Pertussis (Whooping Cough)

By: Jeanna Reed

Etiological Agent

- **Bacterium:** Bordetella pertussis. “The genus Bordetella contains the species *B. pertussis* and *B. parapertussis*, which cause pertussis in humans. Other members of the genus are *B. bronchiseptica*, causing respiratory disease in various animals and occasionally in humans, and *B. avium* as well as *B. hinzii*, which cause respiratory disease in poultry and are very rarely found in humans.” (1) (14)

Transmission

- **Direct Contact / Airborne:** Pertussis is considered an incredibly contagious disease found only in humans. It is spread by an infected individual person to person by coughing, sneezing or sharing the air in close proximity to one another. The height of contagion is approximately two weeks following the beginning of the cough. (1)

Reservoirs

- **Humans:** are the only known reservoirs where *B. pertussis* can cause disease. (2)

Microorganism General Characteristics

- *Bordetella pertussis* is a very small (0.5-1.0 um in size) aerobic gram negative rod. (2)
- It is an encapsulated, non motile, coccobacilli with outer pili and some reports state it is covered in biofilm made of carbohydrate. (2)
- A strict aerobe, Pertussis grows optimally at 35°C to 37°C. Conversely, it is particular in its nutritional requirements needing nicotinamide supplements to grow. (2)
- Growth Inhibition does occur in the presence of fatty acids, metal ions, sulphides and peroxides in the media. (2)

Identification Key Tests

- PCR (polymerase chain reaction), Culture and Serology testing are commonly used to detect Bordetella pertussis. (3)
- Culture has excellent, 100% specificity and is considered to be the “gold standard” for diagnosing this infectious disease. However, antibiotic use must be taken into account because it can lower culture specificity. Collection of a sample for culture is best done via nasopharynx within the first two weeks of the cough. (2) (3)
- PCR testing is used any time there is a suspicion of a Pertussis outbreak but it can lead to inaccurate results without appropriate precautions and best practices considered. It is a rapid test and is typically taken from the nasopharynx specimen. (3)
- While the CDC and FDA have developed Assays that allow for confirmation of Pertussis, several of the serological tests in the US have unverified clinical accuracy. This type of testing while beneficial, is typically only used for detection in later stages of the disease. (3)

Signs and Symptoms of Disease

- There are three stages significant to detection and diagnosis of *Bordetella pertussis* approximately lasting four to eight weeks in total. (4)
- Stage 1: Catarrhal (inflammation of the mucous membranes) which includes coryza, low grade fever and mild cough that worsens over a period of approximately seven to ten days. (4)
- Stage 2: Paroxysmal (sudden attacks) that frequent in number resulting in coughing episodes that increase at night and gradually decrease over a period of three weeks. The patient will experience difficulty expelling mucous, exhaustion and possibly cyanosis and vomiting. A characteristic high pitched “whoop” typically occurs at the end of a paroxysmal attack during this stage. (4)
- Stage 3: Convalescent (recovery) stage can be weeks to months depending on severity of illness and age of patient. (4)

Historical Information
• **15th Century:** Bahaodowle Razi, and Iranian physician born in the late 15th century, is noted to be the first to report a pertussis epidemic 100 years before the 1578 report in Paris. Because of his description in the literature indicating the role of airborne infective agent in transferring the disease, Bahaodowle Razi is now to be considered the original discoverer of pertussis in current documents. [5]

• **1578:** A French scientist by the name of Guillaume De Baillou reported a pertussis epidemic in the literature. [5] [6]

• “In the prevaccine era, the calculated attack rate was 872/100,000 population, and the majority of cases occurred in children <5 years of age. On average, there were 7,300 deaths/year; the death rate began to decline before antimicrobial therapy and vaccination.” [7]

• **1773:** Pertussis is mentioned in the literature and described by William Butter of Edinburgh as “kinkcough”. Other known names were “tussis perennis”, “tussis infantum”, “chink cough”, and “chine cough”. [8]

