ORIGINAL RESEARCHES

Distribution of SARS-CoV-2 seroprevalence among residents of the Tyumen Region during the COVID-19 epidemic period

Anna Yu. Popova[1], Elena B. Ezhlova[1], Albina A. Melnikova[1], Tatiana F. Stepanova[2], Galina V. Sharukho[3], Aleksandr N. Letyushev[2,3], Aleksandr Ya. Folmer[4], Anna A. Shepotkova[2], Lyudmila V. Lyalina[5], Vyacheslav S. Smirnov[5]✉, Kseniya B. Stepanova[2], Tsakhik A. Panina[2], Olga N. Sidorenko[2], Natalia A. Ivanova[2], Svetlana S. Smirnova[2], Inna N. Malchenko[2], Elena V. Okhotnikova[2], Elena G. Stakhova[2], Areg A. Totolian[5]

[1]Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, 127994, Moscow, Russia;
[2]Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia;
[3]Department of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing for Tyumen Region, 625026, Tyumen, Russia;
[4]Center for Hygiene and Epidemiology in the Tyumen Region, 625000, Tyumen, Russia;
[5]Saint Petersburg Pasteur Institute, 197101, Saint Petersburg, Russia

Introduction. In late 2019 – early 2020, an outbreak of infection caused by a novel strain of beta coronavirus SARS-CoV-2 was reported. The World Health Organization defined the disease as coronavirus disease 2019 (COVID-19). In the Tyumen Region, the first case of COVID-19 was diagnosed on 31/1/2020. The source of infection was a female student who came from Jinan, Shandong province (China). The number and rate of cases were steadily increasing from the 16th week through 28th week in 2020. The highest rate was 36.87 cases per 100 thousand people. Afterwards, the cumulative incidence kept increasing gradually, but not as quickly.
The purpose of the seroepidemiological study was to measure the level and to identify the structure of herd immunity against the SARS-CoV-2 virus among the population of the Tyumen Region during the rapid spread of the COVID-19 outbreak.
Materials and methods. Volunteers for participation in the study were selected through questionnaire surveys and random sampling. The exclusion criterion was an active COVID-19 infection at the time of the survey. A total of 2,758 individuals were tested for SARS-CoV-2 specific antibodies. The age of the surveyed volunteers ranged from 1 year to 70 years and older.
Results of the study. During the active phase of the COVID-19 incidence, the population of the Tyumen Region showed moderate (24.5%) seroprevalence of SARS-CoV-2. At the same time, the tests revealed a high (97.8%) rate of asymptomatic infection cases in seropositive individuals who had never been diagnosed with COVID-19 and did not have history of positive PCR test results or acute respiratory infection symptoms on the day of testing. The maximum level of herd immunity was identified in children aged 1–6 years (34.7%), which was significantly higher compared to the average level of seroprevalence in the entire cohort. In recovered COVID-19 patients, antibodies were detected in 68.2%. In individuals with positive PCR test results, antibodies were detected in 64%.
Conclusion. The results of the assessment of the level of herd immunity against the SARS-CoV-2 virus are crucial for prediction of the development trend of the epidemic and for planning specific and non-specific COVID-19 prevention measures.

Keywords: *coronavirus; epidemic; seroprevalence; Tyumen Region; population.*

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ОРИГИНАЛЬНЫЕ ИССЛЕДОВАНИЯ

Распределение серопревалентности к SARS-CoV-2 среди жителей Тюменской области в эпидемическом периоде COVID-19

Попова А.Ю.[1], Ежлова Е.Б.[1], Мельникова А.А.[1], Степанова Т.Ф.[2], Шарухо Г.В.[3], Летюшев А.Н.[2,3], Фольмер А.Я.[4], Шепоткова А.А.[2], Лялина Л.В.[5], Смирнов В.С.[5]✉, Степанова К.Б.[2], Панина Ц.А.[2], Сидоренко О.Н.[2], Иванова Н.А.[2], Смирнова С.С.[2], Мальченко И.Н.[2], Охотникова Е.В.[2], Стахова Е.Г.[2], Тотолян А.А.[5]

