# ESTIMATING THE ACTUAL SUSCEPTIBILITY OF DECREED POPULATION TO MEASLES, RUBELLA AND MUMPS

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As the modern society becomes more vaccine-dependent, the need arises for population immunity studies aimed to estimate the prevalence of antibodies against a particular infection in the donors from different populations, including sentinel groups. This work reveals the actual susceptibility of the Russian population to a number of vaccine preventable infections, including measles, rubella, and mumps. The study was conducted using blood serum samples provided by the Blood serum bank of Gamaleya Federal Research Center for Epidemiology and Microbiology (Moscow). Of 866 samples used in the study, 293 and 117 samples had been collected from healthcare workers in 2011 and 2017, respectively; 220 samples had been obtained from military servants in 2016–2017, and 236 samples had been collected from healthy donors in 2016. All samples were studied by solid phase enzyme immunoassay using diagnostic kits by Vector-Best (Russia). We discovered that 19.4 % and 28.8 % of individuals were susceptible to measles and mumps, respectively, which is insufficient for ensuring epidemiological safety (the herd immunity thresholds for these diseases are 7 % and 15 %, respectively) and puts the population at risk of infection spread, should the pathogens enter the country. The proportion of individuals susceptible to rubella was 6.5 %, which is below the herd immunity threshold (7 %).

**Keywords:** preventive vaccination, herd immunity, serological surveillance, measles, rubella, mumps, military servants, healthcare workers

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# ОЦЕНКА ФАКТИЧЕСКОЙ ВОСПРИИМЧИВОСТИ ОТДЕЛЬНЫХ ГРУПП ДЕКРЕТИРОВАННОГО НАСЕЛЕНИЯ К ВИРУСАМ КОРИ, КРАСНУХИ И ЭПИДЕМИЧЕСКОГО ПАРОТИТА

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В условиях формирования «вакцинозависимости» современного общества приоритетным является изучение популяционного иммунитета, основанное на оценке распространенности антител к той или иной инфекции в крови доноров из различных, в том числе индикаторных, групп населения. В работе представлены данные о фактической восприимчивости россиян к таким вакциноуправляемым инфекциям, как корь, краснуха и эпидемический паротит. В качестве материала для исследования использовали образцы сывороток крови из Банка сывороток крови Национального исследовательского центра эпидемиологии и микробиологии имени почетного академика Н. Ф. Гамалеи (Москва): 866 образцов, в том числе 293 и 117 образцов от медицинских работников, полученных в 2011 г. и 2017 г. соответственно, 220 образцов от военнослужащих, полученных в 2016–2017 гг., и 236 образцов от условно здоровых доноров, полученных в 2016 г. Все образцы были исследованы методом твердофазного иммуноферментного анализа с использованием предназначенных для изучаемых инфекций тест-систем компании «Вектор-Бест» (Россия). Была выявлена значительная доля восприимчивых к кори (в среднем — 19,4 %) и эпидемическому паротиту (в среднем — 28,8 %) лиц, что не соответствует критерию эпидемического благополучия для этих инфекций (7 и 15 % соответственно) и создает условия для распространения инфекций в случае попадания возбудителей на территорию страны. Доля восприимчивых к краснухе людей составила в среднем 6,5 %, что отвечает критерию эпидемического благополучия (7 %).

**Ключевые слова:** вакцинопрофилактика, популяционный иммунитет, серологический мониторинг, корь, краснуха, эпидемический паротит, военнослужащие, медицинские работники

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# ОРИГИНАЛЬНОЕ ИССЛЕДОВАНИЕ І ИММУНОЛОГИЧЕСКАЯ ПАМЯТЬ

World Health Organization (WHO) estimates that on average 2 billion people suffer from infections every year; 17 million of them die [1]. Vaccination is the most effective and economically sound tool for controlling infections, given that it is promoted worldwide and the involved healthcare workers are committed to its goals. Due to vaccination, approximately 2 to 3 million infection-related deaths were prevented in 2016; but better coverage could have saved another 1.5 million lives [1].

Good vaccination coverage is one of the key indicators of a successful vaccination strategy. To ensure protection against the majority of vaccine-preventable infections, WHO expects vaccination coverage to be at least 95 % among children and 90 % among adults. Officially [2], Russia has already achieved these high goals and now only maintains the recommended rates. Plummeting incidence and mortality related to vaccine-preventable infections indicate that the chosen vaccination strategy is effective.

