



The Status of Humoral Immunity to Parvovirus B19 in Population of Certain Geographical Regions

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Introduction. In a number of countries, including Russia, there is no systematic registration and reporting of parvovirus infection cases; the extent of its spread can be estimated by using humoral immunity rates.

Purpose of the study: Assessment of seroprevalence of parvovirus B19 (B19V) in different age groups of population of Russia, Central Asia, and West Africa.

Materials and methods. A total of 1,732 blood serum samples from residents of Saint Petersburg and Nur-Sultan, migrant workers from Uzbekistan and Tajikistan, residents of the Republic of Guinea were studied for IgG antibodies to B19V.

Results. The highest seroprevalence rates were identified in Saint Petersburg and Nur-Sultan (62–65%); the lowest rates were registered among migrant workers from Uzbekistan and Tajikistan (47%). The results for the Republic of Guinea showed a B19V seroprevalence rate of 53%. It was found that there is an increasing trend of seropositivity with age; the percentage of seropositive individuals clearly increases in older age groups: up to 55% — among migrant workers from Central Asia and residents of the Republic of Guinea; up to 80–85% — among residents of Saint Petersburg and Nur-Sultan.

Discussion. The obtained results confirm the worldwide occurrence of parvovirus infection. People susceptible to infection can cause infection spreading in high-risk groups — among pregnant women, immunodeficient patients, blood product recipients, and cancer patients.

Keywords: *parvovirus infection; humoral immunity; seroprevalence; Russian Federation; Central Asia; Republic of Guinea.*

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Состояние гуморального иммунитета к парвовирусу В19 у населения отдельных географических регионов

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Введение. В ряде стран, в том числе в России, отсутствуют регистрация и учет заболеваемости парвовирусной инфекцией; о распространении этой инфекции можно судить по показателям гуморального иммунитета.

Цель исследования: оценка серопревалентности к парвовирусу В19 (PVB19) в разных возрастных группах населения России, Средней Азии, Западной Африки.

Материалы и методы. На IgG-антитела к PVB19 исследованы 1732 сыворотки крови жителей Санкт-Петербурга, Нур-Султана, трудовых мигрантов из Узбекистана и Таджикистана, граждан Гвинейской Республики.

Результаты. Наибольшие показатели серопревалентности выявлены в городах Санкт-Петербурге и Нур-Султане (62–65%); наименьшие — среди трудовых мигрантов из Узбекистана и Таджикистана (47%). Показатель серопревалентности к PVB19, полученный в Гвинейской Республике, составил 53%. Установлена общая тенденция повышения доли серопозитивных лиц в старших возрастных группах: до 55% — у мигрантов из Средней Азии и граждан Гвинейской Республики; до 80–85% — у жителей Санкт-Петербурга и Нур-Султана.

Обсуждение. Полученные результаты подтверждают факт распространения парвовирусной инфекции в разных странах мира. Наличие восприимчивых к заражению лиц может привести к распространению инфекции в группах риска — среди беременных женщин, лиц с иммунодефицитами, реципиентов препаратов крови, онкологических больных.

Ключевые слова: парвовирусная инфекция; гуморальный иммунитет; серопревалентность; Российская Федерация; Средняя Азия; Гвинейская Республика.

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Introduction

The medical significance of parvovirus infection (PVI) is attributed to specific features of its pathogen — human parvovirus B19 (B19V). The virus has a teratogenic effect becoming especially manifest during the second trimester of pregnancy [1–3]. The fetal infection results in development of congenital PVI, the most frequent manifestation of which is nonimmune hydrops fetalis [4–7]. B19V is also characterized by a unique tropism for erythroid progenitor cells (pre-erythroblasts) [8]. As a result, B19V infection causes disruption of erythropoiesis, which may lead to serious complications in patients who are immune compromised or suffer from chronic anemia [9, 10].

