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HERD IMMUNITY TO VACCINE PREVENTABLE INFECTIONS IN SAINT PETERSBURG AND THE LENINGRAD REGION: SEROLOGICAL STATUS OF MEASLES, MUMPS, AND RUBELLA

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Abstract. Specific measles, mumps, and rubella prevention has been the main prerequisite for a striking decline in the incidence of such infections in Russia. An increase in the percentage of seronegative individuals observed in recent years resulted in higher measles incidence being directly related to low herd immunity that accounts for a population protection solely under conditions of a high density of immunized individuals and their uniform distribution in the population. The number of immunized individuals may be estimated only while conducting seroepidemiological monitoring of herd immunity. The objective of the study was to assess a level of herd immunity in the St. Petersburg and Leningrad Region population against measles, mumps, and rubella viruses. *Materials and methods.* There were enrolled 6774 residents into the study: volunteers aged from 1 to 70+ years. The representativeness of the surveyed cohort was ensured by using the Web application “Monitoring of herd immunity against socially significant infections”, used at the stage of volunteer enrollment, by randomization and regulation of the sample size in age groups. Participants filled out a questionnaire and agreed to provide venous blood samples to assess IgG antibody levels against measles, mumps, and rubella viruses by using ELISA. Results. In September 2023, in St. Petersburg and the Leningrad Region, herd immunity met the criterion for epidemiological well-being only with respect to rubella. In all age groups, the proportion of seronegative individuals did not exceed 15%, and most volunteers had high Ab levels, both after illness and vaccination. For measles and mumps, the criterion for epidemiological well-being is considered not to exceed more than 7% seronegative individuals. A sufficient level of measles seroprevalence was detected only in older age groups (≥ 60 years old). Sufficient mumps seroprevalence was not detected in any age group. The average population (St. Petersburg, Leningrad Region) seroprevalence magnitude for measles, rubella, and mumps viruses were 81.4%, 95.5%, and 78.4%, respectively. The problematic age groups with low measles seroprevalence (62.4–74.3%) were adolescents (12–17 years) and young adults (18–39 years). Most seropositive individuals vaccinated against measles had low Ab levels; high levels were noted mainly in older measles convalescent individuals. Low mumps seroprevalence (~70%) was more often observed among adults aged 18 to 49 years. The distribution of seroprevalence in various occupational group was relatively uniform, with some predominance of seropositivity among

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pensioners and schoolchildren. *Conclusion*. The system of specific prophylaxis for vaccine-preventable viral infections used in Russia has shown high efficacy and contributed to the formation of herd immunity, which for many years allowed to lower a risk of both sporadic and group infections to minimal levels. Currently, measles and mumps seroprevalence in the local population is maintained at insufficient level to ensure epidemiological well-being. This necessitates making appropriate management decisions and conducting additional preventive measures aimed at enhancing relevant herd immunity.

Key words: *vaccine-preventable infections, herd immunity, measles, rubella, mumps, seroprevalence, antibodies, St. Petersburg, Leningrad Region, population, cohort study.*

ПОПУЛЯЦИОННЫЙ ИММУНИТЕТ К ВАКЦИНОУПРАВЛЯЕМЫМ ИНФЕКЦИЯМ (КОРИ, КРАСНУХЕ, ЭПИДЕМИЧЕСКОМУ ПАРОТИТУ) У НАСЕЛЕНИЯ САНКТ-ПЕТЕРБУРГА И ЛЕНИНГРАДСКОЙ ОБЛАСТИ

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Резюме. *Введение.* Специфическая профилактика кори, краснухи и эпидемического паротита явилась главной предпосылкой радикального снижения частоты этих инфекций в Российской Федерации. Наблюдающийся в последние годы рост доли серонегативных лиц привел к увеличению заболеваемости корью, что напрямую связано с низким популяционным иммунитетом, который обеспечивает защиту населения только в условиях высокой плотности иммунизированных лиц и их равномерного распределения в популяции. Оценить число иммунизированных лиц возможно лишь при проведении сероэпидемиологического мониторинга популяционного иммунитета. Цель исследования — изучение уровня популяционного иммунитета населения Санкт-Петербурга и Ленинградской области к вирусам кори, краснухи и паротита. *Материалы и методы.* В исследовании участвовали 6774 жителя региона (волонтеры) в возрасте от 1-го года до 70+ лет. Репрезентативность обследуемой когорты обеспечивалась Веб-приложением «Мониторинг популяционного иммунитета социально значимых инфекций», использованного на стадии регистрации волонтеров путем рандомизации и регулирования объема выборки в возрастных группах. В ходе исследования участники заполняли анкету и сдавали пробы венозной крови для определения IgG-антител к вирусам кори, краснухи и паротита методом ИФА с использованием тест-систем производства АО «Вектор-Бест» (Россия). *Результаты.* В сентябре 2023 г. в Санкт-Петербурге и Ленинградской области популяционный иммунитет населения соответствовал критерию эпидемиологического благополучия только в отношении краснухи — во всех возрастных группах доля серонегативных лиц не превышала 15%, большинство волонтеров имели высокий уровень антител как после заболевания, так и после вакцинации. Для кори и паротита критерием эпидемиологического благополучия считается наличие не более 7% серонегативных лиц. Достаточный уровень серопревалентности к вирусу кори выявлен только в старших возрастных группах (60 лет и старше), а к вирусу паротита не выявлен ни в одной возрастной группе. Средний уровень серопревалентности населения Санкт-Петербурга и Ленинградской области к вирусам кори, краснухи и паротита составил 81,4%, 95,5% и 78,4% соответственно. Проблемными возрастными группами с низкой серопревалентностью к вирусу кори (62.4–74.3%) оказались подростки (12–17 лет) и молодые взрослые (18–39 лет). Большинство серопозитивных лиц, вакцинированных от кори, имели низкие уровни антител; высокие уровни отмечены преимущественно у лиц старшего возраста, переболевших корью. Низкая серопревалентность к вирусу паротита чаще наблюдалась среди взрослых (около 70%) в возрасте от 18-ти до 49-ти лет. Распределение серопревалентности в зависимости от рода занятий было сравнительно однородным с некоторым преобладанием серопозитивности среди пенсионеров и школьников. *Заключение.* Используемая в РФ система специфической профилактики вакциноуправляемых вирусных инфекций показала высокую эффективность и способствовала формированию популяционного иммунитета, позволившего в течение многих лет до минимального уровня снизить риск появления как спорадических, так и групповых заболеваний. В настоящее время серопревалентность населения Санкт-Петербурга и Ленинградской области к вирусам кори и эпидемического паротита недостаточна для обеспечения эпидемиологического благополучия и требует принятия соответствующих управленческих решений и проведения дополнительных профилактических мероприятий, направленных на повышение популяционного иммунитета к этим инфекциям.

Ключевые слова: *вакциноуправляемые инфекции, популяционный иммунитет, корь, краснуха, паротит, серопревалентность, антитела, Санкт-Петербург, Ленинградская область, население, когортное исследование.*

Introduction

Acute infectious diseases accompany an individual person throughout their life. Most often, they manifest as sporadic cases. Less often, local outbreaks in groups or limited areas occur. A sudden increase in the number of cases above the predicted level among the population of a certain area or region is classified as an "epidemic", and if the population of large regions or continents is involved, it is customary to use the term "pandemic" [50, 56]. A striking example of the evolution of the epidemic process is COVID-19, which began in 2020, soon developing into a pandemic that affected most countries globally. As of 06/04/2024, more than 775 million cases have been registered [68]. Currently, COVID-19 has transformed into a typical seasonal respiratory infection [47]. One of the reasons for this transformation has been the formation of herd immunity, and the use of a wide range of vaccines played a role.

Herd immunity as a protective factor for a susceptible population works only in conditions of a high proportion of immunized individuals and their uniform distribution in the population. Estimating the percentage of truly immune individuals in a population (both as a result of infection or vaccination) is a complex task. Analysis of morbidity based only on registration of laboratory-confirmed manifest forms of illness does not allow for a reliable assessment of post-infectious immunity in the population. The share of individuals with post-vaccination immunity may differ significantly from official vaccination data due to several factors: underestimation of actual population size (e.g., due to migratory processes); ineffectiveness of individual vaccine batches (e.g., due to non-adherence to storage or transportation conditions); or as a result of individuality in the formation of immunological memory in specific individuals.

These factors necessitate monitoring of herd immunity in different age groups living in all Russian administrative regions. The use of analytical methods and laboratory systems in this work allows for the prompt analysis of a large array of data. This provides a scientific basis for understanding the causes behind evolution of the epidemiological situation with respect to specific infections. Such an approach can also clarify forecasts regarding expected epidemiological conditions, events, and burdens. Vaccine-based prevention technologies have made it possible to achieve outstanding success in reducing the spread of such highly contagious infections as measles, mumps, and rubella. Nevertheless, monitoring of ongoing, adequate implementation is a prerequisite for maintaining progress in recent decades and reducing suffering.

Characteristic features of these infections are the airborne transmission mechanism and an absence of pathogen-specific therapeutic choices. In global practice, the trivalent vaccines M-M-P II and Priorix are primarily used for specific prevention, forming effective specific immunity simultaneously to measles, mumps, and rubella [26, 41]. In Russia, the three-component vaccine Vactrivir is used for this purpose [16].

Specific prevention has been the main prerequisite for a radical reduction in the measles incidence in recent decades to sporadic cases, mainly of imported origin. However, some periods have seen fluctuations in incidence, for example from 2012 to 2018. According to Rospotrebnadzor, 6 measles cases were registered in the Leningrad Region in 2022, with 1 case in St. Petersburg. The favorable situation persisted until 2023, when the number of measles cases began to increase rapidly, and currently continues to increase, in all Russian regions.

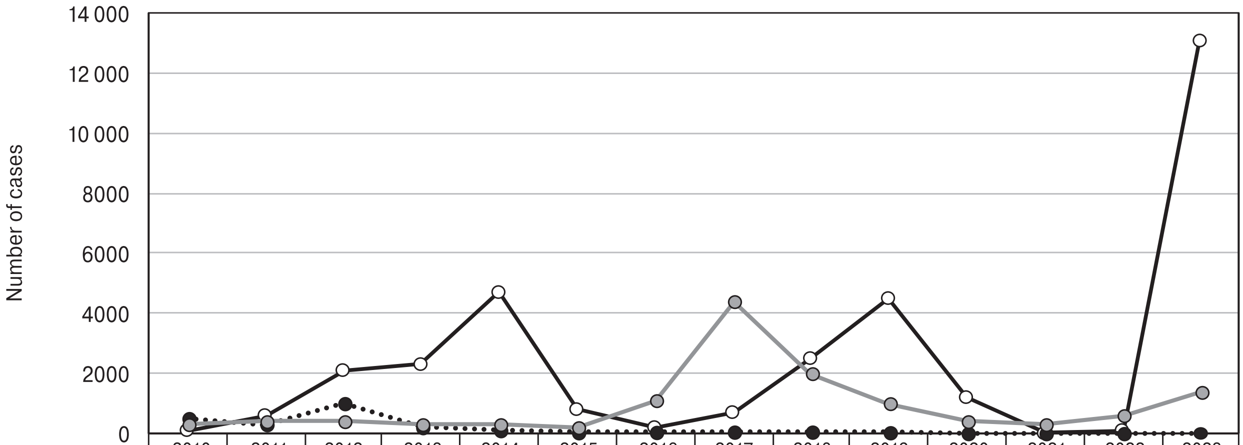
Moreover, most cases are no longer associated with importation, and diseases and/or outbreaks occur, including among the vaccinated population. In 2023, there was a trend towards an increase in measles cases in eight regions of the Northwestern Federal District (NWFD): St. Petersburg; Leningrad Region; Arkhangelsk Region; Murmansk Region; Kaliningrad Region; Vologda Region; the Komi Republic; and the Republic of Karelia.

