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SARS-CoV-2 and mammals: A short revision

SARS-CoV-2 y mamíferos: una breve revisión

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In 2019, an outbreak of pneumonia of unknown origin was reported in China, reminiscent of the Severe Acute Respiratory Syndrome (SARS) virus outbreak during the years 2002-2003. In February 2020, the new virus was identified as a member of the *Coronaviridae* (CoV) family, initially named nCOV-19 and associated with the disease called COVID-19. It was later renamed SARS-CoV-2 by the international committee on taxonomy of viruses (ICTV), as it shares similarities with 6 previously known and described human coronaviruses, including SARS-CoV and MERS-CoV. Bats, reservoirs of many coronaviruses, were the first mammals presumed to be involved in the transmission cycle. The search for the natural reservoir or host of SARS-CoV-2 has focused on bats of the genus *Rhinolophus* (Asian horseshoe bats). However, as with other coronaviruses, intermediate hosts that have not yet been identified may be necessary for transmission to humans. The purpose of this work was to conduct a review of the current knowledge of the mammalian hosts of SARS-CoV-2 and the clinical manifestations they have presented. In addition, potential reservoirs are explored, and intermediate hosts are proposed. Finally, we list the challenges in identifying these key species in the virus transmission cycle and advocate for a One Health approach to prevent future pandemics.

Key words: Coronaviruses; host; pandemic; reservoirs; virus.

En 2019, se reportó un brote de neumonía de origen desconocido en China, que recordaba al brote por el virus del Severe Acute Respiratory Syndrome (SARS) durante los años 2002-2003. En Febrero de 2020 se identificó al nuevo virus como miembro de la familia *Coronaviridae* (CoV), nombrado inicialmente como nCOV-19 y asociado con la enfermedad llamada COVID-19. Posteriormente, fue renombrado como SARS-CoV-2 por el comité internacional sobre taxonomía de virus (ICTV por sus siglas en inglés), ya que comparte similitudes con 6 coronavirus humanos conocidos y descritos previamente, incluidos SARS-CoV y MERS-CoV. Los murciélagos, reservorios de muchos coronavirus, fueron los primeros mamíferos implicados en el ciclo de transmisión hacia los humanos. La búsqueda del reservorio natural u hospedero del SARS-CoV-2 se ha centrado en los murciélagos del género *Rhinolophus* (murciélagos herradura asiáticos). Sin embargo, como ocurre con otros coronavirus, pueden ser necesarios hospederos intermediarios que aún no han sido identificados en la transmisión hacia humanos. El propósito de este trabajo fue realizar una revisión sobre el conocimiento actual de los mamíferos hospederos del SARS-CoV-2 y las manifestaciones clínicas que han presentado. Además, se exploran los reservorios potenciales, y se proponen hospederos intermediarios. Finalmente, se enumeran los desafíos para identificar estas especies claves en el ciclo de transmisión del virus y se aboga por un enfoque de Una Salud para prevenir futuras pandemias.

Palabras clave: Coronavirus; hospedero; pandemia; reservorios; virus.

In December 2019, a message in the platform X (former Twitter) was published stating an outbreak of pneumonia by an unknown cause in a region of China. In 2002-2003 an outbreak of a novel coronavirus named SARS (acronym for Severe Acute Respiratory Syndrome) was also reported in the same country and caused a pandemic alarm as it expanded to several countries with an usually high mortality rate of almost 10 % (Abdelrahman *et al.* 2020; Xu *et al.* 2020). The scientific community was alarmed about the possible reemergence of SARS. Cases seemed similar but with a higher contagious nature and some clinical differences (Guan *et al.* 2020; Wu *et al.* 2020; Zhu *et al.* 2020). In February 2020, the whole genome sequence of a virus found in a clinical sample was published, identifying the virus as a member of the *Coronaviridae* family (Bloom *et al.* 2021; Holmes *et al.* 2021). The novel virus was named novel coronavirus 19 (nCOV-19) and the clinical disease was named by the World Health Organization (WHO) as coronavirus disease 19 (COVID-19; World Health Organization, WHO 2020). However, after analysis performed by the international committee on taxonomy of viruses (ICTV), the virus was renamed SARS-CoV-2, and SARS was renamed SARS-CoV (Holmes *et al.* 2021).

