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SARS-CoV-2 spread in humans and animals

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SUMMARY

Coronaviruses are a large family of viruses and they are wide spread in animals and humans. They can cause respiratory tract illnesses of various severity. The latest recently discovered coronavirus (SARS-CoV-2) is an agent of COVID-19. The first human cases were reported in Wuhan (People's Republic of China) in December 2019. Since then, the disease infected over 153 million people and became the cause of more than 3 million deaths all over the world. Among the leaders in the confirmed cases are the USA, India, Brazil, France, Turkey and Russia. In February 2020, it was determined that some animal species, including domestic cats and dogs, can be infected with SARS-CoV-2. Reports of animal infection in zoos were submitted from the USA, Argentina, Czech Republic, Sweden, Spain, Estonia, RSA and India. Cases of SARS-CoV-2 infection in fur-farmed minks were reported by 13 countries. The most large-scale COVID-19 outbreak in minks that involved about 300 mink farms was reported in Denmark. During the COVID-19 pandemic, the agent's transmission from humans to canines (*Canidae*), felines (*Felidae*), mustelids (*Mustelidae*) and hominids (*Hominidae*) was confirmed. As of early May 2021, the disease cases in animals were reported by 33 countries. Due to COVID-19 epidemic spread and detection of animal infection cases, diagnosis tools and methods were developed in the Russian Federation, and screening tests were performed in susceptible animal populations in different regions of the country. COVID-19 monitoring results demonstrated the virus in two cats (in Moscow and Tyumen).

Keywords: Coronaviruses, COVID-19, SARS-CoV-2, epizootic situation, interspecies transmission, monitoring.

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Распространение коронавируса SARS-CoV-2 среди людей и животных

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РЕЗЮМЕ

Коронавирусы составляют многочисленное семейство вирусов и широко распространены у животных и людей. Они способны вызывать у человека респираторные заболевания различной степени тяжести. Последний из недавно открытых коронавирусов (SARS-CoV-2) является возбудителем заболевания COVID-19. Первые случаи инфицирования людей SARS-CoV-2 были зарегистрированы в городе Ухань (Китайская Народная Республика) в декабре 2019 г. С тех пор данная болезнь поразила более 153 миллионов человек, став причиной более 3 миллионов смертей по всему миру. Лидерами по количеству подтвержденных случаев являются США, Индия, Бразилия, Франция, Турция и Россия. С февраля 2020 г. установлено, что некоторые виды животных, в том числе домашние кошки и собаки, могут заражаться вирусом SARS-CoV-2. Сообщения об инфицировании животных в зоопарках стали поступать из США, Аргентины, Чешской Республики, Швеции, Испании, Эстонии, ЮАР, Индии. О случаях заражения норок SARS-CoV-2 на звероводческих фермах сообщили 13 стран. Наиболее масштабная вспышка COVID-19 среди норок, охватившая около 300 норковых ферм, произошла в Дании. За время пандемии COVID-19 зафиксирована передача возбудителя от человека к представителям семейств псовых (*Canidae*), кошачьих (*Felidae*), куньих (*Mustelidae*), а также гоминид (*Hominidae*). По состоянию на начало мая 2021 г. о заболевании животных сообщили 33 страны. В связи с эпидемическим распространением COVID-19 и выявлением случаев заражения животных в Российской Федерации были разработаны средства и методы диагностики инфекции и проведены скрининговые исследования в популяции восприимчивых животных из различных регионов страны. В ходе мониторинга COVID-19 в России вирус-возбудитель был выявлен у 2 кошек – в Москве и Тюмени.

Ключевые слова: Коронавирусы, COVID-19, SARS-CoV-2, эпизоотическая ситуация, межвидовая передача, мониторинг.

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INTRODUCTION

Coronaviruses (*Coronaviridae*) is a family of related RNA viruses of 46 species, organized in two subfamilies, that cause diseases in mammals (including humans), birds and amphibians. The name is associated with the structure of the virus, the spikes of which resemble the solar corona [1, 2].

