87 Pertussis

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Pertussis is an acute respiratory tract infection affecting all age groups. Pre-vaccine era witnessed a high prevalence of disease with a significant morbidity and mortality. Introduction of vaccine resulted in a significant decrease of the disease in children; however, because of waning immunity following natural disease in 7–14 years or vaccination in 4–12 years and because there is no booster vaccination after 7 years of age, the disease incidence increased in the adolescents and adults resulting in a pool of patients who remained a source for infecting others especially young infants who are not yet vaccinated or have received only one dose of the vaccine.

Because of these factors, the disease remained endemic in most of the countries with 50 million cases occurring annually resulting in 400,000 deaths. Most of the morbidity and mortality occur in young infants. However, the number of global reported cases is less than the estimated one (◉ *Fig. 87.1*).

The affected adolescents and adults usually present with a typical presentation of prolonged cough without classis whoop and therefore remain infectious for a long period.

Organism

Pertussis is mainly caused by *Bordetella pertussis* and *Bordetella parapertussis*. Bordetella is a Gram-negative fastidious aerobic, nonmotile bacillus. Therefore, it requires special media for its growth. The first media introduced was Bordet–Gengou agar. Bordet–Gengou medium is composed of potato, glycerol, and cephalexine. Recently, Regan–Lowe medium is being introduced. It is composed of charcoal agar, defibrinated horse blood, cephalexine, and amphoterecin B. In addition, there is a semisolid transport media of Regan–Lowe formula in case there is anticipated delay in culturing the specimen. Both media have similar yield although some studies showed Regan–Lowe to be superior. *B. pertussis* has also been shown to grow in some other media like buffered charcoal, yeast extract agar, and cyclodextrin solid medium.

Bordetella genus include other related species that may cause human disease but milder than that of *B. pertussis*. These species include:

- *Bordetella bronchoseptica*, which is primarily a pathogen in animals. It occasionally causes mild disease in humans.
- *Bordetella homesii* and *Bordetella hinzii* may be isolated from blood in patients with chronic illnesses. *B. henzii* has also been isolated from the respiratory tract of cystic fibrosis patients.
- *Bordetella trematum* is rarely isolated from wound and ear infections.
- *Bordetella petrii* has been isolated from patient with cystic fibrosis.

Pathogenesis

B. pertussis is acquired by inhalation of infected droplets. Once in the nasopharynx, they may invade the lower part of respiratory tract. It has a high preference for respiratory epithelium without systemic invasion. The attachment to respiratory epithelium is mediated by pertussis toxin and lymphocytosis promoting factor. The local damage is mediated by multiple factors that include in addition to pertussis toxin, tracheal cytotoxin, heat labile toxin, and other toxins. Adenylate cyclase and pertussis toxin inhibit the host immune response both by retarding chemotoxis and preventing phagocytosis and intracellular killing.

Clinical Features

After an incubation period of 7–10 days the symptoms start. The disease proceeds through three stages: catarrhal, paroxysmal, and convalescent.

Catarrhal Stage

In this stage, the child has nonspecific symptoms of fever, runny nose, conjunctivitis, and mild cough. This stage lasts for 1–2 weeks and it is usually very difficult to differentiate from symptoms of other respiratory infections.

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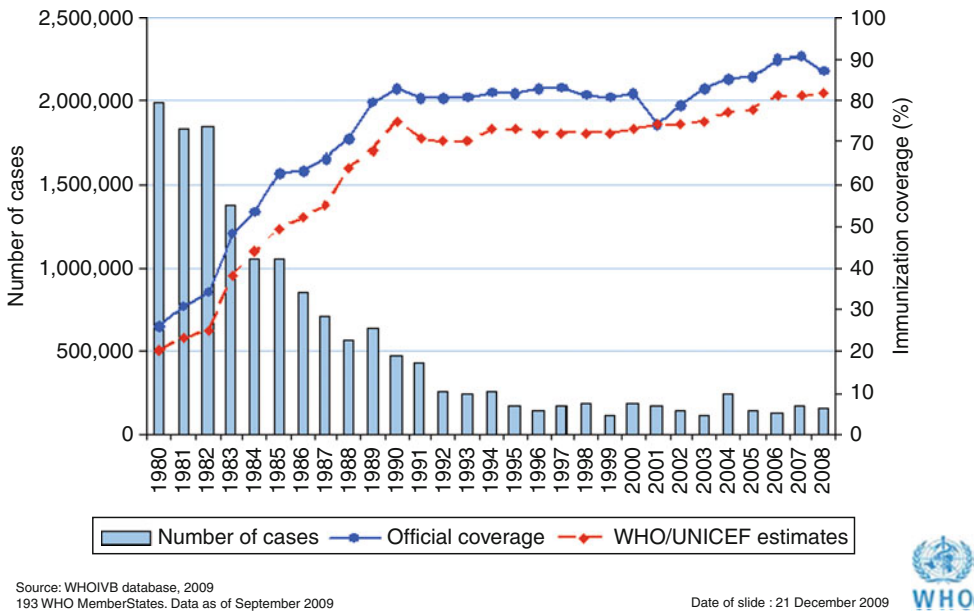

Figure 87.1
Pertussis global annual reported cases and DTP3 coverage, 1980–2008

Paroxysmal Stage

During this stage, the cough evolves into the characteristic pattern of paroxysms. Each paroxysm consists of 10–20 successive coughs that end by deep inspiration that may be associated with whoop due to forceful passage of air through narrow epiglottic opening. Young infants are less likely to have whoop; however, they are prone to develop apneic spells that may be prolonged and result in cyanosis and hypoxia. It is during this stage that hypoxemic insults may result. Such hypoxia may adversely affect brain and thus cause encephalopathy or seizure attacks.

