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Dynamics of *Streptococcus pneumoniae* serotype structure in children for the period 2016–2022

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ABSTRACT

BACKGROUND: The need for microbiological monitoring of the distribution of pneumococcal serotypes is associated with changes that occur during routine immunization of children with pneumococcal vaccines.

AIM: To characterize the changes in the serotype structure of *Streptococcus pneumoniae* obtained from healthy preschool children between 2016 and 2022.

MATERIALS AND METHODS: In total, 1250 healthy children aged <6 years attending kindergartens were examined in multicenter studies (2016–2018 and 2020–2022). Nasopharyngeal pneumococcal isolates (*n*=265) were obtained using the culture method. *S. pneumoniae* serotype was determined using polymerase chain reaction.

RESULTS: Between 2016 and 2018, the prevalence of pneumococcal carriage decreased from 27.3 to 17.3%, and by 2022, it increased to 25.6%. Moreover, the correspondence of *S. pneumoniae* serotypes to the antigenic composition of the 13-valent pneumococcal vaccine decreased from 48.8 to 9.4% and the composition of the 20-valent vaccine from 75.6 to 39.1%. The proportion of "non-vaccine" types of pneumococcus increased from 22% in 2016 to 61% in 2022. Among the "non-vaccine" serotypes/groups, 15AF, 6CD, 23A, and 35F/47F were predominant, and new variants were also discovered: 23B and 35B. The serotypes included in the 13-valent conjugate vaccine were detected among unvaccinated children and were represented by variants 19F, 6A and 6B, 23F. Throughout the observation period, pneumococci of serotypes/groups 15BC, 11AD, and 10A were detected with high frequency.

CONCLUSIONS: Because of the elimination of a significant part of *S. pneumoniae* "vaccine" serotypes in 2016–2022, the concordance of circulating variants with the antigenic composition of pneumococcal conjugate vaccines significantly decreased. In addition, the new types detected with high frequency are not included in existing pneumococcal vaccines, which necessitates the creation of new immunobiological drugs for pneumococcal infection prevention.

Keywords: *Streptococcus pneumoniae*; serotypes; carriage; children.

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Динамика серотипового пейзажа *Streptococcus pneumoniae* у детей за период 2016–2022 годов

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АННОТАЦИЯ

Обоснование. Изменения серотипового пейзажа пневмококков, происходящие на фоне рутинной иммунизации детей пневмококковыми вакцинами, обусловливают необходимость проведения микробиологического мониторинга.

Цель исследования — охарактеризовать изменения серотиповой структуры пневмококков, полученных от здоровых детей дошкольного возраста, в период с 2016 по 2022 год.

Материалы и методы. В ходе многоцентровых исследований (2016–2018 и 2020–2022 годы) обследовано 1250 здоровых детей в возрасте до 6 лет, посещающих детские сады. Назофарингеальные изоляты пневмококка (*n*=265) получены с использованием бактериологического метода. Определение серотипа *Streptococcus pneumoniae* проводилось с помощью полимеразной цепной реакции.

Результаты. В течение 2016–2018 годов распространённость носительства пневмококка снизилась с 27,3 до 17,3%, а к 2022 году вновь возросла (25,6%). При этом соответствие серотипов *S. pneumoniae* антигенному составу 13-валентной пневмококковой вакцины снизилось с 48,8 до 9,4%; составу 20-валентной вакцины — с 75,6 до 39,1%. Удельный вес «невакцинных» типов пневмококка, соответственно, возрос с 22% в 2016 году до 61% в 2022 году. Среди «невакцинных» серотипов / серогрупп преобладали 15AF, 6CD, 23A и 35F/47F; также обнаруживались новые, не встречавшиеся ранее варианты — 23B и 35B. Серотипы, входящие в состав 13-валентной конъюгированной вакцины, выявлялись, как правило, среди непривитых детей и были представлены вариантами 19F, 6A и 6B, 23F. На протяжении всего периода наблюдения с высокой частотой обнаруживались пневмококки серотипов / серогрупп 15BC, 11AD и 10A.

Заключение. В течение 2016–2022 годов вследствие элиминации значительной части «вакцинных» серотипов *S. pneumoniae* произошло существенное снижение соответствия циркулирующих вариантов возбудителя антигенному составу применяемых конъюгированных вакцин. При этом новые, выявляющиеся с высокой частотой сероварианты не входят в состав существующих пневмококковых вакцин, что обусловливает необходимость создания новых иммунобиологических препаратов.

Ключевые слова: *Streptococcus pneumoniae*; серотипы; носительство; дети.

