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Is Pertussis Back? Improvements in Fighting the Forgotten Pediatric Infection

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This article is concerned with the infection, which was one of the major causes of infant mortality more than 60 years ago. With the introduction of vaccination against pertussis into the national programs, physicians rarely face severe pertussis infection forms in their practice. However until now this infectious disease remained a serious problem not only in Russia but in the whole world. Several global reasons contribute to the fact that until now vaccine-preventable infection leads to a prolonged, debilitating cough in schoolchildren, misleading the doctors with the incorrect diagnosis, and is still a real threat to infants.

Key words: *pertussis, vaccination, acellular vaccine, children.*

Pertussis - highly contagious bacterial infection transmitted by airborne droplets. The causative agent of pertussis is *Bordetella pertussis*, which is characterized by tissue tropism ciliary epithelium of the human respiratory tract [1].

Epidemiology. Special features at the current stage. The sources of pertussis are patients with severe clinical forms of pertussis, blurred forms and bacillicarriers. In contact with the diseased, pertussis develops in 90% of the susceptible contingent. Pertussis has the most severe course in infants: at this age it is often joined by complications, high risk of death. More than half of children under one year, who have pertussis, require hospitalization. In one of the five infants pneumonia develops and at least 1 out of 100 infants undergoes seizures. In one case out of 100 pertussis leads to death, mostly at an early age [2].

Incidence of pertussis into older age groups, clinical and subclinical smoothing and smoothing of seasonality characterise modern pertussis. It was found that children at the first years of life have a high level of post-vaccination immunity to pertussis, while causative

infection circulates among other age groups - schoolchildren, students and adults. At the same time there remain the main epidemiological characteristics of this pediatric infection: the high susceptibility of unvaccinated people, mostly children under 1 year; focality, cyclicality, periodicity, life-long postinfectious immunity and low resistance of the pathogen outside of the patient [3].

Originally pertussis infection was considered to be a solely pediatric disease. N.F. Filatov wrote that "pertussis is a really infant disease." According to S.V. Guslitsa and A.M. Adonaylo, in 1940-1950-s pertussis was the most common among children under 5 years old and 84,6-78,8% of the sick lived in Moscow and Leningrad - 81.5% of the total number of patients [1, 4]. However, recent statistical studies have shown that adults are also susceptible to this disease. Pertussis in adults and adolescents is milder and has atypical course, so it is often not diagnosed, which generally contributes to the spread of the pathogen in susceptible society.

In present time seasonality of pertussis infection is not recognized by all clinicians. In pre-vaccinating period pertussis was seasonal. According to T.V. Panteleeva, in one district of Moscow in 1947-1956 there was observed increased incidence (with a maximum in October) among students who returned into educational institutions after the holidays. Epidemiologists associated it with the reduced resistance of the organism, and overcrowding in small areas at this time of year. However, according to the final report of the WHO, conducted in Europe between 1998 and 2002, seasonality of the infection is almost impossible to trace [5-7]. In some countries the rise in the incidence of pertussis was observed in the spring and summer months, while in others, on the contrary, during the cold season.

The main risk factor for pertussis is the lack of immune protection of children due to low immunization coverage, violations of the schemes and terms of vaccinations, unnecessary medical rejections from DPT vaccination.

The difference of susceptibility to pertussis among population is due to genetic characteristics of people, to the character of immunity resulting from vaccination, and to the characteristics of pathogen virulence and the size of infecting dose. When reducing the scope of preventive vaccination of infants up to 30% or less, dynamics and incidence were similar to those before the start of mass vaccination programs.

The clinical picture. Pertussis is characterized by a cyclical flow. There are an incubation period lasting an average of 7-8 days, catarrhal period (7-10 days), the period of spasmodic or whooping cough (an average of 6-8 weeks) and convalescence period, sometimes occupying up to 6 months. In the catarrhal period of pertussis, the patient is of the greatest danger to others. Along with evidently typical forms of pertussis there occur light, abnormal

(abortive and subclinical) and asymptomatic forms - carrying among adolescents and adults (up to 10% of the sick).

Pertussis is characterized by a certain time intervals, which is expressed in the form of raising incidence every 3-4 years. This is due to changes in virulence of circulating pathogens, which inevitably increased with frequency of passage in people with high susceptibility due to the high number of unvaccinated in the community.

Diagnostics difficulties are due to special features of the pathogen. Pertussis bacillus is extremely unstable in the outer environment, thus planting of material must be performed immediately after sampling. The causative agent of pertussis dies quickly under UV irradiation and by simple drying, which sometimes makes it difficult to diagnose the disease. In addition, the frequency of positive results for bacteriological examination depends on the timing of material intake: in the initial period of seeding, rate of pertussis bacillus reaches 95%, in the midst of a period of spasmodic cough (4th week of illness) - already 50% and beginning from the first week of the disease it becomes impossible to discover infectious agent. For example, according to the Department of Health in Moscow, the overall detection of *B. pertussis* in 2009 amounted to only 2.0%, which indicates the absence of bacteriological examination of long-term cough or conduction of surveys in the later stages of the disease. The true incidence of pertussis is much higher due to the so-called undiagnosed pertussis infection (light and smoothed clinical forms) [8].

