

PERTUSSIS: FACTS AND MANAGEMENT

K. Sen*¹, Dr. B. Ray¹ and Prof. S. K. Mahapatra²

¹Gayatri College of Pharmacy, Sambalpur.

²Institute of Pharmaceutical Technology, Salipur, Cuttack.

Received date: 11 February 2020

Revised date: 01 March 2020

Accepted date: 22 March 2020

*Corresponding author: K. Sen

Gayatri College of Pharmacy, Sambalpur.

ABSTRACT

Pertussis, or whooping cough, is an acute respiratory infectious disease caused by the bacterium *Bordetella pertussis*. It can be quite serious, especially for young infants with tiny air passages. Severe cases of whooping cough may require hospitalization, respiratory support, and nutritional and rehydration therapy. Antibiotic are given to control infection followed by other Supportive Therapy. Many times Macrolide group of Antibiotic Shows effectiveness. The treatment, however, has no influence on the course of the disease. Human hyper immune pertussis globulin is still used occasionally, but no reliable data support its efficacy. Further treatment is symptomatic. Preventive Vaccinations are many times effective.

KEYWORD: whooping cough, Direct Fluorescent Antibody, Serological Testing etc. Acellular pertussis Vaccines, Paediatric Formulation (DTaP), Adolescent and Adult Formulation (Tdap).

INTRODUCTION

Pertussis, or whooping cough, is an acute respiratory infectious disease caused by the bacterium *Bordetella pertussis* (*Bordetella parapertussis* can cause milder form of pertussis).

The disease is spread by coughing or sneezing. Thick mucous builds up in the lungs and clogs air passages, triggering violent coughing spells. It can be quite serious, especially for young infants with tiny air passages. The fatality rate is highest in infants under six months of age. The effects of toxins in the *B. pertussis* bacteria can produce high fever, convulsions, brain damage and death. Permanent damage can include continuing seizure conditions, mental retardation, learning disabilities, and chronic illness.

Outbreaks of pertussis were first described in the 16th century, and the organism was first isolated in 1906. In the 20th century, pertussis was one of the most common childhood diseases and a major cause of childhood mortality in the United States. Before the availability of pertussis vaccine in the 1940s, more than 200,000 cases of pertussis were reported annually. Since widespread use of the vaccine began, incidence has decreased more than 80% compared with the prevaccine era. Pertussis remains a major health problem among children in developing countries, with 294,000 deaths resulting from

the disease in 2002 (World Health Organization estimate).^[1]

Bordetella pertussis

Bordetella pertussis was first isolated in pure culture in 1906 by Bordet and Gengou. Today, *B. pertussis* belongs to the genus *Bordetella* in the family *Alcaligenaceae*, which contains several species of closely related bacteria with similar morphology. *B. pertussis* and *B. parapertussis* cause whooping cough (pertussis) in humans. Other members of the genus are *B. bronchiseptica*, which causes respiratory disease in various animals and is only occasionally found in humans. Recent additions to the genus are *B. avium* and *B. hinzii*, which both cause respiratory disease in poultry and are very rarely found in humans.

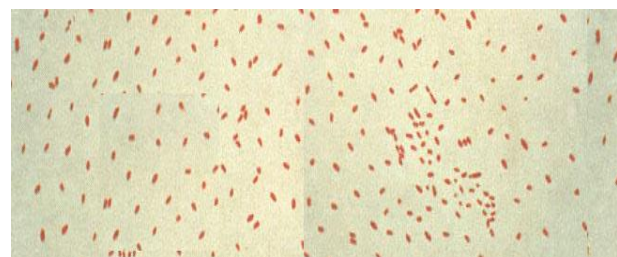
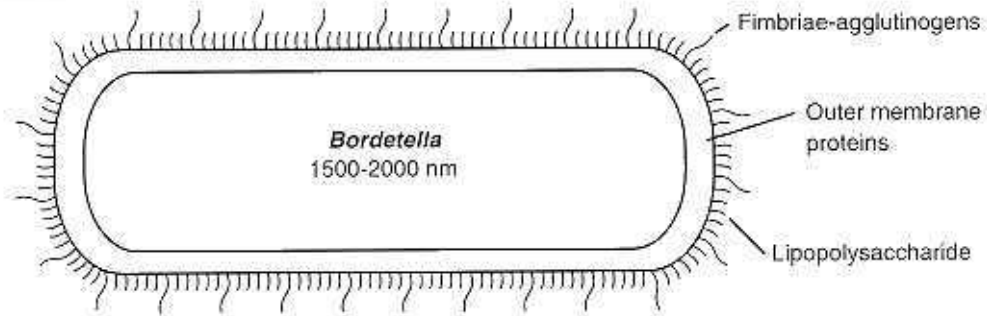


