

## Treatment, prevention and diagnostic methods of the pertussis in a response to increasing number of pertussis cases.

Krztusiec – metody diagnostyki, leczenia oraz zapobiegania w obliczu rosnącej liczby zachorowań.

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### Abstract:

Pertussis is a disease which is the most often caused by *Bordetella pertussis*. It is a severe, highly contagious respiratory tract illness. Risk factors include young or old age, comorbidities, pregnancy and smoking. The highest rise in cases concerns younger infants population, in which the mortality is the most common. Clinical presentation can differ from asymptomatic or mild infection to severe respiratory tract disease that lasts for weeks. Pertussis appears through paroxysms, which occur in 2 to 8 weeks after the beginning of the disease. One of the most common complications of pertussis is pneumonia. Pertussis is a serious problem recently, because an increased number of pertussis cases has been noted. According to the National Institute of Public Health in Poland, in 2024, over 30 000 cases were observed, which is 10 times more compared to 2023. In the face of current outbreak, it seems necessary to pay special attention to prevention methods that allow us to stop further transmission of the pertussis.

**Keywords:** pertussis, *Bordetella pertussis*, vaccination, post-exposure prophylaxis, prolonged cough

**Streszczenie:**

Krztusiec jest wysoce zakaźną chorobą dróg oddechowych, często o ciężkim przebiegu, najczęściej wywoływaną przez Gram ujemną pałeczkę *Bordetella pertussis*. Do czynników ryzyka ciężkiego przebiegu krztuśca należą m.in. młody lub podeszły wiek, choroby współistniejące, ciąża oraz palenie tytoniu. Największy wzrost zachorowań w ostatnich latach dotyczy populacji niemowląt, w której śmiertelność jest najwyższa. Obraz kliniczny może być różny od bezobjawowego lub łagodnego zakażenia do ciężkiej choroby dróg oddechowych trwającej przez wiele tygodni. Krztusiec objawia się napadami kaszlu, które ustępują w ciągu 2 do 8 tygodni od początku choroby. Jednym z najczęściej występujących powikłań jest zapalenie płuc. Zwiększona liczba zachorowań na krztusiec w ostatnim czasie stanowi poważny problem. Według Narodowego Instytutu Zdrowia Publicznego w 2024 roku w Polsce odnotowano ponad 30 000 przypadków zachorowań na krztuśca, co stanowiło dziesięciokrotny wzrost względem roku poprzedniego. W obliczu narastającej liczby zachorowań wydaje się konieczne położenie szczególnego nacisku na metody prewencji oraz zapobiegania dalszej transmisji krztuśca.

**Słowa kluczowe:** krztusiec, szczepienie, *Bordetella pertussis*, profilaktyka poekspozycyjna

## 1. Introduction

*Bordetella pertussis* is a gram-negative bacterial respiratory pathogen that causes the majority of highly contagious acute respiratory infections, known as whooping cough or pertussis. The minority is caused by *Bordetella parapertussis*. Pertussis can be observed in all age groups, mainly in infants and young children [1,2]. The highest risk of a severe course of whooping cough is observed in children under 3 months of age. The youngest patients are especially vulnerable to complications and death [3]. There are a few types of vaccines used in immunization against pertussis. Despite the high immunization rate, cyclical outbreaks are still observed worldwide. In addition, according to the World Health Organization (WHO), pertussis is one of the worst-controlled disease in the world [4]. Moreover, in recent years, there has been a notable growth in the number of pertussis cases. An aspect that plays a key role in spreading whooping cough is the high level of *Bordetella pertussis* contagiousness. That means one person with pertussis can infect up to even 17 people [4,5].

In this review, we would like to summarize information from the previous publications and new recommendations. It seems necessary to pay special attention to the prevention and treatment methods of *Bordetella pertussis*, as it is a highly contagious and life-threatening disease.

## 2. Epidemiology

At the beginning of the previous century, before *Bordetella pertussis* vaccination had been widespread, the disease was a common cause of mortality in children. After introducing the vaccines against *Bordetella pertussis*, the number of cases decreased significantly [5]. Despite the common use of vaccines and high immunization rates, there has been an increased number of pertussis cases in all ages recently [3]. The highest rise in cases concerns the younger infant population, in which mortality is the most common [3]. It has been observed that pertussis outbreaks turn out in a cyclical pattern, more specifically, every 3 to 5 years [5]. It is also said that low trust in medical health services and difficulties in vaccine accessibility lead to decreased vaccination rates. Furthermore, COVID-19 pandemic caused the interruption of regular vaccination schedules [6]. It is believed that all the above mentioned factors could lead to the current growth of pertussis cases.