In CHRC of RAMS during the examination of coughing children (n = 339, 188 boys and 151 girls) for more than two weeks, it was discovered that much of pertussis was not diagnosed (Prof. N. Mayansky). Age of those surveyed - 2 months - 18 years. Vaccination status of patients was not analyzed. It should be noted that none of the children had any clinical and radiological data for pneumonia. There was performed analysis of the results of serological examination of children for pertussis (Table 1).

IgM-antibodies to *B. pertussis*, indicating acute infection, were detected in 37.5% of children coughing for a long time. Also, in 21.5% of patients with questionable levels of immunoglobulin (Ig) M, there could not be excluded acute pertussis infection. At the same time the level of antibodies of class G in IgM-positive patients is higher by more than 3 times than that of IgM-negative patients, which can be logically explained by acute infection of *B. pertussis* antibody along with antibodies of M-class. It is important to note that among patients with pertussis (114), 94 patients (82%) were over 3 years. Even if these children were vaccinated in a timely manner in the first two years of their life, immunity usually reduces gradually. Studied IgM-negative patients usually have the much lower level of antibodies of G-class. The absence of IgM in these patients does not allow to exclude the recent pertussis occurred.

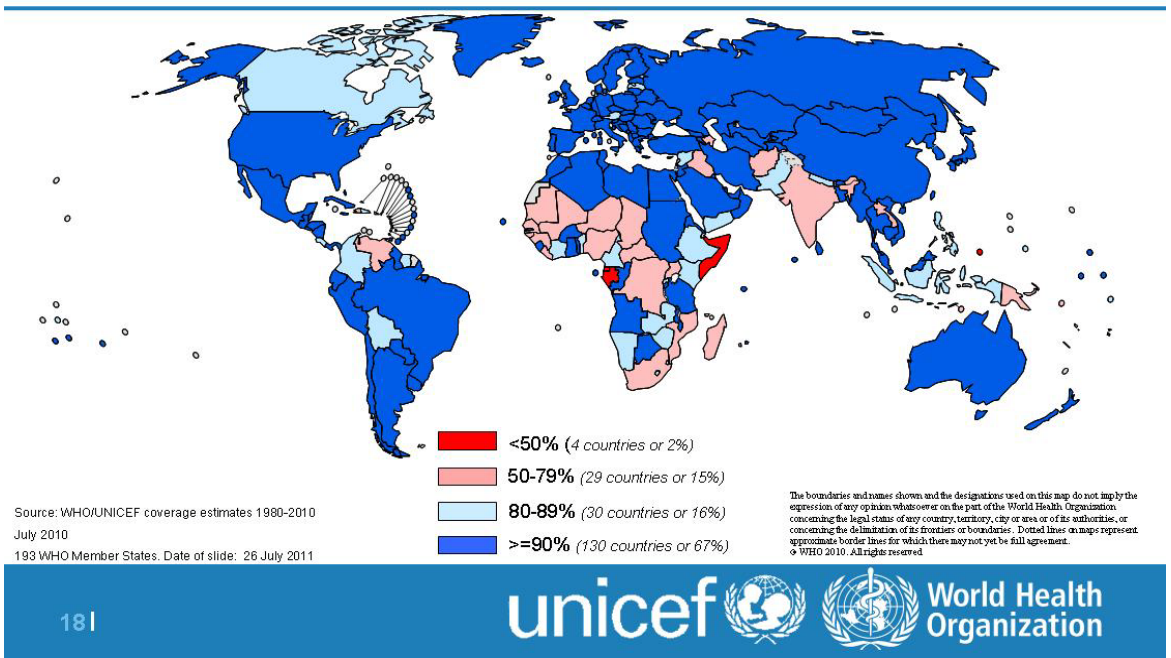
Pertussis is widespread, but the incidence in different countries and continents varies greatly. Even in the European Region there are 3 groups of countries with different levels of disease (from a few to 100 per 100 thousand of population), which primarily depend on the national vaccination programs, and are directly related to the percentage of the grafted population.

According to WHO, in 2009 in the world there were recorded 106.207 million of pertussis infection cases, while 195 thousand people died from this vaccine-preventable disease [9]. At the same time the average coverage of primary vaccination series against pertussis was about 82% that year. For comparison, according to Rospotrebnadzor, the rate of Russian children immunized against pertussis in 2009 totaled more than 96.0%. The number of pertussis patients in 2009 in Russia amounted to 4066 cases.

So, the only reliable means of specific prophylaxis against pertussis is vaccination [10, 11]. The first pertussis vaccine was created in the U.S. in 1941, and the first combined DTP vaccine was put into practice abroad in the late 1940-s. At present, DTP vaccines are included in the mandatory collection, recommended by WHO. Vaccination against pertussis is performed in all world countries, most of which achieved high coverage (Fig. 1) [11, 12]. Creation and licensing of acellular pertussis vaccine in 1991 became a major step in improving of the whole-cell DTP vaccine. One of its main advantages was the decline of reactogenicity, and of number of adverse reactions and, therefore, reduction of the number of contraindications to DTP vaccination.

