

RESOLUTION OF THE MEETING OF THE PUBLIC COORDINATION COUNCIL FOR PNEUMOCOCCAL INFECTION AND VACCINATION IN RUSSIA

A regular meeting of the public Coordination Council for the Study of Pneumococcal Infections and Vaccination in Russia took place at the Scientific Center of Children's Health on December 13, 2014. The meeting was dedicated to the launch of pediatric vaccination against pneumococcal infection in the framework of the Russian National Preventive Immunization Calendar from November 2014 and designing approaches to assessing short- and long-term vaccination results.

It involved the top experts of the Russian Ministry of Health in the following spheres: pediatrics – Academician A.A. Baranov of the Russian Academy of Sciences (hereinafter referred to as RAS), epidemiology – RAS Academician N.I. Briko, pediatric infections – RAS Academician Y.V. Lobzin, allergology and immunology – corresponding RAS member L.S. Namazova-Baranova. Besides, the Union of Pediatricians of Russia, the Research Institute of Pediatric Infections of the Russian Federal Biomedical Agency, the Research Institute of Epidemiology of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, the Research Institute of Antimicrobial Chemical Treatment of the Smolensk State Medical Academy (State Budgetary Educational Institution of Higher Professional Education) of the Russian Ministry of Health, and the RAS I.I. Mechnikov Research Institute of Vaccines and Sera delegated their representatives to attend the meeting.

The studies conducted in Russia confirmed epidemiological, clinical, and economic reasonability of introducing vaccination against pneumococcal infection into the National Immunization Calendar [1]. As a result of the work done by the Russian Ministry of Health, the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, the top outside experts of the Union of Pediatricians of Russia, the Society of Pediatric Infectious Disease Specialists of Russia, and the Interregional Association for Clinical Microbiology and Antimicrobial Chemical Therapy, pneumococcal vaccination was introduced into the National Immunization Calendar on January 1, 2014.

The conducted epidemiological studies [2, 3] have shown significance of serotypes 3, 6A, and 19A as causative agents of the disease in Russian children and adults. That is why the 13-valent pneumococcal conjugate vaccine (PCV13) was chosen for cohort immunization of Russian children, as it contains relevant antigens and provides for maximum effectiveness of immunization.

The vaccine was first delivered to regions of Russia at the end of November 2014; this created a difficult situation of a new vaccination program launch, partially due to the seasonal outbreak of acute respiratory diseases as well as a relatively full vaccination schedule (and lack of combined vaccines) for children under 6 months of age.

Meanwhile, the key factors of increasing the effectiveness of pediatric mass immunization are as follows [3]:

- vaccination coverage (≥ 2 vaccine doses in at least 90% of persons to be immunized),
- time before the required coverage is achieved,
- completeness of the patient sample subject to vaccination (this helps to reduce the risk of reasonless exemptions and involve children at risk in the vaccination process),
- strict adherence to the recommended pattern (timely administration of all doses as regulated without unreasonable delays).

At the stage of PCV13 introduction, it is also important to ensure the catch-up vaccination as an option for immunization of the children born in 2014 entitled to protection from pneumococcal infection according to Federal Law No. 157-FZ of September 17, 1998 "On the immunoprophylaxis on infection diseases" (as amended by Federal Law No. 368-FZ of

December 21, 2012) and the updated National Immunization Calendar (Order of the Russian Ministry of Health No. 125 of March 21, 2014 “On the National Immunization Calendar and the Calendar of Immunization for Epidemic Indications”), which also recommends providing vaccination to 2-5-year-old children and adults at risk including draftees.

As of now, development and publication of the Federal Clinical Guidelines for Vaccinal Prevention of Pneumococcal Infection for both children and adolescents alike is required.

Experience of the pilot program of cohort HPV13 vaccination in 2013 to 2014 in Saint Petersburg showed that healthcare workers (administrative staff, doctors, mid-rank personnel) need a broadened educational program on pneumococcal infection and practical issues of immunization.

In Russia, the negative attitude to this vaccine has formed in the recent years not only among certain layers of the population, but also among various medical specialists, including pediatricians. Changes of health parameters in infants, including developmental care after children with very low birth weight, result in an unreasonably broad range of contraindications and, therefore, reduced vaccination coverage and reduced level of population-wide protection.

Council participants have noted the need to develop and implement a general pro-vaccine campaign for a large target audience including parents, journalists, teachers, and representatives of religious denominations. The campaign should be organized with the involvement of social psychology experts and be based on the analysis of primary concerns of different social layers with regard to vaccination. The evaluation of PCV13 for effectiveness and tolerance will be a crucial component for the development of such pro-vaccine campaign.

The World Health Organization recommends obtaining epidemiological data on the prevalence of serotypes (both disease-causing and just circulating among healthy carriers) in a country. Such data should be obtained at least 2 years prior to and over 5 years after the implementation of the population-wide immunization against pneumococcal infection. Complex evaluation of vaccination effectiveness should take into consideration direct impact (reduced morbidity and mortality), indirect impact (population-wide protection, decreased prevalence of antibiotic-resistant strains, serotype distribution dynamics), and impact on the severity of clinical manifestations. What is more, it is important to evaluate effectiveness of conjugate pneumococcal vaccines not in general, but with a breakdown into infection types: invasive infections (meningitis, sepsis, severe pneumonia), non-invasive infections (otitis, sinusitis), and carriage.