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ЭКО•ВЕКТОР

BACKGROUND

Pneumococcal infection represents a group of ubiquitous anthroponotic diseases with aerosol transmission of the causative agent, *Streptococcus pneumoniae*. The clinical manifestations of these diseases range from asymptomatic to invasive, generalized forms of infection, which may be highly fatal, particularly in cases of meningitis and bacteremia [1].

Currently, there are over 100 serovariants of *S. pneumoniae*, differing in the chemical structure of the polysaccharide capsular antigen. The spectrum of epidemiologically relevant serotypes is characterized by variability [2]. A significant factor contributing to the prevalence and etiological significance of certain serotypes is immunization of children within the national schedule of preventive vaccinations with conjugate vaccines containing polysaccharides of *S. pneumoniae* capsule. These polysaccharides play an important role in colonization, virulence, and induction of serotype-specific immune response in the human body [3–6]. The 13-valent conjugate vaccine (PCV13) has been used in the Russian Federation since 2015 as a component of the national schedule of preventive vaccinations and the schedule of preventive vaccinations for epidemic indications. The vaccine contains capsular polysaccharides of pneumococci of the following serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. Each of these serotypes was individually conjugated to the carrier protein CRM197 [7]. Given the prolonged use of PCV13 for routine immunization of both children and adults at risk, it seems reasonable to suggest significant changes in the serotype composition of pneumococci over the past period.

AIM

To assess the prevalence and serotypes of *S. pneumoniae* isolates obtained from preschool children, the primary reservoir for the pathogen, over a period from 2016 to 2022.

MATERIALS AND METHODS

Study design

The SAPIENS [8] international, multicenter, prospective study examined 1,250 healthy children from organized groups in Krasnoyarsk (nursery schools) aged up to 6 years. The children were selected randomly, with a sampling error of 2.75% and 95% confidence level.

Nasopharyngeal swabs were performed once using probe-tampons with Amies liquid transport medium. *S. pneumoniae* was cultured on Colombian agar with addition of ram's blood (5%), nalidixic acid, and colistin (ready-to-use agar, Sredoff LLC) under capnophilic conditions using Campylogas generator bags. Pneumococci were identified using a combination of cultural properties, tests with optochin and bile, and polymerase chain reaction (PCR) of cpsA and lytA genes [9]. Serotypes were determined using multiplex PCR [10].

Eligibility criteria

Inclusion criteria: permanent attendance of a child in an organized group (nursery school), age 0–6 years, informed consent signed by a parent or legal guardian, and no signs of infectious diseases at the time of examination.

Non-inclusion criteria: failure to meet the above age criteria and refusal of parents or guardians to sign the informed consent form.

Exclusion criteria: signs of acute infectious disease at the time of examination.

Study duration

The first phase of the study was conducted between 2020 and 2022, while the second phase was conducted in 2022.

Ethical review

The study was approved by the Ethics Committee of the Krasnoyarsk State Medical University named after Professor V.F. Voyno-Yasenetsky (Protocol No. 69/2016 dated April 28, 2016) and the Independent Interdisciplinary Committee for Ethical Review of Clinical Trials (Protocol No. 1 dated January 17, 2020).

Statistical analysis

Statistical analysis of the obtained results was performed using the STATISTICA10.0.1011 software package. Qualitative attributes were calculated as percentages, whereas quantitative data were calculated as mean values and standard deviations. Distribution of the attributes was evaluated using the Shapiro–Wilk test. If the normality of distribution was confirmed, the Student's *t*-test was used to compare the groups. If normality was not confirmed, the Mann–Whitney test (for quantitative attributes) or the chi-square test (χ^2; for qualitative attributes) was used. The level of statistical significance of the differences was considered to be $p < 0.05$.

RESULTS

Participant characteristics

The mean age of the subjects was 4.12 ± 0.97 years. When the subjects were divided into groups according to the study periods (years), the children examined in 2022 were found to be younger than those examined earlier (Table 1). Additionally, an increase in the number and proportion of children vaccinated in accordance with the schedule was noted during the analyzed period, accompanied by a simultaneous decrease in the proportion of non-vaccinated and once-vaccinated children. Accordingly, in 2022, the majority of children (68.8%) received three doses of the pneumococcal vaccine in accordance with the national immunization schedule, and the percentage of non-vaccinated children was 4.8% (see Table 1).

