A review on the factors contributing to 2019-nCoV virus outbreaks in Wuhan

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Abstract: The new coronavirus (2019-nCoV) in Wuhan has caused virus outbreaks in many provinces and cities in China, and several neighboring countries were also affected. In recent years, coronavirus several outbreaks around the world were reported, however researchers could not predict its onset. Coincidentally, the birthplace of another coronavirus (SARS-CoV) that causes serious public health problems is also in China. This review compares and analyzes the external environment, natural hosts, intermediate hosts, and susceptible populations when these two coronaviruses occurred. Based on the analysis results, we found that the 2019-nCoV virus outbreak in Wuhan was not an accidental phenomenon, but a result of a combination of factors. At the same time, through the conclusions of these analyses, we will be able to get a glimpse of the trajectories of new coronaviruses and curb the virus outbreak in future.

Keywords: 2019-nCoV; SARS-CoV; drought; bat; green light

1. Introduction

The viral pneumonia that broke out in Wuhan in December 2019 was found to be caused by a novel coronavirus, named 2019-nCoV by the World Health Organization [1]. These viruses are called coronaviruses because of a corona-like protrusion appearance on the edges of virus under electron microscope. This type of protrusion is formed by rod-shaped envelope particles of viral spinous processes (S), which are used to connect with host receptor and infect host cells. In addition to 2019-nCoV, there are six known coronaviruses that can infect humans. Four coronaviruses; HCoV-OC43, HCoV-NL63, HCoV-HKU1, and HCoV-229E cause common cold, and two other coronaviruses; SARS-CoV and MERS-CoV cause highly pathogenic respiratory infections [2].

2. Comparative analysis of 2019-nCoV and SARS-CoV

In this review, we addressed the environment during the virus outbreaks, source of the virus, and route of transmission. These information can help in preparing countermeasures against novel coronaviruses in future.

2.1 Environmental factor

First, we investigated the similarities of the environment conditions of 2019-nCoV and SARS-CoV during the outbreak. SARS-CoV virus was found in Foshan, Guangdong Province in November 2002, while 2019-nCoV virus was found in Wuhan, Hubei Province in December 2019 [3, 4]. November and December are winter months and also the coldest months of the year in China [5]. Generally, body's innate immune response to virus will be lower during winter season. Viruses have a greater probability to spread into respiratory and infect host cells under the stimulation of low

temperature because number of immune cells decreases when blood supply reduced during capillary contraction in nasal mucosa [6].

Secondly, *China Statistical Yearbook* reported that the average annual precipitation in both places are greater than 1100 mm [5,7]. The global average annual rainfall is 990 mm, of which over land it is only 715 mm [8]. It indicates that the average annual rainfall in both places are higher than the world average. However, the annual rainfall in Foshan in 2002 reached its lowest value in just 50 years, which was only 393.1 mm. In fact, data showed that drought occurred in Guangdong that year, causing more than 1,300 reservoirs to dry up and 286,000 hectares of farmland suffered drought [9]. Coincidentally, Wuhan also suffered the worst drought in nearly 40 years, with rainfall only 26 mm totally in December 2019 [10,11].

Many studies have shown that temperature and absolute humidity are correlated with risk of virus infection [12,13]. During the cold winter, air-dried virus particles are not only the most dangerous form of virus, but also survive longer and more likely to float around with airflow or dust [14]. Low humidity can reduce the capacity of cilia cells in airway removing virus particles and secreting mucus as well as repair ability of airway cells. In addition, human cells release signal proteins after infection with virus to alert neighboring cells to consider the danger of virus invasion. However, in low-humidity environments, this innate immune defense system disappears [15]. More seriously, low humidity can cause nasal passages mucus to become dry, the lining of nasal cavity becomes fragile, or even ruptured, and the entire upper respiratory tract is more vulnerable by viruses invasion [16]. Due to the above reasons, the success rate of viruses invading human respiratory tract has significant increase in low humidity.

