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# The biological diversity of coronaviruses: where will the new threat come from?

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## Abstract

The recent outbreak of COVID-19 rose a new wave of interest to coronaviruses though the first coronaviruses were discovered in the first half of the XX century. That time coronaviruses were considered as a quite serious veterinary problem but they were not believed to become highly dangerous for humans. However, such ideas were revised in 2002 when SARS-CoV was transferred to human population in the Southeast Asia assumably from the bats, and later in 2012 when natural focus of the MERS-CoV was discovered in the Arabian countries. Due to the increased interest a large number of new Coronaviridae family members was revealed in the first decades of the XXI century. Since then taxonomic structures of coronaviruses underwent significant changes. This review is focused on the need for continued monitoring of the biological diversity of coronaviruses. The structural studies of coronaviruses regardless of the host species may allow us to identify early changes that can affect the evolutionary drift process of a particular HCoV species involved in viral transmission from bats or birds to humans.

**Key words: coronavirus, Coronaviridae, SARS-CoV, MERS-CoV, SARS-CoV-2, COVID-19, taxonomy.**

## Background

The modern Humanity will definitely cope with the new coronavirus, but it is still unclear at

what cost. There are still too many variables in the equation called the COVID-19 pandemic, and prognosis is greatly depending on the changes of the SARS-CoV-2 virus itself. Evidently it is mutating, and it is not clear whether it will become more dangerous or transform into a relatively harmless virus with which we will be peacefully coexisting.
This is not the first coronavirus that humanity has encountered. Coronaviruses became known in the mid-1960s. In 2002, the SARS-CoV coronavirus caused an epidemic of severe acute respiratory syndrome (SARS). A total number of 8,437 cases were reported, of which 813 resulted in the death of the patients. 10 years later, another coronavirus, MERS — CoV began to rage, causing Middle East respiratory syndrome (MERS), which has a mortality rate of 35 percent.
Coronaviruses belong to the Coronaviridae Family of the Order Nidovirales which includes more than 40 species. The Orthocoronavirinae subfamily is closely related to the winged animals that are natural reservoirs for these viruses: bats for Alphacoronavirus and Betacoronavirus, birds for Deltacoronavirus and Gammacoronavirus. Currently 7 species of that family have the significant medical importance: they cause natural focal infections and nowadays provoke pandemic multi-pathological processes. Though different types of coronaviruses do not have the same way of distribution and infection among people, some species belong to the group of sporadic infections, other species have the ability for epidemic, and even pandemic spread. According to the current International Health Regulations (2005), some types of coronaviruses cause infectious processes which require the public health emergencies of international importance and should be assessed as the cases of diseases that are unusual and can have a serious impact on public health [1]. No intermediate host has yet been identified for the new SARS-CoV-2 coronavirus. Analysis of the S-protein receptor-binding domain indicates that these may be pangolins. But there is another study on phylogenetic analysis, in which scientists suggest that there is no intermediate host, and the virus migrated to humans directly from bats.

**The timeline of coronaviral research**

For the first time, the coronavirus was isolated by Schalk A.F., Hawn M.C. (1931), which caused a "new respiratory disease" in chickens and was identified as an infectious bronchitis virus (IBV), currently called Avian coronavirus (Avian coronavirus - aCov) [3]. In the following years and decades many different types of coronaviruses (HCoV) were discovered, isolated from mammals and birds, but only in 1968 they were merged into the group Coronaviruses [4]. In the catalogues of the International Committee on Taxonomy of Viruses (ICTV) a group of coronaviruses appeared in 1971, when they were combined into a separate genus, and in 1976 - their taxonomic rank increased to a family [5, 6].
Further progress of the classification of coronaviruses was based on the described viral proteins and their structure. In 1996, at the X International Virological Congress a taxonomic group was proposed – an order called Nidovirales (from Lat. Nidos – nest), since the expression of the genome in viruses involves the synthesis of 3' - coterminal nested subgenomic mRNAs [7].
By the end of the twentieth century scientific virological societies considered the role of HCoV mostly in the veterinary pathology, which was poorly related with the human infection diseases. However, the beginning of the XXI century changed these ideas, as new viruses were detected by not only causing diseases in various mammals and birds, but also provoking vivid epidemic manifestations in humans [8].
In 1965, for the first time the human coronavirus HCoV 229E was detected, causing the disease-human coronavirus 229E [9].
In 1966, the human coronavirus HCoV OS43 was isolated from humans, which acts as the etiological factor of the disease-human coronavirus OS43. Diseases caused by both viruses mainly occurred with mild clinical manifestations resembling well-known acute respiratory viral infections (ARVI) [10-12].

