

Department of Medicine
Medical Grand Rounds Webinar: COVID-19 Updates
May 5, 2020
7:30 a.m. to 8:30 a.m.

Questions submitted by participants during webinar

The answers provided are relative to a specific point in time and are subject to change as the management and care for COVID-19 patients continues to evolve

1. Why are people so certain there will be a second spike in cases when SARS went away? Is it possible Covid-19 will go away?

Answer: Many experts agree that a second and even a third wave are likely. The rationale for this includes data from past pandemics like the 1918 influenza outbreak; the fact that still, most of the world has not been infected (i.e., lack of herd immunity); the virulence and attack rate of the organism; and some have said the possibility that the virus may mutate. Some estimates are that until 60-70% of the world's population is immune (from infection or vaccination), we will not have herd immunity. A vaccine is not expected to be available before the second wave. It is possible that COVID-19 will go away like SARS-CoV but this is not expected. We can certainly mitigate the response if a second wave does occur by preparing now with testing, contact tracing, isolation of exposed and infected individuals, and possibly with novel therapeutics that we may have before the fall.

2. Is there a plan to do IgG testing for healthcare workers to see seroprevalence? How will this be rolled out?

Answer: Yes, we are working on a plan now. This will be voluntary testing of our workforce. We will share details soon.

3. Is it known how long the serologic test from Abbott, IgG and IgM, remain positive, after the RT-PCR becomes negative?

Answer: IgM begins to rise at about 5.5 days, peaks at about 12 days, and starts to fall around 35 days. IgG begins to rise shortly after IgM, peaks at about 17 days and remains positive for at least 49 days (when studies were stopped). We do not know durability of IgG at this time.

4. When will serologic testing be available at NM to all outpatients desiring testing? Will NM physicians be tested?

Answer: Outpatients can be tested now by placing an order in EPIC as a miscellaneous send out lab order. Tell the sendout lab which test you want. We currently can send samples to Viracor (IgM and

IgG), Mayo (IgG only) and Quest (IgG only). We will offer voluntary testing to the NM workforce. Details will be coming soon.

5. I have used the abbott platform serology test (offered from quest) to confirm patients had COVID19 (they had known exposure and classic symptoms but couldn't get PCR testing when they were symptomatic in March). I have seen false negatives. Why? If the 'threshold' for 'positive' on a qualitative test set too high?

Answer: *Some reasons for false negative include testing too early and mild disease. Also true negatives are possible—had disease but did not mount an antibody response to the specific antibody the test is designed to detect.*

6. Is there thought to using two serology tests, one for Nucleocapsid for sensitivity, and one for spike protein for specificity?

Answer: *Yes, some companies are designing such serologic tests.*

7. Can you reiterate the serologic positive predictive value. Patients are clamoring for this, but correct that at present prevalence, a positive test is more likely to be a false positive, right?

Answer: *The sensitivity (true positive/all who truly have disease), specificity (true negative/all who truly do not have disease), positive predictive value (true positive/all positive tests) and negative predictive value (true negative/all negative tests) vary among the assays. The prevalence (true positive/all tested) is linked to positive and negative predictive value. As the prevalence increases, a positive test is likely to be real and a negative test is less likely to be real. We cannot say at this time what the PPV is because we do not know the prevalence in the population yet—we need community serostudies to help place our individual results in better context. Current estimates are that if prevalence is less than 5% in a population, a positive test is more likely to be a false positive*

8. Do you know which antibody test(s) the commercial labs (e.g., Quest, LabCorp) are using?

Answer: *Viracor (IgM and IgG), Mayo (IgG only) and Quest (IgG only). The lab sent me data today as follows: Viracor sensitivity IgM 78%, IgG 97.5% and specificity IgM 91% and IgG 97%; Mayo sensitivity 100% after day 14 from symptom onset, specificity 99.3%. Quest sensitivity 80% for specimens collected more than 10 d after symptom onset, specificity 99%.*

9. Do you recommend the Quest test?

Answer: *As long as you understand the benefits and limitations of serology testing, I think any of these can provide some useful data.*

10. What is timeframe for staff testing?

Answer: I do not have a firm answer yet. We are actively working on this.