As of September 2023, 271 verified measles cases were registered (2 per 100 000 pop.). In 70% of cases, the disease developed among unvaccinated individuals, and 5% of patients could not confirm or deny a history of vaccination. In 10% of cases, the disease developed among those vaccinated once. In 15%, occurrence was after revaccination. Most illnesses were associated in some way with importation from other countries, mainly Tajikistan. In all cases, the measles virus genotype D8 MeaNS 8248 was identified.

Rubella cases have not been registered in the Northwestern Federal District since 2021, which can probably be explained by a high level of herd immunity among the population.

Despite mumps vaccination within the framework of the national schedule, manifest cases of this disease are still observed in the city and region. In 2022, 12 cases were detected (0.09 per 100 000 pop.), mainly in St. Petersburg, and 13 cases were already registered in the first 9 months of 2023. Mumps is often observed in vaccinated individuals worldwide, which is apparently associated with a decrease in the intensity of post-vaccination immunity according to time elapsed after immunization [28, 34, 57]. Summarized data on the incidence of these infections (measles, mumps, rubella), illustrating the information above, are shown in Fig. 1.

Thus, despite vaccination against these airborne transmissible pathogens, cases of vaccine-preventable infections are still registered. The only factor capable of preventing the spread of such pathogens is the formation of herd specific immunity [2, 38, 53]. Clearly, progress in this area is impossible without an assessment of the status and strength of herd immunity, including the possible influences of age,



	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Measles	100	600	2100	2300	4700	800	200	700	2500	4500	1200	1	102	13 083
Rubella	500	300	1000	200	100	30	40	50	50	30	3	1	1	0
Mumps	300	400	400	300	300	200	1100	4400	2000	1000	400	300	600	1375

Figure 1. Annual incidence dynamics of measles, mumps, and rubella in the St. Petersburg population (2010 to 2023)

region, and professional category [30, 40]. The aim of the study was to assess herd immunity to measles, mumps, and rubella viruses in a cohort of volunteers living in St. Petersburg and the Leningrad Region.

Materials and methods

Characteristics of the analyzed volunteer cohort

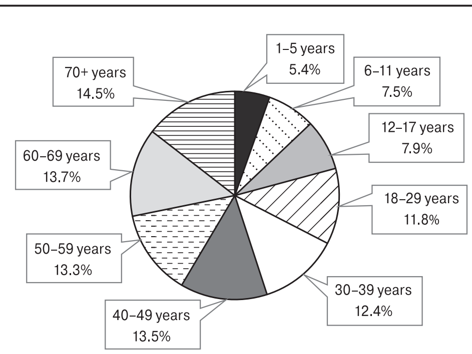
A cross-sectional, randomized study was conducted under the Rospotrebnadzor program "Assessment of herd immunity to vaccine preventable and other relevant infections in the St. Petersburg and Leningrad Region Population", as approved by the local ethics committee of the St. Petersburg Pasteur Institute. All participants, or their legal representatives, were familiarized with the purpose and methodology of the study and signed informed consent. Random selection of volunteers for the study was carried out using a web application with a questionnaire. The selected volunteers were stratified into nine age groups: 1–5 years; 6–11 years; 12–17 years; 18–29 years; 30–39 years; 40–49 years; 50–59 years; 69–69 years; and 70+ years. The size of a representative sample was calculated using a formula based on the Moivre–Laplace limit theorem [8, 15]. The total number of volunteers in the cohort surveyed was 6774 people.

Child volunteers (1–17 years) made up 20.8% of the total number of those surveyed and were divided into three groups: 1–5 years (5.4%); 6–11 years (7.5%); and 12–17 years (7.9%) (Table 1). The proportions of volunteers in adult age groups were approximately the same and differed in numbers by 1.5–2.5%. In total, the cohort consisted of 1789 men (26.4%) and 4985 women (73.6%). Hence, women participated in the study more actively (by a factor of 2.8). Representatives of various fields of activity took part in the study (Table 2).

As follows from Table 2, the largest numbers of volunteers belonged to the groups of pensioners and medical workers. The smallest was IT specialists. The predominance of pensioners and medical workers in the cohort can be explained, to a certain extent, by the greater social activity, and more responsible attitude to their health, of volunteers in these two categories.

Table 1. Age structure of the volunteer cohort (St. Petersburg, Leningrad Region)

Age, years	N, persons	Share, % (95% CI)
1–5 years	369	5.4 (1.3–9.0)
6–11 years	510	7.5 (6.9–8.2)
12–17 years	536	7.9 (7.3–8.6)
18–29 years	796	11.8 (11.0–12.5)
30–39 years	838	12.4 (11.6–13.2)
40–49 years	915	13.5 (12.7–13.4)
50–59 years	900	13.3 (12.5–14.1)
60–69 years	930	13.7(12.9–14.6)
70+ years	980	14.5 (13.6–15.3)
Total	6774	6774



Note. 70+ designates volunteers aged ≥ 70 years.

Research methods

During a wide information campaign, individuals who expressed a desire to participate in the study filled out an online questionnaire with personal data which was sent to the Web application for subsequent analysis. The collected information included: full name; gender; age; area of residence; field of activity; presence of chronic diseases; and contact information. Individuals who met the inclusion criteria (absence of acute illness at the time of the study) were invited to provide additional information and blood for subsequent laboratory testing in person. The methodology for organizing and conducting the study has been described earlier in detail [12].

At the blood collection point, the registrar and volunteer filled out an extended questionnaire, including questions about medical history (measles, mumps, rubella, other vaccine-preventable infections). Also recorded were vaccinations and revaccinations against the listed infections (including vaccine names and dates of administration). The information was taken from the vaccination certificate provided by the volunteer, or clarified from other medical documentation.

In addition to the survey using a specially designed questionnaire, all volunteers were tested for the presence of antibodies to the measles, mumps, and rubella viruses.

Blood samples were taken from the ulnar vein into vacutainers containing ethylenediaminetetraacetic acid solution (K_3EDTA). Vacutainers were centrifuged at room temperature. Blood plasma was separated from cellular elements, transferred to microtubes, and stored at 4°C until testing.

ELISA testing was performed using reagent kits manufactured by Vector-Best (Russia) according to manufacturer instructions: “VectoMeasles-IgG” for the presence and level of antibodies (Abs) to the measles virus; “VectoRubella-IgG” for the presence and level of Abs to the rubella virus; and “Vecto-Parotit-IgG” for the presence of Abs to the mumps virus. The quantitative content of antibodies to measles and rubella viruses was expressed in IU/ml. The study flow chart is shown in Fig. 2.

Table 2. Distribution of volunteers by field of activity

Field of activity	Volunteers, N	Share, %	Confidence Interval (95%)
Healthcare	1366	20,2	19.2–21.1
Pensioner	1157	17,1	16.2–18.0
Schoolars	815	12	11.3–12.8
Education	592	8,7	8.1–9.4
Office worker	563	8,3	7.7–9.0
Preschooler	433	6,4	5.8–7.0
Other	292	4,3	3.8–4.8
Industry	269	4	3.5–4.5
State-military service	262	3,9	3.4–4.4
Unemployed	252	3,7	3.3–4.2
Student	213	3,1	2.8–3.6
Business	158	2,3	2.0–2.7
Research	117	1,7	1.4–2.1
The arts	101	1,5	1.2–1.8
Transportation	100	1,5	1.2–1.8
Information tech. (IT)	84	1,2	1.0–1.5
Total	6774	100	–

Statistical processing

Statistical processing was performed using methods of variation statistics and the Excel 2011 package. The relationships between age and seroprevalence

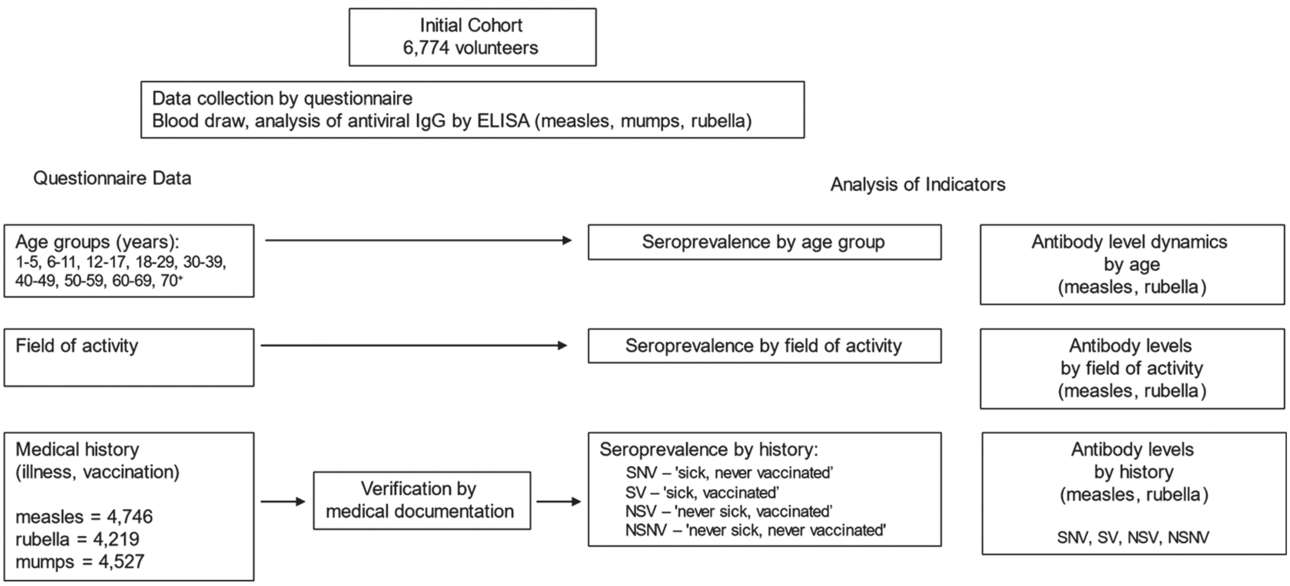


Figure 2. Study flow chart

levels were calculated using the Pearson method. Statistical processing of proportions was performed using the method of A. Wald and J. Wolfowitz [65], as modified by A. Agresti and B.A. Coull [23]. Calculation of the statistical significance of differences in shares was performed using the z test [5]. When assessing diefferences in the compared indicators, a probability level was used to estimate significance ($p \leq 0.05$, unless indicated otherwise).

