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PERTUSSIS- EPIDEMIOLOGY, DIAGNOSTICS, TREATMENT. LITERATURE REVIEW

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ABSTRACT

Introduction and purpose. The bacterium *Bordetella pertussis* causes pertussis, an infectious respiratory disease. Despite the introduction of an expanded vaccination programme over the past decades, pertussis remains a public health concern. This literature review aims to compare clinical and laboratory diagnostics. Additionally, we will focus on the impact of the Covid-19 pandemic on the increase in cases of the disease.

State of knowledge. The illness has three phases: an initial stage lasting one to two weeks; a second stage characterised by coughing fits lasting up to four weeks; and a final recovery phase. Although antibiotics used during the second stage reduce infectiousness, it is unclear whether they reduce the duration of illness. During the first two weeks, patients may experience flu-like symptoms. Culture testing is considered the gold standard, providing 100% specificity. This enables identification of the strain and antibiotic susceptibility testing. This method is most effective within the first two weeks of illness, while viable bacteria are still present.

The number of cases fluctuates from year to year, but there has been a marked decrease among young children and an increase among adolescents and adults. Following the discontinuation of protective measures against SARS-CoV-2, significant pertussis outbreaks have occurred.

Material and methods. This review analyzes the epidemiology, diagnosis, and treatment of whooping cough, with a particular focus on the years from 2019 to the present. The article was based on sources from scientific databases such as PubMed.

Summary. Researchers have linked the increase in pertussis cases in recent years to the lifting of restrictions during the post-Covid period. It is therefore important to raise public awareness of the need for revaccination and to continue scientific research into the epidemiology and diagnosis of this disease.

KEYWORDS

Bordetella Pertussis, Pertussis, Disease Outbreaks, Macrolides, Diagnostics

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Introduction and Purpose

The bacterium *Bordetella pertussis* is the cause of pertussis, an infectious disease of the respiratory tract.[1] Nowadays, the infection primarily affects adolescents and adults, as well as newborns and infants. The latter age group is characterised by the most severe symptoms and the highest risk of death. [2,3] The disease can be divided into three phases: an initial flu-like stage lasting 1–2 weeks; a second stage characterised by coughing fits lasting up to 4 weeks; and a final recovery phase. During the final phase, the cough gradually weakens, but persistent bronchial hypersensitivity triggered by factors such as the cold can cause coughing fits. The total duration of the illness is up to three months, hence the term '100-day cough'. [4]

Despite the implementation of expanded vaccination over the past three decades, pertussis remains a public health problem. Although antibiotics implemented in the second phase of the disease reduce infectiousness, they have no proven effect on reducing the duration of illness.[5]

This literature review aims to compare clinical and laboratory diagnostics. We will also examine the benefits to patients of implementing treatment at different times. Additionally, we will consider the impact of the increase in disease caused by the Covid-19 pandemic.[6,7]

Research Materials and Methods.

This review analyzes the epidemiology, diagnosis, and treatment of whooping cough, with a particular focus on the years from 2019 to the present. The article was based on sources from scientific databases such as PubMed and Google Scholar, with special attention given to the most recent systematic reviews and meta-analyses.

Description of The State of Knowledge

Epidemiology

Despite the general belief that pertussis has been eradicated through vaccination, it remains a significant challenge in clinical practice.[4,8] The number of cases of the disease fluctuates from year to year, but there has been a marked decrease in cases among young children and an increase in cases among adolescents and adults.[9] Since 2022, many high-income countries have reported a resurgence of pertussis, particularly in the European region, but the disease has also caused outbreaks in middle- and low-income countries, despite their less developed disease surveillance capacity.[7] A Swedish study conducted between 2020 and 2021 revealed a decline in cases of whooping cough among infants. This has been attributed to the protective measures introduced during the pandemic.[10] Other sources indicate that since the withdrawal of protective interventions against the SARS-CoV-2 virus, significant outbreaks of pertussis have occurred, which could be partially mitigated by a higher percentage of vaccinated individuals in the population. [7,11]

