Return of the *Whoop!* The Resurgence of Pertussis

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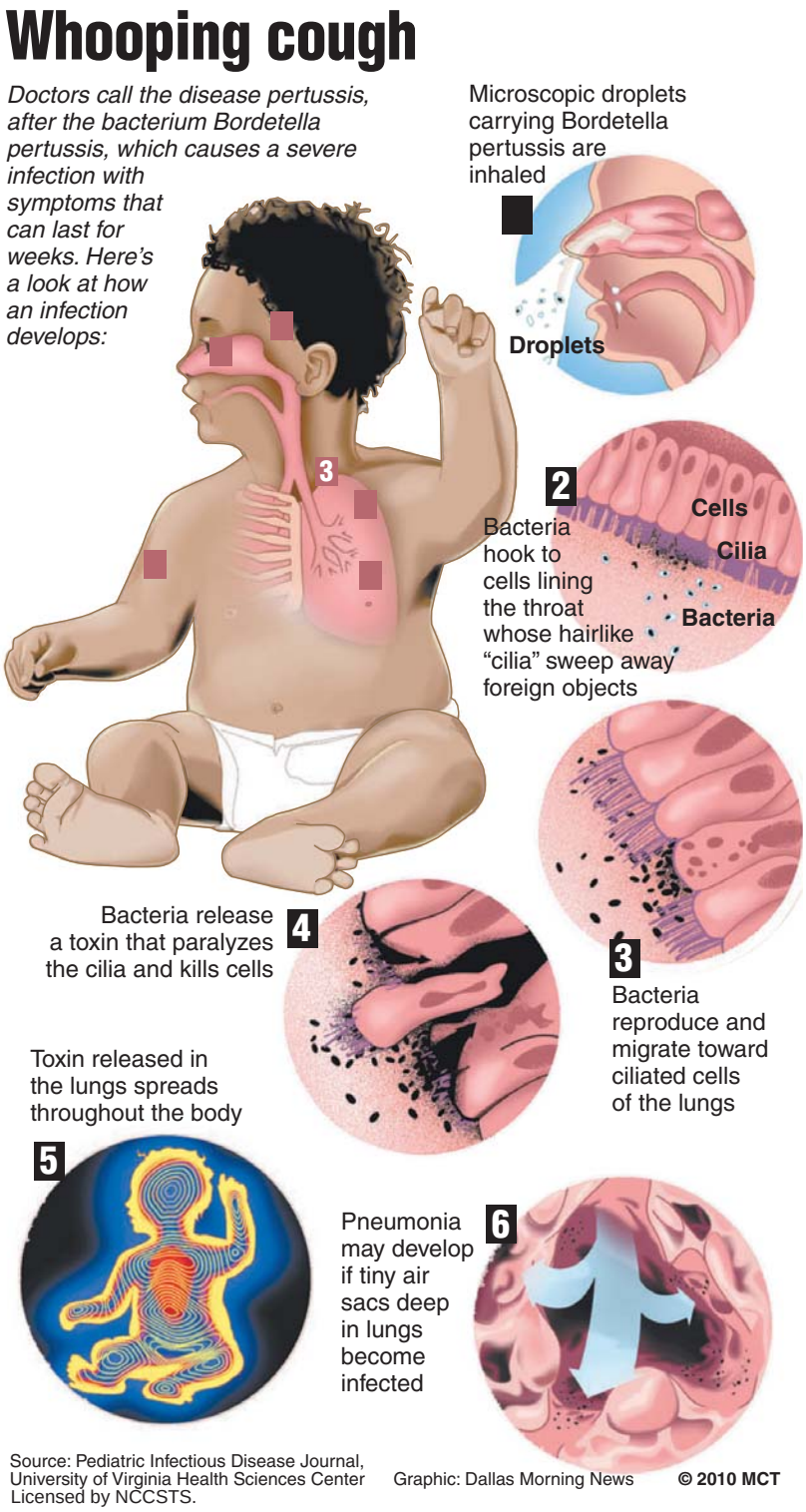

Part I – The History of Whooping Cough

The year was 1893, and Pearl Kendrick was a young girl growing up in Wheaton, Illinois, when she contracted "whooping cough."

Whooping cough, or pertussis, as it is sometimes called, is an illness that dates back to the year 1540. The first epidemic was documented in France in 1578. It is a respiratory illness that is transmitted from one person to another through aerosol droplets. The illness begins as a mild respiratory infection, progresses to a cough, develops into paroxysms of cough (whoop) before symptoms finally wane over weeks to months (duration typically 6–10 weeks).