[1]Федеральная служба по надзору в сфере защиты прав потребителей и благополучия человека, 127994, Москва, Россия;
[2]ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия;
[3]Управление Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека по Тюменской области, 625026, Тюмень, Россия;
[4]ФБУЗ «Центр гигиены и эпидемиологии в Тюменской области», 625000, Тюмень, Россия;
[5]ФБУН «Санкт-Петербургский научно-исследовательский институт эпидемиологии и микробиологии им. Пастера» Роспотребнадзора, 197101, Санкт-Петербург, Россия

Введение. В конце 2019 г. — начале 2020 г. была зарегистрирована вспышка инфекции, вызванная новым штаммом бета-коронавируса SARS-CoV-2. ВОЗ определила идентифицированное заболевание как «коронавирусная болезнь 2019» (COVID-19). В Тюменской области первый случай заболевания COVID-19 был диагностирован 31.01.2020 г. Источником инфекции была студентка, приехавшая из Цзинаня, провинция Шаньдун (КНР). С 16-й по 28-ю неделю 2020 г. наблюдался устойчивый рост заболеваемости. Максимальный уровень составил 36,87 на 100 тыс. человек. Впоследствии кумулятивная заболеваемость постепенно увеличивалась, хотя и с меньшей интенсивностью.
Целью сероэпидемиологического исследования было определение уровня и структуры популяционного иммунитета к вирусу SARS-CoV-2 среди населения Тюменской области в период интенсивного распространения COVID-19.
Материалы и методы. Отбор добровольцев для исследования проводился путем анкетирования и рандомизации. Критерием невключения являлась активная инфекция COVID-19 на момент обследования. На наличие специфических антител к SARS-CoV-2 были обследованы 2758 человек. Возраст опрошенных добровольцев составлял от 1 года до 70 лет и старше.
Результаты исследования. Среди населения Тюменской области в активной фазе заболеваемости COVID-19 наблюдалась умеренная (24,5%) серопревалентность к SARS-CoV-2. Одновременно с этим выявлена высокая (97,8%) частота случаев бессимптомной инфекции у серопозитивных людей, у которых в анамнезе не было заболевания COVID-19, положительного результата ПЦР и симптомов острых респираторных вирусных инфекций в день обследования. Максимальные показатели коллективного иммунитета, установленные у детей 1–6 лет (34,7%), были статистически значимыми по сравнению со средним уровнем серопревалентности для всей когорты. У реконвалесцентов COVID-19 антитела обнаруживались в 68,2% случаев. У лиц с положительным результатом ранее проведенного ПЦР-анализа антитела выявляются в 64% случаев.
Вывод. Результаты исследования состояния коллективного иммунитета к вирусу SARS-CoV-2 необходимы для разработки прогноза развития эпидемиологической ситуации, а также для планирования мероприятий по специфической и неспецифической профилактике COVID-19.

Ключевые слова: *коронавирус; эпидемия; серопревалентность; Тюменская область; население.*

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

The COVID-19 pandemic, which began on 11/2/2020, is an unprecedented event in the modern history of human civilization. Having started with a single infected case at the seafood market in Wuhan (China), the infection spread rapidly around the world, having affected almost every region of the globe. It has spared a few small countries in Africa so far. Besides, there is no information about COVID-19 cases in Turkmenistan and North Korea. As of the first decade of July 2020, the global case tally hit 12.5 million confirmed COVID-19 cases, out of which 6.89 million patients had recovered and 560 thousand patients had died[1].

In Russia, according to official data from the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing (Rospotrebnadzor), as of 12/7/2020, a total of 727,162 cases were reported; the number of recovered patients was 561,061 and the number of the deceased was 11,335. Coronavirus cases are recorded across the country. The highest incidence is recorded in Moscow; the lowest number of cases is recorded in the Chukotka District, Yamalo-Nenets District and Arctic islands of the Russian Federation.