Coronaviruses are widespread in the animal world. Viruses of the *Coronaviridae* family affect bats, cats, dogs, pigs, cattle, birds and other species [2].

The new SARS-CoV-2, which caused an outbreak of the dangerous infectious disease COVID-19, was first detected in December 2019. The World Health Organization (WHO) declared it a public health emergency of international concern on 30 January 2020, and announced it a pandemic on March 11, i.e., a disease that broke out on a global scale and covered several continents.

The detection of antibodies to the viral virion components confirms the previous disease or asymptomatic carrier state and indicates the presence of immunity. The duration and strength of the immunity to the SARS-CoV-2 in different species is currently understudied. To detect antibodies to animal coronaviruses, various methods are used: neutralization test, enzyme-linked immunosorbent assay, immunofluorescence assay [3–8].

Due to the wide spread of COVID-19 in the world and the potential interspecific transmission, the goal was to develop domestic tools and methods for diagnosing the disease in animals, as well as to conduct screening studies of biological material from susceptible animals in various regions of the Russian Federation.

One of the tasks of the work carried out was to determine the target animal populations and conduct COVID-19 primary screening in these populations using laboratory diagnostic methods.

MATERIALS AND METHODS

The data on COVID-19 animal cases were collected based on statistical data from the WAHID/WAHIS database of the World Organization for Animal Health (OIE), as well as on scientific publications of foreign and domestic authors and data from the mass media. Data on human morbidity were taken from the archived data of the Johns Hopkins University (USA) and the World Health Organization (WHO) on COVID-19 outbreaks. Mapping and analytics were performed in the FGBI "ARRIAH" using the ArcGIS ESRI services.

For screening tests, Veterinary Services of 20 Russian Federation Subjects with the participation of the Rosselkhoznadzor Territorial Administrations and inter-regional veterinary laboratories collected samples from animals (nasopharyngeal/oropharyngeal swabs, rectal swabs, fresh feces) using viscose-tipped sterile applicators. Domestic cats, dogs, and mustelids (minks, sables, and ferrets) were identified as the target population for sampling, from which 1,312 samples of biological material

