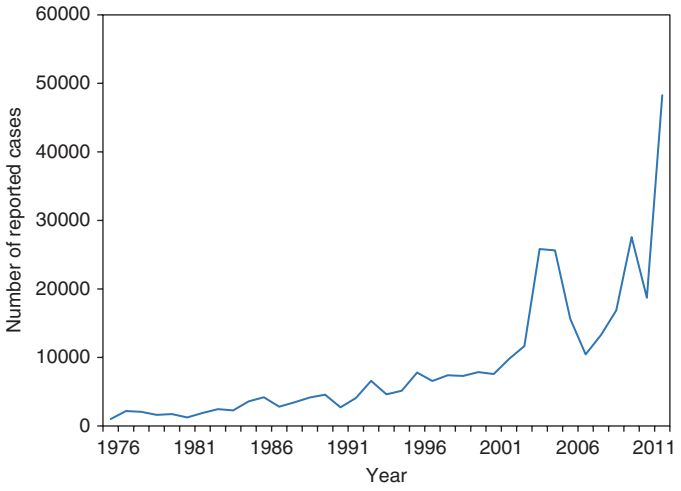


**FIGURE 185-2 Reported cases of pertussis by year—United States, 1976–2012.** *(From the Centers for Disease Control and Prevention, www.cdc.gov/pertussis/surv-reporting/cases-by-year.html. Accessed December 17, 2013.)*

Before the institution of widespread immunization programs in the developed world, pertussis was one of the most common infectious causes of morbidity and death. In the United States before the 1940s, between 115,000 and 270,000 cases of pertussis were reported annually, with an average yearly rate of 150 cases per 100,000 population. With universal childhood immunization, the number of reported cases fell by >95%, and mortality rates decreased even more dramatically. Only 1010 cases of pertussis were reported in 1976 (Fig. 185-2). After that historic low, rates of pertussis slowly increased. In recent years, pertussis epidemics have been reported with increasing frequency worldwide. The United States experienced widespread outbreaks of pertussis in 2005, 2010, and 2012 at levels not seen in 40–50 years (>40,000 reported cases in 2012).

Although thought of as a disease of childhood, pertussis can affect people of all ages and is increasingly being identified as a cause of prolonged coughing illness in adolescents and adults. In unimmunized populations, pertussis incidence peaks during the preschool years, and well over half of children have the disease before reaching adulthood. In highly immunized populations such as those in North America, the peak incidence is among infants <1 year of age who have not completed the three-dose primary immunization series. An increase in pertussis incidence among adolescents and adults began in the late 1990s and led to the introduction of an adolescent booster across North America by 2006. While the disease burden among adolescents has started to decrease, children 7–10 years of age have recently emerged as a high-risk group. In major outbreaks in 2010 and 2012, the incidence of pertussis among children 10 years of age, most of whom were fully immunized, was as high as that among infants <6 months of age. Although adults contribute a smaller proportion of reported cases of pertussis than do children and adolescents, this difference may be related to a greater degree of underrecognition and underreporting. A number of studies of prolonged coughing illness suggest that *B. pertussis* may be the etiologic agent in 12–30% of adults with cough that does not improve within 2 weeks. In one study of the efficacy of an acellular pertussis vaccine in adolescents and adults, the incidence of pertussis in the placebo group was 3.7–4.5 cases per 1000 person-years. Although this prospective cohort study yielded a lower estimate than the studies of cough illness, its results still translate to 600,000–800,000 cases of pertussis annually among adults in the United States.

Severe morbidity and high mortality rates, however, are restricted almost entirely to infants. In Canada, there were 16 deaths from pertussis between 1991 and 2001; all those who died were infants ≤6 months of age. Similarly, in the United States between 1993 and 2004, all pertussis deaths and 86% of hospitalizations for pertussis involved infants ≤3 months of age. Although school-age children are the source of infection for most households, adults are the likely source for cases in high-risk infants and may serve as the reservoir of infection between epidemic years.

## PATHOGENESIS

Infection with *B. pertussis* is initiated by attachment of the organism to the ciliated epithelial cells of the nasopharynx. Attachment is mediated by surface adhesins (e.g., pertactin and filamentous hemagglutinin), which bind to the integrin family of cell-surface proteins, probably in conjunction with pertussis toxin. The role of fimbriae in adhesion and in maintenance of infection has not been fully delineated. At the site of attachment, the organism multiplies, producing a variety of other toxins that cause local mucosal damage (tracheal cytotoxin, dermonecrotic toxin). Impairment of host defense by *B. pertussis* is mediated by pertussis toxin and adenylate cyclase toxin. There is local cellular invasion, with intracellular bacterial persistence; however, systemic dissemination does not occur. Systemic manifestations (lymphocytosis) result from the effects of the toxins.

The pathogenesis of the clinical manifestations of pertussis is poorly understood. It is not known what causes the hallmark paroxysmal cough. A pivotal role for pertussis toxin has been proposed. Proponents of this position point to the efficacy of preventing clinical symptoms with a vaccine containing only pertussis toxoid. Detractors counter that pertussis toxin is not the critical factor because paroxysmal cough also occurs in patients infected with *B. parapertussis*, which does not produce pertussis toxin. It is thought that neurologic events in pertussis, such as seizures and encephalopathy, are due to hypoxia from coughing paroxysms or apnea rather than to the effects of specific bacterial products. *B. pertussis* pneumonia, which occurs in up to 10% of infants with pertussis, is usually a diffuse bilateral primary infection. In older children and adults with pertussis, pneumonia is often due to secondary bacterial infection with streptococci or staphylococci. Deaths from pertussis among young infants are frequently associated with very high levels of leukocytosis and pulmonary hypertension.

## IMMUNITY

Both humoral and cell-mediated immunity are thought to be important in pertussis. Antibodies to pertussis toxin, filamentous hemagglutinin, pertactin, and fimbriae are all protective in animal models. Pertussis agglutinins were correlated with protection in early studies of whole-cell pertussis vaccines. Serologic correlates of protection conferred by acellular pertussis vaccines have not been established, although antibody to pertactin, fimbriae, and (to a lesser degree) pertussis toxin correlated best with protection in two efficacy trials. The duration of immunity after whole-cell pertussis vaccination is short-lived, with little protection remaining after 10–12 years. Recent studies have demonstrated early waning of immunity—i.e., within 2–4 years after the fifth dose of acellular pertussis vaccine in children who received acellular pertussis vaccine for their primary series in infancy. These data suggest that boosters may be needed more frequently than every 10 years, as previously thought. Although immunity after natural infection was thought to be lifelong, seroepidemiologic evidence demonstrates that it clearly is not and that subsequent episodes of clinical pertussis are prevented by intermittent subclinical infection.

## CLINICAL MANIFESTATIONS

Pertussis is a prolonged coughing illness with clinical manifestations that vary by age (Table 185-1). Although not uncommon among adolescents and adults, classic pertussis is most often seen in preschool and school-age children. After an incubation period averaging 7–10 days, an illness develops that is indistinguishable from the common cold and is characterized by coryza, lacrimation, mild cough, low-grade fever, and malaise. After 1–2 weeks, this *catarrhal phase* evolves into the *paroxysmal phase*: the cough becomes more frequent and spasmodic with repetitive bursts of 5–10 coughs, often within a single expiration. Posttussive vomiting is frequent, with a mucous plug occasionally expelled at the end of an episode. The episode may be terminated by an audible whoop, which occurs upon rapid inspiration against a closed glottis at the end of a paroxysm. During a spasm, there may be impressive neck-vein distension, bulging eyes, tongue