In the Tumen Region, the first case was detected on 31/1/2020; the source of infection was a female Chinese citizen who came from Jinan, Shandong province. Sporadic cases had been recorded till April 9, 2020. The steady increase in the incidence started from the 16th week in 2020; the peak was reached during the 28th week with 36.87 cases per 100 thousand people. Afterwards, the cumulative incidence rose gradually to demonstrate a 195% increase during the period from the 26th to the 30th week (**Fig. 1**). Therefore, any announcement of the successful breakthrough in elimination of the COVID-19 outbreak in the Tumen Region would be premature.

Both the current COVID-19 situation and the urgent need for effective epidemic control measures bring herd immunity assessment studies to the fore. The herd immunity threshold can be reached in two ways: through natural infection by increasing the number of people who had the infectious disease, i.e. COVID-19, in a symptomatic or asymptomatic form, or through vaccination covering at least 60% of susceptible people [1, 2]. No matter how fast scientists and manufacturers are moving to create a vaccine, its development takes time; its safety, specificity and efficacy require thorough examination [3]. Then, the only realistic solution is to rely on developing herd immunity resulting from apparent symptomatic infection or inapparent seroconversion. The common assumption is that at least 50–60% of the vulnerable population must develop immunity to a particular infection to stop the spread of infection [2]. Careful attention should be given to the dynamics of the process and to the degree of population heterogeneity, which can significantly affect the development of both individual and community resistance to infection with SARS-CoV-2 [4].

Considering the aforesaid, the **purpose** of the conducted seroepidemiological study was to measure the level and to identify the structure of herd immunity against the SARS-CoV-2 virus among the population of the Tyumen Region during the rapid spread of the COVID-19 outbreak.

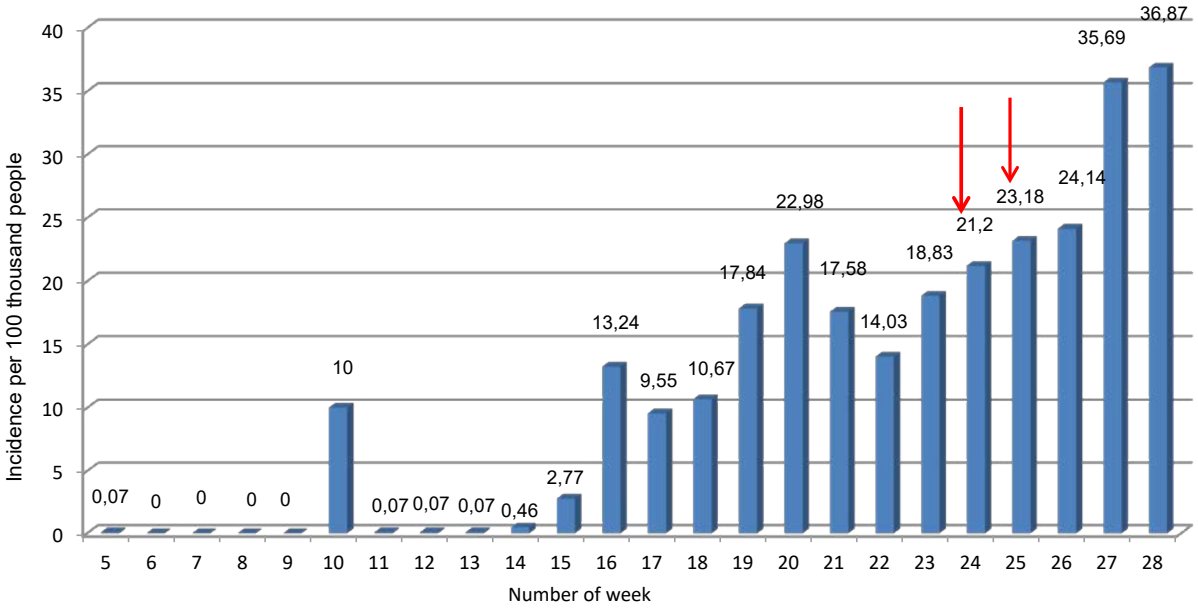

Fig. 1. COVID-19 incidence in Tyumen Region.
The arrows show the period when the seroprevalence study was conducted (the 24th–25th week of the year).