Table 1. Characteristics of examined children by age, gender, vaccination status, and prevalence of *Streptococcus pneumoniae* carriage

Parameter	2016	2017	2018	2022	Significance of differences
Number examined	150	450	400	250	–
Mean age	4.25 ± 1.00	4.09 ± 0.96	4.19 ± 0.87	3.78 ± 1.06	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
Gender, *n*/%	Male: 84/56 Female: 66/44	Male: 244/54.22 Female: 206/45.78	Male: 215/53.75 Female: 185/46.25	Male: 133/53.20 Female: 117/46.80	Not found
Triple-vaccinated, *n*/%	1/0.67	6/1.33	12/3.00	172/68.80	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
Double-vaccinated, *n*/%	2/1.33	26/5.78	25/6.25	51/20.40	$p^{2,1} = 0.0250$ $p^{3,1} = 0.0170$ $p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
Once-vaccinated, *n*/%	35/23.33	120/26.67	131/32.75	15/6.00	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
Non-vaccinated, *n*/%	112/74.67	298/66.22	232/58.00	12/4.80	$p^{3,1} = 0.0003$ $p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
S. pneumoniae culture isolated, *n*/%	41/27.33	91/20.22	69/17.25	64/25.60	$p^{3,1} = 0.0080$ $p^{4,3} = 0.0100$

Primary findings

The prevalence of pneumococcal carriage, having decreased by 10% by 2018, increased by 8.3% by 2022, amounting to 25.6% (see Table 1).

Analysis of compliance of circulating *S. pneumoniae* serotypes with the antigen composition of pneumococcal vaccines showed that in 2022, only 9.4% of isolated cultures belonged to the serotypes included in PCV13, used for routine immunization of infants and toddlers (Table 2). Additionally, a progressive reduction in serotype overlap between PCV20 and PPSV23 (the 23-valent pneumococcal polysaccharide vaccine recommended for children over 2 years of age and adults) was observed, accompanied by a simultaneous increase in the proportion of *S. pneumoniae* variants not included in available vaccines, commonly referred to as "non-vaccine" (see Table 2).

A detailed analysis of *S. pneumoniae* serotypes revealed that during the period between 2016 and 2018, the most prevalent variants were the vaccine serotypes such as 19F, 6A, 6B, and 23F. However, in 2022, these serotypes were only identified in single cases (Fig. 1). The circulation of pneumococci belonging to serogroups 11 and 15 (11AD and 15BC), as well as serotype 10A, was observed throughout the analyzed period. Remarkably, a significant increase in the proportion of non-vaccine serotypes/serogroups, including 15AF, 6CD, 23A, and 35F/47F and the emergence of novel variants, such as 23B and 35B, was revealed in 2022 (see Fig. 1).

A study of *S. pneumoniae* serotypes by vaccination status showed that serotypes included in PCV13 were detected in 5.8% of triple-vaccinated children. The most frequently detected serotypes were 6A, 6B, and 19A (Table 3). In nearly half of the cases (45.5%), the carriers of PCV13 serotypes did not comply with the recommended schedule of vaccination and revaccination, including late start of vaccination and non-compliance with the recommended intervals between vaccinations. The serotypes included in PCV15 and PCV20, as well as the non-vaccine serotypes, were primarily detected in the 2022 cohort (see Table 3). The overall frequency of their detection in triple-vaccinated children was 22.5%.

No PCV13 serotypes were identified in double-vaccinated children. PCV20 serotypes were detected in 13.5% of cases, along with non-vaccine serotypes (see Table 3).

Table 2. Correspondence of isolated *Streptococcus pneumoniae* cultures to the serotype composition of pneumococcal vaccines

Serotypes	2016	2017	2018	2022	Significance of differences
Vaccine serotypes, *n*/%:					
PCV13	20/48.78	37/41.11	31/44.93	6/9.38	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
PCV15	20/48.78	39/43.33	33/47.83	8/12.50	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0000$
PCV20	31/75.61	67/74.44	45/65.21	25/39.06	$p^{4,1} = 0.0002$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0025$
PPSV23	32/78.05	70/77.77	45/65.21	25/39.06	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0025$
Non-vaccine serotypes, *n*/%	9/21.95	21/23.08	24/34.78	39/60.94	$p^{4,1} = 0.0000$ $p^{4,2} = 0.0000$ $p^{4,3} = 0.0025$