Fig. A. Coverage of primary DPT vaccination in the world. WHO data for year 2010

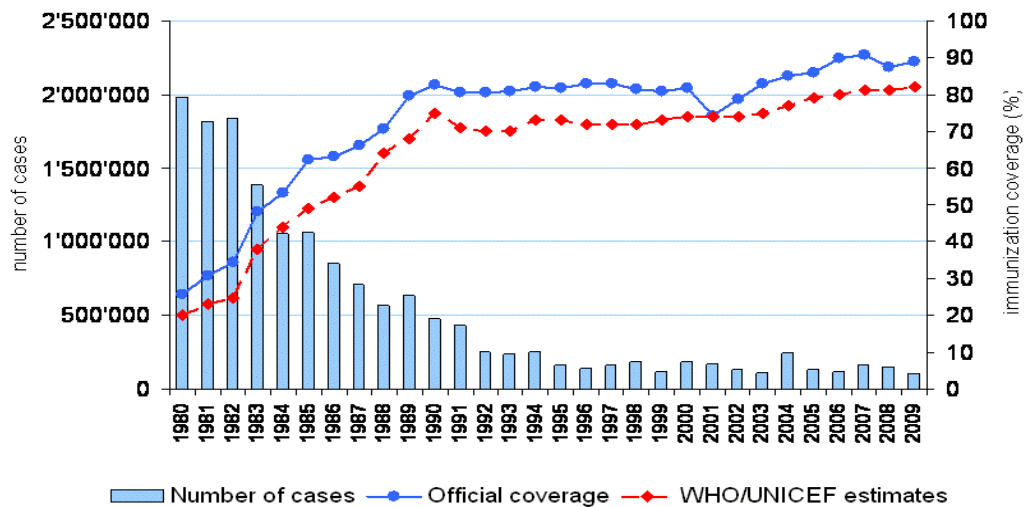
Immunization coverage with DTP3 vaccines in infants, 2010



It is due to annual vaccine that the medical community prevent more than 35 million cases of pertussis and 600 thousand deaths every year. Effect of mass vaccination on the incidence of pertussis in the world is perfectly illustrated in Fig. 2 using data from the WHO; it displays the inverse relationship between them. In addition, long-term and widespread use of pertussis vaccine contributed to changes in the nature of the epidemic process and the clinical picture of this infection. Pertussis has become less severe, and mortality decreased significantly.

Fig. Two. The global incidence of pertussis and coverage of DPT vaccine for the period 1980-2009 (according to WHO)

Pertussis global annual reported cases and DTP3 coverage, 1980-2009



Source: WHO/IVB database, 2010
193 WHO Member States. Data as of September 2010

Date of slide: 08 September 2010



Initial three-time series of pertussis vaccine at 82% coverage of all children living in the world, annually prevents 85 million illnesses each year and 762 thousand deaths from pertussis in children [13]. Number of prevented disabilities exceeds a million. The greatest effect was registered in developed countries where the incidence of clinically diagnosed pertussis was only 3.10 cases per 100 thousand population, and in some European countries (Belgium, Bulgaria, Czech Republic, Iceland, Luxembourg, Portugal), this figure was below 1 per 100 thousand.

Like any vaccine-preventable disease, pertussis has repeatedly demonstrated the direct dependence on the coverage of preventive vaccination. Thus, in different parts of the world, given the slowdown in vaccination, there flared a whole epidemic of pertussis infection very quickly.

In the history of epidemiology there is a vivid example of refusal of vaccination against pertussis in the UK in the 70s: despite the fact that the incidence of pertussis has been reduced to sporadic levels, after immunization coverage fell from 81 to 31%, in a short period of time a real epidemic broke out. In England and Wales there fell ill more than 200 thousand children annually and up to 100 children died. Achieve a decline of morbidity and mortality was possible only after the increase in coverage to 90% of vaccinees. A similar situation occurred in Japan: an end to immunization against pertussis led to the fact that during the 1975-1980 period there were over 36 thousand of pertussis cases. On the territory of Germany from 1979 to 1982 there were 80 thousand cases of pertussis, with 1520 patients had serious complications on lung, 61 - on the

nervous system with 15 deaths. Cessation of vaccination in Sweden in the 1980s led to the fact that 60% of children under 10 years fell sick.

