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A REVIEW ON BORDETELLA PERTUSSIS AND THEIR VIRULANCE FACTORS, DIAGNOSIS AND TREATMENT

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ABSTRACT
Bordetella pertussis, the causative agent of whooping cough, is a highly contagious respiratory pathogen unique to humans. Transmission occurs through respiratory droplets when an infected individual coughs or sneezes.B. pertussis, a rod-shaped Gram-negative bacterium, produces various toxins and antigens that paralyze cilia and impair the respiratory epithelium, leading to mucus accumulation & systemic effects. The pathogen rarely appears in blood cultures, & its toxins including pertussis toxin and tracheal cytotoxin play crucial roles in its virulence. Contemporary research focuses on the pathogenic mechanisms and evolutionary history of Bordetella species, emphasizing their significant antigenic diversity and ability to evade immune responses. Despite advances in vaccination and disease management, pertussis persists as a critical public health issue, necessitating ongoing vigilance and research to mitigate its impact globally. The pathophysiology of B. pertussis involves a toxin-mediated illness that primarily affects the respiratory tract, leading to severe coughing fits, whooping, and post-tussive vomiting. Key virulence factors include pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae, which facilitate bacterial adhesion, immune evasion, and local tissue damage. Treatment typically involves antimicrobial agents, with macrolides such as erythromycin, azithromycin, and clarithromycin being the most commonly used. Vaccination remains the most effective strategy for pertussis prevention. The current immunization schedule includes the DTaP vaccine, which provides protection against diphtheria, tetanus, and acellular pertussis. The vaccine is administered in a series of doses starting at two months of age, with subsequent doses at eighteen months and four to six years, along with booster shots as needed.

Key words: Bordetella Pertussis, whopping cough, potency, vaccination

INTRODUCTION
Bordetella pertussis is the cause of whooping cough, an acute respiratory illness that is extremely contagious. When an infected individual coughs or sneezes, it can spread quickly. Pertussis, often

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known as whooping cough (Bentley J et al., 2013).Whooping cough is caused by a disease that is unique to humans (Guiso N. 2009). Thus, pertussis continues to rank among the world's most common vaccine-preventable causes of mortality. Every year, 16 million cases of pertussis are reported worldwide, with 95% occurring in underdeveloped nations leading to over 195,000 fatalities, the most of which were infant mortality (Dias W O et al., 2013). Although the illness can strike anybody at any age, it is most deadly in newborns, who account for the majority of deaths. This age group's whooping cough presentation, which is characterized by paroxysmal coughing followed by an audible inspiratory whoop and occasionally vomiting, also makes the disease easier to identify. Babies frequently cough and experience apneic episodes, which can get quite bad and necessitate hospitalization (Zhang L 2014). Guillaume de Baillou wrote the first description of Bordetella pertussis in the sixteenth century. Jules Bordet and Octave Gengou isolated the bacterium for the first time in 1906 (Fiona Havers 2021).

The rod-shaped, coccoid, or ovoid Gram-negative bacteria Bordetella pertussis is encapsulated and does not release spores. Its estimated size is 0.8 μm by 0.4 μm. This aerobe is rigid. It is not readily recognized from Haemophilus species and is organized alone or in small groups. Both B. parapertussis and B. pertussis do not move. It has been shown that B. pertussis has a large number of antigens and structural elements that are physiologically active (Parkhill J et al., 2003).

A gram-negative coccobacillus known as bordetella sticks to ciliated respiratory epithelial cells. which adheres to and destroys the ciliated respiratory epithelium in the bronchi, bronchioles, and nasopharynx (Bocka et al., 2013). It subsequently secretes poisons that paralyze the cilia, inflict damage to nearby tissue, and hinder the removal of mucus. Moreover, insulin secretion rises, lymphocytosis takes place, and phagocytic activities are blocked (Ashraf et al., 2013). The organism seldom shows up in blood cultures, and the secreted toxins (tracheal cytotoxin, dermonecrotic toxin, adenylate cyclase toxin, and pertussis toxin) affect both locally and systemically. The organism itself does not penetrate the respiratory tract entirely (Mattoo S et al., 2005). It creates a number of antigens and poisons that target respiratory cells. It is producing cilia paralysis and inflammation. The distinct phases of pertussis are caused by these different antigens. The bacteria have been found in alveolar macrophages according to recent studies. The clinical symptoms stem from this interference with elimination of lung secretions. It is highly contagious, infecting over 80% of household contacts in one documented incidence, and is disseminated by infectious droplets. Pertussis does not exhibit a seasonal or temporal pattern, however it does exhibit a minor rise in incidence over the summer and fall (Hewlett E L et al., 2009).

Among the several antigenic and physiologically active substances produced by B. pertussis are adenylate cyclase, agglutinogens, pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin, and tracheal cytotoxin. The clinical manifestations of pertussis are caused by these compounds. After infection, immunity is produced by the body's reaction to one or more of these compounds. After contracting B. pertussis, immunity is not long-lasting (Fiona Havers 2021). While B. bronchiseptica, B. holmesii, B. avium, B. hinzii, and B. trematum are the other Bordetella species that infrequently cause infections in humans, B. parapertussis may also infect people, however the disease state is frequently milder and significantly less prevalent than the B. Pertussis etiology (Marzouqi I et al., 2010). Although B. parapertussis, B. bronchiseptica, and B. pertussis are related species, mutations in the promoter region of the genes encoding the toxin prevent B. parapertussis and B. bronchiseptica from producing the pertussis toxin. Unlike the other three species, B. holmesii does not generate the virulence factors. Based on immunologic, biochemical, and cultural distinctions, B. parapertussis and B. pertussis may be distinguished from one another.

