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Pertussis in Children

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Abstract

The term Pertussis which is known as whooping cough or '100 day cough' literally translates into violent cough. This disease was first elaborated in the epidemic of Paris in the year 1578. The organism Bordetella pertussis was described first in 1906 and the vaccine was first developed in 1940s. The disease was a major contributor to mortality and morbidity in infants. The disease spreads easily by aerosols. It affects all household contacts who have not been immunized. The disease inhabits ciliated cells of lower respiratory tract and induced inflammatory changes. These inturn release toxins namely pertussis toxin, dermonecrotic toxin, adenylate cyclase toxin, and tracheal cytotoxin which may act at site of invasion and also produce systemic effects. Strangely the organism per se doesn't invade the cells completely nor does it show in blood cultures. As the disease is of high severity, the prevention of pertussis has been considered an important public health issue for many years. Over the years the classical presentation of whooping cough has become uncommon, hence the diagnosis of pertussis has become difficult. Atypical clinical picture with nonspecific investigatory findings make this even more difficult. The key to managing pertussis lies in early detection and prompt treatment. This study aims to study an overall picture of Pertussis including the epidemiology pathogenesis clinical picture and treatment. It also aims to put light over outbreak control, immunity as a result of vaccination and disease exposure and future directives.

Keywords: Pertussis; whooping cough; Bordetella pertussis.

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INTRODUCTION

Whooping cough or pertussis is a communicable disease of the lower respiratory passage with acute presentation seen in infants and children below 5 years of age. The disease is caused by the bacteria Bordetella of which the species bordetella pertussis and bordetella parpertussis cause major share of the disease. Other species like Bordetella bronchoseptica may cause infections in immuno compromised individuals.

EPIDEMIOLOGY

In the past 15-20 years the incidence of Pertussis has been on the rise worldwide.[1,2] Even though the global vaccination coverage nears 85% the recent estimation of caseload is around 24 million annually which also is found to reportedly cause 160,000 deaths in children less than 5 years of age.In 2017, India had a reported 23,766 reported pertussis cases, making it one of the highest reported number of cases of the year.[1]

The species causative of this disease is Bordetella which comes in the family of Alcaligenaceae consisting of ten species that have their own distinct character in terms of genetics. Bordetella pertussis is mostly considered the prime agent of causation of whooping cough while other species like Bordetella parapertussis and Bordetella holmessi also cause a disease pattern similar to whooping cough. Bordetella pertussis comes under gram negative group of coccobacilli and can be made out from other species on the basis of growth and other characteristics. It is a pleomorphic aerobic organism that grow optimally on growth agars like Bordet Gengou or Regan Lowe agar in an optimal growth temperature of 35 to 37 degree Celsius. B. pertussis is a fastidious, nonmotile, catalase- and oxidase positive species. Bordetella species grow slowly on blood supplemented medium and on synthetic medium containing appropriate growth factors, such as nicotinamide.

The disease is spread by aerosolization of drops when a person coughs, which is then disseminated within the ciliated pathways of the lower part of the respiratory system in a host that is susceptible to the disease. The only reservoir known for the disease is humans. Adults and children who cough are the most common sources for the transmission of the infection in infants and children. Incubation period of this disease is variable, ranging from a minimum of one week to a maximum of 3 weeks, an average being ten days.

Studies of infectious disease transmission estimated the basic reproductive number (R0) for various infectious diseases, including pertussis. R0 is defined as the expected number of secondary cases produced by a confirmed primary case in a completely susceptible population. Based on R0 estimates, pertussis is considered far more contagious than polio, smallpox, rubella, mumps, and diphtheria. Secondary attack rates of 50 to 100 percent in susceptible household contacts, depending upon the nature of the exposure.[1]

S. Dahiya *et al*[3] conducted a study on the outbreak rate and pattern of Pertussis. In their study they observed that these outbreaks have occurred in a cyclical pattern since the year of 1980. A surge of cases were noted in some specific years like 1983 1986 1990 and 1993 which have been documented by the Centers of Disease Control and Prevention 1995. They also noticed in their study that despite use of vaccine there have been a recent uprise in cases.

Bokhari H *et al*[4], in a study which was done in Pakistan, noticed that among the causative species of potential cases of whooping cough during 2005 -2009 all of them were identified as Bordetella parapertussis with only a minute fraction of bordetella pertussis isolated in the PCR testing. This study also showed the importance of developing vaccine strategies directed towards both species rather than focusing only on Bordetella pertussis.

SIGNS AND SYMPTOMS

The classic clinical features are a prolonged respiratory illness with paroxysmal coughing often followed by forced inspiratory effort causing a "whoop". The disease presents in different ways clinically based on a lot of factors including the age and status of vaccination in a child. When the disease presents in adults or adolescents the signs and symptoms are at par with those seen in children. But most of them present with a milder form of disease as compared to infants and children.

