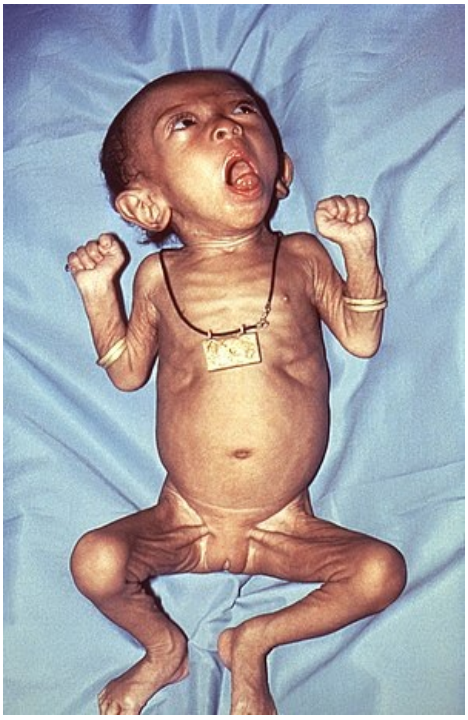
Pertussis

Whooping cough or **pertussis** is a highly contagious respiratory tract infection that spreads via respiratory droplets.[1] It is widespread worldwide, but more than 90% of cases are reported from developing countries. The causative agent is the gram-negative bacterium *Bordetella pertussis*. Most affected individuals are between the ages of 15 and 19 years. In adolescents and adults, pertussis tends to be mild or atypical, remaining unnoticed, and is thus not reported. These undiagnosed patients are a source of infection for infants and toddlers, for whom whooping cough is a serious, life-threatening disease since their immune systems are underdeveloped. In recent years, there have been 4 deaths in the Czech Republic of young, unvaccinated children who have become infected by family members.[2]

Regular pertussis vaccination began in the Czech Republic in 1958. In 2003, an acellular vaccine was introduced, and on 1 January 2007, basic vaccination with a six-component vaccine with an acellular pertussis component was introduced. Vaccination cannot be started until the 9th week of life. Post-vaccination immunity against the causative agent gradually decreases with age (as well as after the disease), so since 2009, children between the ages of 10 and 11 are given boosters. For the same reason, although the vaccination rate of children in the Czech Republic is high, it is possible for children to get sick within 3-5 years after vaccination. Nevertheless, vaccination is very important because it reduces the likelihood of a severe course of the disease and reduces the circulation of the agent in the population.[2]

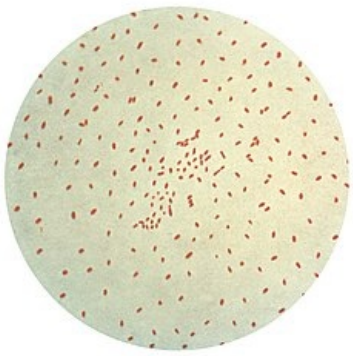
Pathogenesis



Whooping cough in infant

- Infectious agent: ***Bordetella pertussis***, which is a strictly aerobic gram-negative coccobacillus.
- It produces several biologically active substances, some of which play a key role in adhesion and colonization (pertussis toxin, filamentous hemagglutinin, pertactin) or shape the typical clinical picture (pertussis toxin, dermonecrotic toxin, adenylate cyclase, tracheal cytotoxin). Pertussis toxin improves the binding of microbes to the cilia of the airway epithelium and promotes mucus production and systemic manifestations (e.g., histamine effect, lymphocytosis).
- It causes inflammation and eventually necrosis of the ciliated epithelium of the respiratory tract.
- Bordetellae multiply and colonize the ciliated epithelium of the airways after entering the susceptible organism. During the *catarrhal stage*, they reside mostly in the larynx and nasopharynx, where they cause **catarrhal inflammation and eventually necrosis of the mucosal epithelium**, but do not enter the bloodstream. The typical picture of the disease is **peribronchitis**. The halting of mucociliary transport produces an **irritating cough**, which is typical of the *paroxysmal stage.* In this stage, viscous secretion stagnates in the bronchioles, and there may be small atelectasis and emphysema. **Bordetella toxins enter the bloodstream** and cause long-term systemic symptoms even after antibiotic treatment.
- Pertussis complications can also be caused by the mechanical effects of persistent cough.
- **Parapertussis**: a similar disease with a shorter duration of symptoms and mostly with a milder course. The causative agent is *Bordetella parapertussis*.[3]

