

Coronaviruses of wild animals in Russia

Rustam Gilmutdinov^{1,*}, *Guzel Shalamova*¹, and *Sergey Domolazov*¹

¹Kazan state Academy of veterinary medicine Bauman Institute of medicine, Kazan, Russia

Abstract. The review considers wild animal coronaviruses that live in Russia and present certain epidemic and epizootic risks. It is believed that coronaviruses entered the human population from representatives of the wild fauna and bats (the main hosts are natural reservoirs), as well as snakes, pangolins, civets, camels (intermediate hosts) are proposed as candidates. Meanwhile, this list is much wider and the intermediate link may be feline (tigers, leopards, Pallas's cats, caracals, European wildcat and eurasian lynx), mustelidae (american minks, ferrets and siberian weasel), rodents (mice and rats), marine mammals (harbour seal, bottlenose dolphin and beluga whale), as well as insectivores, namely hedgehogs (European, Amur and other species). The majority (60-75 %) of viral pathogens enter the human population from animals, of which at least 70% are wild. The influence of the exploitation of wild animals by mankind on the appearance of pandemics has been observed, which in itself provokes the emergence of new viruses in nature. Flora and fauna, adapting to the growing anthropogenic impact, are geographically redistributed.

1 Introduction

Coronaviruses, considered until the 1960s exclusively "avian respiratory pathogens", by the beginning of the XXI century were already considered as a serious veterinary problem also for pig breeding, and, in part, for cattle breeding (young animals). However, epidemiologists did not classify them as particularly dangerous agents. The appearance of first SARS, then MERS, and finally COVID-19 at the end of 2019, caused a significant increase in the level of epidemic danger of this group of viruses. In this regard, we must be very careful about the forecasts for Russia. Thus, according to COVID-19, they were not only contradictory, but also contradictory, often characterized by excessive complacency.

The probability of new dangerous coronavirus diseases in humans and domestic animals from wild fauna, primarily from wild birds and mammals, is estimated to be high. For example, more than 10 mammalian species have been shown to be susceptible to SARS-CoV or related viruses. Moreover, some coronaviruses (all of them from mammals) are not limited to reproduction or the occurrence of disease in a single host. The same SARS-CoV has a fairly wide range of hosts.

Meanwhile, the volume of Russian scientific literature on wild animal coronaviruses does not exceed 5% of the world's total, while it is mainly of a review nature and wild

* Corresponding author: gilmrust@rambler.ru

fauna is considered only in passing. Thus, it should be recognized that research in this direction is not actually conducted in Russia. As the well-known infectionist Supotnitsky M. V. (2020) rightly notes, "We can only regret the lack of attention in the past among Russian scientists to ... study the pathogens of coronavirus infections and their host ecosystems on the territory of Russia." The species spectrum of the domestic fauna, which is known about coronaviruses, is limited; almost all data were obtained by foreign researchers and, as a rule, in species with a wide range of habitats that cover the territories of other countries.

Hare-like. Coronaviruses have been recorded in European wild rabbits (*Oryctolagus cuniculus*) in Canada, the Netherlands, the United States, China, Spain and France (Monchatre-Leroy E. et al., 2017, etc.). Unlike hares (*Lepus* sp.), whose coronaviruses belong to the alphagroup, in rabbits they are included in the betagroup, but there is a close relationship between them (the identity of the genome sequence is 97-98%). Lau S. et al. (2012) identified and characterized the rabbit coronavirus (RbCoV HKU14), which is assumed to have appeared relatively recently and is an independent species. Although antibodies to RbCoV were found in 67 % of rabbits, the actual variants neutralizing the virus among them did not exceed 5 %.

2 Materials and Methods

The incidence of coronaviruses in hares is about 8 %. Symptoms of the corresponding infection in rabbits are distinguished by a significant variety, in particular, cardiomyopathy and intestinal pathology are observed. The latter is more common. The virus is also found in healthy individuals.

The high identity of the rabbit ACE2 protein to the human one in the critical areas where SARS-CoV-2 connects allows using these animals in the study of human coronavirus infection.

