National Collaborating Centre
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Understanding COVID-19 Antigen Tests

COVID-19 Antigen Tests can provide information on whether a patient is actively infected with SARS-CoV-2 by detecting its viral antigens.

This document provides a brief description of the Antigen Test. It provides basic information on how this test can be used in the diagnosis and surveillance of a pathogen such as SARS-CoV-2 virus, the cause of COVID-19 Pandemic.

What are antigens?

Antigens are molecules and proteins with unique surfaces that are recognized by the immune system as foreign and thus can activate the immune system. When recognized by the immune system, there is a series of reactions that lead to the recruitment and activation of immune cells to eliminate this foreign entity.

The SARS-CoV-2 virus has several antigens, including its nucleocapsid protein, phosphoprotein, and spike protein. Of these antigens, the nucleocapsid protein has been the most common candidate for antigen tests. The nucleocapsid protein is an early and accurate diagnostic marker for SARS-CoV-2 and can be detected as early as one day before symptoms appear (1,2). Consistently, the nucleocapsid protein is also one of the most produced proteins of the SARS-CoV-2 virus (3). Patients with active SARS-CoV-2 infection harbour the virus' antigens. Immunoassays known as antigen tests have been developed to detect SARS-CoV-2 infection by targeting its viral antigens.

How do most COVID-19 antigen tests work?

Antigen tests are designed based on lateral flow assays; an inexpensive technology that uses paper-based platforms to detect chemical analytes within short durations of time. To begin the test, a nasal swab is collected from the patient and soaked into an extraction solution that will disrupt the virus to release its antigen proteins. A liquid sample of this extraction is then applied to a test strip, where it will migrate through the paper strip and interact with SARS-CoV-2-antigen-specific antibodies that have been conjugated with luminescent indicators. If SARS-CoV-2 antigens are present in the sample, they will be captured by the antigen-specific antibodies and then seen as coloured lines on the strip test, indicating a positive test for COVID-19.

Result	Meaning	Interpretation & Action
Positive Test	SARS-CoV-2 antigen is detected in the patient sample.	Patient is actively infected with SARS-CoV-2. Immediate Public Health action required. Depending on the clinical context, patient may require a confirmatory RT-PCR test.
Nagative Test	No SARS-CoV-2 antigen detected in the patient sample.	Inconclusive information. Confirm with RT-PCR diagnostic test.

Applications for Surveillance

Nucleic Acid Amplification Test (NAAT), including RT-PCR, is the gold standard for diagnosing COVID-19 due to its high specificity and sensitivity. However, this type of testing requires extensive laboratory equipment, trained personnel, and results may be delayed. Although antigen tests have lower sensitivity, they tend to have equally high levels of specificity. Thus, antigen tests are an excellent tool for disease surveillance programs in local communities and at point-of-care (POC) settings. By screening populations for COVID-19, this public measure identifies potential sources of transmission and outbreaks as businesses, schools, and institutions begin to open up. Antigen tests are feasible for large-scale surveillance programs due to their ability to produce rapid results (20 minutes). According to the CDC, antigen tests are also effective screening testing in high-risk **congregate settings** (5) including **retirement homes** (6) and have contributed to the rapid identification and isolation of COVID-19 cases (Figure 1).