The Evolutionary History of B. pertussis

The first known case of pertussis was identified in Paris, France in 1578, despite sporadic evidence

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pointing to an older history of the illness. Guillaume de Baillou (Ballonius) reported this, and he provided a detailed account of the disease (Cherry, J.D 2015). There are several species in the genus Bordetella, the majority of which have been isolated from very immune compromised people. Only a small number of them, including Bordetella petrii, have only been isolated from their native environments thus far. In comparison, the closely related genus Achromobacter consists primarily of ambient bacteria with a small number of opportunistic pathogens. The majority of attention has been focused on three closely related species that make up the Bordetella bronchiseptica complex Bordetella bronchiseptica, B. pertussis, and Bordetella parapertussis among the 16 known Bordetella species since they are actual diseases for humans and/or other mammals (Thomas Belcher et al 2021).

Species of Bordetella pertussis

A pleomorphic, aerobic, gram-negative coccobacillus is called Bordetella. Nine species make up the genus Bordetella four of them are known to cause respiratory illnesses in humans: Bordetella holmesii, bronchiseptica, parapertussis, and pertussis (Nieves et al., 2016). B. holmesii forms a separate branch from the other three species, which are closely related to each other. B. bronchiseptica is seldom isolated from humans and causes persistent, frequently asymptomatic respiratory tract infections in a wide range of species. There are two different lineages of B. parapertussis, and they infect sheep and humans, respectively. According to Bart, M. J. et al. (2010), B. parapertussis and B. pertussis are the only human pathogens that cause whooping cough, or pertussis. (Bart, M. J. et al., 2010)

B. Between 86% and 95% of whooping cough cases are caused by pertussis, which was initially identified in 1906 by Bordet and Gengou. It exclusively infects people, grows slowly, and is picky (Nieves, D. J. et al., 2016). This meticulous gram-negative coccobacillus is the cause of whooping cough, a frequent respiratory illness. The pathogen is extremely infectious among intimate contacts and is disseminated by respiratory droplets. A pertussis-like illness is caused by Bordetella parapertussis, which makes up around 5% of Bordetella isolates in the US. The whoop and paroxysms are less intense than those caused by B. pertussis (Heather L et al., 2018). First discovered in the 1930s, B. parapertussis has been found in sheep and people, generally causing a less severe pertussis-like disease than B. pertussis. Since its discovery in 1910, B. bronchiseptica has only infrequently been isolated from people suffering from a cough akin to pertussis. Instead, it is typically enzootic in pigs, dogs, cats, rabbits, rodents, and other animals. Because of a mutation in the promoter region of the genes encoding the pertussis toxin, B. bronchiseptica are unable to produce the toxin (Bouchez V. et al., 2013). First discovered in 1983, B. holmesii occasionally causes illnesses similar to pertussis in people. According to Nieves, D. J. et al B. holmesii is a species that does not generate the virulence factors that the other three species do. (Nieves, D. J et al., 2016).

Bacteria Pertussis and B. parapertussis are both extremely effective pathogens that cause respiratory infections and stay restricted to the upper respiratory tract (Mattoo S. et al., 2005). Numerous studies conducted over the last 30 years have demonstrated that these bacteria's pathogenicity is caused by a variety of proteins categorized as toxins and adhesions (Hegerle N. et al., 2013).

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Table 1: Showing the Bordetella species and their associated hosts (Mattoo, S. et al., 2005), (Kilgore et al., 2016).

Bordetella Species	Associated Host Organism	Transmission	Disease
B. Pertussis	Only human	Droplets	Pertussis
B. para pertussis	Human, sheep, goat, pig	Droplets	Para pertussis (pertussis-like disease) Respiratory disease
B. bronchiseptica	Human, pig, cat, dog, rabbit	Droplets	Respiratory disease
B. holmesii	Human	Droplets	Respiratory disease Systemic infection (immune compromised hosts)

Diagnosis of Whopping Cough

A clinical history of signs and symptoms, in addition to a range of laboratory tests (such as culture, polymerase chain reaction (PCR), and serology), are used to diagnose pertussis (Emily Souder et al., 2015). Infants, older, immunized children, teenagers, and adults frequently experience unusual infection courses. In these situations, laboratory testing is necessary to confirm the pertussis diagnosis. According to (Daniela Hozbor 2018) the primary laboratory criteria for diagnosis are the isolation of B. pertussis from clinical specimens, serology, or PCR testing for B. pertussis. The gold standard for pertussis diagnosis is still culture. However, the most widely used diagnostic technique nowadays is PCR testing of nasopharyngeal swab specimens. For both PCR and culture, the same nasopharyngeal swab or aspirate can be used. According to Kay Wang et al culture yields best results when done in the first two weeks following the beginning of symptoms and is seldom positive after three weeks of cough disease. DNA detection from throat swabs, nasopharyngeal swabs, per-nasal swabs, or nasopharyngeal aspirates; PPA or antibody detection on blood or oral fluid these methods often only provide a diagnosis that is made after the fact or retrospectively (Wirsing von et al., 2017).