[1]https://www.who.int/ru/emergencies/diseases/novel-coronavirus-2019

Materials and methods

The study was conducted during the first stage of Rospotrebnadzor's large-scale project aimed at assessment of herd immunity to the SARS-CoV-2 virus in the population of Russia, following the protocol recommended by the World Health Organization [5]. The study was approved by the research ethics committee of the Pasteur Research Institute of Epidemiology and Microbiology. Prior to the study, all the participants or their legal representatives were informed about the purpose and methods of the study; all of them signed the informed consent.

Volunteers for participation in the study were selected through questionnaire surveys and random sampling. The exclusion criterion was an active COVID-19 infection at the time of the survey. The sample size was calculated by using the formula:

$$n = \frac{t^2 \times p(1-p)}{m^2},$$

where:
n — a sample size;
t — a precision level (for a 95% CI $t = 1.96$);
p — expected prevalence of the studied phenomenon (at 50% $p = 0.5$);
m — a margin of error of 5% [6].

A total of 7,163 volunteers were surveyed; out of them, 3,030 people had their venous blood samples collected for further tests for SARS-CoV-2 specific antibodies. A total of 2,758 samples had been tested.

The age of the examined volunteers ranged from 1 to 70 years and older (**Table 1**).

In all the age groups, the number of volunteers was comparable, except for the significantly smaller number of volunteers in the senior-age group. Taking into account the specifics of child development, the first group was divided into three subgroups: 1–6, 7–13 and 14–17 years. The individuals who had COVID-19 in the past accounted for 0.7% (22 people) of the total number of volunteers. On the testing day, no volunteer had clinical symptoms of acute respiratory infections.

Blood samples were collected in EDTA-containing vacutainer tubes and centrifuged. Plasma was separated from cellular elements, collected in plastic tubes and stored at 4°C till the commencement of the test. The amount of antibodies to SARS-CoV-2 was measured with an enzyme-linked immunosorbent assay (ELISA) kit for human blood serum or plasma tests for detecting SARS-CoV-2 nucleocapsid specific immunoglobulin G (IgG) antibodies; the kit is made by the State Research Center for Applied Microbiology and Biotechnology of Rospotrebnadzor. The results were assessed by using qualitative methods and were deemed positive when the cut-off level was exceeded.

The statistical processing included variation statistics methods, an Excel statistical package and WinPepi software (version 11.65). Due to the absence of a representative sample for districts of the Tyumen Region, most of the statistical indicators were calculated by using the results obtained from the volunteers from Tyumen. The probability value of $p < 0.05$ was used to assess significant differences between variables.

Results

Assessment of seroprevalence

The seroprevalence among the residents of the Tyumen Region totaled 24.5 ± 1.6% (677 out of 2,758); in the age groups, it ranged from 13.4 ± 5.5% to

Table 1. Seroprevalence in residents of Tyumen Region, different age groups

Age group, years		Number of the examined, persons	Including		Seroprevalence, % ($M \pm m$)
			seropositive	seronegative	
1–17		356	94	262	26.4 ± 4.6
Including:	1–6	75	26	49	34.7 ± 10.8
	7–13	144	33	111	22.9 ± 6.9
	14–17	137	35	102	25.5 ± 6.3
18–29		485	125	360	25.8 ± 3.9
30–39		452	119	333	26.3 ± 4.1
40–49		447	108	339	24.2 ± 4.0
50–59		482	126	356	26.1 ± 3.9
60–69		387	85	302	22.0 ± 4.1
70 and older		149	20	129	13.4 ± 5.5
Total		2758	677	2081	24.5 ± 1.6

26.4 ± 4.6% (**Table 1**). The maximum level of seroconversion was detected in the child-age group (mostly in the subgroup of 1–6 years). The senior age group (70 years and older) had the lowest level of seroprevalence (13.4 ± 5.5%), which can be explained by the insufficient size of the sample. The seropositivity did not show any significant gender differences and amounted to 21.5 ± 2.7% in the males and 26.0 ± 2.0% ($p > 0.05$) in the females, though the females demonstrated a clear trend to seroconversion prevalence. The seroprevalence level was 24.5 ± 1.6% in city of Tyumen, exclusive of non-representative data from regional districts.

