

COVID-19: A New Pandemic

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In November-December 2019, a novel respiratory disease emerged in Wuhan China, which rapidly spread within China and then spread globally to cause the most severe pandemic to afflict humans for at least a hundred years, i.e. since the 1918 “Spanish flu”. Within 5 months (as of 31st of May 2020) it has caused over 6 million confirmed cases and over 360,000 deaths. Countries with major international air-travel hubs (i.e. Europe and North America) were affected early but no continent or country is likely to be spared in the months ahead. The causative agent is a new coronavirus closely related to SARS which emerged out of China in 2003 and has been designated SARS coronavirus 2 (SARS-CoV-2), while the disease is named coronavirus disease 2019 (COVID-19).^{1,2}

Four coronaviruses are already endemic in humans, 229E, OC43, HKU-1 and NL-63, largely causes of mild upper respiratory illness. Two novel coronaviruses SARS-CoV in 2003 and MERS-CoV in 2013 emerged from animals, bats and dromedary camels respectively, to cause more severe respiratory diseases in humans. It is now known that the endemic human coronaviruses 229E and OC43 also jumped from animals (camels and cattle respectively) to humans within the past few hundred years, but are now endemic world-wide.³ Thus coronaviruses, like pandemic influenza, have the capacity to successfully cross species to become epidemic in humans. Both SARS-CoV and SARS-CoV-2 have ancestrally closely related viruses in Rhinolophid bats.⁴ SARS-CoV crossed from bats to humans via intermediate mammalian species (civet cats, racoon dogs) in the wild-game animal markets in Southern China. The means by which SARS-CoV-2 adapted to humans is less clear but it may have also had an intermediate host before adaption for transmission in humans.

The main modes of transmission are infected respiratory droplets and fomites. Coughing, sneezing or even breathing, can generate infected respiratory droplets which may travel a few meters and may deposit on the eyes, nose or mouth of a susceptible individual, leading to transmission of disease. The virus is known to remain viable on smooth surfaces (stainless steel, glass, plastic) for many days and therefore hands touching such contaminated surfaces may transfer the virus to the nose, eyes or mouth.⁵ Thus it is important to be aware of the risk of transfer of virus by contaminated hands, especially when in crowded places such as public transport. Avoiding touching your eyes, nose and mouth until you have an opportunity to effect hand hygiene is an important preventive measure. It is now known that transmission can occur prior to a patient developing symptoms and even from asymptotically infected persons who may never develop symptoms.⁶ Although there is no experimental evidence from SARS-CoV-2, studies on other human coronaviruses have shown that surgical masks reduced the spread of infected respiratory droplets⁷. This is the rationale for now recommending face-coverings in the community, i.e. not to protect oneself from infection, but more to protect others from your own respiratory droplets in case you are asymptotically infected.

Since transmission may occur prior to onset of clinical symptoms, the role of rapid diagnosis and contact tracing becomes critical if chains of transmission are to be interrupted. Social distancing is also proven to reduce transmission, because it prevents the virus finding uninfected persons to maintain itself in an ongoing chain of transmission.

The disease spectrum can range from asymptomatic infection to severe viral pneumonia leading to acute respiratory distress syndrome and

death but a range of atypical presentations may occur, including diarrhoea.¹⁸ The incubation period may range from 2-14 days (median 4-6 days) and initial presenting symptoms include cough, shortness of breath or difficulty breathing, fever, chills, muscle pain, sore throat and loss of taste or smell. Children and young adults have asymptomatic or mild infections but may transmit infection to others. Age and underlying co-morbidities such as hypertension, cardiovascular disease, diabetes and obesity are associated with adverse clinical outcome. Factors associated with a more severe outcome include lymphopenia, elevated D-dimer levels and a high Sequential Organ Failure score. Thrombotic events are being increasingly recognised in patients with severe disease and death⁹.

Virological diagnosis is best confirmed by detection of virus RNA by RT-PCR assays in throat and nose swabs, sputum or endotracheal aspirates from patients who are intubated¹⁰. Deep throat saliva has been used as a less invasive self-collected specimen for surveillance purposes¹¹. Though less sensitive as a clinical specimen, it has advantages as a specimen that can be self-collected by the patient with no infection risk to health-care workers carrying out surveillance in community settings. Antibody responses appear towards the end of the first week of illness and are not ideal for early diagnosis of cases.¹² However, serology has a place in sero-epidemiological investigations, and perhaps in deciding on discharge of patients from isolation (see below).