Etiopathogenesis

The disease is spread by droplet infection, especially in the home environment, day nurseries and kindergartens. It can also be contracted from a person who has been vaccinated but has fallen ill. The gateway to infection is the upper respiratory tract. The incubation period for pertussis is 3-14 days.[12] The bacterium releases toxins such as pertussis toxin. It has local and systemic effects on the patient's body. The toxin has several effects, including suppressing the immune system's ability to produce antibodies, stopping the process of phagocytosis, and preventing early neutrophil recruitment.[13]

The peak infectivity is during the first phase of the disease. Pertussis can occur repeatedly during life, because the immunity gained after contracting the disease is not long-lasting.[14] Studies show that protection against *Bordetella pertussis* infection persists for an average of five to 10 years after vaccination and seven to 20 years after natural survivorship. Antibiotic-treated patients become non-infectious by the fifth day of properly administered therapy.[15]

Clinical presentation

During the first two weeks, there is a mild onset of the disease with a gradual deterioration of general wellbeing. The patient may present with low-grade fever, weakness, dry cough, lacrimation and nasopharyngitis. In the following period called paroxysmal, the symptoms may include: apnea associated with paroxysms, chest and abdominal soreness, leukocytosis, lymphocytosis, weight loss, paroxysmal coughing (periods of rapid succession coughing during one exhalation), posttussive emesis, cyanosis, and exhaustion. In some cases, scleral haemorrhage may occur. The most characteristic symptom is whooping on inspiration after coughing. In the final phase of the disease, a decrease in coughing intensity may be observed.[4,5,8] If left untreated, the condition can lead to serious complications. These include pneumonia, pulmonary hypertension, convulsions, encephalopathy and secondary infections. These can be life-threatening, particularly for vulnerable groups such as infants.[16]

Diagnostics

A laboratory test is required to confirm a diagnosis of pertussis. Accurate identification of the clinical features of pertussis is important to prompt testing, because early detection and treatment are critical to reducing transmission.[17] The results of systematic reviews indicate that in adults only four symptoms are of diagnostic relevance. These are: paroxysmal cough, vomiting after a coughing fit, whooping on inspiration and lack of fever. Paroxysmal cough and absence of fever had high sensitivity (93.2% [CI 83.2-97.4] and 81.8% [CI 72.2-88.7]) and low specificity (20.6% [CI 14.7-28.1] and 18.8% [CI 8.1-37.9], respectively) for the diagnosis of pertussis. Whooping on inspiration and vomiting occurring after a coughing fit showed low sensitivity (32.5% [CI 24.5-41.6] and 29.8% [CI 8.0-45.2]) but high specificity (77.7% [CI 73.1-81.7] and 79.5% [CI 69.4-86.9]) in the diagnosis of pertussis. In children (aged 0-18 years), only one symptom is relevant for the clinical diagnosis of pertussis - vomiting after a coughing fit; this symptom had 60.0% sensitivity (CI 40.3-77.0) and 66.0% specificity (CI 52.5-77.3). Clinical symptoms alone are not definitive, as they overlap with other respiratory infections.[18]

Tests used for diagnosing pertussis include polymerase chain reaction (PCR) testing, culturing and serological testing.. PCR is the most accurate and rapid test for pertussis, offering high levels of sensitivity and specificity. It can detect *Bordetella pertussis* DNA, even when the bacteria are no longer viable. Best performed within the first 3 to 4 weeks after cough onset. Sensitivity decreases after this period as bacterial DNA diminishes. Such a test can be performed using a nasopharyngeal swab taken during a primary care visit.[19]

Culture is considered to be the gold standard and is 100% specific. It enables strain identification and antibiotic susceptibility testing. It is the most effective within the first two weeks of illness, while viable bacteria are present. Sensitivity decreases significantly after this period. It needs to be remembered that culture results take longer (7–10 days) and may be affected by prior antibiotic use or vaccination.[4,17]

