

# Editorial

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## COVID-19 Pandemic - An Apocalypse of Our Time

Hundreds of coronaviruses naturally circulate in a variety of mammals but there are only 7 known human coronaviruses which probably originated from bats. Four of these viruses 229E, NL63, OC43, and HKU1 are endemic that commonly cause relatively mild cold-like illnesses while the other 3 have caused outbreaks and epidemics namely the SARS-CoV in 2002-2003, MERS-CoV in 2012 and the SARS-CoV-2 that is responsible for the current pandemic Covid-19. The three coronaviruses that caused the epidemics belong to the *Betacoronavirus* genus.<sup>1,2</sup> Both SARS-CoV and SARS-CoV-2 viruses share the angiotensin converting enzyme ACE2 as receptor for attaching to and infecting pneumocytes in the lungs, however, MERS-CoV/SARS has a different receptor called dipeptidyl peptidase 4 (DPP4 or CD26) found in non-ciliated bronchial cells and in kidney cells. MERS has the highest case fatality rate of about 30% while SARS has a case fatality rate of about 10% and Covid-19 has an estimated crude global fatality rate of about 4.6% (26494 deaths/571678 cases) with most deaths affecting older age group and those with risk factors. As for the ability of person to person spread, MERS has the lowest potential and Covid-19 the highest.<sup>2,3</sup>

A plethora of research articles, editorials and reports have already been published about this novel coronavirus appropriately designated as SARS-CoV-2 which seems to have suddenly emerged from bats as reservoir host and infected the pangolin as an intermediate mammalian host, that is considered as a delicacy in China, from which it probably infected humans and successfully maintained itself by human to human transmission with an estimated rate of transmission of infection (R0) of about 2.2 in a naïve population with no immunity.<sup>4</sup> This implies that once the infection is established in a community where random transmission occurs, it will follow a logistic model curve where it spreads exponentially by a certain factor unless prompt effective measures are taken to interrupt the chain of transmission or a large proportion of the population become immune (herd immunity) as a result of infection or vaccination. Since a vaccine is not yet available, only transmission chain interruption measures will mitigate the epidemic by flattening

and broadening the peak of the COVID-19 curve and thus lessen the disruptive impact on the community. This provides the health services time to prepare and continue functioning without being overwhelmed. It will also provide scientists and clinical investigators sufficient critical time for the development and testing of therapeutic drugs and vaccines.

However, containing the infection and aborting the epidemic requires immediate drastic measures as successfully demonstrated in China by active detection and tracing infections and interrupting all man-to-man transmission by strict quarantine and disinfection measures at multiple levels. Similar measures were successful in not only curtailing but also in eradicating the SARS epidemic within 2 years. Although the heaviest toll by cumulative number of confirmed cases and deaths was initially in China, the USA and western Europe have now exceeded China as the new epicenters of the infection while other countries are still struggling with the rapidly rising number of confirmed cases and associated mortalities. This situation is mainly due to delays in the authority's reaction to the pandemic. The delays were probably driven mainly by fear of economic losses but unfortunately it has caused and will continue to cause not only more economic losses but more importantly loss of precious human lives.

The variably reported fatality rates by different countries until now are not representative of true 'case fatality' rates due to the lack or limited active mass screening that will allow detection of mild or subclinical infections. Thus, much higher mortality rates are reported in countries like Italy as compared to S. Korea where more active mass screening tests were employed. Differences in fatality rates may also be due to variation in virulence of the virus strains but this requires further verification. Mass screening by the relatively expensive and labor-intensive nucleic acid amplification assays would detect new cases and provide valuable information about the incidence of the disease. The relatively less expensive and automated serological tests would supply further important information about the epidemiology of the disease, but reliable approved tests are not yet commercially available.

COVID-19 should be taken extremely seriously by all countries and all groups and individuals. As of 30<sup>th</sup> March, the total number of cases worldwide had exceeded 737,900 with >35,000 deaths. In Malaysia, the total number of confirmed cases is steadily rising and stands at more than 2000. Nationwide movement control order is currently in force till 14<sup>th</sup> April, 2020.

WHO has also nicknamed the COVID-19 pandemic as “Infodemic” due to the widespread misinformation and sometimes incorrect data or interpretation of data. The abrupt emergence and spread of the virus since December 2019 have raised speculations among the public and even scientific media as to its origin and timing. There are plenty of stories and views about conspiracies related to biological warfare research in USA and China as means for destroying the economy and hence weakening political and military power. These baseless views have been and are still expressed and circulating in the news and social media. Although bioengineered weapons of mass disruption ‘if not destruction’ is a realistic worry that has been made more plausible and relatively easily practicable with the current huge advances in biotechnology, one should not overlook the fact that microorganisms like viruses and bacteria are better genetic engineers than molecular biologists as can be depicted from history. Many of these organisms can adapt, overcome new constraints on their successful survival and propagation and even jump to new hosts by modifying their genomes through mutations and genetic recombination. The SARS-CoV-2 virus has already undergone mutations within a short time since its first appearance in the epicenter Wuhan in mainland China. The two SNP (single nucleotide polymorphism) types are labeled L and S with differences in prevalence and pathogenicity.<sup>2</sup>

In conclusion the COVID-19 pandemic is still controllable, although not containable for most countries. This requires global political, social and personal commitment to take appropriate measures to stop the chain of transmission. Knowing the mode of transmission which is mainly by droplet infection that travel short distances of not more than 2 meters, more recent research has shown some worrying data that the virus can survive on surfaces for periods ranging from hours to days and that the virus may remain viable as airborne droplet nuclei for a period of few hours which may explain the relative ease with which it spreads.<sup>4</sup> These data would entail

paying more attention at the importance of personal hygiene and modifying personal habits, increasing frequency of sanitizing or disinfecting surfaces, abolishing gatherings and minimizing socialization and unnecessary travel especially by public transport. These measures probably need to be propagated and continued for the near future even in countries where the epidemic has subsided because of the fear of reintroduction and respread especially if a new naturally modified strain of the virus emerges.

Vaccine candidates are under development utilizing reverse vaccinology (in silico) and machine learning tools to predict the components of the viral proteome that would serve as safe and effective vaccines.<sup>5</sup> Also various known antiviral drugs that interfere with the function of the viral RNA-dependent RNA-polymerase, protease inhibitors that affect the cleavage of the viral polyprotein into functional polypeptides and the antimalarial drug hydroxychloroquine that interfere with early phases of the viral replication have been tested and were found to be effective in in-vitro studies. Currently some of these agents are directly subjected to clinical trials as they are previously known and approved drugs for other infections.<sup>6</sup> Convalescent serum from recovered patients has also been shown to protect cultured cells from infection and may also be effective in vivo if available. However, antiviral drugs for COVID-19 as is the case with other known respiratory viral infections such as influenza probably need to be given early to beneficially alter the course of the disease. Addition of drugs that suppress the ‘cytokine storm’ in ARDS patients are also been considered.

There is no magic pill. It will take several months for a reliable and effective vaccine to be developed and at least a year for it to be available for mass use. This pandemic in the interim can result in a global apocalypse as evidenced by its adverse impact not only on the health sector but crucially on the socioeconomic status worldwide from the most affluent to the poorest of nations.

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