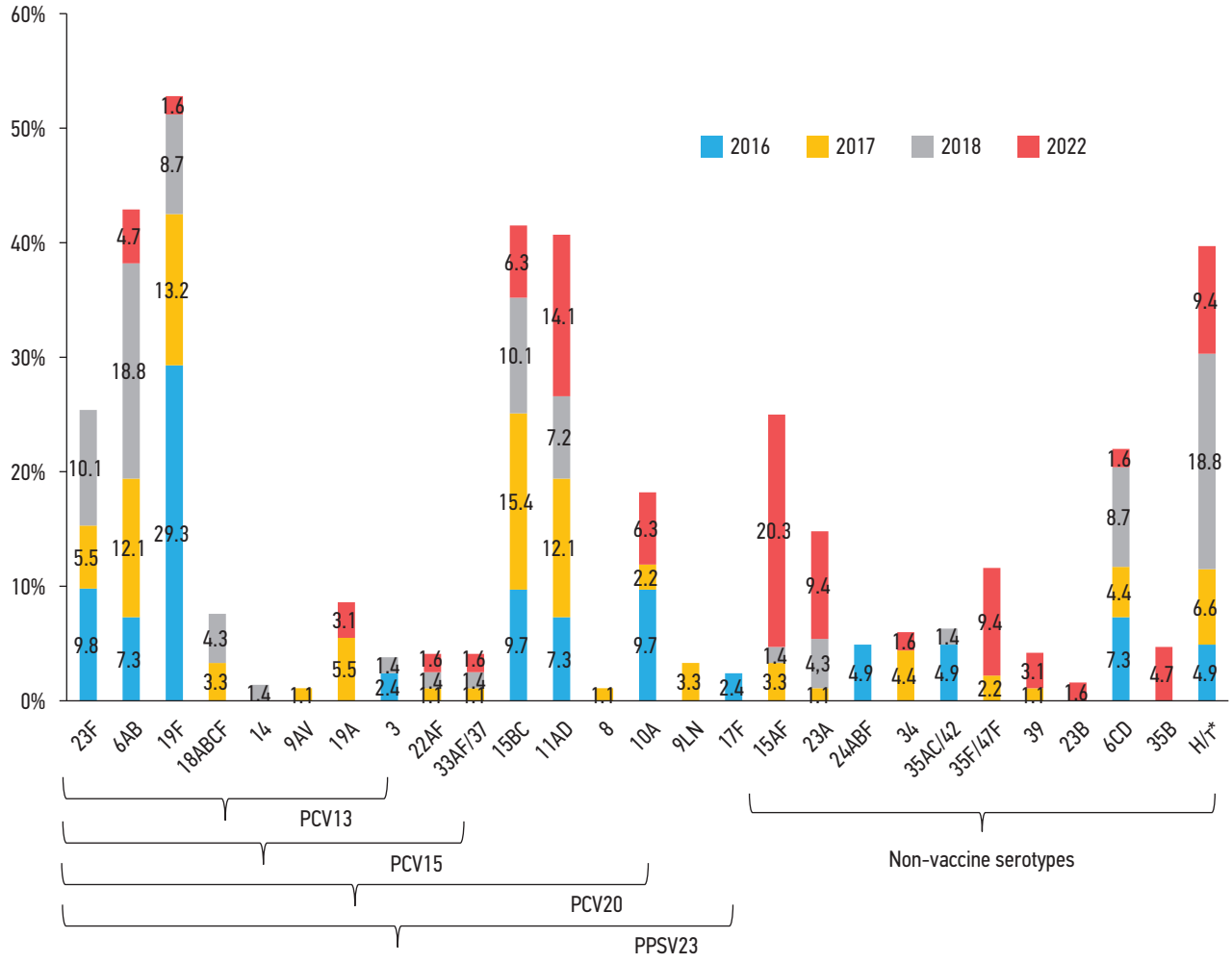

Fig. 1. Dynamics of *Streptococcus pneumoniae* serotype distribution in healthy preschool children in 2016–2022. *H/т — strains which serotype has not been determined (not included in the standard serotyping scheme).

Table 3. Distribution of *Streptococcus pneumoniae* serotypes in children by vaccination status (%)

