

# Animal Hosts of Coronavirus: Unsung Reason behind Recurring Outbreaks



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## Abstract

The world has witnessed severe recurrent outbreaks of highly infectious human diseases caused by deadly coronaviruses such as severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and novel coronavirus (2019-nCoV). Compared to the previous incidence of coronavirus diseases, the ongoing outbreak of COVID-19 caused by 2019-nCoV is more severe, spreading rapidly all over the globe and has been declared as a pandemic by WHO. Previously, SARS-CoV and MERS-CoV was reported to have originated from their natural ecological reservoir i.e. bats, and then passed to humans through intermediate hosts palm civets and camels, respectively. While many reports suggest the bat origin of 2019-nCoV, but substantial evidence for animals as intermediate hosts is still lacking. Understanding of how a virus from a reservoir adapts to new host (s) is essential for disease management. The present review provides the latest results on animal hosts of human coronaviruses. As the new coronavirus is rapidly spreading around the world, future research should aim to investigate for the next potential coronavirus animal hosts.

**Keywords:** COVID-19, 2019-nCoV, SARS-CoV, MERS-CoV, Intermediate host, Pandemic

## Introduction

The world is now facing a massive emergency due to the biggest ongoing outbreak of COVID-19 caused by a highly infectious and pathogenic novel coronavirus designated as severe acute respiratory syndrome coronavirus 2 (2019-nCoV). The virus emerged in Wuhan, China in December, 2019 and eventually spread all over the countries to become pandemic as declared by WHO. There is no drug developed yet for COVID-19, but innovative research on development of specific drug primarily based on the knowledge of viral association with host receptor (Ace2) by its spike protein is expanding in many countries [1]. Bats are thought to be the source of 2019-nCoV which transmitted to humans possibly through another animal as intermediate host [2].

The coronaviruses are known for their ability to infect a variety of economically important vertebrates (such as pigs and chickens) including humans with acute respiratory syndromes. Among them, two strains of coronaviruses, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus

(MERS-CoV) are zoonotic, which also triggered outbreak, but less severe than the ongoing one, particularly based on the infectivity.

Like 2019-nCoV, Ebola, Sars, Nipah viruses are also believed to have reached humans from their probable natural reservoir, the bats. In November 2002, a viral respiratory disease that led to the first major pandemic of the new millennium originated from southern China and crossed the boundaries of other countries, with over 8,000 confirmed cases at the end of June 2003, with a mortality rate of ~9.6% [3]. The etiologic agent of this respiratory disease identified as SARS-CoV was found to be a betacoronavirus of bat origin that adapted to infect the intermediate host palm civet and finally jumped into humans [3]. A decade after the SARS-CoV outbreak, in June 2012, MERS-CoV, emerged in Saudi Arabia, causing similar respiratory disease as SARS [3]. In comparison to SARS-CoV, human-to-human transmission was considered limited, but two major outbreaks in 2012 (Saudi Arabia) and 2015 (South Korea) occurred with more than 2000 cases (mortality rate of ~35%), globally. Like SARS-CoV, MERS-CoV was found to have

originated from bats, whereas unlike SARS-CoV, it was adapted to dromedary camels as intermediate hosts [3].

During the SARS outbreak, raccoon dogs (*Nyctereutes procyonoides*) and masked palm civet (*Paguma larvata*) were identified to carry SARS-CoV like viruses, before the virus was detected in bamboo bats (*Tylonycteris pachypusa* and *Pipistrellus sp.*). Until recently, civets are considered as a “bypass” reservoir and the immediate zoonotic source of SARS-CoV in the Guangdong SARS outbreak [4]. The emergence of MERS-CoV, has identified dromedary camels as a potential intermediate host and also indicated the mode of zoonotic transmission from camels to humans via three possible ways: organs, flesh, and discharges such as faeces and camel milk, since serum evidences revealed that butchers and shepherds have higher infection rates than individuals in other occupations [5]. Alpacas, centrally housed with camels were also identified with MERS-CoV and it was further observed that the MERS-CoV effectively interacts with alpaca-DPP4 (dipeptidyl peptidase 4, receptor of MERS-CoV) followed by infection. Though the role of alpacas is not clear in the MERS-CoV outbreak, but it can be hypothesised that the increasing export of alpacas might have handsome contribution in increasing the risk of 2012 outbreak [5].

