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INFLUENCE OF VACCINE PREVENTION ON THE SPREAD AND SEROTYPE COMPOSITION OF *STREPTOCOCCUS PNEUMONIAE* IN MILITARY COLLECTIVES

I.S. Mukhachev[1]*, A.S. Blagonravova[2], I.V. Feldblyum[2], M.Kh. Alyeva[2]

[1]1026 Center of State Sanitary and Epidemiological Surveillance, Yekaterinburg,
[2] E.A. Wagner Perm State Medical University, Russian Federation

ВЛИЯНИЕ ВАКЦИНОПРОФИЛАКТИКИ НА РАСПРОСТРАНЕННОСТЬ И СЕРОТИПОВОЙ СОСТАВ *STREPTOCOCCUS PNEUMONIAE* В ВОИНСКИХ КОЛЛЕКТИВАХ

И.С. Мухачев[1]*, А.С. Благонравова[2], И.В. Фельдблюм[2], М.Х. Алыева[2]

[1]1026 центр государственного санитарно-эпидемиологического надзора, г. Екатеринбург,
[2]Пермский государственный медицинский университет имени академика Е.А. Вагнера, Российская Федерация

Objective. To study the effect of pneumococcal infection vaccination on the spread and serotype composition of *S. pneumoniae* in military personnel.

Materials and methods. The study was conducted in a military unit of Sverdlovsk region, 369 military men took part in it. Determination of the frequency and serotype of *S. pneumoniae* was carried out on admission and 1.5 months after stay in the military collective using the multiplex PCR method.

Results. After 1.5 months of stay in the military collective, a significant activation of pneumococcal circulation was established ($\chi^2_{McNemar} = 24.038$; $p < 0.001$). The risk of *S. pneumoniae* infection in unvaccinated military personnel was 1.39 times higher than in the vaccinated ones (*RR* = 1.39; 95 % *CI* 1.209–1.596). In the

tel. +7 912 260 61 31
e-mail: faust.78@mail.ru
[Mukhachev I.S. (*contact person) – Head of 1026 Center of State Sanitary and Epidemiological Surveillance, Chief State Health Officer of Central Military District, ORCID: 0000-0003-2669-7144; Blagonravova A.S. – MD, PhD, Acting Rector, ORCID: 0000-0002-1467-049X; Feldblyum I.V. – MD, PhD, Professor, the Head of the Department of Epidemiology, ORCID: 0000-0003-4398-5703; Alyeva M.Kh. – Candidate of Medical Sciences, Associate Professor of the Department of Epidemiology, ORCID: 0000-0002-4467-4707].

тел.: +7 912 260 61 31
e-mail: faust.78@mail.ru
[Мухачев И.С. (*контактное лицо) – начальник – главный государственный санитарный врач ЦВО, ORCID: 0000-0003-2669-7144; Благонравова А.С. – исполняющая обязанности ректора, доктор медицинских наук, ORCID: 0000-0002-1467-049X; Фельдблюм И.В. – заведующая кафедрой эпидемиологии, доктор медицинских наук, профессор, ORCID: 0000-0003-4398-5703; Алыева М.Х. – доцент кафедры эпидемиологии, кандидат медицинских наук, ORCID: 0000-0002-4467-4707].

group of unvaccinated military personnel, the frequency of occurrence of vaccine serotypes was 2.6 times higher than in vaccinated ones ($\chi^2 = 6.25$; $p = 0.01$).
Conclusions. The proactive influence of immunization against pneumococcal infection on the spread and serotype composition of *S. pneumoniae* has been determined: a low spread of vaccine serotypes and a predominance of non-typeable serotypes have been revealed among vaccinated individuals.
Keywords. Military personnel, carriage, *S. pneumoniae*, serotype landscape, vaccinated and unvaccinated.