Insectivorous – tight grip. Since all alpha - and betacoronaviruses are found in insectivorous bats, a search for them in European hedgehogs – *Erinaceus europaeus*), also insectivorous mammals, led to the discovery of a new, closely related MERS - and SARS-CoVs, betacoronavirus in faecal samples of individuals raised in an animal shelter in Germany (Corman V. et al., 2014), which was named *Erinaceus coronavirus - EriCoV*. Later, a high incidence of this coronavirus was shown among European hedgehogs in Western Europe as a whole (Monchatre-Leroy E. et al., 2017; Saldanha I. et al., 2019, etc.). Recently, Lau S. et al. (2019) isolated 1 more betacoronavirus from Amur hedgehogs (*Erinaceus amurensis*) endemic to the Russian Far East. It is closely related to the European hedgehog coronavirus (identity 79.6 %) and, to a lesser extent (68.4 %), to the mers-CoV of DROMEDARY camels. Does not exclude the presence of coronaviruses in other species of urchins (shchelkanov M. Yu et al. 2020). In hedgehogs, the prevalence of coronaviruses is higher than in rabbits, rodents, and bats, and Supotnitsky M. V. (2020) considers domestic hedgehog species to be an actual source of dangerous coronaviruses for the population. Coronaviruses affect the intestinal mucosa of hedgehogs, where they are found in very high concentrations, and are secreted with feces; diarrhea and other manifestations are absent.

3 Results

Predators Are Martens. Coronaviruses have been studied in forest ferrets (*Mustela putorius*), American Minks (*Neovison vison*) and columbines (*Mustela sibirica*). In addition, the absence of antibodies to the virus of infectious cat peritonitis in the Netherlands kept in the zoo Taira (*Eira barbara*) – a representative of the family of Martens.

In the European part of Russia, there is a significant population of ferrets. There are 2 subspecies of deltacoronaviruses that infect them. These are ferret enteritis coronavirus (Ferret enteric coronavirus - FRECoV), which causes epizootic catarrhal enteritis and ferret systemic inflammation coronavirus (Ferret systemic virus - FRSCoV), which causes systemic pyogranulomatous inflammation. FRECoV is highly contagious and highly lethal for adults-old individuals; it is found in saliva and feces, through which it is transmitted; it only damages the intestinal mucosa; enteritis is characterized by a short incubation period. Pyogranulomatous inflammation caused by FRSCoV is similar to the granulomatous form of infectious cat peritonitis and it is mainly affected by young ferrets.

Mink alphacoronavirus, which causes epizootic catarrhal gastroenteritis in them, is genetically similar to ferret coronaviruses. The disease is registered all over the world, including in our country, although the focus is on North America and Europe (Decaro N., 2011). It occurs seasonally, infection is oral-fecal and aerogenic, covers 25-80 % of the population, high contagiousness, lethality-up to 5 %, but when complicated by other infections increases. More often, mink are sick older than 4 months, the incubation period is 5-8 days. Sometimes there is a subclinical carrier (Gorham J. et al., 1990). Clinic: apathy, anorexia, diarrhea with copious discharge of green, yellow or pinkish mucus. There may be relapses. Due to anorexia, the animal also loses the quality of its skin, which is an economic problem for producers. Treatment is symptomatic. Information about the coronavirus column is very sparse (Tidona C., Darai G., 2011).

Predators are feline. Coronavirus is a contagious and significant pathogen of wild felines. Infection can cause both moderate enteritis (Feline Enteric Coronavirus – FECV) and fatal peritonitis (feline infectious peritonitis virus – FIPV) in non-domestic cats, depending on the form of the pathogen (Terio K. et al., 2018).

Intestinal and systemic variants of feline coronavirus are considered as biotypes FECV replicates in enterocytes, causing clinical disease leading to diarrhea, or asymptomatic infection; FIPV replicates in macrophages, leading to systemic infection.

Lesions and clinical signs of the disease in domestic and non-domestic cat species are comparable, in particular, high protein content in effusions in the abdominal and / or thoracic cavities and pyogranulomatous inflammation focused on the vessels.