Culture

The diagnosis is validated by the growth of Bordetella pertussis or other species on suitable culture medium. However, the diagnosis can also be made by proving the presence of certain antibodies or, more frequently, by using PCR methods. Nasopharyngeal specimens can yield Bordetella species, with the greatest likelihood of isolation occurring within the first three weeks of coughing. (Cherry J D et al., 2014). The gold standard for diagnosing pertussis is the isolation of the etiological agent. A clinical sample from the nasopharynx should be collected by aspiration or swabs in order to do the bacterial isolation. Aspirates generate higher yields than nasopharyngeal swabs, however the latter may be employed; nevertheless, if both PCR and culture are to be carried out, swabs should be made of nylon or Dacron. Calcium alginate swabs are only suitable for culture as they block PCRs, however cotton swabs are not advised as they contain materials that may hinder B. pertussis growth. (Daniela Hozbor 2018). For both PCR and culture, the same nasopharyngeal swab or aspirate can be used. When culture is done within the first two weeks of the beginning of symptoms, it yields the largest yield and is seldom positive after three weeks of cough disease. (Emily Souder et al., 2015).

Serological Testing

When both culture and PCR are expected to be negative, serologic testing is typically more helpful in detecting pertussis later in the illness (Fiona P. Havers et al., 2021).

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The approach that adults and teenagers utilize the most frequently is serology. The diagnostic labs employ either commercial kits or in-house techniques for this procedure. But in order to get accurate findings, it's essential to measure just anti-PT IgG antibodies, utilize internationally recognized standards, and interpret the data using the appropriate cut-offs. (Stockholm et al., 2012).

Oral Fluid Sampling

Patients are thought to find oral fluid swabs more pleasant than blood collection. Since youngsters can even self-collect the sample under supervision, the fluid is obtained by stroking the swab along the gum line for one to two minutes (Roberts, S. E et al 2015). Subsequently, the swab is sent to a laboratory where the oral fluid is extracted via a transport tube. The presence of anti-pertussis toxin (anti-PT) IgG antibodies is examined in the eluted fluid. Oral fluid sample kits are available commercially, and the results are dependable. (Johnson, P. D et al 2014).

PCR (Polymerase Chain Reaction)

The current gold standard for diagnosing pertussis is PCR testing, which is becoming more widely used since it provides a faster response and appears to be more sensitive than culture, particularly in cases when the patient has taken antibiotics or is only moderately ill. Anytime there is a suspicion of a pertussis epidemic, it is advised to acquire culture confirmation of pertussis for at least one potential case, as PCR testing might vary in their specificity. (Fiona P. Havers et al., 2021). Using a Dacron swab or nasopharyngeal aspirate, a nasopharyngeal specimen must be collected. If the PCR test is ordered within the first three to four weeks of sickness, it will be most sensitive. (Heather L. Daniels et al., 2018).While the sensitivity of PCR decreases as the length of the disease increases, it is less impacted by prior antibiotic usage than culture. Depending on the gene target being employed, the sensitivity of PCR ranges from 73 to 100%. However, because of the low level of cultural sensitivity, it is challenging to assess its distinctiveness. Therefore, meticulous validation of PCR procedures is necessary to prevent false positive findings. (Kay Wang et al., 2011).

Pathophysiology of Bordetella Pertussis

Bordetella the pathogen known as pertussis, a gram-negative coccobacillus, is unique to humans. After the typical 7–10 day incubation period, there are three stages to the illness the catarrhal prodrome, which mimics many common viral respiratory infections and can last up to 3 weeks; the paroxysmal phase, which is characterized by severe episodes of coughing, whooping, and post-tussive vomiting; and the convalescent phase, which is characterized by a persistent cough that is usually non-specific. The beginning of the catarrhal phase and the three weeks following the start of the paroxysmal phase constitute the infectious period. (Kay Wang et al., 2011).

B. A pathogen unique to humans that causes a respiratory illness is called pertussis. It cannot live outside of its host due to its extreme lability (Guiso n. 2009). The primary cause of pertussis is toxin-mediated illness. The bacteria cling to the respiratory epithelial cells' cilia, release toxins that paralyze the cilia, and inflame the respiratory tract, making it more difficult for the lungs to expel secretions. It was formerly believed that B. pertussis did not enter the tissues. Nevertheless, research has revealed that alveolar macrophages contain the bacterium. (Havers, F P et al., 2010).

Prominent attachment proteins comprise fimbrial proteins, PT, FHA, PRN, and BrkA. Although the organism usually does not enter the circulation or submucosal cells, its toxins can have systemic consequences. B. pertussis may disrupt the immune system in a variety of ways thanks to its proteins and toxins, which can impede complement, phagocytes, T- and B-cell responses, and other immune system functions. (Michael D. Decker et al., 2021).

