Canadian Public Health Laboratory Network Statement on Point-of-Care Serology Testing in COVID-19

Respiratory Virus Infections Working Group[1]

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Introduction

Point-of-care (POC) serology tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), detect the human antibody response to infection or vaccination and not the virus itself. Most are qualitative immunochromatographic (lateral-flow)-based assays that detect IgG+/-IgM from a finger prick blood sample and can provide results in less than 30 minutes. While there is widespread interest in adopting POC serology tests for COVID-19, there are currently significant limitations to this testing modality, including the incomplete understanding of the immunological response in COVID-19, suboptimal clinical validation data, uncertain correlation (or lack thereof) with clinical laboratory-based serology tests and wide variability in performance among different POC tests. Many of the key points outlined below also apply to laboratory-based COVID-19 serology testing.

Current position for acute diagnostics

Serology POC tests for COVID-19 are not recommended for use as a diagnostic tool for acute infection and only three products are approved by Health Canada to date. In general, these tests are not able to detect antibodies until at least a week or more after symptoms have started, and therefore are not suitable for diagnosis of acute SARS-CoV-2 infection at this time. We recommend that nucleic acid detection (e.g. real-time polymerase chain reaction) remain the first line test for the diagnosis of acute SARS-CoV-2 infection, as advised by the World Health Organization (1).

Key points

- It can take at least 7–14 days, and sometimes longer, after symptom onset for antibodies to develop, therefore the use of serology POC tests in the early phase of infection can result in a false negative COVID-19 diagnosis at a time when patients are most infectious (i.e. a negative result does not rule out infection).
- False negative interpretations may occur in elderly and immunocompromised patients, who are unable to mount an adequate antibody response.
- Since serology POC tests do not detect virus, a positive or negative result does not determine whether a person is infectious.
- Positive results may be due to past or recent infection with SARS-CoV-2 or from COVID-19 vaccination.
- Most POC serology tests are unable to differentiate antibodies developed from previous infection from those generated in response to COVID-19 vaccination. Given the rapid expansion of COVID-19 vaccination, this further limits the use of serology POC tests.
- As with other COVID-19 serological platforms, false positive results may occur if these kits cross-react with antibodies from recent or past exposure to other coronaviruses, including human coronaviruses.
- Other infections, as well as non-infectious conditions (e.g. rheumatoid factor-positive diseases), may also cause false positive results.
- False positive results are more likely in areas of low prevalence and low vaccine uptake. The local epidemiology and pretest probability of the individual (i.e. clinical and epidemiological risk factors) need to be taken into consideration when interpreting POC serology results.

- Due to the visual interpretations of most POC serology tests, false positive and negative results may arise from incorrect or subjective reading.
- As per recommendations from the National Advisory Committee on Immunization, there is no indication for serology prior to or after COVID-19 vaccination.
- Any kits used need to be thoroughly evaluated for performance characteristics (sensitivity, specificity) before being used clinically, including in-field use conditions.

An evolving and exceptional use for POC serology testing may be considered when laboratory-based serology testing is not available or is unable to meet the necessary rapid turnaround times to help identify COVID-19 patients most likely to benefit from anti-SARS-CoV-2 monoclonal antibody therapy. Serology testing currently has limited clinical utility; however, some jurisdictions have recommended its use to help inform treatment decisions for COVID-19 patients, as early clinical trial data showed that some monoclonal antibody therapies (e.g. casirivimab + imdevimab) were most effective in seronegative patients. Even in this context, we recommend that serology POC tests be performed in a laboratory setting to help mitigate some of the risks outlined above and validated before use as described below. When possible, laboratory-based SARS-CoV-2 serology testing is preferred.

Current position for use as "immunity certificates or passports"

There has been ongoing discussion around the use of antibody testing as evidence of immunity to facilitate individual movement in public areas and to permit international travel. The knowledge around immunity to SARS-CoV-2 is rapidly evolving; however, at this time, the correlates of protection and duration of immunity are not well understood. As such, we do not recommend using serology, including POC tests, for determining individual immunity or for establishing exemptions from public health measures.

Key points

- Since there is currently no correlate of protection, it is unknown if the levels of antibodies detected by serology POC tests are sufficient for protection.
- Since POC tests do not provide a quantitative result, their utility may be limited even once a correlate of protection is established.
- COVID-19 antibodies may persist for at least six months; however, the rate at which antibodies decline over time varies by age, immune status of the individual and severity of disease.
- Binding antibodies detected by serology POC tests may not correlate with neutralizing (i.e. protective) antibodies.
- Since it takes at least 7–14 days (longer in some individuals) to mount an antibody response, a negative result does not exclude an active infection or rule out infectiousness; therefore, it does not confirm that an individual cannot transmit SARS-CoV-2. Serology tests should not replace molecular (or antigen) testing for travel or other screening purposes.
- Although reinfection or infection after vaccination is relatively rare, a positive serology result does not guarantee protection from infection, especially with intense exposures and the emergence of SARS-CoV-2 variants that have immune escape potential.
- Since serology POC tests do not detect T-cell mediated immunity to SARS-CoV-2, which is also important for long-term protection, a negative result is not proof that an individual is not immune.
- Modelling has shown that public health measures, such as masking and physical distancing, will be required to control the spread of SARS-CoV-2 until the time that population vaccine coverage and adequate population immunity are achieved. Thus, a positive serology result, including from POC testing, may provide a false sense of protection from SARS-CoV-2 infection at the individual level.

Important considerations is implementing point-of-care testing

The role of serology in the diagnosis of SARS-CoV-2 infection, patient management and immunity testing is of limited utility. Once the dynamics of the serological response in COVID-19 are better understood and a correlate of protection is identified, serology may play an important role in the population-based public health response. If serology POC testing is implemented for a specific purpose (e.g. testing for monoclonal antibody treatment), the following should be considered:

- Extensive validation of the test(s) against a gold standard (viral neutralization assays or another laboratory-based serological assay). Performance characteristics (sensitivity, specificity, positive and negative predictive values, cross-reaction to other coronaviruses) should be established using sera from patients infected with SARS-CoV-2 (ancestral and variants), other respiratory viruses, including seasonal coronaviruses, and healthy controls.
- Provide adequate training to healthcare/laboratory workers to perform the test and interpret the result.
- Performing a risk assessment for infection with SARS-CoV-2 and bloodborne infections for the operator. We recommend that universal protective measures to prevent bloodborne pathogen transmission (at a minimum, gloves and gowns) be used when running POC assays until the risk to the operator can be formally assessed.
- Establishing an ongoing quality control/quality assurance program prior to implementation.

- Establishing provisions to ensure the capture of testing data for individual patient records and surveillance purposes and the requirement for participation in external quality assessment to maintain high-quality testing.

Based on currently available information, the Canadian Public Health Laboratory Network recommends that COVID-19 POC serological assays not be used for routine clinical or immunity testing at this time. In line with recommendations by the National Advisory Committee on Immunization (2), serology testing should not be used to document vaccination status or to assess response to COVID-19 vaccination. As more information becomes available on immunological correlates of protection, duration of immunity, test performance and assays are validated against gold standard serological methods, clinical application of POC assays will be re-evaluated. Molecular testing, such as real-time polymerase chain reaction, remains the primary test method for laboratory confirmation of acute SARS-CoV-2 infection and diagnosis of COVID-19.

References

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