Assessment of risk factors

Among the participants who had symptomatic COVID-19, the proportion of seropositive individuals was 68.2 ± 19.5%, while among the participants who had not been previously diagnosed with this infection, the proportion was significantly lower — 24.2 ± 1.6% ($p < 0.05$), and completely correlated with the results obtained during the examination of residents from other regions [5, 7].

In the group of individuals who had never been exposed to COVID-19 patients, the proportion of seropositive people amounted to 21.1 ± 1.6%, while among the individuals who had work or household contacts with those who were diagnosed with COVID-19, the proportion of volunteers with detected anti-SARS-CoV-2 antibodies increased to 32.1 ± 7.2%. It suggests the possibility of household development of an immune response resulting from transmission of the pathogen from a COVID-19 patient, though in small amounts. The absence of significant differences, while the proportion of seropositive people increased by 1.5 times, is indicative of the insufficient size of the sample.

The assessment of the seropositivity level among volunteers who had positive PCR test results for virus RNA is of particular interest. The test results showed that among PCR positive individuals the seroprevalence level was 64%, while among PCR-negative volunteers, the seroprevalence level is 24.24%. The differences are significant at probability of $p < 0.05$. The obtained results convincingly demonstrate the presence of a strong functional relationship between the virus RNA circulation and antibodies to the SARS-CoV-2 virus. The above assumption was verified through the analysis of the relationship between incidence and seroprevalence (**Fig. 2**).

The conducted analysis shows that there is a direct linear relationship between the variables. The Pearson correlation coefficient and the Spearman rank correlation coefficient amounted to 0.44 ($p < 0.1$). Although the significance of the revealed relationship is not high, it leads to the obvious conclusion implied by the direct relationship between the variables: an increase in the incidence rate is accompanied by an increase in the seroprevalence (**Fig. 2**).

Estimation of the proportion of asymptomatic cases

The asymptomatic infection is typical of COVID-19 and, as assumed, can act as significant factor of virus transmission [8]. From this perspective, estimation of the percentage of asymptomatic cases in the population is highly important for the analysis of infection transmission among healthy individuals [9] and can help significantly in adjusting the range and focus of epidemic prevention measures [10].

The proportion of asymptomatic cases among seropositive individuals was estimated through measuring the proportion of individuals who did not have at least one of the following: the COVID-19 diagnosis

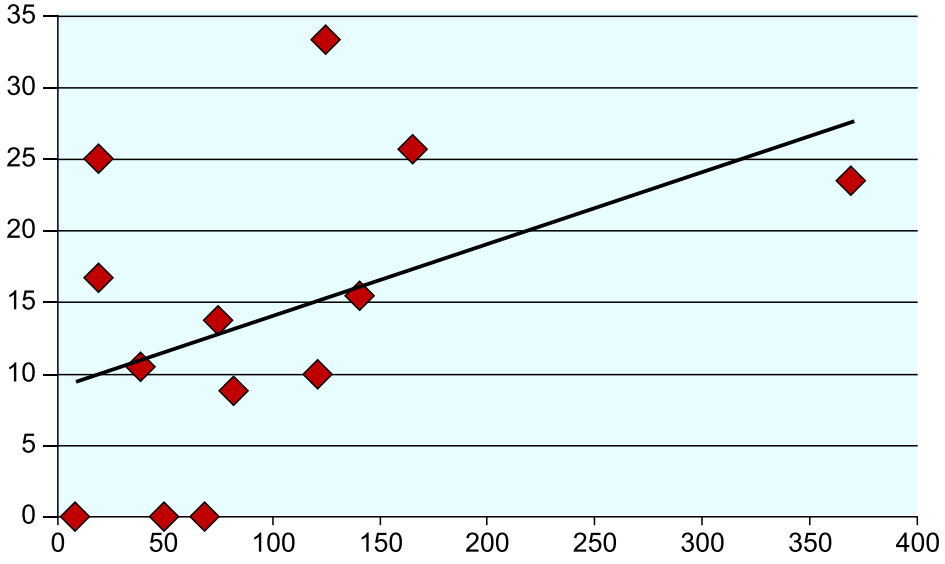

Fig. 2. Correlation between the incidence rate and seroprevalence.
The vertical axis shows seroprevalence, %; the horizontal axis shows the incidence per 100 thousand people.