To identify the potential non-human hosts for SARS and MERS coronaviruses, scientists have infected various animals in laboratory condition and identified several animals that are likely to get infected and carry out viral replication efficiently. Rhesus macaque (*Macaca mulatta*) and common marmoset (*Saguinus mystax*) were identified to support the maintenance of SARS and MERS coronaviruses, whereas cynomolgus (*Macaca fascicularis*), african green monkeys (*Chlorocebus aethiops sabaeus* or *Cercopithecus aethiops sabaeus*) mice, golden syrian hamster, ferret, domestic cats, captive civet cat, squirrel, monkeys, mustached tamarins were observed to be affected by SARS-CoV and these animals were also potent for successive disease transmission [4]. Mers-CoV infection was observed in alpaca, sheep, goats, horses and New Zealand white rabbit. The identification of nonhuman hosts not only helped in understanding the host range of SARS and MERS but also, in designing experiment to investigate the susceptibility of coronaviruses in these animals and finally select an ideal model in drug efficacy test and control of diseases [4].

Not only SARS-CoV and MERS-CoV, several coronaviruses like HCoV-NL63, HCoV-229E and a majority of alphacoronaviruses and betacoronaviruses, also found to have originated from diverse bat species, whereas HCoVOC43 and HCoV-HKU1 likely to have originated in rodents [6]. Compared to the outbreak from these viruses, the recent outbreak of 2019-nCoV has become so severe that the world is now under complete lockdown. Global confirmed cases as of today stands 3,015,298 with 207,933 fatalities [7]. Despite the severity and fatality associated with the repeated outbreak of such diseases, coronavirus vaccines and antiviral

drugs are not yet available. The animal model that mimics human disease is thus of an urgent need. Several studies showed that 2019-nCoV shares 96.2% amino acid sequence similarity (taking all the ORFs) with coronavirus isolated from bats and likewise bats are considered to be the natural source of 2019-nCoV [8]. Apart from bats, snakes were thought to be the source or intermediate host of 2019-nCoV but further investigation obliterated the probability [9]. The high sequence similarity (99%) of 2019-nCoV with the coronavirus isolated from pangolin and the presence of typical novel coronavirus granules observed in the animal, suggested pangolin to be the potential intermediate host of the 2019-nCoV [10]. Recently Xuhua Xia [11] has even claimed the dogs to be an intermediate host of 2019-nCoV. Though adequate evidences have proved the animal origin of 2019-nCoV, the natural and intermediate host is still under question. To gain insight into the animal reservoirs of 2019-nCoV and animal management for COVID19 control, Shi et al. [12] evaluated the susceptibility of different animals including model laboratory animals with intranasal application of SARS-CoV-2. From quantification of viral RNA by qPCR and virus titration in Vero E6 cells, it was concluded that 2019-nCoV replicates efficiently in ferrets, but poorly in dogs, pigs, chickens, and ducks. In contrast, many researchers point to its transition to human through an animal such as pig. One report pointed to snakes, for which bats are food [13].

As a natural reservoir of coronavirus, a search for the presence of SARS-CoV, MERS-CoV and 2019-nCoV in bats, concluded that there is no contradiction for bats being the source of these viruses which apparently passes on to humans via an intermediate animal host. Recently, coronaviruses similar to 2019-nCoV were reported from *Rousettus spp.* and *Pteropus spp.* of bat in India [14].

In this global pandemic situation, caused by 2019-nCoV, though the intermediate host is still unidentified, several reports for animals getting infected suggest inter-species transmission, which significantly raise the risk of rapid dissemination and infection among wild animals as well as humans. Recently, a cat in Belgium, two dogs in Hong Kong, and five tigers, eight wild cats and three lions in the Bronx Zoo, New York, were found to have Covid19 disease [15,16] Also, two pet cats in New York were tested positive for the new coronavirus ([https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/sa\\_one\\_health/sars-cov-animals-us](https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/sa_one_health/sars-cov-animals-us)). Previous study with related virus, SARS-CoV showed that cats can be infected and pass it on other cats [17].

It appears that 2019-nCoV may infect a number of domestic and wild animals, however, which animal(s) acts as intermediate host for transmission of the virus in human is still unclear. It also remains a question whether a single strain of 2019-nCoV is capable of infecting different animals or mutational consequence of 2019-nCoV while residing in human expands the host range. Since cats, dogs and other animals are in close contact with humans, emphasis should thus be given to frequent surveillance

for 2019-nCoV perhaps or evaluation of their susceptibility to any new coronavirus so that appropriate precautionary measure can be taken before the onset of any severe devastating outbreak causing economic, social and political disruption. The major reason for the emergence of deadly animal viruses like 2019-nCoV perhaps lies in the destruction of natural habitat of wild animals, it is something like 'throwing stones at a beehive', so let us pay respect to wild animals.

## Conflict of Interest

The authors declare that there was no conflict of interest.

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