Results

Herd immunity to the measles virus

The average measles seroprevalence in the volunteer cohort was 81.4% (95% CI: 80.4–82.3). It was distributed unevenly across age groups, specifically: with maximum values in those > 60 years of age (94.8–96.2%); and with a smaller share of seropositive volunteers in younger age groups from 12 to 49 years (< 80%). The differences were significant at $p \leq 0.05$. Seroprevalence in young children's groups (1–5 years, 6–11 years) did not differ from the a verage cohort value (Fig. 3).

When analyzing seroprevalence, it is necessary to take into account changes in the national measles vaccination strategy. A single vaccination was introduced in 1968.

In other words, vaccinated individuals aged 40–55 were likely vaccinated in childhood once. A full immunization program (2 vaccinations) was introduced in 1986, which correlates with those under 40 years of age. Persons over 55 years of age were likely only vaccinated in adulthood according to epidemiological indications. It was in adults, starting from 50 years of age, that we noted a statistically significant increase in seroprevalence. In the absence of routine childhood vaccination, this may indicate a previous infection. Low measles seroprevalence among adults aged 18–39 may be associated with the socioeconomic situation in the post-Soviet period. Particularly noteworthy is the high proportion of seronegative individuals among children (18.4–25.7%), probably as a result of medical exemptions and parental refusals to vaccinate.

When assessing seroprevalence depending on field of activity, no significant differences were noted by overall professional group. However, the highest seroprevalence level (95.9%; 95% CI: 94.6–96.9) was observed among pensioners (differences with the final value of the indicator were significantly higher, $p < 0.001$), most of whom probably acquired immunity to measles as a result of a childhood infection. The lowest levels were observed among schoolchildren (77.9%; 95% CI: 74.9–80.6) and students (66.7%; 95% CI: 60.1–72.7), which were significantly lower than the final cohort value ($p < 0.05$). These data fully correlate with the age distribution of seroprevalence described above.

In addition to seroprevalence, the study included a quantitative assessment of anti-measles IgG levels in volunteers of different ages (Fig. 4).

The observed trends differed in both shape and direction. The distribution of seronegative individuals (< 0.18 IU/ml) was bell-shaped. The smallest number of such individuals was detected among those aged ≥ 60 years. The share of individuals with low anti-measles IgG levels (0.18–0.5 IU/ml) was the highest among children and gradually decreased with advancing age category. It should be noted that such dynamics are not accidental, as the correlation coefficient shows ($\rho = - 0.85$; $p < 0.01$).

A negative trend was observed in relation to the average IgG level (0.5–1.0 IU/ml). As in the previous group, the largest share of individuals with average levels was detected among children. The smallest was seen among those aged ≥ 60 years ($\rho = -0.85$;

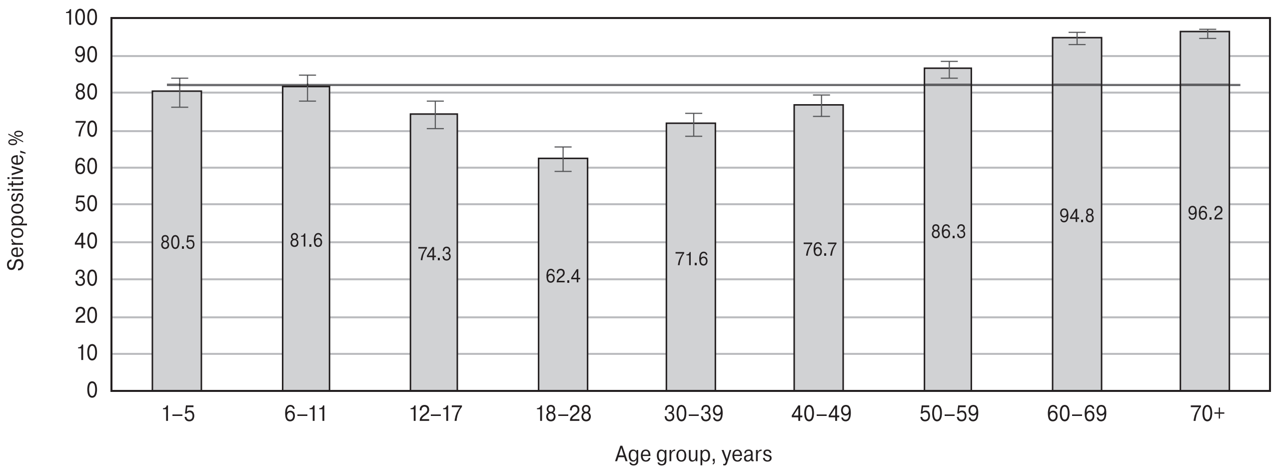
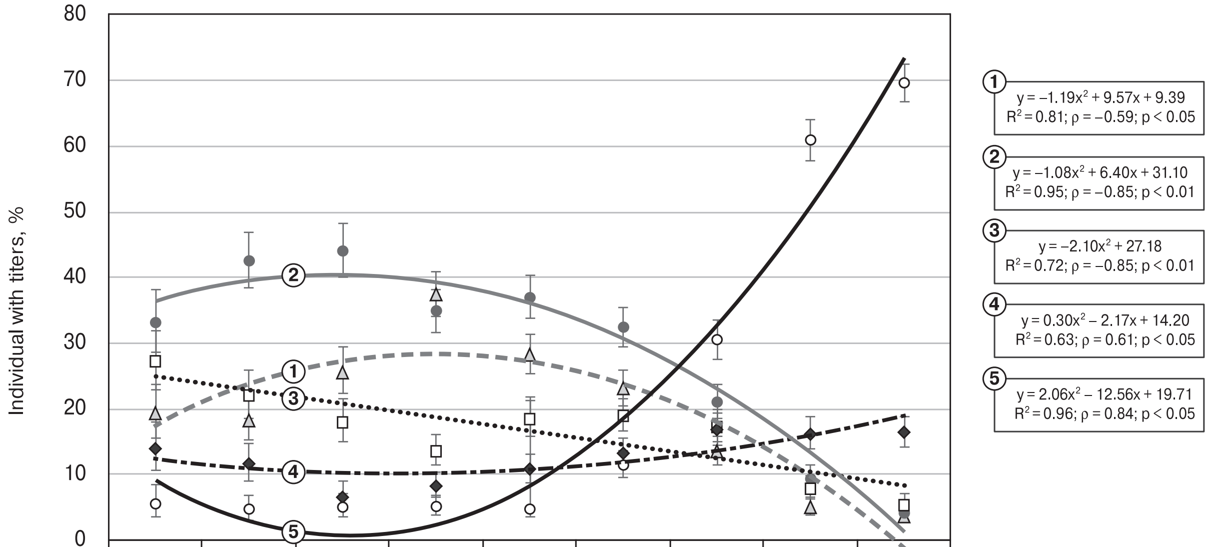


Figure 3. Measles seroprevalence (IgG presence) by age group

Note. Vertical black lines are confidence intervals; horizontal translucent band is the 95% confidence interval of the final value for the entire sample (81.4%; 95% CI: 80.4–82.3). Numerical values and statistical significance indicators are given in Supplementary Table 1S.



		1–5 years	6–11 years	12–17 years	18–28 years	30–39 years	40–49 years	50–59 years	60–69 years	70+ years
1	△ < 0.18 IU/ml	19.5	18.4	25.7	37.6	28.4	23.3	13.7	5.2	3.8
2	● 0.18–0.5 IU/ml	33.3	42.7	44.2	35.1	37.1	32.6	21.2	9.5	4.3
3	□ 0.51–1.0 IU/ml	27.4	22.2	18.1	13.7	18.6	19.1	17.4	8	5.5
4	◆ 1.01–2.0 IU/ml	14.1	11.8	6.7	8.4	11	13.4	17	16.3	16.6
5	○ > 2.0 IU/ml	5.7	4.9	5.2	5.3	4.9	11.6	30.7	61.1	69.8

Figure 4. Trends in the quantitative distribution of anti-measles IgG levels by age group
Note. Numerical values are shown in the upper left: regression equations; determination coefficients (R^2); Spearman correlation coefficients (ρ); p values. Quantitative Ab levels are in IU/ml. Vertical black lines are 95% confidence intervals. Numerical values and statistical significance indicators are given in Supplementary Table 2S.

$p < 0.01$). The distributions of seropositive individuals with high (1.01–2.0 IU/ml) and very high (> 2.0 IU/ml) IgG levels are interesting. In the group with high levels, the trend changed from negative to positive, although with a low determination coefficient (ρ = 0.61; insignificant at $p > 0.05$). The most interesting finding was seen regarding the distribution of seropositivity with the highest anti-measles IgG levels (Fig. 5). The regression curve remained almost at the same level (4.9–5.7 IU/ml) in age groups from 1–3 years to 30–39 years, and then increased almost exponentially to 69.8% (95% CI: 66.8–72.6).

Thus, low and medium anti-measles IgG levels were predominantly detected in individuals under 50 years of age, while high Ab levels were detected in individuals aged ≥ 50 years. It can be assumed that the higher share of seropositive individuals with the maximum IgG concentration in older age groups is due to a history of manifest infection.

The surveyed cohort was heterogeneous in terms of infectious and vaccinal status. Overall, 4746 individuals provided information about a history of measles and vaccination in the questionnaire. After verification of questionnaire data against medical records, 2,628 individuals for whom reliable information was available (Supplementary Table 3S) were divided into 4 groups: "sick, never vaccinated" (SNV, n = 105); "sick, vaccinated" (SV, n = 58); "never sick, vaccinated" (NSV, n = 2,061); and "never sick, never vaccinated" (NSNV, n = 404). It is necessary to acknowledge that such a division is somewhat arbitrary since information about vaccination was confirmed by medical records, yet a history of illness or lack thereof was not documented by most volunteers. Information on the relationship between history, the presence of measles seropositivity, and anti-measles Ab levels was of interest (Fig. 5).

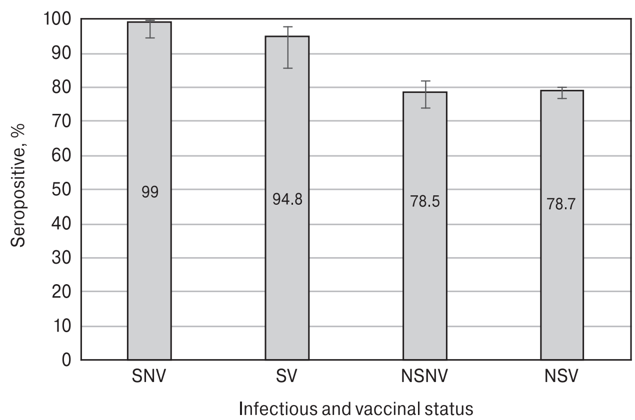
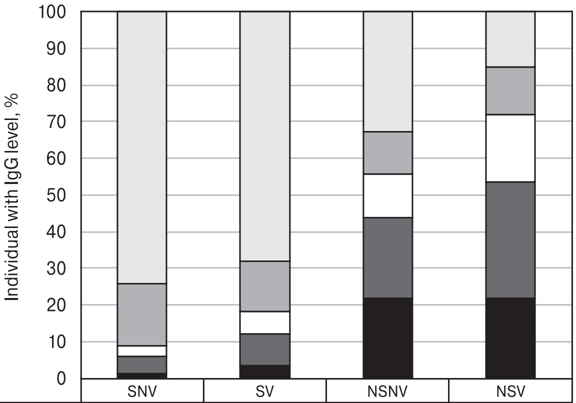


Figure 5. Measles seroprevalence by infectious and vaccinal status
Note. SNV — "sick, never vaccinated"; SV — "sick, vaccinated"; NSV — "never sick, vaccinated"; NSNV — "never sick, never vaccinated". Numerical values and statistical significance indicators are given in Supplementary Table 4S.