Epidemiology

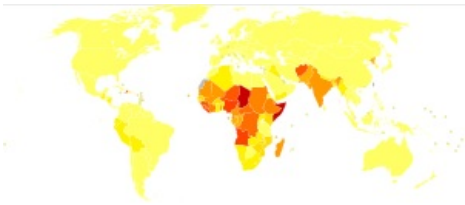


Bordetella pertussis

Pertussis occurs worldwide (139,786 reported cases in 2014), including in European countries.[4] In the Czech Republic, infectious diseases are compulsorily reported and long-term monitored. In 2014, the incidence in the Czech Republic was 24/100,000.[5] In the period before the introduction of vaccination, the morbidity reached tens of thousands of cases per year (with a maximum in 1956). After the introduction of nationwide compulsory vaccination in 1958, the number of cases of whooping cough declined rapidly, but never reached zero. An increasing trend in the disease has been registered since 1993.[6] Previously, most reported patients were 10–14, but since 2012, most reported patients are aged 15–19. In the adult population, the disease is often underdiagnosed and rarely reported.[7][2]

- Incubation period: 6-21 days. The incidence of the disease fluctuates in 3-7 year cycles and this trend also persists in the immunized population. For susceptible individuals, the infectivity is up to 90%.
- Transmission: close contact, droplets, aerosol
- The most infectious individuals are in the catarrhal stage of the disease and the first 2 weeks after the onset

of cough. An infant, whose immune system is underdeveloped, becomes infection-free in 6 weeks, whereas a vaccinated adolescent requires only 2 weeks.
- Bordetella from a nasopharyngeal swab can be detected even on the fifth day of macrolide treatment. During this time, it is advisable to **isolate** the patient. After illness, there is a strong long-term, but not lifelong immunity.
- There is no cross-immunity between B. pertussis and B. parapertussis.
- Transplacental transmission of IgG antibodies is insufficient; therefore, infants under the age of 3 months who have not yet been vaccinated can become ill.[3]



Pertussis in the world - 2004 (WHO)

Clinical manifestation

Pertussis cough is a cough lasting at least 2 weeks with one of the following symptoms:

- Coughing fits
- Whooping cough
- Vomiting after a cough attack without other obvious causes
- Apnea pause in infants[2]

The incubation period is 7 to 21 days.[2]

The disease usually lasts 6 to 8 weeks and has **3 stages**:

1. Catarrhal (1 to 2 weeks);
2. Paroxysmal (2 to 6 weeks);
3. Convalescent (1 to 3 weeks).[2]

The period of infectivity begins at the end of the incubation period, is highest in the early period of the catarrhal stage, then gradually decreases and usually ends 3 weeks after the onset of the paroxysmal stage or 5 days after antibiotic treatment.[2]

The clinical manifestation depends on, among other factors, age and the state of immunity. The classic course is observed in children under 10 years of age and can be divided into 3 stages:

1. ***Catarrhal stage:***
   - Colds, coughing, usually lasting 10-15 days. It is usually clinically indistinguishable from other upper respiratory catarrhs, which impedes early diagnosis and effective antibiotic treatment.
   - General symptoms such as anorexia, fever, fatigue are insignificant and may not be present.
2. ***Paroxysmal stage:***
   - Numerous typical fits of **irritating cough.**
     - At the height of the attack, there may be pauses (apnea) followed by loud wheezing ("crowing" inspiration). Children of the youngest age groups are particularly prone to **apnea**.
     - Paroxysms of cough recur daily for 6-10 weeks, but even longer in older children and more than half of adolescents. Spasms are more common at night and are quite exhausting. They can be caused by any external stimulus, food, emotions, and/or temperature change.
   - At the same time, **cyanosis** occurs, which is accompanied by hypoxia, **nausea, and vomiting**.
   - With long-term exhaustion, younger children may experience **hypoventilation** due to respiratory muscle fatigue and develop dangerous hypercapnia.
   - **The condition between coughing fits is completely asymptomatic**, which distinguishes pertussis from other respiratory infections.
3. ***Convalescence stage:***
   - There is an increased readiness to cough after minimal stimuli, but the severity of spasms and their frequency decreases.[3]

Complications

The frequency of complications is inversely related to the patient's age.

- Complications related to the mechanical effect of persistent cough include **subconjunctival hemorrhage, epistaxis, subarachnoid and intraventricular hemorrhage, and rupture of the tongue.**
- Bacterial **superinfection**: Streptococcus pneumoniae → **otitis and pneumonia.**
- Frequent vomiting → dehydration and development of metabolic acidosis with tetanus seizures.
- **Encephalopathy** accompanied by convulsions or disorders of consciousness.
- Elevated intrathoracic and intra-abdominal pressure result in atelectasis, pneumothorax, pneumomediastinum, and hernias.
- **Pertussis in non-immunized infants has the most severe course.** Cyanosis apnea attacks may not be accompanied by a typical cough. Mortality in this group reaches 1%.[3]

