VCHIP CHAMP VDH COVID-19

June 29, 2020 | 12:15-12:45pm Call Notes*

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Practice Issues: Update on COVID-19 Outbreaks, Serology, & Vaccines

William Raszka, MD & Benjamin Lee, MD, UVMCH Pediatric Infectious Disease Specialists

William Raszka, MD, UVMCH: We don't have any good news at all. That's the short story. If you hang out and drink together, you will transmit disease very efficiently. Again, I want to emphasize the importance of testing symptomatic and asymptomatic people after a known COVID-19 exposure, which is very different from just looking at the percent testing positive from a random sample of individuals. Asymptomatic people play an important role in the continuation of the pandemic. Clearly people are infectious prior to the onset of symptoms and even with very mild symptoms. The take-home message is really do not congregate together and avoid bars. The State of Florida decided to do a large trial on this, and they found disease transmission becomes very common without physical distancing or cloth facial coverings.

We've discussed serology on multiple occasions and Dr. Lee and I are a part of the Serology Task Force for the Governor. As previously stated, you should never use serology for a decision about immunity or return to work or daycare. In a national study, the CDC looked at a sample of 12,000 blood specimens from commercial laboratories at six sites where specimens were analyzed. This cannot be considered a true random sample. If you look at the NYC metro region, they found a 6.93% seroprevalence estimate for the week of March 23rd-April 1st. The vast majority of Americans have yet to be infected. The accuracy of good tests is 91-93%.

There is no data after 35 days, which limits our knowledge of the antibody titers. Unfortunately, there is some bad news regarding the persistence of neutralizing antibody titers. If you look at asymptomatic versus symptomatic people at the convalescent phase, the antibodies for COVID-19 don't persist very long, and we are still unsure if they have anything to do with immunity.

Benjamin Lee, MD, UVMCH: I wanted to give a brief overview on where things stand on the vaccine front. *The New York Times* has a good page tracking coronavirus vaccine development (https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html). There is one vaccine listed as approved. It's a Chinese vaccine approved to give to their military. It's nothing to get excited about. If you look at all the vaccines currently undergoing evaluation, there are some that are in or undergoing Phase 3 clinical trials.

The University of Oxford single dose vaccine is called AZD1222, and it uses a non-replicating adenovirus vector (ChAdOx1). It shouldn't cause uncontrolled replication. This group is pacing the field in terms of where they are in development. It doesn't hurt that they received $1 billion from the U.S. to advance development. You can't tell how well a vaccine is working if too few people are getting infected. In England, the target enrollment is 10,000 participants for Phase 2/3. The Phase 3 trials in Brazil and South Africa (dosing this week) have a target of 2,000 participants each. The U.S. study planned for September proposed 30,000, but may be too late to meet the goal of distributing vaccines by October. There will be a pediatric

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trial as well. They are scaling up manufacturing capacity in parallel with clinical trials and at known risk. They know there's a chance the vaccine will not work. However, they're willing to take the risk of manufacturing a lot of doses during trials, so it can be rapidly distributed if the trials are successful. They have a lofty goal of distributing 2 billion doses (400 million available to US and UK by September). They also guaranteed 1 billion doses to low- and middle-income countries via license to Serum Institute of India (400 million by end of 2020).

Unfortunately, there is at least some cause for concern regarding this vaccine. The only data available is from a pre-published study in monkeys. Vaccinated monkeys had lower average clinical severity scores than non-vaccinated monkeys when inoculated with the virus. The amount of viral RNA recovered was significantly lower in the animals vaccinated. This vaccine prevented monkeys from getting pneumonia when they were exposed to the virus. For nasal swab specimens, there was not a significant difference in viral RNA volume between vaccinated and unvaccinated monkeys, indicating the vaccine may not actually prevent infection or transmission, but just prevent critical illness resulting from infection.

BBIBP-CorV is a 2 dose inactivated whole virus vaccine under development by Sinopharm. A new phase 3 trial is launching in United Arab Emirates tomorrow. This vaccine does prohibit infection in monkeys. 7 days post-challenge, those who received the highest dose of vaccine had no detectable viral RNA. This is more promising that the Oxford data, but the manufacturing of the vaccine will take much longer. There are many vaccines in Phase 2 trials. Other than the Merck vaccine, which uses VSV vector (used in Ebola vaccines), all of the other tests are using approaches to vaccines that have failed in the past. A lot of the animal data is encouraging, but there's no substitute for human data. The biggest most established vaccine manufacturers are taking a slower approach. The duration of immunity is not well-understood and it could be much shorter than we need it to be. Distribution by this winter is unrealistic and potentially dangerous for a vaccine. Too much emphasis is being placed on rapid deployment of novel technologies without enough support for "tried and true" methods (despite longer development time). A widely available vaccine with solid safety and efficacy data is unrealistic to expect before Fall/Winter 2021 and maybe beyond.

Wendy Davis, MD, VCHIP: Is there overlap with the work you all are doing?

Benjamin Lee, MD, UVMCH: All of us here at the Vaccine Testing Center are not involved in definite plans for COVID-19 vaccine work. It's unlikely that we would have enough infected people to warrant participation in any Phase 3 trials. We are not actively doing anything yet, but opportunities may arise for us as development progresses.

Becca Bell, MD, UVMCH PICU & AAP-VT Chapter President: Thank you both for this important info. It underscores the importance of prioritizing re-opening schools (safely) and not just "waiting for a vaccine."

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