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Transmission of COVID-19 between Animals and Humans: a Challenge for the Scientists

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ABSTRACT

In recent decades, some 30 new human pathogens have been identified, of which 75% were spillovers from animals. In late 2019, human infections with a new coronavirus from an unknown origin emerged in China and later spread worldwide. The zoonotic source of severe acute respiratory syndrome coronavirus 2 remains unknown, and there is only some limited information about the close association between the first human cases of COVID-19 and visiting animal markets. Now, bats and pangolins are suspected as natural hosts, and large cats, raccoon dogs, dogs, minks, ferrets, and pangolins as intermediate hosts. There is not enough evidence to prove that animals can transmit COVID-19 infection to humans, but there are some data about the transmission of SARS-CoV-2 between humans and some animal species.

INTRODUCTION

The pathogen spillover event typically occurs when zoonotic pathogens are transmitted from an animal to a human for the first time. According to the National Institutes of Health (NIH), almost 16% of all deaths worldwide can be attributed to infectious diseases, whereas zoonoses account for 60% of known infectious diseases and 75% of emerging infectious diseases [1]. In recent decades, 30 new human pathogens have been identified, of which 75% are spillovers from animals [2]. Considering that most susceptible-to-mutation RNA viruses can adapt to the new host, scientists encounter different features of emerging diseases with combined symptoms and unusual types of human-to-animal transmission [3]. The risk of disease transmission from pets or wild animals to their owners increases by close contact and feeding the animals. Moreover, using lands for cultivation, urban spatial expansion, buildings, and other manipulation of nature have disrupted animal ecosystems resulting in more encounters between humans and animals.

Origin of COVID-19

As the largest city in central China, Wuhan has several desirable conditions for the new emerging zoonotic virus. This city has an extensive transportation hub and is a fundamental core of manufacturing, trade, and tourism ventures. In late 2019, the Wuhan Municipal Health Commission (WMHC) confirmed 27 human infections with a virus from an unknown origin that rapidly spread to other countries [4]. Later, WMHC reported that most of the infected cases had eaten some seafood obtained from the live animal markets in Wuhan, which could have been the reason for infection [5]. The COVID-19 pandemic is caused by a coronavirus named SARS-CoV-2, short for severe acute respiratory syndrome coronavirus [2].

SARS-CoV-2 structure

Coronaviruses are enveloped RNA viruses with spikes on the surface and infect a wide range of animals and humans [1,3].

SARS-CoV-2 belongs to a genetically modified SARS-CoV viral community and several other bat-isolated CoVs. Currently, the zoonotic source of SARS-CoV-2 is unknown, and there is only limited information about a close relationship between the first human cases of COVID-19 and wet markets in Wuhan. Local samples taken from wet markets in Wuhan in Dec. 2019 were positive for SARS-CoV-2, providing further evidence that this market was the outbreak source or played an

essential role in the initial disease outbreak [6].

Intermediate reservoir animals

Sequence analysis of human-collected samples demonstrated that detected viruses were closely and genetically related to coronaviruses isolated from the bat, especially the horseshoe bat (*Rhinolophus genus*) found in Asia, Africa, the Middle East, and Europe. SARS-CoV, the cause of the SARS outbreak in 2002-2003, was similar to coronaviruses isolated from the bats that infected civet cats (*Civettictis civetta*) [7,8]. The bats were probably the SARS-CoV ecological reservoir, and the virus seems to have jumped from an intermediate reservoir animal, e.g., civet cats, to humans and then spread amongst humans [9].

Similarly, SARS-CoV-2 is thought to have leaped the species boundary, jumping from animal hosts and infecting humans. Due to limited encounters between humans and bats, it is more likely that the SARS-CoV-2 transmission to humans occurred via an intermediary host, i.e., another animal species, most likely handled by humans. This intermediary animal host could be a wild or a domesticated animal that has not been identified until now [5,10].

Further genetic sequence analyses suggest that the spillover from an animal source to humans might have happened during the last quarter of 2019 [3]. Since detected SARS-CoV-2 is not genetically related to other known coronaviruses found in farmed or domestic animals, the relationship between detected infectious animal species and the rest of the animals remains unknown [4].

Additionally, the identified coronaviruses in pangolins (*Manis javanica*) from southern China differed from SARS-CoV-2 [10]. Pangolins, a possible intermediate animal host, might be the missing link for transmitting the new coronavirus from the bats to the humans [5] (Fig. 1).