In 2022, 62,500 cases were reported worldwide by WHO [7]. In the European Union, a rapid increase in pertussis cases was also noted. Only in the first quarter of 2024, there have been 32,000 cases, which corresponds to the amount of reported pertussis in the whole of 2019 [8]. There were over 10,000 confirmed cases in the United Kingdom in the first half of 2024, while in the whole 2023 year, 856 cases were reported [9]. There is also a remarkable growth of pertussis cases reported in Poland in 2024 compared to 2023. According to National Institute of Public Health in Poland (NIZH), 14,584 cases of pertussis were reported from January to mid-September 2024, and over 1,700 had to be hospitalized. Compared to 2024, in 2023 there were 559 confirmed pertussis cases in the same period of time [10]. In 2016, there were 6,828 cases, and approximately half of them (3,631) had been hospitalized [11]. However, total number of pertussis cases is unknown due to diagnostic difficulties and non-specific clinical demonstration.

## 3. Risk factors

Establishing the disease's risk factors can be helpful to make an effective strategy against pertussis, including a vaccination programme and post-exposure prophylaxis [12]. Age, chronic medical diseases, some occupational groups, including teachers and health-care workers, pregnancy, or smoking tend to have an increased risk of pertussis morbidity, severity, or even hospitalization [11]. Whooping cough occurs most commonly in infants, young children, teenagers, and seniors. Infants are at the highest risk of morbidity and mortality [4]. Patients suffering from asthma, chronic obstructive pulmonary disease (COPD), immunodeficiency, and obesity are more vulnerable to pertussis, and the symptoms can be more intensified [12].

#### 4. Diagnosis

The pertussis illness duration is between 6 and 12 weeks [13]. The first symptoms develop after 7 to 10 days of the incubation period, which can be prolonged even to 4 weeks [14,15]. Symptoms can vary from many factors, including the patient's age, previous infection, presence of passively acquired antibody, and antibiotic treatment [13]. Clinical presentation can differ from asymptomatic or mild infection to severe respiratory tract disease that lasts for weeks [16]. The time from vaccination or previous infection with whooping cough influences the symptoms severity [17].

Pertussis consists of 3 stages such as catarrhal, paroxysmal and convalescent stage. The first phase lasts approximately 1 to 2 weeks. The main symptoms are rhinorrhoea, nasal congestion, weakness, and sore throat or mild cough, similar to common viral infections. Moreover, lacrimation with conjunctival infection can be present [5,18]. In the next few weeks cough is getting stronger, more frequent, and tenacious. The second is a paroxysmal stage (2-8 weeks), in which paroxysms occur, characterized by a few rapid and forced coughs during a single expiration after which the patient is forced to inhale with a loud, „whooping” sound. A paroxysm may be followed by vomiting or apnoea. Several paroxysms can follow one another within minutes, which makes a patient fatigued. The cough usually occurs in the evening or at night. Furthermore, the patient can experience cyanosis, eye proptosis, tongue protrusion, salivation, lacrimation, engorgement of neck veins, and oral mucus production, which is not purulent. In addition, there are other symptoms such as weight loss, respiratory exhaustion, and children can seem apathetic. Usually, the temperature is maintained within normal limits [18]. The last one is the convalescent stage, which lasts approximately 1 to 2 weeks. In this phase, cough becomes less frequent and less severe. Duration of chronic, non-paroxysmal cough can last up to 6 weeks [5,16]. It has been established that approximately 85% of patients showed negative *Bordetella pertussis* culture in 3 to 4 weeks after begging of typical whooping cough symptoms [19]. However, eradication of *Bordetella pertussis* has not been observed within 6 weeks in unvaccinated or untreated infants [20].

The *B. pertussis* infection can be suspected especially when the cough persists at least 2 weeks and coughing fits, apnoea, or vomiting after paroxysms occur. Although clinical presentation is not enough to make a clear diagnosis, it is a important part in diagnostic process of the pertussis. To confirm the infection several diagnostic techniques can be useful, such as culture, serology, and polymerase chain reaction (PCR) of nasopharyngeal swabs. The gold standard in first 2 weeks of cough is culturing *B. pertussis* from na-

sopharyngeal aspirates or swabs that helps confirming the diagnosis. The PCR is highly useful in first 3 weeks of the infection as the optimal sensitivity rate, and the effectiveness of PCR is lowering with the pertussis duration [21]. In the next stages, the serologic tests such as IgG, and IgA level are used to detect the antibodies against the *B. pertussis* in serum samples, and confirm the disease as antibodies increase after 4 weeks from the begging of the pertussis [22]. Serology has its limitations in several groups, such as infants, and people vaccinated in the last 12 months. The IgG rate lower than 40 EU/ml indicates little possibility of the infection. If the IgG rate is 40-100 EU/ml, the IgA rate higher than 12 EU/ml level is used to indicate the current pertussis infection. The IgG level higher than 100 EU/ml confirms presence of pertussis recently [23]. To conclude, a comprehensive diagnostic approach of pertussis consists of clinical presentation, and laboratory methods.