Pearl Kendrick was one of the lucky survivors. She recovered completely from an illness that during the early 1900s claimed more lives than measles, scarlet fever, tuberculosis, diphtheria, and polio combined. Pearl never forgot the illness (Shapiro-Shapin, 2010).

Although a continent away, she followed with great interest the news of two French scientists, Jules Bordet and Octave Gengou, and their work isolating the microbe that causes the "whooping cough," *Bordetella pertussis*.

Pearl developed as a woman, a scientist, and a researcher. She ultimately began her own study into the organism, *Bordetella pertussis*. She studied the disease of pertussis. She remembered how you could feel fine with only sneezing, low fever, and slight cough, and then within several days you would begin "whooping" and be unable to take in any air.

In the year 1943, over 40 years later, Pearl with the help of her partner, Grace Eldering, formulated the first vaccine to combat *Bordetella pertussis*. This was accomplished while Pearl Kendrick was the director of the Western Michigan Branch Laboratory in Grand Rapids, Michigan. Massive vaccination implementation decreased the cases of pertussis more that 80% of what they had been in the pre-vaccine era (Garrett, 2006).

Refer to Figure 1 and fast forward to the year 2013 and the cases of pertussis have tripled since the 1980s. As of the year 2012, 48,277 cases were reported to the Centers for Disease Control and Prevention (CDC). So why is this vaccine-preventable disease on the rise?

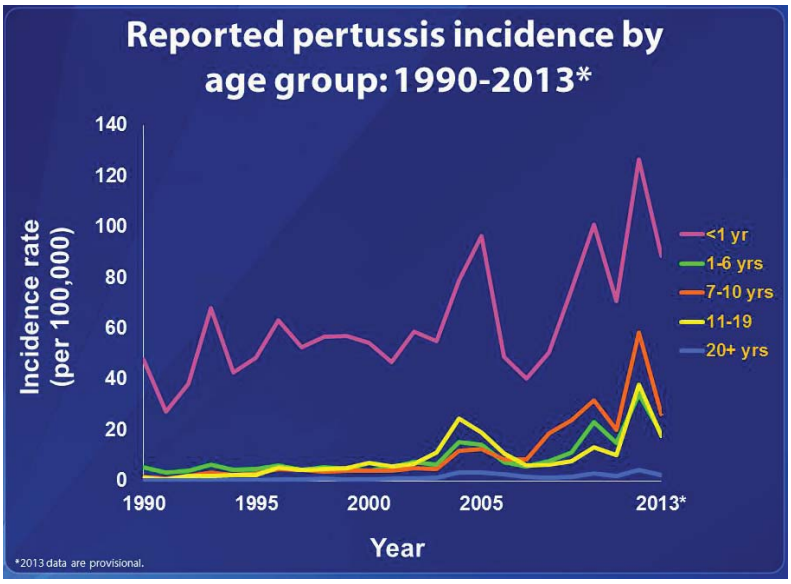

Figure 1. Graph showing the gradual increase in incidence of pertussis by age group. (*Source:* CDC, http://www.cdc.gov/pertussis/surv-reporting.html.)

Question

1. Provide a description for whooping cough. Include symptoms, mechanism, duration, and recovery in your description.

Part II – The Cause of Whooping Cough

As shown in Figure 2, *Bordetella pertussis* is a very small Gram negative rod. It was first isolated and described in 1909 by Jules Bordet and Octave Gengou in Paris. It is a strict aerobe and grows at 35–37 degrees Celsius. The supplemental media used to grow this organism in the laboratory is Bordet-Gengou Media, named after the two scientists credited with discovering the *Bordetella pertussis* bacteria. The media is made up of the following components:

- *Potato infusion*—source of carbon and nitrogen.
- *Peptic digest from animal tissue*—source of carbon and nitrogen.
- *Glycerol*—source of added nutrients.
- *Sheep blood (15%)*—source of added nutrients and provides for possibility of hemolysis.
- *Sodium chloride*—maintains osmotic pressure.
- *Agar*—provides support for growth.

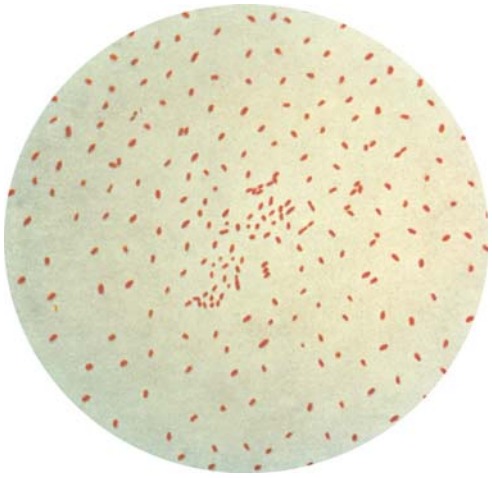

Figure 2. Gram Stain of *Bordetella pertussis* (gram negative rods 0.2 × 0.5 – 2.0 ums). (*Source:* CDC, image #2121, p.d.)