• **1813:** Robert Watt wrote about “chin cough” and felt it was to be considered just as fatal for children next to small pox and measles. [8]

• **1906:** First observed in 1900 by Belgium scientists Jules Bordet and Octave Gengou, the bacteria Bordetella pertussis was officially isolated. [9]

• **1912:** Scientists Bordet and Gengou failed to create a vaccine from killed whole-cell B. pertussis. [10]

• **1922:** The United States reports 107,473 cases of Pertussis this year. 5,099 of those patients died. [11] [12]

• **1948:** Whole-cell pertussis vaccines became available in the early 1920’s for adults but not routinely recommended for children. However, in the 1940’s after Pertussis combined with diphtheria and tetanus toxoids, “DTP” was introduced and further recommended for children despite growing concerns of adverse reactions caused by the whole-cell vaccine. [13] [15]

• **1948-1959:** Vaccines for pertussis are now manufactured by multiple companies and distributed worldwide. This includes a DPT vaccine using the Salk polio vaccine which was found to have a preservative causing serious adverse reactions. In 1968 it was withdrawn from the market. [15]

• **1960-1970:** Over the course of 10 years the total recorded cases for pertussis equaled 110,744. Per year that averaged approximately 11,000 cases reported by the CDC. A further decline is noted in 1976 declaring 1,010 cases the least amount ever recorded to date. [11]

• **1974:** A paper published in Archives of Disease in Childhood describes 36 children who suffered neurological complications following the DPT combination vaccine. Further safety studies were encouraged and consideration of patients with certain known diagnosis (seizures, previous reactions, recent infections and neurological defects) were recommended not to receive this vaccine. [16]

• **1977-1979:** Epidemic of pertussis is recorded in Great Britain totaling over 100,000 cases and 36 deaths. [16]

• **1981-1982:** An FDA sponsored study completed at UCLA to determine the rate of minor and serious reactions to DT and DPT vaccines is published. Findings conclude DPT carries a greater risk of injury than DT alone. Public advocacy groups call for additional investigation and termination of the whole-cell vaccine entirely. [16]

• **1984:** After multiple hearings and conflicting findings regarding safety of the DT and DPT vaccines, Wyeth Laboratories discontinues marketing its whole cell DPT vaccine leaving two manufacturers to sell pertussis vaccines in the US. [16]

• **1986:** NCVIA (National Childhood Vaccine Injury Act) is passed by US Congress to address growing public concerns of adverse reactions following vaccine administration. NVICP (National Vaccine Injury Compensation Program) was also included in the NCVIA to allow compensation to individuals for table injury and non table injury claims. Pertussis (DTaP, DTP, DTP-Hib, P, and Tdap) vaccines are listed as compensable. [17]

• **1990:** Per CDC (Centers for Disease Control) and WHO (World Health Organization) pertussis cases for the US were recorded as 4,570. Globally the data reflects 476,374 cases reported. [11] [18]

• **1999:** Whole cell pertussis vaccine (DPT) is replaced on the US recommended vaccine schedule (but still available) with a new acellular version of the vaccine, now called “DpAT”. This new vaccine was developed to cause less adverse side effects by using parts of the pertussis pathogen to infer immunity. [10]

• **2000-2009:** Despite multiple options for vaccination in the US, cases of pertussis begin to increase with a marked rise in cases reported by the CDC in 2005 and 2005. In 2009, NNDS (National Notifiable Disease Surveillance) reported 194 pertussis-related deaths. [19]

• **2012-2016:** Peaks in disease have been recorded in recent years. 2012 documented a significant increase reporting 48,277 pertussis cases nationwide. Heightened provider and public awareness, improved diagnostic testing, waning immunity from acellular pertussis vaccines, and possibly molecular changes within the pertussis bacterium are many factors that have probably contributed to the increase of cases reported. [20]

**Virulence Factors**
• "Bordetella pertussis" produces a number of virulence factors, including pertussis toxin, adenylate cyclase toxin, filamentous hemagglutinin, and hemolysin. Aglutinogens and other outer membrane proteins are important antigens. (14)

