

PRACA POGLĄDOWA
REVIEW ARTICLE

MODERN APPROACH TO THE PROBLEM OF PERTUSSIS

NOWOCZESNE PODEJŚCIE DO PROBLEMU KRZTUŚCA

Valentyna I. Ilchenko, Liudmyla M. Sizova, Svitlana M. Tanianskaia, Inna N. Nesina, Kateryna V. Pikul
UKRAINIAN MEDICAL STOMATOLOGICAL ACADEMY, POLTAVA, UKRAINE

ABSTRACT

Introduction: Recently, there has been a tendency to increase the incidence of pertussis in many countries of the world and this disease in these countries is among 10 most serious causes of death in young children.

The aim of the work – is to analyze specialized scientific literature for generalization of data and present a modern look at questions of etiology, epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment and immunoprophylaxis of pertussis.

Materials and methods: Available scientific sources over the past years, devoted to the problem of pertussis are studied by the methods of overview, system and content analysis.

Review and conclusions: The main questions of pertussis are outlined. Timely diagnosis, treatment and immunoprophylaxis allow adjusting the actions of doctors to solve the issues of the decrease of the incidence of pertussis. This is greatly helped by modern guidelines for the management of patients with this pathology.

KEY WORDS: pertussis, children, treatment, prevention

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INTRODUCTION

Nowadays, the problem of a pertussis does not lose its relevance in the world. According to the WHO, every year in the world are sick with pertussis about 60 million people, and die – 1 million, mostly children under 1 year [1-2]. Recently, there has been a tendency to increase the incidence of pertussis in many countries of the world and this disease in these countries is among 10 most serious causes of death in young children [3-14]. The main risk factor for pertussis is insufficient immunological protection of children due to low immunization coverage, violations of schedules and timing of vaccination, unreasonable medical exclusions from vaccination.

Due to the deteriorating epidemiological situation regarding pertussis in Ukraine (an increase in the incidence of 10 times in the last 3 years in different age groups, as well as a decrease in the preventive vaccinations, due to the difficult economic situation and the refusal of parents), there is difficult task to use opportunities to stop this phenomenon [6, 15-19]. Timely diagnosis, treatment and, most importantly, prevention, allow adjusting the actions of doctors to solve the issues of the decrease of the incidence of pertussis.

THE AIM

The aim of the work is to analyze specialized scientific literature for generalization of data and present a modern look at questions of etiology, epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment and immunoprophylaxis of pertussis.

MATERIALS AND METHODS

Available scientific sources over the past years, devoted to the problem of pertussis are studied by the methods of overview, system and content analysis. The data of world literature are presented and the results of modern research are analyzed.

REVIEW AND DISCUSSION

Pertussis is acute infectious disease which is caused by pertussis rod and it is transmitted through airborne and characterized by the damage of respiratory airways and spastic (convulsive) cough [7, 20].

BRIEF HISTORY

The burst of pertussis was described by G. de Baieu in Paris in 1578, in the XVII century. The description of the epidemic in England was introduced by T. Sydenham, in the XVIII century. In XVIII Hoffman announced about pertussis. The first monograph about pertussis was created by A. Brendel and Bassiville. A detailed description of pertussis was made by N. F. Filatov. In 1900 and 1906 the pathogen was isolated from the mucus, which was isolated with cough and studied in detail by J. Bordet (Belgium) and O. Gengou (France). In 1957, the killed pertussis vaccine was created, and since 1965 vaccinations have been carried out by the associated vaccine. [7, 21-23].

ETIOLOGY

The causative agent of the disease is Bordetella pertussis, a gram-negative, immobile bacterium that has a rod-like

shape and causes a specific damage of the bronchial epithelium. This microorganism produces a large range of toxins and biologically active substances (pertussis toxin, tracheal cytotoxin, adenylate cyclase, endotoxin, filamentous hemagglutinin, pertactin, dermo necrotic toxin, agglutinogens, lymphocyte-producing factor). Bordetella pertussis is not very stable in the environment, it dies under direct sunlight during the year, and at a temperature of 56 °C – 15-30 minutes. It is quickly inactivated under the influence of disinfectants. In dry phlegm, it keeps the viability for several hours [21-22, 24].

EPIDEMIOLOGY

Pertussis presents the most contagious disease and can be presented in 97-100 % of population. People of different age groups are ill with this disease. More than 50 % of pertussis in children of infancy is associated with insufficiency of mother immunity and the absence of transplacental transmission of specific protective antibodies, so disease can occur from the first days of life. Major part of diseases can be present in children up to 2 years old who undergo this disease very bad [3, 25]. Pertussis is epidemic worldwide. In each area the disease becomes epidemic at intervals of 2-4 years. The first case of pertussis usually does not have the natural life-span immunity, but repeated infection (if it occurs), passes easily and often does not differ.

