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Pertussis - A Comprehensive Review of Etiology, Diagnosis, Treatment and Prevention

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Abstract

Introduction and Aim:

Whooping cough, caused by Bordetella pertussis, remains a global health challenge despite widespread vaccination. This review summarizes current data on its epidemiology, pathogenesis, and clinical presentation across age groups.

Materials and Methods:

The review analyzes scientific literature, reports, and guidelines up to June 2025, sourced from PubMed. Search terms included "whooping cough" combined with "epidemiology," "COVID-19," "vaccinations," and "macrolides." Data underwent qualitative and quantitative analysis for accurate presentation.

Results and Conclusions:

Poland saw a surge in whooping cough cases post-COVID-19 restrictions, rising from 182 in 2021 to 32,430 in 2024, driven by waning vaccine immunity. Infants face the highest risk, with a mortality rate of up to 1%. Diagnosis relies on PCR, microbiological culture, and serological tests. Macrolides are used for treatment and prophylaxis, reducing transmission if administered early. Acellular vaccines offer effective protection with fewer side effects but require boosters due to shorter immunity duration. Controlling incidence requires maintaining >95% vaccination coverage, targeted antibacterial treatment, and research into new vaccines to address evolving Bordetella pertussis strains.

Keywords: pertussis, whooping cough, covid-19, infection, macrolides, vaccines, prophylaxis, antibodies.

Introduction

Pertussis (Whooping cough) is an acute and highly contagious respiratory disease caused by the Gram-negative bacterium Bordetella pertussis. It is a pathogen whose toxin (PT) plays a significant role in the pathogenesis of the disease [1]. The risk of infection for an unvaccinated person is as high as 80% [2,3,8]. It is characterized by the highest incidence and mortality among infants, although it can occur at any age [1,4,6]. Currently, it increasingly affects adolescents and adults, particularly the elderly - those with multiple comorbidities, or weakened immune systems [7,8]. This disease most often manifests itself by acute and persistent coughing, often occurring in paroxysms, accompanied by an inspiratory whoop and post-tussive vomiting [4]. Pertussis is transmitted via the droplet route during coughing or sneezing, and the only reservoir is an infected human [1]. For transmission to occur, an infected person does not need to present typical pertussis symptoms and may be oligosymptomatic or asymptomatic [8]. Another, less likely route of infection is contact transmission, which occurs through contact with surfaces contaminated with respiratory secretions from an infected person. In the case of pertussis, the concept of carrier state does not exist [8]. It is a preventable disease for which primary prophylaxis exists - vaccination. Immunization programs against pertussis were introduced from the late 1950s in the form of first-generation vaccines with a whole-cell pertussis component (wPV). At the beginning of the 21st century, second-generation vaccines with an acellular pertussis component (aPV) appeared. Since the introduction of this immunization method, the incidence of pertussis has sharply declined. Currently, combination vaccines - against diphtheria, tetanus, and pertussis - are most commonly used [6]. Whooping cough was first described during an epidemic in Paris in 1578, the causative pathogen - B. pertussis - was discovered in 1906, and the first vaccine was developed in the 1940s [9].

Pathogenesis

Bordetella pertussis is a fimbriated, Gram-negative aerobic coccobacillus [10,11]. It does not form spores [3]. For now, 10 species have been identified, five of which can cause respiratory infections in humans: B. pertussis, B. parapertussis, B. bronchiseptica, B. holmesii, and B.

petrii. Bordetella parapertussis causes infections in both humans and sheep [10]. B. holmesii causes pertussis-like symptoms or invasive infections, such as meningitis, sepsis, pneumonia, or arthritis [12,13]. For B. pertussis, the only reservoir is an infected human. After aspiration into the upper respiratory tract, the bacterium adheres to the epithelium lining the nasopharynx and trachea and begins producing virulence factors. These factors - including toxins and adhesins - prevent the pathogen's clearance from the body, enabling its invasion, multiplication, and spread to the lower respiratory tract [10]. Bordetella pertussis produces numerous toxins: pertussis toxin (PT), tracheal cytotoxin (TCT), adenylate cyclase toxin (ACT), labile toxin, type III secretion system (TTSS), and endotoxin or lipopolysaccharide (LPS) [6,10]. Pertussis toxin (PT) is the most important virulence factor of B. pertussis. Its action causes necrosis of the respiratory epithelium, resulting in impaired mucus secretion and cough reflex. It has a particular affinity for the epithelium of the upper respiratory tract [3]. Processes induced by pertussis toxin manifest as leukocytosis with lymphocytosis, hyperinsulinemia, and an increased risk of anaphylaxis [2]. Other toxins act both locally, causing an inflammatory response, and systemically, destroying cells of the respiratory system, inducing fever, and causing characteristic coughing [2,9]. Additionally, the bacterium produces filamentous hemagglutinin (FHA) and pertactin (PRN). Its cell wall is additionally protected by fimbriae. The survival of B. pertussis in the human body is ensured by its ability to simultaneously disrupt multiple components of the immune system - suppressing T and B lymphocyte responses, impairing the complement system, and disrupting the function of phagocytic cells [11].