Coronaviruses are enveloped, positive-stranded RNA viruses that affect respiratory, intestinal, liver, and nervous system of both humans and wild and domestic animals (Cui *et al.* 2019; Hao *et al.* 2022). Prior to the emergence of SARS-CoV-2, there were 6 coronaviruses known to infect humans (HCOV: human coronavirus): HCOV-229E, HCOV-NL63, HCOV-OC43, and HCOV-HKU1 causing self-limiting respiratory illnesses and causing respiratory diseases and SARS-CoV and Middle-East Respiratory Syndrome coronavirus (MERS-CoV) causing more severe systemic illnesses with a higher mortality rate (Cui *et al.* 2019). These viruses are common zoonotic agents meaning they are maintained in nature by animal reservoirs with distinct hosts. Some of them have already described or known intermediary hosts that serve as bridge for human infection while for others the intermediaries are unknown (Figure 1; Plowright *et al.* 2017; Salata *et al.* 2019; Rahman *et al.* 2020). Many of the definitive hosts in nature of these viruses are bats (Lau *et al.* 2005; Anthony *et al.* 2017; Olival *et al.* 2020; Ruiz-Aravena *et al.* 2022). Bats harbor plenty bat-related coronaviruses (SARSr-Rs-BatCoVs) that might be transmitted indirectly to humans (Lau *et al.* 2005; Li *et al.* 2005, 2022; Poon *et al.* 2005; Delaune *et al.* 2021). Scientific publications dating back to 2005 (Lau *et al.* 2005; Li *et al.* 2005; Poon *et al.* 2005) have proposed that bat-related coronaviruses have a mutation rate capable of originating a novel virus with a potential for epidemic and pandemic outcomes. Due to this potential, the importance of understanding the interaction of these viruses with bats, but also with other mammals, has been the research focus of coronavirus experts around the world. Initially, as some pangolin coronaviruses present in Malayan pangolins (*Manis avania*) were thought to be similar in their sequences to SARS-CoV-2, they were proposed as possible reservoirs, though later dismissed (Xiao *et al.* 2020; Hou *et al.* 2023). The urge to determine the viral reservoir increased because of the unprecedented pandemic caused by SARS-CoV-2 from 2020 to 2023. Particularly, since many reports arise suggesting the reservoir or host of this virus in nature could be a bat of the *Rhinolophus* genus or Asian horseshoe bats (Lau *et al.* 2005; Li *et al.* 2005, 2022, 2023). Nevertheless, as seen with other coronaviruses (Figure 1), one or more intermediate, so far not yet identified, hosts may be required for transmission to humans.

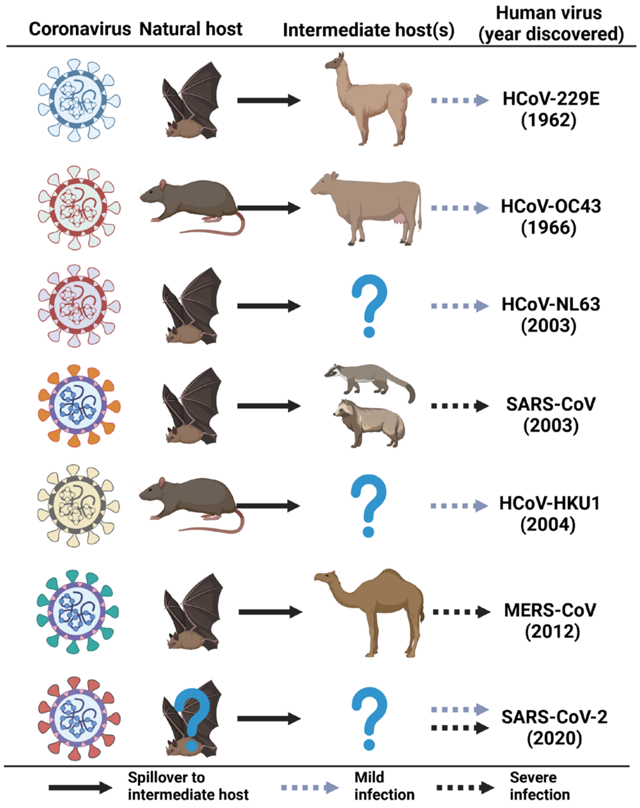

Figure 1. Animal origins of human coronaviruses. Adapted from Cui *et al.* (2019). The depiction uses solid arrows for confirmed data, gray broken arrows for mild infection, and black broken arrows for severe infection.