Apart from the clinically apparent form of the disease most common among children and known as erythema infectiosum or fifth disease, PVI manifestations are quite diversified. They range from asymptomatic forms (30–50% of all cases) or mild exanthem to arthritis and arthralgia (primarily among adults) as well as severe anemia and development of an aplastic crisis (immunodeficient individuals and patients with hematologic disorders) [11–17].

Currently, in a number of countries, including Russia, there is no systematic PVI registration and reporting; the data on its prevalence are limited, including its prevalence in high-risk groups (pregnant women, blood product recipients) [15, 18–21].

Considering the fact that no PVI preventive methods are available and IgG antibodies remain in the blood sera of exposed people for the rest of their life, the extent of PVI spread in a population can be estimated by rates of humoral immunity.

The purpose of this study is to assess the development of humoral immunity to PVI in different age groups of individuals living in the European part of Russia, countries of Central Asia and West Africa.

Materials and methods

A total of 1,732 blood serum samples from relatively healthy adults aged 18–87 were tested for the presence of IgG antibodies to B19V, including 817 serum samples from residents of the Russian Federation (Saint Petersburg), 114 serum samples from migrant workers from Central Asia, 480 serum samples from residents of Kazakhstan (Nur-Sultan), 321 serum samples from residents of the Republic of Guinea (RG). The serum samples were received in 2017–2018 from collections of the virology laboratories of the Saint Petersburg Regional Center for Epidemiological Surveillance of Measles and Rubella in the Northwestern Federal District, the Regional Center for Epidemiological Surveillance of Measles in RG, the HIV Etiology and Immunology Laboratory at the Pasteur Research Institute of Epidemiology and Microbiology.

The sera were tested for anti-B19V IgG antibodies by using the Anti-Parvovirus B19 ELISA IgG test system (Euroimmun AG, Germany) in accordance with the manufacturer's protocol.

The data were processed with MS Excel, Prism 5.0 statistical software (GraphPad Software Inc.). The nominal data were described by indicating absolute values and percentages. The nominal data were compared by using the Pearson chi-square test to assess the significance of the differences between the actual number of outcomes or qualitative data of the sample falling into each category and the theoretical quantity that could be expected in studied groups if the null hypothesis were true. The chi-square (χ^2) value was compared with the critical values for the respective number of degrees of freedom. If the calculated chi-square value was greater than the critical value, it indicated the presence of a statistical relationship between the studied risk factor and the outcome at the respective level of significance.

The Pearson correlation coefficient r_{xy} was used to measure the strength of the relationship between x and y normally distributed variables. The t -test was used to evaluate the statistical significance of the correlative relationship. The values of the r_{xy} correlation coefficient were interpreted in accordance with the Chaddock scale. The probability value of $p < 0.05$ was used as the threshold for significant differences.

Results

The status of humoral immunity to parvovirus B19 among relatively healthy residents of Saint Petersburg (Russia)

Blood serum samples of relatively healthy residents of Saint Petersburg ($n = 317$) were collected from individuals aged 18–87 (the mean age was 42.3 ± 12.09 years; the median age was 39 years). The total percentage of males was 32.8%, while females accounted for 67.2%. The serum samples were divided into 4 age groups. Anti-B19V IgG antibodies were found in $62.1 \pm 2.7\%$ (197 of 317) samples and in each of the four groups (Table 1).

The smallest proportion of seropositive individuals was identified in the 18–20 year-old group where it was $33.3 \pm 11.1\%$. The proportion of positive anti-B19V IgG samples increases with age. The total proportion of positive samples among 18–30 year-old individuals was $53.5 \pm 5.3\%$, while the largest proportion of positive findings ($72.5 \pm 3.6\%$) was identified in the age group of 41 years and older. The identified differences are statistically significant ($df = 3$; $\chi^2 = 17.623$; $p < 0.001$).

The gender analysis did not reveal any substantial differences between seropositive males and females: 66.5 and 62.0% respectively ($df = 3$; $\chi^2 = 2.399$; $p = 0.494$). The proportion of seropositive females was slightly higher in the age groups of 18–20 years and

41 years and older; seropositive males were more frequently found in the age range of 21–40 years.