Figure 1: *Bordetella pertussis*, the agent of pertussis or whooping cough. Gram stain. From the Public Health Image Library (<http://phil.cdc.gov/phil/home.asp>)

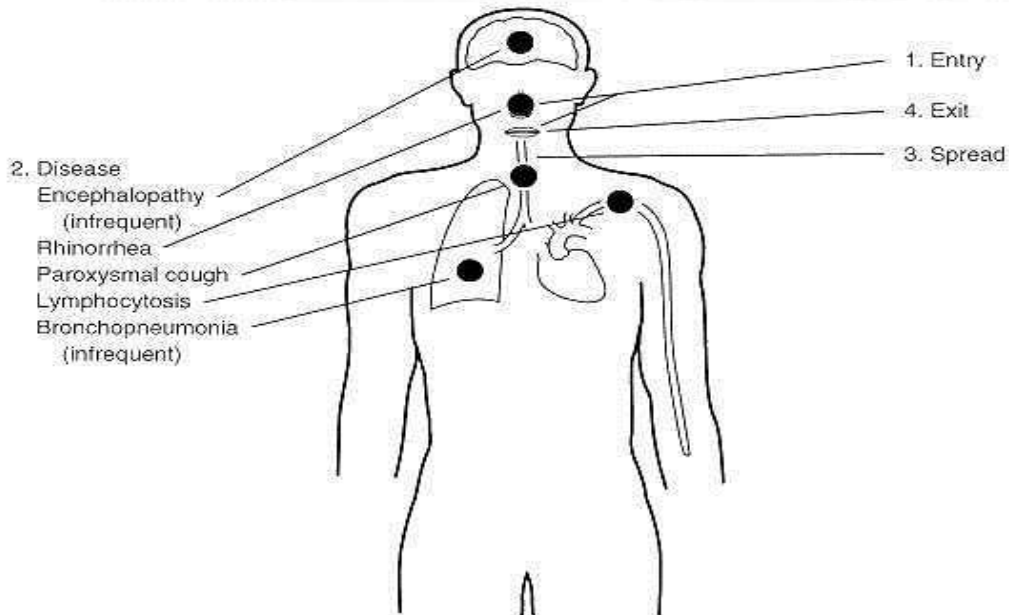
Structure

Bordetella pertussis is a small (approximately 0.8 µm by 0.4 µm), rod-shaped, coccoid, or ovoid Gram-negative bacterium that is encapsulated and does not produce spores. It is a strict aerobe. It is arranged singly or in small groups and is not easily distinguished from

Haemophilus species. *B. pertussis* and *B. parapertussis* are nonmotile. Numerous antigens and biologically active structural components have been demonstrated in *B. pertussis*, although their exact chemical structure and location in the bacterial cell are known only in part.^[2,3]



Pathogenesis



Host Defence

A case of whooping cough confers substantial immunity, which usually lasts for many years. Second infections of adults, usually with atypical symptoms and thus not regularly diagnosed as pertussis, may be more frequent than previously assumed. Immunity acquired after infection with *B. pertussis* does not protect against the other *Bordetella* species. Pertussis toxin is assumed to be one essential protective immunogen, but numerous findings indicate that other components, such as filamentous hemagglutinin, heat-labile toxin, agglutinogens, outer membrane proteins, and adenylate cyclase toxin, may also contribute to immunity after infection or vaccination. The immunogenicity of the substances may be significantly increased by the presence of pertussis toxin. This synergism indicates that

pertussis toxin could function as an adjuvant to a variety of protective antigens of *B. pertussis*. The defense mechanisms are both nonspecific (local inflammation, increase in macrophage activity, and production of interferon) and specific (proliferation of B and T cells). The basis of immunity in whooping cough is, however, incompletely understood. A role of circulating antibody in immunity is indicated by the correlation between protection of human vaccines and their serum agglutinin titers. However, effective immunity does not necessarily depend on the presence of serum agglutinins, and immunity to whooping cough may therefore be mediated essentially by cellular mechanisms. This cell-mediated immunity may be considered the crucial carrier of long-term immunity, and titers of specific humoral antibodies may diminish over the years. This may be the reason

why infants usually do not benefit significantly from maternal antibody.^[4]