Bordetella pertussis colonies appear smooth, raised, and glistening, with a zone of hemolysis (Becton, Dickinson and Company, 2003). Identification of the organism can then be confirmed through biochemical tests, polymerase chain reaction (PCR), direct fluorescent antibody (DFA), and serologic tests.

Pathogenicity

The organism has three major virulence factors for pathogenicity: toxins, hemolysins, and adhesins. These antigenic and disease stimulating components are:

- *Pertussis toxin (PT)*—disruption of phagocytic activity.
- *Filamentous hemagglutinin (FHA)*—adherence to ciliated cells.
- *Adenylate cyclase*—reduction of phagocytic activity and initiation of infection.
- *Pertactin*—attachment to airway linings.
- *Tracheal cytotoxin*—paralysis of ciliated cells.

These substances enable the organism to adhere to the respiratory epithelial cells and paralyze the cilia, causing the infamous "whoop." The virulence of the pathogen then causes inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions and allows mucous to build up. The pertussis toxin mediates colonization and creates errors in phagocytic activity. As the organism proliferates, pertussis toxin leads to lymphocytosis with diminished phagocytosis (Todar, 2013).

Treatment

The treatment of *Bordetella pertussis* relies on the use of early intervention with antibiotics. The principle antibiotics that are most effective in limiting the disease process are Azithromycin, Erythromycin, and Clarithromycin. Antibiotics can stop the patient from being infectious within five days of taking them.

Vaccines are still considered to be the safest and most effective tool currently available for preventing pertussis (CDC, 2013a).

Questions

1. What is a Gram-negative organism? How does the structure of a Gram-negative organism contribute to its virulence?
2. Why is it difficult to grow *Bordetella pertussis* in a laboratory?
3. Discuss and evaluate the methods used to identify *Bordetella pertussis*.
4. What is an antibiotic? Which class of antibiotics works best for *Bordetella pertussis*?
5. What are the pathogenic mechanisms of *Bordetella pertussis*? What are its virulence factors?
6. What other respiratory illnesses mimic whooping cough?

Part III – Vaccines and Consequences of Not Vaccinating

Although Pearl Kendrick along with her partner Grace Eldering introduced the first vaccine to prevent whooping cough in 1943, side effects associated with the vaccine were common. This vaccine is known as a whole-cell vaccine. It is created by growing the bacteria *Bordetella pertussis* on casein supplemented media with agar and charcoal. The bacteria are killed with heat and formaldehyde, creating a suspension of inactivated *Bordetella pertussis* cells, which serve as the foundation of the whole-cell vaccine. After receiving the vaccination, the individual builds up antibodies to the offending bacteria and this action diminishes the potential for evolution of the disease.

The whole-cell pertussis vaccine is given in combination with diphtheria and tetanus and is known as the DPT vaccine or DTwP. The side effects associated with this type of vaccine are numerous, including high fevers, local inflammation at the injection site, and, infrequently, seizures. This vaccine, however, has 70–90% efficacy of preventing pertussis disease after three doses. Whole-cell vaccines are no longer circulated in the United States (CDC, 2012a).

Due to the potential of some severe reactions in the patient, an acellular vaccine was developed as an alternative to the whole-cell vaccine. An acellular vaccine is safer than the cellular variety. This type of vaccine contains inactivated pertussis toxin and one or more bacterial components, which are a much less concentrated form than that found in whole-cell vaccines. This has resulted in the reduction of side effects from vaccination.

The acellular variety of the pertussis vaccine is also combined with the diphtheria and tetanus components and is referred to as DTaP. Although this formulation has greatly reduced the side effects associated with the whole-cell form of the DPT vaccine, current research suggests that there is diminished duration of protection afforded by the acellular variety of the vaccine DTaP (CDC, 2012b).

It should be noted that the Centers for Disease Control and Prevention (CDC) recommends immunization with the acellular variety of the pertussis vaccine. The protocol is delineated in the paragraph that follows.