Цель. Изучение влияния вакцинации против пневмококковой инфекции на распространенность и серотиповой состав *S. pneumoniae* у военнослужащих.
Материалы и методы. Исследование проведено среди 369 военнослужащих воинской части Свердловской области. Определение частоты и серотипа *S. pneumoniae* проведено при поступлении и через 1,5 месяца пребывания в воинском коллективе с использованием метода мультиплексной ПЦР.
Результаты. Через 1,5 месяца пребывания военнослужащих в воинском коллективе установлена достоверная активизация циркуляции пневмококка ($\chi^2_{McNemar} = 24{,}038$; $p < 0{,}001$). Риск инфицирования невакцинированных военнослужащих *S. pneumoniae* был в 1,39 раза выше по сравнению с вакцинированными (*RR* = 1,39; 95 % ДИ 1,209–1,596). В группе непривитых военнослужащих частота встречаемости вакцинных серотипов была в 2,6 раза выше, чем у привитых ($\chi^2 = 6{,}25$; $p = 0{,}01$).
Выводы. Установлено упреждающее влияние иммунизации против пневмококковой инфекции на распространенность и серотиповой пейзаж *S. pneumoniae*: Выявлена низкая распространенность среди привитых вакцинных серотипов и преобладание нетипируемых.
Ключевые слова. Военнослужащие, носительство, *S. pneumoniae*, серотиповой пейзаж, привитые и непривитые.

INTRODUCTION

Respiratory diseases (RD) have long remained a pressing problem for the medical service of the Russian Armed Forces, annually occupying priority positions in the structure of morbidity among military personnel serving both conscript and contract [1–3].

Conscripted military personnel are at the highest risk of developing diseases, which is due to a change in their usual lifestyle in connection with conscription and the need to adapt to new working, living and nutritional conditions [4; 5].

In 2022, the incidence of RD among conscripted military personnel, compared to 2021, increased by 36.8 % (in 2022 – 698 ‰, in 2021 – 510 ‰). In the RD structure the share of acute respiratory infections was 74 % (432 ‰), acute bronchitis – 7.4 % (51.2 ‰), acute tonsillitis – 8 % (45.3 ‰), community-acquired pneumonia – 9.8 % (38.8 ‰), influenza – 0.1 % (0.8 ‰) [6].

The main reasons for the RD emergence and spread are: the introduction of infection into military groups with young recruits from various territories of the Russian Federation; seasonal increase in incidence in the autumn-winter and spring-summer periods, associated with the "mixing" of military personnel during the reception of young recruits and the recirculation of the pathogen among renewed military teams; staffing training military units in a short time with a significant number of personnel [3; 7].

At the same time, it should be noted that recruits arriving in the troops must have immunity against infections relevant to the troops [8], which is provided for by current regulatory documents. Persons sub-

ject to conscription for military service are vaccinated against influenza as part of the National Immunisation Schedule, as well as immunization against varicella, meningococcal and pneumococcal diseases as part of the Preventive Vaccinations Schedule for Epidemic Indications[1].

Pneumococcal Disease (PD), as is known, is represented not only by manifest, but also by non-manifest forms of infection. The impact of immunization of military personnel on the incidence of community-acquired pneumonia is widely discussed in domestic and foreign literature; the importance of military personnel immunization in reducing the incidence of respiratory diseases has been proven. Meanwhile, studies on the effect of vaccination on the prevalence of *S. pneumoniae* in military groups are few, and the results are very contradictory.

In light of the above, *the purpose of the study* is to research the effect of vaccination against pneumococcal disease on the prevalence and serotype landscape of *S. pneumoniae* in military personnel.

MATERIALS AND METHODS

The study was conducted from 2021 to 2023 in the military unit of the Sverdlovsk region. 369 military men aged 18–21 years were examined, including 38.5 % (142) vaccinated with the 23-valent pneumococcal polysaccharide vaccine (PPV23) and 61.5 % (227) of those not vaccinated before conscription.

The study of *S. pneumoniae* carriage included two stages. Biomaterial was collected from the mucous membranes of the nasal cavity and nasopharynx from conscripts upon arrival at the military unit and again after 1.5 months of being in the military collective in order to detect *S. pneumoniae* and determine its serotype[2].

Serotyping was carried out using multiplex PCR using 21 leading serotypes/serogroups of *S. pneumoniae*, including 18 serotypes of the PPV23 vaccine.

Statistical processing of the results was carried out by comparing data for related samples using the nonparametric McNemar test, and for unrelated samples using the Pearson χ^2 criterion. Differences were considered significant at $p < 0{,}05$. Based on the results of the cohort study, the relative risk (*RR*) was determined using the generally accepted method [9].

Statistical processing of the obtained data was carried out using Microsoft Excel 2010, Past 4.14, and an online calculator (https://medstatistic.ru/calculators.html).

RESULTS AND DISCUSSION

Upon arrival at the military unit, carriage of pneumococcus was detected in 12.5 % (46) of the examined conscripts.

