September 17,2020

Ordering and Use of COVID-19 Serology Testing

To: UVMHN Providers

Ordering Information:

Name in EPIC: PATHOLOGY APPROVAL FOR COVID IGG AB UVMMC ONLY
Limitations: Requires Pathology Approval

Recognizing that there are a small number of specific clinical applications for this test (see below) and to alleviate any confusion between serology and the diagnostic PCR test, UVMMC will send IgG serology testing out to our reference lab partner Mayo Clinical Labs but only after pathology approval for the testing. When ordered, this test will notify a Pathology resident to contact you to obtain more information about the patient's clinical scenario. Then through a discussion with the Clinical Chemistry attending pathologist, it will be determined if the request meets the clinical use criteria established for COVID-19 serology testing. This criteria is listed below. If approved, an order will be placed automatically for the collection of the test which will be resulted under the name SARS CORONAVIRUS 2 IGG AB, S (COVID-19).

Guiding Principles on Use of COVID-19 Serology:

1. Antibody testing is useful for:
    a. Understanding how many people COVID-19 has infected (i.e., epidemiology studies, not a clinical application).
    b. Identifying children presenting with Pediatric Multi-System Inflammatory Syndrome associated with COVID-19 (MIS-C).
    c. Assessing COVID-19 convalescent plasma donors.
2. Antibody testing should not be used to acutely diagnose COVID-19 infection.
3. Antibody testing results should not be used to determine a person's COVID-19 immunity status, "return-to-work" decisions, use of masks or other personal protective equipment (PPE), or safety of vulnerable persons to go into public more.
4. A positive antibody test only tells you that an individual has been infected with COVID-19 in the past.
5. Antibody testing results should be interpreted in terms of positive predictive value (PPV), being mindful of the prevalence of COVID-19 in your particular community and the false positive (FP) rate of any given test

Clinical Use Criteria for COVID-19 Serology Testing:

1. Evaluation of Pediatric Multisystem Inflammatory Syndrome associated with COVID-19 (MIS-C)
2. Convalescent plasma donor (This should be coordinated through blood donor center or American Red Cross. Not the UVMMC lab.)
3. A patient that meets **ALL** of the following criteria:
    a. The result of this test should change the management of the patient.
    b. The patient must have ongoing issues related to possible COVID-19 infection and was not positive by PCR. If they had a positive PCR, there is no need for serology in their management at this time.
    c. The patient should have a higher than normal pre-test probability than the general population.

Supporting Information and Rationale:

