

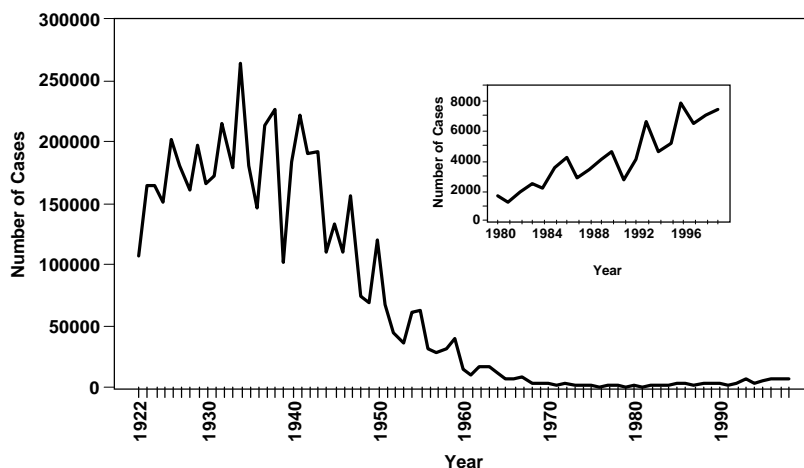
Chapter 1 — Background

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In the early- to mid-1900s, pertussis was one of the most common childhood diseases and a major cause of childhood mortality in the United States. Between 1922 and 1940 the average incidence of pertussis was approximately 150/100,000 population.^{1,2} After the introduction of pertussis vaccine in the 1940s, by 1980 the average incidence of pertussis had decreased to about 1/100,000.³ However, since the 1980s reported pertussis incidence has increased (see **Figure 1-1**); the reasons for this increase are likely to be multifactorial and include improvements in diagnosis and reporting of cases in adolescents and adults.³ As shown in **Figure 1-1**, every 3 to 4 years there is an epidemic of pertussis; the most recent epidemic year was 1996 when 7,796 cases were reported – this was the highest number of reported cases since 1967.

Figure 1-1. Reported Pertussis Cases, United States, 1922-1999.



Approximately 40% of reported pertussis cases are among children aged <5 years.³ In recent years, an increasing proportion of cases has been reported among adolescents and adults, and the number of outbreaks reported among school-age children and adolescents has been increasing.³⁻⁶ Infected adolescents and adults may introduce pertussis into households where susceptible preschool-age children could be exposed (see **Chapter 7: Household Settings**).⁷⁻¹²

Early diagnosis and antimicrobial treatment of cases may lessen the severity of symptoms and limit the period of communicability (see **Chapter 3: Treatment and Chemoprophylaxis**). In addition, prompt identification of cases may help identify un- or undervaccinated children among contacts. Vaccination may help to protect these children (see **Chapter 4: Use of Pertussis Vaccine in Outbreaks**). However, during an outbreak antimicrobial prophylaxis of household and other close contacts is the primary method used to prevent secondary cases. Because pertussis can be very severe among infants,

antimicrobial prophylaxis is especially important in this age group.

DISEASE DESCRIPTION

Pertussis, or whooping cough, is a highly communicable infectious disease caused by the bacterium *Bordetella pertussis*. Pertussis is characterized by spasms of severe coughing (paroxysms). The pertussis paroxysms are continuous without inspiration until the end and are often followed by the characteristic inspiratory whoop and/or post-tussive vomiting. The incubation period is thought to be about 7-10 days (range 4-21 days)^{2,13,14} and rarely may be as long as 42 days.^{15,16} Illness onset is insidious, with symptoms similar to those of a minor upper respiratory infection (i.e., catarrhal period). During the first 1-2 weeks of illness, coryza with an intermittent non-productive cough is common; this period is followed by episodes of paroxysmal coughing which frequently last for several weeks (i.e., paroxysmal period). The disease peaks in severity after one or more weeks of paroxysmal coughing and begins to taper off with an extensive convalescent period of 2-6 weeks that may last up to 3 months in some cases. In a study of 100 culture-confirmed cases among children aged <16 years, the average duration of cough was 8 weeks (range 1 to 16 weeks).¹⁷ In another study performed among 247 children aged <16 years with culture-confirmed pertussis, 75% had a cough for >3 weeks.¹⁸ Patients often experience significant sleep disturbance.^{19,20} Pertussis may occur among persons at any age regardless of vaccination status and may be relatively common among adolescents and adults,^{21,22} although infants aged <1 year have the highest rates of reported disease.^{1,3}

Hospitalization is commonly required for the treatment of infants with pertussis.^{8,13,14,23,24} Complications such as pneumonia are also most common among infants; other less common complications include nutritional problems due to repeated vomiting; neurological complications such as seizures and encephalopathy; otitis media; complications related to apnea such as hypoxia, seizures and hypoxic encephalopathy; and conditions resulting from the pressure effects of severe paroxysmal coughing including rib fracture, pneumothorax, atelectasis, epistaxis, subdural hematomas, hernias, and rectal prolapse. Transient urinary incontinence, hernias and lumbar pain associated with the pertussis cough have been described among adults with pertussis.^{10,25,26} Although a rare event even among children, pertussis encephalopathy has been documented in an adult.²⁷ Primary or secondary bacterial pneumonia is the cause of most pertussis-related deaths.²⁸

Differential diagnoses of pertussis include infections with other etiologic agents of cough illness, including adenoviruses, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and respiratory syncytial virus.^{9,13,14} Parapertussis caused by the bacterium *B. parapertussis* may also cause whooping cough. Two other *Bordetella* species -- *B. bronchiseptica* and *B. holmesii* have occasionally been associated with a pertussis-like cough illness.^{29,30,31,32} Differentiation between *Bordetella* species is based on isolation of the organism in

laboratory culture.

