

Mini Review

Could Rats Be The Intermediate Hosts in the 2019 Wuhan COVID-19 Outbreak?

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Abstract

The pandemic of COVID-19 caused by a novel corona virus now known as SARS CoV-2 which started in Wuhan, China in December 2019 has to date (April 29, 2020) infected more than three million people worldwide with over 227,000 fatalities. Despite rapid identification and sequencing of SARS CoV-2, the origin and mode of transmission of this virus has not been fully elucidated. At the start of the epidemic, it was suggested that bats might be the primary host and wild animals sold in the Wuhan Huanan Seafood Market could be intermediate hosts of the virus. Subsequent epidemiologic studies did not support the market as the origin and sole source of the outbreak. Detailed examination of the timeline of the epidemic suggests that sewer rats might be an important intermediate host between bats and humans. This hypothesis is parsimonious with current observations and can explain in part the limited success of containing the epidemic in Wuhan with strict quarantine of its human population.

INTRODUCTION

In 2003, I published in the Lancet a hypothesis that roof rats might have played a part as intermediate host in the spread of SARS in the Amoy Gardens complex in Hong Kong [1]. One of the weaknesses of this hypothesis at that time was the lack of a rodent model of SARS infection. Since then it has been established that rats can indeed be infected with the SARS CoV and other corona viruses [2,3] and subsequently rats have been used to test vaccines for different corona viruses by researchers around the world [4]. Thus one of the major distractions of the rat hypothesis has been removed. With the sudden disappearance of SARS in the summer of 2003, this hypothesis has never been thoroughly tested or refuted.

ORIGIN OF COVID-19

Scientists still have not fully elucidated the origin and mode of transmission of COVID-19 that started in Wuhan in December 2019. While the Wuhan Huanan Seafood Market has been implicated as ground zero of the epidemic, several observations cast doubt on this hypothesis:

- Three of the first four documented patients had no history of visiting the market or contact with workers in that market [5] they did not know one another or have any epidemiologic links before onset of illness. Among the first 41 documented patients, 14 (34%) had no connection with the Seafood Market [6]
- While bats have been suspected as the primary host and wild animals sold in the Seafood Market as intermediate hosts of SARS CoV-2, no bats were sold in the market at the

time of the outbreak, and the virus has never been isolated from any wild animal on sale [7]. SARS CoV-2 was indeed detected in the Seafood Market but only on inanimate objects such as floors, tables, cages, and other utensils [7]. A group of scientists from South China recently identified a SARS CoV-2 related virus in smuggled dead Malayan pangolin tissues [8] whether live Malayan pangolins were ever sold in Wuhan is not known.

Wild animals sold in the Seafood Market are inefficient intermediate hosts for the spread of SARS CoV-2 to humans. Cross species spill over takes time and opportunity, both of which are scarce in the market. The average stay of an animal in the market is short; it is caged and can only come into contact with a limited number of buyers and sellers. Previous outbreaks of human avian flu took place when there were large concentrations of infected animals. The probability of sporadic animals starting a viral spill over during their brief encounter with humans in the market is small.

CONUNDRUM OF PATIENT ZERO

A report by BBC revealed that documented patient zero (who first became ill on December 1, 2019) was a seventy-year-old bedridden man suffering from dementia [9] A subsequent report from the South China Morning Post indicated that as many as nine earlier cases of COVID-19 (four men and five women aged between 39 and 79, the first a 55-year-old man who fell sick on November 17, 2019) were retrospectively identified in Hubei province. There is no information on whether all or some of them were Wuhan residents, or their connection with the Huanan Seafood Market.

Whether or not documented patient zero was the first person to be infected by an intermediate host of the virus, he was clearly one of the earliest COVID-19 cases identified at the start of the epidemic when person-to-person transmission was uncommon. Phylogenetic analyses of whole genome sequences of SARS CoV-2 suggested that the virus was first introduced into the human population in November or early December 2019 [11,12]. Therefore a large proportion, if not all, of the patients identified in November and December 2019 must have been infected by the intermediate host. This rapid spill over would require multiple intermediate hosts located in different parts of the city.

