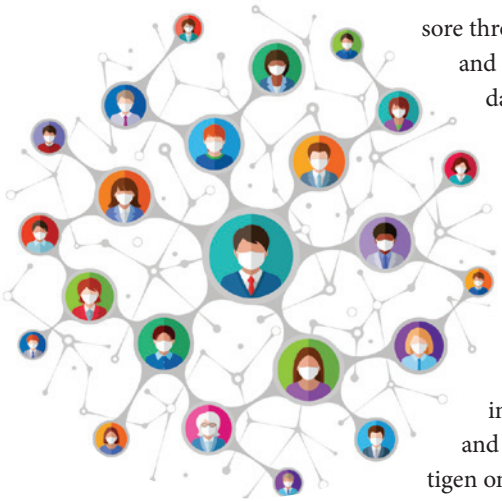
Evidence of symptomatic SARS-CoV-2 reinfection and subsequent transmission



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The first published case of reinfection with SARS-CoV-2, verified by whole genome sequencing (WGS), was reported on August 25, 2020. As of January 31, 2021, there had been more than 15 reports of COVID-19 reinfections that met CDC criteria and several more with evidence supporting reinfection. However, none of these cases reported evidence of transmission as a result of their reinfection, and none were in individuals who had received a dose of a COVID-19 vaccine.

The case we examined was of symptomatic SARS-CoV-2 reinfection and subsequent transmission, 18 days after receiving the initial Pfizer BioNtech COVID-19 vaccine dose and 240 days after initial symptomatic infection.

The patient was a 40-year-old female healthcare worker (HCW) with a history of class III obesity (BMI 45.2) and hypothyroidism, who initially developed symptoms of myalgias, fatigue, chills, sore throat, sore neck and "feeling terrible" on May 11, 2020. A nasopharyngeal sample was collected on May 13, 2020 and tested positive for SARS-CoV-2 by RT-PCR. The patient did not report any known close contacts or travel and did not require hospitalization; acute symptoms resolved after approximately 10 days. She returned to work, with a negative SARS-CoV-2 RT-PCR test on September 28, 2020 and a negative antigen test on October 30, 2020.

The patient received an initial dose of the Pfizer-BioNtech COVID-19 vaccine on December 21, 2020, with no reported adverse reaction. On the evening of January 6, 2021, she developed acute symptoms consistent with COVID-19, including a cough, sore throat, congestion, fatigue, myalgias and headache. On January 8, 2021, 18 days after her first dose of vaccine, she tested positive for SARS-CoV-2 by RT-PCR. She said she had not had any contacts with COVID-19, travel or attendance at large social or holiday gatherings.

On January 11, she received a single infusion of bamlanivimab. That same day, a family member living in her home became symptomatic and tested positive for SARS-CoV-2 antigen on January 12. On January 13, another contact who lives 11 miles away and had last seen the patient on January 9, became symptomatic; that person tested positive for SARS-CoV-2 antigen on January 14. Two other household members developed symptoms of COVID-19 on January 14 and 16.

In order to identify the extent of household transmission, and to obtain samples for SARS-CoV-2 RT-PCR and WGS, anterior nares specimens were collected from the patient, her husband and two adolescent children in their home on January 15, and from her parents, who live about 11 miles away.

WGS was performed by the Minnesota Department of Health (MDH) Public Health Laboratory (PHL) on the five available SARS-CoV-2 RT-PCR positive specimens from the patient and her family members.

Results

The patient had a positive SARS-CoV-2 RT-PCR (Ct value: 19.89) result from the sample obtained on January 8, 2021. The patient was RT-PCR negative on January 15, 2021. SARS-CoV-2 RT-PCR results from the four household contacts taken on January 15, 2021 returned positive. WGS was completed on all four samples. Three of the four samples had identical sequences to the patient sample from January 8, 2021. The fourth had a single nucleotide difference from the patient sequence, but was otherwise identical across the entire SARS-CoV-2 viral genome.

Serologic testing of the serum specimen obtained from the patient on January 21, 13 days after the second positive RT-PCR result, was positive for total antibodies against the viral RBD at a level beyond the reportable range of the assay and negative for total antibodies against the SARS-CoV-2 NC protein. Subsequent serologic analysis, 40 days after the second positive RT-PCR was again positive for total antibodies against the RBD at a level beyond the reportable range of the assay, and also positive for total antibodies against the SARS-CoV-2 NC protein.

Discussion

Duration of immunity after initial SARS-CoV-2 infection, risk of reinfection and transmissibility of infectious virus after rein-

fection are all questions that remain under investigation. Some studies report evidence of extended humoral immunity past 90 days; others report waning antibody levels shortly after infection. A correlation between disease severity and an elevated antibody response has been documented, as has the importance of a strong cellular immune response. However, there is as of yet no defined correlate of protective immunity against re-infection. This patient was seronegative for antibodies to the nucleocapsid antigen, despite testing 15 days following the second onset of COVID-19 symptoms, and seroconverted to anti-nucleocapsid positive by 26 days later. The serologic evidence from this case supports reinfection 240 days after initial infection

This case provides the first molecular and epidemiologic evidence that reinfection can result in viral transmission to contacts, resulting in both positive SARS-CoV-2 RT-PCR and clinical disease.

Since the first WGS-confirmed patient of reinfection by To, et al on August 25, 2020, there have been more than 15 reported cases of reinfection. However, there are no reports of verified transmission from these cases of reinfection. This case provides the first molecular and epidemiologic evidence that reinfection can result in viral transmission to contacts, resulting in both positive SARS-CoV-2 RT-PCR and clinical disease. The patient and her family members did not report any known exposures, gatherings, travel or social events that they attended in the 14 days prior to January 6, the patient's date of symptom onset. She became symptomatic five days before one of her household contacts began developing symptoms and four days before one of her parents, who does not live in the same house. This is consistent with an incubation period of four to five days after exposure. The patient then tested negative by RT-PCR on January 15, the date when her four household contacts were both acutely symptomatic and RT-PCR positive. Finally, three of the four household contacts who tested positive all had identical sequences with the case, and the other sequence had one nucleotide difference.

A limitation on this study is the lack of a sample from the patient's initial infection, so reinfection can't be demonstrated through WGS, which is the only recognized standard of verifying a true reinfection event.

Further clarification on duration of immunity is needed, but this case highlights the need for caution with respect to both previous infection and single-dose administration of COVID-19 mRNA vaccines, and to the risk of subsequent infection. MM

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Funding
This work was supported by Cooperative Agreement Number U60OE000104, funded by Centers of Disease Control and Prevention through the Association of Public Health Laboratories. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of Centers of Disease Control and Prevention or the Association of Public Health Laboratories study participants

Conflicts of interest
Elizta S. Theel is on the advisory board for Roche Diagnostics and Accelerate Diagnostics. The rest of the authors have no conflicts of interest to declare.

Acknowledgements
Richard Danila, Division of Infectious Disease Epidemiology, Prevention and Control, Minnesota Department of Health; Beth Theilen, MD, Division of Pediatric Infectious Diseases, Department of Pediatrics, University of Minnesota Medical School; and Tina Slusher, MD, Pediatric Critical Care Division, Department of Pediatrics, University of Minnesota.

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