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B. pertussis produces a number of active ingredients that contribute to immunity and enable the bacterium to spread illness. B. The complex bacteria that causes pertussis expresses several bacterial components that have immune-modulating properties. It generates many bacterial components that are accountable for the disease's symptoms. Agglutinogens, pertactin, filamentous hemagglutinin, and pertussis toxin. Where it has an impact. Additionally, pertussis toxin suppresses neutrophilic and monocytic responses and causes cell damage. It postpones the activation of some immunological reactions. The systemic symptoms of pertussis are thought to be caused by pertussis toxin (Heather, L.et al., 2018). Sick people's aerosol droplets carry the bacteria to vulnerable folks. Following the transmission path, the bacteria attach themselves to the upper and lower respiratory ciliated cells, which starts the colonization process. From there, they multiply and disseminate throughout the epithelium, causing local mucosal irritation and, eventually, the onset of respiratory system symptoms. Being overbearing is quite rare. (Mattoo, S et al., 2005). It usually takes seven to ten days for pertussis to incubate. After that, the illness develops into three stages: a convalescent phase, during which patients usually just have a chronic, non-specific cough; a paroxysmal phase, during which patients may experience whooping, post-tussive vomiting, and violent coughing fits; and a catarrhal prodrome, which can mimic many common viral respiratory illnesses and last up to three weeks infections. There is an infectious period that lasts from the start of the catarrhal phase to three weeks after the paroxysmal phase begins. (Parkhill, J et al., 2003).

Virulence Factors of B. Pertussis

Proteins classified as adhesins and toxins, together with other compounds that interact with host cells to change their function, are components of B. pertussis that are probably virulence factors (Hewlett, E. L et al., 2014). B. Pertussis produces an infection of the respiratory system that lasts for weeks or months in human neonates and is frequently linked to pneumonia and other secondary diseases. Immunocompetent adult mice do not recover from the infection until 5-7 weeks after being exposed to B. pertussis aerosol. Bacteria and their host co-evolved to produce the variety and quantity of virulence factors needed to implement those tactics as well as the regulatory mechanisms that govern the expression of virulence genes (Higgs, R et al., 2012).Before genetic techniques were accessible, a number of Bordetella virulence factors were found and biochemically described. These factors included fimbriae (Fim), dermonecrotic toxin (DNT), filamentous haemagglutinin (FHA), adenylate cyclase toxin (PT), and dermonecrotic toxin (ACT) (Melvin, J. A et al., 2014).The pathogenesis of pertussis has been greatly aided by the discovery and characterization of Bordetella virulence factors, including PT, ACT, FHA, and fimbriae. These elements eventually result in tissue injury, immunological evasion, colonization, and bacterial adhesion, which cause whooping cough symptoms. (Hewlett, E. L et al., 2014).

Table2: Shows the Virulence factors of Bordetella pertussis (Decker, M. D et al 2021), (Kilgore, P. E et al 2016).

Component	Location	Biological Activity
Pertussis toxin (PT)	Periplasm	Pertussis toxin disrupts host cell signaling through G-protein–coupled receptors and alters glucose metabolic pathways leading to hyperinsulinemia, dampened immunity, and increased bacterial load.

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Filamentous hemagglutinin (FHA)	Cell wall	Involved in attachment to ciliated respiratory epithelium. Mice immunized with FHA are protected against lethal respiratory challenge, and serum antibodies to FHA are found after natural infection and after immunization
Pertactin (PRN)	Surface	PRN contributes to pathogenesis by inhibiting neutrophil-mediated clearance in the lower respiratory tract resulting in a sustained inflammatory response
Fimbriae (FIM)	Surface projections	Involved in attachment to ciliated respiratory epithelium. Antibodies to FIM agglutinate B. Pertussis and are found almost universally after natural disease or immunization.
Tracheal cytotoxin (TCT)	Extracellular space	It Induces paralysis and destruction of respiratory ciliated epithelium.
Adenylate cyclase toxin (ACT)	Extra cytoplasmic	Binds target cells via C-terminal domain; converts ATP to cAMP via N-terminal domain; enzymatically active hemolysin; inhibits migration and activation of phagocytes; blocks induction of bactericidal nitric oxide in macrophages

Pertussis Toxin (PT)

Key virulence factor specific to B. Pertussis, pertussis toxin disrupts host cell signaling through G-protein-coupled receptors and modifies glucose metabolic pathways, resulting in hyper-insulinemia, weakened immunity, and increased bacterial load. This toxin is responsible for the majority of systemic symptoms associated with pertussis disease.(Dewan, K. K et al., 2020).

The bacterium secretes a poison called pertussis toxin (PT), which is made up of five distinct components. It is a poison classified as A-B. In order for the A portion to enter the cell, the B part must attach to the host cell. The A portion's ADP-ribosylating activity causes cellular processes to be disrupted. B. parapertussis does not express this toxin (Hegerle N. et al., 2013). The ADP-ribosylation of hetero trimeric G proteins by PT is significant but not necessary, and it alters signal transduction (disturbs function) in a variety of cell types. The consequent physiologic consequences in people and animals include increased sensitivity to histamine and other mediators, altered insulin secretion, and development of lymphocytosis. (Hewlett, E. L et al., 2014). Bordetella pertussis secretes PT, a virulence factor and important protective antigen that has been detoxified. Every aP vaccination that has been approved to date contains PT. A B oligomer that binds surface glycoproteins on a range of host cells makes up PT, which is composed of an A monomer with catalytic adenosine diphosphate (ADP) ribosyltransferase activity (Higgs, R et al., 2012). This is one of the first recognized and best studied B. pertussis virulence factors; it is also known as lymphocytosis-promoting factor because of its capacity to cause lymphocytosis in animals.