Thus, among the relatively healthy residents of Saint Petersburg, around 62% were identified as B19V-seropositive and their proportion tends to increase in older age groups, without demonstrating any significant gender-based differences.

A totally different pattern of building herd immunity against B19V was observed in the organized group made up staff and cadets (having special living accommodations) of a military college in Saint Petersburg. 500 blood serum samples from individuals aged 18–60 (the mean age was 25.2 years; median age was 21 years) were tested. Most of the examined were males (91.6%). In the organized group, the B19V seroprevalence was much higher ($p = 0.005$) than its average rate observed among city residents, and amounted to $85.8 \pm 1.56\%$ (Table 2). The distinctive feature of the above population is a large number (190 of 223) of B19V-seropositive individuals among the cadets of 18–20 years: Their proportion was $85.2 \pm 2.38\%$. The high level of humoral immunity remained in all examined age groups, without any statistically significant changes.

The proportion of IgG-positive samples was higher among males ($86.7 \pm 1.59\%$) than among females ($69.0 \pm 7.13\%$), though the low number of the females examined in this population (42 females of 500

Table 1. Identification of anti-B19V IgG antibodies in the blood serum of relatively healthy residents of Saint Petersburg ($n = 317$) in different age groups

Age, years	The number of examined sera	Of these, IgG+ to B19V	
		abs.	%, $M \pm m$
18–20 ¹	18	6	$33,3 \pm 11,1$
21–30 ²	68	40	$58,8 \pm 5,9$
18–30	86	46	$53,5 \pm 5,3$
31–40 ³	78	40	$51,3 \pm 5,6$
$\geq 41^4$	153	111	$72,5 \pm 3,6$
Total	317	197	$62,1 \pm 2,7$

Note. Significance of differences: $p_{1-4} < 0.001$.

Table 2. Identification of anti-B19V IgG antibodies in blood samples of healthy individuals from an organized team ($n = 500$) in different age groups

Age, years	The number of examined sera	Of these, IgG+ to B19V	
		abs.	%, $M \pm m$
18–20	223	190	$85,2 \pm 2,3$
21–30	173	145	$83,8 \pm 2,8$
31–40	64	60	$93,8 \pm 3,0$
≥ 41	40	34	$85,0 \pm 5,6$
Total	500	426	$85,8 \pm 1,5$

individuals) provides no conclusion that the identified gender differences can be deemed significant.

Thus, in the environment characterized by long-term close contact (living in barracks) the herd immunity against B19V was actively developing among the individuals of the first age group (18–20 years), which presumably can be explained by undetected circulation of the virus in this population.

The status of humoral immunity to parvovirus B19 among migrant workers from countries of Central Asia

Lately the spread of bacterial and viral infections has demonstrated an increasing trend due to active migration processes. A large number of migrant workers come annually to Russia from countries of Central Asia. Generally, there is no information about circulation of pathogens of infectious diseases, including PVI, in this group.

Below are the results obtained by the study of humoral immunity to B19V among Central Asian migrant workers staying in Saint Petersburg on a work visa. The proportion of IgG-positive individuals should be estimated to identify the significance of this population in PVI prevalence among migrant workers and among permanent residents of Saint Petersburg.

To identify IgG antibodies to B19V, a total of 114 blood serum samples were studied. The samples were collected from migrant workers from Uzbekistan and Tajikistan (104 males and 10 females) aged 18–56 years (the mean age was 33.4 years; the median age was 33.5 years) and divided into three age groups (Table 3). Altogether, the quantity and proportion of IgG-positive samples amounted to 54 of 114 ($47.4 \pm 4.6\%$). Anti-B19V IgG antibodies were found in each age group.

On the whole, IgG-positive serum samples collected from 18–30 year-old individuals accounted for $38.0 \pm 6.8\%$ of the samples. In individuals older than 31 years, the proportion of samples containing IgG antibodies to B19V increased on average to 54.6% and stayed at this level.

