Using Virus Sequencing to Determine Source of SARS-CoV-2 Transmission for Healthcare Worker

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Whether a healthcare worker's severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is community or hospital acquired affects prevention practices. We used virus sequencing to determine that infection of a healthcare worker who cared for 2 SARS-CoV-2–infected patients was probably community acquired. Appropriate personal protective equipment may have protected against hospital-acquired infection.

Healthcare workers (HCWs) are at the front lines of the coronavirus disease (COVID-19) pandemic; their interactions with patients and in the community put them at risk for infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (*1*,*2*). Concern about whether HCWs are adequately protected from exposure while caring for patients has been fueled by limited availability of recommended personal protective equipment (PPE), in particular N95 respirators. Determining an HCW's source of SARS-CoV-2 infection—community versus healthcare system—is crucial for evaluating the effectiveness of hospital infection control and PPE practices. Although SARS-CoV-2 infections in HCWs are often presumed to be acquired during the course of patient care, few reports unambiguously identify the source of acquisition. Forensic genomics, using viral sequencing, may be a promising approach.

We report a case of SARS-CoV-2 infection of an HCW at the University of Wisconsin–Madison (Madison, WI, USA) who performed direct care for 2 non–critically ill patients with confirmed SARS-CoV-2 infections (patients 1 and 2). The University of Wisconsin–Madison Institutional Board deemed this study to be quality improvement rather than research and therefore exempt from review.

At the time of this investigation, community prevalence of SARS-CoV-2 in Dane County, Wisconsin, was relatively low (cumulative prevalence ≈0.06% as of April 17, 2020). During this time, precautions in place included universal masking for HCWs, universal face covering for hospital visitors, and masking of symptomatic patients when entering the healthcare system. Hospitalwide hand hygiene compliance rates were 93%–96%.

While caring for patients 1 and 2, the HCW in this study wore a barrier facemask made to ASTM International (https://www.astm.org) standards, a face shield, reusable gowns, and nonsterile gloves. Four days after providing care for these patients, the HCW began experiencing headache, fever, and sore throat. A nasopharyngeal swab sample was positive for SARS-CoV-2 viral RNA. To establish the possible source of infection, we interviewed the HCW's family member, who had experienced a febrile illness 8 days before the HCW's onset of symptoms but was not tested initially because of limited testing availability. A nasopharyngeal swab sample from the family member was also positive for SARS-CoV-2 (Figure 1).

We sequenced viral RNA isolated from nasopharyngeal swab samples from patients 1 and 2, the HCW, and the family member. To determine whether the HCW most likely acquired infection in the healthcare setting or in the community, we compared consensus SARS-CoV-2 sequences from these 4 persons.

All 4 samples were prepared for sequencing by using the ARTIC protocol (https://artic.network/ncov-2019/ncov2019-bioinformatics-sop.html) and were sequenced on an Oxford Nanopore GridION device (Nanopore Technologies, https://nanoporetech.com/products/gridion). Consensus sequences were derived by using a modified version of the ARTIC bioinformatics protocol (https://www.protocols.io/view/ncov-2019-sequencing-protocol-bbmuik6w), which analyzes data after 100,000 reads have been obtained from each sample (analysis pipelines are available at GitHub, https://github.com/katarinabraun/SARS-CoV-2_sequencing/tree/master/Pipelines_to_process_data/Nanopore_pipeline_ARTIC).

The sequence from the HCW was identical to that of the HCW's family member but distinct from that of patients 1 and 2 (Figure 2). Although we cannot with absolute certainty exclude the possibility that the HCW was infected by another asymptomatic, untested hospitalized patient, the identical virus sequences from the HCW and the HCW's family member provide strong circumstantial evidence for a chain of virus transmission outside of the hospital.

Within 2 days of the positive SARS-CoV-2 test result for the HCW, sequencing of the virus identified the probable source of infection as community transmission. This finding offers reassurance to HCWs

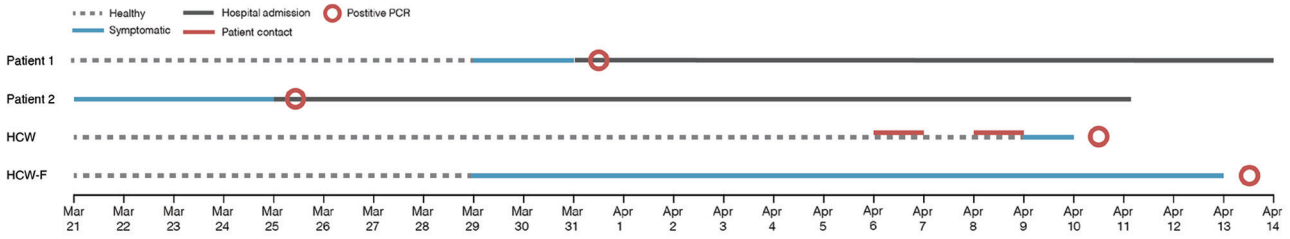
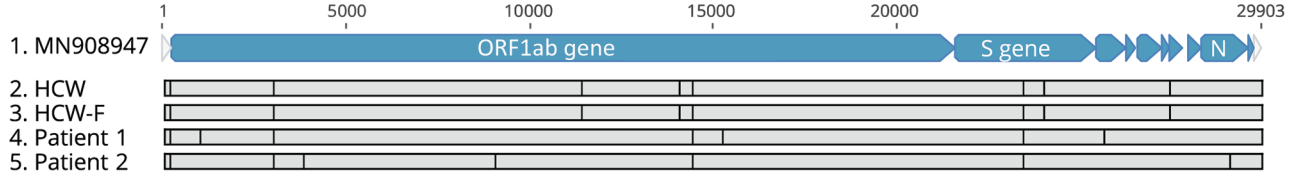