2.2 Natural host

In both outbreaks, the natural host of coronavirus were confirmed to be of bat origin. Research by Zhengli Shi's team from Wuhan Academy of Sciences confirmed that SARS-CoV virus originated from horseshoe bats in a cave in Yunnan province [17]. The team also confirmed that 2019-nCoV has 96% homology with bat coronavirus [18]. Meanwhile, the genome of 2019-nCoV is approximately 89% identical nucleotides to bat-SL-CoVZC45 virus that was found in bats from Zhoushan, Zhejiang Province [19]. Through phylogenetic tree analysis, we found that 2019-nCoV virus and bat-SL-CoVZC45 virus share a common ancestor. (Figure 1)

Why bats in Zhejiang infect animals and humans thousands of miles away in Wuhan? Bats have the ability to migrate more than 1,000 kilometers and usually to insect-rich areas [20]. A study on horseshoe bats in Hong Kong and Guangdong showed that the viruses carried by horseshoe bats in these two places are different. The researchers also reported that the mating and foraging activities by the migrated horseshoe bats with the local horseshoe bats seemed to promote spread of the viruses and found some bats carried both viruses subsequently [21].

Why migrating bats gather near Wuhan Huanan Seafood Market, and what attracts them? We regard that there are at least two factors that can attract bats to gather at this place. Bats are attracted to artificial green lights and become disoriented during their migrations, hence they gather around the green lights area [22]. Yangtze River Bridge, only 20-minute drive from Huanan Seafood Market, have two rows of endless green lights that attract the attention of bats every night, disorienting and gathering them here during migration. Additionally, bats are attracted to insect-rich areas during migration or activity. Abundant of insects found at Huanan Seafood Market due to the long-term sales of various animals and animal carcasses makes this place a suitable habitat for these bats [20].

2.3 Intermediate host

According to the transmission route of SARS-CoV virus, we consider that there may be more than one intermediate host for 2019-nCoV virus. During SARS-CoV virus outbreak, civet cat was considered as natural host, and it was not redefined as an intermediate host until researchers discovered SARS-CoV virus in Yunnan horseshoe bats. In addition to civet cats, researchers also found SARS-CoV virus from domestic cat, red fox, Lesser rice field rat, goose, Chinese ferret-badger and wild boar in Guangdong's seafood market. The virus was transmitted to civet cats from Yunnan horseshoe bats, and civet cats carrying the virus were transported to Guangdong, which led to SARS-CoV virus outbreak in Guangdong [23].

Study has shown that 2019-nCoV has the same codon usage bias as snakes. Therefore, snake may be the intermediate host for 2019-nCoV [24]. However, David Robertson, a virologist from University of Glasgow, UK, stated: "Nothing supports the invasion of snakes." At the same time, Paulo Eduardo Brandão, a virologist from University of St. Paul, also said: "There is no evidence that snakes can be infected by this new coronavirus and act as hosts" [25]. Nanshan Zhong, the leader of 2019-nCoV virus treatment expert group predicted that the intermediate host of 2019-nCoV to be bamboo rat [26].

At present, there is no evidence to prove the origin of bamboo rats in Huanan Seafood Market. Therefore, there are maybe two places where bamboo rats could have been infected with 2019-nCoV. The first site is the bat habitat in Zhoushan. Due to the promotion of bamboo rats breeding by Huanong Brothers in 2018, the amount of bamboo rats breeding and market demand increased significantly [27]. Since the market demand increases, the new bamboo rat breeding base may not be far from the local habitat of 2019-nCoV carrying bats. At the same time, because Zhejiang is a natural habitat for bamboo rats, it is possible that some farms directly introduced wild bamboo rats, which were already infected with 2019-nCoV virus. For the above reasons, the bamboo rat carrying 2019-nCoV virus were transported from the infected place to the incident site in the same way as civet cat spread SARS-CoV. The second site is Wuhan, the place of bat migration. Zhengli Shi's team from Wuhan Academy of Sciences isolated a live SARS-like strain in the feces of horseshoe bats [28]. This suggests that the way of bats spread virus not only via direct contact, but also through fecal feces. Therefore, when bats carrying 2019-nCoV virus forage at Huanan Seafood Market, they may pass the virus directly or indirectly to human and animals.