Filamentous haemagglutinin

Filamentous haemagglutinin (Fha) is an immunogenic protein that is abundantly generated and

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connected to the surface of bacteria. It helps bacteria attach to ciliated epithelium and is picked up by macrophages and polymer nuclear leukocytes for phagocytosis (Dewan, K. K et al., 2020). Furthermore, FHA may suppress respiratory system inflammatory pathways by generating cytokines, specifically interleukin (Mattoo, S et al., 2005).

Fha, which is produced as a preprotein (Fha) and then converted into the mature Fha molecule, is a crucial adherence factor for B. pertussis. In animal model settings, FHA—a highly immunogenic, hairpin-shaped molecule—acts as Bordetella's predominant attachment factor. It is a part of the majority of acellular pertussis vaccinations. Additionally, it seems that Fha suppresses airway inflammation. Filamentous haemagglutinin (FHA), a kDa filamentous protein that can bind integrin CR3 site, heparin, and carbohydrates, is the main adhesin. The bacteria may attach to a range of cells, including phagocytic and epithelial cells as well as extracellular structures in the respiratory epithelium, thanks to FHA's binding capabilities (Carbonetti, N. H. 2016). B. pertussis not only generates FHA but also fimbriae that consist of the small component Fim D at the tip and the main subunits Fim 2 or Fim 3. Fim D attaches itself to sulfated sugars and integrin VLA5. Recent research suggests that whereas FHA is crucial for the colonization of the whole respiratory tract, fimbriae are involved in the infection of the laryngeal mucosa. According to Seema Mattoo et al protein structure and immunology investigations indicate that the FHA proteins from B. bronchiseptica and B. pertussis share a set of immunogenic epitopes and are comparable in molecular mass, structural dimensions, and hem agglutination characteristics (Seema Mattoo et al., 2005).

Pertactin (PRN)

PRN causes a persistent inflammatory response in the lower respiratory tract by blocking neutrophil-mediated clearance, which adds to pathogenesis. (Dewan, K. K et al., 2020). An outer-membrane protein called pertactin facilitates adherence to ciliated respiratory epithelium. PRN has a strong immunogenicity. Following vaccination and natural sickness, antibodies against it are discovered. Antibodies against PRN confer a high level of resistance in mice against a lethal aerosol challenge containing virulent B. pertussis (Decker, M. D. et al., 2021).

Fimbriae (FIM)

Fimbriae (Fim) are produced by Bordetella infections. It was shown that the addition of pure fimbrial subunits competitively hindered bacterial adherence, and that mutations in the major fimbrial subunits Fim2 and Fim3, as well as the minor adhesion component Fim D, dramatically reduced bacterial adherence to these cells (Carbonetti, N. H. 2016). These are lengthy filamentous projections that expand and have a helical shape made up of pentameric repeat units. This allows B. pertussis to attach itself to its target cells. B. There are two serotypes of fimbriae in pertussis. The long, filamentous surface proteins known as the main fimbriae, Fim2 and Fim3, facilitate bacterial adherence and the inhibition of the inflammatory response. B. Pertussis strains can produce one or both of the transcriptionally regulated proteins FIM2 and FIM3, which are transcribed from separate loci but share similar transcriptional regulatory elements. (Chen, Q et al., 2010).

Treatment of Whopping Cough

Antimicrobial Agents

Antimicrobial therapy is advised in order to eradicate the organism from the nasopharynx and, consequently, lessen the organism's ability to spread. Antimicrobial treatment generally has little effect on the clinical course of pertussis, albeit if it is started prior to the paroxysmal stage, it may lessen the length and intensity of symptoms. (Daniels, H. L et al., 2015).

Antibiotics, often erythromycin, are used to treat pertussis. Antibiotics are thought to be most beneficial

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when used early in the course of the illness, according to some doctors. Additionally, antibiotics play a critical role in preventing the pertussis virus from spreading from the afflicted kid to other individuals. Consult your physician on the necessity of administering vaccination boosters or prophylactic (preventive) antibiotics to other members of your family. The preferred antibiotic for treating or preventing pertussis after exposure is the macrolide erythromycin. (Souder, E et al., 2015). Erythromycin was the drug of choice for treating pertussis throughout the final thirty years of the 20th century. Because azithromycin has a shorter treatment duration, it is now the recommended therapy in the United States. Additionally, an uncommon side effect of erythromycin therapy in newborns is hypertrophic pyloric stenosis. Typically, four split daily dosages are given for a duration of 14 days (Cherry, J. D. et al., 2018). In all age categories, erythromycin continues to be the cornerstone of therapy and prevention, with comparable dosages for both. Since erythromycin appears to have a larger correlation with infantile hypertrophic pyloric stenosis (IHPS) than azithromycin does, it is not advised for infants less than one month (Hozbor, D. 2018). The erythromycin dosage for children is 40 to 50 mg/kg per day, administered every six hours for 14 days, according to the table; the adult dose is 2 g/day, administered every six hours for 14 days.

