains purified, inactivated components of *B. pertussis* cells. Several acellular pertussis vaccines have been developed that contain different components in varying concentrations. Acellular pertussis vaccines were first licensed for the fourth and fifth doses of the pertussis series in 1991, and for the primary series in 1996.

Three acellular pertussis vaccines are currently licensed for use in the United States. All three vaccines are combined with diphtheria and tetanus toxoids as DTaP. *Infanrix*[®] (GlaxoSmithKline) contains 3 antigens, mostly pertussis toxin (PT) and FHA. *Tripedia*[®] (Aventis-Pasteur) contains two components, FHA and PT, in equal amounts. *DAPTACEL*[™] (Aventis-Pasteur) contains four components, PT, FHA, pertacin, and fimbriae types 2 and 3.

IMMUNOGENICITY AND VACCINE EFFICACY

Since 1991, several studies conducted in Europe and Africa have evaluated the efficacy of DTaP vaccines administered to infants. These studies varied in type and number of vaccines, design, case definition, and laboratory method used to confirm the diagnosis of pertussis, so comparison among studies must be made with caution. Point estimates of vaccine efficacy ranged from 80% to 85% for vaccines currently licensed in the United States. 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 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 February 2002, only Tripedia is approved for the fifth dose following a series of 4 doses of DTaP.

For children who have started the vaccination series with whole cell DTP, **DTaP should be substituted for any remaining doses of the pertussis series**. A pertussis vaccination series begun with whole cell DTP should be completed with DTaP.

Data are insufficient to determine the safety, immunogenicity, and efficacy of using DTaP vaccines from different manufacturers in a mixed sequence. For this reason, ACIP recommends that whenever feasible, the same brand of DTaP vaccine should be used for all doses of the vaccination series. However, the vaccine provider might not know or have available the type of DTaP vaccine previously administered to a child. In this situation, any available DTaP vaccine should be used to continue or complete the vaccination series. Providers should not miss the opportunity to administer a dose of acellular pertussis vaccine for which the child is eligible if the vaccine used for the earlier doses is not available.

No pertussis-containing vaccine is currently licensed for **persons 7 years of age or older**. Vaccine reactions are thought to be more frequent in older age groups, and pertussis-associated morbidity and mortality decrease with increasing age. Vaccination with DTaP is not recommended after the 7th birthday. Studies are currently underway to determine if a booster dose of acellular pertussis vaccine administered to older children or adults may reduce the risk of infection with *B. pertussis*. This may in turn reduce the risk of transmission of *B. pertussis* to infants and young children who may be incompletely vaccinated.

No single antigen pertussis vaccine is available.

Interruption of the recommended schedule or delayed doses does not lead to a reduction in the level of immunity reached on completion of the primary series. **There is no need to restart a series regardless of the time that has elapsed between doses.**

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

School Entry (fifth) Dose

- Fifth dose recommended when 4th dose given before age 4 years
- Only Tripedia currently licensed for 5th dose after DTaP series

Interchangeability of Different Brands of DTaP Vaccine

- No efficacy or safety data available for "mix-and-match" DTaP schedules
- Series should be completed with same brand of vaccine
- Use different brand of DTaP if necessary

DTaP-Hib Combination Vaccine

- Do not use for primary immunization at 2, 4, or 6 months of age
- May be used as the booster dose of the Hib series at ≥12 months of age following any Hib vaccine*

*booster dose should follow prior dose by ≥2 months

Pertussis Vaccine Use in Children with Underlying Neurologic Disorders

<u>Underlying Condition</u>	<u>Recommendation</u>
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

DTaP - HIB COMBINATION VACCINE

One combination DTaP - Hib vaccine is available in the United States (TriHIBit[®], Aventis Pasteur). The vaccines are provided in separate vials, and the DTaP component (Tripedia) is used to reconstitute the Hib component (ActHIB[®]). No other brand of DTaP and Hib vaccine may be used to produce this combination (e.g., Infanrix must not be substituted for Tripedia). In addition, when supplied as TriHIBit, the DTaP and Hib components have a single lot number. Providers should generally use only the DTaP and Hib supplied together as TriHIBit. However, it is acceptable to combine Tripedia and ActHIB that have been supplied separately (i.e., not packaged as TriHIBit). In this situation, the lot numbers of both vaccines should be recorded in the child's chart.