Epidemiology

Pertussis still remains a significant epidemiological threat despite organized vaccination campaigns worldwide, including in Poland since the 1960s [8]. In 2023, 922 cases were reported in Poland (2.45/100,000), which is a decrease in comparison to 2016 (6,828 cases, 17.77/100,000) [14,19]. The introduction of social restrictions by the government due to the COVID-19 pandemic reduced the prevalence of pertussis in the environment, contributing to a decline in cases, as evidenced by 2021 data (182 confirmed cases, 0.48/100,000) [16,23]. However, with the lifting of restrictions in 2022 (371 cases, 0.98/100,000), a significant upward trend can be observed. It was confirmed by 2024 data, when 32,430 cases were reported (86.33/100,000) - the highest number since before the introduction of mass vaccinations in Poland [8,14]. The significant upward trend since 2023 highlights the growing scale of the problem and the need for intensified epidemiological surveillance [1,8,14].

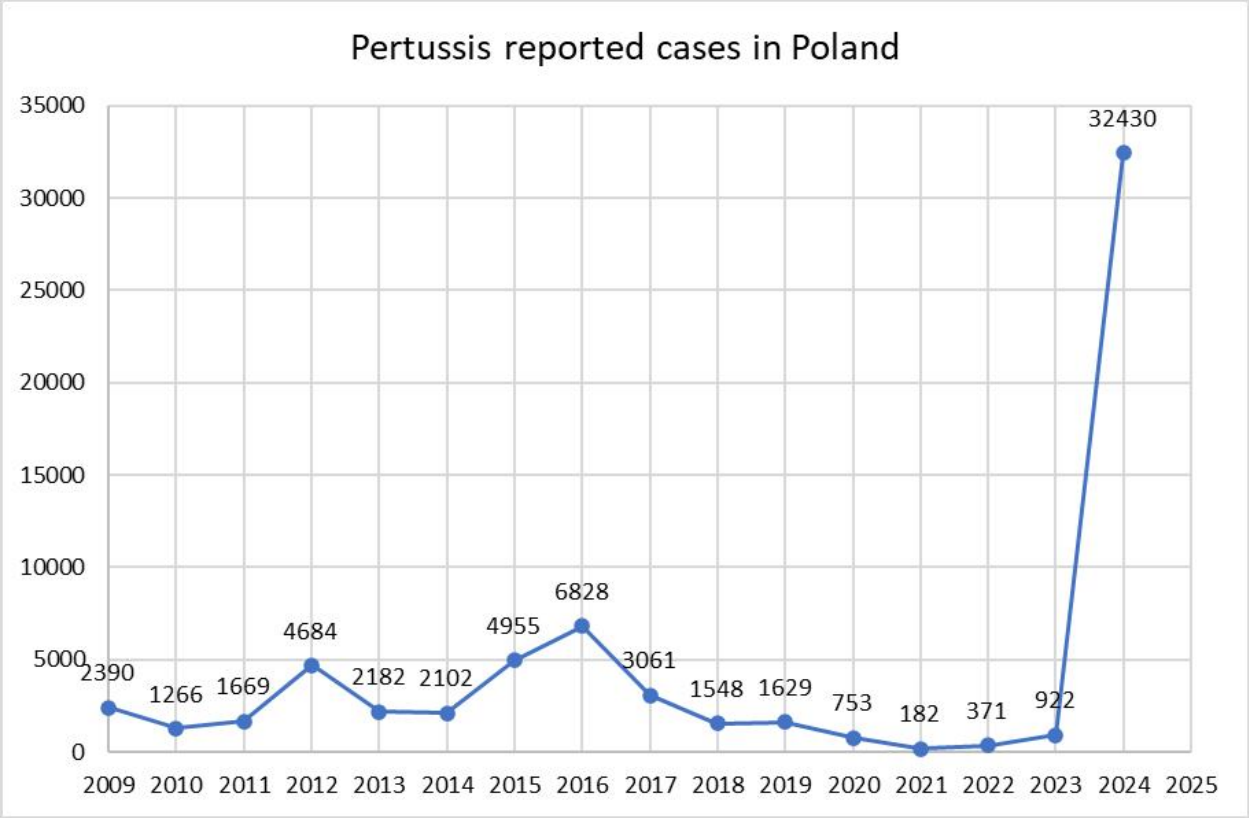

Fig. 1. Reported cases of pertussis in Poland from 2009 to 2024 [14, 16-23].

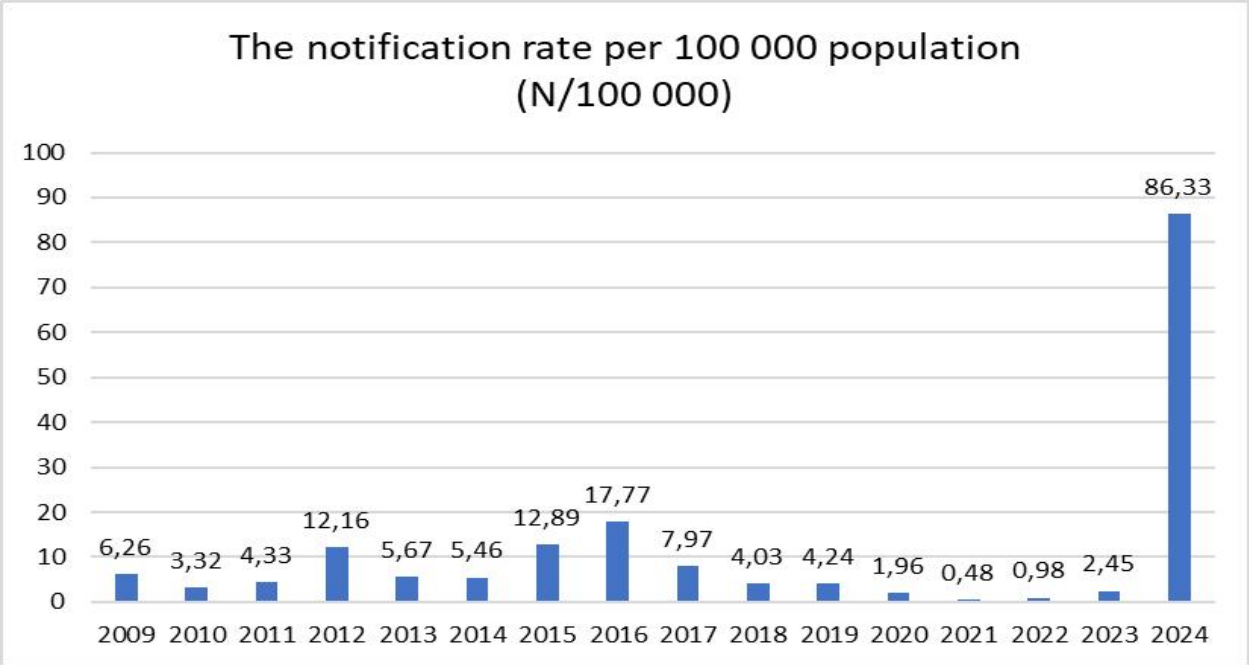

Fig. 2. The notification rate per 100 000 population (N/100 000) of reported pertussis cases in Poland from 2009 to 2024 [14,16-23].

Clinical Manifestation

The incubation period for pertussis ranges from 5 to 21 days, typically around 2 weeks [8]. The course of the disease and symptoms depend largely on age and immune status [1]. The infection progresses through three consecutive phases: catarrhal, paroxysmal cough, and convalescence [1,8].

In the first, catarrhal phase, lasting 1–2 weeks, flu-like symptoms predominate, such as malaise, chills, runny nose, mild cough, and nasal congestion. A low-grade fever may occur but is not characteristic. During this period, the patient is the most contagious [8,24].

