



# New Virus, New Challenge

Yi Shi<sup>1,\*</sup>

The ongoing COVID-19 pandemic has made us to consider the emergence of potential viral diseases in the future. Animals can carry vast and diverse virus species, most of which we do not understand yet, and the spillover events of the viruses from the unknown pool in animals to human population always occurred in the past. To effectively prevent and control the emerging viral diseases, we should make efforts to explore the unknown virus species in nature and prepare in advance.

Viruses are everywhere on our Earth. Although virologists' efforts have characterized over 5,000 virus species, public health and biosafety may face a global threat due to emerging infectious diseases (EIDs). Most EIDs are zoonotic in origin, capable of crossing the species barrier to infect humans. In December 2019, an outbreak of acute respiratory disease caused by a novel coronavirus emerged, and quickly afterward this disease had spread to more than 200 countries.<sup>1</sup> The disease was named “coronavirus disease 2019” (COVID-19) by the World Health Organization, and the coronavirus study group of the International Committee on Taxonomy of Viruses suggested the name of the new coronavirus as “severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2) based on genome comparisons. Although some patients may have shown certain connections with a seafood and wildlife market, the origin of SARS-CoV-2 has yet to be identified, because some patients showed no exposure to the market.<sup>2</sup> The median incubation period of the disease was 4 days.<sup>3</sup> Most patients have mild symptoms, such as fever and dry cough. However, older patients, those with a higher Sequential Organ Failure Assessment (SOFA) score and d-dimer  $>1 \mu\text{g/L}$  on admission have a higher risk of death.<sup>4</sup> On the other hand, younger patients showed a long incubation period (6.6 days) and fewer complications during treatment.<sup>5</sup> Compared with SARS in 2002/2003, COVID-19 displays higher transmissibility with a lower fatality rate. Common public health measures, such as quarantine of infected and suspected patients, have been taken to prevent and control the spread of COVID-19.

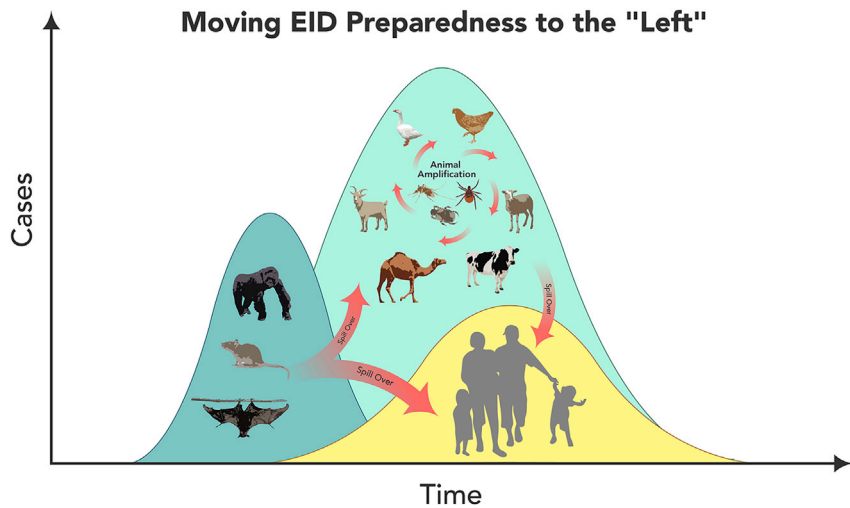
Regardless, scientists are still sprinting to outpace the spread of SARS-CoV-2. Virologists have isolated this novel coronavirus and reported the first genome of SARS-CoV-2 on January 10, 2020, developed the first diagnostic kit on January 15, 2020, and published the first report of the clinical features of COVID-19 on January 27, 2020.<sup>1</sup> Subsequently, it has been shown that SARS-CoV-2 uses the same entry receptor angiotensin converting enzyme 2 (ACE2) as SARS-CoV, and the structures of the viral spike protein and its complex with the ACE2

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\*Corresponding author:  
Email: [shiyi@im.ac.cn](mailto:shiyi@im.ac.cn)

<sup>1</sup>CAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Beijing, China



**Figure 1** The Ecology of the Emergence of Infectious Disease

There are three main populations related to the transmission cycle of zoonotic infectious disease: natural reservoirs, intermediate animals, and the human population. The pathogens in natural reservoirs can spill over into the human population directly or indirectly after amplification in intermediate animals. To efficiently deal with the potential threat of emerging infectious disease (EID), we should enhance the surveillance of the pathogens in the natural reservoirs and intermediate animals and establish epidemic preparedness.

receptor have been solved by structural virologists,<sup>6</sup> providing a basis for the rational design of vaccines and drugs against SARS-CoV-2.

Bats harbor the SARS-related coronaviruses that are most closely related to SARS-CoV-2.<sup>7</sup> Hence, scientists suspect that a wild bat may be the source of SARS-CoV-2, yet the exact intermediate animal host has not been identified or confirmed. The scientific community strongly condemns the conspiracy theories about the origin of the coronavirus and supports the notion that the COVID-19 pandemic is an unexpected viral “spill-over” event from nature.

Overall, we know very little about virus populations in nature. There are 6,000 viral species that are known to infect animals, plants, and bacteria. It is estimated that more than 1 million virus species exist in mammals, and the number of unidentified mammalian viruses is currently unknown! The viral “spillover” from this vast “unknown” pool is becoming more and more frequent (Figure 1), but we have few technological countermeasures available to respond to these “spillovers.”

How can we effectively tackle EIDs? Vaccines are the best way to prevent infectious diseases at the population level, but their development requires a relatively long time, usually several years. Broadly reactive anti-pathogen drugs are also an effective measure to provide first-line treatment against the EIDs. The Gilead com-

pany has collaborated with hospitals to initiate a phase 3 clinical trial of the reactive antiviral drug remdesivir for the treatment of COVID-19. The mechanism of action of remdesivir is associated with the RNA synthesis process by the viral polymerases, which is a promising target for the design of broadly reactive drugs against different types of viruses.<sup>8,9</sup> Another approach is to mine the databases of old drugs. For example, chloroquine phosphate, a widely used anti-malaria drug, is highly effective at inhibiting SARS-CoV-2 infection *in vitro*.<sup>10</sup> Traditional Chinese medicine also shows potential in the clinic. More effective chemical drugs and monoclonal antibodies are under development to treat patients in the future.

The twenty-first century may see accelerating emergence of diseases like COVID-19, driven by population growth and its related impacts on the environment. The world, however, is ill-prepared to respond to such a threat. Our ability to deploy effective measures is much limited and challenged by what we “don’t know” about the future threats, which calls for a change in the scientific community from a reactive culture to a proactive one.

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