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Question: Can we use serologic testing to gauge immunity to COVID-19 at this time?

As serologic testing for SARS-CoV-2 becomes available commercially, multiple issues such as test quality and interpretation need to be addressed. We agree with the primer from the Infectious Diseases Society of America (IDSA), which states that: "The sensitivity, specificity and predictive value of all current antibody testing options have not been clinically verified. Unlike molecular tests for COVID-19 (e.g., PCR), antibody tests may be better suited for public health surveillance and vaccine development than for diagnosis. Further, until more evidence about protective immunity is available, serology results should not be used to make staffing decisions or decisions regarding the need for personal protective equipment."

The Food and Drug Administration (FDA) has authorized a handful of antibody tests for COVID-19, and loosened restrictions to allow companies to sell other antibody tests that have not been scientifically reviewed by the FDA with the important caveat that these companies validate their tests and notify the FDA of the results of these validation studies. Over 90 companies now have tests on the market, but it's not clear how well their individual serologic tests work and how their tests compare to other commercially developed tests. As so little is currently known about immunity to COVID-19, there is a real risk that widespread antibody screening will lead to a false sense of security and lead in turn to unwise decisions about risk of infection in patients with positive antibody tests.

The World Health Organization and IDSA have published statements that current evidence regarding use of antibody tests to determine immunity is lacking. **Potential drawbacks of serological assays include false negative results if performed too early, especially in mild disease, and false positive results particularly with tests for Immunoglobulin M (IgM) and the potential for cross-reactivity with common cold coronaviruses (e.g. HKU1, NL63, OC43, 229E). Moreover, a positive antibody test doesn't guarantee immunity. Some FDA-authorized COVID-19 antibody tests are estimated to have 96-98% specificity, which would mean that a positive test result is more likely a false-positive result than a true positive result if the prevalence or pretest probability is 5% or less.**

These additional considerations have been outlined in the latest IDSA guidelines for serologic testing:

- No universal standard for reporting is available and test detection limits are variable. Some assays provide semi-quantitative results and others are designed to be qualitative (i.e. antibody detected or not).
- Combination IgG/IgM tests can provide unclear value given the potential for cross-reactivity with other coronavirus antibodies and the often-poor specificity of IgM.

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- Currently available commercial assays do not have titers, and without this information it is unclear how to identify individuals for plasma donation.
- Nucleic acid amplification tests (NAATs) perform differently than antibody testing, and this has implications for interpretation. The NAATs that were developed for SARS-CoV-2 are very specific. In patients with signs and symptoms of infection, a positive NAAT result has a very high positive predictive value (PPV) for true infection. Conversely, both the negative and PPV of antibody testing are likely to be lower, given the low prevalence of prior exposure to SARS CoV-2 in the U.S. population and imperfect sensitivity and specificity of the test.
- As a result, antibody tests will be most useful as surveillance tools to estimate (with surrounding confidence intervals) relative proportions of different populations that have been exposed to SARS CoV-2. They will have less utility as diagnostic tools for individual patient assessment.
- Privacy concerns: As we roll out antibody tests, the federal government should clarify several key questions regarding privacy: Who will collect antibody samples? How might they be saved and used in the future (i.e. by government, by law enforcement)? Will there be federal privacy protections for patient samples? What type(s) of applications are intended? Applications must mitigate concerns about privacy violations and hacking; advertiser tracking; potential test error; and faulty phone/wireless signals.'

References:

- "Immunity passports" in the context of COVID-19 – WHO Statement
- IDSA COVID-19 Antibody Testing Primer
- **COVID-19 Testing April Newsletter by DICON**
- Double-Edged Spike—Are SARS-CoV-2 Serologic Tests Safe Right Now?