The next phase, paroxysmal cough, lasts approximately 2–8 weeks. It is dominated by exhausting, paroxysmal, choking cough with characteristic tongue protrusion and expectoration of thick mucus at the end of an attack. During the following inhalation, a typical inspiratory whoop occurs [1,4,8].

Coughing attacks, initially appearing mainly at night, may end with vomiting, periods of apnea, and cyanosis [1]. They occur spontaneously or may be triggered by external factors: light, noise, feeding, or mechanical pressure, e.g., with a spatula during examination. In children under 1 year, attacks may present without the whoop, ending only with apnea [15].

In the convalescence phase, lasting at least 1–2 weeks but often much longer, the intensity of coughing and other symptoms gradually decreases [1]. However, complete resolution takes weeks or months. The dominant symptom is often post-pertussis cough. Within a few months of recovery, paroxysmal cough may recur as a complication of excessive physical exertion or upper respiratory infections.

Infants, especially those under 4 months, are at the highest risk of severe pertussis, with a mortality rate of 1% in this group [15]. Unlike the typical course, the catarrhal phase may be shortened or absent, and the paroxysmal cough phase may manifest with apnea, cyanosis with sudden drops in saturation during respiratory disturbances, choking, vomiting, bulging eyes, tachycardia, or bradycardia [1,14,15]. Paroxysmal cough may not occur at all. Life-threatening complications, such as pneumonia, multi-organ failure, seizures, or shock, are significantly more common than in older populations [1,15]. This course may be fatal, making timely diagnosis and treatment critical.

In vaccinated adolescents and adults, the disease is much milder, often limited to prolonged coughing, which can significantly delay correct diagnosis [1,24].

Diagnosis

Pertussis diagnosis requires confirmation via one of three methods: microbiological culture, PCR, or serological tests [8,14].

PCR has the highest sensitivity (70–99%), especially within 3–4 weeks post-infection, making it the primary confirmatory method [21]. It detects pathogen DNA, so live bacteria isolation is unnecessary. However, sensitivity may be reduced with prior antibiotic therapy for at least 5 days or previous pertussis vaccination [21].

Culture requires special media (Regan-Lowe or Bordet-Gengou) and depends on throat or deep nasal swabs [1,24]. Dacron or calcium alginate swabs are essential to avoid false negative results [24]. It is considered the gold standard up to 2 weeks from cough onset, with sensitivity of 12–60%, but vaccinations and antibiotics are the reason for nearly 50% false negatives [8,21,24]. Its major advantage is nearly 100% specificity and the ability to determine bacterial antibiotic sensitivity [1,21,24].

Serological tests rely on analyzing IgM, IgA, and IgG antibody levels against various B. pertussis antigens [8]. The lack of standardization due to varying methodologies, reference ranges, and validation levels across laboratories is problematic [24]. According to the European Centre for Disease Prevention and Control (ECDC), serological diagnosis should be based on detecting specific IgG antibodies against pertussis toxin in two serum samples, collected 3–5 weeks apart [1,24]. Diagnosis is confirmed by a 100% increase or 50% decrease in antibody titers between blood collections [8,24]. If two samples cannot be obtained or results are inconclusive, additional antibody classes may be tested. IgMs are diagnostically valuable only in unvaccinated infants or adults unvaccinated for at least 10 years [23]. A positive result then indicates infection. For IgA, a level ≥20 IU/ml may be considered positive in individuals over 2 years, regardless of vaccination status [23,24]. IgG measurement is the most reliable, independent of age, considering the time since the last vaccine dose [8,23]. Levels ≥150 IU/ml within ≤5 years of vaccination or ≥100 IU/ml >5 years post-vaccination are regarded positive [23]. A characteristic feature of pertussis is leukocytosis of 20,000–30,000/µl with lymphocyte predominance. However, leukocyte counts may be normal in adolescents and adults [24].

Due to maternally transferred antibodies, serological tests are not applicable in newborns [1,23,24]. Their use in infants is debated due to the lack of a reliable method determining an

age at which results are valid. Reliable antibody testing is suggested for children over 4 months due to low maternal antibody levels or in cases of no vaccination history in the past 12 months. Despite limitations, serological tests are crucial for diagnosing pertussis in later stages when other methods are no longer applicable [8,24].