The source of infection of pertussis is a sick person with any form of the infectious process: mild, moderate, severe, and especially with subclinical forms. The causative agent is contained in droplets of saliva released during coughing. The period of infectivity begins with the first day of the onset of clinical symptoms. The most contagious patients in the catarrhal period and the first week of spastic cough – in the 90-100% excreted pathogen. During the second week of spastic cough, infectivity decreases and the pathogen can be isolated in 60-70 % of patients. The susceptibility to pertussis does not depend on age, but is due to the presence of immunity to it. The index of contagiousness is 0.7, and with close contact – 0.9 [4-5, 17, 21-22, 24].

PATHOGENESIS

Bordetella pertussis produces several toxins, the main as pertussis toxin, which increases the sensitivity of tissues to histamine, leads to dysfunction of lymphocytes and stimulates insulin secretion. After fixation of the bacterium to the flashing airway epithelium (due to adenylate cyclase and pertussis toxin), epithelial cells are damaged, the drainage function of the epithelium of the respiratory tract is damaged, which prevents the rapid elimination of bacteria from the body. Tracheal cytotoxin and dermanecrotic factor increase the production of mucus and contribute to the absorption of pertussis toxin. Most clinical symptoms of pertussis are associated with damage to the epithelium cells of respiratory tract. Firstly, to suffer the drainage function of the mucous membranes, this leads to the accumulation of viscous mucus. The thick, viscous mucus reduces the permeability of small bronchi and bronchioles. This leads to the development of atelectasis, nonspecific bronchopneumonia, and emphysema. The mechanism of elimination of mucus is a cough, which becomes frequent, obsessive and paroxysmal. The accumulation of viscous secretion in the throat provokes vomiting. As a result of frequent cough attacks in the respiratory center, as an excitation center of the dominant type is formed, which can spread to other parts of the nervous system such as vascular, vomiting, and others. During an attack, spasm of the vessels, vomiting, and increased blood pressure may occur. In the future, attacks of spasmodic cough may occur when irritated receptive fields that are not associated with cough reflex (for example, with strong acoustic stimuli, throat examination, injections). The dominant hotbed is stored for a long time, so spastic cough can be observed after elimination of infection. However, in the emergence of stronger excitation centers, the dominant hotbed is braked-due to the cessation of attacks during an exciting game.

In general, in the pathogenesis of the pertussis, hypoxemia, hypoxia and the state of acidosis, which occur as a result from impaired of pulmonary ventilation, circulation and oxidative processes is important. Also, in the mechanism of spastic cough, the allergenic effect of Bordetella pertussis plays a role, while bacteremia does not have a significant effect [7, 21, 24].

CLINICAL MANIFESTATIONS

The incubation period varies within 3-14 days, preferably it is about a week. During the course of the disease, there are three periods such as: catarrhal, spasmodic cough, and recovery.

The catarrhal period develops gradually. It manifests in moderately catarrhal phenomena in the form of dry cough, the body temperature remains normal, but more often increases to subfebrile values, the general state of patients remains satisfactory. Gradually, the cough intensifies, and becomes hard. At the end of this period, it can manifest itself in the form of attacks, especially at night, in spite of the treatment. This should cause a pediatrician or family doctor opinion about pertussis, but not an acute respiratory viral infection or bronchitis. In this case, it should be carefully collected the epidemiological history and assign or repeat a general blood test in which you can see the characteristic changes of the pertussis: high leukocytosis, lymphocytosis and normal erythrocyte sedimentation rate. The catarrhal period lasts 3-14 days, and the infant is reduced to 5-7 days.