The most common complication of *Bordetella pertussis* infection is pneumonia and otitis media. What is more, severe coughing fits can conduce to cerebral hypoxia and in consequence, to encephalopathy and seizures. Also, it can lead to interstitial emphysema in consequence of rupture of alveoli. Rare complications include rib fracture, umbilical or inguinal hernia, apnoea or subarachnoid, and intraventricular hemorrhage [18].

The symptoms of pertussis are non-specific, which means that many other pathogens can conduce to similar clinical manifestations. While making a diagnosis, other potential diseases should be taken into consideration, including illnesses caused by adenoviruses, respiratory syncytial viruses, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Mycobacterium tuberculosis*, and endemic fungi [5]. In differential diagnosis of pertussis, it is important to take into account other causes of prolonged cough, such as sinusitis, gastroesophageal reflux disease, foreign body inhalation, asthma, or cystic fibrosis [24]. Lack of significant fever and posttussive vomiting distinguishes pertussis from other respiratory infections [5].

## 5. Treatment

The treatment of pertussis consists of antibiotic therapy, which should be initiated in the first 3 weeks to shorten the duration of symptoms, eradicate *Bordetella pertussis* from the upper respiratory tract, and reduce further transmission. Introducing antibiotics in the further stages of pertussis is controversial because of their low effectiveness, especially in severity and illness duration [25,26]. There are several antimicrobial agents to treat pertussis. The mainstay of treatment is newer macrolide antibiotics, such as azithromycin

and clarithromycin rather than older ones (erythromycin) because of undesirable adverse effects. Furthermore, it has been found that a short-term treatment with azithromycin for 3 to 5 days was as effective as a long-term erythromycin treatment (10 to 14 days) to eradicate *Bordetella pertussis* [16]. Antibiotic choice should depend on the patient's age, antibiotic tolerance and predicted adverse effects. An important example of undesirable effects is hypertrophic pyloric stenosis, which can occur in neonates treated with erythromycin [27]. In addition, erythromycin can lead to gastrointestinal side effects in treated adults [28]. On the other side, there is azithromycin that is well tolerated and characterized by a high safety profile. That is why azithromycin is the only recommended agent for the treatment of pertussis in infants less than 1 month old [26].

An alternative to macrolides treatment of pertussis is trimethoprim/sulphamethoxazole (also known as co-trimoxazole). It can be used in patients who do not tolerate macrolide antibiotics or when there is bacterial resistance to macrolides [26,29]. Usage of co-trimoxazole is limited to patients older than 1 month due to a higher risk of kernicterus. Other antibiotics are not recommended. Research has shown that ampicillin, cephalosporin, tetracycline, and fluoroquinolones have no positive impact on pertussis-treated patients [26]. Studies have consistently shown that there is a lack of evidence-based symptomatic pertussis treatment that is effective. That is why symptomatic agents such as bronchodilators, corticosteroids, or antitussives are not recommended [16]. However, optimal hydration, nutrition, and removing provoking factors are crucial for proper recovery. Some patients require hospitalization, especially those with pneumonia as a result of pertussis. Oxygen therapy and mechanical ventilation can be helpful in severe cases [5].

**Table 1.** Antimicrobial agents used in treatment and post-exposure prophylaxis of pertussis

| Antimicrobial agent                           | Dosing                                                | Duration of therapy |
|-----------------------------------------------|-------------------------------------------------------|---------------------|
| Azithromycin                                  | 500 mg once on day 1, then 250 mg per day on days 2-5 | 3 - 5 days          |
| Clarithromycin                                | 500 mg twice a day                                    | 7 days              |
| Erythromycin                                  | 500 mg four times a day                               | 10 -14 days         |
| trimethoprim/sulphamethoxazole                | 180 mg of TMP and 800 mg of SMX twice a day           | 14 days             |
| TMP – trimethoprim<br>SMX - sulphamethoxazole |                                                       |                     |

## 6. Prevention

### 6.1 Vaccination

Vaccines are one of the most important parts of preventing the spread of the infectious diseases [30]. People can gain immunity to *Bordetella pertussis* in different ways, including infection and vaccination. Active natural immunity occurs after infection, when patients' immune system produce antibodies against pertussis. Studies have shown that it can last from 3,5 to 30 years [31]. Artificial active immunity appears after exposure to antigens during vaccination.