[1] On approval of the National Immunisation Schedule, the Preventive Vaccinations Schedule for Epidemic Indications and the Procedure for Carrying out Preventive Vaccinations: Order of the Ministry of Health of the Russian Federation dated December 6, 2021 No. 1122n. 2021; 15.

[2] Laboratory diagnosis of community-acquired pneumonia: guidelines. M.: Federal Center for Hygiene and Epidemiology of Rospotrebnadzor 2014; 39.

After 1.5 months of the conscript's stay in the military team, an increase in the circulation of pneumococcus was detected, as a result of which the number of carriers among the examined military personnel increased by 2 times and amounted to 26.0 % (96) ($\chi^2_{McNemar}$ = 24.038; p < 0.001). At the same time, in 20.8 % of those examined (77), *S. pneumoniae* was isolated for the first time.

A comparative assessment of the hidden component of the epidemic process of pneumococcal disease in dynamics among vaccinated and unvaccinated military personnel revealed significant differences. Among unvaccinated military personnel, after 1.5 months, the number of *S. pneumoniae* carriers increased 3 times (from 17 to 52; $\chi^2_{McNemar}$ = 26.064; p < 0.0001), and amounted to 36.6 % (Fig. 1). In vaccinated military personnel, the number of carriers increased only 1.5 times (from 29 to 44; $\chi^2_{McNemar}$ = 3.947; p = 0.047), amounting to 19.4 %, which indicates the proactive effect of immunization on the risk of military personnel infection with *S. pneumoniae*.

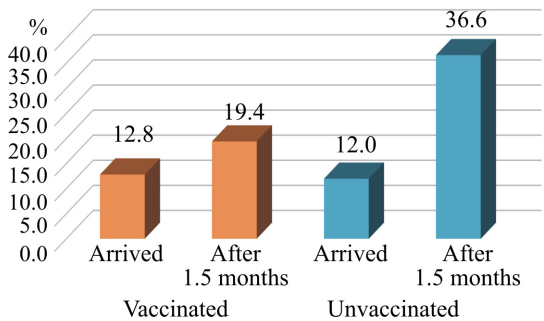

Fig. 1. Frequency of S. pneumoniae carriage in vaccinated and unvaccinated military personnel, %

The risk of *S. pneumoniae* infection in the group of persons not vaccinated against PD was 1.39 times higher compared with vaccinated persons (*RR* = 1.39; 95 % CI 1.209–1.596).

Upon arrival at the military unit, the serotype landscape of pneumococci was represented by four vaccine isolates 1, 3, 4, 18A/B/C/F (1.9 %) and non-typeable serotypes (10.6 %).

After 1.5 months of stay in the military collective, the serotype composition of the isolated pneumococci changed significantly: the leading role belonged to non-typeable serotypes (20.1 %), the proportion of vaccine isolates of pneumococcus significantly increased to 5.4 % ($\chi^2_{McNemar}$ = 6.76; p = 0.01), with a predominance of serotypes 3 and 12F/A/B/44/46, the latter was not detected during the initial examination. The long stay of military personnel in a closed military collective led to the emergence of new serotypes: three 9AV, 9LN, 6A/B/C/D, which are part of PPV23, and a nonvaccine serotype – 16F. Four examined persons (1.08 %) had mixed carriage after 1.5 months – a combination of two serotypes (Fig. 2).

When assessing the serotype landscape of *S. pneumoniae* in vaccinated and unvaccinated military personnel, it was found that upon arrival at the military collective, the frequency of occurrence of non-typeable serotypes was the same in both groups and amounted to 10.6 %, vaccine serotypes were represented in three (1, 3, 4 – 2.2 %) in vaccinated and one (18A/B/C/F – 1.4 %) in unvaccinated military personnel (table).