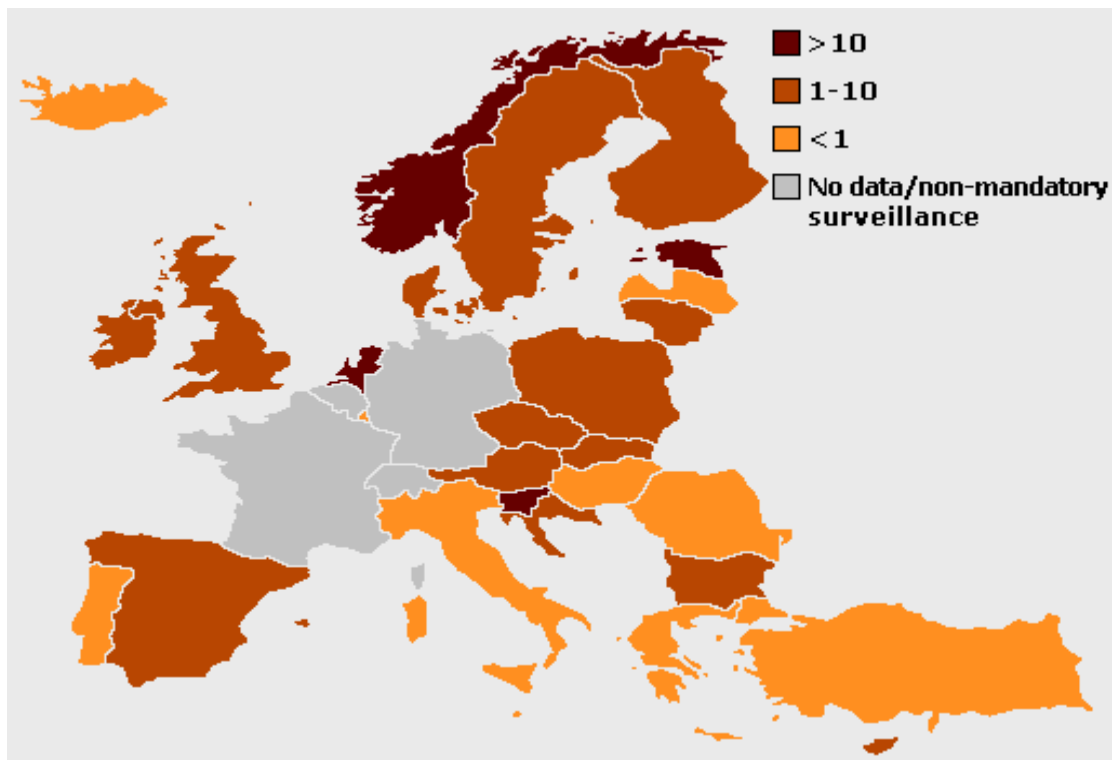
In Russia in the pre-vaccinating period the incidence of pertussis was 400-800 per 100 thousand people and took 2nd place after measles among the causes of death in children under one year. After the introduction of vaccination in general practice in 1959 there was a significant reduction in the incidence of pertussis - by 100 times by 1990. In addition, one of the most important achievements of specific prevention is a sharp decline (by 1000 times), mortality from pertussis. Subsequently, the incidence rate has stabilized at rates of 10-20 cases per 100 thousand (Fig. 3). This average rate is combined of various parameters recorded in all areas across the country, all of which also depend on the level of coverage of the child population. Once the coverage is reduced, the incidence increases. For example, in the 1990s, there was a significant rise in the incidence of pertussis, and in some regions, its level in 1994 was 100-140 per 100 thousand population. In the early 2000s, as a result of vigorous immunization activities it became possible to prevent pertussis epidemics, and illness in general has declined to the level of 3,8-8,7 per 100 thousand population. In 2008, the incidence of pertussis in Russia fell to 2.51 per 100 thousand population, which indicated that the task set by the subprogram "Vaccine" (2005-2011) to achieve the level of pertussis incidence to 3-5 cases per 100 thousand population in 2010, was successfully completed.

Fig. Three. The incidence of pertussis in the Russian Federation



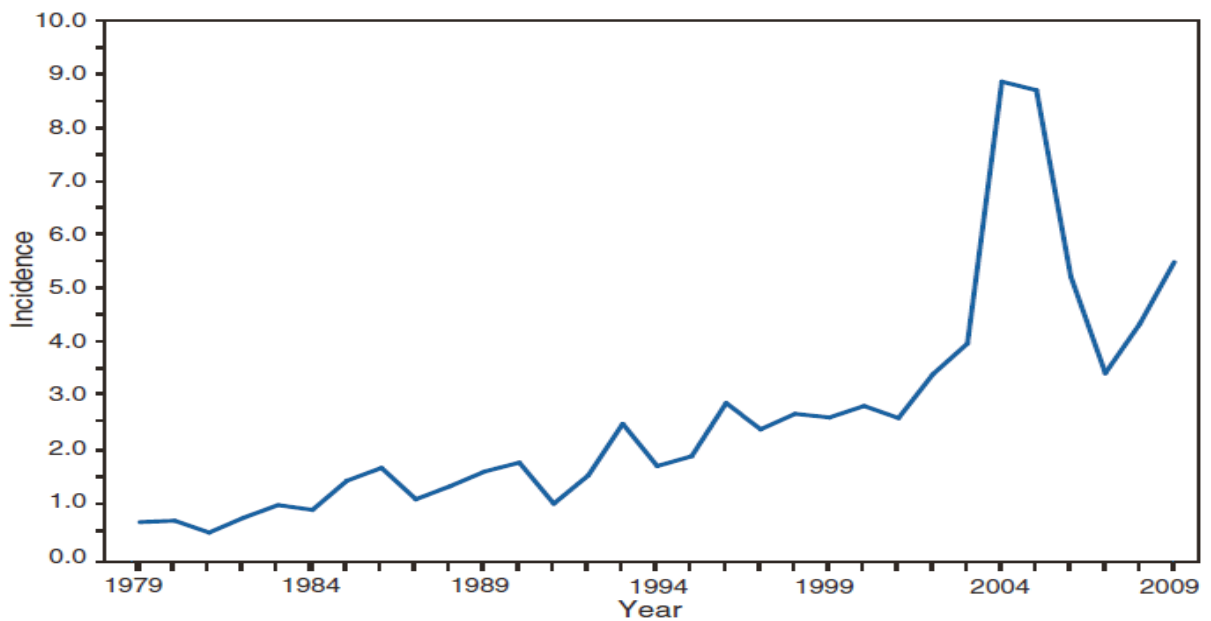
It should be noted that according to reports of WHO, over the past 10 years the incidence of pertussis in European countries has had a tendency to increase (Fig. 4). Thus, for the period 2003-2007 incidence rate was 4.1 per 100 thousand population, while only for 2009 it rose up to 4.9 [7, 14].