The period of spasmodic cough (convulsive period) develops also gradually. Cough presents as an attack and develops more frequent, becomes convulsive. An attack of the cough can occur suddenly, but more often, patients are anticipating it: they have a tingling sensation, a feeling of pressure in the chest, anxiety. The attack begins with several coughing shocks during one breath. During the breath there is a whistling sound, which is the result of spastic narrowing of the vocal cavity. During one attack, coughing and reprises alternate and

can be repeated several times. During an attack, the patient swells the cervical veins, the face becomes inflated, hyperemic, often cyanogenic, looks scared, tears flow, the mouth is open, the tongue is as much as possible protruding, it forms a «shuttle», the bridle can be damaged. In severe cases, there are nosebleeds, hemorrhages in the sclera, involuntary urination and defecation. The attack often ends with vomiting movements with the release of viscous mucus, sometimes actually vomiting, and in severe cases it is possible to stop breathing. In infants, cough attacks are not accompanied by reprisals and often cause apnea. Due to the lack of teeth in children of this age group, there is no damage to the tongue bridle. Body temperature is normal. Fever can be and indicates the possibility of complications. There are dry rales in the lungs and arterial pressure can be increased. Coughing attacks can provoke different external stimuli (oropharynx examination, breastfeeding, feeding, solid food, negative emotions). The period of coughing attack lasts 3-4 weeks and in children up 1 year old lasts to 6-8 weeks. Number of attacks gradually decreases and their intensity reduces.

There are three main types of pertussis: mild, moderate, severe. During the mild type, the frequency of attacks to 15 per day, the number of reprises is to 5, attacks are typical, short, vomiting is relatively rare, the general state of health of patients is not damaged. During the moderate type the number of attacks increases to 25 per day, the number of reprises includes 10, often at the end of the attack, vomiting occurs. General health status deteriorates. During the severe form of pertussis, the number of attacks increases to 30-50 per day or more, attacks is severe, can last up to 15 minutes, have more than 10 reprises and almost always end with vomiting, sleep disturbance, lack of appetite, lethargy, weight loss, prolonged fever. In newborn babies, even with moderate frequency and short duration of cough attacks, pertussis can be very difficult.

In addition to the main forms, there is often an eroded form of pertussis, characterized by the absence of typical cough attacks with reprisals and reduced flow. In such cases, tracheitis or tracheobronchitis is often diagnosed. Such forms are more commonly seen in vaccinated children. There is also an asymptomatic form of pertussis, in which there are no clinical manifestations, although in the body there are cyclic immunological and sometimes hematological changes; X-ray changes that are often detected, blood-filling of the lungs, changes in the capillary system are also described.

During the stage of reconvalescence, or even after the complete elimination of all the symptoms of pertussis, sometimes there is a recurrence of typical cough attacks - these are false relapses. They occur already after the body is released from the pertussis and is not accompanied by a typical reaction to pertussis. These «recurrence» occur in patients when they recover after any infectious disease (acute respiratory viral infection, tonsillitis) [4, 7, 17, 20-21, 24].

COMPLICATIONS

Complications are connected mainly with the activation of secondary bacterial flora. Among these complications ones are dominated by pneumonia and less common diseases are presented by otitis, mastoiditis, pyelitis and other bacterial complications. The serious complication of this disease is the lesion of the central nervous system (seizures, fainting, paralysis) and encephalopathy. They are associated with a disturbance of the oxygenation of the brain tissue, dyscirculatory and dystrophic disorders in it. Often there are severe consequences such as paralysis, mental disorder, deafness, blindness.

Sometimes complications are associated with cough strength: pneumothorax, atelectasis, mediastinal and subcutaneous emphysema, umbilical and inguinal hernia, rectal incontinence, urinary incontinence, and complications of hemorrhagic nature: skin and subconjunctious hemorrhages, bleeding from the tympanic membrane and its rupture, brain hemorrhage. During the first months of life, pertussis passes badly and is accompanied by the number of complications. The most commonly used type of complication such as pneumonia, which is the main cause of death in the case of pertussis [20-21].

DIAGNOSTICS

There are bacteriological, serologic and PCR methods of pertussis diagnostics [4-5, 7, 20-21, 24, 26].

Bacteriological method (sowing the material from the nasopharynx and cultivating it on the nutrient medium) is informative at an early stage. The study is carried out on an empty stomach in 2-3 hours after drinking or eating. The material is taken from the oropharyngeal surface during 5-7 days of the disease twice. The preliminary result can usually be obtained in 3-5 days and the final one – in 5-7 days. The sensitivity of the test varies depending on the quality and terms of the study from 20 to 90 %. In the early days of the disease, it determines reliable result in 86-98 % of cases, but over time, the accuracy indicators are reduced to 15-20 %, especially with the use of antibiotics.

The «Gold Standard» for the diagnosis of pertussis is the reaction of the immunoassay. It allows detecting different classes of immunoglobulin's (Ig A, M, G) in the serum of blood, which helps the doctor to diagnose accurately and determine the stage of the infectious process and find out strong the immune system is to pertussis. The diagnostic sensitivity of this method is 66.6 %, the specificity is 100 %. Blood test is performed on an empty stomach, not earlier than 4 hours after the last meal. After that, serum is released from the blood, which is a material for the research. The research can be either qualitative (positive/negative result) or quantitative. IgM antibodies occur during the acute stage of pertussis during about 2 weeks of the disease. In 2-3 weeks IgA is detected. During the third week, IgG antibodies begin to occur – they are responsible for the formation of persistent immunity.