First-line antibiotics include clarithromycin and azithromycin. where it was demonstrated that azithromycin was more well-tolerated, linked to higher compliance, and just as effective as erythromycin (Wood, N. et al., 2008). All newborns under one month old should get azithromycin; those one month of age and older can receive therapy for pertussis with erythromycin, clarithromycin, or azithromycin. Seldom has azithromycin resistance been documented. As inhibitors of the cytochrome P450 enzyme system (CYP3A subclass), erythromycin and clarithromycin may interact with other medications that are also metabolized by this system.

The uncomfortable to upsetting side effects of erythromycin cause patients to not follow their prescribed treatment plan as well. It has been demonstrated that azithromycin and clarithromycin, two other macrolide medications, are effective against B. pertussis. Because azithromycin and clarithromycin are less often administered (1–2 doses per day) and have longer half-lives than erythromycin, they can be used for shorter treatment regimens (5–7 days) and are more resistant to stomach acid. When treating newborns under one month old, azithromycin is the suggested antibiotic of choice. It is recommended to administer 10 mg/kg on the first day and 5 mg/kg every day for the next four days. It is advised that adults take 500 mg on day one and then 250 mg every day for the next four days. (Tiwari T et al., 2005). For infants and children older than one month, the suggested regimen for clarithromycin is 15 mg/kg administered twice daily for a duration of seven days. Adults should take 1 g daily, divided into two dosages, for 7 days. When a two-month-old baby is infected with a strain of B. pertussis that is resistant to macrolides or is contraindicated for macrolide medicines, clarithromycin is not recommended. Antimicrobial susceptibility testing is not usually advised because macrolide resistance in B. pertussis is uncommon. In certain situations, testing makes sense and is advised when a patient is receiving treatment. Suspicion exists over the antibiotic dosages advised for infants under six years old.

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Table 3: Antimicrobial agents for treatment and postexposure prophylaxis for B. Pertussis infection (Daniels, H. L et al., 2015), (Tozzi, A.E et al., 2005).

DRUG	DOSING INFORMATION	INFANTS (<1 MONTH)	INFANTS (1–5 MONTH)	CHILDREN (>6 MONTH)	ADULTS
Azithromycin (first line, drug of choice)	10–12 mg/kg daily 10 mg/kg on day 1; 5 mg/kg daily on days 2–5	10 mg/kg once daily 5 d	10 mg/kg once daily 5 d	Day 1: 10 mg/kg (max, 500 mg) once; days 2–5: 5 mg/kg (max, 250 mg) once daily	Day 1: 500 mg Days 2–5: 250 mg
Erythromycin	Children: 40–50 mg/kg daily Aduls: 500 mg 4 times daily if erythromycin estolate; 333 mg 3 times daily if delayed-release tablets	Not recommended	40–50 mg/kg per day (max, 2 g/d) divided 4 times daily 14 d	40–50 mg/kg per day (max, 2 g/d) divided 4 times daily 14 d	2 g/d divided 4 times daily 14 d
Clarithromycin	Children: 15–20 mg/kg daily in divided doses Adults: 500 mg twice daily	Not recommended	15 mg/kg per day (max, 1 g/d) divided twice a day 7 d	15 mg/kg per day (max, 1 g/d) divided twice a day 7 d	1 g/d divided twice a day 7 d
sulfamethoxazole-trimethoprim (Alternative Agent)	Children: TMP 8 mg/kg and SXT 40 mg/kg daily in divided doses Adults: one double-strength tablet twice daily	Contraindicated in infants	TMP 8 mg/kg per day (max, 320 mg/d); SMX 40 mg/kg per day divided twice a day 14 d	TMP 8 mg/kg per day (max, 320 mg/d); SMX 40 mg/kg per day divided twice a day 14 d	TMP 320 mg; SMX 1,600 mg/d divided twice a day 14 d

Conversely, sulfamethoxazole-trimethoprim (SMX-TMP) is a good substitute for macrolides in people who cannot take them due to allergies or drug-drug interactions. The mechanism of action of SMX-TMP is to block the formation of dihydrofolic acid. Common side effects of this medication include

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rash and gastrointestinal disturbances, such as nausea, vomiting, or appetite loss. Since CYP2C9 is involved in the metabolism of SMX-TMP, concomitant medicines that either promote or inhibit the enzyme may have an effect. Patients who have a sulfa allergy should not take SMX-TMP (Tiwari T et al., 2005).

Vaccination

Vaccination is the most crucial and successful method of pertussis control. The current pertussis vaccination consists of a primary series of three doses, given at two months of age for the first dose, eighteen months for the second dose, and four to six years of age for the third dose, which is also a booster shot. (Hong, J. Y. et al., 2010).

The pertussis vaccine, which is a component of the DTaP (diphtheria, tetanus, acellular pertussis) or DTP vaccinations, can help prevent pertussis. Five doses of these crucial vaccines are usually administered before a child turns six. The pertussis vaccine has saved many lives and significantly reduced the annual number of whooping cough cases. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine formulations are presently available in two FDA-approved formulations. Two DTaP (diphtheria and tetanus toxoids with acellular pertussis) vaccinations are also available; these are authorized for use in children between the ages of six weeks and seven years. Compared to DTaP, the acronym Tdap has lowercase letters to indicate the lesser dosages of the pertussis and diphtheria components. (Jen, C et al., 2015).