Fig. 4. The incidence of pertussis in 28 European countries in 2009 (final report of the WHO)



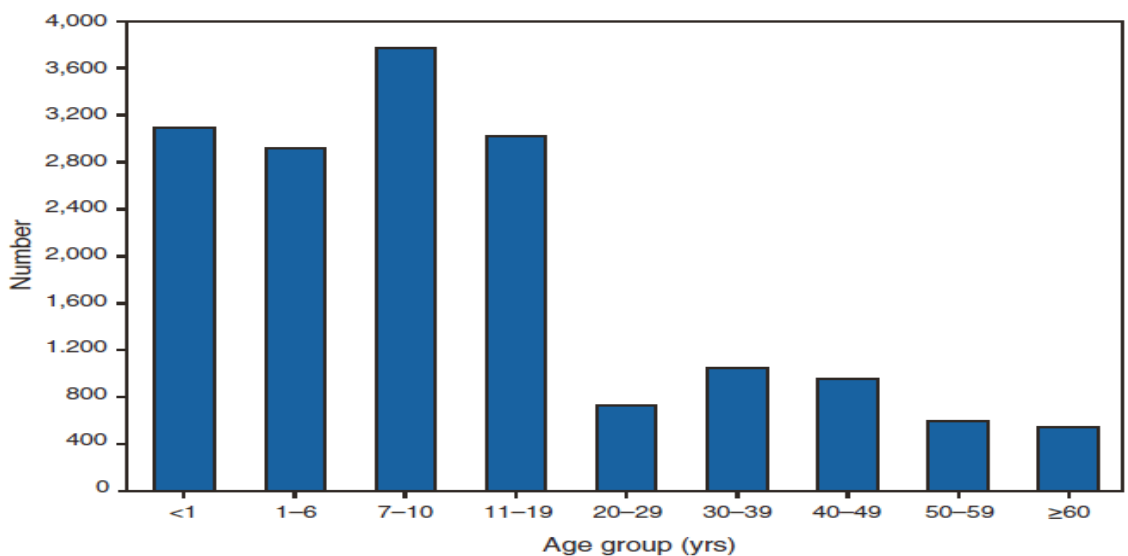
In addition, since the 2000s in many European countries there has been a structural redistribution of cases of pertussis by age group, and increase in overall incidence rate of in children aged 7-14 and adults. In 2003-2007 there were more diseased children under one year (about 35%, or 35.5 cases per 100 thousand), but in 2009 these figures practically equalled with incidence among children aged 10-14 years (22 and 20 cases per 100 thousand, respectively) [7, 8]. Since 2004 in the U.S. there has been a significant jump in the incidence of pertussis (Fig. 5). In addition, in various states is not the first recorded outbreak of this infection. Basically, all sick children are either unvaccinated or have not received a full course of vaccinations. Described outbreaks often occur in crowded bands of religious communities, who reject vaccination for ideological reasons. For example, in 2010 in California there were reported 9143 cases of disease, and according to statistics, 10 babies died then. It is the largest outbreak in the last 63 years (in 1947, 9394 people fell ill).

Fig. 5. The incidence of pertussis in the United States, 1979-2009 (per 100 thousand population) [15]



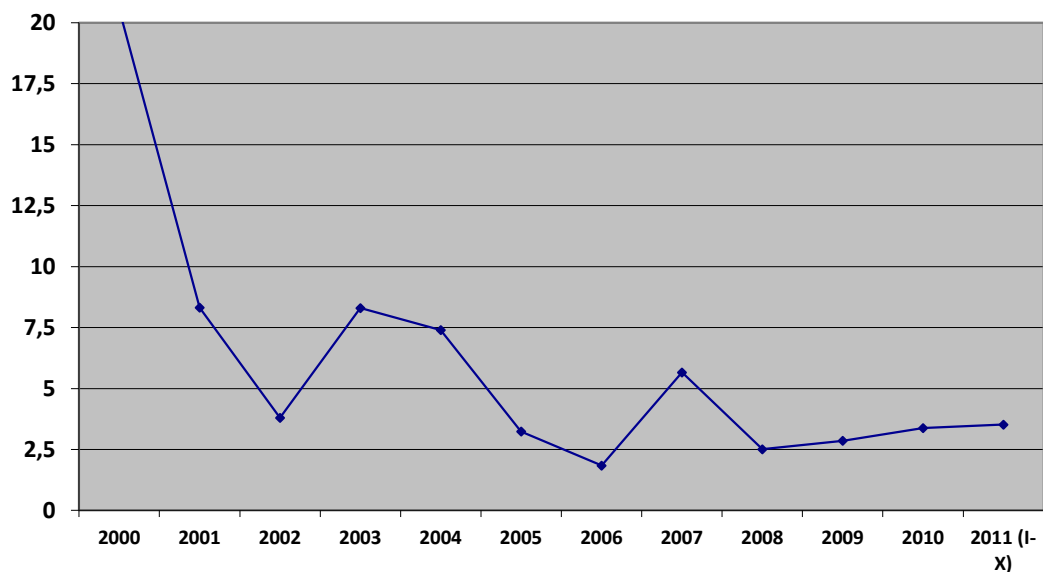
Age characteristic of pertussis indicates primary lesion of first-year infants and children aged 7-10 (Fig. 6). Given this shift in incidence, annually reviewed national scheme of preventive vaccination in the U.S. now includes 3 age groups: 15-18 months, 4-6 years and 11-12 years (see Table. 1).