Streptococcus pneumoniae serotype	Triple-vaccinated				Double-vaccinated				Once-vaccinated				Non-vaccinated			
	2016 *n*=1	2017 *n*=6	2018 *n*=12	2022 *n*=172	2016 *n*=2	2017 *n*=26	2018 *n*=25	2022 *n*=51	2016 *n*=35	2017 *n*=120	2018 *n*=131	2022 *n*=15	2016 *n*=112	2017 *n*=298	2018 *n*=232	2022 *n*=12
PCV13 serotypes																
23F	–	–	–	–	–	–	–	–	–	–	0.8	–	3.6	1.7	2.6	–
6AB	–	16.7	16.7	1.7	–	–	–	–	–	1.6	0.8	–	2.7	2.7	4.3	–
19F	–	–	–	0.6	–	–	–	–	5.7	–	0.8	–	8.9	4.0	2.2	–
18ABCF	–	16.7	–	–	–	–	–	–	–	–	1.5	–	–	0.7	0.4	–
14	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0.4	–
9AV	–	–	–	–	–	–	–	–	–	–	–	–	–	0.3	–	–
19A	–	16.7	–	1.2	–	–	–	–	–	–	–	–	–	1.3	–	–
3	–	–	–	–	–	–	–	–	–	–	–	–	0.9	–	0.4	–
Total	0.0	50.1	16.7	3.5	0.0	0.0	0.0	0.0	5.7	1.6	3.9	0.0	16.1	10.7	10.3	0.0
Additional PCV15 serotypes																
22AF	–	–	–	0.6	–	–	–	–	–	0.8	–	–	–	–	0.4	–
33AF/37	–	–	–	0.6	–	–	–	–	–	0.8	–	–	–	–	0.4	–
Total	0.0	0.0	0.0	1.2	0.0	0.0	0.0	0.0	0.0	1.6	0.0	0.0	0.0	0.0	0.8	0.0
Additional PCV20 serotypes																
15BC	–	–	–	1.7	–	–	4.0	2.0	–	4.2	2.3	–	3.6	3.0	1.3	–
11AD	–	–	–	4.7	–	–	4.0	–	5.7	1.6	0.8	–	0.9	3.0	1.3	8.3
8	–	–	–	–	–	–	–	–	–	–	–	–	–	0.3	–	–
10A	–	–	–	0.6	–	–	–	3.9	–	–	–	–	3.6	0.7	–	8.3
Total	0.0	0.0	0.0	7.0	0.0	0.0	8.0	5.9	5.7	5.8	3.1	0.0	8.1	7.0	2.6	16.6
Additional PPSV23 serotypes																
9LN	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
17F	–	–	–	–	–	–	–	–	–	–	–	–	0.9	1.0	–	–
Total	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.9	1.0	0.0	0.0
Non-vaccine serotypes																
15AF	–	–	–	4.7	–	3.8	–	5.9	–	0.8	–	–	–	0.3	0.4	16.6
23A	–	–	–	3.5	–	–	–	–	–	–	–	–	–	0.3	1.3	–
24ABF	–	–	–	–	–	–	–	–	2.9	–	–	–	0.9	–	–	–
34	–	–	–	–	–	–	–	–	–	3.3	–	6.7	–	–	–	–
35AC/42	–	–	–	–	–	–	–	–	2.9	–	0.8	–	0.9	–	–	–
35F/47F	–	–	–	2.3	–	3.8	–	2.0	–	0.8	–	6.7	–	–	–	–
39	–	16.7	–	–	–	–	–	3.9	–	–	–	–	–	–	–	–
23B	–	–	–	0.6	–	–	–	–	–	–	–	–	–	–	–	–
6CD	–	–	–	0.6	–	–	–	–	2.9	1.6	0.8	–	1.8	0.7	2.2	–
35B	–	–	–	1.7	–	–	–	–	–	-	–	–	–	–	–	–
Non-typeable	–	–	8.3	2.3	–	–	–	2.0	–	–	3.8	6.7	1.8	2.0	3.0	–
Total	0.0	16.7	8.3	15.7	0.0	7.6	0.0	13.8	8.7	6.7	5.4	20.1	5.4	3.3	6.9	16.6

In the cohort of once-vaccinated children, the prevalence of PCV13 serotypes was 3%, the main serotypes of *S. pneumoniae* were 6A, 6B, and 19F. Furthermore, additional types included in PCV15 and PCV20, as well as non-vaccine types, were identified in 12% of cases (see Table 3).

The highest detection rate for PCV13 serotypes (11.3%) was observed in the group of non-vaccinated children, with a notable diversity of serotypes compared to other groups. Additional and non-vaccine types of pneumococcus were detected in 12.4% of cases, with the highest diversity observed in this group (see Table 3).

Notably, 4 of 13 serotypes included in PCV13 (serotypes 1, 4, 5, and 7F) were not detected in the examined children. Additionally, the serotypes/serogroups included in PCV15 (22AF and 33AF/37), as well as PCV23 (9LN and 17F), were rarely detected. Conversely, there was a high detection rate of non-vaccine *S. pneumoniae* serovariants, including 15AF, 23A, 34, 35F/47F, and 6CD.