Inspiring results of vaccination drove WHO to announce a new era in healthcare: smallpox had been eliminated by 1980, no incident cases of polio have been reported in Russia since 2002. Although measles and rubella had not been eradicated by 2010, as planned, there is hope for this to happen in the future. In 2000, the USA declared elimination of measles [3]; however, in 2010 the situation changed: measles incidence rates started to increase in both Americas, Europe, Africa, and the former Soviet Union, including Russia [4]. Therefore, the deadline for measles elimination was extended to 2015 and then beyond 2020.

Growing measles incidence was alarming, prompting the medical community to question the reliability of key indicators of vaccination effectiveness. A few new factors were discovered negatively affecting vaccination outcome, including weak cold chains, unsubstantiated contraindications, increasing vaccine hesitancy among parents and failure to adhere to vaccination schedules. Unfortunately, vaccine hesitancy is becoming a pressing issue in Russia. Polibin et al. [5] indicate that in Russia the population tends to avoid any preventive measures, including vaccination. Parent surveys show that only 80 % of infants below 2 years of age are vaccinated.

Many authors believe that the troubling situation with measles resulted from reduced herd immunity, i. e. the proportion of people susceptible to infection [6–8]. The only way to measure it is to resort to serological surveillance [8, 9]. The proportion of seronegative (or susceptible) individuals is calculated using laboratory serum tests. Seronegativity rates of <7~% and 15 % for measles and mumps, respectively, are epidemiological health thresholds.

In Russia, serological surveillance is not perfect. One of its downsides is the inability to compare results of studies of serum samples collected in different years, accounting for the rapid evolution of laboratory diagnostic techniques and standards. Besides, serological studies ignore professional occupation of the participants (for example, vaccination requirements for decreed population groups are stricter) and their general health (infections affect humoral immunity). Serum banks may provide a solution here.

A number of Russian researchers argue that healthcare workers contribute to the risk of infection outbreaks in healthcare facilities [10, 11]. Healthcare personnel is regarded by the law as a decreed population group; members of this group must be vaccinated against measles before turning 55 (or 35, in the case of rubella and mumps) [12]. These people are not only at risk of getting infected; they also indirectly signal the epidemiological status of the population.

This study aimed to evaluate the actual susceptibility of the Russian population to measles, rubella and mumps by analyzing the samples from the Serum bank of N. F. Gamaleya Federal Research Centre for Epidemiology and Microbiology, Moscow.

#### **METHODS**

We studied 866 serum samples, including:

- 293 samples collected in 2011 from healthcare workers residing in the Central Federal District (CFD);
- 117 samples collected in 2017 from healthcare workers residing in CFD;
- 220 samples collected in 2016-2017 from contracted soldiers (military recruits) serving in Moscow region;
- 236 samples collected in 2016 from seemingly healthy individuals residing in Moscow and Moscow region.

In 2011 the situation with measles significantly deteriorated in Russia, and in 2017 extra preventive measures were taken supported by the State, including immunization of previously unvaccinated population groups and increasing the vaccination age for medical workers from 35 to 55 years [8, 12]. Outbreaks of measles, rubella and mumps are, however, still reported in the armed forces, demonstrating a problem of a closed susceptible group [13].

In our study, vaccination histories of sample donors were unknown, no documented evidence on their vaccination status was available.

The study was designed and conducted in compliance with the guidelines of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing [9]. Serum samples were studied using ELISA and a number of testing kits, including Vecto-Measles IgG, Vecto-Rubella IgG, Vecto-Mumps IgG (by Vector-Best, Russia), according to the manufacturer's protocol.

Statistical analysis was performed in Microsoft Excel and Statistica 6.0 (StatSoft, USA). Significance of differences between the groups was calculated using the chi squared test and Yates' correction. Mean values (m) were calculated for all studied parameters; a 95 % confidence interval was calculated using the Clopper–Pearson method.

#### **RESULTS**

In the course of our study, we evaluated immunity to vaccinepreventable infections among different population groups. Results are shown in Table 1.

The table shows that all studied groups were protected against rubella: the proportion of seronegative samples did not exceed the 7 % threshold.

A considerable proportion of study participants were susceptible to measles, military recruits being the most vulnerable group, where the proportion of seronegative samples reached the maximum of 25.5 %, which is 3.6 times higher than the epidemic threshold. Among medical workers, susceptible individuals accounted for 7.7 %.

Among the healthy donors residing in Moscow and Moscow region, the proportion of susceptible individuals was quite large (21.2 %). This people may contribute to the spread of measles, forming epidemic foci, especially in the armed forces, should the pathogen find its way into the region. Thus, the current situation with measles in Moscow and Moscow region can be characterized as unstable.

