

Dr. Delgado COVID-19 Update 4-23-20

MORE ON SEROLOGIC TESTING

I am well aware that the current timeline to institute serologic testing appears pressing to all of us, but choosing any serological test for the sake of expediency won't just do. We must proceed with caution and sensibility and do so in a methodical fashion. This approach remains paramount.

There is no rush. I continue to reiterate that point. Regardless of your presumed serologic results or status, the approach that best suits our community is to continue with the current restrictions of social distancing.

A test's methodology needs to be considered. Moreover, its probability of yielding accurate results, superseding any sense of expediency, is absolutely critical. Any potential interpretations and assurances of immunity cannot be considered infallible at this juncture.

The data from the many serologic tests becoming available is varied and is based on self generated studies that have only begun over the last few months. They have not been for the most part replicated, peer reviewed or validated. Only 4 tests have received Emergency Use Authorization to this point and many more (>90) are currently commercially available.

The current tests available mostly involve fingersticks of blood reacting with reagent strips. It appears that a blood test involving phlebotomy and processed will be more accurate. Using venipuncture to obtain the blood and the separating out the serum (where antibodies would

concentrate) will likely offer both greater sensitivity and specificity as to the quantitative and qualitative antibody response.

Several large companies, including Abbott, are just now releasing phlebotomy based tests using ELISA technology. Early reports from several thousand patients from Abbott suggest a near 100% true positive rate and a 99% false negative rate at the end of 14 days. If this data holds true, as they apply this to millions in real world conditions, it could be a significant breakthrough.

A conundrum remains though. Antibodies are produced in response to antigens from a virus. This allows them to recognize the virus antigens if they reappear and may initiate an immune response to minimize or prevent future infections by binding to these antigens.

The problem is that these serologic tests, even the ELISA format, may be detecting viral antigens that are not critical to producing immunity itself, but elicit a positive test result. Simply, not all antigens or proteins on a virus can penetrate a cell and cause infection. An immune response that provides immunity targets very specific antigens.

Therefore, any IgG response representing a positive result could be insignificant as to immunity. We still don't know if these tests will offer this level of differentiation. Only time and further study will clarify this issue.

It appears the majority (not all) of patients infected with Covid-19 develop antibodies. The level of antibodies produced or how "robust" the antibody response has a wide variance in the population. It remains unclear if an

antibody response confers “true” immunity (see above) and if so what specific level quantitatively is required to achieve any level of immunity? Also, do we assume that those previously infected without a noted antibody response can become re-infected?

Unfortunately, not enough time has passed to ascertain if antibodies that provide immunity will remain effective for an extended period of time. For Sars, data reflected antibody detection 2 years after infection and for Mers slightly more than a year. How long can we assume, if immunity is conferred, for a Covid-19 response to last? Also, once the antibody levels start to wane at what point does that immunity recede?

WHAT DOES THIS MEAN TO ME?

First, sequential serologic testing is indicated. One result will not be sufficient. Repeated tests with consistent results, ideally via different labs or methods, would increase the likelihood as to the accuracy of your immune status. We need these tests validated as to their accuracy.

We all need to see this next phase-testing for possible immunity-for what it is. It’s an initial step and it will not be a panacea individually if any one test shows a positive response. It’s too early in the process and social distancing remains crucial regardless of your “presumed” immunologic status.

INTRA-OFFICE TESTING

We have procured some initial serologic tests and our supply is very limited. We are currently proceeding with a small control group to determine if our test kits appear accurate.

Once we decide to scale up and receive the bulk of our order, we will proceed accordingly and notify all of you immediately. Please remain patient and we respectfully request you minimize any calls or correspondence to our office for updates on this status.

We will proceed accordingly and grant initial availability to our older population and those that have multiple risk factors for serious illness with a Covid-19 infection. I expect to be able to get through most of the available tests, when they arrive, relatively quickly.

If you are able to obtain testing elsewhere, I would urge you to do so, forward your result and then proceed with a repeat via our test. Sequential testing will only increase the validity of your presumed immune status. During our testing you will be asked if you wish to have your results confidentially shared with any other studies.

Lastly, deep breaths everyone. We continue to move in the right direction.

R. Delgado, MD & Staff