Pertussis

What the Pediatric Infectious Disease Specialist Should Know

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Abstract: Pertussis is a bacterial disease that is transmitted very efficiently from human to human by droplets. It occurs at any age, is endemic in any population, and can cause outbreaks in highly variable frequencies. Hallmark of the disease is cough with or without paroxysms, whoop, and vomiting. Diagnosis relies on clinical suspicion followed by laboratory confirmation (PCR, Serology) and should be followed by prompt antibiotic treatment to stop spread of the bacteria to contact persons. Control of pertussis by acellular vaccines is possible to some extent if immunization coverage is high and booster doses are given lifelong. However new vaccines with higher efficacy rates are warranted.

Key Words: pertussis, *Bordetella,* epidemiology

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Almost all cases of pertussis (or whooping cough) are caused by *Bordetella pertussis* (Bp) or, less frequently, *Bordetella parapertussis* (Bpp) infection.[1] In rare cases, *Bordetella bronchiseptica* (which causes kennel cough in dogs) or *Bordetella holmesii* is found as the cause of cough in a patient. *Bordetella* species are fimbriated Gram-negative rods that express a variety of virulence factors, including pertussis toxin (PT, expressed by Bp only), which is the cause of leukocytosis in unimmunized patients, filamentous hemagglutinin (FHA), and pertactin (PER).

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TRANSMISSION

Bp and Bpp are effectively transmitted from human to human by droplets. Pertussis is highly contagious with an R_0 in the range of 15 to 17, that is, 1 primary case can cause as many as 17 secondary cases. This scenario assumes that the primary case transmits large amounts of bacteria and that exposed contact persons are fully susceptible. However, dynamics of contagiousness are influenced by pertussis-specific preexisting immunity of both the primary case and exposed contact persons.[2]

EPIDEMIOLOGY

The variable contagiousness of Bp explains why pertussis occurs in what appear to be single cases (Bp or Bpp); localized outbreaks (almost exclusively Bp) in families, day-care centers, schools, hospitals, and other institutions; and epidemics (Bp only) like most recently in the United States.[3,4] Pertussis is not an exclusive childhood disease but has long been known to affect individuals of any age, including newborns, and can truly be called a "family affair."[5] Notably, young infants are frequently exposed to this potentially devastating disease by their family members, that is, parents, siblings, or even grandparents.[6] Pertussis leads to individually variable degrees of specific immunity; however, immunity wanes over time leading to more or less symptomatic reinfections life long.

DISEASE

Pertussis is a chameleon that can present as anything from rhinitis and unspecific mild cough (often not leading to a physician visit or not recognized as pertussis in daily practice) to classic textbook presentation with paroxysmal coughing spells, post-tussive whooping, and vomiting. Any of these cough manifestations can last between a few days to several weeks or even months.[7] Pertussis is at least unpleasant for the patient, as these symptoms frequently interfere with daily activities and can cause significant sleep disturbances. Fever occurs in less than 20% of cases. Type and frequency of complications are dependent on age and immunity. They most commonly present as bronchoalveolar pneumonia (any age) or apnea (newborns and young infants) and more rarely as respiratory distress syndrome, seizures, and other signs of encephalopathy.[8] Pertussis in young infants can be fatal.[9]

DIAGNOSIS

Typical pertussis disease can be diagnosed clinically, but this manifestation is only the tip of the iceberg. More often, pertussis presents in a child or adolescent as an unexplained prolonged cough that does not appear to improve after 7 to 14 days' duration. Even in typical disease, clinicians are unable to distinguish Bp from Bpp infection; this distinction requires laboratory confirmation. Traditionally, bacterial culture from nasopharyngeal secretions (NPS, aspirated or obtained by a swab) has been the diagnostic gold standard. However, sensitivity of culture is low, especially in breakthrough disease (despite previous immu-

