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BRIEF REPORT

Viral Genomics to Inform Infection-control Response in Occupational Coronavirus Disease 2019 (COVID-19) Transmission

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Healthcare workers are at increased risk of occupational transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We report 2 instances of healthcare workers contracting SARS-CoV-2 despite no known breach of personal protective equipment. Additional specific equipment cleaning was initiated. Viral genomic sequencing supported this transmission hypothesis and our subsequent response.

Keywords. COVID-19; genomics; occupational; transmission.

Healthcare workers (HCWs) are at increased risk of infection with coronavirus disease 2019 (COVID-19). Our experience in Australia has to date consisted predominantly of imported cases in returned travelers, and clusters related to travelers and other high-risk settings [1]. A coordinated response to extensively test and isolate suspected and confirmed COVID-19 cases has been initiated, alongside social-distancing measures and use of personal protective equipment (PPE). At our large 2200-bed, quaternary health service in Melbourne, Victoria, Australia, as of 1 June 2020, 21 patients confirmed with COVID-19 have been admitted, with 2 HCWs diagnosed with COVID-19 suspected as occupational acquisitions. Both had a history of direct contact with patients with COVID-19, but without a clear PPE breach. Service-wide PPE at this time consisted of a tiered approach, with droplet and contact precautions for all patients with suspected and confirmed COVID-19, and airborne and contact precautions when patients were unwell with pneumonia or had aerosol-generating procedures. All PPE was single-use in the facility at the time, except for eyewear (goggles), which was in low supply; goggles were reused after a single-step clean by the wearer, with a bleach solution. We investigated these HCW infections using genomics to better understand the source of infection and inform appropriate institutional responses.

METHODS AND RESULTS

Putative Transmissions

Patient 1 was a 46-year-old man with mild asthma who returned to Australia from international travel and entered home quarantine. He developed dyspnea on the third day of quarantine and was hospitalized 4 days later due to worsening exertional dyspnea. On day 7 of his illness he clinically deteriorated, requiring high-flow oxygen via nasal prongs, and ultimately requiring intensive care unit admission for intubation and ventilation the same day. Healthcare worker 1, a 43-year-old nurse, directly cared for patient 1 on days 6 and 7 of his illness, during which time airborne and contact precautions were used including a negative-pressure room. She did not provide concurrent care for any other patients with known COVID-19. Six days after her first contact with patient 1, HCW 1 developed a sore throat and fever, and was diagnosed with COVID-19 based on positive polymerase chain reaction (PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on nasopharyngeal swab the following day. She reported no breach from protocol for PPE use, no other contacts or epidemiological risk factors for COVID-19 infection, and she recovered without hospitalization.

Patient 2 was the mother-in-law and a suspected close contact of patient 1, as a household contact during his quarantine. Along with another household member she subsequently contracted SARS-CoV-2. The patient was an 84-year-old woman with no comorbidities who became unwell after exposure to patient 1 with fever and sore throat and was hospitalized the same day at a different hospital site from patient 1. Healthcare

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worker 2, a 43-year-old doctor, assessed the patient on day 5 of her illness over a 20-minute period, followed recommended PPE with airborne and contact precautions, a negative-pressure room, and included the use of a "spotter"—that is, a trained staff member to check appropriate PPE use at the donning and doffing stages. Patient 2 subsequently deteriorated clinically with increased oxygen requirements on day 6, and passed away on day 9 of her illness. Healthcare worker 2 became unwell with fever and sore throat 6 days after contact with patient 2, with a positive SARS-CoV-2 PCR from a nasopharyngeal swab on the same day. Healthcare worker 2 did not provide clinical care for any other patients with known COVID-19, no other potential COVID-19 exposures or risk factors were identified, and clinical course was mild. Three other staff members and a patient were furloughed (because of HCW 2 contact) but remained well. No contact was identified between HCW 1 and HCW 2.

In response to these cases, and because no other PPE breach was identified, the cleaning step for goggle reuse was hypothesized as the potential exposure. A second step of chlorine immersion outside the clinical area was added. With the overall low infection rate in our hospital, it has not been possible to confirm this as the mode of transmission, although no further transmissions have been identified linked to goggle reuse.