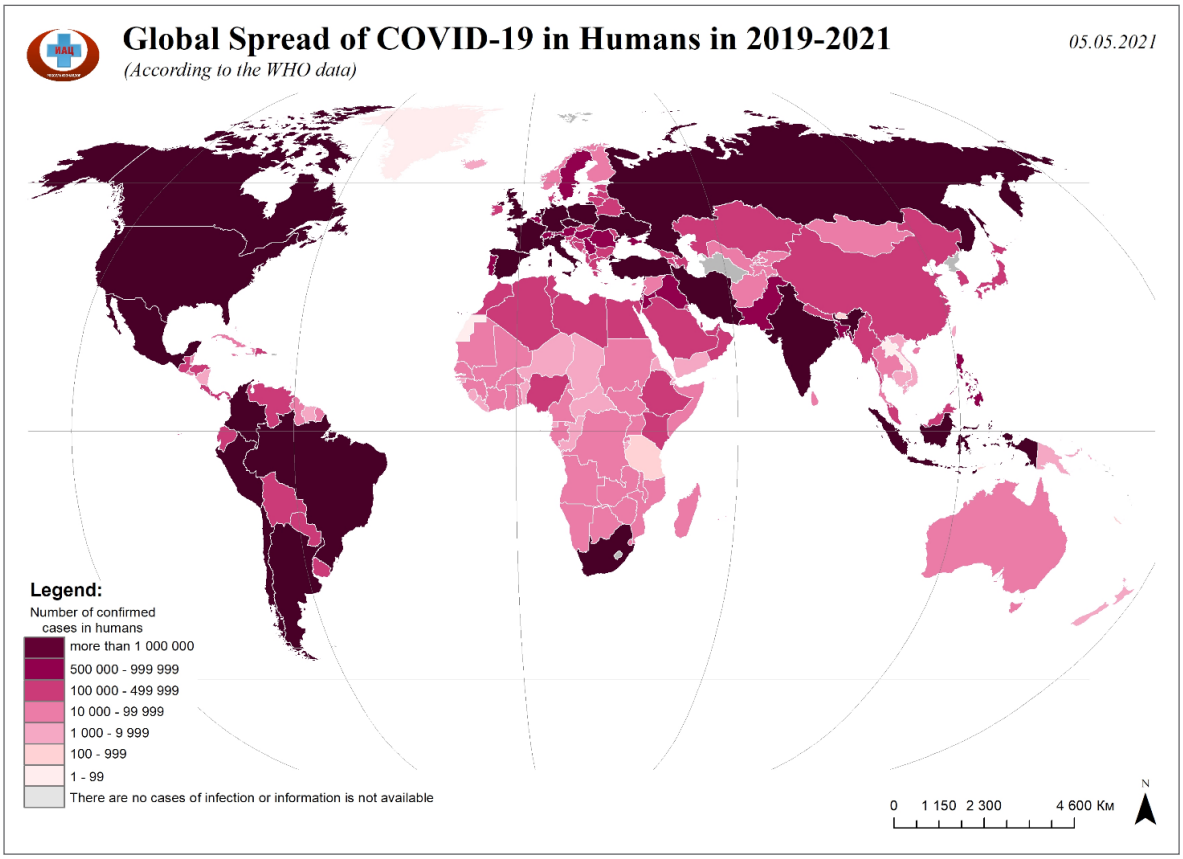

Fig. 1. Global spread of COVID-19 in humans, 2019–2021

Рис. 1. Распространение COVID-19 среди людей в мире с 2019 по 2021 г.

were collected. In addition, in order to determine the presence of infected animals in the populations of wild and domestic birds, as well as in the livestock populations (cattle, small ruminants, pigs), 122 samples of biomaterial from 26 Russian Federation regions were collected and tested. The collected samples were transported to the FGBI "ARRIAH" at a temperature of 4–8 °C. For analysis, a PCR test kit was used to detect the SARS-CoV-2 RNA (SARS-CoV-2 real-time RT-PCR, FGBI "ARRIAH") as recommended by the manufacturer.

Table 1
Number of SARS-CoV-2 infected humans across the world [11]

Таблица 1
Количество зараженных коронавирусом SARS-CoV-2 людей в мире [11]

Region	Number of cases	% of cases	Number of deaths	% of deaths
America	62,713,257	40.7	1,529,597	47.5
Europe	52,275,954	34.0	1,092,527	33.9
Southeast Asia	23,837,189	15.5	291,762	9.0
Eastern Mediterranean	9,274,240	6.0	185,875	5.8
Africa	3,330,385	2.2	83,259	2.6
Western Pacific	2,522,720	1.6	38,019	1.2
Total	153,953,745		3,221,039	

RESULTS AND DISCUSSION

SARS-CoV-2 spread in the human population

In December 2019 in China, there was an increase in the number of pneumonia cases. Investigations revealed that the disease was caused by a previously unknown virus, which was later identified as the new SARS-CoV-2 coronavirus. The infection spread quickly enough to other countries (Fig. 1) [9].

According to the WHO data, as of May 5, 2021, the number of coronavirus infected people in the world exceeded 153 million, of which more than 3.22 million died (Table 1). According to Johns Hopkins University, more than 155.2 million people were infected worldwide, and more than 3.24 million died [10]. The leader in the number of confirmed cases remains the United States, where 32.1 million infected people were recorded. In second place is India (20.7 million), in third – Brazil (14.8 million), in fourth – France (5.6 million), in fifth – Turkey (4.9 million), in sixth – Russia (4.8 million) [11].

SARS-CoV-2 spread in animal populations

The first official notification of the OIE on the transmission of the SARS-CoV-2 from humans to animals was received on February 26, 2020 from Hong Kong. The dog was quarantined after its owner was hospitalized due to the COVID-19 infection. Samples of biological material taken from the dog tested positive for SARS-CoV-2. At the same time, the animal had no clinical signs of the disease. Later, there were reports of SARS-CoV-2 detections in domestic cats and dogs in Europe, Asia, and America (Fig. 2).