DISCUSSION

Summary of the primary study results

Over the period between 2016 and 2022, changes in the serotype structure of *S. pneumoniae* were observed among healthy, organized bacterial carriers under 6 years of age. There was a significant decrease in the proportion of serovariants included in available pneumococcal vaccines (PCV13, PCV15, PCV20, and PPSV23), with a simultaneous increase in the proportion of non-vaccine isolates. The prevalence of pneumococcal carriage exhibited a decrease from 27.3% to 17.3% between 2016 and 2018, followed by an increase to 25.6% by 2022.

Discussion of the primary study results

Microbiological monitoring of the prevalence and serotype spectrum of circulating *S. pneumoniae* strains is needed both for predicting the effectiveness of immunization and for monitoring the ongoing "serotype substitution" [11]. A typical example of "serotype substitution" is the increase in the incidence of invasive forms of pneumococcal infection caused by serotype 19A in children vaccinated with PCV7 and PCV10 [12]. Moreover, the release of PCV13 resulted in the global dissemination of non-PCV13 pneumococcal serovariants, including 22F, 12F, 33F, 24F, 15C, 15B, 23B, 10A, and 38 [13]. Recent studies conducted in Asian countries revealed the prevalence of non-PCV13 and non-vaccine types *of S. pneumoniae* in invasive (22F, 11A, 10A, 34, 23A, and 35B) [14] and non-invasive (15BC, 11AD, 10A, 23A, 34, 15AF, 21, 35B, 31, and 33FA/37) [4, 15] clinical forms of pneumococcal infection.

The studies conducted in various regions of the Russian Federation showed that the main serotypes/serogroups of *S. pneumoniae* in nasopharyngeal carriage in children were 15AF, 6, 11AD, 23A, 9LN, and 16F in recent years [16, 17]. The proportion of children with PCV13 serotypes decreased from 59.2% in 2016–2018 to 24.8% in 2020–2023, and the proportion with PCV20 decreased from 73.7% to 46.4%, respectively [16].

Our data indicate a significant decline in concordance of detected *S. pneumoniae* serotypes with the antigenic composition of PCV13, from 48.8% in 2016 [15] to 9.4% in 2022. Moreover, the most frequent non-PCV13 serotypes/serogroups among healthy organized children in Krasnoyarsk were 15BC, 11AD, and 10A. The main non-vaccine serotypes were 15AF, 6CD, 23A, and 35F/47F. The primary reservoir for non-PCV13 and non-vaccine types was children who received three doses in accordance with the national immunization schedule.

The serotype concordance of detected *S. pneumoniae* isolates with the PCV20 composition decreased by 36.5% (from 75.6% in 2016 to 39.1% in 2022).

CONCLUSION

Thus, the obtained data show that the circulating serotypes of *S. pneumoniae* do not correspond to the antigenic composition of the currently available pneumococcal conjugate vaccines in most cases. This discrepancy may result in increased incidence of various clinical forms of infection caused by non-vaccine pneumococcal serovariants. For more complete information, monitoring of serotypes and epidemic clones of *S. pneumoniae* is needed both at the regional and national levels.

ADDITIONAL INFORMATION

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REFERENCES

1. Avdeev SN, Alyeva MH, Baranov AA, et al. Federal Clinical Guidelines on Vaccination of pneumococcal infection in children and adults. *Russian Journal of Preventive Medicine.* 2023;26(9-2):3–23. (In Russ). doi: 10.17116/profmed2023260923

2. Ganaie F, Maruhn K, Li C, et al. Structural, genetic, and serological elucidation of Streptococcus pneumoniae serogroup 24 serotypes: discovery of a new serotype, 24C, with a variable capsule structure. *J Clin Microbiol.* 2021;59(7):e0054021. doi: 10.1128/JCM.00540-21

3. Huang H, Lin CY, Chiu NC, et al. Antimicrobial susceptibility and serotype replacement of Streptococcus pneumoniae in children before and after PCV13 introduction in Taiwan. *J Microbiol Immunol Infect.* 2023;56(2):299–310. doi: 10.1016/j.jmii.2022.08.018

4. Yokota SI, Tsukamoto N, Sato T, et al. Serotype replacement and an increase in non-encapsulated isolates among community-acquired infections of Streptococcus pneumoniae during post-vaccine era in Japan. *IJID Reg.* 2023;8:105–110. doi: 10.1016/j.ijregi.2023.07.002

5. Janssens E, Flamaing J, Vandermeulen C, et al. The 20-valent pneumococcal conjugate vaccine (PCV20): expected added value. *Acta Clin Belg.* 2023;78(1):78–86. doi: 10.1080/17843286.2022.2039865