2.4 Ultimate host

Same as the source of first SARS-CoV virus patient in 2002, the first 2019-nCoV virus patient also comes from a trade center that sells seafood, poultry and game. At the outset, 2019-nCoV virus may have species barrier before it can be transmitted to humans. However, due to human activities the virus has expanded its scope of infection. In fact, when humans, poultry, and wild animals live together, the risk of spreading the virus across species increases (Figure 2). A study in the United States showed that coronavirus has selective pressure adaptation, in which they can cross the species barrier to infect target cells by altering the accumulation of mutations in spikes [29].

In addition to coronaviruses, other types of viruses have also undergone adaptation in history. AIDS virus was originally carried by chimpanzees in West Africa rainforests, but its infected humans only in the 1940s. A common view is that the disaster originated due to human invading deep forests and came into contact with chimpanzees which are carriers of the virus. Due to human invasion, number of chimpanzee populations has decreased. As a result, a new biological demand has been created, simian immunodeficiency virus needs find its new host, human [30].

Bats have inhabited near Yangtze River Bridge and Huanan Seafood Market due to the conducive environment and may have transmitted the coronavirus to intermediate hosts in this area since then. Therefore, vendors in the Huanan Seafood Market may already have long term contact with infected intermediate hosts. In addition, some Wuhan people have a habit of eating bats. Besides, bat feces have been used in traditional Chinese medicine to improve vision. [31]. All of these

significantly increases the chance of 2019-nCoV virus expanding the range of host due to selective stress adaptation.