Genomic Sequencing and Analysis

In the state of Victoria, all SARS-CoV-2 PCR–positive samples are forwarded to the Doherty Institute Public Health Laboratories for genomic sequencing and analysis. Extracted RNA from samples underwent tiled amplicon PCR (ARTIC protocols) and Illumina sequencing as previously described [1]. Reads were aligned to the reference genome (Wuhan Hu-1; GenBank MN908947.3) with *minimap2*, and consensus sequences were generated (*SAMtools*, *ivar consensus*). A multiple-sequence alignment was generated using *MAFFT* (version 7.453) and cleaned up with *arbow* (version 0.4.0; https://github.com/MDU-PHL/arbow), generating a maximum likelihood tree using IQ-Tree (version 1.6.12). The median time from sample collection to sequence data availability was 16 days (range, 11–21 days). Sequences have been uploaded to GISAID and GenBank (Supplementary Data File 1), and protocol references are detailed in Supplementary Data File 2.

Phylogenetic Analysis

Samples from all 4 cases (patients 1 and 2 and HCWs 1 and 2) were highly related by genomics, all clustering in the same part of the phylogenetic tree (Figure 1). Specifically, the sequences from patient 1, HCW 1, and HCW 2 (and a household contact) were indistinguishable, while the sequence from patient 2 was very closely related with only 1 single nucleotide polymorphism difference (Figure 1, insert). This may be due to natural evolution in vivo or, alternatively, due to RNA degradation during sample processing and sequencing [2]. While the phylogenetic model was uncertain of the internal structure of the cluster (some branches with bootstrap support values <10), the branch defining the cluster was very well supported, indicating that all samples in the cluster were consistently more closely related to each other than to any other samples in the tree, confirming the hypothesis that the HCWs likely acquired SARS-CoV-2 from the respective patients. Additional cases in the same cluster included 2 people who attended the same overseas event as patient 1 (one with contact with patient 1), 1 household contact of a traveler to this event, and a smaller number of cases without known epidemiologic links to these cases. Additional information including a global context tree is available in published data by Seemann et al [1].

DISCUSSION

Healthcare workers are at increased risk of contracting SARS-CoV-2 due to workplace exposure: for example, over half of infected HCWs in the United States reported occupational exposure as their only known risk factor for COVID-19 [3]. Use of PPE is an important step in protecting HCWs from contracting coronaviruses and other infectious diseases but requires appropriate training to reduce the risk of accidental contamination, in addition to support from the work environment to access appropriate PPE and vigilance for potential causes of PPE failure.

Despite strict PPE policy and adherence, we observed 2 likely HCW COVID-19 transmissions. These events were treated as significant events and led to changes in our policy relating to goggle cleaning, a step suggested by both HCWs as a potential weak point in preventing transmission. Optimal PPE to protect against COVID-19 has been a topic of ongoing debate: a recent systematic review [4] identified a paucity of evidence relating to best PPE combination and doffing procedures, including no studies investigating the use of goggles or face shields. To assist with analysis of whether our 2 cases of presumed transmission were due to an unexpected failure of PPE, genomic sequencing was performed and confirmed a close relationship between the 4 cases consistent with epidemiological suspicion.

A combined approach integrating epidemiological and genomic surveillance data is being increasingly used for bacterial and viral healthcare outbreaks [5] and can help inform infection-control responses to outbreaks. Whole-genome sequencing was used to track nosocomial influenza transmission in a high-risk inpatient group, identifying unexpected viral introduction and allowing a tailored infection-control response [6]. Genomic sequencing has been used since the early stages of the SARS-CoV-2 pandemic to map transmission dynamics and help model predicted spread [7]. While genomic diversity is relatively limited among SARS-CoV-2 sequences [7, 8], in practice there is usually adequate resolution to support or refute putative transmission events in order to inform infection-control and public health investigations [9, 10]. In our setting, rapid genomic analysis supported the hypothesis that transmission occurred due to unexpected