Figure 1. Timeline of infection, contact, and testing of HCW, HCW's family member, and coronavirus disease patients 1 and 2, Madison, Wisconsin, USA, 2020. HCW, healthcare worker; HCW-F, HCW's family member.

caring for patients with COVID-19 that appropriate PPE may protect against hospital-acquired SARS-CoV-2 infection. Conversely, had sequencing demonstrated nosocomial transmission, that would have provided an impetus for revisiting infection control strategies. On the basis of these results, sequencing of SARS-CoV-2 from HCWs and known contacts, within and outside of patient care settings, should be an essential component of a comprehensive strategy to protect the health of HCWs and other frontline workers.



Position	Location	Reference	HCW	HCW-F	Patient 1	Patient 2	Annotation
241	3' UTR	C	T	T	T	T	
1059	ORF1ab	C	·	·	T	·	T265I
3307	ORF1ab	C	T	T	T	T	Synonymous
3871	ORF1ab	G	·	·	·	T	K1202N
9053	ORF1ab	G	·	·	·	T	V2930L
11417	ORF1ab	G	T	T	·	·	V3718F
14073	ORF1ab	T	C	C	·	·	Synonymous
14408	ORF1ab	C	T	T	T	T	P4715L
23403	S	A	G	G	G	G	D614G
23947	S	A	G	G	·	·	Synonymous
25563	ORF3a	G	·	·	T	·	Q57H
27348	ORF6a	T	G	G	·	·	Y49*
29008	N	T	·	·	·	C	Synonymous

Figure 2. Severe acute respiratory syndrome coronavirus (SARS-CoV-2) consensus-level single-nucleotide variants (SNVs) from investigation of SARS-CoV-2 infection in HCW, Madison, Wisconsin, USA, 2020. The top alignment image depicts the SARS-CoV-2 genome for all persons evaluated in this investigation and highlights SNVs identified relative to the original SARS-CoV-2 reference isolate from Wuhan, China (GenBank accession no. MN908947.3). The table contains additional information about each of these SNVs. Light blue shading indicates A2a clade-defining mutations. Dots indicate identity with reference sequence. Asterisk indicates a tyrosine-to–stop codon change. HCW, healthcare worker; HCW-F, HCW's family member; ORF, open reading frame; UTR, untranslated region.

Acknowledgment

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About the Author

Dr. Safdar is an infectious diseases physician, scientist, and hospital epidemiologist. Her research focuses on patient and healthcare worker safety in healthcare settings.

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Disappearance of SARS-CoV-2 Antibodies in Infants Born to Women with COVID-19, Wuhan, China

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We report the detection and decline over time of severe acute respiratory syndrome coronavirus 2 antibodies in infants born to women with coronavirus disease. Among 11 infants tested at birth, all had detectable IgG and 5 had detectable IgM. IgG titers with positive IgM declined more slowly than those without.

Although the diagnosis of coronavirus disease (COVID-19) by reverse transcription PCR (RT-PCR) is efficient and specific, IgM and IgG production and decay are useful to assess past or recent infection, especially for patients with negative nucleic acid tests (*1*). Evidence of IgM and IgG in adults with COVID-19 appeared around 13 days after illness onset (*2*). Plateau IgM levels lasted for 4 weeks and gradually declined (*3*). Although IgG lasted for a longer time, only 19.5% patients had a ≥4-fold increase in titers during convalescence, a finding that was helpful for diagnosis of existing or acute infection (*2*,*3*).

However, to our knowledge, antibody persistence in infants born to women with COVID-19 has not yet been reported. IgM is the antibody isotype produced initially in the immune response and the first immunoglobulin class to be synthesized by a fetus or infant. Maternal IgM does not cross the placental barrier intact; therefore, positive IgM in early infants is potential evidence of intrauterine vertical transmission (*1*). Although IgG is transferred passively from mother to fetus through the placenta, the duration of passive immunity from maternal IgG is still unclear.

We implemented assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–specific antibodies and SARS-CoV-2 nucleic acid tests in 64 infants admitted to the neonatal section of Tongji Hospital (Wuhan, China) during January 19–April 12, 2020. Among these, 24 infants (ranging in gestational age from 31 weeks to 41 weeks, 2 days) were born to women with PCR-confirmed COVID-19 (Table) and 40 infants (ranging in gestational age from 35 weeks, 3 days, to 41 weeks, 3 days) were born to women without COVID-19. Because antibody testing was implemented in early March, the timing of antibody testing in infants was inconsistent. We conducted SARS-CoV-2 nucleic acid tests by using a qualitative SARS-CoV-2 RT-PCR (DAAn GENE Biotech, http://www.daangene.com). We performed quantitative assessment of IgG and IgM by using the IFlash3000 Chemiluminescence Immunoassay Analyzer (YHLO Biotech, http://en.szyhlo.com), which has been proven to be a highly accurate method to detect SARS-CoV-2 antibodies (*4*). We considered IgM or IgG titers >10 AU/mL to be positive.