In Southern China (2002) the unknown diseases that caused atypical pneumonia had appeared and later spread to different countries and continents, causing epidemics. Special virological and molecular genetic studies have established the etiological cause of those diseases, which was associated with an unknown coronavirus SARS-CoV (from the English severe acute respiratory syndrome-related coronavirus - SARS coronavirus), causing the disease – severe acute respiratory syndrome (SARS) [13, 14].
Dutch scientists (2004) in the study of material taken from a person with respiratory syndrome, identified as the previously unknown coronavirus HCoV-NL-63 (from the English sample number 63 from the Netherlands - human coronavirus NL63), causing the disease - human coronavirus NL63 [15-17].
Employees of the University of Hong Kong later in 2005 found in the material from a patient with clinical manifestations of bilateral pneumonia another new coronavirus-HCoV HKU1 (from the English Hong Kong University with the number 1-human coronavirus HKU1), causing the disease - human coronavirus HKU1 [18]. Both new viruses generally caused mild respiratory symptoms, but sometimes these types were also responsible for severe SARS-syndrome [18].
In Saudi Arabia (Jeddah, 2012), a new virus MERS-CoV (from the English middle east respiratory syndrome coronavirus) causing clinically Middle East respiratory syndrome (MERS) with the ability to spread epidemically in the world, was isolated during the study of nasopharyngeal discharge obtained from a man with SARS [19].
In Wuhan (Hubei Province, China, December 8, 2019) the first case of human disease caused by an unknown pathogen was officially registered [20].
On December 31, 2019, the City Health Commission submitted the first official report to the Ministry of Health (Beijing, China) about the appearance of diseases in the city that was initially registered as SARS of unclear etiology [21].
On January 7, 2020, a new virus belonging to the Coronaviridae family was identified and received the temporary name 2019-nCoV (from the English - novel coronavirus 2019) [22].
On January 10, 2020, for the first time GenBank published the complete genome of the first strain of the 2019-nCoV virus (Wuhan-Hu-1 under the number MN908947, RefCeq NC_045512) [23, 24].
On January 30, 2020, due to a large number of infected people and fatal cases of the disease, first in Wuhan, and then in other territories of China and in some closely located countries, the World Health Organization (WHO) declared the ongoing outbreak caused by the 2019-nCoV virus a public health emergency of international importance [25].
On February 12, 2020, WHO assigned a new name to diseases caused by the 2019-nCoV virus - COVID-19 (from the English coronavirus disease - 2019) and determined its position in the International Classification of Diseases by assigning codes [26]. Based on the results of studying several hundred genomes of coronaviruses of the 2019-nCoV strains detected during the ongoing epidemic process in the world, ICTV decided to rename the 2019-nCoV virus to the SARS-CoV-2 virus (from the English - severe acute respiratory syndrome 2 – SARS coronavirus 2), which causes the coronavirus infection COVID-19 [26 - 27].
On March 11, 2020, due to the expansion of the geographical scope of the epidemic and diseases recorded on most continents and in almost all countries of the world caused by SARS-CoV-2, WHO declared the COVID-19 epidemic - the COVID-19 pandemic [28 - 30].