11. Does the inhibition of binding and fusion of SARS-CoV-2 to host cells by polyclonal antibodies imply immunity in a patient with positive IgG serology? Does it at least suggest likely immunity?

Answer: This was only presented as an interesting study to show that infecting mice with SARS-CoV and then harvesting their polyclonal antibodies in the presence of SARS-CoV-2 can block SARS-CoV-2 entry through hACE-2 receptor. This is useful to show that blocking function of spike protein is a useful target to try to elucidate neutralizing antibody and potentially help with vaccine targets and development. It was not meant to say that IgG to some part of SARS-CoV-2 (different serologic assays use different targets; the Abbott platform we have here is to nucleocapsid, not spike) lets you know you are immune. If we could identify the neutralizing antibody/antibodies to SARS-CoV-2 and then detect these specific antibodies in serologic test, you would have a better estimate of immunity. We currently know nothing about the duration of immunity even if it exists.

12. Is there any estimate for when we will be able to determine if the antibodies to SARS-CoV-2 are protective? Assuming titers are the same, will the antibody protectiveness be equivalent for everyone or could it still vary person-to-person for other reasons?

Answer: Researchers are working on identifying neutralizing (i.e., protective) antibodies now. There is likely to always be person-to-person variation in immunity.

13. Is our present covid test a serologic test?

Answer: We have tests here to detect viral RNA and tests to detect IgG to nucleocapsid.

14. For Dr. Zembower - sorry - came in late, so apologize if you had discussed this. Sounds like antibody testing is tough to interpret, yet we will be offering to employees. Do you recommend we get it (and why if yes)? Thanks!

Answer: I recommend for you get it if you want it. I think it should be voluntary and those getting the test should understand its potential benefits and its limitations. There is some optimism, based on immunity to SARS-CoV literature, that if you have had infection, you will have some degree of immunity. Having a large population tested can also help determine disease prevalence which can help put everyone's individual tests in perspective in terms of positive and negative predictive value.

15. Should we actively recommend testing in Peds, newborns for exposed, asymptomatic or minimally symptomatic patients? IDPH puts it as "available" but is it mandatory? What ways will it help?

Answer: I think testing different populations will help determine disease epidemiology. I do not think this should be mandatory. The biggest advantages now are to help with public health data to see how many people have recently been infected—this can help determine things like herd

immunity. It can help diagnose people with acute disease if RT-PCR tests are negative. It can help identify potential plasma donors for possible therapies for severely ill patients, and it has the potential to tell people whether they might have some degree of immunity—but this is far from certain with current serologic tests.

16. when will antibody testing be available for our outpatients? we get this question all day long

Answer: *It is available now as a send out test. See my answers to questions 4 and 8.*

17. Is there a role to use remdesivir in patients with covid and comorbidities before they require hospitalization. Should we try to admit them earlier to start the medication earlier in the disease.

Answer: *Preliminary data suggest that patients with severe illness benefit more than those with mild to moderate disease so at this time patients must have hypoxemia to be eligible through the EUA; however, optimal timing of drug administration needs to be defined. Given limitations of drug supply and burden on hospital system I would not recommend admitting patients solely for remdesivir at this time.*

18. Of all the JAK inhibitors, baricitinib has the strongest data to suggest a prothrombotic side effect. Since we are already concerned about thrombotic complications from COVID-19, are there plans to test the other two “potentially safer” JAK inhibitors?