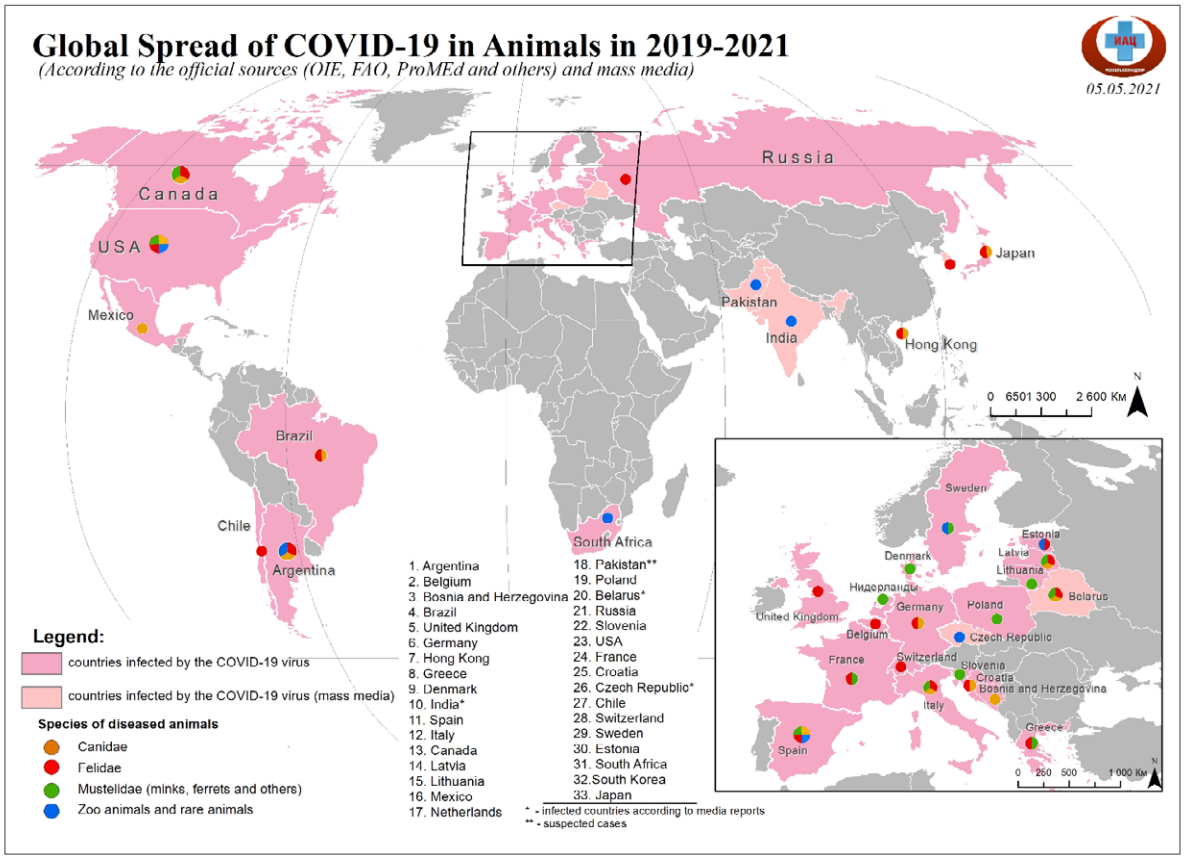

Fig. 2. Global spread of COVID-19 in animals, 2019–2021

Рис. 2. Распространение COVID-19 среди животных в мире с 2019 по 2021 г.

In Russia, the infection of animals with SARS-CoV-2 was confirmed by the FGBI "VGNKI" and the FGBI "ARRIAH". The virus was detected in two cats from Moscow and Tyumen. In the course of further COVID-19 screening tests in the populations of domestic, farm and fur animals (minks, ferrets, sables), conducted in 2020, no cases of the disease/virus carrier state were detected.