**Taxonomic position of coronaviruses**

By the end of the first decade of the XXI century, the modern classification of coronaviruses began to form: the genus Coronavirus was formed as part of the family Coronaviridae, and the subfamily Orthocoronavirinae. The division into lower taxonomic categories: genera, subgenera, and species occurred later after a detailed study of viruses and their cellular receptors, which were not associated with their differences in species of biological objects

(humans, mammals, and birds) [31-33].
The study of cellular receptors in various coronaviruses, including those that play the significant role in human pathology, showed that some different features were revealed. Coronaviruses of the first group have a cellular receptor N-aminopeptidase (aminopeptidase-N - APN), known as the cluster of differentiation CD13. CD is named according to the nomenclature of human leukocyte differentiation antigens and is a receptor between interacting viruses and host cells. The group was divided into two subgroups due to differences in the structure of the 3'terminal set of genes. Subgroup 1a, which included mammalian and avian viruses, did not differ from each other. Subgroup 1b included both coronaviruses that play a role in human pathology (HCoV-229E, HCoV-NL63) and those that cause pathology in animals and birds, when the genome contained an additional reading frame for one or two non - structural proteins between the S and E genes [8, 33-39].

The current taxonomic structure of coronaviruses turned out to be mosaic, which required a change in the classification in the direction of increasing the rank of taxa. The proposal was implemented in the IX Taxonomic Catalog of ICTV (2011): the genus Coronavirus was transferred to the category of the subfamily Coronaviridae. Instead of the genus Coronavirus, four new genera are described, designated by letters of the Latin alphabet: the first genus - Alphacoronavirus (group 1), the second genus-Betacoronavirus (Group 2), the third genus - Gammacoronavirus (group 3 with subgroups 3A and 3B), the fourth genus - Deltacoronavirus (group 3 with subgroup 3C) [40].
In 2018, the taxonomic structures of coronaviruses underwent two more significant changes. First, a new taxonomic category of coronaviruses - subgenus-was introduced and some ranks (subgenus, genus, family) were mathematically evaluated. The division into subgenera and other taxonomic categories was based on the allocation of phylogenetic distances (the sum of differences in the set of traits between two nodes of the phylogenetic tree, measured along the edges connecting them), built on the basis of the study of full-fledged genomes. The assessment of these taxonomic categories established the size criteria for coronaviruses: for the subgenus-0.186, for the genus-0.789, for the subfamily-1.586, but in the future possible changes are assumed depending on the number of coronaviruses studied [41]. Secondly, there was a replacement of two subfamilies with one, which was named Orthocoronavirinae. The researchers found that the subfamily is associated with winged animals that are a reservoir of coronaviruses: bats - for the genera Alphacoronavirus and Betacoronavirus, birds - for the genera Gammacoronavirus and Deltacoronavirus. The appearance of amphibian infectious agents among coronaviruses, on the one hand, violates the ecological integrity of this family, which was only recently acquired after the exclusion of the subfamily Torovirinae, which contained fish viruses and now has the rank of an independent family Tobaniviridae. On the other hand, there is hope to find traces of the older evolution of coronaviruses as a result of the expansion of the spectrum of potential hosts. This can the result of the expansion of the host reservoir spectrum in coronaviruses, due to their broad ecological plasticity, and has allowed some HCoVs to cause diseases in humans and show their epidemiological significance [8, 33, 38].
The results of genetic, phylogenetic, phenotypic and evolutionary analyses of the genomes of various HCoV strains were obtained from the two databases Genbank and the Global Initiative on Sharing All Influenza Data (GISAID), where data on HCoV genomes was entered. These materials were used by scientists from different countries to create a modern classification of HCoV, including those of medical significance (table 1) [38, 42, 43].