Before introducing the pertussis vaccination, whooping cough was a severe, death-dealing illness [30]. In 1920, the first vaccine against pertussis was presented, and since the late 1940s, vaccination has been spreading worldwide with positive results [32]. In 1960, pertussis vaccination was launched in Poland [4]. The introduction of DTP (Diphtheria, Tetanus, and Pertussis) vaccines gave a notable decrease in pertussis outbreaks in many countries. However, concerns about the safety profile of the whole-cell DTP vaccine (DTwP) have been raised. Main objections against DTwP were associated with „vaccine encephalopathy” and sudden infant death syndrome (SIDS), which have been refuted [18,33]. Despite this, DTwP is connected with many adverse effects such as fever, redness of skin at the injection site, drowsiness, anxiety, vomiting, and persistent crying [34]. In response to the side effects of DTwP, diphtheria, tetanus toxoid, and pertussis acellular vaccines (DTaP) were developed. The DTaP does not have lipopolysaccharide (LPS), which is why it is less reactogenic than DTwP. As a result, DTaP gives less adverse effects. In the 1990s, due to its better safety profile, DTaP were commonly used worldwide [5]. It is said that DTwP vaccination leads to 5 to 14 years of protection [35]. While using acellular vaccine provides only 4 to 7 years of immunity [36]. In recent years, using acellular vaccination has been controversial. A number of researchers have demonstrated that acellular pertussis vaccination has no influence on nasopharynx colonization, transmission, and inducing herd protection [14]. On the other side, there are many epidemiological data showing the efficacy of acellular vaccines [37]. There are many different immunization timetables for DTP and DTaP vaccines in several countries. However, the Centers for Disease Control and Prevention (CDC) guidelines recommend 5 doses of DTaP vaccination at 2, 4, 6, 15 to 18 months, and 4 to 6 years old. Moreover, the Advisory Committee on Immunization Practices (ACIP) introduced a single dose of Tetanus toxoid, reduced Diphtheria toxoid, and acellular pertussis (Tdap) vaccine for adolescents and adults [38]. Vaccination against pertussis schedule in Poland in 2025 consists of 4

doses of DTP at 2, 3 to 4, 5 to 6, and 16 to 18 months old, one dose of DTaP in 6 years old, and a booster of Tdap in 14 years old [39]. There are few studies evaluating Tdap booster in adults, showing positive results of additional vaccination [40]. However, further research is needed to establish the effectiveness of a Tdap booster [41]. According to the ACIP's latest recommendations, it is said that the tetanus, diphtheria vaccine (Td) or Tdap vaccine booster should be retaken by adults every 10 years, because prior infection or vaccination does not provide immunity for a whole life [11].

As mentioned in the CDC recommendations, every pregnant woman should receive a Tdap vaccination within 27 to 36 weeks of pregnancy [42]. Tdap vaccination features a high safety profile for both pregnant women and children. It is an effective protection against pertussis for infants in the first two months of life [4].

## **6.2 Post-exposure prophylaxis**

Cost-effective strategy for pertussis post-exposure prophylaxis (PEP) has been an object of recent studies. [30]. PEP should be considered for patients who have had close contact with pertussis cases of all ages and for household members. Moreover, patients with pertussis should be isolated for 5 or more days after introducing the treatment to prevent the transmission of pathogens [1]. Introducing the PEP does not depend on immunization status. Antibiotics used in prophylaxis of pertussis aim to prevent severe pertussis, complications, death, and shorten the illness duration. It is recommended to introduce macrolides within 21 days of exposure. The antibiotic and doses of antimicrobial agents in the PEP are the same as those in the treatment of pertussis [38]. In the cost-effective strategy, the main choice is azithromycin as it is a short-term therapy. The research demonstrated that the PEP is a key strategy, especially in epidemics [30].

On the other hand, in spite of these findings about the role of PEP in preventing the development of severe pertussis infection, research in this area also has shown no difference in symptoms or laboratory tests while taking or not PEP among household contacts of pertussis patients [43].

## **7. Summary**

In the face of the latest pertussis outbreak, it is crucial to prevent further spreading of this highly infectious and dangerous disease. More and more new cases of pertussis remind us that it is an important issue with areas for further research. An increased number of pertussis cases should make practitioners more careful while diagnosing patients with prolonged cough. It is essential to educate and aware people of the importance of prevention

methods, which seems to be one of the crucial aspects in avoiding further epidemic outbreaks. According to WHO, vaccination is the best way to prevent whooping cough [7]. Despite unclear data, following research is needed to evaluate the effectiveness of DTaP in developing herd immunity. Further studies should be also undertaken to investigate the legitimacy of using PEP in pertussis and its effectiveness in reducing the transmission rate. Due to diagnostic difficulties, it seems necessary to ease access to diagnostic tests, which could be helpful in the proper treatment of patients with prolonged cough.

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