Fig. 6. The incidence of pertussis by age group in the U.S. in 2009 [15]



The epidemiological situation on pertussis in the territory of Russia is relatively stable, but with a tendency to an increase in morbidity. After epidemic of pertussis had place in the 1990s, due to the reduction of vaccine rejections and increase in immunization coverage with DPT vaccine, by 2002 it became possible to dramatically reduce the incidence of this infection. During the analysis of pertussis incidence in the past 12 years, there was revealed a chain of ups and downs, which may indicate a lack of control of the infection (Fig. 7). In addition, over the last three years there could be seen a steady increase in the number of pertussis cases.

Fig. 7. The incidence of pertussis (absolute number per 100 thousand population) in the Russian Federation in the period 2000-2011 (FC of Hygiene and Epidemiology)



Only during the first 9 months of 2011, the incidence of pertussis increased by 7.7% and comprised 2.21 per 100 thousand of population versus 2.06 comparing with the same period of January-September 2010. The highest incidence of pertussis (4, 4-10,9 cases per 100 thousand population) were registered in Samara, Yaroslavl and Penza regions, Karelia, Ingushetia, St. Petersburg and Moscow. Increase in the incidence of pertussis in 3 or more times was registered in Dagestan, the Republic of Udmurtia, Perm and Trans-Baikal regions, Vladimir and Chelyabinsk regions [16]. Using the analysis of long-term dynamics of the epidemic process, there could be made an assumption on the similar rise in the incidence following the recession in 2009. Not only the reduction of immunity tension among adolescents and adults vaccinated in childhood, and mutation of the pathogen, but also improved diagnosis of this infection [16] are considered to be possible explanations of these outbreaks.

Samely as in Europe, in the Russian Federation the epidemic process of pertussis is characterized by a growing incidence of children of older age groups. In particular, in Moscow in 2009 the share of pupils in the structure of children with pertussis incidence was 45.0%, while the rate of this age group increased by 1.5 times comparing with 2008. In 2009, 42 cases of pertussis were registered in organized groups, and 31 of them - in schools (73.8%) [10].

Vaccination. At present time, in the whole world and in this country there are two types of DTP vaccines: whole-cell and modern acellular ones. The main preventive drug used in the Russian Federation, is a whole-cell DTP vaccine, which is a domestically produced vaccine, which often provoked vaccinal reactions and in rare cases - complications of the central nervous system (including encephalopathy). That is why DTP vaccine continues to be regarded as a drug

that causes the greatest number of adverse reactions [7, 13]. Because of these adverse reactions in some countries (UK, Japan, Germany, Sweden) in 1970-1980s there had place massive rejections from usage of DPT vaccine, which led to the sharp rise in pertussis with an increasing number of severe and fatal outcomes. At the present time developed countries prefer acellular vaccines, whose advantage is the lower frequency postvaccine reactions along with the same immunogenicity. There are two acellular vaccines in the Russian market: "Infanriks" (from 2004 to 2011 this drug has a statute of domestic drug, its production is controlled by Russian enterprise "SmitKlyanBichem-Biomed") and "Pentaxim" (since 2009), but, as in many other countries, they are rarely used due to the high cost of drugs and lack of production in each country. Given these obstacles, WHO continues to recommend the use of whole-cell vaccine in mass immunization programs as of effective and safe [15].

Immunization with acellular vaccine is recommended in cases of contraindications to the use of whole-cell vaccine. Acellular DTP vaccine with a reduced content of diphtheria and tetanus toxoids (eg, "Bustriks», GSK) is also recommended for revaccination of children older than 4 years who have contraindications to the use of whole-cell vaccines due to possible severe adverse reactions [12, 14].