Because of evidence of reduced immunogenicity of the Hib component when used as a combination, TriHIBit is not approved by the Food and Drug Administration for use as the primary series at 2, 4, or 6 months of age. It is approved only for the fourth dose of the DTaP and Hib series. If TriHIBit is administered as one or more doses of the primary series at 2, 4, or 6 months of age, the Hib doses should be disregarded, and the child should be revaccinated as age-appropriate for Hib. The DTaP doses may be counted as valid and do not need to be repeated.

Although TriHIBit cannot be used in the primary series at 2, 4, or 6 months of age, it may be used as the booster (final) dose following a series of single-antigen Hib vaccine or combination hepatitis B - Hib vaccine (COMVAX[™]). Therefore, TriHIBit can be used if the child is aged ≥12 months, and has received at least one prior dose of Hib vaccine ≥2 months earlier, and TriHIBit will be the last dose in the Hib series. For example, TriHIBit can be used for the booster dose at 12-15 months of age in a child who has received COMVAX or PedvaxHib[®] at 2 and 4 months of age, or 3 prior doses of HibTiter[®] or ActHib. TriHIBit can also be used at 15-59 months of age in a child who has received at least one prior dose of any Hib-containing vaccine. TriHIBit should not be used if the child has received no prior Hib doses.

OTHER DTaP ISSUES

Infants and children with recognized, possible, or potential **underlying neurologic conditions** present a unique problem. These children appear 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 chance of a significant vaccine reaction 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 should not be counted, and the person should be revaccinated according to age.**

Children who have recovered from satisfactorily documented pertussis do not need additional doses of pertussis vaccine.

Satisfactory documentation includes recovery of *B. pertussis* on culture or typical symptoms and clinical course when epidemiologically linked to a culture-proven case, as may occur during outbreaks. When such confirmation of diagnosis is lacking, vaccination should be completed, because presumed pertussis syndrome may have been caused by other *Bordetella* species, *Chlamydia trachomatis*, *Mycoplasma pneumoniae*, or certain viruses.

As noted above, pertussis accounts for a significant proportion of cough illnesses among adults. In addition, older children and adults with pertussis are often a source of infection for unimmunized or underimmunized children. However, no pertussis vaccine available in the United States is approved for use among persons aged 7 years or older. Studies have shown that acellular pertussis vaccine is safe and immunogenic among adults. However, it is not clear that administration of acellular pertussis vaccine to older children and adults will reduce the risk of their becoming infected with *B. pertussis*, or will reduce the risk of transmitting pertussis to young children. Administration of acellular pertussis vaccine to persons aged ≥ 7 years is not recommended. A pertussis vaccine for adults was recently approved in Canada, and may be available in the U.S. in the future.

ADVERSE REACTIONS FOLLOWING VACCINATION

As with all injected vaccines, administration of DTaP may cause **local reactions**, such as pain, redness, or swelling. Local reactions appear to be more frequent after the 4th and/or 5th doses of DTaP. **Mild systemic reactions** such as fever, drowsiness, fretfulness, and low grade fever may occur after either whole-cell DTP vaccination or DTaP vaccination. However, mild reactions following the first four doses are less common among children who receive DTaP. For instance, fever of $>101^{\circ}$ F is reported in 3%-5% of DTaP recipients

Pertussis Vaccination of Children Who Have Recovered From Pertussis

- If documented disease, do not need additional doses of pertussis vaccine
- Satisfactory documentation of disease:
 - recovery of *B. pertussis* on culture, OR
 - typical symptoms and clinical course when epidemiologically linked to a culture- proven case

Pertussis Vaccine in Adults

- No pertussis vaccine licensed for use in adults in the United States
- Acellular pertussis vaccine safe and immunogenic in adults
- Impact on disease or transmission unknown
- Not routinely recommended at this time

