COVID-19 Serology Testing – What is Known and Unknown as of <mark>May 4, 2020</mark>

COVID-19 tests designed to evaluate patients for active infection rely on molecular (usually Reverse transcription polymerase chain reaction, RT-PCR) and antigen testing methods that detect the presence of the SARS-CoV-2 virus circulating in the respiratory tract. Virus is detected in persons who are currently infected (although some persons may have detectable levels for some weeks following infection). Since we know that COVID-19 infections can also be asymptomatic, these persons likely have not been tested. As a result, we don't know the true burden of COVID-19 infection.

Serological tests detect evidence of the body's immune response to an infection (antibodies), which can provide information on whether an individual was ever infected with COVID-19. Current evidence indicates that COVID-19 antibodies begin to develop approximately 6 to 10 days after infection. IgM antibodies are the first ones to develop and appear to peak approximately 12 days after SARS-CoV-2 infection. They can persist in sufficient quantities for as long as 35 days, after which the quantity declines rapidly. IgG antibodies, which take longer to develop and are generally longer lasting, have been observed to peak approximately 17 days after SARS-CoV-2 infection and to persist for at least 49 days.

Serology testing for COVID-19 may be used to identify people who were previously infected with COVID-19. Serology testing should not be used to diagnose current COVID-19 infection since antibody responses to infection may take days to weeks to be detectable; a negative serologic test does not rule out active infection; and a positive serologic test may reflect prior infection with a human coronavirus other than SARS-CoV-2.

Serology is an important tool, however, for public health professionals to understand the prevalence of COVID-19 (how many people have been exposed to the virus), disease severity, and potentially to understand levels of population immunity. There is a lot of interest in serology testing to know if an individual is "immune" so they can go back to work or resume normal activities. While serology is an important tool in understanding the impact of the COVID-19 outbreak overall, there are several questions that are unknown and that limit its effectiveness as an individual-level proof-of-immunity tool. As we learn more about COVID-19, these questions may be answered. Current limitations of serology testing include:

1. Uncertain test validation: There are many tests that are being marketed which have not been completely validated nor reviewed by the FDA. These tests may not be accurate and may not be comparable. A false positive result may give people a false sense of security thinking they are "safe" from infection and not needing to take precautions. Healthcare providers and laboratories should consider whether tests have received FDA EUA and the setting in which they are authorized to operate (https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd).

2. <u>Cross-reaction to seasonal coronaviruses:</u> Each year, seasonal coronaviruses circulate and cause (usually mild) respiratory illnesses. It is unknown if a positive COVID-19 serology test detects only SARS-CoV-2 or would also detect antibodies to another coronavirus.

3. <u>Do antibodies equal immunity</u>? While it is thought that there may be some degree of immunity to COVID-19 after an individual recovers from the disease, it is unknown how long that immunity might last or if there is a minimum level of antibodies needed to confer immunity. These questions won't be answered until people who have IgG antibodies are exposed again to SARS-CoV-2 and researchers can study whether any of them are infected again. Time is also needed to determine how long the IgG antibodies will last.

Serology can be useful at a regional or state level but given the inaccuracies in available tests and the uncertainty about how the test results correlate to immunity, it is not advised to use serology to help individuals understand their personal risk.

<u>References</u>:

Developing a National Strategy for Serology (Antibody Testing) in the United States. The Johns Hopkins Center for Health Security. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2020/200422-national-strategy-serology.pdf