The proportion of seropositive migrant workers aged 30 years and younger was slightly lower than the proportion of seropositive residents of Saint Petersburg in the same age group: 38.0 and 53.5% respectively (the differences are not statistically significant). Signi-

ficant ($p = 0.05$) differences are found in the group of individuals aged 41 years and older: 54% seropositive individuals among the migrant workers and 72.5% seropositive individuals among permanent residents of Saint Petersburg.

The proportion of seropositive males and females was comparable: $48.1 \pm 7.1\%$ against $40.0 \pm 7.1\%$ respectively. However, females accounted for less than 10% of the examined in this group, thus giving no proof of significance of the obtained results.

The examined blood samples were collected from migrant workers who came to Saint Petersburg from Central Asian low-density areas. This fact may explain the lower number of B19V-seropositive individuals among residents of Uzbekistan and Tajikistan as compared to residents of Saint Petersburg. On the other hand, there can also be a correlation between the B19V herd immunity rate and the ethnic affiliation of the examined individuals.

To prove this assumption regarding IgG antibodies to B19V, we examined blood samples from residents of another country of the Eurasian continent — Kazakhstan.

The status of humoral immunity to B19V among relatively healthy residents of Nur-Sultan (Republic of Kazakhstan)

The comparative study was performed by using samples collected from individuals living in Nur-Sultan, the capital of Kazakhstan. The city is comparable with Saint Petersburg by density of population, the number of educational (secondary and higher) institutions, manufacturing companies, military schools, etc. The city is characterized by active internal and external migration supported by well-developed rail and air traffic.

A total of 480 blood serum samples were studied. The samples were collected from relatively healthy Nur-Sultan residents aged 18–59 years (the mean age was 30.5 ± 9.8 years; the median age was 28 years). The males and females accounted for 73.7% and 26.3% , respectively. Anti-B19V IgG antibodies were found in $65.2 \pm 2.2\%$ of the samples. The serum samples were divided into 5 age groups; IgG-positive samples were found in each of them. The analysis of the data from Table 4 revealed a growth trend for the proportion of seropositive samples in older age groups ($r = 0.225$; $p = 0.000001$). The lowest proportion of seropositive serum samples accounting for $48.6 \pm 5.8\%$ was identified among individuals aged 18–20 years. In the age groups of 21–30 and 31–40 years, the proportion of seropositive individuals increased to 62.0 ± 3.3 and $69.9 \pm 4.3\%$ respectively. In the group of individuals aged 41 years and older, the proportion of those who were IgG positive to B19V reached $80.5 \pm 4.2\%$. The found differences are statistically significant ($df = 3$; $\chi^2 = 19.696$; $p < 0.001$). The proportion of males with IgG antibodies to B19V was higher than the proportion

Table 3. Identification of anti-B19V IgG antibodies in blood samples of labor migrants from Central Asia ($n = 114$) in different age groups

Age, years	The number of examined sera	Of these, IgG+ to B19V	
		abs.	%, $M \pm m$
18–30	50	19	$38,0 \pm 6,8$
31–40	33	18	$54,5 \pm 8,6$
≥ 41	31	17	$54,8 \pm 8,9$
Total	114	54	$47,4 \pm 4,6$

Table 4. Identification of anti-B19V IgG antibodies in the blood serum of relatively healthy residents of Nur-Sultan ($n = 480$) in different age groups

Age, years	The number of examined sera	Of these, IgG+ to B19V	
		abs.	%, $M \pm m$
18–20 ¹	72	35	48,6 ± 5,8
21–30 ²	208	129	62,0 ± 3,3
18–30	280	164	58,6 ± 2,9
31–40 ³	113	79	69,9 ± 4,3
≥41 ⁴	87	70	80,5 ± 4,2
Total	480	313	65,2 ± 2,2

Note. Significance of differences: $p_{1-4} < 0.001$.

of seropositive females: $69.5 \pm 2.9\%$ and $53.2 \pm 6.1\%$ respectively ($df = 1$; $\chi^2 = 10.368$; $p = 0.002$).