The following agenda has been proposed to evaluate contribution of PCV13 vaccination to the pediatric healthcare in Russia.

1. Analysis of the morbidity dynamics of pneumonia, diseases of the ear and mastoid process, and meningitis based on the official statistical report forms (forms 2, 12, and 14 of the Federal Statistical Monitoring) with breakdown by age (0 to 1 years, 1 to 14 years, adults) three years prior to and after the population-wide immunization against pneumococcal infection.
2. Continuation of monitoring prevalence of pneumococcus serotypes and dynamics of serotype distribution at the functioning monitoring centers (Research Institute of Pediatric Infections [Federal State Budgetary Institution] of the Federal Biomedical Agency, Scientific Center of Children’s Health [Federal State Budgetary Scientific Institution], Research Institute of Epidemiology [Federal Budgetary Scientific Institution] of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, and the Research Institute of Antimicrobial Chemical Treatment of the Smolensk State Medical Academy [State Budgetary Educational Institution of Higher Professional Education] of the Russian Ministry of Health). The network of centers in non-capital regions should be expanded to cover all federal districts. Monitoring results should be reported annually with due account of reporting expansion and peculiarities of population-wide PCV13 vaccination implementation.
3. The Russian Center for Epidemiological Control over Meningococcal Infection and Septic Bacterial Meningitis of the Central Research Institute [Federal State Scientific Institution] of Epidemiology of Russian Federal Service for Surveillance on Consumer Rights Protection and

Human Wellbeing will continue septic meningitis monitoring in the Russian Federation with due account of long-time average annual morbidity in under-2 children. This value should be determined two years prior and two years after the implementation of the population-wide vaccination against pneumococcal infection (as soon as at least one cohort has been vaccinated according to the 2 + 1 pattern).

4. Pilot case control study based on the corrections to the statistical report forms in the federal districts (one region per district) with the evaluation of general respiratory infection morbidity, extramural pneumonia morbidity, acute otitis media (the most frequently formally reported ENT disease) morbidity requiring hospitalization, and sinusitis morbidity in PCV13-vaccinated and non-vaccinated children with due consideration of immunization coverage and fulfilment of the vaccination pattern. It is also necessary to conduct a study of carriage in organized and non-organized children communities using a unified protocol.

5. Aside from the proposed approaches to the evaluation of PCV13 efficacy, it is recommended to implement monitoring of vaccination tolerance using the standard report forms for post-vaccine responses. The ongoing experience of statistical report usage in the Republic of Kazakhstan since 2010 has confirmed viability of this technique in terms of both understanding the safety and tolerance of the updated infant immunization pattern and providing new information to healthcare workers.

6. Evaluation of economic outcomes of vaccination (on the basis of the obtained data) 2 and 3 years after commencement of the population-wide immunization as compared to the predicted effect [4], as well as analysis of impact factors and prediction of further effects.

7. Adjustment of the proposed approaches to the evaluation of PCV13 immunization effectiveness on the basis of the data analysis carried out after 18-24 months.

The National Immunization Calendar approved by Order of the Russian Ministry of Health No. 125 of March 21, 2015 “On the National Immunization Calendar and the Calendar of Immunization for Epidemic Indications” states that vaccination against pneumococcal infection is indicated to all the children at the age of 2 months, 4.5 months, and 15 months. Paragraph 7 of this order states that “Children who were not vaccinated against pneumococcal infection within the first 6 months of life should be vaccinated twice with a 2-month-long time gap between administrations.” If the vaccination schedule is violated, vaccination should be carried out according to the patterns presented in the pharmaceutical leaflet [5].

At the same time, the number of children at specific risk is relatively small during the infancy, as the risk groups are formed after the age of 12 months [6]. Premature infants should be vaccinated according to the 3 + 1 pattern, i.e. 3 initial doses separated by at least a month, and re-vaccination at the age of 12-15 months [6].

If Prevenar 13 was used for initial vaccination, it is recommended to use it for final administration as well [7]. Prevenar 13 leaflet contains the following immunization patterns (see tb.).

Table. Immunization patterns

Age at initial vaccination	Vaccination pattern	Time gaps and dosage
2-6 months	3 + 1 or 2 + 1	Personal immunization: 3 doses with at least a 4-week-long time gap. The initial dose may be administered within the second month after birth or later. One-time revaccination at the age of 11-15 months Population-wide immunization of children: 2 doses with at least a 8-week-long time gap. One-time revaccination at the age of 11-15 months
7-11 months	2 + 1	2 doses with at least a 4-week-long time gap. One-time revaccination within the second year of life
12-23 months	1 + 1	2 doses with at least a 8-week-long time gap
2-5 years and 50+ years	1	Single administration

Shall the time gap between administrations according to any of the aforementioned vaccination patterns exceed the aforesaid values, no additional Prevenar 13 doses are required [7].

For the purpose of increasing immunization effectiveness and a better exercise of children's right to protection against pneumococcal infections, the Public Coordination Council deems it necessary to recommend catch-up immunization in 2014/2015 in accordance with the patterns contained in the Prevenar 13 leaflet to cover all the children born in 2014 being over 2 months of age at the time of initial vaccination. From the mid-2015, vaccination can be carried out as planned.

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