Out of 197 countries, whose data is available, 129 begin to vaccinate children against pertussis at the age of 6 weeks-2 months in order to quickly protect their most vulnerable period of life. In almost all countries, DTP vaccination is allowed to be performed in one day with other vaccines of the National Calendar; 4 -, 5 - and 6-component vaccines, including DTP component, are more and more widely used. The basic scheme of a specific pertussis immunization consists of three time vaccination and one-time revaccination. However, taking into consideration the increase in the incidence of pertussis in school age, an increasing number of developed countries include into their national immunization schedules additional 2nd revaccination at the age of 5-11 (Belgium, France, Germany, Spain, Portugal, USA, Japan, etc.). Austria, Finland and Switzerland perform third vaccination at the age of 11-15 [13, 15]. In England, there remains only one vaccination against pertussis - in 3 years, in New Zealand - 4 years, and in Denmark - in 5 years. For revaccination in all countries except Brazil, acellular vaccine is used. This is due to the advantage in the lower reactogenicity of the acellular vaccines comparing to whole-cell [17]. Below is a table which shows the scheme of vaccination / revaccination against pertussis in developed countries (Table 2).

The vaccination system of the Russian Federation includes three vaccinations in the first year of life and one revaccination in 1.5 years, but even at high coverage it provides insufficient immunity duration, which begins to decline as early as in 5-7 years [7]. As a result, there is created a high non-immune layer - the condition for the circulation of the pathogen [3], which in

turn contributes to infecting children in the first six months of their life, have not yet got adequate vaccination protection. In many countries, this problem is solved by a second and a third dose of DTP-boosted vaccination. In Russia, this question remains open. It is also proved by a retrospective study of sera from 81 children with prolonged cough in the presence of specific IgG antibodies to B. Pertussis; study was conducted in 2010-2011 in CHSC, RAMS (candidate work of Volkov K.S.).

Among those surveyed there were 55 preschool and 26 school-age children. The vast majority of children (69 of 81) were inoculated in accordance with the National immunization schedule, one child had withdrawal for medical reasons. In 11 cases, vaccination status was unknown. Table 3 shows the results of a survey of children on the presence of antibodies to B. pertussis. It should be noted that for 18 children surveyed (22.2%), G-class antibodies were not detected. They were mostly children aged 5-6 years. It should be noted that most of them (14 out of 18, according to their mothers) have been vaccinated against pertussis. Lack of protective antibodies may be due to the fading of immunity to pertussis by the age of 6 years.

In most cases (65.4%) antibody levels ranged from 10 to 50Ed/ml. In 10 seropositive cases IgG levelled above 50 U / ml. All these children had previously been vaccinated against pertussis. Of the 10 children with relatively high titers of antibodies to B. Pertussis, two children were aged 3 years, that is, increased titer is associated with recent vaccination. For other children, due to their high levels of antibodies to B., pertussis could not be excluded from the history. Thus, in 3 of 8 children over three years, the disease might have been detected by the presence in history of typical clinical symptoms of pertussis: dry paroxysmal cough, until vomiting. For other five children with elevated levels of IgG to B. Pertussis, prolonged cough was different from the typical pertussis cough in nature and developed after respiratory infection with clinical manifestations of catarrhal and adenoiditis tubootitis. However, it should be noted that one out of four children examined, in the absence of IgG to B. Pertussis, are at risk for pertussis.

Patients and methods

In the center of the vaccinal prevention in CHSC RAMS, the vaccine 'Infanriks' has been used since June 2006 (more than 5500 shots made), Pentaxim - from December 2008 (more than 5000 shots made). From the very beginning of using the acellular pertussis vaccine there was a significant interest to it not only from pediatricians, but also from child neurologists, and neonatologists. In recent years the range of contraindications to DPT vaccination has significantly narrowed. In addition, those parents who were afraid of adverse reactions or have been exposed to it after the application of whole-cell vaccines, have shown great interest in the safe acellular vaccine. Indeed, parents whose children have developed a high temperature before

the reaction and / or febrile seizures after vaccination whole-cell vaccine (DTP or "Tetrakok"), reported good tolerance of acellular vaccines.

During the entire period of observation of children who have received "Infanriks" and "Pentax", there has not been a single serious adverse event. The body temperature rose at no more than 5% of children; no more than 1% of vaccinated children had body temperature above 38,0 ° C.

Tolerability of vaccination "Infanriks" in children older than 4 years is of particular interest. The vaccine "Pentax" can not be used for these purposes because it contains the polio component.

In the center of the vaccinal prevention in CHSC, RAMS, where the portability of vaccination "Infanriks" in children older than 4 years is of particular interest, a special survey is being held. Considering that this vaccination is not provided by the National and Regional immunization schedule for this age, only 83 children participated in a study.

Patients and methods

Selected for the vaccination were children aged 4-12 years, who came to the vaccination or revaccination of DPT. Parents were given an explanation, including age indications, described in the instructions for children under 4 years old. Given that currently there are no analogues in Russia for vaccination of children older than 4 years against pertussis, parents reacted adequately and were sympathetic to the proposal. In addition, for many children immunoprophylaxis using the studied vaccine was began prior age of 4, and continued afterwards. All parents signed informed consent. Distribution of children receiving the vaccine is given in Table 4.

The second revaccination was performed on 36 children (43.4%) without affecting the schedule - at the age of 7 years. For these children Infanriks substituted revaccination that was provided for them in the age of 7, ADS-M(without pertussis component). Taking into account their age, 47 remaining children (56.6%), had a broken schedule of vaccinations.