**Table 1. Taxonomic structure of medically important Coronaviridae family (Nidovirales)**

| Taxon | Latin name | Prototype strains | Source of isolation | Genbank ID |
|---|---|---|---|---|
| Kingdom | Ribovirus | | | |
| Order | Nidovirales | | | |
| Suborder | Cornidovirinae | | | |
| Family | Coronavirus | | | |
| Subfamily | Orthocoronavirinae | | | |
| Genus | Alphacoronavirus | | | |
| Subgenus | Davinalovirus | | | |
| Species | HCoV-229 | Inf-1 | Homo sapiens | NC002645 |
| Subgenus | Setracovirus | | | |
| Species | HCoV-NL-63 | Amsterdam 1 | Homo sapiens | AY567987 |
| Genus | Betacoronavirus | | | |
| Subgenus | Embecovirus | | | |
| Species | HCoV-HKU1 | HKU1 | Homo sapiens | NC006577 |
| Species | Betacoronavirus (HCoV-OC-43) | HCoV-OC-43/ATCC | Homo sapiens | AY391777 |
| Subgenus | Merbecoronavirus | | | |
| Species | MERS-CoV | Jeddan/ Camel | Camelus dromedarius | KF917527 |
| Subgenus | Sarbecovirus | | | |
| Species | SARS-CoV | GDOI | Homo sapiens | AY278489 |
| Species | SARS-CoV-2 | Wuhan-flu-1 | Homo sapiens | NC045512 |
| Genus | Gammacoronavirus | | | |
| Genus | Deltacoronavirus | | | |

Note: Prototype strains, isolation sources, and Genbank identification number (ID) are listed for coronavirus species of medical significance [8].

The current taxonomic classification of coronaviruses consists of taxonomic groups: kingdom – Ribovirus, order – Nidovirales, suborder – Cornidovirinae, family – Coronavirus, subfamily – Orthocoronavirinae, genera - Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus. The results of the phylogenetic study of genomes were used to determine the taxonomic structure of the intragenital classification [44].
The genus Alphacoronavirus includes 2 subgenera, each containing one species ofcoronavirus of medical significance: the subgenus Davinalovirus includes the species HCoV 229E, the subgenus Setracovirus-the species HCoV NL63.
The genus Betacoronavirus includes 5 species of coronaviruses of medical significance, which are divided into 3 subgenera: the subgenus Embecovirus includes two species HCoV HKU1, HCoV OS43; the subgenus Merbecoronavirus includes one species MERS-CoV; the subgenus Sarbecovirus contains two species: SARS-CoV and SARS-CoV-2.
In addition to the HCoV species isolated from humans, these genera Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus include other HCoV species. The specific names of HCoV, which did not cause disease in humans, were derived from the specific names of those mammals and birds from which they were isolated (cats, dogs, pigs, ferrets, minks, bats of various species, mice, rats, cattle, rabbits, Chinese ferret badgers, palm civets, bats, club - footed kozhans, night bats, chickens, turkeys, pheasants, lake gulls, belugas, ducks, geese, pigeons, nightingales, leopards, reed warblers, magpie warblers, astrilds) [8, 38-40].
The SARS-CoV, MERS-CoV, and SARS-CoV-2 viruses, which caused major epidemics, and SARS-CoV-2 and a pandemic, have become epidemic in the human population. Diseases caused by these coronaviruses are characterized by some features that allow them to be classified as a group of particularly dangerous viruses. Their distinctive abilities determined by the receptor specificity for α2'-3' sialosides like some of the influenza A virus that determine the ability to penetrate into the lower respiratory tract [45 - 47] and can cause serious infectious diseases, epidemics and pandemics, which indicates naih a danger to others (viruses belong to the 2nd group of pathogenicity of microorganisms, which require set bioderived precautions required for work with dangerous biological agents with biological safety level - BSL-3) [48].
SARS-CoV, MERS-CoV and SARS-CoV-2 viruses are genetically heterogeneous and cause different diseases: SARS-CoV - SARS virus (2002); MERS-CoV - MERS virus (2012); SARS-CoV-2 - COVID-19 virus.
Other viruses of the Coronavirinae family, Orthocoronavirinae subfamily: HCoV 229E, HCoV NL63, HCoV HKU1, HCoV OS43 cause diseases in humans, but they differ in the spectrum of clinical manifestations and severity, and some show differences in the morphology of the virus, and this separates them from the group of particularly dangerous coronaviruses. All four coronaviruses are spread globally and cause from 15 to 30% of cases of human diseases in the structure of the incidence of SARS. Infected people do not demonstrate a high degree of contagiousness, as in particularly dangerous HCoV; the overwhelming number of diseases occurs in the form of mild forms; severe clinical manifestations are rarely recorded in the lower respiratory tract in children, the elderly and patients with weakened immunity. These arguments allow these representatives to be combined into another group that differs from one of particularly dangerous coronaviruses.

