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.
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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 last stage, 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. 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.
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.

**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.
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 gradually increased during the 1990's. A total of 7,796 cases was reported in 1996, the largest number since 1967 (2.9 per 100,000 population). A provisional total of 6,031 cases was reported in 1999. 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 1980 through 1998, 58% of all reported cases were in children <5 years of age. Thirty-nine percent of reported cases were children <12 months of age. During this 19 year period, 14% of reported cases were in persons >20 years of age. However, older persons have accounted for a larger proportion of cases in recent years. In 1985-1987, 75% of reported cases were among children <10 years of age and 25% of cases were among persons >10 years. In contrast, in 1995-1997, children <10 accounted for 58% of reported cases, while persons 10 years of age or older accounted for almost 42% of reported cases of pertussis.
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.

- 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

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.

Four acellular pertussis vaccines are currently licensed for use in the United States. All four vaccines are combined with diphtheria and tetanus toxoids as DTaP. Acel-Imune® (Wyeth Lederle) contains 4 components, predominately filamentous hemagglutinin (FHA). Infanrix® (SmithKline Beecham) contains 3 antigens, mostly pertussis toxin (PT) and FHA. Tripedia® (Aventis-Pasteur) contains two components, FHA and PT, in equal amounts. Certiva® (North American Vaccine) contains only PT.

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 71% to 84% for vaccines currently licensed in the United States.
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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
Interchangeability of Pertussis Vaccines
- DTaP preferred for all doses of the series
- DTaP may be substituted for any dose of the pertussis series
- Series begun with whole cell vaccine may be completed with DTaP

Interchangeability of Different Brands of DTaP Vaccine
- No efficacy or safety data available for "mix-and-match" DTaP schedules using different brands of DTaP
- Series should be completed with same type of vaccine
- Use different type of DTaP vaccine if necessary

DTaP Fifth Dose
- Children who are eligible for 5th dose of an acellular pertussis series:
  - use Acel-Imune if possible
  - use another DTaP if Acel-Imune is not in stock
  - do NOT miss opportunity to administer the 5th dose

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 whole-cell DTP or 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 vaccines are as efficacious as whole cell pertussis vaccines when administered to infants as the primary series. In addition, local reactions, fever, and other systemic adverse events occur substantially less often after DTaP administration than after administration of whole cell DTP. As a result, DTaP vaccines are recommended for all five doses of the vaccination schedule. For children who have started the vaccination series with whole cell DTP, **DTaP may be substituted for any doses of the pertussis series.** A pertussis vaccination series begun with whole cell DTP may be completed with DTaP.

There are no data regarding the safety, immunogenicity, and efficacy of using DTaP vaccines from different manufacturers for successive doses of the primary or booster vaccination series ("mix and match"). Whenever possible, the same brand of DTaP vaccine should be used for all doses of the vaccination series. However, the type of vaccine previously administered may not be known, or the type of vaccine used for earlier doses may not be available to a vaccine provider. In these circumstances,
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**
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

Children who have recovered from satisfactorily documented pertussis do not need 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.

Adverse Reactions Following Vaccination

As with all injected vaccines, administration of DTaP may cause local reactions, such as pain, redness, or swelling, particularly following the 5th dose. Mild systemic reactions such as fever, drowsiness, fretfulness, and low grade fever may occur after either whole-cell DTP vaccination and DTaP vaccination. However, mild reactions following the first four doses are less common among children who receive DTaP. For instance, fever of >101°F is reported in 3%-5% of DTaP recipients 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 ≥105°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.

The number of children included in the DTaP trials was insufficient to estimate the risk for rare severe reactions, such as encephalopathy or anaphylaxis. Surveillance for rare adverse events will continue as acellular pertussis vaccines are used more widely.

In 1991 and 1993, the Institute of Medicine (IOM) conducted comprehensive reviews of all available data on the relationship of encephalopathy and whole cell pertussis vaccine. The 1991 report concluded that the available evidence suggests a causal relationship between the receipt of whole cell pertussis-containing vaccine and acute encephalopathy, and estimated the excess risk as 0-10.5 cases per million doses administered. In 1993, the IOM concluded that the available evidence suggests a causal relationship between receipt of whole cell pertussis vaccine and chronic encephalopathy, based largely on data from the National Childhood Encephalopathy Study conducted in Great Britain from 1976 to 1979. However, the IOM concluded that there was no evidence of chronic
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 ≥40.5°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.

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**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
Vaccine Storage and Handling

DTaP and DTP vaccines should be stored continuously at 2°-8°C (35°-46°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.

Other Considerations About the Pertussis Vaccine Controversy

In addition to the adverse events following whole cell DTP vaccination already discussed, other issues about the safety, efficacy, and benefit of whole cell pertussis vaccine have been raised by its opponents. They argue that (1) a number of other events, including SIDS and infantile spasms, may be related to DTP vaccination; (2) the decline in pertussis incidence is due to improvements in living conditions and not to pertussis vaccine; (3) modern medical therapy makes pertussis disease a relatively trivial illness. To summarize, they argue that the risks of vaccine usage outweigh the benefits. It is important to examine each of these issues in greater depth. These issues have not been raised for acellular pertussis vaccines.

There is no distinct syndrome resulting from vaccine administration, and therefore many temporally associated adverse events probably represent background illness rather than illness caused by vaccine. This distinction is critical, as the first year of life is also the time when many congenital neurologic disorders first become manifest. Further, the known febrile and other systemic effects of DTP vaccination may stimulate or precipitate inevitable symptoms of underlying central-nervous system disorders, such as febrile seizures and epilepsy, particularly since DTP may be the first pyrogenic stimulus an infant receives.

Sudden infant death syndrome (SIDS) has occurred among infants who had recently received DTP or DT. The largest SIDS study to date was conducted by the National Institute of Child Health and Human Development at the National Institutes of Health (NIH). In the study, SIDS cases were actually less likely to have recently received DTP than non-SIDS cases.
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
United Kingdom during this epidemic. Studies carried out in Great Britain during this epidemic showed a vaccine efficacy of 70%-90%. A risk-benefit analysis has been performed for the U.S. to compare the outcomes with or without a vaccination program using a hypothetical cohort of 1 million children from birth to 6 years of age who received or did not receive pertussis vaccination. The ratio of overall costs without a program to those with a program was 5.7:1. The benefit-cost ratio (reduction in disease costs divided by program costs) was 11.1:1. Without a program, the estimated annual number of residual defects from encephalitis (both vaccine and disease induced) would decrease from 54 to 29 cases. However, the estimated annual deaths from pertussis would increase more than 10-fold, from 44 to 457.

**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 the Morbidity and Mortality Weekly Report (MMWR) office. 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 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.
Selected References