Infected patients can have viral RNA detected from the respiratory tract, and sometimes, the gastro-intestinal tract for 3-4 weeks or sometimes longer.¹¹ The conventional criteria for discharge of patients from hospital isolation has been two consecutive negative RT-PCR test results with at least 24 hours between them. But since recovered patients may have detectable virus by RT-PCR for many weeks thereafter, discharge of patients may be difficult and led to a shortage of isolation beds for those who need it most, i.e. those in early stages after onset of symptoms. It is clear that transmission is maximal just prior to symptom onset and in the first few days after symptom onset. Thus, Hong Kong is now considering release of patients from isolation if the patient is

clinically fit for discharge, at least ten days have passed since the onset of illness, and either two clinical specimens of the same type (i.e. respiratory or stool) have tested negative for RT-PCR for SARS-CoV-2 taken at least 24 hours apart or have tested positive for SARS-CoV-2 antibody even if RT-PCR remains positive at low viral load (RT-PCR CT values >34).¹³ The rationale for this decision is that a) infectious virus cannot be cultured from patients after 9 days after onset of illness even though RT-PCR may remain positive¹⁴ and b) antibody responses generally develop around 10-14 days after onset of symptoms which is likely the reason why virus cannot be cultured (i.e. is non-infectious) even if RT-PCR remains positive.^{12,14}

In the early phases of this pandemic, there were no proven antiviral therapeutics but there was no shortage of claims, often poorly substantiated, or supported by poorly conducted clinical trials. It is important to carefully assess evidence that is presented in support of such antiviral therapies, especially since, with good symptomatic and supportive care, the overall case fatality is relatively low. Overall case fatality in Wuhan was estimated to be 1.4% but those above 59 years were 5.1 times more likely to die than those aged 30-59.¹⁵

Although social distancing measures and “lock-downs” may suppress virus transmission in a community¹⁶, the threat of re-emergence from hidden foci of infection or re-introduction from other affected countries will continue to pose a threat to public health. As this is a novel virus, the human population has no immunity to it and remain highly susceptible to infection. The pandemic will only be contained once adequate “herd immunity” has developed in the population (i.e. 50-60% of the population is immune) and this can only occur through natural infection or vaccination. Since neither of these are on the short-term horizon, we need to accept that we are in a longer-term containment phase with the virus. This it is important to maintain sustainable social distancing measures that can be applied for many months more. Vaccines, though some are in phase 1 clinical trials, are unlikely to be available until next year, at the earliest.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *New England Journal of Medicine* 2020;20:382(8):727-733. <https://doi.org/10.1056/NEJMoa2001017>
2. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, et al. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nature Microbiology* 2020;5(4):536-544. <https://doi.org/10.1038/s41564-020-0695-z>
3. Corman VM, Eckerle I, Memish ZA, Liljander AM, Dijkman R, Jonsdottir H, et al. Link of a ubiquitous human coronavirus to dromedary camels. *Proceedings of the National Academy of Science of the United States of America* 2016;30:113(35):9864-9. <https://doi.org/10.1073/pnas.1604472113>
4. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579(7798):270-273. <https://doi.org/10.1038/s41586-020-2012-7>
5. Chin AWH, Chu JTS, Perera MRA, Hui KPY, Yen HL, Chan MCW, et al. Stability of SARS-CoV-2 in different environmental conditions. *Lancet Microbe* 2020;20. [https://doi.org/10.1016/S2666-5247\(20\)30003-3](https://doi.org/10.1016/S2666-5247(20)30003-3)
6. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature Medicine* 2020;26:672-675. <https://doi.org/10.1038/s41591-020-0869-5> [Epub ahead of print]
7. Leung NHL, Chu DKW, Shiu EYC, Chan KH, McDevitt JJ, Hau BJP, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine* 2020;26:676-680. <https://doi.org/10.1038/s41591-020-0843-2>
8. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;15:395(10223):507-513. [https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)
9. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. *Annals of Internal Medicine* 2020 May 6. <https://doi.org/10.7326/M20-2003> [E pub ahead of print]
10. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Eurosurveillance* 2020;25(3). <https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045>
11. To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infectious Diseases* 2020;20(5):565-574. [https://doi.org/10.1016/S1473-3099\(20\)30196-1](https://doi.org/10.1016/S1473-3099(20)30196-1)
12. Perera RA, Mok CK, Tsang OT, Lv H, Ko RL, Wu NC, et al. Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020. *Eurosurveillance* 2020;25(16). <https://doi.org/10.2807/1560-7917.ES.2020.25.16.2000421>
13. Centre for Health Protection, Hong Kong Special Administrative Regions, China. 6th May 2020. <https://www.info.gov.hk/gia/general/202005/06/P2020050600679p.htm>
14. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;581:465-469. <https://doi.org/10.1038/s41586-020-2196-x> [Epub ahead of print]
15. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nature Medicine* 2020;26(4):506-510. <https://doi.org/10.1038/s41591-020-0822-7>
16. Cowling BJ, Ali ST, Ng TWY, Tsang TK, Li JCM, Fong MW, et al. Impact assessment of non-pharmaceutical interventions against coronavirus disease 2019 and influenza in Hong Kong: an observational study. *Lancet Public Health* 2020;5(5):e279-e288. [https://doi.org/10.1016/S2468-2667\(20\)30090-6](https://doi.org/10.1016/S2468-2667(20)30090-6)