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Pathogenicity and transmissibility of 2019-nCoV—A quick overview and comparison with other emerging viruses

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ABSTRACT

A zoonotic coronavirus, tentatively labeled as 2019-nCoV by the World Health Organization (WHO), has been identified as the causative agent of the viral pneumonia outbreak in Wuhan, China, at the end of 2019. Although 2019-nCoV can cause a severe respiratory illness like SARS and MERS, evidence from clinics suggested that 2019-nCoV is generally less pathogenic than SARS-CoV, and much less than MERS-CoV. The transmissibility of 2019-nCoV is still debated and needs to be further assessed. To avoid the 2019-nCoV outbreak turning into an epidemic or even a pandemic and to minimize the mortality rate, China activated emergency response procedures, but much remains to be learned about the features of the virus to refine the risk assessment and response. Here, the current knowledge in 2019-nCoV pathogenicity and transmissibility is summarized in comparison with several commonly known emerging viruses, and information urgently needed for a better control of the disease is highlighted.

2019-nCoV is the third coronavirus to cross species to infect human populations (probably transmitted from bats or another host) in the past two decades [1–3]. The previous two are the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012 [4,5]. Since 2019-nCoV can cause a severe respiratory illness like SARS and MERS and was found to be adept at human-to-human transmission, China launched an emergency response at an early stage of the outbreak. The World Health Organization (WHO) has not yet, but may soon declare the outbreak a global health emergency (PHEIC). Successful isolation of the 2019-nCoV [4,5] has promoted the understanding of viral origin and the feature of its infectivity, however, at this stage much remains unclear and to be investigated.

1. Pathogenicity of 2019-nCoV

Of the first 41 cases of laboratory confirmed infections with 2019-nCoV, all had viral pneumonia and almost a third of the patients developed acute respiratory distress syndrome (ARDS) requiring intensive care and 6 patients (14.6%) died [6]. Since the fatality rate of the early reported case is often high due to bias towards more severe cases, the true mortality risk might be much lower. As of Jan 27, 2020, about 3000 cases have been confirmed in China, and cases were also reported in Japan, South Korea, Thailand, Singapore, the United States, and Australia, all of which were exported from China. The total number of deaths from the pneumonia-related disease accounts for less than 3%. In addition, most of those who have died had underlying health conditions such as hypertension, diabetes or cardiovascular disease that compromised their immune systems. Although the fatality rate will continue to change until all infected people recover, it appears that 2019-nCoV is less pathogenic than SARS-CoV (~10%), and much less than MERS-CoV (~40%).

Coronaviruses are a group of viruses that cause a significant percentage of all common colds in human adults and children. Four human coronavirus including 229E, OC43, NL63, and HKU1 are prevalent and typically cause common cold symptoms in immunocompetent individuals. SARS-CoV which causes SARS, has a unique pathogenesis because it causes both upper and lower respiratory tract infections. 2019-nCoV is classified as a novel betacoronavirus belonging to the sarbecovirus subgenus of Coronaviridae family. The genome sequence of 2019-nCoV is about 89% identical to bat SARS-like-CoVZXC21 and 82% identical to human SARS-CoV [7]. It has been reported that 2019-nCoV uses the same cell entry receptor, ACE2, to infect humans, as SARS-CoV [8], so clinical similarity between the two viruses could be expected,

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particularly in severe cases. Notably, there are signs, from what is still very limited data, that the clinical features of 2019-nCoV seem to be more variable.

2. Transmissibility of 2019-nCoV

The 2019-nCoV outbreak was started from a local seafood market in winter, similar environment as SARS. Two-thirds of the first 41 confirmed cases were found to have a link with the Huanan Seafood Wholesale Market (also sold live animals). Initial reports indicated that human-to-human transmission of the virus was nonexistent or limited, however, it is now quite clear that efficient human-to-human transmission exists and is a requirement for the large-scale spread of 2019-nCoV [9]. Like SARS-CoV, 2019-nCoV can be passed directly from person to person by respiratory droplets, and emerging evidence suggested that it may also be transmitted through contact and fomites. Further investigations are required to explore the origin of 2019-nCoV and to reveal how easily the virus can pass between humans. In addition, the asymptomatic incubation period for individuals infected with 2019-nCov was estimated to range from 1 to 14 days (most likely 3–10 days), longer than that of SARS-CoV. Although it remains unclear whether those without symptoms have high enough viral titers for spreading the virus, great attention should be paid to minimize related risks.