Infants aged <1 year

Among infants aged <6 months, apnea may occur, and whoop or paroxysms may be absent. In young unvaccinated children, leukocytosis and lymphocytosis are common findings during the early paroxysmal stage.^{17,18,33,34} Infants are more likely than older children or adults to have severe disease, to suffer from complications, to require hospitalization, or to die.^{1,3,17,28,35-38}

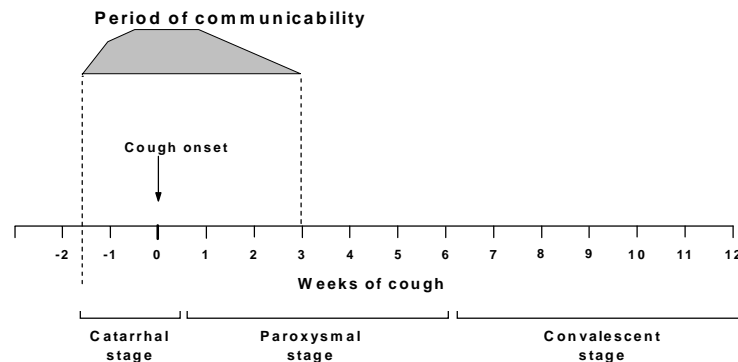
Adolescents and adults

Compared with un-immunized children, adolescents and adults with pertussis are more likely to have milder illness (i.e., an illness resembling an upper respiratory infection or an acute cough illness without paroxysms, whoop, or post-tussive vomiting).^{26,39-41} However, some infections may result in severe illness with significant morbidity.^{26,39-41} Similar to children, adolescents and adults with pertussis often do not have symptoms of a respiratory illness between coughing attacks.^{21,26} Because pertussis is not always considered as a cause of cough illness among adolescents and adults, these patients may be mis-diagnosed as having bronchitis or asthma.^{26,40} Additionally, not all pertussis infections result in a cough illness.^{17,25,42-47} In a prospective household contact study to evaluate the efficacy of DTaP vaccines in children, the spectrum of symptoms among adults was also studied. Among the 121 families with at least one pertussis case in a child, 79 adults had evidence of infection with *B. pertussis*.²⁵ Of these 79 adults, 9% had no cough, 91% had a cough, 63% had paroxysms, 52% had sleep disturbed by cough, 53% had cough followed by choking and/or vomiting, and 8% had whoops.²⁵ Amongst the 72 adults with a cough, the cough lasted an average of 54 days (median: 49 days); 63 (80%) of these had cough \geq 3 weeks.²⁵

TRANSMISSION

B. pertussis is transmitted from person to person via aerosolized droplets produced from a cough or sneeze or by direct contact with secretions from the respiratory tract of infectious individuals. Pertussis is highly contagious, with 80% secondary attack rates among susceptible persons (i.e., persons who have not been immunized or have not had a prior case of pertussis).^{15,48,49} Persons with pertussis are most infectious during the catarrhal period and the first 2 weeks after cough onset (i.e., approximately 21 days) (see **Figure 1-2**); some individuals, such as infants who remain culture-positive for several weeks, may be infectious for a longer period. However, compared to other infectious diseases, less is known about pertussis transmission such as the dose required or length of exposure needed to cause infection in a susceptible person.

Figure 1-2: Period of communicability of pertussis



In several studies, household members have been documented to have been the source of pertussis in infants.^{7,12,37,50,51} In a study of pertussis cases among 430 hospitalized children aged <2 years, the source of pertussis in the child was suspected to be a parent in 20%, a sibling in 53%, a child relative in 12%, a neighbor in 8%, and a day care contact in 3%.³⁷ However, the epidemiology of pertussis in Canada has been very different from that in the U.S. – with a much higher incidence, likely due to the use of an ineffective whole-cell DTP vaccine.⁵² A study of source of infection among infants aged <1 year in the U.S. is on-going.