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nization) and in reinfections where the number of bacteria in the NPS is typically low.[10] Therefore, today, NPS from patients with suspected pertussis are most commonly analyzed by specific polymerase chain reaction (PCR).[11] Depending on PCR primers used in your laboratory, specific Bp can not only be distinguished from Bpp but also from other rare *Bordetella* species. Although PCR (or culture) is most promising in the early phases of the disease (weeks 1 and 2), serology is the preferred diagnostic tool thereafter. It is important that enzyme-linked immunosorbent assays based on specific antigens such as PT (specific for Bp) and FHA rather than sonicated bacteria are used. Unlike with other infectious diseases, sensitivity of IgM antibodies is low, and diagnosis mainly relies on detection of specific and IgA and/or IgG antibodies. Unfortunately, serologic tests are poorly standardized, and most laboratories do not take immunization status of patients into account. This is important, as tests cannot discriminate vaccine induced antibodies from those elicited by wild-type bacterial infection. However, in the absence of recent pertussis immunization (within previous 6 months), an anti-PT antibody value ≥27 IU/mL is sensitive and specific for pertussis.[12]

TREATMENT

Bordetellae are susceptible to a variety of antibiotics among which macrolides are most commonly used. When given early during the disease, symptoms may become ameliorated, but this is unlikely when initiated during the progressed paroxysmal stage.[13] The main indication for treatment is interruption of the infection chain by eliminating contagiousness within 5 to 7 days after onset of treatment compared with up to several weeks in untreated patients. Preferred antibiotics are clarithromycin (if ≥1 month of age, 7.5 mg/kg bid for 7 days; maximum, 1 g per day) or azithromycin (<6 months of age: 10 mg/kg as a single dose for 5 days; ≥6 months of age: day 1, 10 mg/kg as a single dose; days 2–5, 5 mg/kg as a single dose; maximum, 250 mg/d).[14] Other medications including beta mimetics, steroids, and cough-relieving drugs are not of proven benefit. In patients with lung failure, aggressive treatment such as extracorporeal membrane oxygenation (ECMO) is indicated.[8]

PREVENTION

Postexposure antibiotic prophylaxis (same drugs, dosages, and duration as for treatment) may be considered in the most vulnerable individuals, that is, young infants, and as a supplementary measure in addition to active immunization to control outbreaks. There is 1 controlled trial that demonstrated efficacy of antibiotic prophylaxis, and clinical observations also support its recommendation.[14,15]

Most developed countries today use multicomponent (PT + FHA ± pertactin ± fimbriae) so-called acellular vaccines (ACV), whereas most resource-limited countries still use the older whole-cell vaccines (WCV) consisting of inactivated whole Bp bacteria. Both types of vaccines have been shown to be safe, immunogenic (although substantial lot to lot variability has been demonstrated for WCV), and efficacious, with efficacy estimates against typical disease caused by Bp ranging from 78% to 85% for ACV and 38% to 92% for WCV in infants and young children after 3 to 4 doses.[16] Vaccine efficacy against Bpp is lower (50% for ACV in one study[17]) and that against other *Bordetellae* is not known. National recommendations in almost all countries recommend 2 or 3 doses in infants, followed by booster doses at highly variable numbers and time points. Of note, protection against complicated pertussis is already demonstrable after the first dose of vaccine, underlining timely initiation of the immunization series.[18] Furthermore, it is important to achieve high immunization coverage in the population for herd protection, given that vaccine efficacy on an individual level is suboptimal.[19]

Few countries, mainly in Europe, America, and Australia, have introduced universal booster doses for adolescents and even fewer a universal booster dose in adults.[1] Because there are no monovalent pertussis vaccines available, it is important to note that a single tetanus–diphtheria–acellular pertussis combination vaccines with reduced antigen contents ("Tdap") can be given regardless of the interval from the last diphtheria and/or tetanus vaccine.[20] Two studies in 387 adults aged 18 to 76 years have demonstrated that intervals as short as 3 weeks do not lead to an increased risk for local reactions when compared with intervals longer than 2 years, and no serious adverse events occurred.[21,22] This is encouraging information when rapid protection from pertussis in an adult with a recent history of diphtheria- and/or tetanus immunization is warranted.

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