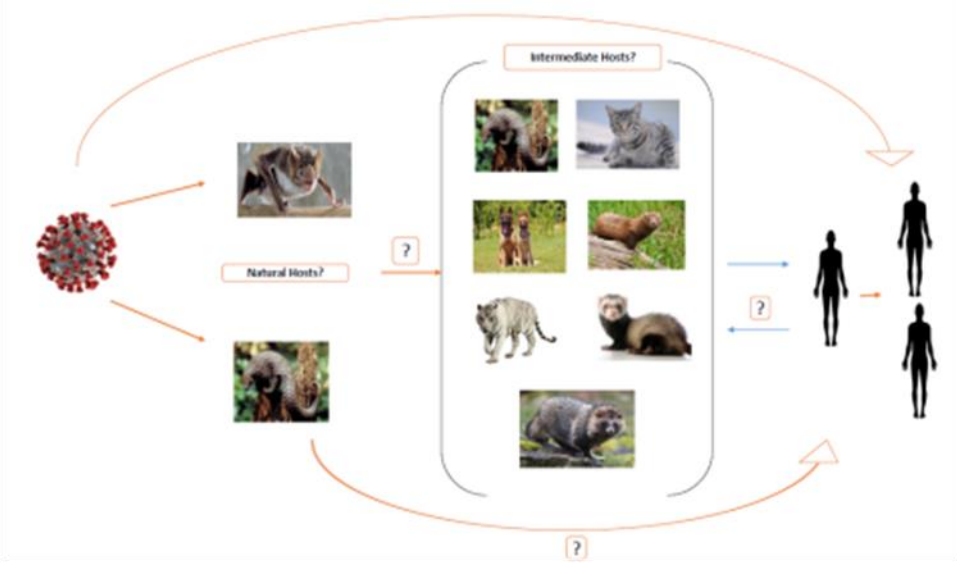

Fig. 1. Schematic representation of Covid-19 transmission. Bats and pangolins are suspected as natural hosts, and large cats, raccoon dogs, dogs, minks, ferrets, and pangolins as intermediate hosts.

COVID-19 in animals

A few pets, including dogs, cats, and minks, were confirmed by the Centers for Disease Control and Prevention (CDC) to be infected with COVID-19 after close contact with humans. A previous study showed that the virus replication was low in pet animals such as dogs, pigs, chickens, and ducks, while its efficient amplification in ferrets and cats makes them capable of transmitting the virus by respiratory droplets [11]. In Hong Kong, two dogs (*Canis lupus familiaris*) with close contact with positive COVID-19 humans showed to harbor the virus with no clinical manifestation [12].

In the United States, New York City Zoo, a tiger (*Panthera tigris*) with the respiratory disease was the first animal to test positive for COVID-19. Public health authorities assumed that the big cat became infected following close contact with an infected zookeeper, which was the first concrete evidence showing the COVID-19 virus transmission from humans to animals [13].

Additional studies revealed cats (*Felis catus*) susceptibility to the COVID-19 virus and transmission of the virus among these animals. In Belgium, the SARS-CoV2 virus was detected in a cat's feces and vomit,

showing the clinical signs of digestive and respiratory disease. This finding was not surprising to scientists and veterinarians due to the natural susceptibility of cats to coronaviruses. Until now, there is no evidence that cats can pass COVID-19 to humans [14].

On the other hand, ferrets (*Mustela putorius furo*) showed to be susceptible to SARS-CoV-2 infection and may develop the illness. Since June 2020, Danish authorities have confirmed that COVID-19-causing SARS-CoV-2 has spread widely over mink farms in Denmark [13-15].

So far, several animal species have been tested positive for SARS-CoV-2 due to close interaction with humans. Based on the reports from animal research facilities, natural and experimental COVID-19 infections have occurred in some animals, including American mink (*Neovison vison*), dogs, cats (domestic), raccoon dogs (*Nyctereutes procyonoides*), and big cats (tigers, lions, and puma), rabbits (*Oryctolagus cuniculus*), raccoon dogs (*Nyctereutes procyonoides*), cattle (*Bos taurus*), pigs (*Sus scrofa*), golden Syrian hamsters, marmosets (*Callithrix jacchus*), and macaques (*Macaca fascicularis* and *Macaca mulatta*) [16].

CONCLUSION

Based on experimental animal models, the incubation period in all animals was similar to the human, i.e., during two weeks, the transmission among animals happened via direct contact, e.g., droplets. The infected animals presented the virus in the respiratory tract and lungs. Wuhan's animal sales markets were shut down after the COVID-19 outbreak; however, many similar markets remained active worldwide. While animal viruses continue to pose significant threats to human health, people have never tried to cut their contact with animals in some countries. It is time to make recommendations to substantially minimize extensive contact with animal tissues, excreta, and fluids. Nowadays, One Health approach authority is required to protect the human population from zoonosis pathogens [16]. According to the One Health approach, all relevant divisions across the human-animal-environment interface are involved in addressing health in a coordinated way that is more effective and sustainable. This collaboration is required to detect, assess and respond to zoonotic diseases [17].

It is not surprising that two bat coronaviruses BatCoV RmYN02 and BatCoV RaTG13, identified in horseshoe bats *Rhinolophus malyanus* and *R. affinis*, respectively, showed to be the closest known relatives to SARS-CoV-2. Both Bat-CoVs detected in 2019 in bats from Yunnan province, China, exhibited an average of ~93% identity with SARS-CoV-2 in the genetic structure, especially nucleotide identity [18]. Nevertheless, there is not enough clear evidence that animals, primarily pets and farm animals, can transmit COVID-19 infection to humans, but there are some published data about the transmission of SARS-CoV-2 between humans and some species such as cats, minks, ferrets, bats, raccoon dogs, and pangolins. Pet owners and veterinarians should closely follow hand-washing and other precautions to prevent the transmission of animal-related diseases.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests associated with this manuscript.

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