



## LITERATURE REVIEW ON EVALUATION AND MANAGEMENT OF PERTUSSIS

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### ABSTRACT

Pertussis is an acute respiratory tract infection that is also known as whooping cough. It affects all age groups but in young children, it may lead to severe complications. In children younger than 5 years old, pertussis is considered the fifth fatal but vaccine-preventable disease worldwide. However, it is still considered a major health dilemma. To review the published literature that discussed pertussis, clinical evaluation, and management. PubMed database was used for articles selection, and the following keys were used in the mesh ("Pertussis"[Mesh]) AND ("management"[Mesh]) OR ("evaluation"[Mesh]). Early detection of the infection leads to earlier intervention and prevention of the complication. Clinical complications are more likely to appear in missed or delayed cases of all age groups' patients. Therefore, a combination of various methods should be used instead, matching culture or PCR results with serologic test results to confirm the diagnosis adequately and quickly. Regarding management, the recommended first therapeutic step to treat pertussis is antibiotics as the literature states frankly that antibiotics should be started in suspected cases of pertussis even before confirming the diagnosis. Antibiotics hasten the bacteria clearance from the upper respiratory tract within the first couple of days of the disease's course.

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### Introduction

Pertussis is an acute respiratory tract infection caused by *Bordetella pertussis* bacteria [1, 2]. It is also known as whooping cough and it affects all age groups but in young children, it may lead to severe complications like pneumonia, pulmonary hypertension, apnea attacks, seizures, cardiogenic shock, and hyperleukocytosis, and respiratory failure. This can be described as malignant pertussis [3].

Worldwide and Brazil, in particular, experienced a surprising increase in pertussis incidence. This increase is seen more in unvaccinated infants [3-5]. More than 30 million pertussis cases are registered yearly and the death rate is 160,000 deaths each year in children younger than 5 years old, in the developing countries mostly [6]. In older children and adults, the clinical presentation of pertussis is atypical in most cases. Generally, the main source of transmission is the infected mothers [6, 7]. In children younger than 5 years old, pertussis is considered the fifth fatal but vaccine-preventable disease worldwide. However, it is still considered a major health dilemma [7].

Understanding pertussis, and its complications, and how to face such a disease is important for every pediatrician. Therefore, we aim in this article to review the published literature that discussed pertussis, clinical evaluation, and management.

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## Materials and Methods

PubMed database was used for articles selection, and the following keys were used in the mesh (“Pertussis”[Mesh]) AND (“management”[Mesh]) OR (“evaluation”[Mesh])).

In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics: Pertussis, evaluation, and management.

Exclusion criteria were all other articles, which did not have one of these topics as their primary endpoint.

### *Clinical presentation*

Pertussis has 3 phases; it begins with a catarrhal phase after the incubation period. This phase might last from one to two weeks and the patients in this phase are considered the most contagious. In the catarrhal phase, the disease presents vaguely and the physician mostly cannot distinguish between the disease and mild upper respiratory tract infection. Patient’s cough’s frequency and severity increase along with the progression of the catarrhal phase.

Next is the paroxysmal phase, and it lasts for 3 to 6 weeks. It is characterized by the presence of whooping cough and other symptoms such as cyanosis, post-tussive vomiting, and apnea attacks [8].

In the convalescent phase, the symptoms’ severity decreases gradually but this phase lasts up to several months. Several factors can influence the clinical course of pertussis including sex, age, and immunization status of the patient. After the age of 3 years, the spasmodic cough lasts around 1 week longer in girls than in boys [9].

Most of the infants below 6 months old do not have whooping cough; meanwhile, the most common clinical manifestations in this age group are recurrent apnea attacks, bradycardia, cyanosis, and hypoxia-induced seizures. This age group experiences a more complicated and more prolonged disease course [8]. In this age group, the patients mostly face malignant pertussis, which is considered fatal, and the mortality rate increases with the presence of hyperleukocytosis (white blood cells are between 30,000 and 100,000) and the presence of severe pulmonary hypertension.

