AMA cautions about limitations of antibody testing for SARS-CoV-2

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CHICAGO — With a growing number of tests claiming to identify people who have been exposed to SARS-CoV-2 and potentially immune to COVID-19, the American Medical Association (AMA) today announced guidance to help ensure physicians and the general public are aware of the limitations and potential uses of serological testing, also known as antibody testing. Through the new guidance, the AMA cautions physicians and the general public about using these tests to determine individual immunity and warns that the discontinuation of physical distancing should not be made on the basis of antibody test results.

"Given that we do not yet have scientific evidence showing if, when and for how long individuals might become immune to COVID-19, physicians and the general public should not use antibody testing to consider anyone immune to the disease—doing so may lead individuals to falsely assume they can stop physical distancing and further the spread of illness," said AMA President Patrice A. Harris, M.D., M.A. "Although many are using these tests to determine whether an individual had COVID-19, we encourage physicians to only use antibody tests authorized by the Food and Drug Administration (FDA) and only for the purposes of population-level studies, evaluating recovered individuals for convalescent plasma donations, or along with other clinical

information as part of a well-defined testing plan for groups or individuals."

The AMA's new guidance provides physicians and the general public with an overview of the current state of antibody testing for SARS-CoV-2, including their limitations, potential uses, and how they are and are not regulated. This guidance can be found online as part of the AMA's COVID-19 Resource Center.

While antibody tests may play an important role in determining the overall prevalence of COVID-19 in the U.S. population, including asymptomatic infection, inherent limitations exist in using them to identify prior infection in individuals. Many of the antibody tests currently on the market may return a significant number of false positive results, as well as show cross-reactivity—meaning the tests also identify antibodies for other coronaviruses, such as those causing the common cold. Given these limitations, the AMA recommends that currently available antibody tests not be used as the sole basis of diagnosing COVID-19, and not be offered to individuals as a method of determining immune status, and not be used to inform decisions such as returning to work, discontinuing physical distancing, or as the basis for "immunity certificates."

Additionally, concerns continue to mount about the performance and fraudulent labeling of many of the SARS-CoV-2 antibody tests currently available. The vast majority of more than 120 tests on the market have not been authorized by the FDA, despite marketing claims to the contrary. The AMA urges physicians to pay close attention to the regulatory status of all available SARS-CoV-2 antibody tests. A list of all antibody tests authorized by FDA for SARS-CoV-2 can be found on FDA's website.

The AMA continues to recommend physical distancing to reduce the spread of COVID-19.

Limitations

Physicians and the general public need to be aware that serology tests have several inherent limitations that make correct interpretation of the results critical. Serological tests for SARS-CoV-2 antibodies present even greater challenges, as much is still unknown about immune status for the novel virus. Some limitations to be aware of include:

- **False positive results**: Serological testing for disease with a low prevalence in the population presents inherent challenges with interpretation of positive results. Even high performing tests (e.g. high sensitivity and specificity) will return false positive results when disease prevalence is low, as is currently the case with COVID-19. Take, for example, a community of 100 individuals with a disease prevalence of 5%. If a serological test with a specificity of 95% was used in this population, it would be expected to return 5% false positives, so 5 out of the population of 100. Five true positives would also be expected, as the disease prevalence is 5%. Overall, this test would return 10 positive results, however, only 50% of the results would be accurate, showing the inherent limitation of these types of tests in low disease prevalence states. Once disease prevalence is higher, the concern about false positives becomes somewhat mitigated, however, this is not the current reality with COVID-19.
- **Cross-reactivity:** While this may not be true of all serology tests for SARS-CoV-2, cross-reactivity has been a noted concern among some offered tests. Cross-reactivity occurs when a test for antibodies for SARS-CoV-2 identifies not only antibodies for this virus, but also for other coronaviruses, such as those causing the common cold. For tests where cross-reactivity is possible, antibodies for other coronaviruses may result in a

positive test result for SARS-CoV-2 even when the patient in question was not infected.

- **Immune status:** Given that SARS-CoV-2 is a novel virus, there is much we do not know about what, if any, immunity it may confer to those exposed and recovered from infection. According to the WHO, there is no currently available evidence showing immunity to COVID-19 after infection. While individuals typically develop some type of immune response after exposure to most viruses, it is not yet clear when an immune response develops after COVID-19 infection, how strong this immune response may be, and how long the immune response may last.