Of the species that have the coronavirus registered, Russia is interested in tigers (*Panthera tigris*), leopards (*P. pardus*), manuls (*Otocolobus manul*), caracals (*Caracal caracal*), forest cats (*Felis silvestris*) and common lynx (*Lynx lynx*). The Amur tiger and the Amur leopard inhabit the Russian far East; single individuals Caracal can be found in the foothills and deserts of Dagestan; the Pallas' cat habitat is represented by the Eastern, TRANS-Baikal and Tuva-Altai areas; the Caucasian subspecies of wild cat lives in the Caucasus mountains, the lynx found in Central, up to Kamchatka and Sakhalin.

Meanwhile, we met only 1 domestic publication on wild cat coronavirus infection. Thus, Seredkin I. V. et al. (2015) identified antibodies to feline coronaviruses in 43% of the studied Amur tigers of the Sikhote-Alin biosphere reserve. By Wu C. et al. (2020), wild cats are susceptible to SARS-CoV-2 and can act as intermediate hosts, as evidenced by the discovery of SARS-CoV-2 in Malay and Amur tigers at the Bronx zoo, New York.

According to Thalwitzer S. et al. (2010), there were almost no seropositive feline coronavirus individuals among free-living leopards in Namibia.

Meanwhile, the same researchers note 100 % seroprevalence in caracals; however, typical signs of the disease, such as fever, anorexia, discharge from the eyes or nose, are absent.

Low levels of exposure to coronaviruses (4 and 6 %) have been reported in forest cats in mainland Europe (Leutenegger C. et al., 1999) and in Scotland (Daniels M. et al., 1999). Seroprevalence in free-living populations of forest cats in the UK is not found at all. It is

believed that infection with feline coronavirus in forest cats is not supported due to their solitary social habitat system (Leutenegger C. et al., 1999).

In the common lynx, clinical disease has been registered in captivity (Poelma F. et al., 1971), while in free-living populations there is a low level of seroprevalence. This fact, as in forest cats, is associated with their solitary social system of habitat (Ryser-Degiorgis M. et al., 2005).

Marine mammal. Coronaviruses have been described in common seal (*Phoca vitulina*), bottle-nosed Dolphin (*Tursiops truncatus*), Indian bottlenose Dolphin (*Tursiops aduncus*), and Beluga (*Delphinapterus leucas*) (Bossart G., Schwartz J., 1990; Mihindikulasuriya K. et al., 2008; Nollens H. et al., 2010; Woo P. et al., 2014). Officially, the international Committee on taxonomy of viruses (ICTV) classifies only the Beluga gammacoronavirus as a species. All these animals live on the territory of Russia. Common seals are found in all seas adjacent to the Arctic ocean. The bottle-nosed Dolphin is common in the Baltic, Black and Mediterranean seas. Beluga inhabits the White, Bering and Okhotsk seas, sometimes entering the Baltic sea. Clinical signs include acute necrotic enteritis, pneumonia, or liver pathology.

The relationship between strains identified in the Indian bottlenose Dolphin and Beluga whales and classified as gammacoronaviruses is shown (Mihindikulasuriya K. et al., 2008; Woo P. et al., 2014).

The common seal has been identified as an alphacoronavirus; its members of this genus that are pathogenic to domestic animals and some of them, namely HCoV229E and HCoV-NL63, often infect humans.

The clinical manifestations of the disease vary significantly from left-sided infection to acute necrotic enteritis (Bossart G., Schwartz J., 1990), acute liver failure (Mihindikulasuriya K. et al., 2008) or pneumonia with congestion, compaction and hemorrhage in the lungs (Nollens H. et al., 2010). Severe leukocytosis, dehydration, hypernatremia and hyperchloremia are detected.

Rodents. They are a significant reservoir of zoonotic viruses, which outnumber all mammals (68). Evolutionarily, they are older than bats and more closely related to humans. Although rodents represent a significant reservoir of RNA viruses, they were not considered such for a long time in relation to coronaviruses. Rodents do not differ in the species diversity of coronaviruses, and only one species is known from their own pathogens - murine coronavirus OrMCoV (Lau S. et al., 2015, etc.).