PATHOGENESIS

Pathogenesis by *B. pertussis* is poorly understood and studies are needed to better understand the host-organism interaction. However, several virulence factors have been described including filamentous hemagglutinin (FHA), pertactin (PRN), fimbriae (FIM), pertussis toxin (PT), endotoxin (lipo-oligosaccharide), tracheal colonization factor, tracheal cytotoxin, and adenylate cyclase toxin. It is thought that after introduction of the organism into the respiratory tract via aerosol droplets, the organism attaches to ciliated cells in the nasopharynx, and unless there is an immune response to thwart it, proliferates and spreads into ciliated cells in the trachea and bronchi causing paralysis and death of these cells.⁵³ Bacteremia does not occur.¹⁴ It has been found that *B. pertussis* can enter and survive within phagocytic leukocytes and non-phagocytic cells, but how this impacts on pathogenesis and the host immune response is unclear.^{53,54} Virulence factors (such as pertussis toxin, adenylate cyclase toxin, and others that have yet to be identified) cause the clinical characteristics of pertussis. *B. pertussis* infection can cause a primary pertussis pneumonia with subsequent respiratory failure and death.^{38,53,54}

IMMUNITY

The mechanism of immunity to pertussis is not well understood. Studies in mice support a role for both humoral and cell-mediated immunity. In most patients, after natural infection there is a rise in antibodies to PT, FHA, or PRN, as well as an increase in IgA in the respiratory mucosa that corresponds with the disappearance of *B. pertussis* from the nasopharynx.¹⁴ Acellular pertussis vaccines containing only inactivated PT have been

demonstrated to be effective in prevention of pertussis, suggesting that immunity to PT is sufficient to prevent disease; some experts believe that multi-component vaccines including other components of *B. pertussis* (PRN, FIM, or FHA) may be more effective than mono-component vaccines.⁵⁵ However, available data are insufficient to allow comparisons of the effectiveness of currently licensed acellular pertussis vaccines.

Immunity to pertussis has been shown to wane 5-10 years after vaccination with whole-cell pertussis vaccines.⁴⁶ Waning immunity following vaccination with acellular pertussis vaccines may also occur but data are currently limited. Immunity following natural disease may wane over time and exposure to the organism with asymptomatic or symptomatic infection may be needed to maintain effective protection.⁴¹ However, some experts believe that immunity following natural disease is lifelong.^{14,56} To our knowledge, there are no published reports of positive culture results from 2 separate episodes of pertussis among children aged <7 years, although there are anecdotal reports of studies in which adult patients self-report a past episode of pertussis.^{21,41} Attack rates among adults in a household study in Germany (where vaccination coverage was minimal and pertussis is endemic) did not differ by recall of past pertussis; 26% of adults had typical pertussis.⁵⁷ Neonates and unimmunized infants are susceptible to pertussis, suggesting that maternal antibodies that cross the placenta are insufficient to protect against pertussis.

The effectiveness of vaccines licensed in the U.S. for protection against moderate to severe pertussis was estimated to range from 60% to 90% .^{56,58} The routine use of pertussis-containing vaccines has greatly reduced the incidence of pertussis, but their use in outbreak control is limited because multiple doses are required for protection and no product is currently licensed for use in persons ≥ 7 years of age (see **Chapter 4: Use of Pertussis Vaccine in Outbreaks**).

CULTURE CONFIRMATION

Obtaining a positive culture result from a person with pertussis can be affected by several factors such as how the specimen is handled (see **Chapter 2: Diagnosis and Laboratory Methods**), the stage of illness at the time of specimen collection, the use of antimicrobial therapy prior to culture, immunity from past infection or from vaccination, and age of the case-patient.

Several studies have shown that specimens obtained for culture within 3 weeks of cough onset had a higher proportion of culture-positive results compared with specimens taken later in the illness.^{18,59,60} In the absence of treatment, the culture positivity rate may be greater than 50% from specimens obtained within the first 3 weeks after cough onset; after 6 weeks of cough the rate of culture-positivity is less than 20%.^{18,49,59,60} In addition, the use of an nasopharyngeal aspirate instead of a swab results in a higher proportion of culture-positive results.⁶¹ Lastly, plating of culture medium immediately and directly

(i.e., without transport) after specimen collection increases yield.^{18,49,59,60}

Treatment with erythromycin or trimethoprim-sulfamethoxazole prior to culture decreases the likelihood of a positive culture result.^{18,60} After initiation of either antibiotic, *B. pertussis* is rapidly cleared from the nasopharynx (see **Chapter 3: Treatment and Chemoprophylaxis**).⁶²

Among pertussis case-patients, older persons are less likely to have positive culture results than are young children.^{18,60} Similarly, a smaller proportion of vaccinated children with pertussis have positive culture results compared with unvaccinated children.^{18,60,63} For example, in one large study, 28% of 424 vaccinated children aged ≤ 10 years with pertussis were culture-positive compared with 46% of 1426 unvaccinated children with pertussis.⁶⁰

CARRIAGE

Long-term carriage (e.g., several months) of *B. pertussis* probably does not occur. However, it has been documented that persons can become infected and remain asymptomatic.^{42-47,64} Transmission from asymptomatic infected persons to others may occur but is less likely than for symptomatic persons since asymptomatic persons do not have a cough.⁶⁵ It is unknown how asymptomatic infection impacts on pertussis epidemiology. Transmission from asymptomatic persons may explain the occurrence of pertussis in patients who have not been in contact with a known case.⁴²

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