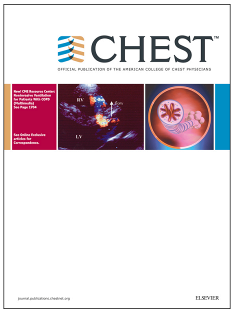

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A novel coronavirus (COVID-19) outbreak: a call for action

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In December 2019, Wuhan, Hubei province, China, one of the six megalopolises with a population of 14 million, became the center of an outbreak of pneumonia of unknown cause. Considering the early cases were linked to the Huanan seafood market, the market was shut down on January 1, 2020. One week later, on January 7, 2020, Chinese health authorities confirmed that they had identified a novel coronavirus (COVID-19). On January 30 2020, the WHO Director-General made the final decision on the determination of a Public Health Emergency of International Concern (PHEIC), regarding the outbreak in China, with exportations to other countries.[1]

As of mid-February, more than 50,000 cases with laboratory confirmed COVID-19 have been detected in China, of whom more than 1600 have died. It has spread to all 34 provinces in China within one month. The Spring Festival travel rush, in which an estimated 5 million people traveled from Wuhan to throughout the country, was one of the key factors that led to the rapid intercity spread. Approximately 680 exported cases of COVID-19 infection have been reported in more than 25 countries.

This outbreak is the third time that a zoonotic coronavirus has crossed species to infect humans in the past two decades. During the epidemics of the other two betacoronaviruses, SARS-CoV and MERS-CoV, more than 10,000 cumulative cases occurred, with lethality rates of 10% for SARS-CoV and 37% for MERS-CoV. [2,3] Learning from the 2003 SARS outbreak, Chinese health authorities have taken rapid measures to isolate suspected or confirmed patients, trace and quarantine their close contacts, educate the public on both food and personal hygiene, and alert and train health-care workers on compliance to infection control against emerging pathogens.

The Chinese Center for Disease Control and Prevention (China CDC) issued an epidemic update and risk assessment of COVID-19 in late January. [4] The document describes evidence of what is known about the causative pathogen, the epidemiology and clinical features of the illness, diagnosis and management essentials, and public prevention measures. The CDC provided practical guidance for the public to protect themselves from the infection, including a recommendation that travelers avoid all nonessential travel to China (on Jan 27, 2020).[5]

Molecular Characterization

Within only one month from the detection of the incident case, several Chinese scientists isolated the virus, sequenced its full-length genome and described its specific morphology. The initial genome sequence was shared with the WHO on January 12, 2020. Several investigative teams have independently isolated and characterized the viral genome, and the sequences were made publicly available on the Global Initiative on Sharing All Influenza Data [GISAID] platform (https://www.gisaid.org).

Zhou et al. showed that COVID-19 shared 79.5% sequence identity with SARS-CoV. It was then isolated from the bronchoalveolar lavage fluid of a critically ill patient and was found to be neutralized by sera from similarly infected patients. It was also confirmed that COVID-19 uses the same cell entry receptor, angiotensin converting enzyme 2 as SARS-CoV, which is highly expressed in airway epithelial cells. [6]

Zhu et al. also identified and characterized COVID-19. They reported the isolation of the virus and provided the initial description of its specific cytopathic effects and morphology. COVID-19 seems to be the seventh member of the family of coronaviruses that infect humans. Notably, COVID-19 grew more readily in primary human airway epithelial cells than in standard tissue-culture cells, unlike SARS-CoV or MERS-CoV, suggesting the potential for increased infectivity.[7] Homology modelling revealed that COVID-19 had some amino acid variations at key residues benchmarked with SARS-CoV.[8] It is not clear whether these changes lead to the facilitation of virus infection.

The information produced by this research allows the medical and scientific community to better understand the transmission of COVID-19, to develop rapid diagnostic tests and efficient epidemiological control, and to facilitate the development of antiviral therapies and vaccines.