The mucous membranes of the human respiratory tract are the natural habitat for *B pertussis* and *B parapertussis*. Although *B pertussis* can survive outside the body for a few days and so may be transmitted by contaminated objects, most infections occur after direct contact with diseased persons specifically, by inhalation of bacteria-bearing droplets expelled in cough spray. The

patient is most infectious during the early catarrhal phase, when clinical symptoms are relatively mild and noncharacteristic (Fig.8). Subclinical cases may have similar epidemiologic significance. Healthy carriers of *B pertussis* or *B parapertussis* are assumed to play no significant epidemiologic role. The natural habitat of *B bronchiseptica* is the respiratory tract of smaller animals such as rabbits, cats, and dogs. Therefore, human infections with *B bronchiseptica* are extremely rare and occur only after close contact with carrier animals.^[5]

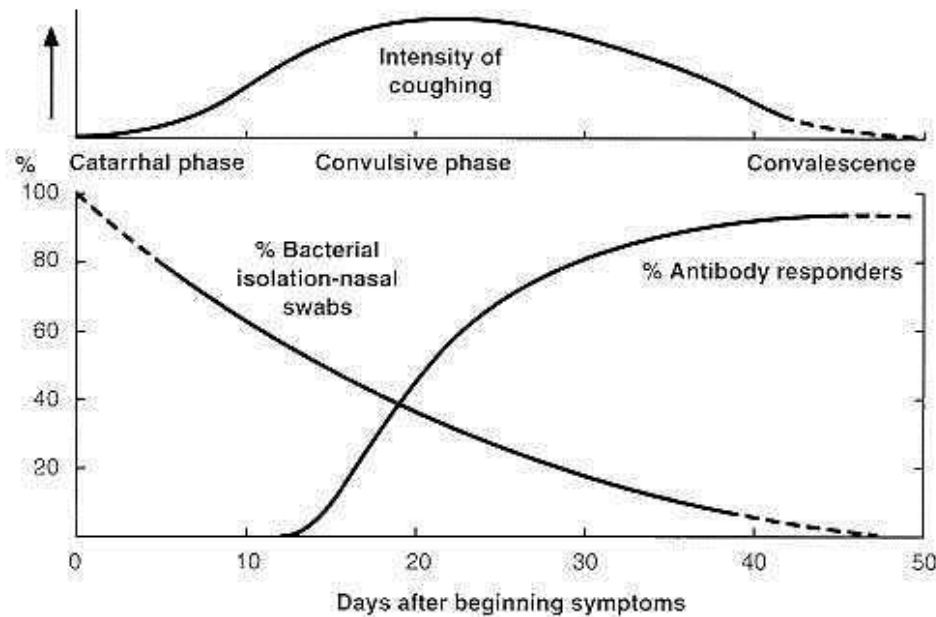


Figure 8: Relationship of *B pertussis* to the developing antibody response during whooping cough (<http://www.textbookofbacteriology.net>).

1.Catarrhal Stage: The first stage, the catarrhal stage, is characterized by the insidious onset of coryza (runny nose), sneezing, low-grade fever, and a mild, occasional cough, similar to the common cold.

2.Paroxysmal Stage: The cough gradually becomes more severe, and after 1–2 weeks, the second, or paroxysmal stage, begins. Fever is generally minimal throughout the course of the illness.

It is during the paroxysmal stage that the diagnosis of pertussis is usually suspected. Characteristically, the patient has bursts, or paroxysms, of numerous, rapid coughs, apparently due to difficulty expelling thick mucus from the tracheobronchial tree. At the end of the paroxysm, a long inspiratory effort is usually accompanied by a characteristic high-pitched whoop. During such an attack, the patient may become cyanotic (turn blue). Children and young infants, especially, appear very ill and distressed. Vomiting and exhaustion commonly follow the episode. The person does not appear to be ill between attacks. Paroxysmal attacks occur more frequently at night, with an average of 15 attacks per 24 hours. During the first 1 or 2 weeks of this

stage, the attacks increase in frequency, remain at the same level for 2 to 3 weeks, and then gradually decrease. The paroxysmal stage usually lasts 1 to 6 weeks but may persist for up to 10 weeks. Infants younger than 6 months of age may not have the strength to have a whoop, but they do have paroxysms of coughing.