6. Abdul Rahman NA, Mohd Desa MN, Masri SN, et al. The molecular approaches and challenges of Streptococcus pneumoniae serotyping for epidemiological surveillance in the Vaccine Era. *Pol J Microbiol.* 2023;72(2):103–115. doi: 10.33073/pjm-2023-023

7. Prevenar 13 (pneumococcal polysaccharide conjugate adsorbed vaccine, thirteen-valent) (Prevenar). *Register of Medicines of Russia* [Internet]. Available at: https://www.rlsnet.ru/drugs/prevenar-13-vakcina-pnevmokokkovaya-polisaxaridnaya-konyugirovannaya-adsorbirovannaya-trinadcativalentnaya-42222 (In Russ).

8. Sidorenko S, Rennert W, Lobzin Y, et al. Multicenter study of serotype distribution of Streptococcus pneumoniae nasopharyngeal isolates from healthy children in the Russian Federation after introduction of PCV13 into the National Vaccination Calendar. *Diag Microbiol Infect Dis.* 2020;96(1):114914. doi: 10.1016/j.diagmicrobio.2019.114914

9. Laboratory diagnosis of community-acquired pneumonia of pneumococcal etiology: Guidelines. Moscow: Federal Service for Supervision of Consumer Rights Protection and Human Wellbeing; 2017. 64 p. (In Russ).

10. Streptococcus Laboratory. *Centers for Disease Control and Prevention* [Internet]. Available from: https://www.cdc.gov/streplab/pneumococcus/resources.html

11. John J. The remaining challenges to laboratory-based surveillance of invasive pneumococcal disease. *Indian Pediatr.* 2015;52(3):199–200. doi: 10.1007/s13312-015-0606-1

12. Beall BW, Gertz RE, Hulkower RL, et al. Shifting genetic structure of invasive serotype 19A pneumococci in the United States. *J Infect Dis.* 2011;203(10):1360–1368. doi: 10.1093/infdis/jir052

13. Balsells E, Guillot L, Nair H, Kyaw MH. Serotype distribution of Streptococcus pneumoniae causing invasive disease in children in the post-PCV era: A systematic review and meta-analysis. *PLoS One.* 2017;12(5):e0177113. doi: 10.1371/journal.pone.0177113

14. Kim GR, Kim EY, Kim SH, et al. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae causing invasive pneumococcal disease in Korea between 2017 and 2019 after introduction of the 13-valent pneumococcal conjugate vaccine. *Ann Lab Med.* 2023;43(1):45–54. doi: 10.3343/alm.2023.43.1.45

15. Protasova IN, Sidorenko SV, Feldblum IV, Bakhareva NV. Epidemiology of Streptococcus pneumoniae serotypes in children before and after pneumococcal vaccination. *Fundamental and Clinical Medicine.* 2022;6(4):54–66. (In Russ). doi: 10.23946/2500-0764-2021-6-4-54-66

16. Sidorenko SV, Lobzin YuV, Rennert W, et al. Changes in serotype distribution of Streptococcus pneumoniae circulating among children in the Russian Federation after 13-valent pneumococcal conjugate vaccine introduction. *Journal Infectology.* 2023; 15(2): 6–13. (In Russ). doi: 10.22625/2072-6732-2023-15-2-6-13

17. Tyurin YuA, Bayazitova LT, Isaeva GSh. Molecular genetic identification and typing of pneumococci in biosamples obtained from organized children in the Republic of Tatarstan. *Bacteriology.* 2021;6(3):71. (In Russ). EDN: AJQXAC

СПИСОК ЛИТЕРАТУРЫ

1. Авдеев С.Н., Алыева М.Х., Баранов А.А., и др. Вакцинопрофилактика пневмококковой инфекции у детей и взрослых. Методические рекомендации // Профилактическая медицина. 2023. Т. 26, № 9-2. С. 3–23. doi: 10.17116/profmed2023260923

2. Ganaie F., Maruhn K., Li C., et al. Structural, genetic, and serological elucidation of Streptococcus pneumoniae serogroup 24 serotypes: discovery of a new serotype, 24C, with a variable capsule structure // J Clin Microbiol. 2021. Vol. 59, N 7. P. e0054021. doi: 10.1128/JCM.00540-21

3. Huang H., Lin C.-Y., Chiu N.-C., et al. Antimicrobial susceptibility and serotype replacement of Streptococcus pneumoniae in children before and after PCV13 introduction in Taiwan // J Microbiol Immunol Infect. 2023. Vol. 56, N 2. P. 299–310. doi: 10.1016/j.jmii.2022.08.018

