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From Hendra to Wuhan: what has been learned in responding to emerging zoonotic viruses

Published Online
February 11, 2020
https://doi.org/10.1016/
S0140-6736(20)30350-0

As the world watches the rapid spread of the 2019 novel coronavirus (2019-nCoV) outbreak, it is important to reflect on the lessons that can be learned from this and previous emerging zoonotic viruses (EZV) in a comparative and analytic way. Although the source of 2019-nCoV is yet to be confirmed, early findings suggest a high possibility of a bat origin.[1] There have been six major EZV outbreaks in the past 25 years caused by proven or suspected bat-borne viruses (table).[2–7] With these in mind, four major points are worth considering in the context of the 2019-nCoV outbreak.

First, are Koch's postulates still relevant in the era of next-generation sequencing (NGS)? In the heat of the debate about the early response to the 2019-nCoV outbreak, insufficient attention was paid to how the initial aetiological evidence came from NGS analysis requested by clinicians. To our knowledge, all previous EZV outbreak investigations started with a live virus isolation, including the 2012 Middle East respiratory syndrome coronavirus (MERS-CoV) discovery.[5] The preliminary sequence data indicating the presence of a severe acute respiratory syndrome (SARS)-related coronavirus in patients' lung lavage samples were obtained on Dec 26, 2019, by NGS.[8] The Chinese authorities ruled out SARS and MERS, as well as a few other non-coronaviruses, on Jan 5, 2020, and confirmed a novel coronavirus as a potential cause on Jan 9, 2020.[4] However, the genome sequence—crucial for rapid development of diagnostics needed in an outbreak response—was not released until Jan 12, 2020,[7] 17 days after the preliminary sequence data were obtained. These events raise challenging questions. Should a national response team report a highly suspected pathogen sequence before confirming an aetiological live agent? Are current national and international policies and regulations adequate to deal with a sequence-based outbreak reporting system? While they have evolved over time, the postulates formulated by Robert Koch and Friedrich Loeffler in 1884 included the isolation of a live agent as a key criterion.[9] We believe that it is time to establish an NGS-based reporting system that can alert to the presence of a new aetiological agent(s) rather than requiring the isolation of aetiological agents.

Second, clinicians and scientists have a crucial role in responding to such EZV outbreaks. In past EZV outbreak investigations, clinicians have largely had supportive roles. This situation is likely to change now that more clinician scientists are better trained and have academic appointments, especially in China. In fact, it was the clinicians who led to the early detection of and warning about the 2019-nCoV outbreak in China. In investigating severe pneumonia cases of unknown cause, clinicians in two hospitals in Wuhan independently sent lung lavage samples from patients for NGS analysis by commercial NGS companies. Alarm bells rang, not only through the different levels of the official Chinese Center for Disease Control and Prevention (China CDC) reporting system but also through social media traced back to eight doctors who were wrongly accused of spreading "fake news". These doctors were later cleared of any wrongdoing and praised by the government authorities for their brave action in early alerting.[10]

Achieving the right balance between information sharing and scientific publication is important during an EZV outbreak response. This is not a new challenge but greatly amplified in the 2019-nCoV outbreak when anger in China was directed towards a few leading scientists who were alleged to have held back sharing data about

	Year of first or major outbreak	Countries or regions affected	Bat origin status	Main intermediate animal host responsible for human infection	Different virus names used or suggested
Hendra[2]	1994	Australia	Confirmed	Horses	First named "equine morbillivirus"
Nipah[3]	1998–99	Malaysia and four other countries	Confirmed	Pigs	First named "Hendra-like virus"
SARS[4]	2002–03	China and 25 other countries	Confirmed	Civets	First named "atypical pneumonia"
MERS[5]	2012	Saudia Arabia and 26 other countries	Suspected	Camels	First named "hCoV-EMC"
Ebola[6]	2014	Guinea and six other countries	Highly suspected	Non-applicable*	..
2019-nCoV[7]	2019–20	China and 24 other countries	Suspected	Presently unknown	Suggested name "HARS-CoV"

SARS=severe acute respiratory syndrome. MERS=Middle East respiratory syndrome. hCoV-EMC=human coronavirus Erasmus Medical Center. 2019-nCoV=2019 novel coronavirus. HARS-CoV=Han acute respiratory syndrome coronavirus. For 2019-nCoV, data are for Feb 9, 2020. *Although the 2014 Ebola outbreak was believed to start with a direct bat-to-human transmission, non-human primates have been indicated in previous Ebola outbreaks.

Table: **Summary characteristics of major outbreaks of emerging zoonotic viruses in the past 25 years**

the virus to publish their findings. These unsubstantiated allegations consumed media attention and created media panic that was counterproductive to the outbreak response. Clear national and international guidelines are needed on how to achieve the right balance in the leadership provided by public health and research experts facing an outbreak of an EZV.

Third, a One Health approach[11] in EZV outbreak responses and control is vital. In August, 2003, after WHO declared the end of the SARS outbreak, it organised a special mission with international and Chinese scientists to investigate the origin and early transmission events of SARS-CoV. Among the eight international experts invited, seven were veterinarians or those working in animal health. By contrast, the six-member Chinese team only had one participating veterinarian or animal scientist. While recognising the tremendous effort by the China CDC team in the early response to the 2019-nCoV outbreak, the small number of team members trained in animal health was probably one of the reasons for the delay in identifying an intermediate animal(s), which is likely to have caused the spread of the virus in a region of the market where wildlife animals were traded and subsequently found to be heavily contaminated. Unfortunately, what animal(s) was involved in transmission remains unknown. There is an urgent need to know the risks associated with the presumed animal to human transmission of 2019-nCoV, and the measures that can be taken to prevent such transmission in the future. For example, should the sale of wild animals be restricted in Chinese wet markets? We recommend that a comprehensive One Health team be involved in all future EZV investigations. Indeed, this approach has international implications, with risks of exotic zoonotic diseases associated with the huge quantities of illegal bush meat from central and west Africa being imported into Europe and North America.[12]

Finally, naming of a new virus is important not only for virologists in the long term but also for effective communication to the general public. In all the major EZV events over the past 25 years, naming of the new virus has not been straightforward and most went through a renaming process (table). This is also true for the 2019-nCoV outbreak. There has been intensive discussion now among virologists worldwide about an alternative name for 2019-nCoV. To continue the tradition of using a syndrome, as in SARS and MERS, and to avoid the sensitivity of using a city name, we propose to name this new virus Han acute respiratory syndrome coronavirus (HARS-CoV). Han is the abbreviation of Wuhan in Chinese. Such a name is, we believe, preferable to the names being used in media headlines, such as "Wuhan virus" or "China virus", and it retains the historical fact that the outbreak started in Wuhan.

Now is not a time for blame. Rather, there are lessons the global health community can and should learn and act on so that we can better respond to the next EZV event, which is almost certain to happen again. These lessons are definitely not unique to China.

L-FW and JSM are members of the WHO IHR Emergency Committee. L-FW is also a member of the WHO Consultation Group on nCoV Reagents and Cross–Reactivity; WHO Working Group on Prioritization of nCoV vaccine; and OIE World Organisation for Animal Health Advisory Group on 2019-nCoV. We declare no other competing interests.

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