The purpose of this review is to explore the current knowledge of SARS-CoV-2 infection in various mammals. We will define basic concepts of reservoir, host, and intermediate host. We will enumerate the possible reservoirs, the potential intermediate hosts suggested until December 2023, and the difficulties to name these key species in the transmission cycle of the virus. Finally, we will propose from the perspective of clinical virology, strategies for the prevention of future pandemics where a One Health approach must be followed.

Concepts for understanding viral transmission. Concepts needed to be explained for better understanding of viral transmission include the terms natural reservoir, intermediate host, host, and spillover. A natural reservoir is defined as the animal that maintains that virus in its ecological niche. The reservoir should harbor the virus continuously and for a long term (Haydon *et al.* 2002). Usually, the virus does not cause disease in them since they control the infection by physiological, immunological, or genetic barriers (Plowright *et al.* 2017) or for example, may only excrete the virus under stress (Drexler *et al.* 2010). A host is an animal that maintains the virus, with or without symptoms, and it can transmit it to another animal from the same or a different species. The host allows the virus to fulfill its reproductive cycle and start a new infectious cycle in another host. An intermediate (or amplifier) host plays a critical role in disease emergence by bringing viruses, from animals which would normally have little to no contact, into close contact (Parrish *et al.* 2008), for example domestic animals can be intermediate hosts between wildlife and humans. Finally, spillover is the spread of a pathogen to a novel host (Plowright *et al.* 2017).

Coronaviruses and their zoonotic potential. Within the realm of potentially zoonotic viruses, CoVs hold significant importance owing to their propensity for easy transmission via the respiratory or fecal-oral route (Drexler *et al.* 2010; Wong *et al.* 2021). This attribute renders them capable of sparking epidemics and increases the likelihood of different host species transmission or spillover events (Drexler *et al.* 2010; Wong *et al.* 2021). CoVs boast the largest genome among RNA viruses thus, granting them with a remarkable capacity for mutations and other genome modifications (Lai and Cavanagh 1997; Wang *et al.* 2006; Bolles *et al.* 2011). The substantial genetic diversity within CoVs gives rise to the phenomenon known as quasispecies (Lai and Cavanagh 1997; Bolles *et al.* 2011), where a delicate equilibrium in the mutation rates exists, resulting in the viral population forming a cloud of variants centered around a consensus genetic sequence. This cloud of viral variants continuously expands and contracts in various directions, providing an ample possibility of genome variants that allows the persistence of the virus by increasing the possibility of adaptation to environmental changes with some variants being more frequent than others (Lai and Cavanagh 1997). Genetic variation in coronaviruses facilitates rapid adaptation to novel hosts and ecological niches, alterations in tissue tropism, and even the emergence of new coronavirus variants, lineages, or species (Steiner *et al.* 2024). Some researchers have predicted that the infection of different wild, peridomestic, and domesticated animals may present a fertile ground for the emergence of new SARS-CoV-2 variants, as it was suggested with the Omicron variant (Wei *et al.* 2021; Du *et al.* 2022). CoVs form a large family of numerous different viruses, and many have been described in mammals, although most coronaviruses have been detected in birds and a few in reptiles (Salata *et al.* 2019; Raveloman-antsoa *et al.* 2020; Ye *et al.* 2020; Wong *et al.* 2021). Despite of their high genomic diversity, most coronaviruses have constraints to sustain transmission within human populations because their replication, excretion, and transmission nature have not yet adapted to humans (Woo *et al.* 2009; Bolles *et al.* 2011; Wong *et al.* 2021).