Documented patient zero was bedridden and stayed at home most of the time. He never visited the Seafood Market and his human interactions were limited. None of his contacts tested positive for SARS CoV-2 at the time of his illness. How did he get the disease?

If patient zero was not infected by another person but rather an animal in his own apartment, the possibilities are quite limited. It was unlikely to be a pangolin. Bats were also improbable as most of them were still hibernating at this time of the year. Hong Kong recently reported two dogs, a 17-year-old Pomeranian and a 2-year-old German shepherd, infected by their owners who had COVID-19 [13,14] These dogs however had no symptoms of the disease. There was no history that patient zero or his family kept a dog.

THE IDEAL INTERMEDIATE HOST

The most likely animal to have infected patient zero at home was the sewer rat. Rats are ubiquitous, roam around wet markets and households, and can leave infectious material wherever they go. An infected rat could easily contaminate the household of patient zero and caused the infection. The epidemic might have started when wild animals carrying SARS CoV-2 in the Seafood Market infected some of the local rats that in turn started waves of infection among rats in the neighborhood. The contacts between wild animals and rats in the market are close, multiple, and frequent. In some of these encounters, rats could have been infected by contaminated animal feed or excrement. When the number of infected rats reached a critical mass, they began leaving sufficient infectious material around to infect humans in and out of the Seafood Market.

There are some theoretical concerns on whether rats and mice can be optimal intermediate hosts of SARS CoV 2 based on the structure of their angiotensin-converting enzyme 2 (ACE2) receptor [15] However, as long as the virus can replicate within the host, a low viral load is actually advantageous so as not to cause fulminating infections.

It is unlikely that rats were the original intermediate host infected by bats in their natural habitat. Most of the suspected bat species live thousands of miles from Wuhan. Even if bats could infect rats in the wild, it would be a long journey to Wuhan unless rats could hitch hike a ride on trucks carrying wild animals to the Wuhan market. Chances are the first intermediate host between bats and humans is another wild animal favored as food by the Chinese.

There is another possibility: the Wuhan Centre of Disease

Control runs an animal laboratory about 280 meters from the Seafood Market. This laboratory specializes in collecting and identifying pathogens from animals including bats [16]. Rats could have picked up SARS CoV-2 directly from infected bats housed in this facility without going through another intermediate host. In this scenario, rats would be the only intermediate host responsible for the spill over of the virus.

DISCUSSION

The rat hypothesis explains in part the severity of the Wuhan outbreak (with 61% of Chinese cases) compared to the rest of the country. Rats in Wuhan had a head-start in developing a viral outbreak among themselves that subsequently led to human infections in the beginning of the epidemic. To infect a large number of people in a short period of time required a sizable reservoir of infected rats. It might have taken months or even years to build up such a reservoir. In cities outside Wuhan human-to-human transmission was probably the dominant mode of spread and thus the resulting outbreaks were less severe. It is also possible that a particular type of rat found in Wuhan is especially susceptible to SARS CoV 2 and became super-spreaders of the disease.

It can also explain why the epidemic continued unabated for a long time in Wuhan (new cases still occurring up to March 23, 2020) despite a complete lockdown of the city on January 23 and draconian restrictions of human movement in mid-February 2020. Human quarantine does not stop rats from moving around households, buildings, and neighbourhoods. As long as there are infected rats moving freely in the community, they will continue to act as reservoirs of the virus and the chain of transmission will not be broken. People tend to relax their infection control measures at home. They may not wash their hands as frequently and food items may be left uncovered and exposed to contamination by rats.

The rat hypothesis has important public health implications and can be tested by thoroughly investigating rats in Wuhan. They should be examined for live viruses as well as antibodies to the virus. Experimental studies should be done to understand the natural history of murine SARS CoV-2 infection, transmission mechanisms, pathogenesis and pathology, duration of viral shedding and specific body fluids that are high in viral load.

If rats are found to be carriers of SARS CoV-2, their extermination has to be an integral part of epidemic control. Besides communal efforts to eradicate rats, people should be warned of the hidden dangers in their household and the measures they can take to protect themselves. They should always keep a keen vigilance for rat infestations in their neighbourhood and their home. This pandemic can only be contained when we unravel the origin of the disease and stop all important routes of transmission.

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