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Table 1. Immunity to measles, rubella and mumps in different population groups residing in Russia (2016–2017)

Population groups	Seronegativity to measles virus, % [CI of 95 %]	Seronegativity to rubella virus, % [Cl of 95 %]	Seronegativity to mumps virus, % [Cl of 95 %]
Healthcare workers	7.7* [3.6; 14.1]	5.1 [1.9; 10.8]	20.5 [13.6; 29.0]
Military recruits	25.5 [19.8; 31.8]	4.6 [2.2; 8.2]	29.6 [23.6; 36.1]
Healthy individuals	21.2 [16.2; 27.0]	8.9* [5.6; 13.3]	32.2 [26.3; 38.6]
Total	19.4 [16.2; 22.9]	6.5 [4.6; 8.8]	28.8 [25.1; 32.7]

Note. \* — differences in comparison with the epidemiological health thresholds (7 %) are statistically insignificant (p > 0.05).

Table 2. Herd immunity in healthcare workers

Population groups	Seronegativity to measles virus, % [Cl of 95 %]	Seronegativity to rubella virus, % [Cl of 95 %]	Seronegativity to mumps virus, % [Cl of 95 %]
Healthcare workers (2011)	18.7 [14.5; 23.7]	4.7 [2.6; 7.9]	38.2 [32.6; 44.1]
Healthcare workers (2017)	7.7 [3.6; 14.1]	5.1 [1.9; 10.8]	20.5 [13.6; 29.0]

A considerable proportion of individuals was found to be susceptible to mumps in all studied groups (29.6 % of military recruits, 32.3 % of healthy donors), which is on average twice as high as the epidemic threshold (< 15 %) and may promote infection in the population.

Serum banks accumulate samples obtained before the actual study, making retrospective serological research possible. In our study we used blood serum samples collected from healthcare workers in 2011 when measles incidence rates where increasing in Russia in general and Moscow in particular. Statistical differences (p < 0.05) between two sample groups were observed for measles and mumps (Table 2).

Between 2011 and 2017, the proportion of people susceptible to measles considerably decreased and reached the recommended threshold: from 18.7 % in 2001 to 7.7 % in 2017, which may be a result of an additional round of vaccination prompted by the epidemiological situation. The proportion of individuals seronegative to mumps decreased from 38.2 % to 20.5 % but did not reach the recommended threshold, which indicates the need for an additional vaccination round.

#### DISCUSSION

Based on the obtained results, we conclude that susceptibility to rubella in some population groups and population in general is low and does not go beyond the outbreak threshold (the proportion of seronegative samples in our study was 6.5 %). These results correlate with the official statistics on sporadic rubella incidence of 0.11 per 100,000 population in 2016, with no congenital rubella cases reported [14]. Importantly, over the last 6 years the proportion of seronegative individuals has not changed, which is a good prognostic sign.

There is a risk of measles epidemic, should the pathogen find its way into the country, because in all studied groups the

proportion of susceptible individuals (an average of 19.4 %) was above the outbreak threshold. The most vulnerable group was the military recruits (25.5 % of seronegative samples). Another study [15] conducted in contracted soldiers revealed that the proportion of seropositive individuals was 72.4  $\pm$  2.3 %.

The proportion of mumps-susceptible individuals was maximal in healthy donors (32.3 %, with an average rate of 28.8 %). According to the official statistics, mumps rates tend to grow, but only in the case of sporadic incidence [14].

Measles, mumps and rubella are traditionally seen as viral infections with similar epidemiological patterns. The vaccines against these infections are attenuated and administered at the same age (12 months, 6 years). The differences observed by the authors of this works and other researchers [16] regarding the proportion of susceptible individuals may be explained by different immunogenicity of measles, rubella and mumps components contained in the vaccine, whose effectiveness were estimated to be 97 % (67–100 %), 97 % (94–100 %) and 88 % (66–95 %), respectively [17].

## CONCLUSIONS

As a method for monitoring herd immunity, serological surveillance allows evaluating vaccination effectiveness, predicting epidemics and planning preventive measures. Our study demonstrates the need for additional immunization campaigns covering the unvaccinated subpopulations, including the armed forces. The large proportion of individuals susceptible to mumps among the studied groups increases the risk of an outbreak in the nearest future. Preventive measures need to be taken now. The situation with rubella is benign, giving hope for complete eradication of this disease in the future.

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