Natural reservoirs and hosts of coronaviruses. The emergence of SARS-CoV in 2002-2003 is attributed to the process of genome recombination with bat SARS-related coronaviruses (SARSr-Rs-BatCoVs; Li *et al.* 2005, 2020; Lau *et al.* 2015). This recombined virus initially infected civets (*Paguma larvata*) in China and subsequently humans before triggering the SARS epidemic. On the other hand, MERS-CoV is believed to have spill overed from different bats species *Taphozous perforates* (Memish *et al.* 2013), *Neoromicia* sp. and *Pipistrellus* sp. (Ithete *et al.* 2013), *Vespertilio superans* (Yang *et al.* 2014), which have been found positive for related viruses to dromedary camels (*Camelus dromedarius*) years ago. Later it became prevalent in dromedary camel populations and was detected for the first time in Saudi Arabia in 2012 (Reusken *et al.* 2013; El-Kafrawy *et al.* 2019). HCoV-229E and HCoV-NL63 typically induce mild infections in immunocompetent individuals and recent discoveries have uncovered progenitors of these viruses in African bats *Triaenops afer* and *Hipposideros* spp. (Pfefferle *et al.* 2009; Corman *et al.* 2015; Tao *et al.* 2017), with camelids such as *Vicugna pacos* (only in American continent; Crossley *et al.* 2012) likely serving as intermediate hosts for HCoV-229E. Similarly, HCoV-OC43 and HKU1, which generally cause mild infections in humans, are thought to have originated in rodents, but with HCoV-OC43 having an intermediate host in bovines (Forni *et al.* 2017; Cui *et al.* 2023). For SARS-CoV-2 the most likely reservoir in nature has been hypothesized also to be bats (Figure 2). The genome of SARS-CoV-2 has only 79.6 % of identity with SARS-CoV while it bears a striking 96 % similarity to the bat coronavirus RaTG13 (Li *et al.* 2021; Liu *et al.* 2021; Pei and Yau 2021). This high level of homology between them suggests that bats might be indeed the natural reservoirs of SARS-CoV-2. Despite this high percentage of homology, the RaTG13 RBD, receptor binding domain needed for cell infection after attachment and determinant for virus tropism, is very divergent from the RBD of the SARS-CoV-2 (Liu *et al.* 2021; Pei and Yau 2021). Thus, it is possible that the SARS-CoV-2 RBD underwent selective pressure after evolving in horseshoe bats and evolved even further in a putative non-bat intermediate animal species before its spillover to humans. Nevertheless, the exact amino acid identity between SARS-CoV-2 and any other virus found before the pandemic started has yet to be found. SARS-CoV-2 has been detected in many different mammals, though the source of their infection, if it was transmitted by the reservoir (enzootic event) or from another mammal (enzootic event) or from a human being (reverse zoonotic event) has yet to be determined. Because of the numerous transmission and spillover events recorded so far, finding the definite and original host and/or the intermediate host in nature of SARS-CoV-2 remains a difficult task.

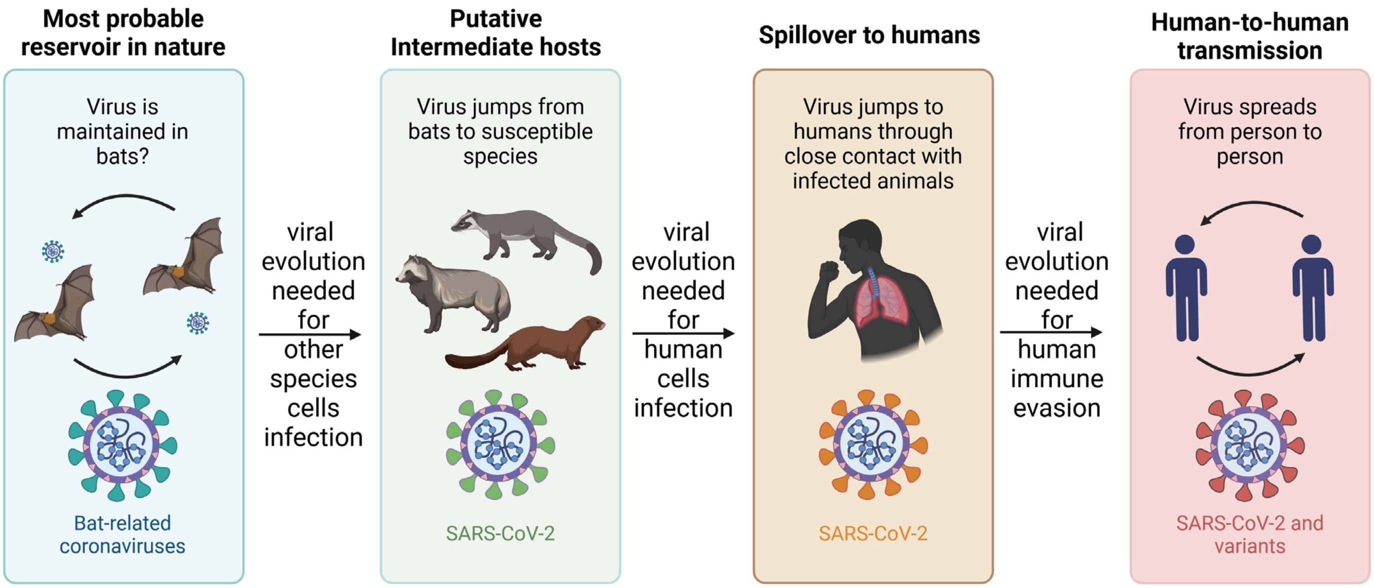

Figure 2. Probable zoonotic transmission of SARS-CoV-2 and adaptation to humans. Adapted from Pekar *et al.* (2022).