In adults, the disease course goes through the 3 phases but the patients mostly experience only protracted cough. Smokers and asthmatic patients experience a longer duration of cough and more attacks of apnea [10]. However, in vaccinated patients, the disease clinical course is significantly lesser in severity [8, 9].

However, asymptomatic infections can occur especially in vaccinated individuals. Therefore, alertness is important to suspect pertussis infection in mild chronic cough [11]. The cough can last for 34 weeks or more especially in patients with mild illness. It has been shown in a study that 5% of healthy-looking infants had polymerase chain reaction (PCR) evidence of pertussis [11, 12].

### *Diagnosis*

The laboratory markers of pertussis are leukocytosis and lymphocytosis, which can be very useful in diagnosing the disease along with the typical presentation of pertussis. Traditionally, the laboratory tests that were relied on in the detection of B. pertussis are nasopharyngeal secretions culture and serologic testing for pertussis-specific antibodies [8, 13].

The nasopharyngeal secretions cultures should be collected by aspiration or swabbing. The culture process should include enrichment of the specimen and specific media use to prevent the growth of other organisms from the upper respiratory tract. The culture sensitivity is high in unvaccinated individuals, and in severe cases [14].

However, the sensitivity and the specificity of the laboratory tests had been affected with time because of the extensive vaccination coverage and the misdiagnosed mild cases. The results can be affected also by antibiotics use [8].

Serologic testing depends on the detection and identification of a significant variation in IgA or IgG titers against the factors of B. Pertussis. However, the strength and reliability of the seroconversion are affected by previous infection or vaccination. Therefore, it is not recommended in vaccinated or adult individuals [15]. The reasonable threshold for a positive test result of serology for pertussis is serum IgG anti-pertussis toxin antibody level above 100–125 EU/mL [16].

The polymerase chain response (PCR) testing method increases the likelihood of confirming B. pertussis. Since the probability of false-positive results is high, PCR tests require specific research facility experience and the availability of proper specimens. The accuracy of PCR testing decreases with the duration of the disease course since the technique depends on the recognition of the microorganism [17].

The variability of results, the usefulness of this method only late in the clinical course of the disease, and the lack of standardized commercial test kits make serologic testing difficult to use in common practice with reproducible results. A combination of various methods should be used instead, matching culture or PCR results with serologic test results [16].

### *Complications*

Early detection of the infection leads to earlier intervention and prevention of the complication. Therefore, clinical complications are more likely to appear in missed or delayed cases of all age groups’ patients. However, young infants are more susceptible to develop severe complications such as respiratory failure and death [18]. Approximately half of the infants that are infected with pertussis require hospitalization and the mortality rate is 1% due to pertussis complications [19]. The complications that have been seen in hospitalized cases of pertussis are mostly apnea, pneumonia, and convulsions [20]. Pulmonary hypertension is also one of the most dangerous complications that are associated with a high rate of mortality in infants with pertussis [21].

In a British study, respiratory syncytial virus (RSV) was a coinfection accompanied in one-third of the hospitalized infants with pertussis infection. Generally, viral infections should be suspected in patients with pertussis such as influenza A virus, and Rhinovirus. Some studies also found adenoviruses with infants with pertussis [22, 23]. Moreover, pertussis can be accompanied by mixed pathogens as synergistic superimposed bacterial or viral infections can be present along with the pertussis infection. Examples of these pathogens include adenovirus, influenza A and B viruses, parainfluenza virus, and RSV. In addition, parasitic and helminthic organisms have been also reported to be associated with coinfections along with pertussis infection, for example, *Fasciola hepatica* and *Plasmodium falciparum* [18, 24]. Nevertheless, when rhinovirus and adenovirus accompany pertussis as a coinfection in infants and young children, the colonization of the infection mostly occurs in the upper respiratory tract and the clinical course is mostly asymptomatic or mild. On the other hand, such infections in adult patients appear to cause serious complications such as apnea, syncope, weight loss, insomnia, urinary incontinence, and rib fracture. They also may lead to the development of pneumonia infection and death [25, 26]. The risk factors for life-threatening complications in adults with pertussis include diabetes mellitus, chronic obstructive pulmonary disease, multiple sclerosis, and multiple myeloma [10]. Hospitalization is needed for around 12% of adult patients with coinfections [18].