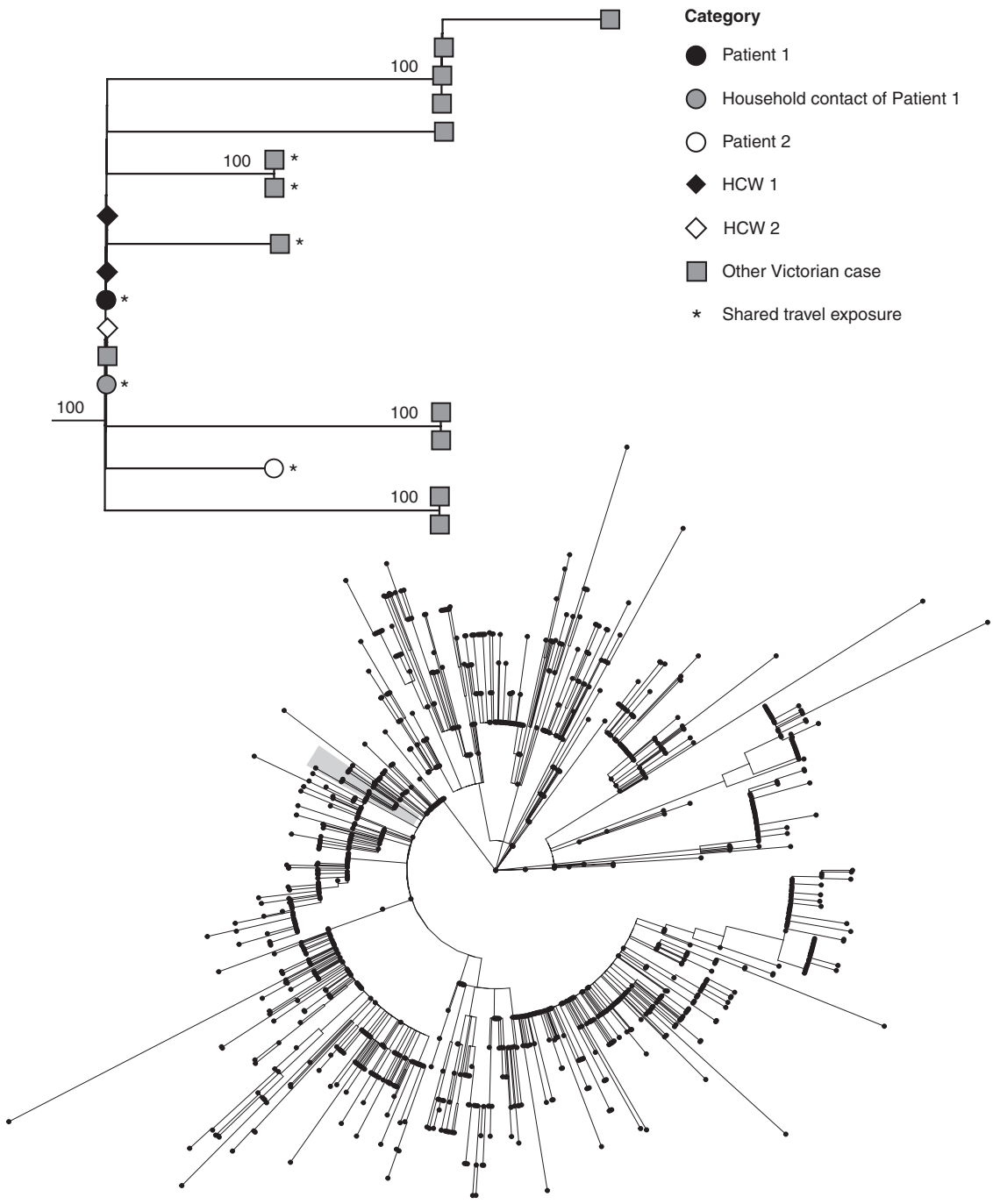

Figure 1. Phylogenetic tree of Victorian SARS-CoV-2 sequences available on 1 June 2020. A subtree of the cluster containing the 4 cases is shown in the top left, and its location in the larger tree shaded in dark gray. The tips are colored different shades by case category, and the diamond tip shape indicates common epidemiological exposure. The tree includes sequences from 2 samples for HCW 1, collected on separate days. Bootstrap values for branch support in the subtree are shown if ≥70%. Abbreviations: HCW, healthcare worker; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

PPE failure, enabling prompt changes to infection-control protocols and the decision to add postcontact cleaning for reusable goggles. This approach was particularly helpful given the epidemiology in Australia at this time, with multiple introductions of diverse SARS-CoV-2 strains by returned travelers with subsequent limited community transmission. Conversely, genomics may be more challenging in contexts with limited genomic diversity, such as in large clonal outbreaks.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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