ICTV in 2008 included this species in the genus Betacoronavirus (Holmfeldt K. et al., 2015), and in 2011 divided it into subspecies: mouse hepatitis virus (Murine hepatitis virus – MHV) and rat coronavirus (Rat coronavirus – RtCoV) (King A. et al., 2012).

MHV is represented by a variety of genetically and antigenically related strains that vary significantly in virulence and tropism to organs. This is due to the high tendency of the coronavirus to mutations and recombinations. Although the name MHV contains the word "hepatitis-hepatitis", the virus is not always hepatotropic. So, initially, in 1949, it was determined in mice with neurological pathology, but later it was often isolated from clinically ill mice with different manifestations. In mice, the coronavirus affects the liver, CNS, and is phylogenetically closely related to some human coronaviruses (Forni D. et al., 2017).

In the experiment, MHV can infect suckler rats and for some time it was considered a common pathogen for mice and rats. But in 1970, Parker J. et al. we described an independent rat coronavirus (RtCoV) that causes damage to the respiratory tract and lungs (Parker's coronavirus), as well as sialodacrioadenitis (sialodacriionitis coronavirus). Individuals of all ages are sensitive to RtCoV, but newborn rat pups are the most susceptible, with a mortality rate of up to 40 %.

Coronaviruses of sialodacryoadenitis and Parker is very contagious, but discretely and is transmitted by direct contact or aerosol. Parker virus is present in the body for about 1 week, often subclinically, but can cause rhinotracheitis and mild interstitial pneumonia. Sialodacryoadenitis of the coronavirus circulated among rats, causing clinically significant inflammation and swelling of the lacrimal glands, cervical.

SARS and MERS in mice and rats are mild, differing in symptoms and pathogenesis from human disease, and mice are generally resistant to COVID-19.

Cheiroptera. This very important topic is not covered in this review due to the limited scope of the publication, although it is, as already noted, quite relevant for Russia, since its territory is inhabited, according to various sources, from 30 to 60 species. To quote Supotnitsky M. V. again (2020): "the study of natural reservoirs of coronaviruses on the territory of the Russian Federation looks depressing. Bats that live directly near the Russian-Chinese border, as well as their viruses, are poorly studied."

Most of the genetic diversity of alpha and betacoronaviruses is associated with infections in bats. Bats are carriers of the main types of alphacoronaviruses (according to various data, 7 or 10 out of 17, 6 out of 11) and betacoronaviruses (4 or 7 out of 12), which can spread to humans and cause diseases. For some bat species, it is common for more than two viruses to co-exist in a single individual. Many human coronaviruses originate from bats (Forni D. et al., 2017).

Today, bats are considered the largest reservoir, the main hosts, of these viruses; they play an important role in their evolution and interspecies transfer. Regional patterns of bat CoV outbreaks at the species level can be inferred from the population distribution of the respective bat hosts.

References

1. I. V. Seredkin, D. M. Goodrich, D. Lewis, infectious and endoparasitic diseases of the Amur tiger Bulletin of krasgau **12**. 185-191 (2015)
2. M. V. Supotnitsky the New SARS-CoV-2 coronavirus in the aspect of global epidemiology of coronavirus infections Bulletin of the rchb protection troops **4**, 1, 32-653 (2020)
3. M. Yu. shchelkanov, A. Yu. Popova, V. G. Dedkov history of studying and modern classification of coronaviruses (Nidovirales: Coronaviridae) Infection and Immunity **10**, 2, 221-246; (2020)
4. G. Bossart, J. Schwartz Acute necrotizing enteritis associated with suspected coronavirus infection in three harbour seals (*Phoca vitulina*) *J. Zoo Wildl. Med* **21**, 84-87 (1990)
5. V. Corman, R. Kallies, H. Philipps Characterization of a novel betacoronavirus related to middle east respiratory syndrome coronavirus in european hedgehogs, *J. Virol* **88** (1), 717-724 (2014)
6. M. Daniels, M. Golder, O. Jarrett, D. Macdonald Feline viruses in wildcats from Scotland *J. Wildl. Dis* **35**, 121-124 (1999)
7. N. Decaro Alphacoronavirus. Coronaviridae Alphacoronavirus. The Springer Index of Viruses, *Springer*, 371-383 (2011)
8. D. Forni, R. Cagliani, M. Clerici, M. Sironi Molecular Evolution of Human Coronavirus Genomes *Trends Microbiol* **25** (1), 35-48 (2017)
9. J. Gorham, J. Evermann, A. Ward Detection of coronavirus-like particles from mink with epizootic catarrhal gastroenteritis *Can. J. Vet. Res* **54**, 383-384 (1990)

