LITERATURE REVIEW

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PROLONGED SARS-COV-2 CELL CULTURE REPLICATION IN RESPIRATORY SAMPLES FROM PATIENTS WITH SEVERE COVID-19

Article: https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00095-1/fulltext
Journal: *Clinical Microbiology and Infection*

Background:
COVID-19 infected patients can remain PCR positive (due to prolonged SARS-CoV-2 RNA shedding) well beyond recovery or even in the absence of symptoms. Recovering viable SARS-CoV-2 by virus culture is a better indicator of infectivity, however culture of SARS-CoV-2 is difficult, requiring a BSL-3 facility and considerable technical expertise. These technical challenges may account for variability between studies that suggest particular clinical or laboratory thresholds (e.g. days past symptom onset, PCR cycle values, or neutralizing antibody titers) may correlate to lack of virus recovery and thus lack of infectivity.

Results:
This study correlated culture positivity results to patient symptoms and recovery, PCR cycle threshold (Ct) values, and neutralizing antibody titers for 193 clinical samples from 189 adult COVID-19 patients who were either asymptomatic, had moderate COVID-19 or had severe symptoms requiring hospitalization. This group showed viable virus (indicated by cytopathic effect in Vero E6 cell culture) in 47% (91/193) samples across all patient groups, and most frequently (69%, 75/109) in the initial clinical sample collected. Patients with severe disease had significantly higher culture positivity (47%) than outpatients (18%). Similar to other studies, viral culture positivity correlated to lower Ct values in both mild and severe COVID-19 (>90% culture positive for Ct <25). But unlike other studies, patients with severe disease had viable SARS-CoV-2 recovered in over half of patients up through week 3 of symptoms, and in 25% of patients beyond week 3. Notably, samples with Ct values >/= 35 also showed viable virus, although less frequently (5% in moderate, 15% in severe COVID-19). Additionally, while half of severe COVID-19 patient sera samples tested (14/30) had high neutralizing antibody titers (>1:1024) greater than 10 days beyond onset of symptoms, 21% (3/14) of these were from patients with positive virus cultures.

What does this mean?
Like other studies, highest periods of viable virus were detected early (< 10 days) in disease course and when PCR Ct values were lower. However, this study further showed that especially in cases of severe disease and even in the presence of neutralizing antibodies, viable SARS-CoV-2 can be shed beyond 3 weeks of illness. This may further inform infection prevention recommendations and promote caution in interpreting absence of virus culture positivity.

Further Considerations:
Infectivity is more than a metric of having any culture-competent virus present in respiratory samples. Future experimental or epidemiological studies will help determine infectious doses and host factors that lead to active infection. Standardization or lab-to-lab viral culture comparisons to determine why this group was atypically successful in culturing SARS-CoV-2 from clinical samples may also be valuable.

BINDING AND NEUTRALIZING ANTIBODY TITERS AFTER A SINGLE VACCINE DOSE IN HEALTH CARE WORKERS PREVIOUSLY INFECTED WITH SARS-COV-2

Article: https://jamanetwork.com/journals/jama/fullarticle/2777171
Journal: *JAMA*

Background:
The SARS-CoV-2 vaccine clinical trials have almost exclusively been performed in individuals without prior COVID-19. Given that over 115 million people worldwide have been confirmed with COVID-19, not counting asymptomatically infected individuals, the question regarding need for complete, dual-dose vaccination of previously infected patients using mRNA-based vaccines has emerged. This study evaluated the immune response following administration of a single dose of an mRNA-based vaccine in healthcare workers (HCWs) with prior confirmed SARS-CoV-2 infection.

Results:
59 HCWs were enrolled in the study, of whom 17 were SARS-COV-2 naïve (eg, SARS-CoV-2 antibody negative), 16 had asymptomatic infections and 26 had prior symptomatic disease. Binding and neutralizing antibody (nAb) levels were monitored at days 0, 7 and 14 after the first SARS-CoV-2 mRNA vaccine dose. That authors found that compared to the SARS-CoV-2 naïve HCWs, both binding and nAb levels were statistically higher for HCWs with prior symptomatic or asymptomatic COVID-19.

What does this mean?
These data suggest that a single SARS-CoV-2 mRNA-based vaccine may be sufficient to 'boost' the immune response in previously infected individuals, eliminating the need for a second vaccine dose. This has also been proposed by a separate pre-print study, which likewise showed significantly elevated antibody levels in previously infected COVID-19 patients versus naïve individuals, following administration of a single mRNA-based SARS-CoV-2 vaccine dose. That study further indicated that antibody levels following a single vaccine dose were significantly higher than antibody levels achieved following the second vaccine dose in previously uninfected individuals.