PCR testing can be done during the first 4 weeks of the disease. The sensitivity of this test exceeds bacteriological research. The specificity of the method is 100 %. The smear is taken from the nose or from the oropharynx. It should be taken to pick up the material on an empty stomach

or 2-3 hours after drinking and eating, pre-rinse is not required. In the laboratory, in the recovered material, specific portions of the DNA of the bacteria causing pertussis are determined. The positive result determines disease or bacteriocarrier [5, 7, 21].

The final diagnosis is determined:

- by the basis of characteristic symptoms of illness in the absence of the possibility of conducting laboratory diagnosis or with negative results of laboratory research;
- by the confirmation of the previous diagnosis by laboratory methods (isolation of culture or DNA of the pathogen or anti-infectious antibodies);
- by the basis of the characteristic symptoms of the disease, determining the presence of an epidemiological link with the source of the infection.

TREATMENT

The presence of Bordetella pertussis in the body defines either pertussis or asymptomatic course of disease. The treatment is required in any of these cases. Patients who are 1 year old, as well as patients with severe forms of pertussis and they had the presence of complications must be hospitalized. The bed regime is prescribed when there are fever and severe complications. All other patients show prolonged stay in the open air. It is very good for such patients to have cool and humid air – improves ventilation of the lungs, oxygen exchange and, possibly, reflexively affects the central nervous system and cough attacks are becoming rarer and weaker. The child should spend outdoors the most part of the day in the warmer days of the year, and in the cold – for several hours a day. During winter months walks should be carried out in closed areas from the drafts. Walking is allowed at air temperature not lower than -10 °C, however, overcooling is not allowed. It is also necessary to ensure continuous careful ventilation of the room in which the patient is located.

Much attention should be paid to educational work with children such as leisure activities, various activities, games, etc. It is necessary to exclude all sorts of stimuli such as emotional, physical which can provoke cough attacks.

Feeding should be complete. After feeding, you must especially protect the child from stimuli that provoke the development of cough attacks. If you have vomiting after eating, it should be repeated. There is a need for parenteral fluid administration when vomiting frequently presents.

To all patients in the first 3 weeks from the onset of the disease appoint erythromycin or other antibiotics from the group of macrolides in doses corresponding to the child's age within 14 days (for such antibiotic as Azithromycin the duration should be prescribed during 5 days). Trimethoprim (sulfamethoxazole) and ampicillin are used for intolerance to macrolides. These drugs are also prescribed for 14 days. However, from the perspective of evidence based medicine, optimal medications are Azithromycin and Clarithromycin. It should be noted that for the treatment of children during the first months of life, the administration of erythromycin is not recommended as the connection between its use and stenosis of the pyloric stomach is confirmed. The administration of an etiotropic therapy after 3 weeks from the onset of the disease pathogenetically unreasonable and is solved individually (in this period, antibiotic therapy should be prescribed to patients who may be in contact with non-immune individuals).

To prevent cough attacks 2.5 % of Aminazine solution in 1-2.5 mg/kg is administered intramusculary twice a day (before the day and night sleep). In newborn babies solutions of Aminazine of 1.0 ml * 3.0 ml of Novocain solution is prescribed. Dosage calculation is done through Aminazine. Besides, Diazepam of 0.3 mg/kg can be used once a day. Elder children Diazepam is administered orally. There is experience with the use of salbutamol: for children 2-7 years – 1-2 mg 2-3 times a day, 8-14 years – 2 mg 3 times a day.

To decrease the intensity and frequency of cough, children at the age of 2 years can be prescribed antitussive drugs containing dextromethorphan hydrobromide, geyfenazine and on the basis of butamirati hydrocyterate.

According to evidence-based medicine, immunoglobulin's, corticosteroids, ß-adrenergic antagonists are not recommended for the treatment of pertussis.

Supervision of infants involves vital functions monitoring, episodes of apnea, frequent suction of mucus from the respiratory tract, providing adequate oxygenation, parenteral hydration, correction of hypoglycemia, parenteral nutrition.