3.Convalescent Stage: In the convalescent stage, recovery is gradual. The cough becomes less paroxysmal and disappears in 2 to 3 weeks. However, paroxysms often recur with subsequent respiratory infections for many months after the onset of pertussis. Adolescents and adults and children partially protected by the vaccine may become infected with *B. pertussis* but may have milder disease than infants and young children. Pertussis infection in these persons may be asymptomatic, or present as illness ranging from a mild cough illness to classic pertussis with persistent cough (i.e., lasting more than 7 days). Inspiratory whoop is not common. Even though the disease may be milder in older persons, those who are infected may transmit the disease to other susceptible persons, including unimmunized or incompletely immunized infants. Older persons are often

found to have the first case in a household with multiple pertussis cases, and are often the source of infection for children.

Complication

The most common complication, and the cause of most pertussis-related deaths, is secondary bacterial pneumonia. Young infants are at highest risk for acquiring pertussis-associated complications. Data from 1997–2000 indicate that pneumonia occurred in 5.2% of all reported pertussis cases, and among 11.8% of infants younger than 6 months of age. Neurologic complications such as seizures and encephalopathy (a diffuse disorder of the brain) may occur as a result of hypoxia (reduction of oxygen supply) from coughing, or possibly from toxin. Neurologic complications of pertussis are more common among infants. Other less serious complications of pertussis include otitis media, anorexia, and dehydration. Complications resulting from pressure effects of severe paroxysms include pneumothorax, epistaxis, subdural hematomas, hernias, and rectal prolapse.^[6,7]

Diagnosis

The diagnosis of pertussis is based on a characteristic clinical history (cough for more than 2 weeks with whoop, paroxysms, or posttussive vomiting) as well as a variety of laboratory tests (culture, polymerase chain reaction [PCR], direct fluorescent antibody [DFA] and serology). The different tools for Diagnosis are Isolation by culture, PCR, Direct Fluorescent Antibody, Serological Testing etc.^[8]

Treatment

Whooping cough should always be treated with antibiotics and never with only alternative therapies. The following complementary therapies may reduce symptoms and speed recovery. Supportive treatment involves careful monitoring of fluids to prevent dehydration, rest in a quiet, dark room to decrease paroxysms, and suctioning of mucus. Sitting up during coughing attacks may help.

Allopathic Treatment

Treatment with the antibiotic erythromycin is clearly helpful only in the very early stages of whooping cough, during incubation and early in the catarrhal stage. In general, however, physicians have used this antibiotic both for treatment of whooping cough itself and to prevent its spread to others in the patient's community. This type of preventive measure is known as prophylaxis. Unfortunately, the benefits of antibiotic prophylaxis and treatment for whooping cough are limited because erythromycin-resistant strains of *B. pertussis* have spread throughout the United States since the first case of erythromycin resistance was identified in Arizona in 1994. Although erythromycin is still used as of 2003 for both treatment and prophylaxis of whooping cough, the Centers for Disease Control (CDC) is

monitoring the five resistant strains of *B. pertussis* that have been identified so far.^[9,10]

Herbals

The following herbal remedies may help to support antibiotic treatment of whooping cough:

- Bryonia (*Bryonia alba*) tea: spasmodic coughing
- Butterbur (*Pinguicula vulgaris*) infusion: infection and spasms
- Evening primrose (*Oenothera biennis*) oil
- Jamaican dogwood (*Piscidia erythrina*) root or bark: spasms
- Lobelia (*Lobelia inflata*) tea or tincture: spasmodic coughing
- Pansy (*Viola tricolor*) tea or tincture: spasms
- Red clover (*Trifolium pratense*) tea
- Santonica (*Artemisia cina*) powder, tablets, or lozenges
- Sea holly (*Eryngium planum*) infusion: infection and spasms
- Skunk cabbage (*Symplocarpus foetidus*) powder, extract, or tincture
- Sundew (*Drosera rotundifolia*) infusion: infection and spasms
- Thyme (*Thymus vulgaris*) infusion: infection and spasms
- Wild cherry (*Prunus serotina*) bark infusion or syrup: infection, and spasmodic coughing.