Table 2. Proportion of asymptomatic cases in the total number of seropositive residents of different age groups in Tyumen Region

Age group, years	Total number of seropositives	Asymptomatic seropositives	Proportion of asymptomatic cases, % ($M \pm m$)
1–17	94	93	98.9 ± 2.1
18–29	125	119	95.2 ± 3.8
30–39	119	115	96.6 ± 3.3
40–49	108	108	100.0 ± 1.9
50–59	126	123	97.6 ± 2.7
60–69	85	84	98.8 ± 2.3
70 and older	20	20	100.0 ± 4.4
Total	677	662	97.8 ± 1.1

or a positive PCR test result or acute respiratory infection (ARI) symptoms. Among residents of the Tyumen Region, the asymptomatic cases accounted for 97.8 ± 1.1%, reaching the highest levels in two age groups: 40–49 year-old and over 70 years old (**Table 2**).

Thus, similar to other regions, the absolute number of seropositive individuals demonstrates asymptomatic infection. Keeping in mind that seropositivity is not necessarily connected with the virus RNA circulation, we can reasonably assume that asymptomatic infection has more advantages than downsides, as it is highly probable that the presence of antibodies to the SARS-CoV-2 nucleocapsid protein can be connected with the increased resistance to infection with a pathogenic virus and can contribute to reduction in the epidemic tension among people. The same tendency underlies the relationship between the seroprevalence to the SARS-CoV-2 virus and COVID-19 incidence (**Fig. 1**).

Discussion

The examination of the population of the Tyumen Region represented mainly by Tyumen residents showed that the seroprevalence level among the volunteers ranged from 13.4 ± 5.5 to 34.7 ± 10.8%. Similar to other regions (St. Petersburg and Leningrad Region) [1, 2], the highest seroprevalence was detected among children. At present, this phenomenon cannot be explained adequately and to the fullest. It can be assumed that the development of the landscape of antibodies to coronavirus in children is affected by cross-reactive antibodies resulting from acute respiratory infections caused by other types of β-coronaviruses, which have common determinants in nucleocapsid proteins [11]. The other age groups did not show any substantial differences in seroprevalence levels. The fairly low proportion of individuals with SARS-CoV-2 antibodies in the senior-age group can be explained by the small number of people of this age in the group.

The analysis of other parameters of seroprevalence did not reveal any unusual findings. As expected, the seroprevalence level was significantly higher among people recovered after COVID-19, people who had work or household contact with COVID-19 patients, and viral RNA carriers having positive PCR test results.

As for asymptomatic cases, they demonstrate a high level of seroprevalence. The phenomenon can be caused by two factors: On the one hand, it is a typical characteristic of SARS-CoV-2 [10, 11]; on the other hand, it can be produced by inapparent seroconversion when a humoral immune response can develop even without manifest symptoms of the infection [5, 7].

Conclusions

1. The herd immunity of the total population of the Tyumen Region was 24.5%. The highest level of seroprevalence was found in individuals aged 1–6 years (34.7%); the lowest level was identified in the group of individuals aged 70 years and older (13.4%).