	SNV	SV	NSNV	NSV
> 2.0 IU/ml	74.3	68.4	32.9	15.1
1.01–2.0 IU/ml	17.1	13.5	11.4	13.2
0.51–1.0 IU/ml	2.9	6.3	11.9	18.2
0.18–0.5 IU/ml	4.8	8.4	22.3	31.9
< 0.18 IU/ml	1	3.4	21.5	21.6

Figure 6. Anti-measles IgG levels by infectious and vaccinal status

Note. SNV — "sick, never vaccinated"; SV — "sick, vaccinated"; NSV — "never sick, vaccinated"; NSNV — "never sick, never vaccinated". Numerical values and statistical significance indicators are given in Supplementary Table 4S.

In the groups of volunteers who had had measles (SV, SNV), regardless of vaccinal status, seroprevalence and Ab levels were generally higher than in the groups who had not had measles (NSV, NSNV), also regardless of vaccination.

As expected, the highest share of seropositive individuals was found among volunteers who had indicated a history of illness in the questionnaire, regardless of vaccinal status (groups SNV, SV). In these groups, seroprevalence was 94.8–99.0% (Fig. 5), and the vast majority (~80%) had high Ab levels (≥ 1 IU/ml) (Fig. 6).

In the groups with no official history of measles (NSNV, NSV), seronegativity was about 22%. Seropositivity in these groups was quite high (~78%) regardless of vaccinal status, although significantly lower than the value for those with a measles history ($p < 0.001$). The share of individuals with high Ab levels (> 1 IU/ml) was significantly lower than that of those who had had measles. Regarding high Ab level individuals: they were 44.0% among the unvaccinated (NSNV) (of which 32.9% had Abs > 2 IU/ml); and they were 22.8% among those vaccinated (NSV) (of which 10.1% had Abs > 2 IU/ml). These results are apparently explained by the structure of these two groups. Half of the volunteers in the NSNV group were over 50 years old. As shown earlier, seropositivity at this age is about 90% and higher. This indicates childhood measles infection which the volunteer did not remember, or did not know about. This is understandable, especially if the illness was mild. In any case, if infection occurred, then post-infectious immunity was formed, which is usually accompanied by high Ab levels. Unvaccinated individuals have a significantly higher chance of getting measles than vaccinated people. This is confirmed by the greater share of people with high Ab levels in the unvaccinated group.

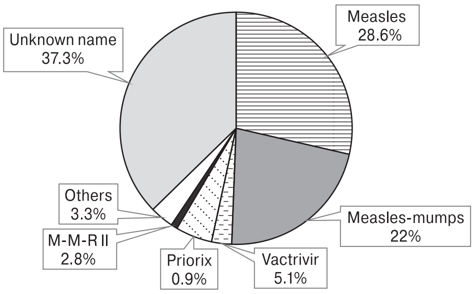


Figure 7. Structure of preparations used for measles vaccination (St. Petersburg, Leningrad Region)

Note. Numerical values and statistical significance indicators are given in Supplementary Table 5S.

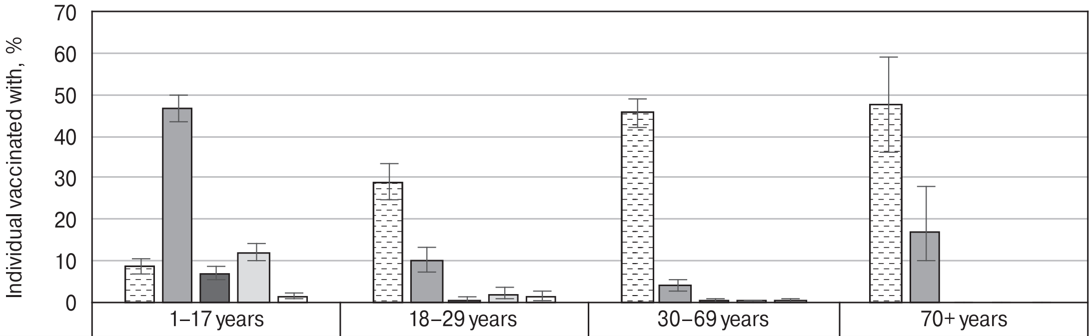
In the largest group, "never sick, vaccinated" (NSV), the majority were children and people under 60 years of age who were vaccinated according to the national schedule. They would be expected to have post-vaccination immunity. However, more than 20% of those in this group did not have anti-measles antibodies, and only 28% of volunteers had high levels.

Of the total, 2,297 volunteers were vaccinated against measles. About 40% of individuals did not have a specific vaccine name listed on their certificate. Approximately equal numbers of volunteers were vaccinated with measles vaccine (28.6%; 95% CI: 26.8–30.5) and measles-mumps vaccine (22.0%; 95% CI: 20.4–23.8). The total share of other vaccines (Priorix, M-M-R II, Vactrivir, etc.) was about 12% (Fig. 7).

Significant differences in vaccines were noted depending on volunteer age. This is likely due to the domestic availability of various vaccines used at different times (Fig. 8). Adult volunteers from 30 to 69 years old were combined into one group due to an absence of significant differences.

Most children were vaccinated with two-component (measles, mumps) or three-component (measles, mumps, rubella) vaccines. Regarding the latter, both imported (Priorix, M-M-R II) and domestic (Vactrivir) preparations have been used. The share of children vaccinated with monovalent measles vaccine was below 10%.

Most adult volunteers, especially the elderly, were vaccinated with a monovalent measles vaccine. Vaccination with it increased proportionally with age: from 29.1% (95% CI: 24.9–33.8) in the group "18–29 years old" to 47.8% (95% CI: 36.5–59.4) in the group ≥ 70 years. In adult volunteers aged 30–69 years, two- and three-component vaccines were practically not used. About 10.1% (95% CI: 7.5–13.5) of persons aged 18–29 years had been vaccinated



	1–17 years	18–29 years	30–69 years	70+ years
Measles	8.6	29	46	48
Measles-mumps	47	10	4	17
Vactrivir	7	0.3	0.2	0
Priorix	12	2	0.1	0
M-M-R II	1.5	1,3	0.2	0

Figure 8. Preparations used for measles vaccination, by age group
Note. Numerical values and statistical significance indicators are given in Supplementary Table 5S.

with two-component measles-mumps vaccine since 2002 (when it entered serial production). Among volunteers aged ≥ 70 years, there were also persons vaccinated with measles-mumps vaccine (17.5%; 95% CI: 10.0–28.0), probably during vaccination of the adult population during periods of increased incidence in recent years.

When summarizing measles herd immunity among local volunteers (St. Petersburg, Leningrad Region), it can be stated that the threshold level of immunity sufficient to prevent epidemic spread of the pathogen (≤ 7% seronegative individuals) has been achieved only in the age groups of 60 years and older. Among adult volunteers under 50 years of age, seroprevalence did not reach 80%. In the range 18–29 years old, the minimum values were noted (62.4%). It is noteworthy that about 20% of children who should have been vaccinated according to the national schedule did not have antibodies to the measles virus.

Herd immunity to the rubella virus

As noted earlier, the rubella situation in 2021–2022 was favorable. There were no sporadic cases, let alone epidemic outbreaks, in St. Petersburg or the Leningrad Region. Despite the fact that rubella is milder than other airborne infections (COVID-19, influenza, measles), it is a significant public health concern due to its teratogenic potential and association with autism [42]. Rubella is one of the most common infections causing fetal abnormalities (congenital rubella syndrome) in pregnant women.

The first live attenuated rubella vaccine was created by P.D. Parkman and H.M. Meyer Jr. in 1966 [48]. Inclusion of the rubella vaccine in national immunization schedules has increased vaccination coverage to 89.0% in most developed countries. Russia is no exception, and rubella vaccination has been included in the national schedule since 1997. Routine immunization occurs at several points: children at 1 year old; children at 6 years old; and girls aged 13 years. Additional immunization is performed for children aged 1 to 17 years: who have not had rubella; who have not been vaccinated; or have been vaccinated only once. Young women 18 to 25 years old may also receive vaccination if they have not had rubella or been vaccinated previously.

The absence of rubella cases does not preclude large-scale studies of herd immunity against vaccine-preventable infections. Vigilance regarding these pathogens, including rubella, is an important prerequisite for maintaining epidemiological well-being, without setbacks, in the country. The long-term use of a live attenuated vaccine in Russia has resulted in a high level of herd immunity (95.5%; 95% CI: 94.9–95.9) in the St. Petersburg and Leningrad Region population (Fig. 9).

The highest rubella seroprevalence values were found in the subgroups of elderly (60–69 years) and older (70+ years) people. The lowest were among those middle-aged (30–39 years). Differences with the overall seroprevalence value were significant ($p < 0.05$). Despite some seroprevalence differences among various age groups, the average level of herd immunity exceeds 95%. Since the criterion for epidemic well-being regarding rubella is the detection of ≤ 7% seronegative individuals, the situation in St. Petersburg and the Leningrad Region can be considered favorable. This is confirmed by the absence of rubella cases in recent years in the regions analyzed. As expected, given the high overall seroprevalence of the population, differences by field of activity were not seen. Anti-rubella IgG levels were determined in volunteers depending on age (Fig. 10).

