Coronavirus Infections—More Than Just the Common Cold

Human coronaviruses (HCoVs) have long been considered inconsequential pathogens, causing the “common cold” in otherwise healthy people. However, in the 21st century, 2 highly pathogenic HCoVs—severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)—emerged from animal reservoirs to cause global epidemics with alarming morbidity and mortality. In December 2019, yet another pathogenic HCoV, 2019 novel coronavirus (2019-nCoV), was recognized in Wuhan, China, and has caused serious illness and death. The ultimate scope and effect of this outbreak is unclear at present as the situation is rapidly evolving.

Coronaviruses are large, enveloped, positive-strand RNA viruses that can be divided into 4 genera: alpha, beta, delta, and gamma, of which alpha and beta CoVs are known to infect humans.1 Four HCoVs (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults. Coronavirus are ecologically diverse with the greatest variety seen in bats, perhaps the natural hosts. These reservoirs; however, as more viral sequence data accumulates, it is impossible to predict the next pathogenic HCoV.

While the trajectory of this outbreak is impossible to predict, effective response requires prompt action from the standpoint of classic public health strategies to the timely development and implementation of effective countermeasures.

The surface spike (S) glycoprotein is critical for binding of host cell receptors and is believed to represent a key determinant of host range restriction.1

Until recently, HCoVs received relatively little attention due to their mild phenotypes in humans. This changed in 2002, when cases of severe atypical pneumonia were described in Guangdong Province, China, causing worldwide concern as disease spread via international travel to more than 2 dozen countries.2 The new disease became known as severe acute respiratory syndrome (SARS), and a beta-HCoV, named SARS-CoV, was identified as the causative agent. Because early cases shared a history of human-animal contact at live game markets, zoonotic transmission of the virus was strongly suspected.2 Palm civets and raccoon dogs were initially thought to be the animal reservoir(s); however, as more viral sequence data became available, consensus emerged that bats were the natural hosts.

Common symptoms of SARS included fever, cough, dyspnea, and occasionally watery diarrhea.2 Of infected patients, 20% to 30% required mechanical ventilation and 10% died, with higher fatality rates in older patients and those with medical comorbidities. Human-to-human transmission was documented, mostly in health care settings. This nosocomial spread may be explained by basic virology: the predominant human receptor for the SARS S glycoprotein, human angiotensin-converting enzyme 2 (ACE2), is found primarily in the lower respiratory tract, rather than in the upper airway. Receptor distribution may account for both the dearth of upper respiratory tract symptoms and the finding that peak viral shedding occurred late (~10 days) in illness when individuals were already hospitalized. SARS care often necessitated aerosol-generating procedures such as intubation, which also may have contributed to the prominent nosocomial spread.

Several important transmission events did occur in the community, such as the well-characterized mini-outbreak in the Hotel Metropole in Hong Kong from where infected patrons traveled and spread SARS internationally. Another outbreak occurred at the Amoy Gardens housing complex where more than 300 residents were infected, providing evidence that airborne transmission of SARS-CoV can sometimes occur.3 Nearly 20 years later, the factors associated with transmission of SARS-CoV, ranging from self-limited animal-to-human transmission to human superspreader events, remain poorly understood. Ultimately, classic public health measures brought the SARS pandemic to an end, but not before 8098 individuals were infected and 774 died.2 The pandemic cost the global economy an estimated $30 billion to $100 billion.1 SARS-CoV demonstrated that animal CoVs could jump the species barrier, thereby expanding perception of pandemic threats.

In 2012, another highly pathogenic beta-CoV made the species jump when Middle East respiratory syndrome (MERS) was recognized and MERS-CoV was identified in the sputum of a Saudi man who died from respiratory failure.3 Unlike SARS-CoV, which rapidly spread across the globe and was contained and eliminated in relatively short order, MERS has smoldered, characterized by sporadic zoonotic transmission and limited chains of human spread. MERS-CoV has not yet sustained community spread; instead, it has caused explosive nosocomial transmission events, in some cases linked to a single superspreader, which are devastating for health care systems. According to the World Health Organization (WHO),...
as of November 2019, MERS-CoV has caused a total of 2494 cases and 858 deaths, the majority in Saudi Arabia. The natural reservoir of MERS-CoV is presumed to be bats, yet human transmission events have primarily been attributed to an intermediate host, the dromedary camel.

MERS shares many clinical features with SARS such as severe atypical pneumonia, yet key differences are evident. Patients with MERS have prominent gastrointestinal symptoms and often acute kidney failure, likely explained by the binding of the MERS-CoV S glycoprotein to dipeptidyl peptidase 4 (DPP4), which is present in the lower airway as well as the gastrointestinal tract and kidney.\(^1\) MERS necessitates mechanical ventilation in 50% to 89% of patients and has a case fatality rate of 36%.\(^2\)

While MERS has not caused the international panic seen with SARS, the emergence of this second, highly pathogenic zoonotic HCoV illustrates the threat posed by this viral family. In 2017, the WHO placed SARS-CoV and MERS-CoV on its Priority Pathogen list, hoping to galvanize research and the development of countermeasures against CoVs.

The action of the WHO proved prescient. On December 31, 2019, Chinese authorities reported a cluster of pneumonia cases in Wuhan, China, most of which included patients who reported exposure to a large seafood market selling many species of live animals. Emergence of another pathogenic zoonotic HCoV was suspected, and by January 10, 2020, researchers from the Shanghai Public Health Clinical Center & School of Public Health and their collaborators released a full genomic sequence of 2019-nCoV to public databases, exemplifying prompt data sharing and the importance of sustained preparedness.

Scores the perpetual challenge of emerging infectious diseases and the importance of sustained preparedness.


Opinion Viewpoint

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REFERENCES