The greatest differences were observed in the group of young people aged 18–20 years; the proportion of seropositive males was 2.7 times as high as the proportion of females protected against infection: 67.5 ± 2.9 and $25.0 \pm 5.2\%$ respectively. The differences are statistically significant ($p = 0.0004$). In the age group of 21–30 years, the differences tend to decrease: $65.1 \pm 3.4\%$ of seropositive males and $47.2 \pm 6.1\%$ of seropositive females; in the group of individuals aged 31 years and older, the proportions of seropositive males and females become equal.

The status of humoral immunity to B19V among relatively healthy residents of RG

The obtained results helped identify special characteristics of building herd immunity against B19V in Eurasian countries interconnected through close communication, migration flows, trade, cultural and interpersonal contacts. The African continent geographically remote from Eurasian countries has its own economic, social, and ethnic distinctive features. The herd immunity against B19V and its development were assessed through examination of blood samples collected from RG residents living in Conakry and Kindia, the Mamou, Labé, Nzérékoré, Kankan, Faranah, and Boké regions.

A total of 321 blood serum samples from males and females aged 18–83 years (the mean age was 35.6 years; the median age was 32 years) were examined and divided into 4 age groups. When divided by gender, the number of samples was almost the same. The males accounted for 50.1%, while the females accounted for 49.9% of the samples.

Anti-B19V IgG antibodies were found in each age group. On the whole, the proportion of IgG-positive samples was $53.9 \pm 2.78\%$ (173 of 321). The results are shown in **Table 5**.

The lowest proportion of seropositive samples was registered in the group of 18–20 years ($44.4 \pm 11.7\%$). In the age group of 21–30 years, the proportion of se-

ropositive samples increased to $53.8 \pm 5.6\%$. In total, the proportion of seropositive individuals aged 18 to 30 years was $52.1 \pm 5.1\%$ and showed no considerable changes in the older age groups.

Generally, the proportions of seropositive males and females did not demonstrate any substantial differences: 57.4 and 47.9% respectively. However, the age groups of 18–20 and 31–40 years demonstrate a significantly larger number of seropositive males as compared to the females protected from infection: 57.1% against 36.4% and 59.4% against 31.6%, respectively. In the groups of 21–30 years as well as those of 41 years and older, the proportions of seropositive males and females did not show any substantial differences, staying at the level of 51.2–57.1%.

Thus, IgG antibodies to B19V were found nearly in fifty percent of the samples from the first age group (18–20 years). Comparable data were also obtained for individuals of this age group in other regions (Russia, Kazakhstan).

Discussion

With no virus-specific preventive measures, there is clear evidence of continuous B19V circulation in different regions of the world [22]. In this study, IgG antibodies to B19V were found in all age groups of relatively healthy residents of Russia, Central Asia (Eurasia) and RG (West Africa). The study also revealed that B19V seroprevalence rates tend to increase among individuals of older ages in all studied groups, thus supporting the data obtained by other authors [12, 17, 18]. At the same time, the study also revealed differences in development of herd immunity among residents of different countries.

The highest rates of seroprevalence were identified in Saint Petersburg and Nur-Sultan; the lowest rates were found among migrant workers from sparsely populated regions of Uzbekistan and Tajikistan. The B19V seroprevalence rate fell in between the estimated rates for blood samples collected both from residents of the capital (Conakry) and from residents of sparsely populated regions of RG.

Table 5. Identification of anti-B19V IgG antibody in blood samples of healthy residents of the Republic of Guinea ($n = 321$) in different age groups

Age, years	The number of examined sera	Of these, IgG+ to B19V	
		abs.	%, $M \pm m$
18–20	18	8	44,4 ± 11,7
21–30	78	42	53,8 ± 5,6
18–30	96	50	52,1 ± 5,1
31–40	88	47	53,4 ± 5,3
≥41	137	76	55,5 ± 4,2
Total	321	173	53,9 ± 2,7

Large metropolitan cities (Saint Petersburg and Nur-Sultan) characterized by high density of population, pronounced migration processes, high percentage of organized children attending preschool and school, a large number of students of secondary and higher schools (including military schools), where nonresident students live in dormitories and barracks, produce conditions favorable for active circulation of B19V.