Homeopathy

Homeopathic remedies are chosen based upon the family of symptoms displayed by each patient. Remedies for symptom families include:

- Kali bichromicum: coughing up yellow, stringy mucus.
- Drosera: dry and tickly feeling in throat; violent coughing that induces vomiting; symptoms worse after midnight.
- Kali carbonicum: dry, hard, hacking cough at 3 A.M.; puffy eyelids; exhaustion; chilly feeling.
- Coccus: coughing worse when warm; drinking cold water brings relief; vomiting stringy, transparent mucus.
- Cuprum: coughing spasms cause breathlessness and exhaustion; blue lips; toe and finger cramping; drinking cold water brings relief.
- Belladonna: stomach pain before coughing; coughing worse at night; retching with coughing attacks; red face; puffy eyelids.
- Ipecac: sick feeling most of the time; paleness, rigidity, breathlessness, and then relaxation precede vomiting.

Other Remedies

Other remedies may assist in the treatment of whooping cough.

- Dietary supplements include vitamins A and C, beta carotene, acidophilus, lung glandulars, garlic, and zinc.

- Dietary changes include drinking plenty of fluids, eating fruits, vegetables, brown rice, whole grain toast, vegetable broth, and potatoes, and avoiding dairy products.
- Juice therapists recommend orange and lemon juice or carrot and watercress juice.
- Hydrotherapy treatment consists of wet clothes or other material applied to the head or chest to relieve congestion.
- Aromatherapy uses essential oils of tea tree, chamomile, basil, camphor, eucalyptus, lavender, peppermint, or thyme.

Medical Management

The medical management of pertussis cases is primarily supportive, although antibiotics are of some value. Erythromycin is the drug of choice.

This therapy eradicates the organism from secretions, thereby decreasing communicability and, if initiated early, may modify the course of the illness. An antibiotic effective against pertussis (such as azithromycin, erythromycin or trimethoprim-sulfamethoxazole) should be administered to all close contacts of persons with pertussis, regardless of age and vaccination status. All close contacts younger than 7 years of age who have not completed the four-dose primary series should complete the series with the minimal intervals. Close contacts who are 4–6 years of age and who have not yet received the second booster dose (usually the fifth dose of DTaP) should be vaccinated. The administration of Tdap to persons 10 through 64 years of age who have been exposed to a person with pertussis is not contraindicated, but the efficacy of postexposure use of Tdap is unknown.

Pertussis Vaccines

Pertussis vaccine is produced from smooth forms (phase I) of the bacteria as a killed whole-cell vaccine. Whole-cell pertussis vaccine is composed of a suspension of formalin-inactivated *B. pertussis* cells. It was developed in the 1930s and used widely in clinical practice by the mid-1940s. Based on controlled efficacy trials conducted in the 1940s and on subsequent observational efficacy studies, a primary series of four doses of whole-cell DTP vaccine was 70%–90% effective in preventing serious pertussis disease. Protection decreased with time, resulting in little or no protection 5 to 10 years following the last dose. The different variety of Pertussis vaccines are-Whole cell Pertussis vaccines, Acellular pertussis Vaccines, Pediatric Formulation (DTaP), Adolescent and Adult Formulation (Tdap).^[11,12,13]

Vaccination for Pregnant Women

Any woman who might become pregnant is encouraged to receive a single dose of Tdap if she has not already received a dose. Women who have not received Tdap (including women who are breastfeeding) should receive a dose in the immediate postpartum period, before discharge from the hospital or birthing center, if 2 years or more have elapsed since the last Td. Shorter intervals

since the last Td can be used if necessary. If Tdap cannot be administered before discharge, it should be given as soon as feasible. The dose of Tdap replaces the next routine dose of Td. ACIP recommends Td when tetanus and diphtheria protection is required during pregnancy. However, pregnancy is not a contraindication for use of Tdap. A clinician may choose to administer Tdap to a pregnant woman in certain circumstances, such as during a community pertussis outbreak. When Td or Tdap is administered during pregnancy, the second or third trimester is preferred to avoid coincidental association of vaccination and spontaneous termination of a pregnancy, which is more common in the first trimester.^[14]

Clinicians can choose to administer Tdap instead of Td to pregnant adolescents for routine or “catch-up” vaccination because the incidence of pertussis is high among adolescents. Others for whom Tdap might be considered during pregnancy are pregnant healthcare personnel and child care providers (to prevent transmission to infants younger than 12 months of age and to other vulnerable persons) and pregnant women employed in an institution or living in a community with increased pertussis activity.