Serological testing is an effective way of confirming a pertussis infection in later stages of the illness, as it identifies the antibodies produced in response to the toxins. The test yields the most accurate results between two and eight weeks after the cough begins, when antibody concentrations are at their highest. This method is not suitable for people who were recently vaccinated, as the vaccine can cause a temporary rise in antibody levels, potentially affecting the test's accuracy. When using serological testing for diagnosis, an IgG antibody assay that specifically targets pertussis toxin (PT) should be relied upon. [19,20] If the results are inconclusive or a second blood sample cannot be obtained, an additional IgA antibody test is recommended. It is important to note that serological testing is not suitable for newborns and infants as they may not produce their own antibodies or may carry maternal antibodies, which can interfere with the interpretation of results.[21]

Treatment

According to current recommendations, macrolide antibiotics are the primary group used in the treatment of pertussis, with azithromycin and clarithromycin being the most commonly chosen. Erythromycin is used less frequently due to its more common gastrointestinal side effects. For patients who cannot take macrolides due to an allergy or intolerance, cotrimoxazole is an alternative treatment option. Starting treatment in the initial, non-infectious phase of the disease can alleviate its progression, whereas in the paroxysmal cough phase, antibiotics do not affect symptom severity, but reduce the patient's infectiousness. The main aim of therapy is to protect vulnerable individuals, such as newborns and infants, from infection and severe symptoms.[4,22,23]

Recently, macrolide resistance in *B. pertussis* has been reported worldwide, particularly in China. The reasons why macrolide resistance has been centered on this country over the last decade can only be speculated about, but the dominant *B. pertussis* lineage differs between China and most high-income countries. [24-26]

Prophylaxis

The primary strategy for preventing cases of pertussis is the widespread use of vaccines containing antigenic components of *Bordetella pertussis*. In Poland, vaccination is carried out at one, two and six years of age. This cycle consists of primary vaccination, which consists of three doses administered in the first year of life (at 2, 3–4 and 5–6 months of age), and a booster vaccination in the second year of life (16–18 months of age); and a booster vaccination at 6 years of age. [27] Due to the gradual waning of post-vaccinal immunity, booster doses are recommended for adolescents and adults every 10 years. It is particularly important to vaccinate women in the third trimester of pregnancy, as this allows passive immunisation of the newborn through the transfer of maternal antibodies across the placenta. Cell-free vaccines are used for this purpose [2, 28]. Vaccinating members of the immediate environment of infants aims to protect the most susceptible individuals, in a strategy known as 'cocooning'. In addition to pregnant women, the vaccination programme should cover household members, caregivers of newborns and medical personnel. Unfortunately, the effectiveness of this strategy is limited by the low level of health awareness among adults and the expense of vaccines. [29,30]

Post-exposure prophylaxis

Precise guidelines have been developed for preventive action among individuals who have been in contact with a confirmed case of whooping cough. The aim of the antibiotic prophylaxis is to reduce the likelihood of whooping cough and its associated complications in individuals in the patient's immediate environment and to prevent the further spread of the disease among vulnerable groups, such as newborns and women in their third trimester of pregnancy. According to the Centers for Disease Control and Prevention (CDC) guidelines, prophylactic medication should be administered to individuals who have come into contact

with the patient as soon as pertussis is diagnosed and within 21 days of the first cough symptoms appearing. Antibiotics from the macrolide group are recommended, at a dosage similar to that used to treat the disease.[15,21]

Conclusions.

Despite widespread vaccination, pertussis continues to pose a significant epidemiological threat. There has been an increase in incidence among adolescents and adults, which is associated with waning immunity following vaccination. Early diagnosis, particularly through PCR testing, and the prompt implementation of macrolide treatment, which reduces infectivity, are crucial.

The temporary decline in transmission caused by the pandemic was followed by new outbreaks after restrictions were lifted. Further research is needed into the effectiveness of vaccination and population immunity, as well as the increasing resistance of bacteria to antibiotics. Educating physicians and the public, and updating vaccination programmes, remain key to effectively controlling pertussis.

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