2. After the symptomatic COVID-19 infection, antibodies are detected in 68% of the patients.

3. Antibodies were detected in 64% of individuals with positive PCR test results.

4. The COVID-19 incidence rate has a strong relationship with SARS-CoV-2 seroprevalence.

5. The proportion of asymptomatic cases totaled 97.8% of the seropositive residents of the Tyumen Region.

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ЛИТЕРАТУРА

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Information about the authors

Anna Yu. Popova — D. Sci. (Med.), Prof., Head, Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, 127994, Moscow, Russia.
ORCID ID: http://orcid.org/0000-0003-2567-9037.
E-mail: depart@gsen.ru

Elena B. Ezhlova — Cand. Sci. (Med.), Deputy Head, Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing, 127994, Moscow, Russia.
E-mail: ezhlova_eb@gsen.ru

Albina A. Melnikova — Cand. Sci. (Med.), Deputy Head, Epidemiological surveillance department, Federal Service for

Информация об авторах

Попова Анна Юрьевна — д.м.н., проф., руководитель Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека, 127994, Москва, Россия. ORCID ID: http://orcid.org/0000-0003-2567-9037.
E-mail: depart@gsen.ru

Ежлова Елена Борисовна — к.м.н., зам. руководителя Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека, 127994, Москва, Россия. E-mail: ezhlova_eb@gsen.ru

Мельникова Альбина Андреевна — к.м.н., зам. начальника Управления эпидемиологического надзора Федеральной

Surveillance on Consumer Rights Protection and Human Wellbeing, 127994, Moscow, Russia.
ORCID ID: http://orcid.org/0000-0002-5651-1331.
E-mail: melnikova_aa@gsen.ru

Tatiana F. Stepanova — D. Sci (Med.), Prof., Director, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-6289-6274.
E-mail: stepanovatf@tniikip.rospotrebnadzor.ru

Galina V. Sharukho — D. Sci (Med.), Head, Department of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing in the Tyumen Region, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0003-0772-8224.
E-mail: nadzor72@tyumen-service.ru

Aleksandr N. Letyushev — Cand. Sci. (Med.), leading researcher, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia; Head, Epidemiological surveillance department, Department of the Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing in the Tyumen Region, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-4185-9829.
E-mail: nadzor72@tyumen-service.ru

Aleksandr Ya. Folmer — Cand. Sci. (Med.), chief physician, Center for Hygiene and Epidemiology in the Tyumen Region, 625000, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0001-8321-5637.
E-mail: tocgsen@fguz-tyumen.ru

Anna A. Shepotkova — medical statistician of the laboratory of epidemiological analysis and mathematical modeling, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-1930-5635.
E-mail: shepotkovaaa@tniikip.rospotrebnadzor.ru

Lyudmila V. Lyalina — D. Sci. (Med.), Prof., Head, Laboratory of epidemiology of infectious and non-infectious diseases, Saint Petersburg Pasteur Institute, 197101, St. Petersburg, Russia.
ORCID ID: https://orcid.org/0000-0001-9921-3505.
E-mail: lyalina@pasteurorg.ru

Vyacheslav S. Smirnov✉ — D. Sci. (Med.), Prof., leading researcher, Saint Petersburg Pasteur Institute, 197101, St. Petersburg, Russia.
ORCID ID: https://orcid.org/0000-0002-2723-1496.
E-mail: vssmi@mail.ru

Kseniya B. Stepanova — Cand. Sci. (Med.), leading researcher, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-5420-0919.
E-mail: stepanovakb@tniikip.rospotrebnadzor.ru

Tsakhik A. Panina — junior researcher, Laboratory of clinic and immunology of biohelminthiasis, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0003-2490-4592.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Olga N. Sidorenko — junior researcher, Laboratory of clinic and immunology of biohelminthiasis, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-9032-1603.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Natalia A. Ivanova — junior researcher, Laboratory of clinic and immunology of biohelminthiasis, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0001-6964-0039.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Svetlana S. Smirnova — junior researcher, Laboratory of clinic and immunology of biohelminthiasis, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0002-2797-7570.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Inna N. Malchenko — physician, Clinical department, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0003-2550-868X.
E-mail: info@tniikip.rospotrebnadzor.ru

службы по надзору в сфере защиты прав потребителей и благополучия человека, 127994, Москва, Россия.
ORCID ID: http://orcid.org/0000-0002-5651-1331.
E-mail: melnikova_aa@gsen.ru

Степанова Татьяна Федоровна — д.м.н., проф., директор ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-6289-6274.
E-mail: stepanovatf@tniikip.rospotrebnadzor.ru