Adverse Effects of DTaP

- Local reactions, such as pain, redness, or swelling.
- Mild systemic reactions such as drowsiness, fretfulness, and low-grade fever may also occur.
- Temperature of 101°F or higher is reported in 3%–5% of DTaP recipients. These reactions are self-limited and can be managed with symptomatic treatment with acetaminophen or ibuprofen.
- Moderate or severe systemic reactions (such as fever [105°F or higher], febrile seizures, persistent crying lasting 3 hours or longer, and hypotonic hyporesponsive episodes) have been reported after administration of DTaP but occur less frequently than among children who received whole-cell DTP.
- Swelling at the site of injection occurred in 2% of patients after the first dose of Tripedia, and in 29% following the fourth dose.
- Increases in the frequency of fever after the fourth dose have also been reported, although the increased frequencies of other systemic reactions (e.g., fretfulness, drowsiness, or decreased appetite) have not been observed.
- Swelling involving the entire thigh or upper arm has been reported after booster doses of certain acellular pertussis vaccines. The limb swelling may be accompanied by erythema, pain and fever. Although the swelling may interfere with walking, most children have no limitation of activity. The pathogenesis and frequency of substantial local reactions and limb swelling are not known, but these conditions appear to be self-limited and resolve without sequelae.

CONCLUSION

Even there is Suitable New generation antibiotic available to treat this infection, the disease need proper Diagnosis by culture of bacteria and Sensitivity to Antibiotic for effective treatment as well as to prevent emergency of Resistance. Other remedies may assist in the treatment of whooping cough like Dietary supplements include vitamins A and C, beta carotene, acidophilus, lung glandular, garlic, and zinc. Research need to be developed Globally to meet the challenge associated with Complication of this Infection.

REFERENCE

1. Introduction and overview. Description of whooping cough. [Online], 2002. [Cited 2005 Dec 25]; Available from: URL: <http://www.doh.gov.za/facts/statsnotes/2002/whooping.pdf>.
2. Schellekens J, Wirsing von Konig C, Gardner P. Pertussis sources of infection and routes of transmission in the vaccination era. *Pediatr Infect Dis J*, 2005 May; 24(5): s19- 24.
3. Spearing NM, Horvath RL, McCormack JG. Pertussis: adults as a source in healthcare settings *Med J Aust* 2002 November, 18; 177: 568-69
4. Cherry JD, Grimprel E, Guiso N, Heininger U, Mertsola J. Defining Pertussis epidemiology; clinical, microbiologic and serologic perspectives. *Pediatr Infect Dis J*, 2005 May; 24(5): S25-34.
5. Hozbor D, Mooi F, Flores D, Weltman G, Bottero D, Fossati S, et al. Pertussis epidemiology in Argentina: trends over 2004– 2007. *J Infect*, 2009; 59(4): 225–31. 9. Pan American Health Organization. Meeting Report of Technical.
6. Centers for Disease Control and Prevention: Recommended antimicrobial agents for treatment and post-exposure prophylaxis of Pertussis 2005 guidelines *Morb Mortal Wkly Rep Surveill Summ*, 2005 December 9; 54(RR14): 1- 16
7. Black R, Cousens S, Johnson H, Lawn J, Rudan I, Bassani D, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet*, 2010; 375(9730): 1969–87.
8. Fry NK, Tzivra O, Ting Li Y, McNiff A, Doshi N, Maple PAC, Crowcroft NS et al. Laboratory diagnosis of pertussis infections: the role of PCR and serology. *J Med Microbiol*, 2004; 53: 519.
9. Muller FC, Hoppe JE, Wirsing von Konig C. Laboratory diagnosis of pertussis; State of the art in 1997. *J Clin Microbiol*, 1997 October; 35(10): 2435-43.
10. Centers for Disease Control and Prevention: Recommended antimicrobial agents for treatment and post-exposure prophylaxis of Pertussis 2005 guidelines *Morb Mortal Wkly Rep Surveill Summ*, 2005 December 9; 54(RR14): 1- 16.
11. Crowcroft NS, Pebody RG. Recent developments in pertussis. *Lancet*, 2006 Jun 10; 367(9526): 1926-1936.
12. Dabrera G, Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, et al. A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012-2013. *Clin Infect Dis* 2015 Feb, 2015; 60(3): 333-337.
13. Edmunds WJ, Brisson M, Melegaro A, Gay NJ. The potential cost-effectiveness of acellular pertussis booster vaccination in England and Wales. *Vaccine*, 2002 Jan 31; 20(9-10): 1316-1330.
14. Donegan K, King B, Bryan P. Safety of pertussis vaccination in pregnant women in UK: observational study. *BMJ*, 2014 July 12; 349: 4219.