Classical Presentation Consists of three Stages: Catarrhal, Paroxysmal, and Convalescent

Catarrhal phase:This phase presents in a way that resembles the common cold with cough and coryza which lasts for upto 14 days. Fever is not usually seen and if its present is usually of low grade. The cough which initially presents in a mild variant tends to worsen as the disease progresses.

Paroxysmal phase: Coughing persists and severity increases, occurring in paroxysmal attacks, either spontaneously or triggered by external stimuli. The paroxysm is a long series of coughs during which the child may develop gagging and cyanosis. Whooping is the noise of the forced inspiratory effort following a coughing attack during the paroxysmal phase. Post-tussive emesis is frequent. The paroxysmal stage lasts for two to six weeks. Paroxysms increase in frequency during the first one to two weeks, remain at the same intensity for two to three weeks, and decrease gradually there after.

Convalescent Phase: The cough subsides gradually

over several weeks to months. Episodic coughing may reappear.

Atypical presentations occur in young infants wherethe catarrhal stage is very short or absent, and the "whoop" may not be seen. Early symptoms can include feeding difficulties, tachypnea, and cough. The infant can appear deceptively well between episodes of coughing. In vaccinated children clinical presentation and course of infection are generally less severe. In older children and adolescents they present with waning immunity.

E Yaari *et al*[5], in a study conducted to study presentation of pertussis in vaccinated individuals found that in children and adults alike, when they have been previously immunized pertussis presents as amild version with atypical symptoms and a clinical course which isn't severe. They usually suffer from persistent and prolonged cough.

DIAGNOSIS

Clinical diagnosis: For endemic or sporadic cases, a clinical case of pertussis is defined as an acute cough illness lasting at least 14 days accompanied by one of the following: Paroxysms of coughing, Inspiratory whoopand Posttussive vomiting. In an outbreak or following household contact to a known case, a clinical case is defined as a cough illness for at least 14 days; presence of the typical pertussis associated features is not required.

Centers for Disease Control and Prevention case Definition for Pertussis

A confirmed case is defined as a personwith an acute cough illness of any duration, who is culture-positive from nasopharyngeal secretions, who meets the clinical case definition with laboratory confirmation by PCR from nasopharyngeal secretions and who meets the clinical case definition and is epidemiologically linked directly to a case confirmed by either culture or PCR from nasopharyngeal secretions.[6]

A probable case is defined as a person who meets the clinical case definition without laboratory confirmation or an epidemiologic link to a laboratory confirmed case.

Various tests used for the laboratory diagnosis arebacterial culture (cough plate culture on Bordet Gengou media),polymerase chain reaction (PCR), direct fluorescent antibody (DFA) testing, and serology.

The absolute lymphocyte count is often ≥ 10,000 lymphocytes per micro L. Marked leukocytosis (eg, >60,000 cells/microL) has been associated with increased pertussis severity, (including pertussis pneumonia, and pulmonary hypertension).

Radiographic findings: In uncomplicated pertussis, chest radiographs may be normal, or demonstrate subtle abnormalities such as peri bronchial cuffing, perihilar infiltrates, or atelectasis.

Differential Diagnosis

B. parapertussis and B. bronchiseptica, Mycoplasma pneumoniae, Chlamydia spp, tuberculosis, and viral pathogens (RSV, adenovirus, parainfluenza, influenza A and B, and rhinovirus), reactive airway disease and foreign body aspiration need to be ruled out.

COMPLICATIONS

In patients of all ages, delayed clinical recognition of pertussis is more likely to result in clinical complications and sequelae. Overall, young infants are at highest risk for severe outcomes, such as respiratory failure and death. Infants hospitalized for pertussis have been shown to present with apnea, pneumonia, and convulsions. Complications of Pertussis can be divided system wise as below:

Respiratory: apnea, pneumonia, otitis media, emphysema, bronchiectasis, pneumothorax and/or pneumomediastinum.

Neurological: seizures, encephalopathy.

Malnutrition: weight loss secondary to feeding difficulties and post-tussive vomiting. Reactivation of Tuberculosis.

Difficulty sleeping, Bleeding: epistaxis, subconjunctival hemorrhage and subdural hematoma, Rectal prolapse, urinary incontinence, inguinalhernia, Rib fractures and Death.

TREATMENT

Antimicrobials within 21 days of onset of illness, may shorten the duration of symptoms and decrease transmission to susceptible contacts eradicating pertussis from the nasopharynx.

Treatment is recommended forall children with clinical pertussis (with or without laboratory confirmation), children with culture or polymerase chain reaction (PCR) confirmed pertussis even if asymptomatic at the time of confirmation and patients who have had more than 21 days of symptoms, particularly those likely to be in contact with high-risk individuals.