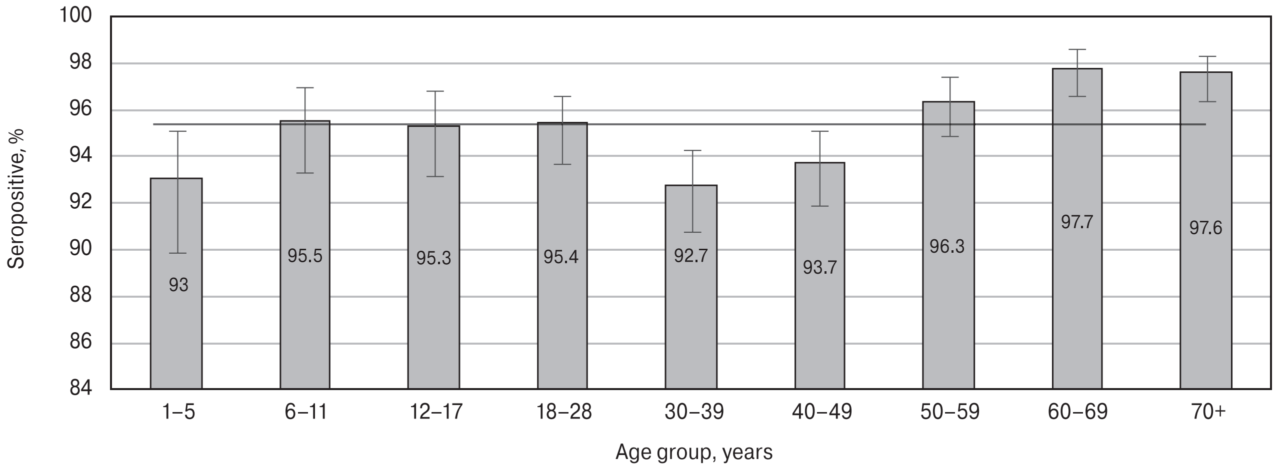
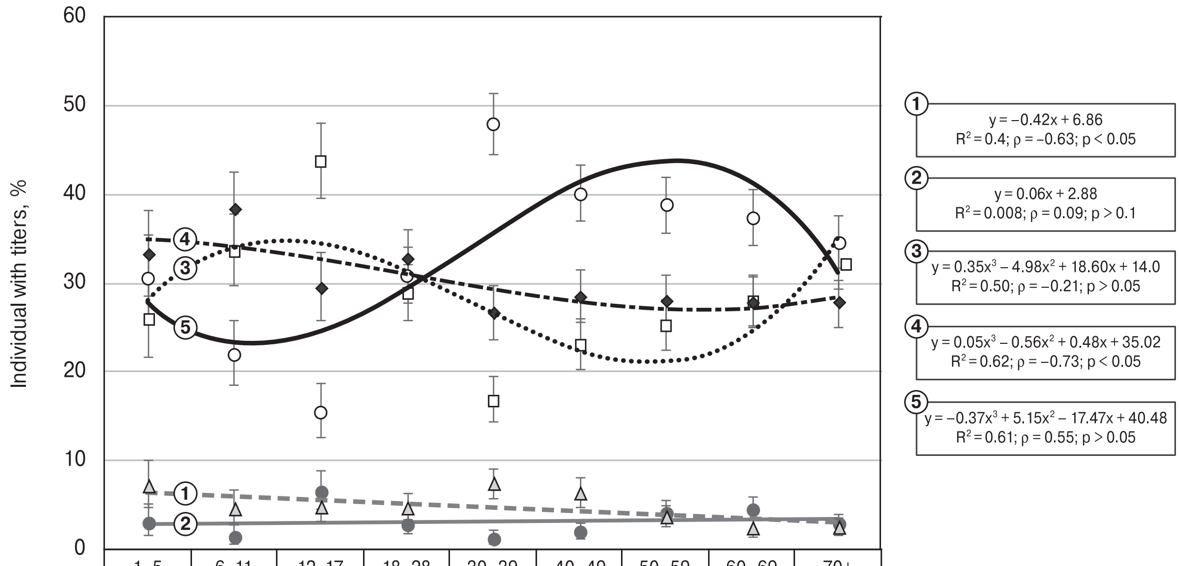


Figure 9. Rubella seroprevalence (IgG presence) by age group

Note. Vertical black lines are 95% confidence intervals; horizontal translucent stripe is the 95% confidence interval of the final value for the entire sample (95.5%; 95% CI: 94.9–95.9). Numerical values and statistical significance indicators are given in Supplementary Table 6S.

The data reflect a complex, heterogeneous structure regarding the distribution of anti-rubella Abs present in the population. The share of seronegative individuals and those with minimal Ab levels was distributed relatively uniformly. It was described by linear regression, with virtually no dependence on age. The trends change with higher Ab levels, requiring a more complex approximation described by 3rd degree polynomials. Significant heterogeneity in the results is noteworthy, including opposing trends describing certain Ab concentration distributions: 25–100 IU/ml (average) and > 200 IU/ml (maximum).

Within the age intervals 6–11 years and 12–17 years, an increase in average Ab levels, and a decrease in maximum levels, are observed. In the range 18–29 years, there is a turning point in trends.



		1–5 years	6–11 years	12–17 years	18–28 years	30–39 years	40–49 years	50–59 years	60–69 years	70+ years
①	△ < 10 IU/ml	7	4.5	4.7	4.6	7.3	6.3	3.7	2.3	2.4
②	● 10.0–25.0 IU/ml	3	1.4	6.5	2.8	1.2	2	4.1	4.5	2.9
③	□ 25.1–100.0 IU/ml	26	33.7	43.8	28.9	16.8	23.1	25.3	28	32.2
④	◆ 100.1–200.0 IU/ml	33.3	38.4	29.5	32.8	26.7	28.5	28	27.8	27.9
⑤	○ > 200.0 IU/ml	30.6	22	15.5	30.9	48	40.1	38.9	37.4	34.6

Figure 10. Trends in the quantitative distribution of anti-rubella IgG levels by age group

Note. Numerical values are shown in the upper left: regression equations; determination coefficients (R^2); Spearman correlation coefficients (ρ); p values. Quantitative Ab levels are in IU/ml. Vertical black lines are 95% confidence intervals. Numerical values and statistical significance indicators are given in Supplementary Table 7S.

By the age range 50–59 years, the largest share of volunteers had Abs at maximum levels, and a statistically significant proportion of seropositive individuals had only average levels. Considering that for both trends the determination coefficient varies within a range (0.5–0.61), it can be considered that this form of regression is not random. It likely reflects real processes, and statistically significant features, of the quantitative Ab distribution.

Among volunteers of all age groups, the shares of individuals with medium, high, or very high Ab levels were distributed evenly. No more than 7% of volunteers had low Ab levels (10–25 IU/ml). Nevertheless, in children from 6 to 17 years old, high IgG levels were detected significantly less often than in children 1–5 years old or adults ≥ 18 years.

As with measles, those volunteers (4219 people) who provided information about their illness and vaccination in the questionnaire were divided into four groups (Suppl. Table 8S). Depending on infectious and vaccinal status after verification of their questionnaire data against medical records (2302 people), these were: SNV (n = 180); SV (n = 43); NSNV (n = 813); and NSV (n = 1266).

The age distribution of volunteers by infectious and vaccinal status is related to the national schedule, which has included rubella vaccination since 1998. In this regard, only people under 25 years of age were routinely vaccinated against rubella. People over 25 years of age, primarily women, may have received unscheduled vaccination based on epidemiological indications. It can be assumed that the groups of those who have had the disease (SNV, SV) should be mostly represented by people aged ≥ 30 years. The NSV group is most likely to be children and young people (18–29 years old). The NSNV group is volunteers of different ages who were not vaccinated, either due to medical exemptions, refusal (children and adults < 25 years), or because of age (people > 25 years). Such a classification is largely arbitrary since the actual number of people who have had rubella may be higher due to the prevalence of mild and asymptomatic cases. Furthermore, people of any age may have received rubella vaccination based epidemiological measures, especially women, for whom the presence of rubella constitutes a risk of developing pre- and postnatal lesions in newborns [27, 33, 42].

Given the high overall rubella seroprevalence in the cohort (95.5%), and its uniform distribution across age groups, one would not expect to find significant differences in seroprevalence in volunteers of different infectious and vaccinal status (Fig. 11, 12).

Although significant differences were not found between groups, seroprevalence exceeded 95% among volunteers who had experienced rubella or were vaccinated (SNV, SV, NSV), which is higher than the value for those who denied a history of vaccination or illness (NSNV, 88.6%). As with measles,

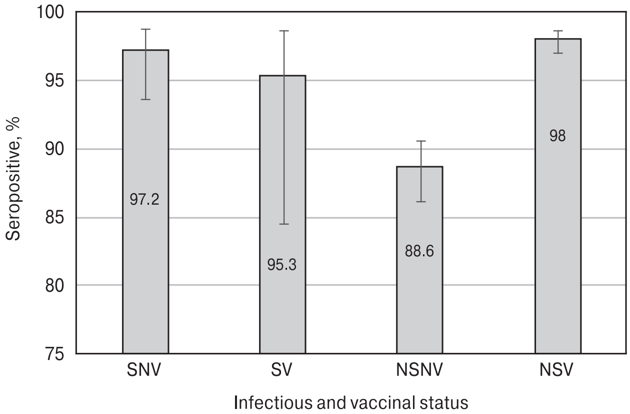
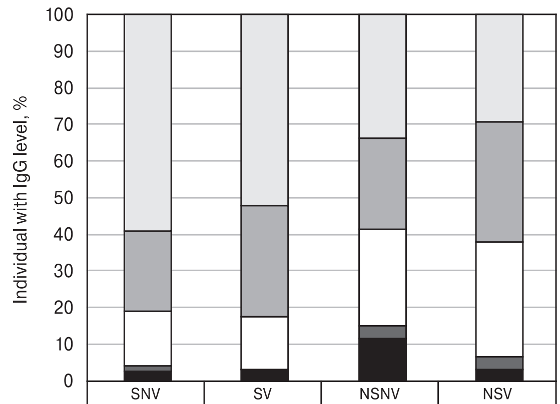


Figure 11. Rubella seroprevalence by infectious and vaccinal status

Note. SNV — "sick, never vaccinated"; SV — "sick, vaccinated"; NSV — "never sick, vaccinated"; NSNV — "never sick, never vaccinated". Vertical black bars are 95% confidence intervals. Numerical values and statistical significance indicators are given in Supplementary Table 9S.

the vast majority of volunteers who had had the disease (> 80%) had high IgG levels (> 100 IU/ml), including about 60% with levels higher than 200 IU/ml.

Despite the absence of a history (disease and/or vaccination) among NSNV, the share of those with high antibody levels was also high, reaching almost 89%. This fact indicates that the share of people who had actually experienced rubella is undoubtedly higher due to the prevalence of mild or asymptomatic cases, which nevertheless leave a trace in the form of circulating IgG [16]. Furthermore, among volun-



	SNV	SV	NSNV	NSV
> 200 IU/ml	58.9	51.9	33.6	29
100.1–200 IU/ml	22.2	30.5	25	33
25.1–100 IU/ml	15	14.3	26.2	31.3
10–25 IU/ml	1.1	0	3.8	3.6
< 10 IU/ml	2.8	3.3	11.4	3.1

Figure 12. Anti-rubella IgG levels by infectious and vaccinal status

Note. SNV — "sick, never vaccinated"; SV — "sick, vaccinated"; NSV — "never sick, vaccinated"; NSNV — "never sick, never vaccinated". Numerical values and statistical significance indicators are presented in Supplementary Table 9S.

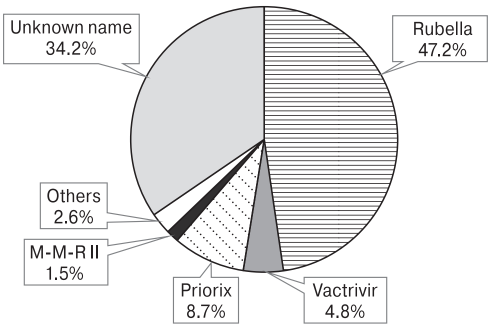


Figure 13. Structure of preparations used for rubella vaccination
Note. Numerical values and statistical significance indicators are given in Supplementary Table 10S.

teers who had not had rubella, Ab levels were lower than in those who had been ill: IgG exceeded 100 IU/ml in almost 60%, including about 30% with a value higher than 200 IU/ml (Fig. 12).