A very important threshold quantity associated with the viral transmissibility is the basic reproduction number, which is usually denoted by R_0 (pronounced "R naught"). The epidemiological definition of R_0 is the average number of people who will catch a disease from one contagious person. It specifically applies to a population of people who were previously free of infection and not vaccinated. Three possibilities exist for the potential spread or decline of a disease, depending on its R_0 value: 1. If R_0 is less than 1, each existing infection causes less than 1 new infection. In this case, the disease will decline and eventually disappear. 2. If R_0 equals 1, the disease will stay alive, but there won't be an epidemic. 3. If R_0 is greater than 1, cases could grow exponentially and cause an epidemic or even a pandemic. From what we currently know, the calculated R_0 value for 2019-nCoV is significantly greater than 1. A preliminary R_0 estimate of 1.4–2.5 was presented in WHO's statement regarding the outbreak of 2019-nCoV, 23 Jan 2020 [1]. S. Zhao et al. estimated the mean R_0 for 2019-nCoV in the early phase of the outbreak ranging from 3.3 to 5.5 (likely to be below 5 but above 3 with rising report rate) [10], which appeared slightly higher than those of SARS-CoV (R_0: 2–5). In contrast, previous studies have suggested that the R_0 for MERS-CoV is less than 1, meaning that it is unlikely to cause a pandemic [11]. Super-spreading events have been implicated in 2019-nCoV transmission, as that in SARS-CoV and MERS-CoV, but their relative importance is still unclear and the super-spreaders are difficult to track. J Read. et al. estimated the R_0 for 2019-nCoV to be 3.6–4.0, indicating that 72–75% of transmissions must be prevented in order to stop the increasing trend [12], however, the authors assumed that there is little heterogeneity in reproductive numbers, so the true R_0 value could be smaller. Nevertheless, in view of avoiding the 2019-nCoV outbreak turning into an epidemic or even a pandemic, it is better to overestimate rather than underestimate the transmissibility of 2019-nCoV.

It should be noted that estimation of R_0 during the pre-epidemic stage can be plagued by data uncertainty and variability [13]. For example, the estimated R_0 was 0.80 (95% CI 0.54–1.13) for pre-epidemic SARS-CoV in southeast Asia (2002–2003). Additionally, R_0 might change seasonally according to climate or yearly gatherings such as the Chinese Spring Festival that put individuals in closer proximity to one another. Because of these, China is now under enormous pressure to make difficult decisions with an incomplete and rapidly changing understanding of the viral transmissibility. Considering the complexity of R_0, continuing research is required, including updated R_0 estimates and methodological refinements. Fortunately, a main trend is that the estimated R_0 value for 2019-nCoV is getting reduced as case information accumulates. And with the control measures implemented, the effective reproduction number (R_e) has been shown to drop to 2.08 (1.99–2.18) as of 22 Jan 2020 [14].

3. Relationship between viral pathogenicity and transmissibility

The severity of disease is most often an important indirect factor in a virus's ability to spread. Because coronaviruses have error-prone RNA-dependent RNA polymerases (RdRP), mutations and recombination events frequently occur [4], resulting in quasispecies diversity that is closely associated with adaptive evolution and the capacity to cause disease. Previous studies have shown that SARS-CoV mutated over the 2002–2004 epidemic to better bind to its cellular receptor and replication in human cells, enhancing virulence. It is thus important to examine whether 2019-nCoV behaves like SARS-CoV to adapt to the human host and whether this would increase the R_0 value and change its virulence. By contrast, MERS-CoV has not mutated substantially since it was discovered, which may be due to that the functional cellular receptor (CD26) used by MERS-CoV is quite unique so the virus has a very limited potential to mutate without losing fitness. Notably, ACE2, the receptor protein of both SARS-CoV and 2019-nCoV, is abundantly present in humans in the epithelia of the lung and small intestine [15], and coronaviruses can infect the upper respiratory and gastrointestinal tract of mammals. In this regard, identifying the possible route of infection will also have implications for the pathogenesis and treatment of disease caused by 2019-nCoV.

Table 1 gives estimates of case fatality rate as well as R_0 value of several commonly known emerging virus infections based on data collected from literatures [16,17], WHO and CDC. It is clear that airborne viruses tend to have a higher R_0 value than those spread through contact. Besides, from the table, we can find a trend that higher pathogenicity is often associated with lower transmissibility, which may also apply to a certain virus of different subtypes and strains. A good example is the influenza virus. Whereas the pandemic H1N1 virus binding to receptors in the upper respiratory tract caused relatively mild disease and became endemic in the population, the H7N9 virus binding to receptors in the lower respiratory tract has a fatality rate of approximately 40% and has so far resulted in only a few small clusters of human-to-human transmission. Another example is that Measles virus and

Table 1
Case fatality rate and R_0 value of commonly known emerging virus infections.

