185 Pertussis and Other *Bordetella* Infections

Karina A. Top, Scott A. Halperin

Pertussis is an acute infection of the respiratory tract caused by *Bordetella pertussis*. The name *pertussis* means "violent cough," which aptly describes the most consistent and prominent feature of the illness. The inspiratory sound made at the end of an episode of paroxysmal coughing gives rise to the common name for the illness, "whooping cough." However, this feature is variable: it is uncommon among infants ≤6 months of age and is frequently absent in older children and adults. The Chinese name for pertussis is "the 100-day cough," which accurately describes the clinical course of the illness. The identification of *B. pertussis* was first reported by Bordet and Gengou in 1906, and vaccines were produced over the following two decades.

MICROBIOLOGY

Of the 10 identified species in the genus *Bordetella*, only four are of major medical significance. *B. pertussis* infects only humans and is the most important *Bordetella* species causing human disease. *B. parapertussis* causes an illness in humans that is similar to pertussis but is typically milder; co-infections with *B. parapertussis* and *B. pertussis* have been documented. With improved polymerase chain reaction (PCR) diagnostic methodology, up to 20% of patients with a pertussis-like syndrome have been found to be infected with *B. holmesii*, formerly thought to be an unusual cause of bacteremia. *B. bronchiseptica* is an important pathogen of domestic animals that causes kennel cough in dogs, atrophic rhinitis and pneumonia in pigs, and pneumonia in cats. Both respiratory infection and opportunistic infection due to *B. bronchiseptica* are occasionally reported in humans. *B. petrii*, *B. hinzii*, and *B. ansorpii* have been isolated from patients who are immunocompromised.

Bordetella species are gram-negative pleomorphic aerobic bacilli that share common genotypic characteristics. *B. pertussis* and *B. parapertussis* are the most similar of the species, but *B. parapertussis* does not express the gene coding for pertussis toxin. *B. pertussis* is a slow-growing fastidious organism that requires selective medium and forms small, glistening, bifurcated colonies. Suspicious colonies are presumptively identified as *B. pertussis* by direct fluorescent antibody testing or by agglutination with species-specific antiserum. *B. pertussis* is further differentiated from other *Bordetella* species by biochemical and motility characteristics.

B. pertussis produces a wide array of toxins and biologically active products that are important in its pathogenesis and in immunity. Most of these virulence factors are under the control of a single genetic locus that regulates their production, resulting in antigenic modulation and phase variation. Although these processes occur both in vitro and in vivo, their importance in the pathobiology of the organism is unknown; they may play a role in intracellular persistence and person-to-person spread. The organism's most important virulence factor is *pertussis toxin*, which is composed of a B oligomer–binding subunit and an enzymatically active A protomer that ADP-ribosylates a guanine nucleotide-binding regulatory protein (G protein) in target cells, producing a variety of biologic effects. Pertussis toxin has important mitogenic activity, affects the circulation of lymphocytes, and serves as an adhesin for bacterial binding to respiratory ciliated cells. Other important virulence factors and adhesins are *filamentous hemagglutinin*, a component of the cell wall, and *pertactin*, an outer-membrane protein. *Fimbriae*, bacterial appendages that play a role in bacterial attachment, are the major antigens against which agglutinating antibodies are directed. These agglutinating antibodies have historically been the primary means of serotyping *B. pertussis* strains. Other virulence factors include tracheal cytotoxin, which causes respiratory epithelial damage; adenylate cyclase toxin, which impairs host immune-cell function; dermonecrotic toxin, which may contribute to respiratory mucosal damage; and lipooligosaccharide, which has properties similar to those of other gram-negative bacterial endotoxins.

EPIDEMIOLOGY

Pertussis is a highly communicable disease, with attack rates of 80–100% among unimmunized household contacts and 20% within households in well-immunized populations. The infection has a worldwide distribution, with cyclical outbreaks every 3–5 years (a pattern that has persisted despite widespread immunization). Pertussis occurs in all months; however, in North America, its activity peaks in summer and autumn.

In developing countries, pertussis remains an important cause of infant morbidity and death. The reported incidence of pertussis worldwide has decreased as a result of improved vaccine coverage (Fig. 185-1). However, coverage rates are still <50% in many developing nations; the World Health Organization (WHO) estimates that 90% of the burden of pertussis is in developing regions. In addition, overreporting of immunization coverage and underreporting of disease result in substantial underestimation of the global burden of pertussis. The WHO estimates that there were 195,000 deaths from pertussis among children in 2008.

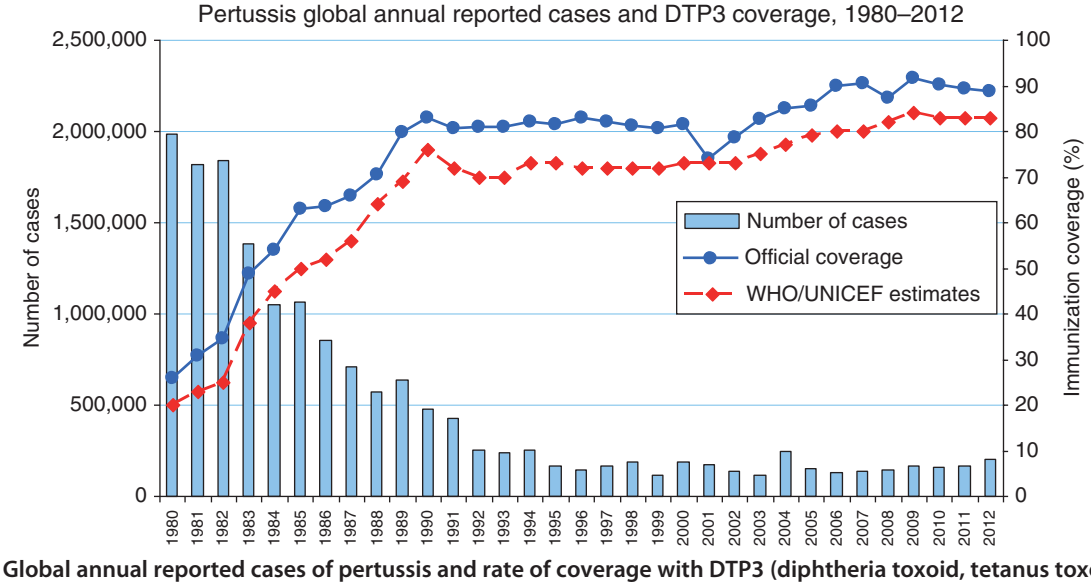

FIGURE 185-1 Global annual reported cases of pertussis and rate of coverage with DTP3 (diphtheria toxoid, tetanus toxoid, and pertussis vaccine; 3 doses), 1980–2012. *(© World Health Organization, 2013. All rights reserved. From www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/Pertussis_coverage.JPG. Source: WHO/IVB database, 2013.)*