The important role of serology for COVID-19 control

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Lancet Infect Dis 2020

Published **Online** April 21, 2020 https://doi.org/10.1016/S1473-3099(20)30322-4

See **Online/Articles** https://doi.org/10.1016/S1473-3099(20)30273-5

As of April 14, 2020, just under 2 million cases of coronavirus disease 2019 (COVID-19) have been reported worldwide.[1] With the pandemic growing at an alarming rate and national governments struggling to control local epidemics because of scant diagnostics and impermanent non-pharmaceutical interventions, we should look to additional epidemiological solutions. Locations such as Singapore and Taiwan have been successful in slowing epidemic growth by using intensive surveillance with broader testing strategies to identify and contain cases.[2,3]

In *The Lancet Infectious Diseases*, Sarah Ee Fang Yong and colleagues[4] report three clusters of COVID-19 cases identified in Singapore in early 2020 by active case-finding and contact tracing and confirmed with RT-PCR. One cluster from a church (Church A) was previously identified[5] and linked to two imported cases from Wuhan, China. The two additional clusters (Church B and a family gathering) were attributable to community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by one individual interacting with both clusters. Serological platforms were developed and assessed for confirmation of SARS-CoV-2-specific antibody responses to capture past infections. By serological analysis, Yong and colleagues identified the missing link between the Church A cluster and the other two clusters—an individual who had twice tested negative by RT-PCR. By linking all three clusters, Yong and colleagues highlight the success of such surveillance measures to capture many cases and effectively slow the spread of COVID-19 in Singapore.

This investigation exemplifies the failings of RT-PCR as a sole diagnostic method in surveillance, because of its inability to detect past infection, and the added value of serological testing, which if captured within the correct timeframe after disease onset can detect both active and past infections.[6,7] In public health practice, serological analysis can be useful for rapid case-identification and the subsequent chain of events to actively identify close contacts, recommend quarantine, and define clusters of cases. Contact tracing, which is a necessary but insufficient means of disease control, needs careful effort and is sensitive to timing to be effective, particularly in highly dense populations. As shown in Singapore, serological analysis can be useful for contact tracing in urban environments and linking clusters of cases retrospectively to delineate transmission chains and ascertain how long transmission has been ongoing or to estimate the proportion of asymptomatic individuals in the population.

Beyond the immediate use of serological data to identify and contain cases, these data can also be used to set control policies. Population serological testing (specifically measuring SARS-CoV-2-specific IgG antibody titres) can estimate the total number of infections by assessing the number of individuals who have mounted an immune response, regardless of whether an infection was subclinical or happened in the recent past (current data suggest antibodies persist for at least 4 weeks).[8] By providing estimates of who is and is not immune to SARS-CoV-2, serological data can be used in at least four ways. First, to estimate epidemiological variables, such as the attack rate or case-fatality rate, which are necessary to assess how much community transmission has occurred and its burden. Second, to strategically deploy immune health-care workers to reduce exposure of the virus to susceptible individuals. Third, to assess the effect of non-pharmaceutical interventions at the population-level and inform policy changes to release such measures, Fourth, to identify individuals who mounted a strong immunological response to the virus and whose antibody isolates can be used to treat patients via plasma therapy.[9]

Although the potential for serological assays to help control the COVID-19 pandemic is substantial, the complexity of developing and validating a diagnostic test is not fully elucidated by Yong and colleagues.[4] Serological assays are currently being developed for widespread use.[10] Yet, several challenges remain: first, assessing the sensitivity and specificity of tests, particularly for determining disease during the acute phase of infection; second, verifying the test is not detecting cross-reactivity with other viral pathogens that result in false-positive results; third, understanding antibody kinetics over time to distinguish thresholds of immunity, because we do not know how long immunity to this novel coronavirus might last; and finally, ensuring the test is reliable for distribution and is cost-efficient. Although RT-PCR diagnostics will still be vital for identifying acute infection, as the SARS-CoV-2 pandemic continues to spread and cases accumulate, serological testing and data will prove increasingly important to understand the pandemics' past and predict its future.

We declare no competing interests.

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