Of the total cohort, only 1,368 volunteers provided medical documentation with information on rubella vaccination. Vaccine name was not indicated in the vaccination certificates of 37.7% of people (Fig. 13). Most volunteers were vaccinated with a domestic monovalent rubella vaccine: 47.2% (95% CI: 44.6–49.9). The usage share of three-component imported and domestic vaccines ranged from 1.5% (M-M-R II) to 8.7% (Priorix).

Age differences were noted regarding vaccines used for rubella vaccination. These are likely associated with the availability of specific vaccines in different time periods (Fig. 14). Adult volunteers aged 30–49 years were combined into one group due to an absence of significant differences.

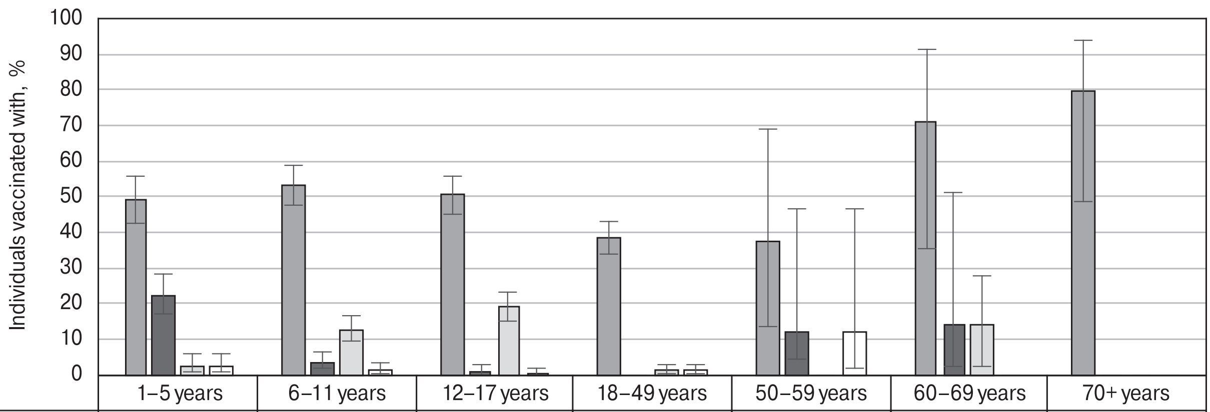
Most volunteers in all age groups were vaccinated with domestic monovalent rubella vaccine. The three-component Vactrivir (measles, mumps, rubella) vaccine has been used in Russia since 2019 as part of the national vaccination schedule. Hence, the maximum share of those vaccinated with Vactrivir was noted among children aged 1–5 years (22.4%; 95% CI: 17.4–28.5). In other age groups, it was apparently used for one-time revaccination in older children, as well as vaccination according to epidemiological indications in adults aged 50–69 years. The imported three-component vaccine Priorix was used for routine vaccination and revaccination of children, as well as vaccination of adults according to epidemiological indications, during the periods when it was available in Russia.

Thus, the conducted serological studies (Ab presence, levels) revealed a high level of herd immunity, indicating that conditions in the region (St. Petersburg, Leningrad Region) are close to the threshold beyond which the rubella virus in the population is completely eliminated.

Herd immunity to the mumps virus

Mumps can be accompanied by numerous complications, the most common of which is orchitis [62, 69, 71]. Less often, meningitis, nephritis, polyneuropathy, pancreatitis, deafness, and other problems, can occur [25, 45, 60, 71]. The infection contributes to the formation of persistent immunity. In Russia, planned vaccination of children (at the age of 12 months) began in 1980. In 2001, mandatory revaccination of children at 6 years of age was introduced. Accordingly, volunteers younger than about 45 years were subject to scheduled mumps vaccination.

Our data shows that the overall seroprevalence in the local volunteer cohort (St. Petersburg,



	1–5 years	6–11 years	12–17 years	18–49 years	50–59 years	60–69 years	70+ years
Rubella	49.5	53.7	50.9	38.6	37.5	71.4	80
Vactrivir	22.4	3.8	1.2	0	12.5	14.3	0
Priorix	2.8	12.8	19.2	1.7	0	14.3	0
M-M-R II	2.8	1.6	0.6	1.4	12.5	0	0

Figure 14. Preparations used for rubella vaccination, by age group
Note. Vertical black lines are 95% confidence intervals. Numerical values and statistical significance indicators are given in Supplementary Table 10S.

Leningrad Region) was 78.4% (95% CI: 77.4–79.3) in September 2023 (Fig. 15). Considering that the share of seronegative individuals should not exceed 15% to ensure epidemiological well-being regarding mumps, it is obvious that the level of herd immunity is insufficient to prevent the spread of infection in the surveyed areas.

The distribution of mumps seroprevalence showed statistically significant age differences relative to the average cohort value. A significantly higher ($p \leq 0.01$) share of seropositive individuals was observed in children aged 6–11 years (probably after revaccination at 6–7 years), as well as in the older groups (≥ 60 years) (likely post-infectious immunity in unvaccinated individuals). In contrast, among young adult and middle-aged volunteers (18–49 years), there was significantly lower seroprevalence ($p \leq 0.0001$). This fact is to be expected since this interval includes those vaccinated once at the age of 1 year (since 1980) before the introduction of revaccination (in 2001).

The distribution of seroprevalence depending on occupation was consistent with the age distribution. The highest values (~86%) were found among schoolchildren and pensioners (children, elderly). The lowest (~70%) were among medical workers, civil servants, and transportation workers (those middle-aged). In all cases, the differences were significant at $p \leq 0.05$. For participants who provided information about illness and vaccination by questionnaire (n = 4527), data were verified against medical records when possible (Supplement Table 12S). Those with documented infectious and vaccinal status (n = 2346) were divided into four groups: SNV (n = 111); SV (n = 25); NSNV (n = 708); and NSV (n = 1502).

As with other vaccine-preventable infections, the groups with volunteers who had experienced symptomatic mumps were represented mainly by adults over 30 years of age. Some of the volunteers who had had the illness were also vaccinated, likely due to epidemiological measures. The NSV group was represented mainly by children and young people under 30 years of age. This is obviously related to the initiation of mumps vaccination in Russia. Older people would have been vaccinated for epidemiological reasons or in accordance with specific regional vaccination programs.

When comparing mumps seroprevalence among volunteers with different infectious and vaccinal status, the highest share of seropositive individuals was observed in the groups who had experienced symptomatic mumps (regardless of vaccination): SNV group — 91.0% (95% CI: 84.2–95.0); and SV group — 92% (95% CI: 75.0–97.8). Seroprevalence among volunteers who indicated no history of mumps (regardless of vaccination) was lower: NSV group — 80.2% (95% CI: 78.1–82.2); and NSNV group — 73.9% (95% CI: 70.5–77.0) (Fig. 16). It is noteworthy that volunteers who denied a history of illness or vaccination, were nevertheless mostly seropositive for anti-mumps antibodies.

Medical documentation with information on mumps vaccination was provided by 1583 volunteers. However, it was impossible to determine official vaccine name in 37.8% of cases (Fig. 17). Most were vaccinated with domestic vaccines: a two-component measles-mumps vaccine (31.5%; 95% CI: 29.3–33.9); a monovalent mumps vaccine (17.9%; 95% CI: 16.1–19.9); and/or the three-component Vactrivir vaccine (4.1%; 95% CI: 3.2–5.2). The share of the two imported, three-component (measles, mumps, rubella) vaccines (Priorix, M-M-R II) did not exceed 9%.

Age differences regarding vaccines used for mumps vaccination were noted. These are likely related to the availability of specific vaccines in different time periods (Fig. 18). Adult volunteers aged 30–49 and 50–69 years were combined due to an absence of significant differences.

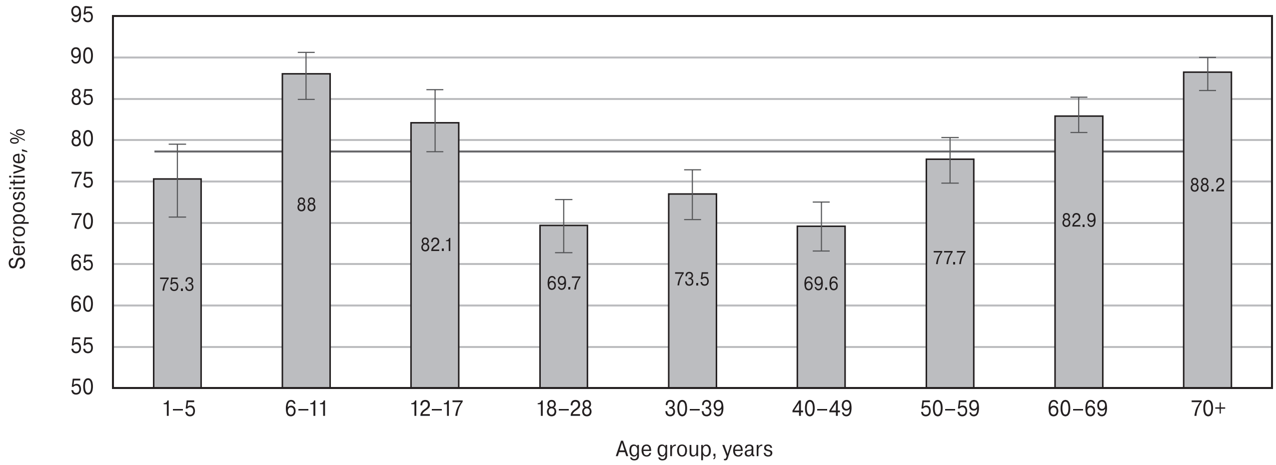


Figure 15. Mumps seroprevalence, by age group

Note. Vertical black lines are 95% confidence intervals; horizontal translucent bar is the 95% confidence interval of the final value for the entire sample (78.4%; 95% CI: 77.4–79.3). Numerical values and statistical significance indicators are presented in Supplementary Table 11S.

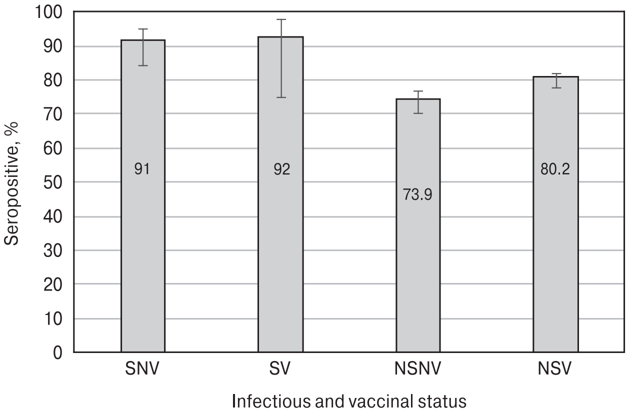


Figure 16. Mumps seroprevalence by infectious and vaccinal status

Note. SNV — "sick, never vaccinated"; SV — "sick, vaccinated"; NSV — "never sick, vaccinated"; NSNV — "never sick, never vaccinated". Vertical black lines are 95% confidence intervals.