Differential Diagnosis

Differential diagnosis of pertussis primarily includes other respiratory infections, such as upper respiratory tract infections, bronchitis, pneumonia, or tuberculosis. Pathogens causing similar symptoms include adenoviruses, RSV, Mycoplasma pneumoniae, Chlamydia pneumoniae, and other Bordetella species [25]. In children, foreign body aspiration should be considered. In adults with chronic cough, COPD should be differentiated. Significant leukocytosis in laboratory tests also warrants ruling out leukemia [9]. However, a distinguishing feature of pertussis, as discussed above, is its characteristic triphasic course and persistent cough without fever.

Treatment

The primary treatment for pertussis relies on macrolide antibiotics: clarithromycin, azithromycin, or erythromycin. When used in appropriate doses, they significantly reduce transmission risk and prevent severe disease progression [1]. However, their use after the catarrhal phase is less effective, as symptoms are then primarily caused by circulating toxins released by B. pertussis, not the bacteria themselves [1,24]. Nonetheless, macrolides in later phases are justified due to proven mortality reduction [26].

Treatment should be initiated in all cases of infant infection under 1 year within 6 weeks of symptom onset and in other patients within 3 weeks if pertussis is suspected [8,23].

Erythromycin, despite its effectiveness, is no longer recommended due to gastrointestinal side effects in nearly 30% of patients, leading to treatment discontinuation [1].

Clarithromycin, better tolerated, is recommended by the American Academy of Pediatrics (AAP) and Centers for Disease Control and Prevention (CDC) for use from 2 months of age at 7.5 mg/kg body weight twice daily for 7 days and 2 x 500 mg doses for adults over the same period [1,27,28].

Azithromycin is recommended for the youngest children, at 10 mg/kg once daily for 5 days up to 6 months of age [27]. Beyond this age, dosing differs [1]. On the first day, 10 mg/kg in a single dose, up to 500 mg. From days 2 to 5 - 5 mg/kg once daily, up to 250 mg. Adult treatment mirrors pediatric dosing: 500 mg in a single dose on day 1 and 250 mg once daily

on days 2 to 5 [1,23,24].

Clarithromycin and azithromycin offer shorter treatment duration and better patient tolerance compared to erythromycin [1].

In cases of treatment failure or macrolide allergy, co-trimoxazole is used at 960 mg every 12 hours for 14 days. It is less effective and less preferred due to side effects [1].

For patients under 6 weeks treated with macrolides, monitoring for 1–2 months post-treatment is necessary due to the risk of hypertrophic pyloric stenosis [30]. Azithromycin presents the lowest risk, making it the first-line treatment in this age group [1,30]. Co-trimoxazole is contraindicated in infants under 2 months due to the risk of kernicterus, which can lead to disability, cerebral palsy, or death [1,24].

Symptomatic treatment should focus on limiting cough triggers [8]. Proper room ventilation and air humidification are also recommended [1]. In infants, smaller feeding portions and lateral positioning post-feeding are advised [24]. No drug has proven effective in alleviating pertussis symptoms [1].

Salbutamol, according to some researchers, reduced cough frequency and duration, but deeper studies did not confirm this effect [31,32]. Similar trials with antihistamines, based on B. pertussis increasing histamine sensitivity and causing acute inflammatory reactions, also failed to prove symptom relief [33].

Systemic corticosteroids and anti-pertussis toxin are not recommended due to lack of evidence for efficacy [34,35].

Post-Exposure Prophylaxis

Post-exposure prophylaxis, involving pharmacotherapy, is applied to unvaccinated individuals with close contact with an infected person [8,9,15]. It should be initiated within 3 weeks of exposure [2,25]. It is particularly necessary for those at risk of severe pertussis: infants under 1 year of age, individuals on immunosuppressive drugs, and patients with cystic fibrosis, other chronic lung diseases, or respiratory failure [8].

Close contacts include:

- A person in contact with an infected individual at a distance <1 meter (pathogen transmission during speaking, sneezing, coughing, bronchoscopy, or suctioning respiratory secretions during medical procedures).

- A person with direct contact with respiratory secretions from an infected person produced during coughing, runny nose, mouth-to-mouth resuscitation, sharing meals, or physical examination of the nose or throat of an infected person.
- A person in the same room as an infected individual at close proximity for >1 hour [8].

Post-exposure prophylaxis is conducted for 5 days using the same drugs and doses as for pertussis treatment [25].