Virus	Case Fatality Rate (%)	R_0
2019-nCoV	3	1.4–5.5[a]
SARS-CoV	10	2–5
MERS-CoV	40	<1
Avian H7N9 (2013)	40	<1
H1N1 (2009)	0.03	1.2–1.6
H1N1 (1918)	3	1.4–3.8
Measles Virus	0.3	12–18
Rhinovirus	<0.01	6
Ebola Virus	70	1.5–2.5
HIV	80[b]	2–4
Small Pox Virus	17	5–7

[a] WHO: 1.4–2.5; S. Zhao et al.: 3.3–5.5; J. Read et al.: 3.6–4.0; M. Shen et al.: 4.5–4.9.
[b] Without therapy.

Rhinovirus have strong transmissibility but low mortality rate. But this is not a given: CoV-NL63 uses the same receptor (ACE2) as 2019-nCoV, whereas it causes disease of very different severity. In the case of 2019-nCoV, there have been some clues suggested that, sometimes, an individual with highly severe 2019-nCoV disease will only cause a few infections, conversely, individuals with a moderate disease or latent infection can occasionally cause many infections, though the molecular mechanism is not yet understood. A possible consequence of this is that viral mutations that pose a low health threat on the individual level may pose a high risk on the population level. Further studies are thus required to fill the knowledge gap in viral mutations and pathogenicity and transmissibility. Related information can help to reveal how the virus is evolving and adapting to new conditions and whether the outbreak has the potential to persist.

Based on above discussions, the current 2019-nCoV seems to have relatively low pathogenicity and moderate transmissibility. However, more information on the biological and epidemiological features of the virus are urgently needed to further refine the risk assessment and response, which will ultimately benefit the 2019-nCoV control and prevention. Besides, because that anti-coronaviral drugs and vaccines are still under development [18,19], fear plays a role in the economic and social consequences, which was also a feature of SARS-CoV outbreak. Educating the communities and strengthening public confidence will thus be important. As long as the transmission of the virus from one person to another could be substantially and consistently interrupted ($R < 1$), it is entirely possible that the outbreak could be controlled and even eradicated, and this requires the joint efforts of the whole society.

Declaration of Competing Interest

The author declared no competing interests.

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References

[1] WHO. Statement on the meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). posting date. 2020 [Online.].
[2] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020. https://doi.org/10.1016/S0140-6736(20)30185-9 [in press].
[3] Perlman S. Another decade, another coronavirus. N Engl J Med 2020. https://doi.org/10.1056/NEJMe2001126 [in press].
[4] Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181–92.
[5] de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol 2016;14:523–34.
[6] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020. https://doi.org/10.1016/S0140-6736(20)30183-5 [in press].
[7] Chan JF-W, Kok K-H, Zhu Z, Chu H, To KK-W, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from patients with acute respiratory disease in Wuhan, Hubei, China. Emerg Microb Infect 2020. https://doi.org/10.1080/22221751.2020.1719902 [in press].
[8] Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. bioRxiv 2020. https://doi.org/10.1101/2020.01.22.914952 [in press].
[9] Chan JF-W, Yuan S, Kok K-H, To KK-W, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020. https://doi.org/10.1016/S0140-6736(20)30154-9 [in press].
[10] Zhao S, Ran J, Musa SS, Yang G, Lou Y, Gao D, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. bioRxiv 2020. https://doi.org/10.1016/j.ijid.2020.01.050 [in press].
[11] Bauch CT, Oraby T. Assessing the pandemic potential of MERS-CoV. Lancet 2013;382:662–4.
[12] Read JM, Bridgen JR, Cummings DA, Ho A, Jewell CP. Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions. medRxiv 2020. https://doi.org/10.1101/2020.01.23.20018549 [in press].
[13] Delamater PL, Street EJ, Leslie TF, Yang YT, Jacobsen KH. Complexity of the basic reproduction number (R0). Emerg Infect Dis 2019;25:1–4.
[14] Shen M, Peng Z, Xiao Y, Zhang L. Modelling the epidemic trend of the 2019 novel coronavirus outbreak in China. bioRxiv 2020. https://doi.org/10.1101/2020.01.23.916726 [in press].
[15] Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004;203:631–7.
[16] Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A novel coronavirus emerging in China — key questions for impact assessment. N Engl J Med 2020. https://doi.org/10.1056/NEJMp2000929 [in press].
[17] van den Driessche P. Reproduction numbers of infectious disease models. Infect Dis Model 2017;2:288–303.
[18] Jiang S, Du L, Shi Z. An emerging coronavirus causing pneumonia outbreak in Wuhan, China: calling for developing therapeutic and prophylactic strategies. Emerg Microb Infect 2020. https://doi.org/10.1080/22221751.2020.1723441 [in press].
[19] Yu F, Ojcis D, Pan C, Jiang S. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan, China. Microb Infect 2020;22:74–9. https://doi.org/10.1016/j.micinf.2020.01.003.