SARS-CoV-2 infection of zoo animals was first reported in March 2020 in the United States. In the Bronx Zoo (New York), a tiger with clinical signs of respiratory disease was diagnosed with SARS-CoV-2 infection during laboratory diagnostics. Five other tigers and three lions, which were kept in two enclosures at the zoo, were also infected with SARS-CoV-2. Then reports of animal infections in zoos began to arrive from other US states: tigers in Indiana, Tennessee, Virginia, Texas and Minnesota; snow leopard in Kentucky; gorilla in California; lion in Pennsylvania [12, 13]. Moreover there was information in the media that in the State of Georgia aquarium, otters got diseased with a coronavirus infection. According to the aquarium staff, the otters had symptoms of respiratory infection: sneezing, runny nose, cough and mild depression [14]. Presumably, employees of the zoos with an asymptomatic disease became a source of infection for the animals.

SARS-CoV-2 infections among zoo animals have been reported in other countries. Laboratory tests confirmed the disease in gorillas and Indian lions at the Prague Zoo (Czech Republic) [15, 16]. Representatives of the Spanish Veterinary Services reported coronavirus positives in four lions at the Barcelona Zoo [17]. In January 2021, a lion was diagnosed with COVID-19 at the Tallinn Zoo (Estonia) [18]. The Swedish National Veterinary Institute (SVA) has confirmed COVID-19 in two tigers and two lions kept at the Boras Zoo. The media reported about the suspected SARS-CoV-2 infection of two white tiger cubs in Pakistan [19]. In India, the coronavirus was found in lions at the Hyderabad Zoo [20]. The OIE also received notifications about the infection of cougars in the zoo in Johannesburg (South Africa) and in Argentina.

In April, two mink farms in the Dutch province of North Brabant in the municipalities of Larbeck and Gemert-Bakel were diagnosed with a coronavirus infection. The animals had a laboured breathing and increased mortality was recorded. Experts believe that the source of infection in minks was a human, because at the same time, some farm employees had symptoms of respiratory disease.

Sporadic cases of the SARS-CoV-2 infection have been reported in domestic ferrets in Slovenia and Spain [21, 22].

A total of 14 countries reported SARS-CoV-2 infection in mustelids (including domestic and wild). As of April 2021 COVID-19 was registered on more than 400 fur farms (Table 2).

The largest COVID-19 outbreak among minks occurred in Denmark. It covered about 300 mink farms, which were located mainly in the north of the country, in Northern Jutland. Human cases of COVID-19 were also reported, caused by new variant strains of SARS-CoV-2 detected in farm minks. To prevent the further spread of the coronavirus variants isolated from minks among people, the Danish authorities took a number of measures, including the culling of mink population on the country's farms [24]. Cases of transmission of the mutated virus from minks

Table 2
COVID-19 outbreaks on mink farms across the world [21, 23–28]

Таблица 2
Регистрация очагов COVID-19 на норковых фермах в странах мира [21, 23–28]

No.	Country	Total mink farms	Number of infected mink farms	Date of outbreak registration
1	Greece	91	23	13.11.2020 – 08.02.2021
2	Denmark	1,147	290	15.06.2020 – 07.12.2020
3	Spain	29	3	03.12.2020 – 15.03.2021
4	Italy	9	3	10.08.2020 – 18.03.2021
5	Canada	98	2	26.11.2020 – 16.12.2020
6	Latvia	9	2	04.2021
7	Lithuania	86	4	26.11.2020 – 30.03.2021
8	the Netherlands	126	69	23.04.2020 – 04.11.2020
9	Poland	350	1	27.01.2021
10	Republic of Belarus	8	1	02.2021
11	the USA	≈245	16	26.07.2020 – 25.10.2020
12	France	4	1	16.11.2020
13	Sweden	40	13	23.10.2020 – 11.11.2020
		Total	427	23.04.2020 – 04.2021

to humans were also detected in other countries (USA, Netherlands) [11, 29].