Susceptibility of different mammalian species to SARS-CoV-2, modes of transmission and clinical manifestations. Various mammalian species have been confirmed to be positive for SARS-CoV-2, either through natural infection due to the contact with humans or animals infected with the virus, or via experimental infection studies conducted in laboratory environments (Haake *et al.* 2020; Muñoz-Fontela *et al.* 2020; Shi *et al.* 2020; Zhai *et al.* 2020; Hobbs and Reid 2021; Meekins *et al.* 2021; Prince *et al.* 2021; Sharun *et al.* 2021; Frazzini *et al.* 2022; Reggiani *et al.* 2022; Li *et al.* 2023; Rao *et al.* 2023; Martínez-Hernández *et al.* 2024). Mammalian species detected to be positive for SARS-CoV-2 can be grouped in 4 different categories: i. those that underwent experimental infections; ii. those found in the wild; iii. those found in zoos; and iv. those found in domestic settings: farming and in close companion (pets) to humans.

Experimental infections have revealed that SARS-CoV-2 infection poses a risk to various animal species including non-human primates, hamsters, ferrets, American minks, cats, dogs, raccoon dogs, North American deer mice, Egyptian fruit bats, Asian small-clawed otters, and white-tailed deer (Murphy and Ly 2021; Yen *et al.* 2022; World Organization for Animal Health 2023). Additionally, instances of animal-to-animal transmission have been documented among hamsters, ferrets, cats, minks, raccoon dogs, fruit bats, deer mice, white-tailed deer, rats and mice (Barrs *et al.* 2020; Freuling *et al.* 2020; Kim *et al.* 2020; Richard *et al.* 2020; Schlottau *et al.* 2020; Zhai *et al.* 2020; Dróżdż *et al.* 2021; Fagre *et al.* 2021; Lu *et al.* 2021; Munnink *et al.* 2021; Shriner *et al.* 2021; Hale *et al.* 2022; Yen *et al.* 2022; Martínez-Hernández *et al.* 2024). Experimental infections are important to conduct research in pathogenicity, pathology, antivirals, antigenicity, vaccines, and virus susceptibility. On the other hand, natural infections of animals showcase a more interesting panorama with differences in susceptibility to virus infection, clinical presentation (Table 1) and putative transmission routes (infection and excretion of the virus; Munir *et al.* 2020; Meekins *et al.* 2021; Fang *et al.* 2024). The finding of naturally infected animals might contribute to identify the natural host or reservoir in nature of the virus and the putative intermediary host (if there is one or several) serving as bridge for the spillover event(s) to humans. It is tempting to speculate that, since a considerable amount of time has elapsed and so many spillover, zoonotic and reverse zoonotic events have taken place since the emergence of the virus, pin-pointing the culprits might be cumbersome. Furthermore, some press releases have confirmed that other mammals have been found positive in diverse zoos located in different countries. Among them a lynx, hyenas, a coati, a snow leopard, a binturong and 2 hippopotamuses have tested RT-PCR positive for the virus (National Center for Immunization and Respiratory Diseases, Division of Viral Diseases 2022). This emphasizes the need for effective biosecurity measures and surveillance strategies to prevent and control SARS-CoV-2 infections and reverse zoonotic events in zoological institutions (Nederlof *et al.* 2024).