Vaccines

In Poland, as in many countries, pertussis vaccination is mandatory [36]. It is most commonly administered as a combination vaccine protecting also against diphtheria and tetanus [1,8]. The pertussis component may be in a high dose (DTP), with variants including whole-cell (DTwP) or acellular (DTaP) components [7,23]. Additionally, the Tdap vaccine with reduced acellular pertussis antigens exists [23]. Acellular vaccines are predominantly used today [8,23]. They contain purified bacterial antigens, causing fewer side effects, and are better tolerated than whole-cell vaccines but provide shorter protection (5–10 years vs. 10–12 years) [1,8,23]. Common side effects include redness, swelling, or pain at the injection site and fever [8,24]. Protecting those most vulnerable to severe pertussis is critical. Current recommendations advise pregnant women to receive the dTap vaccine, ideally in the third trimester between 27 and 36 weeks [24,30]. It is safe for both mother and child [8]. It enables antibody production to protect the infant before it develops its own antibodies. According to the 2025 Immunization Program in Poland, the schedule includes mandatory and booster doses [30].

The first dose is given at 2 months, followed by doses at 4, 6, and 16–18 months using DTPa. The same variant is used as a booster at 6 years. For 14-year-olds, Tdap is used. Revaccination every 10 years is recommended to maintain immunity [30]. A vaccination coverage rate >95% is required for population protection [1]. Rising pertussis cases are attributed to waning vaccine immunity, reduced vaccination rates, and the emergence of bacterial strains lacking pertactin, a protein critical to the current vaccine's mechanism [1,24]. Researchers are currently working on new vaccine variants to provide longer protection and better efficacy against mutating B. pertussis strains [1].

Complications

Persistent coughing paroxysms associated with pertussis infection can cause a range of

mechanical complications, including rib fractures, umbilical or inguinal hernias, urinary or fecal incontinence, back pain, and even carotid artery dissection. Such a sudden increase in intrathoracic and intraabdominal pressure can also lead to pneumothorax, diaphragmatic rupture, subcutaneous emphysema, subconjunctival hemorrhages, nosebleeds, or facial swelling [37,38]. Due to the intense effort during paroxysms, fainting may occur. Literature also describes pertussis infection as a trigger for migraines and even memory loss [37]. Other common complications include pneumonia, otitis media, and sinusitis [4,37]. Pathogens most frequently causing secondary bacterial pneumonia include Streptococcus pneumoniae, Streptococcus pyogenes, Haemophilus influenzae, and Staphylococcus aureus. Viral complications caused by RSV, CMV, or adenoviruses also occur. Due to exhausting coughing paroxysms that may hinder food intake and frequent post-tussive vomiting - nutrient deficiencies and significant weight loss are observed [37].

Central nervous system complications are rare, occurring in less than 2% of cases, and include seizures or acute encephalopathy. The etiology of encephalopathy remains unclear, with suspected factors including hypoxia from severe coughing, hypoglycemia, metabolic disturbances, intracranial hemorrhages due to sudden pressure increases, or direct effects of bacterial toxins. This is a life-threatening complication. It is reported that one-third of children with acute encephalopathy due to pertussis die, and another third survive with permanent brain damage [37]. Equally dangerous is pulmonary hypertension, noted in the literature as a factor contributing to increased mortality in infants due to exacerbated hypotension and hypoxia [9,39].

Complications in the pediatric population primarily occur in unvaccinated children or those who have not received all mandatory vaccine doses. Mortality among hospitalized children with pertussis is approximately 1% [15].

In the elderly, mortality from pertussis is higher due to overall multimorbidity and increased risk of burdensome complications like pneumonia.

Summary and Discussion

Pertussis is a disease caused by the Gram-negative bacterium Bordetella pertussis, characterized by paroxysmal coughing. It poses the greatest threat to the pediatric population, with a mortality rate of 1% in this group [15]. It more frequently causes apnea, encephalopathy, epilepsy, shock, and even death in children compared to adults [15]. In adults and adolescents, the disease is often oligosymptomatic, significantly complicating accurate

diagnosis [8,23]. Currently, a significant upward trend in pertussis cases is observed [14,24], driven by declining vaccination rates and the resumption of human interactions following the lifting of restrictions related to the SARS-CoV-2 pandemic [14,23]. This necessitates intensified efforts to curb pertussis transmission through increased vaccination coverage, antibacterial treatment, and development of new vaccines due to B. pertussis mutations [1].

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