Шарухо Галина Васильевна — д.м.н., рук. Управления Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека по Тюменской области, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0003-0772-8224.
E-mail: nadzor72@tyumen-service.ru

Летюшев Александр Николаевич — к.м.н., в.н.с. ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия; рук. отдела эпидемиологического надзора Управления Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека по Тюменской области, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-4185-9829.
E-mail: nadzor72@tyumen-service.ru

Фольмер Александр Яковлевич — к.м.н., главный врач ФБУЗ «Центр гигиены и эпидемиологии в Тюменской области», 625000, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0001-8321-5637.
E-mail: tocgsen@fguz-tyumen.ru

Шепоткова Анна Анатольевна — медстатистик лаб. эпидемиологического анализа и математического моделирования ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия;
ORCID ID: https://orcid.org/0000-0002-1930-5635.
E-mail: shepotkovaaa@tniikip.rospotrebnadzor.ru

Лялина Людмила Владимировна — д.м.н., проф., зав. лаб. эпидемиологии инфекционных и неинфекционных заболеваний ФБУН НИИ эпидемиологии и микробиологии им. Пастера, 197101, Санкт-Петербург, Россия.
ORCID ID: https://orcid.org/0000-0001-9921-3505.
E-mail: lyalina@pasteurorg.ru

Смирнов Вячеслав Сергеевич✉ — д.м.н., проф., в.н.с. ФБУН НИИ эпидемиологии и микробиологии им. Пастера, 197101, Санкт-Петербург, Россия.
ORCID ID: https://orcid.org/0000-0002-2723-1496.
E-mail: vssmi@mail.ru

Степанова Ксения Борисовна — к.м.н., в.н.с. ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-5420-0919.
E-mail: stepanovakb@tniikip.rospotrebnadzor.ru

Панина Цахик Арутовна — м.н.с. лаб. клиники и иммунологии биогельминтозов ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0003-2490-4592.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Сидоренко Ольга Николаевна — м.н.с. лаб. клиники и иммунологии биогельминтозов ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-9032-1603.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Иванова Наталья Александровна — м.н.с. лаб. клиники и иммунологии биогельминтозов ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0001-6964-0039.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Elena V. Okhotnikova — physician, Clinical department, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0001-8815-0916.
E-mail: info@tniikip.rospotrebnadzor.ru

Elena G. Stakhova — physician, Clinical department, Tyumen Region Infection Pathology Research Institute, 625026, Tyumen, Russia.
ORCID ID: https://orcid.org/0000-0003-4571-8799.
E-mail: info@tniikip.rospotrebnadzor.ru

Areg A. Totolian — D. Sci. (Med.), Prof., Academician of RAS, Director, Saint Petersburg Pasteur Institute, 197101, St. Petersburg, Russia.
ORCID ID: https://orcid.org/0000-0003-4571-8799.
E-mail: pasteur@pasteurorg.ru

Contribution: the authors contributed equally to this article.

Смирнова Светлана Сергеевна — м.н.с. лаб. клиники и иммунологии биогельминтозов ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-2797-7570.
E-mail: lifa@tniikip.rospotrebnadzor.ru

Мальченко Инна Николаевна — врач клинического отделения ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0003-2550-868X.
E-mail: info@tniikip.rospotrebnadzor.ru

Охотникова Елена Владимировна — врач клинического отделения ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0001-8815-0916.
E-mail: info@tniikip.rospotrebnadzor.ru

Стахова Елена Георгиевна — врач клинического отделения ФБУН «Тюменский научно-исследовательский институт краевой инфекционной патологии» Роспотребнадзора, 625026, Тюмень, Россия.
ORCID ID: https://orcid.org/0000-0002-8436-2409.
E-mail: info@tniikip.rospotrebnadzor.ru

Тотолян Арег Артемович — д.м.н., проф., академик РАН, директор ФБУН НИИ эпидемиологии и микробиологии им. Пастера, 197101, Санкт-Петербург, Россия.
ORCID ID: https://orcid.org/0000-0003-4571-8799.
E-mail: pasteur@pasteurorg.ru

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