Indeed, the development pattern for Nur-Sultan residents' herd immunity against B19V correlates to the data obtained from testing blood serum samples of relatively healthy residents of Saint Petersburg. The aggregate portions of seropositive individuals aged 18–30 years were 58.6 ± 2.9 and $53.5 \pm 5.3\%$ respectively, exceeding the proportion identified when testing blood serum samples from migrant workers from Uzbekistan and Tajikistan — $38.0 \pm 6.8\%$. The proportions of seropositive individuals older than 41 years are also comparable: $72.5 \pm 3.6\%$ in Saint Petersburg and $80.5 \pm 4.2\%$ in Nur-Sultan.

The fact that long-term close contacts contribute to the spread of infection is supported by high rates of seroprevalence among cadets of the military college in Saint Petersburg, where the actively developing herd immunity against B19V (85.2% seropositive) was registered among 18–20 year-old individuals and substantially exceeded the seroprevalence rates observed in the similar age group of relatively healthy residents of Saint Petersburg (33.3%).

The examined Central Asian migrant workers came from areas characterized by low density of population, poorly pronounced internal migration, a small number of secondary specialized colleges and higher schools. These features may explain the considerably lower numbers of B19V seropositive individuals among residents of Uzbekistan and Tajikistan as compared to residents of Saint Petersburg. Migrant workers having low herd immunity are undoubtedly a target of B19V infection. The overcrowded accommodation typical of their staying in Saint Petersburg can contribute to active spread of infection, which can involve susceptible permanent residents of the city, including blood donors, pregnant women, individuals with primary and secondary immunodeficiencies, patients suffering from anemia, blood product and bone marrow recipients, cancer patients.

The presence of gender-based differences in development of herd immunity against B19V is most likely connected with social factors and was observed during examination of blood serum samples from residents of Kazakhstan and RG. In Nur-Sultan, humoral immunity to B19V developed more actively among males aged 18–20 years. These results may evidence a more active circulation of the virus among young males of Nur-Sultan.

The examined residents of RG also demonstrated almost a two-fold increase in the number of B19V

seropositive young males as compared to seropositive females of the similar age groups, which is comparable with the gender differences identified among residents of Nur-Sultan. The prevalence of seropositive females was observed in older age groups of RG residents, which may be explained by closer contacts between women and children in families.

In the meantime, in each examined group of residents from different geographical regions there were also identified seronegative individuals, thus suggesting that individuals from high-risk groups can be involved in an infectious process. Previously it was shown that around 50% of the examined pregnant women living in Saint Petersburg were susceptible to B19V infection [23]. It is found that parvovirus B19 infection of patients suffering from chronic anemia as well as cancer patients can aggravate the course and the prognosis of the primary disease [24, 25].

The obtained results confirm the significance of PVI not only for children and teenagers, but also for adults. The continuous identification of PVI cases in different age groups of individuals living in the North-western Federal District is supported by the previously performed studies [26]. The seroprevalence of B19V was assessed by a number of foreign authors studying blood donors from South Africa, Iran, China, Brazil [27–30]. B19V-seropositive individuals were identified in each of the performed studies, thus supporting the fact of wide spread of PVI. Their proportion in the target group ranged from 27.6% (Iran) to 62.2% (RSA), on the whole, correlating to our data and evidencing the existence of factors affecting development of herd immunity against B19V.

Conclusion

The obtained results confirm the PVI prevalence in different geographical regions. Herd immunity develops most actively in long-term close contact environments.

At the same time, the study revealed seronegative individuals in all the groups. The presence of individuals susceptible to infection can lead to spread of infection in high-risk groups — among pregnant women, individuals with primary and secondary immunodeficiencies, patients suffering from anemia, blood product and bone marrow recipients, cancer patients.

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