> *DTaP vaccines should be dispensed to infants beginning at 2 months, 4 months, and 6 months followed by 4th shot at 18 months. A 5th shot should be given between ages 4–6. Adolescents should receive another booster at 11–18 years of age. Adults 19–64 years of age, or older, who have close contact with infants less than 12 months of age, should also receive a booster. In addition, pregnant woman at 27–36 weeks, should be immunized (CDC, 2012b).*

Given the relatively modest cost of whole-cell vaccine, the World Health Organization (WHO) promotes the use of this variety of vaccine (WHO, 2013a). The information in Table 1 outlines the immunization protocol as recommended by WHO.

Table 1: World Health Organization (WHO) Recommended Routine for *Bordetella pertussis* Immunizations for Children

Antigen	*Age of first dose*	*Doses in Primary Series*	*Interval Between 1st and 2nd Dose*	*Interval Between 2nd and 3rd Dose*	*Booster*
DTP	6 weeks minimum	3	4 weeks (min)–8 weeks	4 weeks (min)– 8 weeks	1–6 years of age (*see below)

Source: WHO, 2013b.

** "Recommended three doses during first year of life. In areas where pertussis is of particular risk to young infants, DPT should be started at 6 weeks with 2 subsequent doses at intervals of 4–8 weeks. The last dose of the primary series should be completed by the age of six months.*

** Pertussis vaccine: Neo-natal immunization and vaccination of pregnant women and household contacts against pertussis is not recommended by WHO.*

** Pertussis containing booster: A booster dose is recommended for children age 1–6 years, preferably during the second year of life. The booster should be given > 6 months after the last primary dose. Completion of this schedule (primary series plus booster) is expected to ensure protection against pertussis for > 6 years."*

Regardless of the vaccination approach, pertussis remains one of the most common childhood diseases and a major cause of mortality in the United States. Worldwide, pertussis persists as a major health concern.

Consequently, pertussis is a significant cause of morbidity and mortality in infants less than 2 years of age. Complications of pertussis include pneumonia, otitis media, and epistaxis. Ten to 15% of all pertussis cases are found in infants less than six months of age with a 90% rate of death (CDC, 2012a). Growing cases have also been noted in two different cohorts: children 7–10 years of age and adolescents 13–14 years old (see Figure 1). This experience has led to attempts at improving vaccination coverage and the addition of boosters for these two age cohorts.

Due to the great success rates of the pertussis vaccine between the 1940s and the 1980s there was wide-spread acceptance of vaccines. This ultimately resulted in significant decreases in pertussis disease, epidemics, and pertussis related death. However, due to the amazing benefits of vaccines, a certain amount of complacency has emerged in response to vaccination. Both fear and mistrust of vaccines dating back to the 19th century and a dramatic remission of pertussis have led to a great anti-vaccine movement. Small groups of people have boycotted pertussis vaccines and have on some level contributed to the resurgence of whooping cough. This prevalent fear of side effects secondary to the whole-cell vaccine ultimately led to a complete transition to vaccination with the acellular vaccine in the United States, as is highlighted in the above immunization protocol outlined by CDC. However, safety may have been traded for efficacy as the new acellular vaccine has been implicated in the return of pertussis. Current studies indicate that the older whole-cell vaccine has longer, more enduring immunity (Klein et al., 2012). These two events have contributed substantially to an increase in pertussis leading to whooping cough outbreaks comparable to pre-vaccine era numbers (Shetty, 2010).

The geographical spread of non-immunized persons is significant and sets the stage for pertussis resurgence. If unvaccinated individuals are broadly separated geographically, their immunity remains. However, if persons refusing pertussis vaccine cluster, the potential for an outbreak of pertussis is greatly increased.

Reduced vaccination and lack of adherence to vaccine booster schedules for adolescents and adults can also set the stage for the transmission of pertussis. Although the extent of disease will be milder in this group of individuals, the potential for transmission of pertussis to infants and those victims not immunized will remain (CDC, 2012b).

Vaccination still remains the most effective means for the prevention of the spread of pertussis. Based on recent figures of pertussis epidemics in the state of Washington and elsewhere, efforts should be taken to enforce vaccination schedules to prevent any further increase in a disease (pertussis) that Pearl Kendrick worked so hard to diminish with her vaccine (CDC, 2012b).

Questions

1. What is a vaccine?
2. Compare the differences between a cellular and an acellular vaccine.
3. How does an organism become more powerful in the midst of diminished vaccination?
4. What are some of the reasons why parents may refuse to have their children vaccinated?
5. What are the consequences of diminished vaccination? What impact does reduced vaccination have on herd immunity?
6. Referring to the CDC statistics found in the graph in Figure 1, as well as the research-supported information provided in this case study, provide reasons as to why there is a resurgence of whooping cough.

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