DTaP Adverse Reactions

- Local reactions
- Low grade fever
- More severe adverse reactions uncommon
- Local reactions more common following 4th and 5th doses

Adverse Reactions Following the 4th and 5th DTaP Dose

- Local adverse reactions and fever increased with 4th and 5th doses of DTaP
- Reports of swelling of entire limb
- Extensive swelling after 4th dose NOT a contraindication to 5th dose

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compared with 16% of whole-cell DTP recipients. These reactions are self-limited and can be managed with symptomatic treatment with acetaminophen or ibuprofen. **Moderate to severe systemic events** (such as fever $\geq 105^{\circ}$ F, febrile seizures, persistent crying lasting ≥ 3 hours, and hypotonic hyporesponsive episodes) have been reported rarely after administration of DTaP, and occur less frequently among children administered DTaP than among children administered whole cell DTP.

Information on adverse reactions following a full series of DTaP are also limited. Available data suggest a substantial increase in the frequency and magnitude of local reactions after the fourth and fifth doses. For example, swelling at the site of injection increased from 2% after the first dose of Tripedia to 29% following the fourth dose. Increases in the frequency of fever after the fourth dose have also been reported, although the increased frequencies of other systemic reactions (*e.g.*, fretfulness, drowsiness, or decreased appetite) have not been observed. Further details on this issue can be found in a supplemental ACIP statement published in 2000 (*MMWR* 2000;49(RR-13):1-8).

Swelling involving the entire thigh or upper arm has been reported after booster doses of different acellular pertussis vaccines. The limb swelling may be accompanied by erythema, pain and fever. Although the swelling may interfere with walking, most children have no limitation of activity. The pathogenesis and frequency of substantial local reactions and limb swelling is not known, but these conditions appear to be self limited and resolve without sequelae.

In the absence of a vaccine supply shortage, ACIP continues to recommend that a fifth dose of DTaP be administered before a child enters school. Whether children who experience entire limb swelling after a fourth dose of DTaP are at increased risk for this reaction after the fifth dose is unknown. Because of the importance of this dose in protecting a child during school years, **ACIP recommends that a history of extensive swelling after the fourth dose should not be considered a contraindication to receipt of a fifth dose at school entry.** Parents should be informed of the increase in reactogenicity that has been reported following the fourth and fifth doses of DTaP.

DTaP Contraindications

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

Despite the increased reactogenicity of the fourth and fifth doses, DTaP remains the preferred vaccine for preventing pertussis, diphtheria, and tetanus among children because of the improved safety profile when compared with whole cell pertussis vaccines.

CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Contraindications to further vaccination with 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.

VACCINE STORAGE AND HANDLING

DTaP and DTP vaccines should be stored continuously at $2^{\circ}\text{--}8^{\circ}\text{C}$ ($35^{\circ}\text{--}46^{\circ}\text{F}$). The pertussis antigen is most susceptible to extremes of temperature, although normal ambient temperature up to 4 days will not destroy it. Freezing, on the other hand, substantially reduces the potency of the pertussis component.

PERTUSSIS SURVEILLANCE

Pertussis cases are reported to the Centers for Disease Control and Prevention via two systems. First, the states provide information about cases of pertussis, including age, gender, county of residence, and date of onset, to *Morbidity and Mortality Weekly Report (MMWR)*. Most states provide this information on a weekly basis, but for some there is lengthy delay in reporting. The second system, the Supplementary Pertussis Surveillance System (SPSS), consists of detailed epidemiologic information received on about 80% of cases reported to the *MMWR*. Although many pertussis cases go unreported, the surveillance system is useful for monitoring epidemiologic trends. For instance, the highest incidence of pertussis occurs in

DTaP Precautions (Warnings)*

- Moderate or severe acute illness
- Temperature $\geq 105^{\circ}\text{F}$ (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, 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

infancy, the age group at greatest risk for severe illness and complications. In recent years, the surveillance system has reflected an increase in the incidence of pertussis in all age groups, most notably among adolescents and adults.

Guidelines on pertussis surveillance and outbreak control are available on the National Immunization Program website at <http://www.cdc.gov/nip/publications/pertussis/guide.htm>.

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