54 (65%) of 83 children enrolled in the study had the unfavorable history: 28 (52%) had concomitant pathologies, including allergic diseases and pathology of upper respiratory tract, gastrointestinal tract and nervous system, 2 (3.7 %) - a malformation of the lung, 1 (1.85%) - endocrine abnormalities (diabetes mellitus), 5 (9.25%) belonged to a group of often sickly children.

In more than half (58.8%) of cases, "Infanriks" was administered in combination with other vaccines according to National immunization schedule, including poliovirus (live or inactivated) vaccine against hepatitis B, Haemophilus influenzae type b.

The vaccine was administered at a dose of 0.5 ml intramuscularly into the deltoid muscle. Direct observation of vaccinated children was carried out within 30 minutes after vaccination, and then

controls of the general and local reactions was carried out through phone calls on 2-3rd day after inoculation.

In accordance with conventional methods there were taken into account both local and general reactions.

Research results and their discussion

Adverse reactions (Table 5), that developed in the first 3 days after vaccination, were observed in 23 children (27.7%). There were identified almost an equal number of local and general reactions. All of them were of moderate severity, ie, body temperature rose no higher than 38,4 ° C, local induration and redness were no more than 4-5 cm in diameter. All adverse events were stopped within 3 days along with use of antihistamine or antipyretics and local drug treatment and did not require for medical attention. There have been no strong local or severe general post-vaccinal reaction. It is interesting that all patients that in some way respond to vaccination, suffered from various forms of allergic diseases. Most of them were vaccinated while taking antihistamines.

In general, it should be noted that the acellular DTP vaccine "Infanriks" showed good tolerability and low reactogenicity, even at the older age than it is shown according to the instructions on the drug. This is necessary to consider on children who had not managed to get the full DPT vaccination on time, and to suggest Infanriks for these children. It is important that children who have a long medical exemption from the DPT vaccination, usually suffer from serious chronic diseases (neurological, allergic, etc.), and pertussis is most dangerous for them. It is possible to replace second ADS-M revaccination at preschool age for children who will be in danger of pertussis in older age, too. In addition, not only pre-school age children should be protected, but their younger brothers and sisters as well. Vaccination should be carried out only after preliminary discussions with the child's parents and mandatory written informed consent.

Conclusion

It is a well-known fact that pertussis has not yet been defeated. Moreover, in recent years, the incidence of pertussis in the world has a tendency to increase. Epidemiological and clinical characteristics of infectious disease change as well. Pertussis rate increases among schoolchildren and teenagers, thus requiring for the revision of pertussis immunization scheme. Creation of acellular pertussis vaccines helped to prevent possible disease among older children and adults and in children with a family history of somatic disorders.

Additional revaccination against pertussis is designed not only to protect school children from this infection, but also to reduce the circulation of *B. pertussis* in the community. Otherwise, pertussis can not be killed - school-age children will get sick and infect themselves as

well as not fully vaccinated or unvaccinated infants at the first half of life, for whom pertussis remains one of the most dangerous childhood diseases.

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Table 1. The results of serological examination of coughing children on a long-term

| Ig Class | Number of observations (n) | Negative result (%) | Positive result (%) | Doubtful result (%) |
|-----------------|-----------------------------------|----------------------------|----------------------------|----------------------------|
| IgM | 302 | 123 (41) | 114 (37,5) | 65 (21,5) |
| IgA | 293 | 236 (81) | 49 (16,7) | 8 (2,7) |
| IgG | 333 | 84 (25,3) | 249 (74,7) | - |

Table 2. Schemes of vaccination against pertussis in developed

| Country | Age of vaccinated | | | Age of revaccinated | | |
|----------------|--------------------------|-----------|-----------|----------------------------|-------------|-------------|
| | V1 | V2 | V3 | RV1 | RV2 | RV3 |
| USA | 2 mon | 4 mon | 6 mon | 15–18 mon | 4–6 years | 11–12 years |
| France | 2 mon | 3 mon | 4 mon | 16–18 mon | 11–13 years | - |
| Canada | 2 mon | 4 mon | 6 mon | 18 mon | 4–6 years | - |
| Japan | 3 mon | 4 mon | 5 mon | 6 years | -- | - |
| Germany | 2 mon | 3 mon | 4 mon | 11–14 mon | 5–6years | 9–17 years |
| Russia | 3 mon | 4,5 mon | 6 mon | 18 mon | -- | - |

Table 3. The results of a survey of children on the presence of specific IgG antibodies to *Bordetella pertussis* (n = 81)

| IgG Level, piece/ml | Frequency (%) |
|----------------------------|----------------------|
| 10–50 | 53 (65,4) |
| > 50 | 10 (12,3) |
| < 10 (not detected) | 18 (22,2) |

Table 4. The frequency of posr-vaccinating reactions to the vaccination

| Children in all | Reactions (%) | |
|------------------------|----------------------|--------------|
| | General | Local |
| Vaccination - 23 | 7 (8,5) | 9 (10,8) |
| 1-я revaccination – 24 | 2 (8,3) | - |
| 2-я revaccination- 36 | 1 (2,8) | 4 (11,1) |