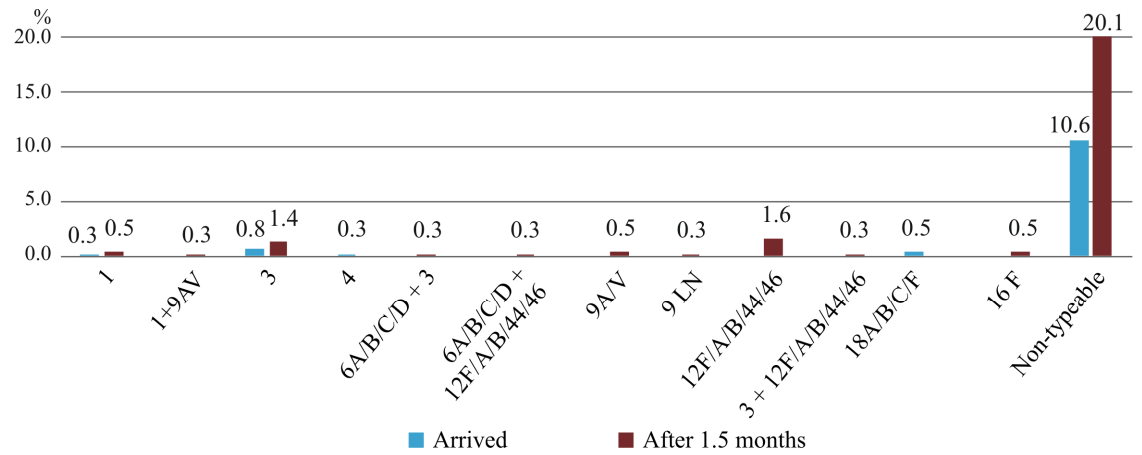

Fig. 2. Serotype composition of isolated S. pneumoniae, %

Structure of *S. pneumoniae* serotypes in vaccinated and unvaccinated military personnel

Serotype (serogroup)	Vaccinated, *n* = 227				Unvaccinated, *n* = 142			
	Arrived		After 1.5 months		Arrived		After 1.5 months	
	number of strains	per 100 examined persons [95 % CI]	number of strains	per 100 examined persons [95 % CI]	number of strains	per 100 examined persons [95 % CI]	number of strains	per 100 examined persons [95 % CI]
6A/B/C/D							2	1.4 [0.4–5.0]
9A/V			1	0.4 [0.1–2.5]			2	1.4 [0.4–5.0]
9LN							1	0.7 [0.1–3.9]
3	3	1.3 [0.5–3.8]	3	1.3 [0.5–3.8]			4	2.8 [1.1–7.0]
12F/A/B/44/46			3	1.3 [0.5–3.8]			5	3.5 [1.5–8.0]
18A/B/C/F					2	1.4 [0.4–5.0]		
1	1	0.4 [0.1–2.5]	2	0.9 [0.2–3.2]			1	0.7 [0.1–3.9]
4	1	0.4 [0.1–2.5]						
16F			1	0.4 [0.1–2.5]			1	0.7 [0.1–3.9]
Non-typeable	24	10.6 [7.2–15.2]	36	15.9 [11.7–21.2]	15	10.6 [6.5–16.7]	38	26.8 [20.2–34.6]

After 1.5 months, both in the vaccinated and unvaccinated groups, predominantly non-typeable isolates were identified: in the unvaccinated – 27.5 %, in the vaccinated – 16.3 %.

In the unvaccinated group, vaccine serotypes were distributed in greater diversity and quantity (6A/B/C/D, 9A/V, 9LN, 3, 12F/A/B/44/46, 1), which was significantly 2.6 times higher that the number of vaccine serotypes in vaccinated persons (9A/V, 3, 12F/A/B/44/46, 1) ($\chi^2 = 6.25$; $p = 0.01$).

Among those vaccinated against pneumococcal disease, a low prevalence of vac-

cine serotypes and a high frequency of non-typeable, including nonvaccine serotypes were revealed, which is consistent with data from similar works by other authors, according to which, against the background of military personnel mass immunization, vaccine strains of *S. pneumoniae* are replaced by serotypes not included in the composition of the vaccines used.

Thus, the conditions of stay of military personnel in military units, characterized by multi-territoriality of arriving conscripts, crowding and the factor of the team "mixing", significantly activate the mechanism of PD epidemic process development in military groups, causing not only an increase of the *S. pneumoniae* carriage frequency, but also the diversity of its serotype landscape, increasing the risk of infection among military personnel. Despite the continued circulation of pneumococcal serotypes in military personnel, the proactive effect of vaccination on the infection process has been proven.

In order to reduce the intensity of pneumococcal circulation and mitigate the risk of infection of military personnel in military units, health authorities of the constituent entities of the Russian Federation need to increase vaccination coverage against PD of persons, subject to conscription for military service.

Conclusions

1. Immunization of military personnel against pneumococcal disease reduces the frequency and diversity of the serotype landscape of circulating *S. pneumoniae*. Among vaccinated persons, a predominance of non-typeable strains was established; vaccine serotypes were found much less frequently than among unvaccinated persons.

2. The proactive impact of vaccination on the prevalence of *S. pneumoniae* among military personnel has been established.

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