Diagnosis

- **Clinical diagnosis** of pertussis based on symptoms alone is difficult in the current epidemiological situation,

especially in adults, whose symptoms are atypical and less pronounced.
- Unvaccinated children typically have **leukocytosis** in their blood counts. Leukocytosis is not a typical finding after vaccination with at least one dose of the vaccine.[8]
- In many cases, **X-ray findings are normal**.
- The gold standard for diagnosis is **cultivation** that has high specificity but low sensitivity. The sensitivity of cultivation decreases with time from the onset of disease symptoms. Another limitation of this diagnostic method is the length of the cultivation period, which delays detection.
- Detection of the causative agent in nasopharyngeal swabs by **PCR**: a limitation of this method is that PCR sensitivity decreases with time from the onset of symptoms of the disease.
- Serological examination of specific anti-PT (pertussis toxin) antibodies of IgG class by **ELISA** method: the main disadvantage of this method is that in patients up to 5 years after the last pertussis vaccination, it is difficult to distinguish between post-vaccination and post-infection antibodies. As a result, examination of so-called paired sera with a 4-6 week interval is recommended, where a minimum 4-fold increase of antibodies is required to confirm the diagnosis. When testing only one serum sample, the recommended diagnostic limit is the amount of anti-PT IgG antibodies > 94-110 EU/mL, which indicates a recent or active infection.[9]

Recommended procedure in case of clinical suspicion:[10]

- Neonates and young children: PCR and/or cultivation of nasopharyngeal swab and/or aspirate soon as possible after the onset of symptoms
- Vaccinated children and adults with a cough lasting less than 2 weeks: nasopharyngeal collection for PCR and culture
- Older children and adults: determination of IgG class anti-PT
- Adolescents and adults with a cough lasting longer than 3 weeks: PCR and anti-PT IgG determination.[2]

Bordetella cultivation requires 3-7 days. It is performed on a special Bordet-Gengou medium. Collection of material (swab from the back wall of the nasopharynx or larynx) is usually performed in the morning on an empty stomach. The tongue is held with a wooden spatula or a clean cloth. Inoculation must be prompt, so the collection of material is best done at the patient's bedside. Negative cultivation does not rule out the disease.[3]

Predictive factors in suspected pertussis

positive factors	negative factors
contact with the disease	fever
incomplete immunization	diarrhea
long interval after vaccination	rash
no difficulty between attacks	enanthem
post-attack vomiting	tachypnea
apnea, bradycardia (in infants)	stridor
dry, irritating cough	murmur
whooping cough	lymphadenopathy
gasping or asphyxia during a cough	neutrophilia
petechiae in the supraclavicular region	neutropenia
lymphocytosis with normal cell appearance	lymphocytosis with atypical lymphocytes

[3]

Differential diagnostics

- Infections that present with "pertussis" cough: pertussis cough syndrome caused by **adenoviruses, RSV, influenza, parainfluenza, H. influenzae, M. pneumoniae, Ch. pneumoniae.**
- Foreign body aspiration or cystic fibrosis should be suspected in case of cough fits, especially in children.[3]

Treatment

The drugs of choice are **macrolides** - azithromycin, clarithromycin, erythromycin. Tetracyclines and cotrimoxazole are also effective. It is important to start antibiotic therapy early, which would lessen the severity of the course of the disease and reduce the risk of transmission to other individuals. It is ideal to start treatment at the catarrhal stage before the destruction of the ciliated epithelium. In the case of late treatment, antibiotics are no longer effective against the paroxysmal course of the disease due to the presence of toxins in the airways, but they can at least minimize transmission to other individuals.[2][9] Corticosteroids are used in the paroxysmal stage.[1]

Post-exposure antibiotic prophylaxis is suitable for susceptible individuals (e.g., immediate relatives) who are expected to be at high risk of a severe course (e.g., infants under the age of 1, especially under 4 months, and pregnant women in the third trimester of pregnancy).[2]

Hospitalization is recommended for infants and older children in case of a complicated course. For infants below the age of 3 months or for children with hypoxia, desaturation, cyanosis, and apnea, placement in the ICU with continuous monitoring of vital functions is necessary.[3]

Prevention

Pertussis vaccination is part of compulsory vaccination in the Czech Republic. In the Czech Republic, an acellular vaccine is used, which is a part of a combined vaccine that also protects against diphtheria and tetanus toxoid:

- DTaP (Infanrix, also part of Pediacel, Hexacima vaccines) - for children above 2 months of age
- Tdap (Adacel, Boostrix) - for children above 7 years of age and adults under 65 years of age. This vaccine has a reduced dose of diphtheria toxoid (or tetanus toxoid) and acellular pertussis subunits.

The acellular pertussis vaccine contains: pertussis toxin, filamentous hemagglutinin, pertactin and fimbriae.[11]

The American Center for Disease Control and Prevention (CDC) recommends vaccinating all women in the third trimester of pregnancy to prevent pertussis in early infancy.[12]

Links

Related articles

- Cough
- Vaccination calendar
- Bordetella parapertussis
- Bordetella pertussis

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