**Structural features of coronaviruses**

All coronaviruses, regardless of the severity of the disease; what are the clinical symptoms; what is the degree of epidemiological danger to others; have the same morphological properties and structure, although some differences exist in some species [46-50].
HCoV virions are spherical in diameter from 80 to 229 nm, the largest among RNA viruses. RNA, which has helical symmetry, is located inside the nucleoprotein (N-protein) and both structures together form a nucleocapsid (60-70 kDa). On the outer surface of the nucleocapsid is a super-capsid shell of complex structure (bilayer lipid shell), under which there are four or

five structural proteins that form the outer layer of the coronavirus and protect the RNA inside. Structural proteins determine not only the structure of the virus, but also take part in the replication of new viral particles, in the assembly and exit of new copies of the virus from the host cell [51-56].

N-protein (50 - 60 kDa) is a phosphorylated protein in chemical structure and protects the RNA virus by keeping it stable inside the viral envelope, while a large number of proteins are connected to each other in a long spiral, wrapping and winding on the RNA [51 – 54, 56, 57].

S-protein (150 - 220 kDa), is located on the surface of the bilipid shell of the virus in the form of club-like processes, so it is called spike protein (from the English spikes-spike), which gives the virus a unique crown shape. S-protein by its chemical structure is a glycoprotein that creates trimers in the form of peplomers that form "crown teeth" with a length of 10-25 nm. These coronaviral proteins have determined the name of the taxonomic group of viruses and ensured the penetration of the virus into the somatic cell. Part of the spike can expand and attach to different proteins in different species, which are present on the cells of the respiratory tract and in the cells of other organs and tissues of different human systems, i.e. determine the adhesion and introduction of the virus into the cell. Probably, a mutation or several mutations that occurred some time ago affected the evolution of the virus, which created the conditions for its transition from bats to humans and determined the ability of spines to bind tightly to human cells [51 – 53, 55 – 58].

M-protein (23-25 kDa) is a structural HCoV protein, located slightly deeper than the spike protein, closer to the nucleocapsid, so it can act as a transmembrane protein, according to the chemical structure of the glycoprotein. The M-protein is part of the outer envelope of the virus and provides the virion form [51-53]. Cryo-electron microscopy and tomography studies have shown that there are two functionally distinct forms of the coronavirus M protein. On most viral particles, the M-protein is tightly packed along the edge, and in some it is characterized as blurry, which does not come into contact with RNA. The general shape, tightly packed along the edge, was called M LONG , and the short blurred one was called M COMPACT. Viral spikes were found on both M LONG and M COMPACT, but were absent on virus membranes without the M protein. The two forms of M-protein represented different conformations of the same peptide chain. The endodomains of the M protein independently assembled into oligodimeric complexes at 37 °C, and a convex, rigid viral envelope was formed, which was called M LONG. M LONG, stabilized by S, N, and E. M protein is a dimeric protein that controls particle size and assembly efficiency [54, 56, 57, 59].