In many instances, the transmission of SARS-CoV-2 to animals is believed to primarily happen via direct contact with infected asymptomatic humans (Fang *et al.* 2024). Research conducted in laboratories has demonstrated that the virus can also spread to animals through airborne droplets. Cats, for example, are vulnerable to contracting the virus through airborne exposure, and infected cats may pass it on to other cats they live with through respiratory droplets or airborne pathways (Shi *et al.* 2020). However, there is so far no indication of transmission occurring through fecal-oral, blood, vertical, or alternative routes between humans and animals (Fang *et al.* 2024). Many of the infected animals are asymptomatic, but contagious, and may function as a source of transmission at the human–animal interface (Halfmann *et al.* 2020). Another potential route for transmission of SARS-CoV-2 to animals, though challenging to be addressed, is through contact with contaminated surfaces and objects, since the virus can maintain its infectiousness on them under certain conditions (Aboubakr *et al.* 2021). The determination of the host range for SARS-CoV-2 and many other coronaviruses primarily pivots on the interaction between the viral S glycoprotein, particularly the spike 1 subunit (S1), and the cellular receptor known as angiotensin-converting enzyme II (ACE2; Luan *et al.* 2020; Rangel *et al.* 2020; Zhai *et al.* 2020; Steiner *et al.* 2024). Nevertheless, other mammal receptors or coreceptors might function as alternative virus receptors needed for infection. *In silico* prediction models analyzing the molecular structure of SARS-CoV-2 receptor and mammal protein ACE2 and their interaction, suggest that it is highly likely for humans, primates, deer, rodents, felids, and ferrets (Damas *et al.* 2020; Rangel *et al.* 2020; Piplani *et al.* 2021) to be infected by this virus. This data was also confirmed doing a comparative *in vitro* infection analysis of 83 cell cultures derived from 55 mammalian species (Li *et al.* 2023). Interestingly, horseshoe bats and pangolin ACE2 receptors scored very low for binding the SARS-CoV-2 receptor (Damas *et al.* 2020). Nevertheless, the possibility to exclude that infection in other species occurs via another cellular receptor beside ACE2 is still pending and the open hypothesis remains if this infection is or will be productive enough to elicit transmission to humans or other mammals.

Public health and future directions. The understanding of the involvement of not only domestic and wild animal species in the spread of SARS-CoV-2 remains still incomplete. Nevertheless, there have been several reported cases of SARS-CoV-2 infection among domestic and wild animals (Table 1; Haake *et al.* 2020; Muñoz-Fontela *et al.* 2020; Shi *et al.* 2020; Zhai *et al.* 2020; Hobbs and Reid 2021; Meekins *et al.* 2021; Prince *et al.* 2021; Sharun *et al.* 2021; Frazzini *et al.* 2022; Reggiani *et al.* 2022; Li *et al.* 2023; Rao *et al.* 2023; Martínez-Hernández *et al.* 2024). This observation is noteworthy, given the millions of human cases and the close interactions between humans, pets, and wildlife under their care (Tan *et al.* 2022). Nonetheless, the susceptibility of some animals to SARS-CoV-2 infection, along with their potential to shed infectious virus through respiratory secretions and/or

Table 1. Mammals described as positive for SARS-CoV-2 in a non-experimental setting. Adapted from Munir *et al.* (2020), Meekins *et al.* (2021), and Fang *et al.* (2024).

Mammal **common name and scientific name**	**Clinical signs**	**Transmission to humans**
Domestic cat, *Felis catus*	Subclinical in most studies (adult/subadult), behavior changes, diarrhea, weight loss in one study; potential severe clinical signs in juveniles	Yes, via direct contact; indirect (aerosol) transmission less likely
Domestic dog, *Canis familiaris*	Subclinical	None reported; dogs may shed virus in nasal secretions
Ferret, *Mustela putorius furo*	Most subclinical; isolated increased body temperature, reduced activity, respiratory signs, reduced activity/appetite, ruffled fur	Yes, via direct contact; indirect (aerosol), transmission less effective
American mink, *Neovison vison*	Many asymptomatic; nasal discharge, respiratory distress, reduced activity/feed intake, mortality	Widespread infection in farms; natural infection from mink to humans, cats, and dogs via indirect (aerosol) transmission
Asian Small-clawed otter, *Aonyx cinereus*	Respiratory signs, lethargy	Yes, via direct contact
White-tailed deer, *Odocoileus virginianus*	Most subclinical; elevated body temperature; some ocular/nasal discharge	Yes, via direct and indirect (aerosol) contact
Western lowland gorilla, *Gorilla gorilla*	Respiratory signs	Yes, via direct contact
Syrian or Golden hamsters, *Mesocricetus auratus*	No evidence of overt illness	Hamster to hamster, hamster to human, via direct and indirect (aerosols) contact. Resulted in further human to human infections
Racoon dogs, *Nyctereutes procyonoides*	Asymptomatic	Possible direct contact between humans and experimentally infected animals
Lions / Tigers *Panthera tigris jacksoni, Panthera tigris altaica, Panthera leo krugeri*	Cough and wheezing with subsequent inappetence, virus associated tissue damage	Probable direct or indirect transmission from humans to lions/ tigers and from tigers/lions to tigers/lions
Rats/ mice *Rattus norvegicus* *Mus musculus*	No evidence of overt illness, since weight was not affected	Probable direct or indirect transmission from humans