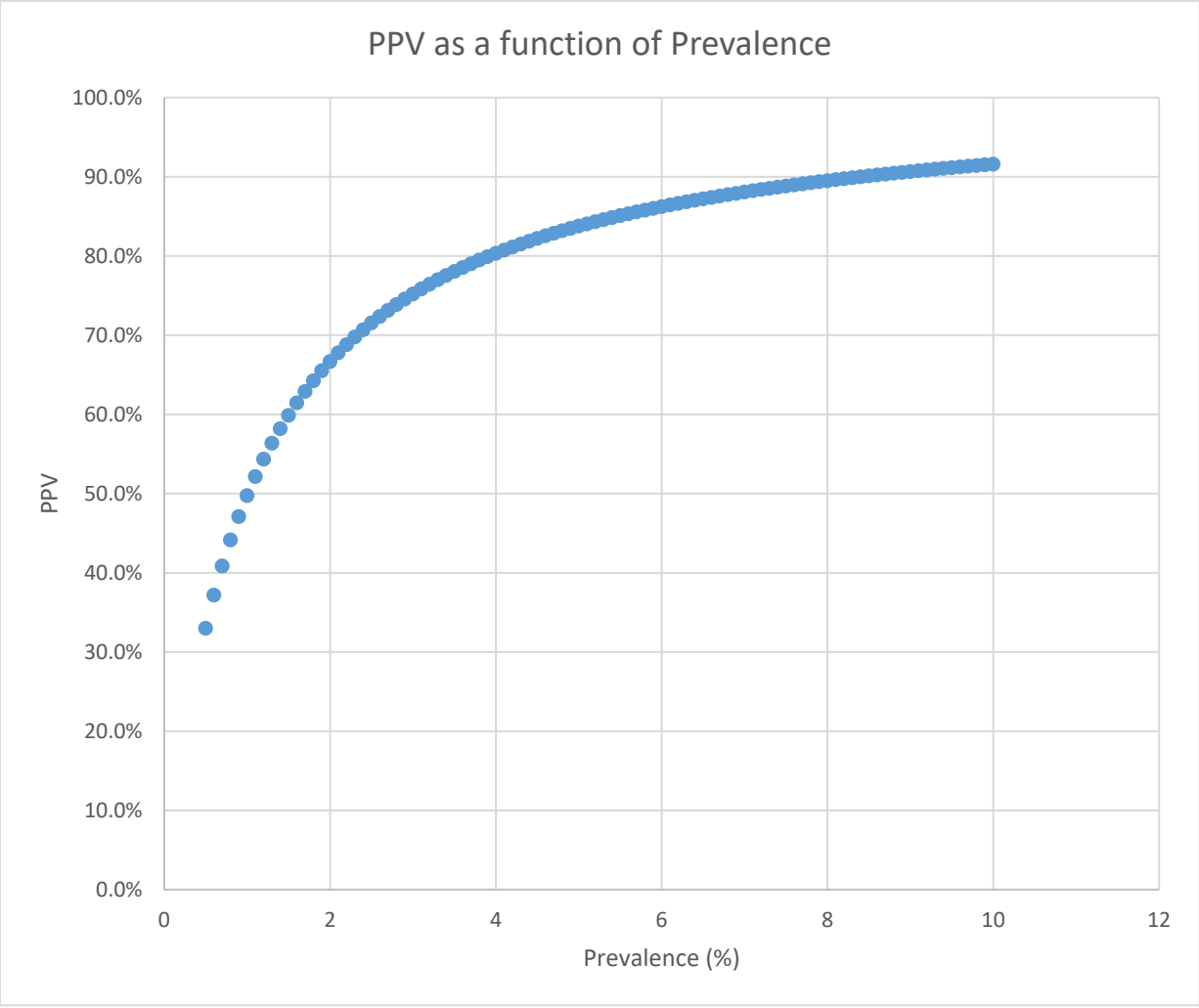
There has been much discussion in the media and lay press on the use of serology (antibody) testing in combating the COVID-19 pandemic. Some of this information has been misleading and promises unrealistic expectations on how the testing can be used to "re-open" the economy and identify a person's COVID-19 immunity status. This letter is to provide you with realistic expectations on the use and limitations of COVID-19 serology testing in our community.

Depending on the type of serologic test, the assay may detect IgM antibodies, IgG antibodies, or both. In general, IgM antibodies are less specific, leading to higher rates of cross-reactivity and false positives. Therefore, IgG should be the primary antibody measured for COVID-19 serology. The sensitivity of the serology assays is dependent on the length of time that has elapsed since symptom development. In patients who have only had symptoms for less than 5 days, sensitivity can range between 0-25%. Sensitivity improves the longer it has been since symptom onset, with 92-100% sensitivity observed in patients tested after 14 days.

Although studies have shown that antibodies developed in response to the virus are capable of neutralizing the virus, the most common COVID-19 serology tests do not differentiate from antibodies capable of virus neutralization and those that cannot. Furthermore, these assays do not predict the duration of antibody response, which has been shown to be as short as 2-3 months following resolution of infection. Early data suggests that the development and the effectiveness of these antibodies likely depend on an individual's age, overall health, and the severity of his/her COVID-19 related illness. In general, those of older age and greater severity of COVID-19 illness are more likely to have developed antibodies in response to COVID-19 infection.

Another factor that complicates using COVID-19 serology, and any laboratory test for that matter, is the risk of a false negative or false positive result. The positive predictive value (PPV),

or likelihood that the positive test result is correct (a “true positive”), is driven by the disease prevalence in combination with the test specificity, or rate of false positive results (FP = 1-specificity). For COVID-19, the assumed prevalence in Northern NY and most of VT is around 1%. The FP rate with even the “best” COVID-19 serology test is 1%. To calculate PPV you divide the prevalence by prevalence plus the FP rate. So a patient who lives in Northern NY or most areas of VT, has a 50/50 chance (coin flip) their positive result is actually a true positive. If the prevalence of COVID-19 is less than 1%, such as in the Northeast Kingdom of VT, or in the case of a “worse” serology test with a higher FP rate, the PPV can decrease to 17% (rolling a 1 on 6-sided dice) or less. Below is a graph of PPV as a function of prevalence for a test with 98% sensitivity and 99% specificity.



Sincerely,

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