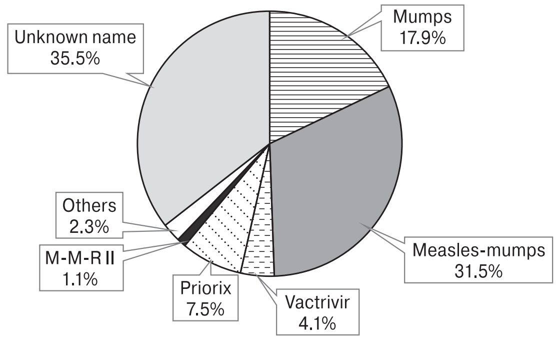


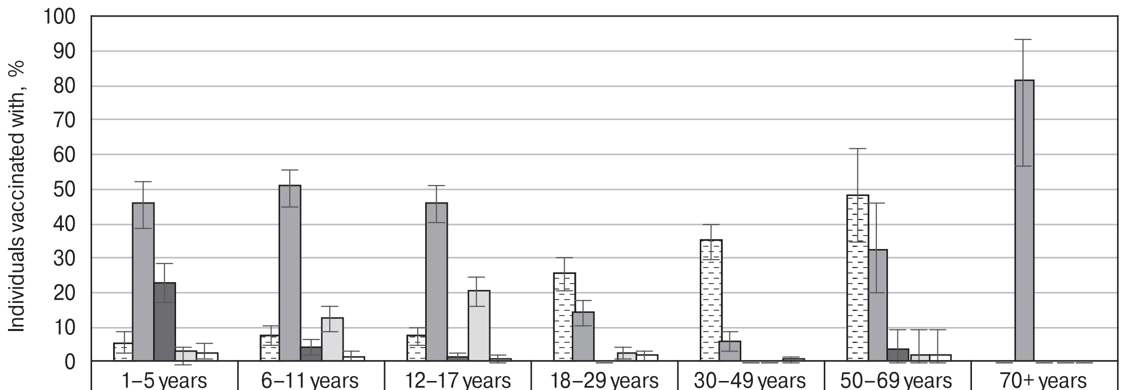
Figure 17. Structure of preparations used for mumps vaccination

Most child volunteers (45.7–50.5%), as well as those over 70 years old (81.3%; 95% CI: 57.0–93.4), were vaccinated with the measles-mumps vaccine. The new domestic three-component vaccine Vactrivir, introduced into practice in 2019, was used to vaccinate children aged 1–5 years (22.4%; 95% CI 17.3–28.5) and 6–11 years (3.8%; 95% CI 2.2–6.5%). In other age groups, only a few such vaccinated individuals were noted. In contrast, those aged 18 to 69 years were vaccinated with monovalent mumps vaccine (25.2–48.2%) or, to a lesser extent, mumps-measles vaccine (5.8–32.1%). Regarding imported, three-component vaccines, Priorix was used in certain young groups (6–11 years, 12–17 years). M-M-R II was used in isolated cases in different age groups.

When summarizing our analysis of herd immunity to mumps, we note that seroprevalence in the local population is close to the threshold for epidemiological well-being (≤ 15% seronegative individuals) only for certain groups: children aged 6–17 years and individuals in the oldest groups (≥ 60 years).

In the volunteer cohort, a separate group consisted of "naive" individuals who denied a history of illness or vaccination. They presumably should have had neither post-infectious, nor post-vaccination, immunity. Nevertheless, for all infections analyzed, high seroprevalence was found among those in the NSNV (never sick, never vaccinated) group: measles virus — 78.5% (95% CI: 74.2–82.2); mumps virus — 73.9% (95% CI: 70.5–77.0); and rubella virus — 88.6% (95% CI: 86.2–90.6).

Age analysis showed that seroprevalence for all infections was minimal in children aged 1–5 years



	1–5 years	6–11 years	12–17 years	18–29 years	30–49 years	50–69 years	70+ years
Mumps	5.2	7.3	7.1	25.2	34.9	48.2	0
Measles-mumps	45.7	50.5	45.8	13.9	5.8	32.1	81.3
Vactrivir	22.4	3.8	1.2	0	0	3.6	0
Priorix	2.9	12.4	20.3	2.2	0	1.8	0
M-M-R II	2.4	1.3	0.6	1.6	0.3	1.8	0

Figure 18. Preparations used for mumps vaccination, by age group

Note. Vertical black lines are 95% confidence intervals. Numerical values and statistical significance indicators are given in Supplementary Table 13S.

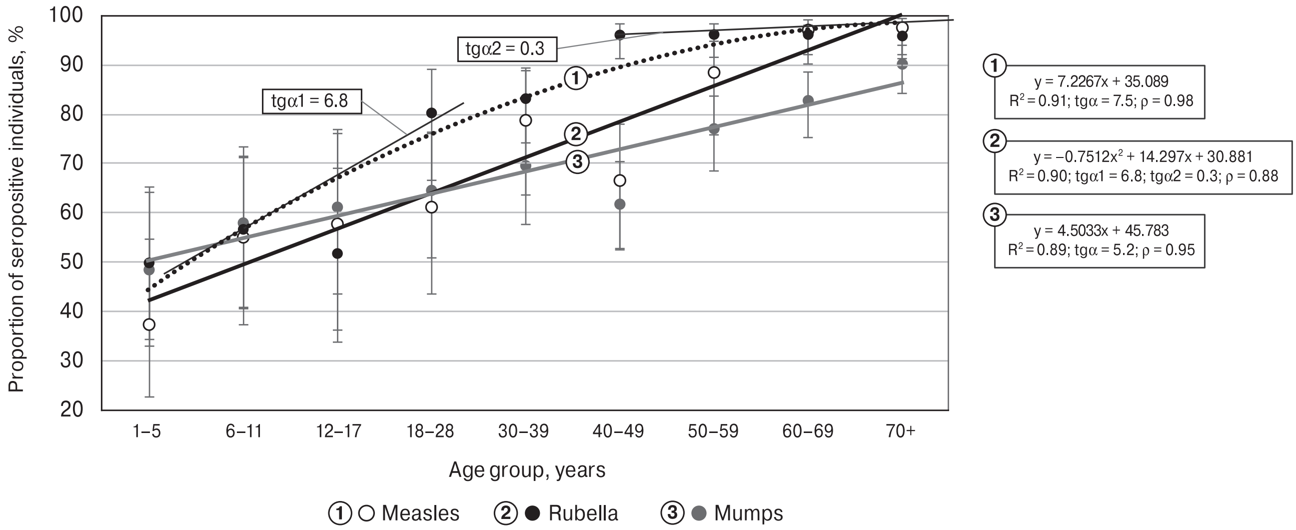


Figure 19. Seroprevalence among “naive” volunteers (never sick, never vaccinated) for vaccine-preventable infectious pathogens

Note. Since the rubella trendline was described by a 2nd degree polynomial, tangents to the curve were calculated for the youngest and oldest categories: tgα1 — slope of the youngest interval (aged 1–11 years), representing rate-of-increase in seropositivity in children; and tgα2 — slope of the oldest interval (aged ≥ 60 years). Trends for measles and mumps were straight lines. As such, their tgα values reflect evenly increasing seropositivity across age groups. Spearman correlation coefficients (ρ) are shown. For statistical significance, all at $p < 0.05$. Numerical values and statistical significance indicators are given in Supplementary Table 14S.

(37.5% for measles, 48.6% for mumps and 50.0% for rubella), with an increase to maximum levels in individuals aged ≥ 70 years (90.3% for mumps, 96.0% for rubella and 97.7% for measles) (Fig. 19). Setting aside that some volunteers, or their parents, may have forgotten illness or vaccination, one aspect becomes apparent. The revealed seroprevalence values indicate insufficient laboratory diagnostics of vaccine-preventable infections. In reality, older volunteers had not only experienced “childhood” infections, they also had likely received a natural booster effect through encounters with infected individuals. This is confirmed by the fact that Ab levels were higher in older age groups than in children.

It is obvious that the dependence in this case is not linear, and the trend can be described by two tangents. The first is tgα1 = 6.8 (steeper), wherein the level of herd immunity is growing at a high rate due to an active transmission process. Adaptive immunity is quickly formed (via childhood immunization or transmission). The second is tgα2 = 0.3, wherein all (or almost all) of those in the oldest groups (> 60 years) have already encountered the virus in their lives through vaccination or illness. In result, the virus practically does not spread in this age group.

Discussion

Herd immunity is the central mechanism for protecting the population from contagious infectious pathogens that tend to spread as epidemics. These include airborne infections, often in childhood (measles, mumps, rubella, diphtheria, whooping cough), as well as acute respiratory viral infections that are not strongly age-specific (influenza, parainfluenza, respiratory syncytial virus, coronaviruses, etc.) [31, 39, 44, 46, 63, 66]. It is also worth mentioning that a number of infections have virtually disappeared in recent times, yet caused a number of deadly epidemics in the Middle Ages [1, 64]. The outcome of all these pandemics was the formation of specific immunity to the pathogen. This process is based on the ability of cellular and humoral mechanisms to block the transmission of pathogens among the population, wherein the prevalence of positive serological results (p) exceeds the critical value of herd immunity (pc), known as the herd immunity threshold [43, 51, 70]. According to researchers, achieving this threshold is realistic (at least for measles, mumps, and rubella) provided that vaccination of different population segments is properly organized [51, 67].

The measles virus is a highly contagious pathogen, the basic reproduction number (R_0) for which is 9–18 [61]. This means that the target vaccination coverage to achieve the protective immunization threshold should be about 95% [29]. The criterion for epidemic well-being regarding measles is the presence of no more than 7% seronegative individuals in the population. Our results show that in St. Petersburg and the Leningrad Region, the measles seroprevalence in the cohort as a whole was 81.4% (95% CI: 80.4–82.3), which is significantly below the threshold. We also note statistically significant heterogeneity in the cohort: the lowest seroprevalence was found among individuals aged 18–39 years (62.4%; 95% CI: 59.0–65.7); and the highest was among those aged ≥ 70 years (96.2%; 95% CI: 94.8–97.2). Similar heterogeneity was found in volunteers depending on field of activity. Higher seroprevalence was noted among pensioners and preschoolers (which corresponds to the age distribution). It was also noted in health workers and educators, both of which are "at risk" groups. Since 2014, they are subject to vaccination until the age of 55 under certain conditions (no history of vaccination or illness) [12, 13].

High anti-measles Ab levels are most typical for older individuals: about 80% of seropositive individuals aged ≥ 60 years had high (1–2 IU/ml), or very high (> 2 IU/ml), IgG levels. The opposite situation was noted in the group "children aged 1–17 years": the overwhelming majority had low or medium Ab levels (0.18–1.0 IU/ml).

Analysis of volunteer histories (measles vaccination, past illness) showed that seroprevalence was mainly influenced by past illness, not vaccination. Among those who had had measles, seroprevalence and Ab levels were higher than among those who had not, regardless of vaccination. Our data on local herd immunity (St. Petersburg, Leningrad Region) are consistent with earlier data from other seroepidemiological studies conducted in various Russian regions. They also noted low measles seroprevalence in children and in adults aged 18–40 years [4, 9, 10, 11, 17, 18].

