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Short communication

SARS-CoV-2 viral shedding in vaccinated and unvaccinated persons: A case series

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\textbf{Abstract}

The preclinical time course of SARS-CoV-2 shedding is not well-described. Understanding this time course will help to inform risk of SARS-CoV-2 transmission. During an outbreak in a congregate setting, we collected paired mid-turbinate nasal swabs for antigen testing and reverse-transcription polymerase chain reaction (RT-PCR) every other day from all consenting infected and exposed persons. Among 12 persons tested prospectively before and during SARS-CoV-2 infection, ten of 12 participants (83%) had completed a primary COVID-19 vaccination series prior to the outbreak. We recovered SARS-CoV-2 in viral culture from 9/12 (75%) of participants. All three persons from whom we did not recover SARS-CoV-2 in viral culture had completed their primary vaccination series. We recovered SARS-CoV-2 from viral culture in 6/9 vaccinated persons and before symptom onset in 3/6 symptomatic persons. These findings underscore the need for both non-pharmaceutical interventions and vaccination to mitigate transmission.

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\section{1. Introduction}

Understanding the time course of shedding using diagnostic indicators such as cycle threshold (Ct) values from reverse transcription polymerase chain reaction (RT-PCR) testing and recovery of SARS-CoV-2 from viral culture, is important to address risk of SARS-CoV-2 transmission. In previous studies, RT-PCR results among SARS-CoV-2 infected persons were positive 1–2 days before symptom onset and remained positive for up to 4 weeks \cite{1,2}. However, viable virus was not recovered from culture after 10 days from the initial positive test \cite{3,4}. Among persons infected with the SARS-CoV-2 Delta variant, vaccinated persons had similar Ct values, but lower viral titers than unvaccinated persons \cite{5}. However, these investigations recruited participants at or shortly after symptom onset, limiting their ability to describe viral shedding during the pre-symptomatic period. During an outbreak of the Delta variant in a federal prison in Texas, we serially tested a cohort of exposed persons and documented the conversion timeline and viral shedding of some participants from exposure to infection and symptom onset.

\section{2. Methods}

During July–August 2021, the US Centers for Disease Control and Prevention (CDC) partnered with the Federal Bureau of Prisons...
(BOP) to investigate a SARS-CoV-2 Delta variant outbreak at a prison in Texas. During this investigation, incarcerated persons were invited to participate in serial swabbing [6]. At the time of the investigation, approximately 80% incarcerated persons in this prison were fully vaccinated.

Trained CDC and BOP personnel collected paired mid-turbinate nasal swabs for antigen testing and reverse-transcription polymerase chain reaction (RT-PCR) every other day from consenting incarcerated persons who were exposed during the outbreak. Exposed persons were placed in quarantine. Participants with a positive antigen test were moved to medical isolation, and study staff collected a single swab daily for 10 days from the date of first positive test. Specimens from infected participants were tested by (RT-PCR) and viral culture.

At the end of the 10-day collection period, all infected participants completed a symptom questionnaire. Demographic characteristics, past medical history, vaccination status, and history of prior SARS-CoV-2 infection were obtained from BOP electronic medical records.

For this case series, we included data from participants with at least one negative SARS-CoV-2 viral test prior to their first positive test to describe infection timelines.

Specimens were tested at CDC by RT-PCR using the CDC Influenza SARS-CoV-2 multiplex assay. Viral culture was performed on remnant aliquots from specimens collected on days 0, 3, 5, 7, and 9 days after first positive test [7]. For more granular analysis across the time-course of infection, viral culture was also performed on a subset of specimens collected on other days.

We performed viral culture using 2-fold serial dilutions of 100 μL clinical specimens in Dulbecco’s Modified Eagle Medium in a 96 well plate and inoculated Vero-E6 cells overexpressing TMPRSS2. Specimen-inoculated cells were incubated at 37 °C in 5% CO₂ and were observed daily for cytopathic effect for 7 days. Cells with observed cytopathic effect were harvested by scraping and used for total nucleic acid extraction and RT-PCR. If the cycle threshold (CT) was ≤ 40, the putative isolate was negative for SARS-CoV-2 RT-PCR targets, or the putative isolate cycle threshold did not meet the criteria of a positive isolate, then it was defined as virus not isolated.

We collected and managed demographic and symptom information using the Research Electronic Data Capture (REDCap) [8]. We analyzed data using R (R Foundation for Statistical Computing, Vienna, Austria) [9]. Viral culture results were classified as positive or negative.

This activity was reviewed and approved by the BOP Research Review Board and CDC’s Human Subjects Protection Office and was conducted consistent with applicable federal laws and CDC policy.²

3. Results

We identified 12 persons who were eligible for this case series analysis (Fig. 1). All were male and all identified as non-Hispanic White. Median age was 43 years (range: 21–65 years). Two persons (17%) withdrew from the investigation before the 10-day collection period was complete, and the outbreak investigation concluded before all 10 daily swabs could be collected for 1 person (8%). Three persons (25%) never had a positive antigen test and were only swabbed every other day.