Convalescent Stage

The cough decreases in its intensity; however, the child may remain to have episodes of cough that usually are not in paroxysm. This stage usually lasts for 1–2 weeks but it may persist for months. Recurrence of brief paroxysmal cough during this stage may occur but rare.

Complications

Pertussis is an acute disease that causes significant morbidity and mortality. Pneumonia whether primary or secondary is the most common complication and the most common cause of death among patients with pertussis. Pertussis results in atelectasis and bronchopneumonia in significant number of patients; however, long-term pulmonary sequelae are rare. Secondary bacterial pneumonia is common and therefore therapy directed for these pneumonias in addition to that of pertussis is required. Most common bacterial cases of pneumonia in such patients are *S. pneumoniae, H. ifluenzae*, and *S. aureus*.

Encephalopathy occurs in 8/1,000 and seizure occurs in 3% of affected patients. The presumed cause of these brain insults is hypoxia, toxins produced by *B. pertussis*, and intracerebral hemorrhage. Other complications include otitis media, sinusitis, subconjunctival hemorrhage, epistaxis, subdural hemorrhage, and melena.

Diagnosis

Culture, PCR, and serology are different methods of diagnosis but each has its limitation.

Culture

B. pertussis is fastidious organism that requires special growth media. Therefore in suspected cases, laboratory should be informed to prepare the appropriate media. Culture requires a collection of nasopharyngeal specimen

with a Dacron or calcium alginate swab and sending it immediately to the laboratory in a specific transport media, to be cultured in Regan–Lowe or Bordet–Gengou medium.

There are a number of factors which decrease the sensitivity of the culture:

1. Culture obtained after 7 days of illness.
2. Previous antibiotic usage.
3. Poor specimen collection or poor transportation or media contamination in the laboratory.
4. Previous immunization as the organism load is usually low.

Therefore, having a negative culture does not necessarily exclude the diagnosis:

PCR

A new modality for the diagnosis with a better sensitivity. It has the advantage of ability to be positive even if collected later in the disease course; however, sensitivity decreases after the 14th day of illness.

Serology

EIISA for IgG, IgA, and IgM against pertussis antigens can be done. The best antigen to be used is pertussis toxin. Previous immunization may result in positive test. Recent vaccination usually results in positive IgM and IgG. In acute infection IgA is usually positive; however, it is better to collect acute and convalescent sera for both IgA and IgG. A twofold rise is suggestive of acute infection. In adolescents and adults, a single IgG more than 100 unit/ml is highly suggestive of acute infection.

Antigen Detection Test

Direct fluorescent antibody (DFA) test is a rapid test that has 95% specificity but it is less sensitive 60%. The advantage of DFA is being rapid with result available in 2–4 h. Other experimental rapid tests are DNA hybridization and PCR-based tests but they are not yet widely used.

Treatment

Treatment of pertussis consists of nonspecific supportive measures and directed antibiotic therapy. Supportive measures include maintaining good nutrition, providing oxygen and supporting ventilation if needed. Nonspecific therapy with steroids and salbutamol has been used in few nonrandomized studies with some benefit; however, it cannot be recommended as a standard of therapy as it is not supported by controlled randomized studies. Young infants with severe leukocytosis exceeding 100,000/mm^3 may suffer from severe respiratory distress and pulmonary hypertension leading to respiratory and circulatory failure. Autopsy of such infants has shown obstruction of small- and medium-sized pulmonary arteries with lymphocytes without thrombosis. In such infants, there is some anecdotal report of some benefit from exchange transfusion to reduce the number of leukocytes. Specific antibiotic therapy is recommended in all patients with proven or suspected pertussis. Erythromycin especially the estolate form is very effective against *Bordetella*. The recommended dosage is 40–50 mg/kg/day in four divided doses. The new macrolides (azithromycin and clarithromycin) have been shown to be of equal efficacy with better tolerance. Use of antibiotic in the catarrhal stage (within 2 weeks of illness onset) may abort or ameliorate the progression of the disease. However, if it is not introduced until the paroxysmal stage is started, then there is no efficacy on the disease course; however, it will accelerate the eradication of the organism and thus its contagiousness. The recommended duration of therapy is 14 days; however, new studies have shown 7 days of therapy is equivalent to the longer duration and this has led many authorities to recommend the shorter course of therapy.

Resistance to erythromycin has been reported in occasional cases. Patients who do not tolerate erythromycin should be treated with cortimoxazol at a dosage of 8 mg of trimethoprim 40 mg of sulfamethoxazole/kg/day in two divided doses for 14 days.

Prevention

Isolation

Children suspected to have pertussis should be isolated if hospitalized until the culture is available or the patient is being treated for 5 days with appropriate antibiotics. They should also be prevented from school or day care attendance until they are 5 days on therapy.

Prophylaxis

Household contacts should be prophylaxed with erythromycin 40 mg/kg/day qid for 14 days.

Immunization

Killed whole cell vaccine has proven to be effective in decreasing the prevalence of pertussis and should be given to all infants. Recently, acellular pertussis vaccine with less side effects is being introduced and it may be the recommended future vaccine (see section on immunization).

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