Position Paper

The Testing Debate for COVID-19: PCR vs. Rapid Antibody Test: *How Rapid Antibody Testing can Identify Potential Immune Patients Quickly*

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Knowledge and clarity empower rational action. The COVID-19 pandemic demands a powerful response, but the absence of a clear understanding of the virus has hamstrung governments' ability to act. The COVID-19 pandemic has now affected over 200 hundred countries and caused disease in over one million, resulting in close to 53,000 deaths. According to the Johns Hopkins Coronavirus Resource Center, United States has the largest number of cases (over 245,000) with close to 6,000 deaths and an epicenter of the disease in New York State (~ 93,000 cases and over 2,500 deaths). The quarantine, staying-home and social-distancing measures instituted throughout the states will help curb the epidemic. These measures are important and powerful tools to slow viral transmission. In of themselves, however, they do not help decision-makers determine the true extent and spread of the disease, nor how best to prepare to meet it. Rapid screening for disease is the cornerstone of curbing an outbreak, because such screening affords an understanding the epidemiology of the virus. Armed with this knowledge, public health policymakers are in a stronger position to more accurately assess and implement strategically meaningful interventions.

The nation struggles with the question "**To Test or Not**" for COVID-19. Testing for SAR-CoV-2 in the US appears to be controversial. The concerns arise from a poor understanding of the testing process and the consequences test results may have on staffing and employment. Fundamentally, however, the implications of testing are far-reaching and concern more than the single individual and a single test. Widespread testing is what enables us to discern disease incidence and prevalence, and to determine who has recovered from infection and is now immune. The faster we can clear individuals from active disease state, the faster we can mitigate the socio-economic downturn and social disruption. In order to do so, we need the ability to clearly identity the following categories of patients:

1. Exposed and now infected (at risk)
2. Infected but asymptomatic (infectious to others)
3. Infected and symptomatic (sick and infectious)
4. Infected and recovered (developed immunity)

Testing that can place patients into one of these categories will allow us to understand if someone is contagious (shedding virus) or non-contagious (not shedding virus). Furthermore, such testing will inform us if an individual has developed a certain level of immunity.

Multiple testing modalities are being used or have recently been developed, to include RT-PCR for viral RNA and rapid antibody testing. Neither of these tests are perfect; neither alone can provide 100% sensitivity or specificity. PCR tests for viral presence, which can vary between patients depending viral load and the patient's degree of exposure. Variability in viral load as well as poor swab technique during testing can lead to false negatives. Administration of the test puts staff at risk because it requires removal of a patient's mask and can cause the patient to sneeze or cough. Furthermore, recent studies have demonstrated that PCR, which has been considered the "Gold Standard," has a high false negative rate, up to 30%. This false negative rate suggests that a third of covid-19 suspected individuals tested negative by PCR may continue to carry and transmit COVID-19 unaware of the risk they pose to others. Moreover, PCR testing requires special equipment and special training, and can provide results only days after testing. By contrast, serologic immunoassay via IgM/IgG is a simple point-of-care, cost-effective test using a finger-stick blood drop. It provides results within minutes and can be used to conduct serial monitoring of populace to see who has been exposed to COVID-19. Importantly, antibody testing allows clinical decision makers to determine who is now clear of active disease and can return to work.

We have been using a rapid antibody IgM/IgG test by Boston Biopharma that has been FDA-approved for sale and is under evaluation for emergency use authorization like most rapid tests available currently. After consideration of the sensitivity/specificity of the PCR test, the inherent danger of spreading the virus during the nasal swabbing, and the test's cost and inconsistent turnaround time, we believe that a rapid antibody test is the better tool to empower our public health. The antibody test for IgM and IgG detects the humoral response (in immuno-competent people) and exposure prevalence. Known immunologic graphs correlate IgM rise with symptom development in covid-19 patients (roughly ~4-7 days since exposure event) and, additionally, the IgM response may also be present in asymptomatic patients. IgG indicates longer-term immune response.

It is important to note that no test on its own can determine patient infectious status. To be effective, testing must be conducted within a clinical screening and evaluation process. Based on our experience, antibody testing is easier to administer, is a better point-of-care (POC) tool, and adds further critical information to that of RT-PCR alone.

Disagreement over testing methodology stems from the evolving understanding of COVID-19 and the varying knowledge of virology by those crafting the public response. It is clear that a stay-

home policy without a means to survey the US population and "clear" individuals of active disease state would be detrimental to the American economy and would create further social disruption and anxiety. This toll on staffing is especially important in the healthcare setting. The use of social-distancing and isolation measures in democratic nations have yielded favorable outcomes and have been able to "flatten the curve." However, the ability to identify individuals who are IgM (-) and IgG (+) is critical if we are to return to some normalcy and reassure labor force mobility. Table 1 describes the various scenarios and the potential outcomes.

Table 1: Interpretation of the Rapid Antibody Test		
IgM	IgG	Status
Positive	Negative	Indicate exposure and probable active infectious state
Positive	Positive	Indicates recent exposure and longer-term immunity development
Negative	Positive	Indicates that individual was exposed and mounted an adequate longer-term immune response. However, we do not know if that IgG is truly giving protective immunity yet nor of its longitudinal value.
Negative	Negative	Indicates that there has been no exposure and the individual is at high risk of acquiring the disease.

At present, there are no definitive nor specific therapeutic agents or vaccines, despite the tremendous commitment to their research and development. While we wait, the disease continues to cause significant morbidity and mortality. Antibody testing affords another benefit: the identification of patients who have recovered from the infection and who are able to provide their own antibodies to others in the form of convalescent plasma. During the 2014 Ebola outbreak, convalescent plasma was recommended as an empirical treatment, and a protocol for treatment of Middle East Respiratory Syndrome (MERS) coronavirus with convalescent plasma was established in 2015. Other studies for viruses such as SARS-CoV, H5N1 avian influenza, and H1N1 influenza suggest the effectiveness of transfusion of convalescent plasma. (1,2,3,4,5) A recent uncontrolled case series of 5 critically ill patients study published by Chenguang Shen et al in JAMA suggests that convalescent plasma transfusion may help in the treatment of critically-ill patients with COVID-19. While awaiting confirmation in randomized clinical trials, the approach continues to hold much promise. (6)

Conclusion:

Rapid POC antibody COVID-19 specific testing is the best means at our disposal to improve our epidemiologic understanding of the virus and to empower a robust public health response. The ability to determine immunity will enable us to safely restore our economy. This will further permit safe and cost-effective way to create a registry of immune individuals whereby enabling collection of convalescent plasma, a possible treatment for patients critically ill with COVID-19.

References:

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