Northwestern Medicine®
Feinberg School of Medicine

Department of Medicine
Medical Grand Rounds Webinar: COVID-19 Updates
May 19, 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. What is strength of scientific evidence that "reinfection" suggested by a positive PCR test indicates (or does NOT) contagiousness?
   Answer: South Korean CDC reported about 1% of cases becoming PCR positive for virus after having tested negative for virus. This was largely associated with mild symptoms and unclear whether this represents reinfection or inadequately cleared prior infection. It has been suggested it could also be related to late detection of fragments of virus RNA or earlier falsely negative tests. The USS Theodore Roosevelt seems to be experiencing approximately the same (~1%) similar incidence. It is not known whether this represents reinfection or not.

2. Is there a minimum level of antibodies (and which type) that suggests immunity for an individual?
   Answer: A minimum level or type of antibody that protects is not known at this time. Currently, serology only examines whether people have been exposed.

3. With high household seropositive levels, should we re-think quarantine at home?
   Answer: More household spread data is needed. We should continue to follow local and state instructions regarding quarantine, including keeping those infected away from other household members.

4. Are all neutralizing antibodies anti-RBD, and vice versa, are all anti-RBD antibodies neutralizing antibodies?
   Answer: The receptor binding domain is the most frequent target of neutralizing antibodies. Not all RBD directed antibodies are neutralizing. And some neutralizing antibodies are directed against parts of the spike glycoprotein other than the RBD.

5. How does RNA-based virus evade RNA-induced immune response?
   Answer: Generally, coronaviruses all encode multiple proteins that deactivate different effectors that are induced by interferons. One of the best characterized is the papain-like protease that not only plays a role in virus replication, but deubiquitinates host factors (including NF-kappa-B and ISG15). SARS-CoV-2 has several ORFs of as-yet unknown function that may also contribute to this. It is of note that the RNA in the Moderna vaccine candidate may also induce some innate immune responses. We will need to learn if this can be helpful in brining immune cells into the injected muscle and whether that can have a beneficial "adjuvant" effect or perhaps in some cases cause unwanted local/systemic reactions. Only short-term production of the SARS-CoV-2 is needed from that vaccine, so it's unlikely that kind of response will prevent antigen exposure.

6. If we know the neutralizing antibodies, why are the commercially available antibody tests, not measuring these?

<u>Answer:</u> Serology assays survey prior exposure. As such, they use whatever viral protein performs well in a given assay. The neutralizing antibodies that are strongly suspected to confer protection (not proved) can only be measured now in a biocontainment laboratory, are very time- and labor-intensive, and cannot be used at scale.