

# The Wuhan SARS-CoV-2—What's next for China

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When an outbreak of pneumonia of unknown etiology occurred in Wuhan City, Hubei Province, China, in December 2019, the mystery<sup>1</sup> was the nature of the causative agent. As many of the patients had visited a fish and wild animal market, the possibility of a recurrence of severe acute respiratory syndrome (SARS) needed to be investigated.<sup>2</sup> Finally, could this outbreak of pneumonia be caused by a novel coronavirus that was different from those causing SARS or Middle East respiratory syndrome (MERS)?<sup>3</sup> Once this outbreak was recognized as a serious threat, a special team consisting of physicians, scientists, and epidemiologists began to investigate these possibilities. Within 9 days, SARS and MERS had been ruled out and a novel coronavirus had been isolated in Wuhan; this coronavirus is now officially named as the SARS-CoV-2 by the International Committee on Taxonomy of Viruses. The breadth and nature of the investigation that identified this novel SARS-CoV-2 is elaborately described by Zhu and colleagues in a recent publication in *The New England Journal of Medicine*.<sup>4</sup> Additional details subsequently have been published in several prestigious journals.<sup>5-14</sup> This study is quite remarkable and praiseworthy.

Given the subsequent spread to other parts of China as well as to other countries, the reasons for this spread should be examined. There are two such reasons that are noteworthy. The first is that the potential threat of these initial cases of pneumonia was not well-appreciated. The second reason is simply the timing of this outbreak; the outbreak began just before the Chinese New Year. By the time the investigation had been completed, the Chinese New Year was underway. The Chinese New Year is one of the most important holidays in China and celebrates the beginning of the new year on the traditional Chinese calendar. The first day of the Chinese New Year was on 25 January 2020. The Chinese New Year is associated with a number of customs; among these is returning home for an annual reunion dinner. Thus, traveling home had already begun by the time Chinese authorities attempted to curtail the spread of

the coronavirus by extending the lunar new year holidays and suspending travel.<sup>14</sup> This made control measure of the outbreak more difficult. The net effect of the initial delay in the investigation and the holiday travel was, in effect, the "Perfect Storm."

The results of the spread within China of the SARS-CoV-2 are considerable and still unfolding. Given the timing of this outbreak, the inability of the Chinese government's measures to control this epidemic and limit most of these cases to Wuhan is understandable. The question then is, "What's next for China?" As earlier suggested, there remains considerable work to be done.<sup>1</sup> This study includes many issues that can be determined in the short term as well as some that will require long-term solutions. Some of these issues are as follows. The timing of colonization, infection, and shedding need to be determined. For example, are infected persons first colonized? Do infected persons shed virus before they have clinical symptoms? Transmission characteristics need to be determined. Is infectious transmission limited to respiratory droplets or can the virus be transmitted by contact with an infected person? Efficient human-to-human transmission is required for large-scale spread (ie, an epidemic or pandemic) of any emerging virus. Therefore, the basic reproductive ratio during this epidemic needs to be determined; the basic reproductive ratio is defined as the average number of secondary cases that an infected person produces during their entire infectious period in a susceptible and uninfected population.<sup>15</sup> The case-fatality rate needs to be accurately determined; the case-fatality rate of the SARS-CoV was around 11%. Some of these questions are already being addressed,<sup>16,17</sup> but further work is needed. Often serology is required in such an epidemic to determine how many persons may have had clinically inapparent infections. Detection and identification methods that are accurate and can be performed in real time at the point of care or in the field need to be developed.<sup>1</sup> The exact relationship between the SARS-CoV-2 and animals (eg, bats)

needs to be determined.<sup>4,18,19</sup> Although bats are suspected, the question of how the virus has moved from bats to the human host needs to be resolved. Does this transmission involve intermediate animal hosts as occurred with SARS-CoV and MERS-CoV? If the SARS-CoV-2 proves to have an animal source, the continued presence of live animal markets in China must be seriously questioned. In the long term, the development of vaccines and antiviral therapy needs to be a higher priority than it has been since the SARS pandemic in 2002 to 2003; the lack of a SARS vaccine or SARS antiviral therapy suggests that such research has not been a priority. For example, Ampligen (poly I:poly C124) has been shown to inhibit SARS-CoV in a murine lung model, yet has not been further evaluated in humans.<sup>20</sup> Similarly, Remdesivir (GS-5734) has been shown to inhibit both epidemic and zoonotic coronaviruses.<sup>21</sup> It is likely that continued investigation of new antiviral agents with activity against coronaviruses in the absence of ongoing active epidemics would be enhanced by government incentives. Another issue in the long term that needs to be addressed is the potential of novel coronaviruses to spread within medical centers to health care workers as has happened with SARS-CoV and MERS-CoV.<sup>22-24</sup> Most medical centers, whether in China or in the United States, are not prepared for such a problem. For example, negative-pressure containment rooms with proper anterooms are either not found or found only in limited numbers in medical centers in the United States.<sup>25</sup>

The recent epidemic in China caused by the SARS-CoV-2 is yet another example of emerging zoonotic viral diseases.<sup>18</sup> Like previous epidemics/pandemics caused by novel members of the coronavirus family, there are many lessons to be learned. Much work remains to be done before this latest coronavirus is fully understood and these lessons can be learned.

## AUTHOR CONTRIBUTIONS

Concept forming: HL and Y-WT. Writing: CWS. Revising and editing: HL and Y-WT.

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**How to cite this article:** Lu H, Stratton CW, Tang Y-W. The Wuhan SARS-CoV-2—What's next for China. *J Med Virol*. 2020;1-2. <https://doi.org/10.1002/jmv.25738>