E-protein (9-12 kDa) or the shell structural protein is adjacent to the nucleocapsid, which is detected only among viruses of the subfamily Orthocoronavirinae. E-protein helps to form an oily bubble of the virus and perform functions while already inside the infected cell. Pentamers of protein E form ion channels and are an important factor in the pathogenicity of HCoV (pentamers in the shell of several copies per virion). The E-protein is embedded in the envelope, can connect with proteins that help regulate genes, actively change the activation pattern of human own genes, and participate in the assembly of the virion and the exit of the virion outside the cell [51 - 53, 55 - 58].

Some coronaviruses (HCoV-OC43 and HCoV-HKU1) have an additional surface hemagglutinin esterase (HE-protein, 9-12 kDa), a glycoprotein by its chemical structure. Viruses that possess the HE-protein demonstrate hemagglutinating and esterase activity, which are used as a mechanism for invading the somatic cell, help in the attachment and destruction of certain sialic acid receptors that are located on the surface of the host cell. A HE-protein is a transmembrane protein dimer consisting of two monomers, where each consists of three domains. These three regions are binding domains: membrane fusion, esterase, and receptor fusion. All especially dangerous viruses SARS-CoV, MERS-CoV, SARS-CoV-2 lack HE-protein [8, 33, 40, 51, 57].

All structures of the viral cell are determined by the virus genes, which show some differences in different viruses, and determine the process of virus variability and replication.

**Possible biological mechanisms of coronaviral spread**

The Orthocoronavirinae subfamily is closely related to the winged animals that are natural reservoirs for these viruses: bats for Alphacoronavirus and Betacoronavirus, birds for Deltacoronavirus and Gammacoronavirus. In 1949, the mouse hepatitis virus (MHV — Murine hepatitis virus) was described, which is extremely widespread among wild and laboratory house mice (Mus musculus), causes liver damage and leads to significant mortality (up to 100%) among suckling mice in vivar colonies [59]. Since 2011, MHV has been known as the "mouse coronavirus" (MCoV — Murine coronavirus) (Betacoronavirus, Embecovirus) [60].

By the beginning of the XXI century, MCoV was the most studied representative of the Coronaviridae (then losing this "title" to particularly dangerous coronaviruses human SARS-CoV and MERS-CoV). Like many other coronaviruses, numerous strains of MHV have been divided into two pathotypes, called enterotropic 5 (causing cytolysis of enterocytes and numerous necrosis of the intestinal mucosa) and polytropic (reproducing in the epithelium of the nasopharynx, affecting the lymph nodes, but not the intestinal epithelium; neurotropic strains are also known) [61].

Under experimental conditions, suckling rats can be infected with MHV, so for a while this virus was considered to be common to mice and rats. However, in 1970, an independent rat coronavirus (RtCoV — Rat coronavirus), which causes damage to the respiratory tract and lungs, as well as sialodacrioadenitis [62].

Animals of all ages are sensitive to rtcov, but newborn pups are most susceptible, among which there is a moderate mortality rate (up to 40%) [62]. Described
in 1948 by J. A. Miles and M. G. Stoker, the puffinosis coronavirus (PCoV — Puffinosis coronavirus), which causes conjunctivitis, blisters on the swimming webs of the paws and spasms of the extensor muscles in common petrels (Puffinus puffinus) on the Skomer Islands and Skokholm off the southwest coast of Wales (UK) [63], was close to MHV and RtCoV. The reason lies in the population interactions of mouse-like rodents and petrels that lay eggs in burrows that are populated by rodents in the inter-nesting period. Currently, MCoV includes RtCov and PCoV as subspecies. Most likely, the Runde virus (RNDV — Runde virus) also belongs to MCoV, and it has remained in the status of unclassified since the 1970s. RNDV was isolated in 1977 from Ixodes uriae, collected in breeding colonies of seabirds on the Norwegian island of Runde [64]. Birds are forced to use crevices for nests rock or burrow [for example, so do the Atlantic puffins (Fratercula arctica)]. The same shelters are then used by rodents, and the saturated ixodids can contain the virus at least in the intestines (since the fact of biological transmission of RNDV is not established). Indirectly, this hypothesis is supported by the absence of coronaviruses among strains isolated from I. uriae on small freshwater-deprived islands where rodents are absent [64].

