SARS-CoV-2: virus dynamics and host response

Since December, 2019, coronavirus disease 2019 (COVID-19) has affected more than 100 000 patients globally.[1] COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has a case-fatality rate of 2·3%, with higher rates among elderly patients and patients with comorbidities.[2] Person-to-person transmission is efficient, with multiple clusters reported. Clinically, patients with COVID-19 present with respiratory symptoms, which is very similar to the presentation of other respiratory virus infections. Radiologically, COVID-19 is characterised by multifocal ground-glass opacities, even for patients with mild disease.[3]

Knowledge of virus dynamics and host response are essential for formulating strategies for antiviral treatment, vaccination, and epidemiological control of COVID-19. However, a systematic study on these aspects has not been done. In *The Lancet Infectious Diseases*, Kelvin To and colleagues[4] report the viral load and antibody profiles of a cohort of 23 patients admitted to hospital with COVID-19. In these patients, the viral load peaked during the first week of illness then gradually declined over the second week. Viral load was also shown to correlate with age. Furthermore, both IgG and IgM antibodies started to increase on around day 10 after symptom onset, and most patients had seroconversion within the first 3 weeks. Finally, the IgG and IgM antibody level against the SARS-CoV-2 internal nucleoprotein and the surface spike receptor binding domain correlated with neutralising activity.

These findings have several practical implications. First, the high viral load during the early phase of illness suggests that patients could be most infectious during this period, and it might account for the high transmissibility of SARS-CoV-2. Furthermore, the high viral load on presentation suggests that SARS-CoV-2 could be susceptible to emergence of antiviral resistance. Second, age was associated with viral load in this study, which could explain the high degree of severe disease in older patients with SARS-CoV-2.[5,6] The high viral load in elderly patients is associated not only with low immunity but also with high expression of the ACE2 receptor (the cell-entry receptor for SARS-CoV-2) in older adults.[7] The timing of antibody seroconversion is crucial for determining the optimum timepoints for collecting serum specimens for antibody testing for diagnosis. Furthermore, this information is important for immunologists to choose the best timepoints for obtaining peripheral blood B cells for development of therapeutic monoclonal antibodies.[8]

The major strength of the study by To and colleagues is the systematic analysis of the serial viral load and antibody profile for up to 4 weeks, which provides insights into viral and host interactions during the acute and convalescent phases. Another notable aspect is that self-collected posterior oropharyngeal saliva samples were used, instead of nasopharyngeal specimens, for viral load monitoring. Collection of nasopharyngeal specimens is an invasive procedure, and it is uncomfortable for the patient and poses an infection risk to health-care workers. Self-collected saliva is much more acceptable to patients and is safer for health-care workers. This study clearly shows the feasibility of using saliva for viral load monitoring.

The information provided by To and colleagues is solid scientific evidence on COVID-19 for clinicians and scientists. Nonetheless, many questions are still outstanding on the viral characteristics and host response during infection. SARS-CoV-2 has been detected in faeces, blood, and urine samples,[9,10] and it is important to ascertain viral load dynamics in such samples, for prevention and control of the pandemic. Furthermore, the relation between viral load and disease severity needs to be further clarified. Studies with a larger sample size are needed to understand how different factors can affect viral load or antibody response. For example, immunocompromised patients might have higher viral load, prolonged viral shedding, and impaired antibody response. Future studies in the paediatric population are vital, because children seem to have much milder disease than in adults. Finally, a more detailed understanding of the innate and adaptive immune response against SARS-CoV-2 is important for understanding the pathogenesis and for designing vaccines.

We declare no competing interests.

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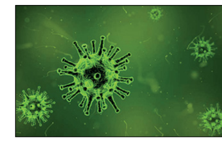

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1 WHO. WHO statement on cases of COVID-19 surpassing 100 000. March 7, 2020. https://www.who.int/news-room/detail/07-03-2020-who-statement-on-cases-of-covid-19-surpassing-100-000 (accessed March 13, 2020).
2 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.
3 Chan JF-W, Yuan S, Kok K-H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020; **395:** 514–23.
4 To KK-W, Tsang OT-Y, Leung W-S, 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 Infect Dis* 2020; published online March 23. https://doi.org/10.1016/S1473-3099(20)30196-1.
5 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; published online March 11. https://doi.org/10.1016/S0140-6736(20)30566-3.
6 Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020; **368:** m606.
7 Chen Y, Shan K, Qian W. Asians do not exhibit elevated expression or unique genetic polymorphisms for ACE2, the cell-entry receptor of SARS-CoV-2. Feb 25, 2020. https://www.preprints.org/manuscript/202002.0258/v2 (accessed March 13, 2020).
8 Lu S. Timely development of vaccines against SARS-CoV-2. *Emerg Microbes Infect* 2020; **9:** 542–44.
9 He Y, Wang Z, Li F, Shi Y. Public health might be endangered by possible prolonged discharge of SARS-CoV-2 in stool. *J Infect* 2020; published online March 5. DOI:10.1016/j.jinf.2020.02.031.
10 Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA* 2020; published online March 3. DOI:10.1001/jama.2020.3204.

Contact precautions: no benefits, no indication

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In view of the global increase in multidrug-resistant bacteria, applying contact precautions during the care of affected patients seems, at first, a rational approach to decrease the spread of these organisms. Increasing the distance between sources of multidrug-resistant organisms and potential recipients and using disposable equipment, such as gloves and gowns, for any contact with the patient and their environment might appear to be logical and harmless precautions. However, as a growing body of evidence has shown, contact precautions do harm. A number of detrimental effects have been reported, including decreased contact with health-care workers, increased frequency of adverse events, and self-reported feelings of stigmatisation and reduced self-esteem.[1,2] Furthermore, contact isolation in single-bed rooms can put hospitals under organisational constraints that might negatively affect patient care. Considering these well studied and far-reaching consequences, validating the potential beneficial effects of contact precautions in clinical trials such that evidence-based recommendations can be made seems crucial.

In *The Lancet Infectious Diseases*, Friederike Maechler and colleagues[3] report on a multicentre cluster-randomised crossover trial comparing standard precautions to contact isolation for preventing the acquisition of extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E). Contact precautions included accommodation in single-bed rooms, side rooms, or cohorting, and the wearing of gloves and gowns for any encounter with the patient or their surroundings. Four hospitals and 20 non-intensive care wards contributed patients to the study. The authors were able to document as many as 38 357 patients admitted to the wards during the study period, of whom 11 368 had a length of stay of more than 1 week and were included in the per-protocol analysis. The results from the main analysis and associated sensitivity analyses are clear: contact isolation did not decrease the number of hospital acquisitions of ESBL-E. Of note, 1543 (73·4%) of 2101 cases of ESBL-E reported on admission or during the study were ESBL-producing *Escherichia coli*.

Being the first multinational cluster-randomised study on the topic, we believe that the study should be seen as a crucial addition to the current evidence base on the widely debated issue of the need for contact precautions.[4] Unlike previous studies, both medical and surgical wards were included and adherence to contact precautions was assessed in detail.[5,6]

However, some limitations of the study should be recognised. A median laboratory turnaround time of 4 days (IQR 3–5) led to a delay in the reporting of ESBL-E-positive samples and, thus, in the implementation of contact isolation. This delay is reflected in the considerable proportion of ESBL-E-positive patient days during which contact precautions were not in place (6040 [32%] of 18 698). However, this lag in detection