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CORRESPONDENCE

Antigen testing and non-infectious shedding of SARS-COV-2

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Dear Editor,

We read with great interest the article by Lanser et al. who studied the sensitivity of rapid antigen testing for SARS-CoV-2 in relation to the cycle threshold (Ct)—a semiquantitative surrogate of viral load obtained by real-time polymerase chain reaction (RT-PCR) [1]. The authors considered a Ct > 33 to be indicative of non-infectious shedding, based on unpublished CDC figure data (dated July 22nd) depicting a Ct > 33 as cut-off for non-replicable virus in cell culture. The authors found low number (16.7%) of positive antigen results in subjects with Ct value > 33, and therefore concluded that a negative antigen result in previously positive subjects could be leveraged "to determine the time point when they are no longer contagious".

We would like to highlight serious limitations of Lanser et al.'s findings and conclusions. First, a statistical comparison of the antigen test results for subjects with Ct above or below 33 is not reported. Second, SARS-Cov-2 Ct values vary considerably between and within platforms, laboratories, and target genes [2]. The quoted CDC data pertain to the N1–N3 genes, while the study's cobas® platforms targets the ORF1-gene. Using the Applied Biosystems 7500 FAST system that targets the ORF1-gene, Ladhani et al. found a Ct > 35 as the cut-off for uncultivable virus [3]. Moreover, the CDC omitted any allusion to the aforementioned data in its October 19th update. Third, while RT-PCR is a highly sensitive method, its sensitivity for SARS-CoV-2 is only ~ 70%, and experts recommend at least two negative swabs prior to ruling out SAST-Cov-2 infection [4]. The authors did not provide any data regarding antigen test results in patients with negative RT-PCR swabs. These data are essential to accurately determine the sensitivity and specificity of the antigen test, assess a plausible correlation between antigen test results and Ct, and correctly inform infection control and public health policies. By limiting antigen testing to hospitalized RT-PCR positive subjects alone, the authors most likely overestimated the true sensitivity of the antigen assay, and were unable to estimate its specificity. Lastly, ample data suggest that Ct values should be interpreted in the clinical context of symptom-onset to test time-interval, as well as illness severity [5–7]. Since all the samples were obtained from hospitalized COVID-19 patients, the study findings are strongly biased toward severe illness, and may not equally apply to public screening as proposed by the authors. Furthermore and as acknowledged by the authors, for a given Ct value—infectivity is much more probable when a swab is obtained at the onset of symptoms, rather than when taken 10 days later. Yet, the authors provided no data regarding the days from onset of symptoms to testing, and they grouped Ct values irrespective of this clinically important variable. While we agree with the authors that "antigen tests… might be suitable and effective for rapidly identifying infectious subjects with symptoms compatible to a COVID-19 infection", studies addressing these limitations will further support the wide-spread implementation of antigen tests.

We agree with the authors that a rapid test with a high sensitivity and specificity for SARS-CoV-2 infection and infectivity would benefit public and occupational health policies, as well as and infection control guidelines.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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