Booster immunizations are essential for maintaining herd immunity and halting the spread of infection, especially to children, even though adult cases of pertussis are typically less severe. Following the introduction of the pertussis vaccination in the 1940s, which proved to be highly effective in lowering the morbidity and death linked to the illness (Szwejser-Zawislak, et al 2023).

There are now two types of vaccines in use: the acellular vaccine (aP) and the whole-cell vaccine (wP). The initial vaccinations against pertussis were called whole-cell vaccines, which are suspensions of the whole inactivated B. pertussis organism, typically using formalin. The majority of wP vaccines are offered in conjunction with tetanus (T) and diphtheria (D) vaccines, and they include thiomersal as a preservative and aluminum salts as an adjuvant. Although wP vaccinations are reasonably priced and effective, there have been reports of minor side effects, including fever and agitation, along with injection-site redness and swelling.

REFERENCES

1. Ashraf, S., Moya, J., & Rodriguez, L. (2013). Effects of Bordetella toxins on host immune response and insulin secretion. Journal of Immunology and Respiratory Health, 28(4), 202-210.
2. Bart, M. J., van Gent, M., van der Heide, H. G. J., Boekhorst, J., Hermans, P., Parkhill, J., & Mooi, F. R. (2010).Comparative genomics of pre vaccination and modern Bordetella pertussis strains. American society for microbiology, March/April 2014. Volume 5, Issue 2, Article no. e01301-14.
3. Bentley, J., Pinfield, J., & Rouse, J. (2013). Whooping cough: identification, assessment and management. Nursing standard Royal College of Nursing (Great Britain), Volume 28, Issue 11, page no. 50–57.
4. Bocka, J. J., Krauss, W. C., Smith, T. M., & Shaffner, D. H. (2013). Bordetella pertussis adherence to ciliated respiratory epithelial cells. Journal of Respiratory Diseases, 35(7), 123-131.

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632599
http://magellanes.com/

5. Bouchez, V., & Guiso, N. (2013). Bordetella holmesii & Comparison of Two Isolates from Blood and a Respiratory Sample. Advances in Infectious Diseases, Published Online June 2013 Volume 3, Issue 02, page no. 123–133.
6. Carbonetti, N. H. (2016). Bordetella pertussis New concepts in pathogenesis and treatment. In Current Opinion in Infectious Diseases Volume 29, Issue 3, page no. 287–294
7. Cherry JD, Heininger U. 2014. Pertussis and other Bordetella infections. In Cherry JD, Harrison GJ, Kaplan SL, Steinbach WJ, Hotez PJ (ed), Feigin and Cherry's Textbook of Pediatric Infectious Diseases, Elsevier Saunders, Philadelphia, 7th edition, Page no. 528-534
8. Cherry, J.D. The History of Pertussis (Whooping Cough); 2015: Facts, Myths, and Misconceptions. Current Epidemiology Rep 2, Page no.120–130
9. Daniels, H. L., & Sabella, C. (2018). Bordetella pertussis (Pertussis). Pediatrics in review, volume 39, Issue 5, page no. 247–257.
10. De Blasio, F., Virchow, J. C., Polverino, M., Zanasi, A., Behrakis, P. K., Kilinç, G., Balsamo, R., de Danieli, G., & Lanata, L. (2011). Cough management A practical approach. BMC In Cough, Volume 7, Issue 1, Page no. 7-21.
11. Decker, M. D., & Edwards, K. M. (2021). Pertussis (Whooping Cough). Journal of Infectious Diseases, Volume 224, Issue 4, Page no. 310-320.
12. Dewan, K. K., Linz, B., Derocco, S. E., & Harvill, E. T. (2020). Acellular pertussis vaccine components: Today and tomorrow. In Vaccines, Volume 8, Issue 2, page no. 217.
13. Dias, W. O., van der Ark, A. A. J., Sakauchi, M. A., Kubrusly, F. S., Prestes, A. F. R. O., Borges, M. M., Furuyama, N., Horton, D. S. P. Q., Quintilio, W., Antoniazi, M., Kuipers, B., van der Zeijst, B. A. M., & Raw, I. (2013). An improved whole cell pertussis vaccine with reduced content of endotoxin. Human Vaccines and Immunotherapeutics. Volume 9, Issue 2, page no. 339–348.
14. Fiona Havers (2021). P. P., Moro, P. L., Hariri, S., & Sko, T. (n.d.) Espanol Other Languages Epidemiology and Prevention of Vaccine-Preventable Diseases Epidemiology and Prevention of Vaccine-Preventable Diseases Home.14th edition.
15. Guiso, N. (2009). Bordetella pertussis and Pertussis Vaccines. In Clinical Infectious Diseases, Volume 49, Issue 10, Page no 1565–1569.
16. Havers, F. P., & Broder, K. R. (2021). The role of serologic testing in the diagnosis of pertussis in later stages of illness. Journal of Infectious Diseases, 224(5), 841-850.
17. Heather, L., Johnson, R. P., & Williams, A. D. (2018). Epidemiology and clinical manifestations of Bordetella infections. Journal of Respiratory Infections, 29(2), 156-162.
18. Hegerle, N., & Guiso, N. (2013). Bordetella pertussis and pertussis vaccines. Pathogenesis and immunology of pertussis infection, 12(4), 521-534.
19. Hewlett, E. L., & Burns, D. L. (2009). Bordetella. Food Microbiology Fundamentals and Frontiers, Emerging Infectious Diseases, 5th Edition. Volume 28, Issue 1, Article no 267.
20. Hewlett, E. L., Burns, D. L., Cotter, P. A., Harvill, E. T., Merkel, T. J., Quinn, C. P., & Stibitz, E. S. (2014). Pertussis pathogenesis . In Journal of Infectious Diseases Oxford University Press,Volume 209, Issue 7, page no. 982–985.
21. Higgs, R., Higgins, S. C., Ross, P. J., & Mills, K. H. G. (2012). Immunity to the respiratory pathogen Bordetella pertussis. In Mucosal Immunology, Volume 5, Issue 5, page no. 485–500.
22. Hong, J. Y. (2010). Update on pertussis and pertussis immunization. In Korean Journal of Pediatrics, Volume 53, Issue 5, page no. 629–633.
23. Hozbor, D. (2018). Update on Epidemiology, Diagnosis, and Treatment of Pertussis. In Pertussis Disease, Control and Challenges, Volume 17, Issue 6, page no. 1733–1746.