Clinical Features

Ren and colleagues reported the clinical manifestations of the infection caused by the novel bat-origin species of human infected CoV virus, including its' potential lethality.[9] On January 24, Huang et al. reported in *The Lancet* on the epidemiological, clinical, laboratory, radiological characteristics, treatment and outcomes.[10] An understanding of the clinical features will help clinicians to recognize these patients and minimize the risk of exposure to others. It was inferred that the target cells might be in the lower airway, due to features of the presentation, such as the lack of prominent upper respiratory tract signs and symptoms and the ground-glass opacities on chest CT images. Older males with comorbidities have been reported to have more severe and even fatal respiratory diseases.[11] Additional studies will help in assessing for host risk factors for disease severity and mortality. Laboratory evaluation has found lymphopenia in 63% patients and a cytokine storm profile in those who are critically ill. The combination of viral replication in the lower respiratory tract and an aberrant immune response may have an impact on the severity of illness, similar to what has been proven in SARS and MERS.[10] Translational research may discover biomarkers and other co-factor triggers in infected patients with different risk stratification.

A familial cluster of pneumonia due to COVID-19 was reported. This finding is consistent with person-to-person transmission, highlighting the risk of spread, which is further supported by reports of infected travelers in other geographical regions.[12] In the last two weeks of January, 13 children were diagnosed, fortunately with a mild clinical presentation. This information suggests the possibility that coronavirus transmission is evolving. The basic reproductive number of COVID-19 was estimated to be 2.2,[13] lower than that of SARS-nCoV (around 3).[14] However, host virus interactions may hasten the birth of potential super-spreaders, leading to major outbreaks.

Treatment of Coronaviruses

Due to the severe lung injury caused by SARS-CoV or MERS-CoV, patients who were infected and required invasive mechanical ventilation and extracorporeal membrane oxygenation had a very high mortality. [2,3,15] Unfortunately, no specific coronavirus antivirals or vaccines have been proven to be effective. In a historical control study, a combination of protease inhibitors, lopinavir and ritonavir, was associated with substantial clinical benefit among SARS-CoV patients.[16] Results from *in vitro* cell and *in vivo* animal studies suggest that a combination of lopinavir/ritonavir and interferon-β1(IFN-β1) may be effective against MERS-CoV. A placebo-controlled trial of IFN-β1 and lopinavir/ritonavir was initiated in patients with laboratory-confirmed MERS requiring hospital admission in Saudi Arabia.[17] Remdesivir, a 1'-cyano-substituted adenosine nucleotide analogue prodrug with broad-spectrum antiviral activity against several RNA viruses, may be evaluated.[18] The first reported patient with COVID-19 infection in the United State was administered remdesivir. Based on worsening clinical status, intravenous remdesivir was given for compassionate use on hospital day 7 (illness day 11). [19] A Randomized controlled trial has been registered to evaluate the safety and efficacy of remdesivir in patients with COVID-19 viral pneumonia (NCT 04252664). Robert and Andrew noticed non-structural proteins (nsp)12 polymerase may be a template for the design of novel antiviral therapeutics to interrupt the assembly of the SARS-CoV core RNA-synthesis machinery.[20] COVID-19 has full-length genome sequences with more than 75% nucleotide identity with that of SARS-CoV[7], which allows the molecular structure information to be used as a model for CoV antiviral design. Clinical studies should assess the effectiveness and safety of monoclonal and polyclonal neutralizing antibody products and aim to discover therapeutic targets against immunopathologic host responses.

China established an effective detection network in response to an outbreak of infectious diseases after the SARS pandemic. It is of great significance to share what is known of COVID-19 genome sequences, the epidemiology and clinical features of the illness. In the era of social media, when an epidemic occurs, a lot of misinformation is available.[21] Hopefully, the early suggestion that COVID-19 infection is of lower lethality than SARS holds true. In contrast, a low health threat on the individual level means there is potential to cause disruptions of global public health systems and a long duration of person-to-person transmissibility. Mild illnesses and asymptomatic carriers may be potential sources of infection, sustaining a local epidemic and global spread. To reduce panic and economic loss, and to manage and save the infected, a lot still needs to be done. The goal is to break the transmission chain of COVID-19. This will require effective programs to trace, diagnose and cure every infected patient. We all need to be aware of the risks of another zoonotic virus crossing species to infect the human population in the future. It is of great imperative that we call for global action to deal with this major public health emergency.

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