feces (McAloose *et al.* 2020; Newman *et al.* 2020; Oreshkova *et al.* 2020), underscores the importance of further research at the intersection of human-animal-environmental dynamics, guided by the principles of One Health (Rubin *et al.* 2014; Kelly *et al.* 2017). These principles mainly describe the promotion of a comprehensive approach that addresses health issues by considering all facets of human, animal, and environmental health as an integrated problem-solving framework highlighting the importance of broadening expertise in public health disciplines and interdisciplinary work (Kelly *et al.* 2017). Particularly, portraying how human behavior and its impact on the environment through globalization, climate change, deforestation, closer contact with wildlife, domestication of wild animals and other alterations of nature promote the emergence and reemergence of diseases. The SARS-CoV-2 pandemic has been a clear example of a global problem that needed to be addressed by several and diverse expertise backgrounds to obtain an integrated, definitive response. It was probably a global problem that arose from the mishandling of wild animals by humans, as it is hypothesized that the spillover event of SARS-CoV-2 to humans and the epicenter of the COVID-19 pandemic occurred in a wholesale market in Huanan were animals were kept in stressful conditions (Worobey *et al.* 2022).

Of note, there is little evidence that pet mammals play a significant role in the spread of SARS-CoV-2 virus to humans even after close contact with aerosols, nasal/lung secretions, or feces (Dróżdż *et al.* 2021; Yen *et al.* 2022). Common among the pandemic CoVs and various other novel viruses affecting humans, such as Ebola, Yellow Fever, and Dengue, is their origin in wild animal hosts (Jones *et al.* 2008; Allen *et al.* 2017; Plowright *et al.* 2017; Ruiz-Aravena *et al.* 2022). Despite an (almost wishful) belief in minimal risk, virologists globally have acknowledged and expressed concerns regarding anthropogenic activities that promote and intensify interactions between humans and wildlife, thereby increasing the risk of zoonotic disease transmission (Allen *et al.* 2017; Kelly *et al.* 2017; Olival *et al.* 2017). The presence of SARS-CoV-2 in animal reservoirs presents an additional obstacle for implementing a suppression/elimination strategy for pandemic mitigation. Instances of back-spill into human populations, as observed in Danish and Dutch mink farms or pet hamsters in Hongkong, appear to be unavoidable, complicating efforts to contain the virus.

From the scope of clinical virology, some mitigation strategies for SARS-CoV-2 and future pandemics could be considered: i) surveillance of identified "hot spots" for potential zoonoses emergence (Carlson *et al.* 2022), developing broad, efficient, and cost effective methodologies, ii) investment in research and development of antiviral and/or vaccine strategies allowing capacity building for clinical trials, licentiate successful candidates and bring to manufacture, and most importantly, invest in tests to define human and mammals protection against infection or a tests that traduce in predicting severity of disease; iii) reduce drivers of spillover and pathogen dissemination by understanding epidemiology, developing sensitizing and educational campaigns to attempt the respect of wildlife by humans, promoting behavioral changes that diminish biodiversity loss and depletion of ecosystems; iv) develop from an interdisciplinary approach counter mechanisms to misinformation and disinformation and promote science education programs to expand public understanding of complex topics; v) strengthen the joint work of multiple, diverse, and inclusive stakeholders in order to provide effective guidance to policymakers and decision-makers based on evidence and vi) global accessibility to information, testing, treatment and vaccines, included with participation in research and guideline creation, as the exclusion of developing countries limits the efficacy of any control mechanisms facilitating viral and disease persistence, with the particularity that disease emergence hotspots are mostly located in these countries (Erkyihun and Alemayehu 2022; Keusch *et al.* 2022; Leifels *et al.* 2022; Lefrançois *et al.* 2023). Future research in wild animals and surveillance are necessary to understand if and how different mammals could be affected by SARS-CoV-2. The most common aim of some viruses is to attain a point of equilibrium with their host and become endemic without causing high mortality in a susceptible host population, we will have to wait to see if SARs-CoV-2 behaves in this form.

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