10. K. Holmfeldt, M. Sullivan, A. Kropinski ICTV taxonomic proposal 001a-dB.A.v2.Cba41virus. Create genus Cba41virus within the family Podoviridae (2015)
11. S. Lau, Y. Feng, H. Chen Severe Acute Respiratory Syndrome (SARS) coronavirus ORF8 protein is acquired from SARS-related coronavirus from greater horseshoe bats through recombination, **89**, 10532–10547; (2015)
12. S. Lau, K. Li, A. Tsang Recent transmission of a novel alphacoronavirus, bat coronavirus HKU10, from Leschenault's rousettes to pomona leaf-nosed bats: First evidence of interspecies transmission of coronavirus between bats of different suborders, *J. Virol*, **86** (21), 11906–11918 (2012)
13. S. Lau, H. Luk, A. Wong Identification of a Novel Betacoronavirus (Merbecovirus) in Amur Hedgehogs from China *Viruses*, **11**, 980 (2019)
14. C. Leutenegger, R. Hofmann-Lehmann, C. Riols Viral infections in free-living populations of the European wildcat, *J. Wildl. Dis*, **35** (4), 678–686 (1999)
15. K. Mihindukulasuriya, G. Wu, St. Leger Identification of a Novel Coronavirus from a Beluga Whale by Using a Panviral Microarray, *J. Virol* **82** (10), 5084–5088 (2018)
16. E. Monchatre-Leroy, F. Boué, J. Boucher Identification of Alpha and Beta Coronavirus in Wildlife Species in France: Bats, Rodents, Rabbits and Hedgehogs, **9** (12), E364 (2017)
17. H. Nollens, J. Wellehan, L. Archer Detection of a respiratory coronavirus from tissues archived during a pneumonia epizootic in free-ranging Pacific harbor seals *Phoca vitulina richardsii* *Dis. Aquat. Organ*, **90**, 113-120 (2010)
18. J. Parker, S. Cross, W. Rowe Rat coronavirus (RCV): a prevalent, naturally occurring pneumotropic virus of rats *Arch. Gesamte Virusforsch*, **31** (3), 293-302 (1970)
19. M.-R. Ryser-Degiorgis, R. Hofmann-Lehmann, C. Leutenegger Epizootiological investigations of selected infectious disease agents in free-ranging Eurasian lynx from Sweden *J. Wildl. Dis*, **41** (1), 58-66 (2005)
20. I. Saldanha, B. Lawson, H. Goharriz Extension of the known distribution of novel clade C betacoronavirus in wildlife host *Epidemiol. Infect* **147**. - e169 (2019)
21. K. Terio, D. McAloose, E. Mitchell In: *Pathology of Wildlife and Zoo Animals*, 263–285 (2018)
22. S. Thalwitzer, B. Wachter, N. Robert Seroprevalences to viral pathogens in free-ranging and captive cheetahs (*Acinonyx jubatus*) on Namibian farmland *Clin. Vac. Immunol*, **17** (2), 232–238 (2010)
23. C. Tidona, G. Darai *The Springer Index of Virus* Springer Science+Business Media, LLC, 2088 (2011)
24. Woo, S. Lau, C. Lam Discovery of a Novel Bottlenose Dolphin Coronavirus Reveals a Distinct Species of Marine Mammal Coronavirus in Gammacoronavirus, *J. Virol*. **88** (2), 1318–1331 (2014)
25. C. Wu, M. Zheng, Y. Yang In Silico Analysis of Intermediate Hosts and Susceptible Animals of SARS-CoV-2 *ChemRxiv*. Preprint. (2020)
<https://doi.org/10.26434/chemrxiv.12057996.v1>