4. Yokota S.-I., Tsukamoto N., Sato T., et al. Serotype replacement and an increase in non-encapsulated isolates among community-acquired infections of Streptococcus pneumoniae during post-vaccine era in Japan // IJID Reg. 2023. Vol. 8. P. 105–110. doi: 10.1016/j.ijregi.2023.07.002

5. Janssens E., Flamaing J., Vandermeulen C., et al. The 20-valent pneumococcal conjugate vaccine (PCV20): expected added value // Acta Clin Belg. 2023. Vol. 78, N 1. P. 78–86. doi: 10.1080/17843286.2022.2039865

6. Abdul Rahman N.A., Mohd Desa M.N., Masri S.N., et al. The molecular approaches and challenges of Streptococcus pneumoniae serotyping for epidemiological surveillance in the Vaccine Era // Pol J Microbiol. 2023. Vol. 72, N 2. P. 103–115. doi: 10.33073/pjm-2023-023

7. Превенар 13 (вакцина пневмококковая полисахаридная конъюгированная адсорбированная, тринадцативалентная) (Prevenar) // Регистр лекарственных средств России [интернет]. Режим доступа: https://www.rlsnet.ru/drugs/prevenar-13-vakcina-pnevmokokkovaya-polisaxaridnaya-konyugirovannaya-adsorbirovannaya-trinadcativalentnaya-42222

8. Sidorenko S., Rennert W., Lobzin Y., et al. Multicenter study of serotype distribution of Streptococcus pneumoniae nasopharyngeal isolates from healthy children in the Russian Federation after introduction of PCV13 into the National Vaccination Calendar // Diagn Microbiol Infect Dis. 2020. Vol. 96, N 1. P. 114914. doi: 10.1016/j.diagmicrobio.2019.114914
9. Лабораторная диагностика внебольничной пневмонии пневмококковой этиологии: Методические рекомендации. Москва: Федеральная служба по надзору в сфере защиты прав потребителей и благополучия человека, 2017. 64 с.
10. Streptococcus Laboratory // Centers for Disease Control and Prevention [интернет]. Режим доступа: https://www.cdc.gov/streplab/pneumococcus/resources.html
11. John J. The remaining challenges to laboratory-based surveillance of invasive pneumococcal disease // Indian Pediatr. 2015. Vol. 52, N 3. P. 199–200. doi: 10.1007/s13312-015-0606-1
12. Beall B.W., Gertz R.E., Hulkower R.L., et al. Shifting genetic structure of invasive serotype 19A pneumococci in the United States // J Infect Dis. 2011. Vol. 203, N 10. P. 1360–1368. doi: 10.1093/infdis/jir052
13. Balsells E., Guillot L., Nair H., Kyaw M.H. Serotype distribution of Streptococcus pneumoniae causing invasive disease in children in the post-PCV era: A systematic review and meta-analysis // PLoS One. 2017. Vol. 12, N 5. P. e0177113. doi: 10.1371/journal.pone.0177113
14. Kim G.R., Kim E.-Y., Kim S.H., et al. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae causing invasive pneumococcal disease in Korea between 2017 and 2019 after introduction of the 13-valent pneumococcal conjugate vaccine // Ann Lab Med. 2023. Vol. 43, N 1. P. 45–54. doi: 10.3343/alm.2023.43.1.45
15. Протасова И.Н., Сидоренко С.В., Фельдблюм И.В., Бахарева Н.В. Эпидемиология серотипов Streptococcus pneumoniae у детей на фоне универсальной вакцинопрофилактики пневмококковой инфекции // Фундаментальная и клиническая медицина. 2022. Т. 6, № 4. С. 54–66. doi: 10.23946/2500-0764-2021-6-4-54-66
16. Сидоренко С.В., Лобзин Ю.В., Реннерт В., и др. Изменения в серотиповом составе Streptococcus pneumoniae, циркулирующих среди детей в Российской Федерации, после внедрения 13-валентной пневмококковой конъюгированной вакцины // Журнал инфектологии. 2023. Т. 15, № 2. С. 6–13. doi: 10.22625/2072-6732-2023-15-2-6-13
17. Тюрин Ю.А., Баязитова Л.Т., Исаева Г.Ш. Молекулярно-генетическая идентификация и типирование пневмококков в биообразцах, полученных от организованных детей в Республике Татарстан // Бактериология. 2021. Т. 6, № 3. С. 71. EDN: AJQXAC

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