As early as in 2020, there were reports of SARS-CoV-2 registered in wild fauna. The US Department of Agriculture confirmed the first case of wild mink infection with coronavirus in Utah. The authorities of the Spanish autonomous community of Valencia also found SARS-CoV-2 in two dead wild minks [12, 25].

Fur animals that have escaped from farms can act as hosts, maintaining the virus circulation in the wild, and cause the transmission of the SARS-CoV-2 to other species of wild susceptible animals. However, there is currently no evidence of the wide spread of coronavirus in the population of wild minks living around animal farms, and the available information is insufficient to assess the likelihood of a SARS-CoV-2 reservoir occurrence in wild fauna [21].

During 18 months from the beginning of the COVID-19 pandemic, the transmission of the pathogen to canines (*Canidae*), felines (*Felidae*) (including the subfamilies of large (*Pantherinae*) and small (*Felinae*) cats), mustelids (*Mustelidae*), as well as hominids (*Hominidae*) belonging to the order Primates was recorded. The World Organization for Animal Health recommends testing of all species susceptible to the coronavirus.

Many tests have been conducted to study the effects of SARS-CoV-2 on different animal species. As shown by the results of recent experimental studies (Table 3), many mammals can be infected with the new coronavirus, including cats, dogs, mice, hamsters, bats, shrews, raccoon dogs, and deer. In laboratory conditions, intraspecific transmission of SARS-CoV-2 was observed in cats, minks, ferrets, raccoon dogs, white-tailed deer, striped skunks, some species of bats and hamsters, as well as rhesus macaques, crab-eating macaques and other Old World monkey species [29, 30]. Also, various foreign studies show that some farm animals (pigs, cattle, rabbits, ferrets, minks) are also susceptible to SARS-CoV-2 [31–34]. Data on experimental infection of cattle are scarce, and reports about pig and rabbit infections are sometimes contradictory.

An international team of biologists studied the properties of 25 amino acids of the ACE2 enzyme (angiotensin-converting enzyme 2), which serves as a receptor for SARS-CoV-2 in humans, and performed genomic and structural analyses of ACE2 in 410 vertebrate species to identify transmission routes and understand which animal species are susceptible to the virus [47, 48]. The results allowed the scientists to divide the animals into five groups.

The highest risk group included 18 species of Old World primates: representatives of the families of marmosets (*Cercopithecidae*), gibbons (*Hylobatidae*) and hominids (*Hominidae*), including humans. The second group included some rodents, marine animals (dolphins, porpoises, beluga whales, narwhals, and other cetaceans), deer, lemurs, and members of the anteater family (*Myrmecophagidae*).

A relatively large group of cloven-hoofed mammals was classified as a medium-risk group for infection. It includes domestic cattle, sheep, goats, as well as some species of cloven-hoofed animals, kept in zoos and wildlife parks (giraffes, okapis, hippos, water buffaloes, Saharan oryxes, Saharan gazelles, yaks, alpacas, bisons, etc.). In felines, the likelihood of infection was average, and in camels, horses, pigs, dogs and some other domestic animals – low. In many representatives of fish, reptiles, amphibians, monotremes, marsupials, martens, rodents and birds, the risk of infection tends to zero.

Table 3
Supposed animal hosts of SARS-CoV-2 [9, 12, 14, 26, 29–46]

Таблица 3
Предполагаемые хозяева SARS-CoV-2 среди животных [9, 12, 14, 26, 29–46]

Possible origin (natural reservoir)	Intermediate hosts (naturally susceptible animals)	Animals susceptible under experimental conditions
bats/reptiles/ pangolins	dogs, cats (domestic cats, cougars, Malay, Amur and Bengal tigers, lions, snow leopards), primates (lowland gorillas), martens (frets, European and American minks, Asian small-clawed otters)	fruit bats (Egyptian rousettes), cats, dogs, minks, ferrets, primates (rhesus macaques, crab-eating macaques, green monkeys, hamadryas, tamarins), pigs, cattle (dairy calves), white-tailed deers, raccoon dogs, tree shrews, striped skunks, North American raccoons, New Zealand rabbits, shrews, rodents (mice, bank voles, hamsters: Syrian, Chinese, deer mice, bushy-tailed woodrats, Roborovski dwarf hamsters)