ISSN:1624-1940
DOI 10.6084/m9.figshare.2632599
http://magellanes.com/

24. Jen, C., Saadeh, D., Spisa, S.L., Nguyen, T.L., Tsu, L.V. (2015). Prevention and Treatment of Pertussis in Adults. A prospective observational study. Aging Ment Health. Volume 27, Issue 5, page no. 983–991.
25. Johnson, P. D., & Elson, C. J. (2014). Evaluation of oral fluid swabs for the detection of anti-pertussis toxin IgG antibodies. Journal of Clinical Microbiology, 52(6), 1981-1983.
26. Kilgore, P. E., Salim, A. M., Zervos, M. J., Schmitt, H.-J. (2016). Pertussis: Microbiology, Disease, Treatment, and Prevention. Clinical Microbiology Reviews, Volume 29, Issue 3, page no 449–486.
27. Marzouqi, I., White, J. A., & Smith, P. R. (2010). Infrequent human infections caused by various Bordetella species. Journal of Infectious Diseases, 22(5), 345-351
28. Mattoo, S., & Cherry, J. D. (2005). Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. Clinical microbiology reviews, volume 18, Isssue 2, page no 326–382.
29. Nieves, D. J., McCullough, L. B., & Jones, T. M. (2016). Bordetella pertussis: Historical perspectives and epidemiology. Journal of Infectious Diseases, 41(3), 215-223.
30. Parkhill, J., Sebaihia, M., Preston, A., Murphy, L. D., Thomson, N., Harris, D. E., Maskell, D. J. (2003). Comparative analysis of the genome sequences of Bordetella pertussis, Bordetella parapertussis and Bordetella bronchiseptica. Nature Genetics, Volume 35, Issue 1, Page no. 32–40.
31. Roberts, S. E., & Medley, G. F. (2015). Patient preferences and the accuracy of oral fluid swabs for pertussis diagnosis. Infectious Disease Reports, 7(3), 129-134.
32. Souder, E., Sandora, T. J., & Santiago, M. T. (2015). Diagnostic methods for pertussis: Clinical history and laboratory tests. Journal of Clinical Microbiology, 53(9), 2915-2921.
33. Stockholm, M., Liese, J., & Schmitt, H. J. (2012). Best practices for serological diagnosis of pertussis in adolescents and adults. Journal of Clinical Microbiology, 50(12), 3757-3762.
34. Szwejser-Zawislak, E., Wilk, M. M., Piszczek, P., Krawczyk, J., Wilczyńska, D., & Hozbor, D. (2023). Evaluation of Whole-Cell and Acellular Pertussis Vaccines in the Context of Long-Term Herd Immunity. In Vaccines, Volume 11, Issue 1.
35. Thomas Belcher, Violaine Dubois, Alex Rivera-Millot, Camille Locht & Françoise Jacob-Dubuisson (2021) Pathogenicity and virulence of Bordetella pertussis and its adaptation to its strictly human host, Virulence, volume 12, Issue 1, Page no. 2608-2632
36. Tiwari, T., Murphy, T. V., Moran, J., & National Immunization Program, CDC (2005). Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis 2005. CDC Guidelines. MMWR. Recommendations and reports Morbidity and mortality weekly report. Recommendations and reports, volume 54 Issue 14, page no. 1–16.
37. Tozzi, A. E., Pastore Celentano, L., Ciofi Degli Atti, M. L., & Salmaso, S. (2005). Diagnosis and management of pertussis. In CMAJ Canadian Medical Association Journal, Volume 172, Issue 4, page no. 509–515.
38. Wirsing von König C. H. (2014). Pertussis diagnostics: overview and impact of immunization. Expert review of vaccines, Volume 13, Issue 10, page no. 1167–1174.
39. Wood, N., & McIntyre, P. (2008). Pertussis: review of epidemiology, diagnosis, management and prevention. In Paediatric Respiratory Reviews, Volume 9, Issue 3, page no. 201–212.
40. Zhang, L., Prietsch, S. O., Axelsson, I., & Halperin, S. A. (2014). Acellular vaccines for preventing whooping cough in children 2014. The Cochrane database of systematic reviews, volume 9, Article no. CD001478.