Answer: *Baricitinib was chosen based on correspondence to The Lancet (Richardson et al. Baricitinib as a potential treatment for 2019-nCoV acute respiratory disease. The Lancet. Feb 3, 2020. 395: e30-31 available at <https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930304-4>) based on the dose that would be required to inhibit viral endocytosis. Patients with a prior history of recurrent or recent VTE (12 weeks prior to enrollment) will be excluded from ACTT-2. Development of VTE during study will require discontinuation of study drug/placebo.*

19. Any pharmaceutical intervention for those patients who are asymptomatic carriers?

Answer: *No, not at this time. There are several studies listed on clinicaltrials.gov looking at various antivirals (mostly chloroquine/hydroxychloroquine) in asymptomatic carriers.*

20. Could you provide (later) a link to the primer on serologic testing?

Answer: *<https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf>*

21. The NM Remdesivir cohort you showed early is relatively young. Is there any data yet on efficacy in older patients?

Answer: The patients who received compassionate use remdesivir at NM ranged from 47-73 years old. The patients we enrolled in the NIAID ACTT ranged from 32 up to 89. The average age in Wang et al. was 66 in Remdesivir group and 64 in placebo group. We will have to wait for the results from ACTT to see the breakdown of outcomes by age.

22. Talk more about the process of deciding which cities, or hospitals or patients will get this drug

Answer: The process of drug distribution is not clear at this time. The FDA EUA states “Given the severity of illness of patients appropriate for remdesivir treatment and the limited availability of drug supply, hospitals with intensive care units and other hospitals that the U.S government deems most in need will receive priority in the distribution of donated remdesivir. The U.S. government will coordinate the distribution of remdesivir to hospitals in regions most heavily impacted by COVID-19.” The IDSA wrote a letter to the white house asking for more transparency in the distribution process <https://www.hivma.org/globalassets/remdesivir-eua-letter-final.pdf>.

23. Will there be virologic data in the NIAID study?

Answer: Yes, the study will perform qualitative and quantitative PCR for SARS-CoV-2 from OP swabs and blood on multiple days throughout the 29 day study period.

24. Do you believe Remdesivir is a good option to use, even though there is a limited data?

Answer: Yes, I think at this time point the potential benefits outweigh the known risks in severe disease (hypoxemia) as the drug seems to be well tolerated and morbidity/mortality is high among those requiring hospitalization. The available data did not demonstrate any major safety concerns. It will still be important to have a discussion with patients or representatives regarding the known benefits and risks prior to administration and to reevaluate the role of remdesivir once we have additional data.

25. Seems like the data suggests remdesivir might be more effective when given earlier in the course (moderate disease) vs waiting until late . . .

Answer: The results from Wang et al. showed a trend toward time to clinical improvement when drug was started between 1-10 days after onset of symptoms compared to those that started drug 11-12 days after onset of symptoms but this was not statistically significant. We are waiting on data from the NIAID trial which has a larger sample size. But from what we know about treatment of other viral respiratory illnesses (specifically influenza) this seems logical. Although many COVID-19 patients have protracted courses with late viral shedding so I think optimal timing will need to be determined.

26. What was the rationale for using anti-nucleocapsid assay at NM?

Answer: This test was developed by Abbott. We already had the Abbott Architect platform here and use it for other types of testing; thus, we could quickly and reliably validate this platform in our lab without additional lab equipment purchases or training. Abbott targeted nucleocapsid for sensitivity.

27. Does NMH have any Remdesivir stocked?

Answer: At time of writing this, no. We will receive remdesivir for clinical trial participants when we start enrolling for ACTT-2. The government will be distributing remdesivir for prescription under the EUA but details on this unclear (see above). Other NM sites that are participating in the expanded access protocol may still be able to obtain directly from Gilead. Gilead will also provide drug through compassionate use to pregnant patients and children with severe disease.

28. Will/when Northwestern's serology testing be available for outpatient use across all campuses?

Answer: See answers above

29. How and when can an NM employee can order the serology test?

Answer: See answers above

30. Based on what we know when should high risk health care workers return to work?

Answer: This is a good question but to answer your question more specifically, I would need to know what you mean by high risk (just because the person is a HCW? Person has underlying medical condition putting them at high risk? Person works on a high risk floor? Etc.). I will refer you to the CDC guidance on this question that likely answers all these questions for you:
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/return-to-work.html>