

SYNOPSIS

02/26/2020

COVID-19 – What We Know So Far About... Zoonotic Origins

Introduction

“What We Know So Far” documents are intended to provide an overview of some of the published and unpublished reports related to emerging issues with respect to coronavirus disease 2019 (COVID-19). The reports are found through ongoing scanning of the published literature and scientific grey literature (e.g. [ProMED](#), [CIDRAP](#), [Johns Hopkins Situation Reports](#)), as well as media reports. It is recognized that there may be additional information not captured in this document. As this is a rapidly evolving situation, the information will be current as of the date written.

Key Points

- Genomic and phylogenetic analyses of COVID-19 sequences show a high similarity with bat SARS-like coronaviruses, suggesting that bats may be the original animal reservoir.
- There is some genomic evidence to suggest that pangolins may be intermediate hosts; however, further studies are required.

Background

Zoonotic infections (also known as “zoonoses”) are infections transmitted from animals to humans. These transmissions have led to the emergence of multiple infectious diseases, including all [of the coronaviruses](#) that are known to infect humans.

- Severe acute respiratory syndrome coronavirus (SARS-CoV) is thought to have originated as a [bat coronavirus](#) transmitted to [palm civets](#) at food markets before subsequently infecting [humans](#). This zoonotic event (“spillover”) is estimated to have occurred [a few months](#) before the first human infection with SARS-CoV was reported.
- Middle East respiratory syndrome coronavirus (MERS-CoV) originated similarly from multiple [bat coronaviruses](#) in the Middle East and Africa, which were then transmitted to dromedary camels as an intermediate reservoir from which [humans](#) later became infected. This spillover event may have occurred around [2010](#) and MERS-CoV infection in humans was first identified in [2012](#).
- The seasonal coronaviruses, which cause mild respiratory illness in humans, also have animal origins. Human coronavirus (HCoV)-NL63 and HCoV-229E possibly [originated in bats](#) and it is hypothesized that HCoV-OC43 and HCoV-HKU1 may have [originated in rodents](#).
- COVID-19 is another coronavirus likely originating from a spillover event.

Bats as the Origin of the Non-Human Precursor Virus

- Using whole genome sequencing and phylogenetic analysis, [three studies independently](#) identified a ~96% sequence similarity between COVID-19 and a bat coronavirus strain (RaTG13, isolated from a *Rhinolophus affinis* bat in Yunnan province in 2013), highly suggestive of an ancestral bat origin.

COVID-19 Adaptation to Human Hosts

- Several studies [show](#) that the Spike protein of COVID-19 can bind the human angiotensin-converting enzyme 2 ([ACE2](#)) [receptor](#). This is the same receptor used by SARS-CoV and is present in the human respiratory and gastrointestinal tract.
- Although similar to bat coronaviruses that do not infect humans, the Spike protein of COVID-19 [differs](#) in key aspects, including (i) a receptor binding domain (i.e., the part of the Spike protein that binds host cells) that may optimize virus binding to human ACE2 receptor and (ii) a unique cleavage site that may enhance cell-cell fusion (an important step in viral entry into human cells).

Role of Intermediate Host(s)

- A [press briefing](#) discussed an unpublished analysis of a metagenome dataset (i.e., a dataset that had genomes from various coronavirus species) that identified a pangolin coronavirus strain exhibiting ~99% sequence similarity to COVID-19.
- Two [non-peer-reviewed](#) studies found [85.5-92.4%](#) sequence similarity between COVID-19 and coronavirus strains found in the *Manis javanica* pangolin (a scaly anteater mammal). Although this level of homology (similarity) is lower compared to the RaTG13 bat strain, the pangolin strains shared the same key binding residues as COVID-19 that are suggested to be important for human infection.
- [Laboratory analysis](#) and [structural modelling](#) of the COVID-19 Spike protein suggests that it may bind ACE2 in a diverse group of animals (pigs, ferrets, cats, non-human primates, civets, bats). If accurate, this would mean that there are other possible intermediate hosts.
- A [study](#) hypothesizing snakes as a potential intermediate host was later [refuted](#) using more extensive analysis.
- Further studies are needed to fully elucidate whether pangolins or other animals serve as an intermediate host.

Location and Timing of the Zoonotic Transfer Event(s)

- The emergence of COVID-19 is associated temporally and epidemiologically with the Huanan Seafood Wholesale Market in Wuhan, Hubei province, China. This market is [one of the largest seafood markets in Central China](#), but also reportedly sold wild animals, including [frogs, snakes and hedgehogs](#), as well as a [variety of other species](#). It is not known whether pangolins were sold at the market since they are illegally poached and trafficked animals.
- According to a [news release](#), the Chinese Center for Disease Control and Prevention isolated COVID-19 virus from 5.6% (33/585) of environmental samples taken at the Huanan Seafood Wholesale Market, with the majority of positive samples taken from the zone where wildlife

trading was concentrated. This is consistent with the observation that this exposure setting was commonly reported in early cases of COVID-19.

- At this time, it is unclear whether the zoonotic transfer event occurred at the market. Of the 47 patients [diagnosed](#) before the market closure in Wuhan, 17 cases (including the [first case](#) with symptom onset on December 1, 2019) had no exposure history to the market, raising questions about the [possibility](#) of transmission events independent of the market.
- The time of the most recent common ancestor, which can be used to infer the emergence of COVID-19, is estimated between [September 28, 2019 and December 21, 2019](#).

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Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 – What we know so far about... zoonotic origins. Toronto, ON: Queen’s Printer for Ontario; 2020.

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