The authors of the study noted that the results obtained *in silico* need to be confirmed experimentally, while they can not be considered absolutely accurate. Nevertheless, the results of the analysis significantly expanded the range of potential intermediate hosts and identified many species that may be at risk of infection with the SARS-CoV-2 through its interaction with the ACE2 receptors. In the future, these studies will help determine which animal species can infect humans with the coronavirus [47, 48].

COVID-19 monitoring studies in animals in the Russian Federation

Since June 2020, screening studies of animal populations from various RF regions have been conducted by the FGBI "ARRIAH" in order to detect the SARS-CoV-2 RNA, using the test kit of its own production. 1,312 samples of biomaterial from different animal species from 20 regions of the country were tested. During the monitoring process, a positive sample from a cat from the Tyumen Oblast was detected (Table 4).

According to the results of the study, the SARS-CoV-2 is detected sporadically in the studied animal populations (cats, dogs, minks, sables, ferrets) in the tested regions of the Russian Federation. The virus was detected in two cats – from Moscow (confirmed by FGBI "VGNKI") and Tyumen (confirmed by FGBI "ARRIAH").

In order to study the possibility of natural coronavirus infection or SARS-CoV-2 transmission to animals with unproven natural susceptibility (large and small cattle, pigs, domestic and wild birds), 122 samples of biomaterial collected on farms in various regions of the Russian Federation were tested (Table 5).

The genome of the new SARS-CoV-2 was not detected in any of the samples from wild and domestic birds, as well as from farm animals.

CONCLUSION

The number of people infected with the SARS-CoV-2 in the world has exceeded 153 million. The leaders in the number of confirmed cases are the United States (32.1 million), India (20.7 million), Brazil (14.8 million), France (5.6 million), Turkey (4.9 million), and Russia (4.8 million).

According to many virologists, humanity will be able to cope with SARS-CoV-2 only through the acquisition of immunity by the planet population. About 20 vaccines against COVID-19 have been registered in the world [11]. However, according to the WHO, as of March 1, 2021, less than 10% of the world's population has antibodies to the coronavirus.

There is currently no evidence that animals play a significant role in the spread of SARS-CoV-2 in humans. Based on the information available to date, the risk of human infection from animals is considered low. The SARS-CoV-2 is primarily transmitted with respiratory droplets from humans to humans [26, 29]. However, cases of the virus transmission from animals to humans have already been reported. For example, in Denmark, the Netherlands and the United States, there was a transmission of the mutated coronavirus from a mink to a human.

At the same time, the coronavirus can be transmitted from humans to animals. A high likelihood of infection is noted for animals that are in direct contact with humans. Thus, COVID-19 cases in companion animals (dogs, cats, ferrets) were reported in Europe, Asia and America.

Table 4
Results of testing biological samples collected from cats, dogs and mustelids for SARS-CoV-2 RNA using FGBI "ARRIAH" manufactured test-kit

Таблица 4
Результаты исследования проб биологического материала от кошек, собак и куницеобразных, полученные в ходе выявления РНК SARS-CoV-2 с использованием тест-системы производства ФГБУ «ВНИИЗЖ»