It can be assumed that the revealed differences are due to a number of medical and social factors. Mandatory single vaccination of children with a live measles vaccine at the age of 1 year was launched in the USSR in 1968. In 1986, revaccination of children before entering school (at the age of 6 or 7 years) was introduced. Thus, subjects who have undergone a full course of measles vaccination within the framework of the national schedule (vaccination, revaccination) can be classified fairly reliably as persons under 40 years of age. Persons aged 40–55 years were most likely vaccinated once. Those over 55 would have been vaccinated only according to epidemiological indications. Interestingly, starting from the age of 50, the share of measles-seropositive persons with high Ab levels steadily increases.

There is no doubt that in the period preceding the introduction of mandatory vaccination, measles incidence was high, and people over 50 years of age were highly likely to have had this infection. The higher seroprevalence in groups over 50 years of age, as well as high Ab levels, indicate a long-term and even lifelong existence of anti-infective immunity. It is believed that the measles vaccination coverage among the adult population aged 18–35 is maintained at the regulated level and is about 99% in Russia [12, 13]. Our data indicate that the real seroprevalence of the population at this age is 60–70%. Data from Russian authors indicate that during periods of increased measles incidence, people in age groups with a low herd immunity are primarily involved in the epidemic process [18]. Also noteworthy is the high share of seronegative individuals among children (18.4–25.7%). Data from official registrations and individual researchers confirm the involvement of unvaccinated individuals in the epidemic process: no more than 5–7% of those infected are vaccinated against measles [3, 21].

Thus, our results confirm the fact that individuals who have had manifest measles (usually older people) have higher immune protection than after vaccination [54]. In addition, older individuals in conditions of high measles incidence in the pre-vaccination period probably encountered the pathogen repeatedly, which strengthened post-infectious immunity (booster effect) and ensured high Ab levels. The immune response formed following the measles vaccine is lower. In addition, the probability of a natural booster effect in vaccinated individuals in conditions of reduced circulation of wild virus is low. This is confirmed by low Ab levels in seropositive young individuals [35].

Rubella, like measles, is a vaccine-preventable infection and, despite the existence of a family of specific vaccines, continues to cause up to 100 000 cases of congenital rubella syndrome worldwide annually [39, 42, 59]. Its basic reproduction number varies from 3–8, potentially up to 12 [49, 56]. It follows that the required threshold of herd immunity in European countries is estimated to be 67–87%, while in developing countries it can reach 90% [39, 51, 52]. Live attenuated MMR vaccine is used worldwide for specific prevention of rubella; it is capable of generating adaptive immunity simultaneously to three pathogens: measles, mumps, and rubella [58].

Rubella immunization in Russia was introduced into the schedule by an order of the Ministry of Health (dated 27.12.97, No. 375), later replaced by a subsequent order (dated 30.09.2015, No. 683H). Accordingly, children are subject to routine immunization at specific points: those aged 12 months; 6 years; and girls aged 13 years. Additional rubella immunization includes: all children from 1 to 17 years who have not been ill, not been vaccinated, or vaccinated only once; as well as young women aged 18–25 years who have not been ill or vaccinated previously [14].

An assessment of rubella herd immunity showed that the overall cohort had the necessary immune protection, regardless of age or occupation. The average rubella seroprevalence was 95.5% (95% CI: 94.9–95.9). The highest level was recorded among volunteers aged 50–70+ years (96.3–97.6%). The lowest was in the age group 30–39 years (92.7%; 95% CI: 90.8–94.3). In other words, the level of herd immunity reached the threshold for epidemic well-being (≤ 7% seronegative individuals in the pop.) in almost all age groups. This is confirmed by the absence of registered of cases of rubella, or congenital rubella syndrome, in 2021–2023 locally (St. Petersburg, Leningrad Region).

Unlike measles, 60–70% of volunteers had high, or very high, anti-rubella IgG levels, and the share of individuals with low Ab levels did not exceed 7%. However, in children aged 6–17 years, high IgG levels were detected significantly less frequently than in children aged 1–5 years or adults. This situation, noted by other authors [20], may be associated with a weakening of immunity 6–10 years after revaccination in the absence of a natural booster effect when encountering wild rubella virus. It is interesting to note that in the group of volunteers who had not been ill or vaccinated against rubella, the share of seropositive individuals was high, 88.6% (95% CI: 86.2–90.7), although significantly lower than in the groups of those who had been ill and vaccinated. In addition, those with full recoveries from symptomatic infections had higher Ab levels. Specifically, in 50–60% of such volunteers, IgG levels exceeded 200 IU/ml, as opposed to 29–33% of those who without a history of manifest rubella.

When summarizing the assessment of herd rubella immunity in the local population (St. Petersburg, Leningrad Region), as well as the data of other domestic authors [7, 9, 11, 17, 18, 20], it is obvious that the existing practice of routine vaccination has contributed to the formation of herd immunity sufficient to interrupt viral spread.

This is reflected in the absence of manifest cases in recent years. Clearly, a high level of herd immunity has been maintained, even in the absence of circulation of the wild strain or natural booster effects through encounters. It is premature, of course, to declare a complete victory over rubella, and the possibility of imported cases cannot be ruled out. However, the risk of epidemic spread among local residents can currently be considered low.

In uncomplicated cases, mumps occurs as a mild, self-limiting infection, but there are also complicated cases with the addition of orchitis in boys, as well as pancreatitis and even neurological complications [60, 69, 72, 73]. The mumps virus is less contagious than the measles virus. Values for the basic reproductive number, depending on regional characteristics, can vary from 4–7 (USA) to 11–14 (Great Britain) [36]. Before the introduction of mass vaccination, illness was widespread globally. In some countries, up to 5–6% of the population has experienced symptomatic forms [22]. A significant change in the epidemiological situation occurred only after the introduction of specific vaccination into clinical practice in 1967. This has enabled a many-fold reduction in mumps prevalence globally [6, 37].

Contemporary mumps epidemiology and its features have been shaped by routine prevention using a live attenuated vaccine. The introduction of vaccines against the virus in Russia has contributed to a decrease in the frequency of clinical mumps cases, primarily due to the formation of strong herd immunity [6]. In Russia, two domestic vaccines based on the Leningrad-3 strain are used: a monovalent mumps vaccine and a divalent (mumps-measles) vaccine. Two imported trivalent (measles, mumps, rubella) vaccines, M-M-R II and Priorix, are also used. Regardless of their origin, all of the listed vaccines create 90% immunity, which lasts up to 5–6 years after administration [16, 19, 24, 32]. The vaccination program against mumps in Russia has undergone changes, which obviously has affected seroprevalence in various age groups. Routine vaccination of the child population (at the age of 12 months) began in 1980. In the year 2000, the attenuated mumps virus content in the vaccine was increased by 2-fold. In 2001, due to an identified decrease in immunity, mandatory booster revaccination of children at 6 years of age (before school) was introduced into the national vaccination schedule.

Taking into account that the average value of the basic reproductive number (R_0) varies within 4.5, it is possible to calculate the threshold level of mumps herd immunity (R_i), which was 77.7%, using the formula $(1\text{-}(1/R_0) \times 100)$. In St. Petersburg and the Leningrad Region, the average cohort value of R_i was 78.4% (95% CI: 77.4–79.3). The highest R_i values were noted among children aged 6–11 years (88.0%; 95% CI: 84.9–90.6) and those ≥ 50 years (88.2%; 95% CI: 86.0–90.0); differences with the average cohort value were significant ($p < 0.001$). The least protected were middle-aged adults aged 18–49 years, among whom seronegativity reached 30%. They were likely vaccinated once before the introduction of revaccination in 2001.

The distribution of mumps seroprevalence by field of activity corresponded with age. The highest seropositivity values were found among schoolchildren and pensioners (children and the elderly). The lowest was among medical workers, civil servants, and transportation workers (middle-aged people). In all cases, the differences were significant ($p \leq 0.05$). As with other vaccine-preventable infections, analysis of infectious history and vaccinal status showed that the highest share of seropositive individuals was noted in groups of volunteers who had experienced symptomatic mumps, regardless of vaccination: 87.6–91.0%.

Thus, the threshold for epidemic well-being with respect to mumps (≤ 15% seronegative individuals) corresponded to the level of herd immunity only among children aged 6–17 years and those > 60 years. The rest of the population, including preschool children and adults aged 18 to 59, are not sufficiently protected from mumps. As such, they can be involved in epidemiological processes.

Analysis of volunteer groups who cannot document, or recall, a history of vaccination or illness (i.e., should not have had significant humoral immunity) shows that there has been insufficient laboratory diagnostics of vaccine-preventable infections. Latent and asymptomatic forms (measles, mumps, rubella) have very likely been overlooked in the past. Seropositivity for these pathogens was noted in all age groups. It increased with age, reaching maximum levels in those aged 70+ (90.3% for mumps, 96.0% for rubella and 97.7% for measles). Many of the older adult volunteers were born in, or have lived through, the pre-vaccination period. Many have had these “childhood” infections, as well as the opportunity to receive a natural “booster effect” in conditions of high morbidity (through contact with infected individuals).

In Russia, live attenuated vaccines are used for specific prevention of these pathogens in the form of monovalent, two-component (measles, mumps), and three-component preparations (measles, mumps, rubella). All available vaccines are safe, effective, and can be equally used within the framework of immunization programs. However, the general trend in vaccination development globally has been a transition to combination vaccines with an increasing number of components. In 2019, the first domestic three-component vaccine, Vactrivir (measles, mumps, rubella) [19], was registered in Russia. Earlier, the foreign vaccines Priorix and M-M-R II were used as three-component vaccines. Multicomponent vaccines are predominantly used for routine vaccination of children. Monovalent vaccines are used for vaccination (and revaccination) of adults according to epidemiological indications, depending on which pathogen is of public health concern.

Conclusions

1. Currently, herd immunity to “childhood” infections in the local population (St. Petersburg, Leningrad Region) ensures epidemiological well-being only with respect to rubella. This is confirmed by the long-term absence of cases of acute infection or congenital rubella. An unfavorable situation is noted with the level of herd immunity to measles and mumps, which corresponds to the situation noted in other Russian regions.

2. The highest share of susceptible individuals was found among young and middle-aged groups. These volunteers typically: have not experienced symptomatic cases of these infections; were vaccinated according to an incompletely established vaccination schedule; and have not experienced a natural booster effect (due to reduced circulation of wild viral strains). The aforementioned factors contribute to a fading of post-vaccination immunity.

3. The least susceptible to these “childhood” illnesses are individuals over 50 years of age who have experienced infection (symptomatically or asymptomatically). They have developed post-infectious immunity (with high Ab levels) and also received a natural booster effect in the pre-vaccination period in conditions of high morbidity.

4. The situation with post-vaccination immunity to measles requires additional analysis. Seroprevalence levels in certain age groups, including children, are insufficient to ensure epidemiological well-being. Currently, outbreaks associated with imported cases of infection are being registered in Russian regions, with subsequent formation of foci among unvaccinated residents.

Supplementary materials

Supplement tables are available at: http://dx.doi.org/10.15789/2220-7619-HIT-17797.

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