It is well-known that natural foci of MERS-CoV are located on the territory of the Arabian Peninsula, where the bats act as the reservoir of the virus [65]. A person can become infected by MERS-CoV as a result of contact with bat secretions or from another unknown intermediate hosts which can be pangolins. Pangolin meat is a delicacy in many countries of South-East Asia, and skin scales are widely used in oriental medicine, making these animals part of the International Red Book as one of the most massive objects of illegal trade [66]. This, in particular, explains why the source of the virus was the Wuhan market.

Serological investigation in the populations of farm animals in the territory Oman has shown that 100% of single-humped camels (Camelus dromedarius) have antibodies against the S1 subunit of the spike protein MERS-CoV [67]. Then, direct evidence was obtained for the circulation of MERS-CoV variants identical to epidemic ones in the body of camels and the possibility of human infection from these animals [68]. Bats can infect camels during their diaries in shelters for farm animals. It turned out that the immune layer for MERS-CoV is found among single-humped camels in Africa, including the Canary Islands. However, specific anti-

MERS-CoV antibodies are absent in single-humped camels in Australia [69], which suggests that these animals may not be the main host of MERS-CoV. Specific anti-MERS-CoV antibodies were found in Qatar-bred alpaca (Vicugna pacos). It is possible that all callosopods (Artiodactyla: Tylopoda) are sensitive to MERS-CoV and may be an intermediate host and a convenient indicator for this virus in the presence of a natural reservoir-bats containing the virus.

## Conclusion

Currently, the modern taxonomic structure of coronaviruses has been not fully formed, it has been going on for more than 80 years and yet will be continued. Nearly 40 species of coronaviruses are found but currently only 7 of them are reported for medical significance. Analysis of literature sources, taxonomic position, morphological characteristics, structure of different species of coronaviruses showed those 7 species should be allocated to 2 groups of coronaviruses: a group of dangerous human coronaviruses (SARS-CoV, MERS-CoV and SARS-CoV-2); a group of «non-dangerous» human coronaviruses (HCoV 229E, HCoV NL63, HCoV HKU1, HCoV OC43). Attention is drawn to the need for the furthers studies of the biological diversity of coronaviruses. These studies should include the structural changes of in coronaviruses, regardless of the host species, and this can also allow us to identify those changes that affect the evolutionary drift process of a particular HCoV species and which probably lead to transmission from bats or birds to humans.

A natural question arises — is this the first and last meeting with SARS-CoV-2 or will we have to face it again after the end of the pandemic? Recall that the Bird flu pandemic subsided in July-August 1918, and then in the fall came the second, more deadly wave. The question of a possible re-encounter with the SARS-CoV-2 virus is now difficult to answer. If everything goes along the way of significantly weakening the virus, then eventually it will turn into one of the non-dangerous circulating viruses that cause common colds. Today it is clear that bat viruses are already adapted to mammalian cells, and it is easier for them to enter human populations, but also avian coronaviruses should not be excluded from the context analysis: their receptor specificity to α2'-3' – sialosides is similar to that of Bird flu A viruses and some variants of epidemic strains can be capable of infecting the lower parts of the human respiratory tract.

Due to the detection of amphibian coronaviruses and the much greater proximity of birds (one of the main hosts of coronaviruses) to reptiles rather than to amphibians we can assume the existence of viruses of this family that can affect reptiles (most likely — as part of a separate subfamily). The presence of subgenera specialized for mammals is the result of the expansion of the spectrum of potential hosts by coronaviruses due to their high ecological plasticity.

Taking into account the migratory abilities of bats and especially birds, it is necessary to not only to include coronaviruses in the ecological monitoring programs, but also to expand the scope and depth of environmental and virological monitoring.

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### Ethics declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

**Availability of data and materials** All data are available on demand.

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