EDITORIAL

Another Decade, Another Coronavirus

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For the third time in as many decades, a zoonotic coronavirus has crossed species to infect human populations. This virus, provisionally called 2019-nCoV, was first identified in Wuhan, China, in persons exposed to a seafood or wet market. The rapid response of the Chinese public health, clinical, and scientific communities facilitated recognition of the clinical disease and initial understanding of the epidemiology of the infection. First reports indicated that human-to-human transmission was limited or nonexistent, but we now know that such transmission occurs, although to what extent remains unknown. Like outbreaks caused by two other pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus [SARS-CoV] and Middle East respiratory syndrome coronavirus [MERS-CoV]), 2019-nCoV causes respiratory disease that is often severe.[1] As of January 24, 2020, there were more than 800 reported cases, with a mortality rate of 3% (https://promedmail.org/).

As now reported in the *Journal*, Zhu et al.[2] have identified and characterized 2019-nCoV. The viral genome has been sequenced, and these results in conjunction with other reports show that it is 75 to 80% identical to the SARS-CoV and even more closely related to several bat coronaviruses.[3] It can be propagated in the same cells that are useful for growing SARS-CoV and MERS-CoV, but notably, 2019-nCoV grows better in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV. Identification of the virus will allow the development of reagents to address key unknowns about this new coronavirus infection and guide the development of antiviral therapies. First, knowing the sequence of the genome facilitates the development of sensitive quantitative reverse-transcriptase–polymerase-chain-reaction assays to rapidly detect the virus. Second, the development of serologic assays will allow assessment of the prevalence of the infection in humans and in potential zoonotic sources of the virus in wet markets and other settings. These reagents will also be useful for assessing whether the human infection is more widespread than originally thought, since wet markets are present throughout China. Third, having the virus in hand will spur efforts to develop antiviral therapies and vaccines, as well as experimental animal models.

Much still needs to be learned about this infection. Most important, the extent of interhuman transmission and the spectrum of clinical disease need to be determined. Transmission of SARS-CoV and MERS-CoV occurred to a large extent by means of superspreading events.[4,5] Superspreading events have been implicated in 2019-nCoV transmission, but their relative importance is unknown. Both SARS-CoV and MERS-CoV infect intrapulmonary epithelial cells more than cells of the upper airways.[4,6] Consequently, transmission occurs primarily from patients with recognized illness and not from patients with mild, nonspecific signs. It appears that 2019-nCoV uses the same cellular receptor as SARS-CoV (human angiotensin-converting enzyme 2 [hACE2]),[3] so transmission is expected only after signs of lower respiratory tract disease develop. SARS-CoV mutated over the 2002–2004 epidemic to better bind to its cellular receptor and to optimize replication in human cells, enhancing virulence.[7] Adaptation readily occurs because coronaviruses have error-prone RNA-

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dependent RNA polymerases, making mutations and recombination events frequent. By contrast, MERS-CoV has not mutated substantially to enhance human infectivity since it was detected in 2012.[8]

It is likely that 2019-nCoV will behave more like SARS-CoV and further adapt to the human host, with enhanced binding to hACE2. Consequently, it will be important to obtain as many temporally and geographically unrelated clinical isolates as possible to assess the degree to which the virus is mutating and to assess whether these mutations indicate adaptation to the human host. Furthermore, if 2019-nCoV is similar to SARS-CoV, the virus will spread systemically.[9] Obtaining patient samples at autopsy will help elucidate the pathogenesis of the infection and modify therapeutic interventions rationally. It will also help validate results obtained from experimental infections of laboratory animals.

A second key question is identification of the zoonotic origin of the virus. Given its close similarity to bat coronaviruses, it is likely that bats are the primary reservoir for the virus. SARS-CoV was transmitted to humans from exotic animals in wet markets, whereas MERS-CoV is transmitted from camels to humans.[10] In both cases, the ancestral hosts were probably bats. Whether 2019-nCoV is transmitted directly from bats or by means of intermediate hosts is important to understand and will help define zoonotic transmission patterns.

A striking feature of the SARS epidemic was that fear played a major role in the economic and social consequences. Although specific anticoronaviral therapies are still in development, we now know much more about how to control such infections in the community and hospitals, which should alleviate some of this fear. Transmission of 2019-nCoV probably occurs by means of large droplets and contact and less so by means of aerosols and fomites, on the basis of our experience with SARS-CoV and MERS-CoV.[4,5] Public health measures, including quarantining in the community as well as timely diagnosis and strict adherence to universal precautions in health care settings, were critical in controlling SARS and MERS. Institution of similar measures will be important and, it is hoped, successful in reducing the transmission of 2019-nCoV.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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