Antimicrobial Therapy and Post-exposure Prophylaxis for Pertussis in Infants, Children and Adolescents:

- Antimicrobial therapy depends on age of child. For children less than one month of age drugs of choice are azithromycin and erythromycin. Azithromycin is given at the dose of 10mg/kg/day once daily for 5 days while erythromycin is given 40mg/kg/day 6th hourly for 14 days. Clarithromycin and Trimethoprim sulfamethoxazole is contra indicated in this age group.
- Between 1-3 months Clarithromycin can also be given at the dose of 15mg/kg/day in two divided doses for a week and Trimethoprim at a dose of 8mg/kg/day and sulfamethoxazole at a dose of 40mg/kg/day in two divided doses can be given for 2 weeks.
- Beyond 3 months dose of Azithromycin is given 10mg/kg on day 1 upto a maximum dose of 500mg and then 5mg/kg upto a maximum of 250mg for days 2-5. Erythromycin dose remains the same upto a maximum dose of 2gm/day. Clarithromycin can be given at a dose of upto 1gm/day.
- In adolescents Azithromycin is given as 500mg single dose od Day 1 and 250mg on days 2-5. Erythromycin is given at 2gm/day 6th hourly for 14 days. Clarithromycin is given at 1 gm/day in two divided doses for 7 days. Trimethoprim is given at 200mg/day and sulfamethoxazole at 1gm/day in two divided doses for 14 days.
- Adjunctive treatments including bronchodilators, corticosteroids, bordetella pertussis immunoglobulin and antitussive agents have not proven to be beneficial. Extracorporeal membrane oxygenation (ECMO)-Infants with severe respiratory failure and pulmonary hypertension secondary to pertussis may need ECMO. Known triggers (eg, exercise, cold temperatures) for coughing paroxysms should be avoided.

Indications for hospitalization include respiratory distress including tachypnea, retractions, nasal flaring, grunting, and the use of accessory muscles, any evidence of pneumonia, the inability to feed, presence of cyanosis or apnea, with or without coughing and seizures.

Antimicrobial resistance to B. pertussis has been reported sporadically over 2 decades. It has been estimated that the occurrence of B. pertussis resistance to macrolides is less than one percent .

Fry *et al*.[7] proposed that the mechanism of resistance is due to a mutation of the erythromycin binding site in 23S rRNA. Muloiwa, R *et al*.[8] conducted a metaanalysis on burden of disease since 45 years of post-vaccination era. Eighty-two studies (49,167 participants) made the inclusion criteria. The overall median point prevalence of PCR-confirmed Bordetella pertussis was 11% (interquartile range (IQR), 5–27%), while culture-confirmed was 3% (IQR 1–9%) and paired serology a median of 17% (IQR 3–23%) over the period. Most deaths occurred in infants less than 6 months of age.

PREVENTION

Routine immunization schedules depends on age. Dtap is given 2, 4, 6 months with booster between 15-18 months and 4-6 years. Tdap is preferred for preteens, pregnant women between 27-36 weeks of each pregnancy and adults.

Outer membrane vesicles (OMV) derived from Bordetella pertussis-the etiologic agent of the resurgent disease called pertussis-are safe and effective in preventing bacterial colonization in the lungs of immunized mice. Vaccine formulations containing those OMV are capable of inducing a mixed Th1/Th2/Th17 profile, but even more interestingly, they may induce a tissue resident memory immune response. This immune response is recommended for the new generation of pertussis vaccines that must be developed to overcome the weaknesses of current commercial acellular vaccines (second generation of pertussis vaccine).[10]

Post exposure chemoprophylaxis in contacts of Pertussis is controversial as there is not much evidence regarding efficacy of post exposure prophylaxis in controlling the outbreak. CDC also actively promotes judicious use of antibiotics among healthcare providers and parents. Directed treatment towards patients who have higher chances of contacting the disease is now preferred by the CDC.

Prophylactic antibiotics after exposure in contacts who haven't developed symptoms within 21 days of first onset of cough in an index case can help to avoid the development of symptoms. For children who haven't been completely immunized and below 7 years of age with well documented infection of pertussis should complete immunization with DTaP rather than with diphtheria-tetanus vaccine. CDC also recommends prophylactic antibiotics in infants, pregnant women, immuno compromised individuals. Erythromycin is considered the drug

of choice for post exposure prophylaxis.[1]

Shweta Alai *et al*.[9], in a study conducted in Pune India, compared the gene structure of the different strains present in whole cell vaccines of India. It revealed high genetic similarity and conserved genome among strains. Phylogenetic analysis showed that clinical and vaccine strains share genetic closeness with reference strain Tohama-I.

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