When there is apnea it is necessary to restore respiratory tract as quickly as possible. Nose, oral cavity is kept from mucus and vomiting masses. Respiratory movements are restored by the rhythmic pressing of the hands on the chest of the child, using manual respirators, oxygen transport through the mask. During frequent, prolonged apnea, the child is transferred to the emergency department and intensive care unit, where the issues of the need for mechanical ventilation and correction of vital functions are solved [4, 7, 17, 20-21].

HOSPITALIZATION

A patient with pertussis is isolated in a hospital or at home for 30 days from the onset of the disease. Isolation should be carried out as early as possible. However, in practice, the diagnosis of pertussis is usually established during the period of spastic cough. Accordingly, isolation is postponed which greatly reduces its epidemiological efficiency. Hospitalization involves patients with a severe or complicated form of pertussis, children who are less than 2 years old, sick children from a family living in unfavorable living conditions, as well as from families with children who are less than 6 months who have not been ill with pertussis [7, 21].

MEASURES

Children who are 7 years old and were in contact with patients, they were previously not ill and were not vaccinated by pertussis vaccine, quarantine for 14 days from the

time of isolation of the patient is determined. If the patient was not isolated and communication with him continued throughout the period of illness, quarantine is determined until the end of the period of contagion in the patient. The final disinfection in the hotbed of infection is not carried out (the causative agent quickly dies in the environment). When there is suspection of pertussis, a bacteriological examination is carried out.

Group of people who are at high risk of severe or complicated course of pertussis is established. People of this group are:

- children under 1 year old, especially the first four months;
- children with chronic pulmonary diseases which are accompanied with mucoviscidosis, diseases with respiratory failure;
- children with immunodeficiency status;
- pregnant women in the third trimester.

People from risk group should avoid patients with pertussis and people who cough. Patient from the group of risk should be administered antibacterial agents during the contact with the patient who is ill with pertussis.

Pregnant women are administered erythromycin or azithromycin if they were in contact with patients who were ill with pertussis [4, 20-21].

PREVENTION

According to the orders of the Ministry of Health of Ukraine № 551 dated August 11, 2014 and № 947 of May 18, 2018, acellular pertussis vaccine is used for active immunization, which is part of the combined vaccines (against diphtheria, tetanus and/or against poliomyelitis, hemophilic infection, viral hepatitis B) or adsorbed pertussis-diphtheria-tetanus vaccine. The next scheme of primary course of vaccination is used: the first dose is administered in 2 months of child's life, the second – in 4, the third – in 6. Revaccination should be done after the first course of vaccination in 18 months. The vaccination can't give life long immunity, disease can occur in late childhood and in adults. Experts recommend late re-vaccination to protect and prevent the spread of pertussis [16-17, 21].

FURTHER PROSPECTS

New strategies of pertussis are developed by scientists. In many countries the second revaccination is administered in pre-school age [4-5, 8-9, 11-12, 27-30]. Acellular pertussis vaccine is administered in the USA and in other countries of Europe, when children are more than 2 months old. The possibility of the first vaccine by newborn babies is proposed. Nowadays transplacental transmission of antipertussis antibodies to the fetus is effectively approved and their protective role is also detected. Efficacy of mother's vaccination contains 89 % in order to prevent disease. Vaccination during pregnancy can decrease the mortality of newborn babies on 33 %, the hospitalization number – on 38 % and the morbidity – on 49 %. Acellular pertussis vaccine Tdap (27-36 weeks of gestation) is recommended for pregnant women nowadays. And to prevent infection of newborn child vaccination is necessary for all members of family. It allows protecting a child during the first 6 months before the formation of immunity [6]. However, in many countries Tdap vaccine is not licensed, that's why vaccination is impossible.

Nowadays scientists develop new effective pertussis vaccines. Live slight vaccine BPZE 1 is developed for intranasal injection. Results of the first stage of clinical identifications of the given vaccine demonstrated favorable advances. The increase of acellular pertussis vaccine efficacy is prognosed [5, 23].

CONCLUSIONS

Pertussis incidence does not leave its relevance, despite the possibility of effective prevention of this disease. Timely diagnosis, treatment and immunoprophylaxis allow adjusting the actions of doctors to solve the issues of the decrease of the incidence of pertussis. This is greatly helped by modern guidelines for the management of patients with this pathology. However, clinical experience matters the doctor and the individual data of a particular patient.

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CORRESPONDING AUTHOR

Valentina I. Ilchenko
Department of endocrinology with children's infectious diseases,
Ukrainian Medical Stomatological Academy
26 Shevchenko St., 36011 Poltava, Ukraine
tel: +380662544335
e-mail: val.ilch@ukr.net

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