No.	Region	Species	Number of tested samples	Number of positive samples
1	Altai Krai	sables	31	0
2	Bryansk Obalst	minks, ferrets	45	0
3	Vladimir Oblast	dogs, cats	50	0
4	Kaliningrad Oblast	minks	90	0
5	Kirov Oblast	minks	30	0
6	Leningrad Oblast	sables	31	0
7	Lipetsk Oblast	minks	69	0
8	Nizhny Novgorod Oblast	cats	30	0
9	Novosibirsk Oblast	minks	35	0
10	Republic of Bashkortostan	minks, sables	70	0
11	Republic of Crimea	minks	30	0
12	Republic of Mordovia	minks	51	0
13	Republic of Sakha (Yakutia)	minks	60	0
14	Republic of Tatarstan	minks, sables	120	0
15	Republic of Udmurtia	minks	60	0
16	Sverdlovsk Oblast	cats, dogs, minks	17	0
17	Tver Oblast	minks	301	0
18	Tula Oblast	ferrets, minks, sables	95	0
19	Tyumen Oblast	cats	67	1
20	Yamalo-Nenets Autonomous Okrug	sables	30	0
		Total	1,312	1

In Russia, the infection of animals with SARS-CoV-2 was confirmed by the FGBI "VGNKI" and the FGBI "ARRIAH". The virus was detected in two cats from Moscow and Tyumen. During the COVID-19 monitoring conducted in 2020 by the FGBI "ARRIAH", no cases of the disease/carrier state were detected in other studied animal populations (dogs, minks, sables, ferrets, cattle and small cattle, pigs, domestic and wild birds).

Infection of zoo animals with SARS-CoV-2 has been reported in the United States, Argentina, Sweden, Spain, Czech Republic, Estonia, South Africa, India. Cases that have occurred on mink farms in the United States, Canada, and several European countries, including Denmark, Greece, Spain, Poland, France, Lithuania, Latvia, Belarus, Sweden, Italy, and the Netherlands, show that the virus can be transmitted from humans to minks. Sporadic cases of SARS-CoV-2 infection have been reported in domestic

Table 5
Results of testing biological samples collected from cattle, sheep and goats, pigs and birds for SARS-CoV-2 RNA using FGBI "ARRIAH" manufactured test-kit

Таблица 5
Результаты исследования проб биологического материала от КРС, МРС, свиней и птиц, полученные в ходе выявления РНК SARS-CoV-2 с использованием тест-системы производства ФГБУ «ВНИИЗЖ»

No.	Region	Species	Number of tested samples	Number of positive samples
1	Belgorod Oblast	pigs	3	0
2	Vladimir Oblast	cattle	7	0
		wild ducks, chickens	10	0
3	Voronezh Oblast	wild ducks	5	0
		pigs	9	0
4	Zabaikalsky Krai	chickens	5	0
5	Ivanovo Oblast	pigs	3	0
6	Kaluga Oblast	cattle	5	0
7	Kostroma Oblast	pigs	3	0
8	Krasnodar Oblast	ducklings	5	0
		pigs	3	0
9	Lipetsk Oblast	pigs	3	0
10	Moscow Oblast	cattle	3	0
		pigs	4	0
11	Nizhny Novgorod Oblast	cattle	3	0
12	Orel Oblast	pigs	3	0
13	Penza Oblast	turkeys	5	0
14	Perm Krai	cattle	3	0
15	Pskov Oblast	pigs	3	0
16	Republic of Bashkortostan	pigs	6	0
17	Republic of Dagestan	small ruminants	2	0
18	Republic of Crimea	swans	3	0
19	Republic of Mordovia	cattle	3	0
20	Republic of Tatarstan	cattle	4	0
21	Rostov Oblast	swans	4	0
22	Samara Oblast	cattle	3	0
23	Stavropol Krai	pigs	3	0
24	Tambov Oblast	pigs	3	0
25	Tula Oblast	pigs	3	0
26	Chelyabinsk Oblast	pigs	3	0
		Total	122	0

ferrets in Slovenia and Spain [21, 22]. Cases of coronavirus infection have also been recorded in wild mink populations in the United States and Spain, but the available information is insufficient to assess the likelihood of a SARS-CoV-2 reservoir occurrence in wild fauna.

Recent experimental studies show that many mammals, including some farm animal species, can be infected with the new coronavirus.

These findings highlight the importance of regular testing of susceptible animal species and the study of SARS-CoV-2 genetic material.

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