3. Conclusions

According to our comparative retrospective analysis, to prevent new coronaviruses emergence in future, we suggest to look into the following aspects. Firstly, to pay attention at an area experiencing drought where this place had high relatively rainfall and humidity throughout, which may be a precursor to novel coronavirus outbreak. Secondly, stimulation such as green light should be switched off or turn to other colors to reduce interference during bats migration. Thirdly, farm owners should explore for the presences of bat habitats nearby when establishing new farms. At the same time, farmers that plan to do wildlife farming should test for coronavirus in this animals. Finally, consumption of meat from wild animals should be limited to curb novel coronavirus.
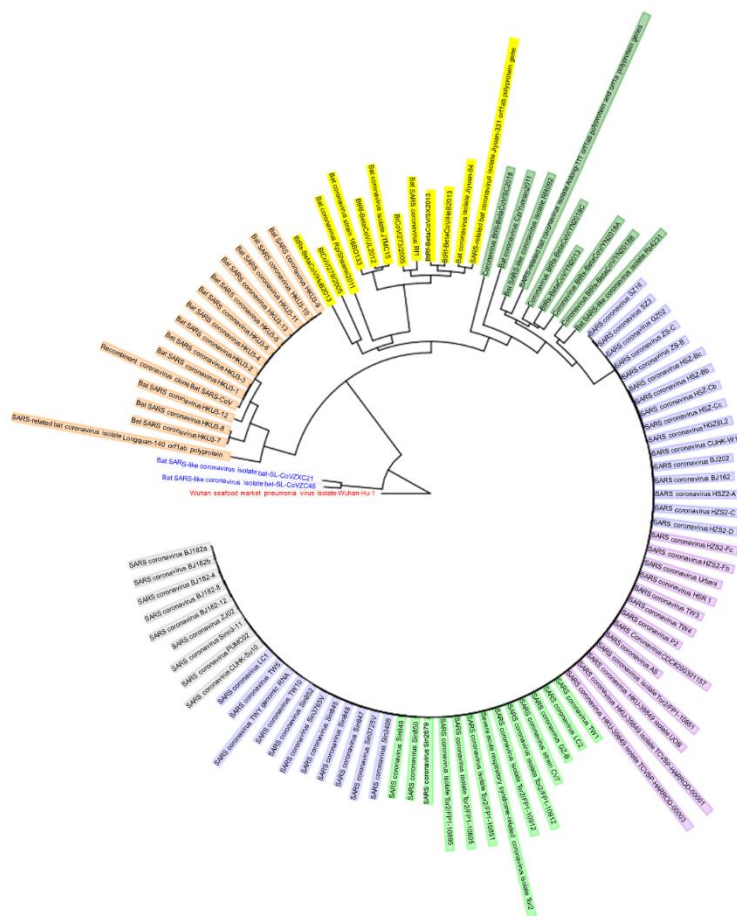
Figure 1. Phylogenetic analysis of 2019-nCoV. Sequence of Wuhan seafood market pneumonia virus isolate Wuhan-Hu-1 was used to BLAST the whole genome sequence database from NCBI. Phylogenetic tree constructed using BLAST pairwise alignments. Wuhan seafood market pneumonia virus isolate Wuhan-Hu-1, Bat SARS-like coronavirus isolate bat-SL-CoVZC45 and Bat SARS-like coronavirus isolate bat-SL-CoVZXC21 share a common ancestor.
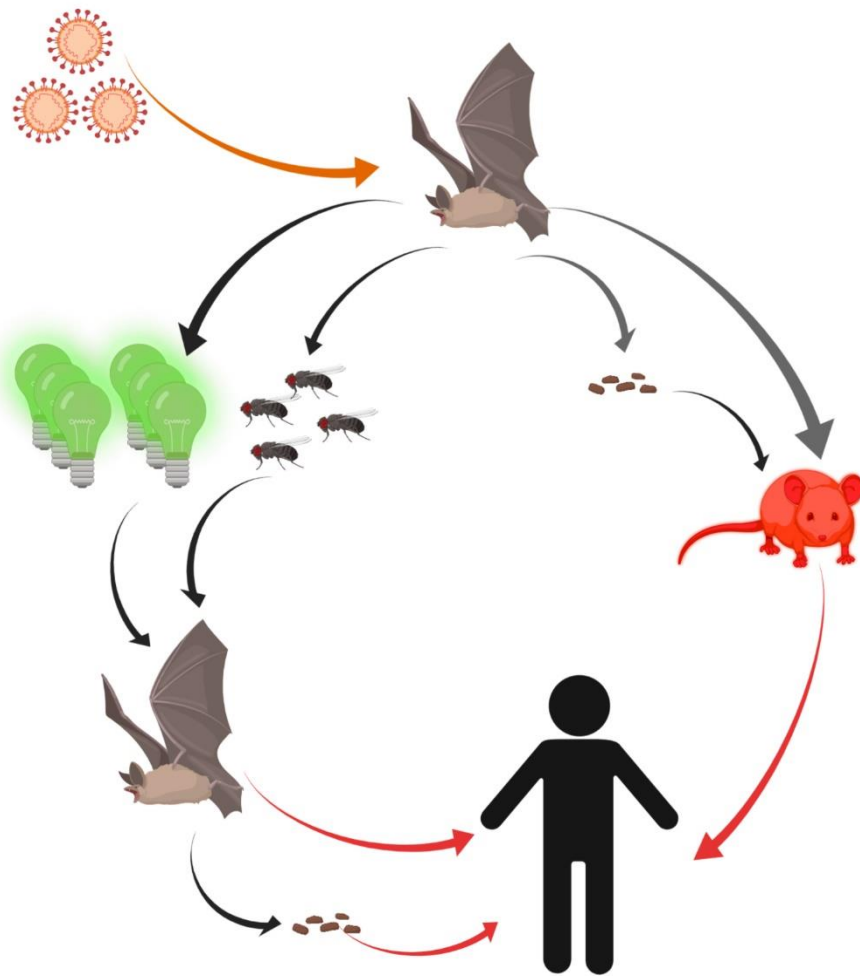
Figure 2. 2019-nCov virus transmission route diagram. Bats carrying 2019-nCoV virus attracted by green lights and insect-rich areas. Bats carrying 2019-nCoV virus transmit the virus to human through its meat and feces, and intermediate host such as bamboo rats.

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