Among participants with a positive antigen test, 5/9 (56%) had positive viral culture results from specimens collected the same day as the positive antigen test; two participants with a negative antigen test on the day of illness onset had positive viral culture results the same day.

Ten of 12 participants (83%) had completed a primary COVID-19 vaccination series prior to the outbreak with either Pfizer/BNT162b2 (4/10, 40%), Moderna/mRNA-1273 (3/10, 30%), or Janssen/JNJ-78436735 (3/10, 30%). Two vaccinated persons had a documented prior SARS-CoV-2 infection (both > 6 months prior to current illness onset). Both of these persons received their COVID-19 vaccination series following infection with SARS-CoV-2.

We recovered SARS-CoV-2 in viral culture from 9/12 (75%) of participants. All three persons from whom we did not recover SARS-CoV-2 in viral culture had completed their primary vaccination series (Moderna 2/3, Janssen 1/3). The median duration of recovery of SARS-CoV-2 from viral culture was 6 days (range 3–9 days).

We detected SARS-CoV-2 RNA using RT-PCR in 12 participants (Fig. 2). Cycle threshold values tended to increase with increasing number of days from the date of first positive test. One of 5 participants with at least one negative RT-PCR result prior to day 10 (Case #8) recorded a positive result after an initial negative. Samples with positive culture results had lower Ct values (median: Ct = 23.5; range: 16.8–32.2) than samples with negative culture results (median: 31.1; range: 26.3–36.0).

Eleven of 12 participants had at least one underlying medical condition, the most common being overweight with body mass index (BMI) > 25 (10/12, 83% including 5/12, 42% with BMI > 30) and history of tobacco use disorder (7/12, 58%). Information on symptoms was available for 10/12 participants (83%). Among these participants, 4 (40%) reported no symptoms. Among persons reporting symptoms, the median symptom duration was 7 days (range 2–15 days). Median symptom onset was 1 day after the first positive RT-PCR test (range 7 days before to 3 days after). Among participants who reported symptoms, 3/6 (50%) had a positive RT-PCR test and positive viral culture results prior to reported symptom onset. Among participants who did not report symptoms, 3/4 (75%) had at least one positive viral culture result following their first positive RT-PCR result; 2/4 (50%) never had a positive antigen test.

4. Discussion

Both vaccinated and unvaccinated persons had positive RT-PCR test results and recovery of virus in culture following infection with SARS-CoV-2, suggesting that both vaccinated and unvaccinated persons can transmit SARS-CoV-2. We found that symptoms most commonly developed after viable virus was recovered in culture; this finding suggests that transmission can occur early after infection and prior to symptom onset. Among these 12 participants, virus was recovered in culture for up to 9 days following the first positive RT-PCR test, even among vaccinated persons. Initial antigen positivity correlated with recovery of culturable virus, but this association was imperfect as evidenced by the person who had virus recovered in culture prior to their first positive antigen test.

We describe the recovery of SARS-CoV-2 in viral culture from vaccinated individuals, which expands upon similar findings [10]; the effect of COVID-19 vaccination was not previously examined. Further research is needed to determine to what extent vaccinated individuals with SARS-CoV-2 infection may be able to infect others, to what extent antigen testing may be used as a proxy for infectiousness, and correlation of viral shedding with clinical illness among vaccinated and unvaccinated persons.

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² See e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.
This investigation has at least five limitations. First, all infections in this outbreak were due to the Delta variant and viral dynamics may differ from other variants. Second, our sample size did not allow for direct comparisons between vaccinated and unvaccinated persons. Third, the high proportion of vaccinated persons in this prison limits our ability to generalize findings to other settings with lower vaccination rates and potentially different transmission dynamics. Fourth, recovery of SARS-CoV-2 in viral culture from a mid-turbinate swab may not correspond with transmissibility of SARS-CoV-2. Finally, we performed antigen testing...

Fig. 1. Summary of vaccination status, medical history, and laboratory findings among persons with COVID-19 infection identified during an outbreak in a federal prison, July-August 2021. Day 0 refers to the date of the first positive SARS-CoV-2 test [either rapid test or reverse transcription polymerase chain reaction (RT-PCR)]. The vaccine manufacturers are listed as BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and JNJ-7843735 (Johnson & Johnson/Janssen).
only for participants who were not already known to be infected, limiting the ability to correlate positive antigen results with infectiousness throughout the disease course.

These results underscore the need for non-pharmaceutical interventions such as masking, physical distancing, and frequent testing of exposed individuals to mitigate SARS-CoV-2 transmission during outbreaks in high-transmission settings such as prisons, as vaccinated persons may be able to transmit SARS-CoV-2. Understanding the time course of viral shedding relative to symptom onset and symptom duration among vaccinated and unvaccinated persons provides key information related to transmission potential and can help to inform isolation and quarantine measures [11]. As new variants continue to emerge, we should remain vigilant for infections in vaccinated persons and consider that vaccinated persons may be capable of transmitting SARS-CoV-2 [12]. Understanding the viral dynamics for these new variants will be critical to align mitigation measures with these variants’ transmissibility.

Data availability

The authors do not have permission to share data.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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