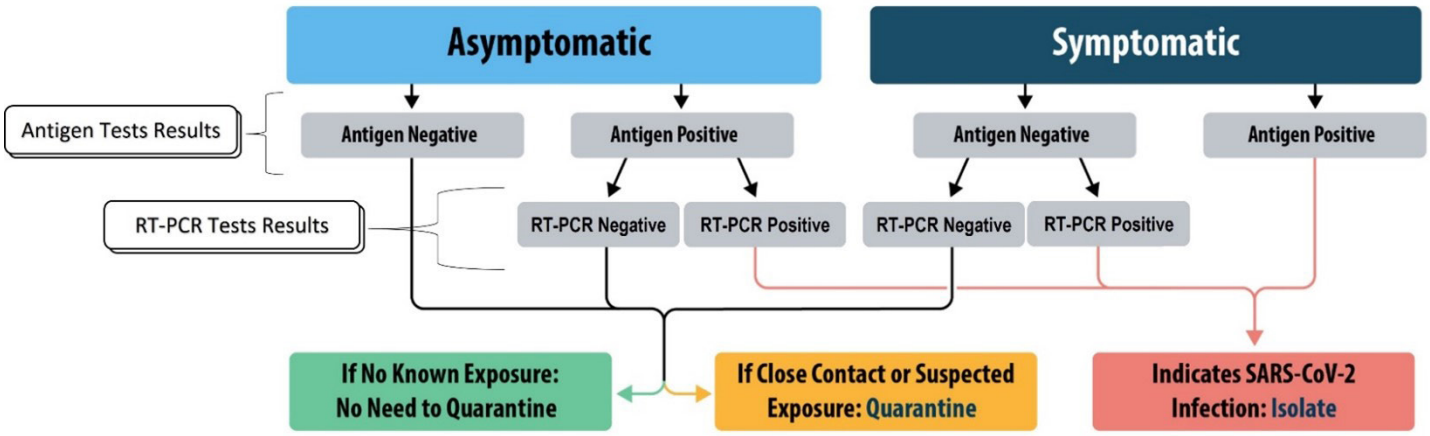

Figure 1. Antigen Test Decision Algorithm for Community Settings (Adapted from CDC)(4)

The value of antigen testing in SARS-CoV-2 disease surveillance was recently demonstrated in Slovakia. In October 2020, Slovakia started a population-wide antigen-testing campaign to identify and reduce transmission of COVID-19 (7). After two rounds of antigen testing, the country was able to reduce its infection prevalence by 58% across 45 counties within a week (8). To accomplish this, the government had to test 66% of its entire population in the first round of the campaign and then 62% in the second round (8). COVID-19 antigen tests were also considered valuable in hospitals, where test results are urgent for decision-making and patient management, in Brazil (9) and in Italy (10).

Despite their feasibility as a screening tool, antigen tests are still less sensitive than RT-PCR in diagnosing patients with low viral loads, as mentioned above. To mitigate this limitation, researchers and public health officers have suggested serial testing (i.e., repeated testing spread out at different time points) as an approach to offset the reduced accuracy of antigen tests (11). For example, one study found that serial testing of 43 adults via antigen tests and RT-PCR at 2-3 times per weeks were associated with improved test sensitivities at >98% compared to testing once per week (12). Likewise, past modelling studies have shown that test frequency was more important than test sensitivity in the prevention and mitigation of an outbreak (13,14). As antigen testing becomes available to the general public, it can be used for repeated testing in community and hospital settings to rapidly identify infected cases and reduce viral transmission (15,16).

What are the advantages and disadvantages of antigen testing?

Pros	Cons
• Inexpensive • Quick results • Increased frequency of testing is possible • Provides information on whether a patient is actively infected with SARS-CoV-2 • An accessible diagnostic test for distanced communities and at point-of-care • High specificity • Serial testing possible • Can be done outside of a laboratory • Does not requires a trained professional	• Different antigen tests have been shown to exhibit different levels of sensitivity (0-94%) and specificity (90-100%) compared to RT-PCR (17). • Lower sensitivity at low viral loads (i.e., antigen tests are not ideal for detecting infection at either early, asymptomatic or recovery stages of infection) • False positives have been reported due to improper use and/or when used for testing populations with low infection prevalence (18). • Misinterpretation of the visualized test results (i.e. faint band lines) can lead to false test results

Approved Antigen Tests Distributed by the Government of Canada

Several antigen tests have been approved by Health Canada and are available in an assortment of settings, including point-of-care settings, hospitals, pharmacies, businesses, federal organizations, and workplace settings. For more updates about antigen tests approved in Canada, check for updates at (**Link**)

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