### *Management*

The recommended first therapeutic step to treat pertussis is antibiotics as the literature states frankly that antibiotics should be started in suspected cases of pertussis even before confirming the diagnosis [27].

It has been shown that antibiotics significantly reduce the severity of the symptoms as well as the disease course duration in the catarrhal phase. They also hasten the bacteria clearance from the upper respiratory tract [3]. In the paroxysmal phase, antibiotics have shown to be effective in reducing transmissibility, which subsequently helps in the elimination of the bacteria in the nasopharynx after starting the treatment within 5 to 7 days.

The first recommended antibiotics for *B. pertussis* eradication are macrolides [3]. Before 1996, studies suggested that erythromycin should be given at a high dose 6 hourly for 1 to 2 weeks. In 1990, studies on the minimum time needed for the eradication of *B. pertussis* were conducted. They suggested that sufficient results can be achieved by lower doses 8 hourly and for 1 week to 10 days. Later, resistance to erythromycin has been observed in *B. pertussis* cases. This led to the search for new drugs that are with no resistance and with fewer side effects than erythromycins such as nausea, vomiting, and diarrhea. Studies on azithromycin and clarithromycin have been performed in 2000 to evaluate their safety and effectiveness. A study conducted in 2004 revealed that treating children with azithromycin for five days reduced the risk of developing acute respiratory infections. A follow-up study was conducted in 2001 revealed that clarithromycin and Erythromycin reduced the risk of hospitalization among children and adolescents with respiratory conditions. Both regimens have shown the same efficacy. The researchers concluded that the reduction of gastrointestinal adverse effects was similar to the effects of clarithromycin and azithromycin [28-30].

### *Hospital care*

In addition to antibiotics, treating severe cases of pertussis requires intensive medical care and advanced life support to avoid potential complications [3]. Hospitalization is considered an option for infants and young children with respiratory conditions or diseases that usually develop complications for example pulmonary, muscular, or neurological disease. Adequate hydration is also very important for the maintenance of blood volume. In addition, oxygen therapy is often needed due to respiratory distress that can be caused by infections, pneumonia, and pulmonary hypertension. Mechanical ventilation might be also needed in infants with hypercapnia [18, 31, 32].

### *Cough treatment*

Corticosteroids, salbutamol, antihistamines, leukotriene inhibitors, and anti-pertussis immunoglobulins are all therapeutic options for the symptomatic treatment of cough in pertussis patients. It is believed that systemic corticosteroids have a significant positive effect on the severity of the disease course [3, 33].

### *Pertussis vaccine*

According to the World Health Organization (WHO), the primary goals of immunization are to reduce the risk of serious disease in infants and to achieve the minimum level of vaccine coverage required (90%) in newborns with three doses. Authorities have recently concentrated on infection control in addition to the goal of preventing the disease in infants and the associated severe forms [34].

The WHO notes that the widespread vaccination program that had been carried out in the 1950s and 1960s resulted in a drop in disease incidence and death numbers in developed countries.

The most recent findings also show the relevance of immunization, which has traditionally been accomplished using two types of vaccines: cellular (old generation) and acellular (new generation).

The two types were mostly used as components of combination products, with a three-dose vaccination regimen. According to the WHO, the best old and new generation vaccinations against severe pertussis have equally outstanding positive effects and characteristics [7, 34].

## Conclusion

Early detection of the infection leads to earlier intervention and prevention of the complication. Clinical complications are more likely to appear in missed or delayed cases of all age groups' patients. Therefore, a combination of various methods should be used instead, matching culture or PCR results with serologic test results to confirm the diagnosis adequately and quickly.

Regarding management, the recommended first therapeutic step to treat pertussis is antibiotics as the literature states frankly that antibiotics should be started in suspected cases of pertussis even before confirming the diagnosis. Antibiotics hasten the bacteria clearance from the upper respiratory tract within the first couple of days of the disease's course.

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