The authors in both studies suggest that given the limited SARS-CoV-2 vaccine supply, previously COVID-19 infected patients may only need a single vaccination dose to boost their natural immunity.

Link to preprint study: https://www.medrxiv.org/content/10.1101/2021.01.29.21250653v1.full.pdf

Further Considerations:
While these studies are compelling, larger cohort sizes and long-term follow up will be necessary to document efficacy of the one-dose option in prior COVID-19 confirmed individuals.

PERFORMANCE OF THE ABBOTT BINAXNOW SARS-COV-2 ANTIGEN TEST IN ADULTS AND CHILDREN

Articles: https://jcm.asm.org/content/early/2021/02/19/JCM.00083-21
Journal: *Journal of Clinical Microbiology*

Background:
Compared to standard SARS-CoV-2 PCR assays, some advantages of rapid antigen detection tests include the ability to provide testing close to or at the point of care, and a shortened reporting time. However, the performance of these assays has been shown to be reduced or limited in certain settings. Specifically, there is

limited data about the performance characteristics of these methods in pediatric patients and asymptomatic adults.

Results:
In a drive-through collection and testing setting, the authors enrolled 1,380 adults and 928 children. Two anterior nasal swabs were collected from each patient and were used for performing the Abbott BinaxNOW antigen assay and a SARS-CoV-2 PCR test, which served as the reference method. In this population, the virus prevalence was 12.7% in adults and 14.5% in children. For patients with < 7 days of symptoms, sensitivity of the antigen test was 96.5% for adults and 84.6% for children, with 100% specificity for both groups. However, a lower SARS-CoV-2 antigen sensitivity was found in asymptomatic adults (70.2%) and children (65.4%), with similarly high specificities (99.6% and 99.0%, respectively).

What does this mean?
Specificity of the Abbott BinaxNow SARS-CoV-2 antigen test is high among the groups of patients in the study. The sensitivity of this assay varies, however, with the highest sensitivity observed in symptomatic adults or children tested < 7 days post-symptom onset. The sensitivity of the BinaxNow antigen assay is significantly lower in asymptomatic patients overall, which is relevant for institutions considering routine screening of asymptomatic individuals using this rapd assay.

Future Considerations:
Result interpretation and confirmation plan should be developed based on disease prevalence since the test result prediction values will change based on different prevalence.

EFFECT OF IVERMECTIN ON TIME TO RESOLUTION OF SYMPTOMS AMONG ADULTS WITH MILD COVID-19 A RANDOMIZED CLINICAL TRIAL

Articles: https://jamanetwork.com/journals/jama/fullarticle/2777389
Journal: *JAMA*

Background:
Ivermectin is a commonly used and safe antiparasitic drug that has shown activity against SARS-CoV-2 both in vitro and in animal models. Due to its positive safety profile as an antiparasitic drug and the preliminary anti-SARS-CoV-2 activity findings, it has been widely prescribed internationally as a potential COVID-19 therapy, despite the uncertainty still surrounding its treatment efficacy.

Results:
A double-blind, randomized clinical trial, looking at the efficacy of ivermectin versus a placebo for the treatment of COVID-19 was performed at a single site in Cali, Columbia. Symptomatic patients with laboratory-confirmed cases of mild COVID-19 were randomly chosen from the health department database, with one cohort of patients (n = 200) receiving a 5-day regimen of ivermectin, while the other cohort (n = 200) were prescribed a placebo. Patients were then tracked, and time to resolution of symptoms within a 21-day follow-up period were measured. The time to resolution of symptoms in the ivermectin-treated group was 10 days vs. 12 days in the placebo group, with a hazard ratio for resolution of symptoms of 1.07 [95% CI, 0.87 to 1.32]; P = .53). In addition, 82% and 79% of patient showed resolution of symptoms by day 21 in the ivermectin and placebo group, respectively.

What does this mean?
These results do not support the use of a 5-day course of ivermectin as a treatment for mild COVID-19, since there was no significant improvement in the time to symptom resolution as compared to the placebo group.

Future Considerations:
This study further adds to our knowledge about the efficacy, or lack thereof, of certain unvalidated therapies, such as ivermectin, that have been widely used for treatment of COVID-19. Studies on the efficacy of all of the drugs currently being utilized as potential COVID-19 treatments will be critical for patient management.