• Of all the factors, PT (pertussis toxin) is considered the most important due to the initial colonization stage of the infection where the known portal of entry is the respiratory tract mucous membranes. PT is also known to cause the majority of the systemic symptoms associated with whooping cough, such as profound leukocytosis which may contribute to poorer outcome in infants. (14)

• Cellular trafficking and activity, modulation of host immune response, B oligomer binding activity, and autoimmunity are all major issues and concerns discussed in the literature surrounding PT. However, "Despite detailed molecular analysis of several virulence-associated factors of B. pertussis, significant gaps remain in our understanding of the pathogenesis of this infection and disease" (21)

Control and Treatment

• Once diagnosed, timing related to treatment of pertussis is extremely important, especially in infants, and can lessen the symptoms. The later the diagnosis and treatment the less chance a patient has of altering the course of disease and the spread of pertussis may or may not be affected. Patients infected with pertussis are thought to be most contagious during the catarrhal stage into the third week following paroxysms or until five days after the start of antibiotic therapy. (23)

• Recommended microbial choices for pertussis are listed as erythromycin, clarithromycin, azithromycin and also include trimethoprim-sulfamethoxasole (a combination antibiotic). (22)

• Erythromycin, while a preferred choice for treatment, does not alter the course of disease but reduces the infectious period to 5 to 10 days. Inactivated whole-cell vaccines are considered greatly effective, but can cause toxic side effects. Safer acellular vaccines have been licensed for booster vaccination and may also be licensed for primary vaccination. (14)

Prevention and Vaccines

• Vaccination and avoidance of infection is currently the best way to protect against pertussis and reduce the risk of severe infection in infants. WHO (World Health Organization) estimates 90% coverage of infants with three doses of superior pertussis vaccination will remain the priority of vaccine programs worldwide especially in areas where pertussis is a serious health problem. (23) (24)

• Available vaccines worldwide include whole cell (wP) and acellular (aP) pertussis vaccines. In the United States, DTaP and Tdap are the recommended immunizations. Globally, acellular vaccines are the preferred choice when affordable due to concerns regarding severe adverse reactions with the whole-cell pertussis vaccine. According to WHO, comparison of vaccines regarding efficacy and effectiveness is somewhat difficult to determine due to different recommended scheduling globally and varying combinations of pertussis vaccines. (24)

• Although vaccination can prevent pertussis in adolescents and adults, there is insufficient evidence to support the addition of vaccine boosters in these age groups for achieving the primary goal of reducing severe pertussis in infants. Countries with demonstrable nosocomial transmission are encouraged to vaccinate health-care workers, particularly maternity and pediatric staff, if economically and logistically feasible. (25)

Local Current Outbreaks/Cases

• There has been a noted rise in reported pertussis cases in Texas and the US. Recent Texas trends show several significant factors that contribute to this increase including waning immunity in adolescents and adults, increased awareness among healthcare professionals and parents, better testing methodologies and improved surveillance of pertussis. (26)

• Three to five year cycles are common for Pertussis. In 2013, 3,985 cases were reported. Of those cases 11% were hospitalized and five deaths were recorded by the Texas Department of State Health Services. The five deaths recorded were noted to be in children under the age of one. (26)

• As of December 17, 2015 no deaths were documented out of the 1,360 cases of pertussis reported in Texas. The age groups most significantly affected were one to six year olds and adults twenty years and older. (27)

Global Current Outbreaks/Cases
• Globally pertussis is still a major health concern. Regardless of high vaccination rates, in some countries pertussis still manages to claim lives. “Estimates from WHO suggest that, in 2008, about 16 million cases of pertussis occurred worldwide, 95% of which were in developing countries, and that about 195,000 children died from the disease.” (28)

• As of 2014, estimates according to data provided by WHO/UNICEF show 172,490 pertussis cases recorded globally. (25)

References


