Viral genomics to inform infection control response in occupational COVID-19 transmission

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ABSTRACT:

Healthcare workers are at increased risk of occupational transmission of SARS-CoV-2. We report two 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

BACKGROUND:

Healthcare workers are at increased risk of infection with COVID-19. Our experience in Australia has to date consisted predominantly of imported cases in returned travellers, and clusters related to travellers and other high-risk settings [1]. A co-ordinated 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 01/06/2020, 21 patients confirmed with COVID-19 have been admitted, with two healthcare workers (HCW) diagnosed with COVID-19 suspected as occupational acquisitions. Both had a history of direct contact with COVID-19 patients, but without a clear PPE breach. Service-wide PPE at this time consisted of a tiered approach, with droplet and contact precautions for all suspected and confirmed COVID-19 patients, 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 eyewear (goggles), which were 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 / 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 dyspnoea on the third day of quarantine and was hospitalised four days later due to worsening exertional dyspnoea. On day 7 of his illness he clinically deteriorated, requiring high flow oxygen via nasal prongs, and ultimately requiring ICU 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 sore throat and fever, and was diagnosed with COVID-19 based on positive polymerase chain reaction (PCR) for 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 hospitalisation.

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 hospitalised the same day to a different hospital site to Patient 1. HCW 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. HCW 2 became unwell with fever and sore throat six days after contact with Patient 2, with positive SARS-CoV-2 PCR from a nasopharyngeal swab on the same day. HCW 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 hypothesised 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 (Supplementary Data)

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. 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* (v7.453) and cleaned up with *arbow* (v0.4.0, https://github.com/MDU-PHL/arbow), generating a maximum likelihood tree using IQ-Tree (v1.6.12). 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), protocol references are detailed in Supplementary Data File 2.

Phylogenetic analysis

Samples from all four 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, whilst the sequence from Patient 2 was very closely-related with only one single nucleotide polymorphism (SNP) 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 two people who attended the same overseas event as Patient 1 (one with contact with Patient 1), one household contact of a traveller 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 healthcare workers in the United States reported occupational exposure as their only known risk for COVID-19 [3]. Use of PPE is an important step in protecting healthcare workers 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 two 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 healthcare workers 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 two cases of presumed transmission were due to an unexpected failure of PPE, genomic sequencing was performed, and confirmed a close relationship between the four cases consistent with epidemiological suspicion.

The use of 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]. Whilst genomic diversity is relatively limited amongst 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 PPE failure, enabling prompt changes to infection control protocols and the decision to add post-contact 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 travellers with subsequent limited community transmission. Conversely, genomics may be more challenging in contexts with limited genomic diversity, such as in large clonal outbreaks.

NOTES

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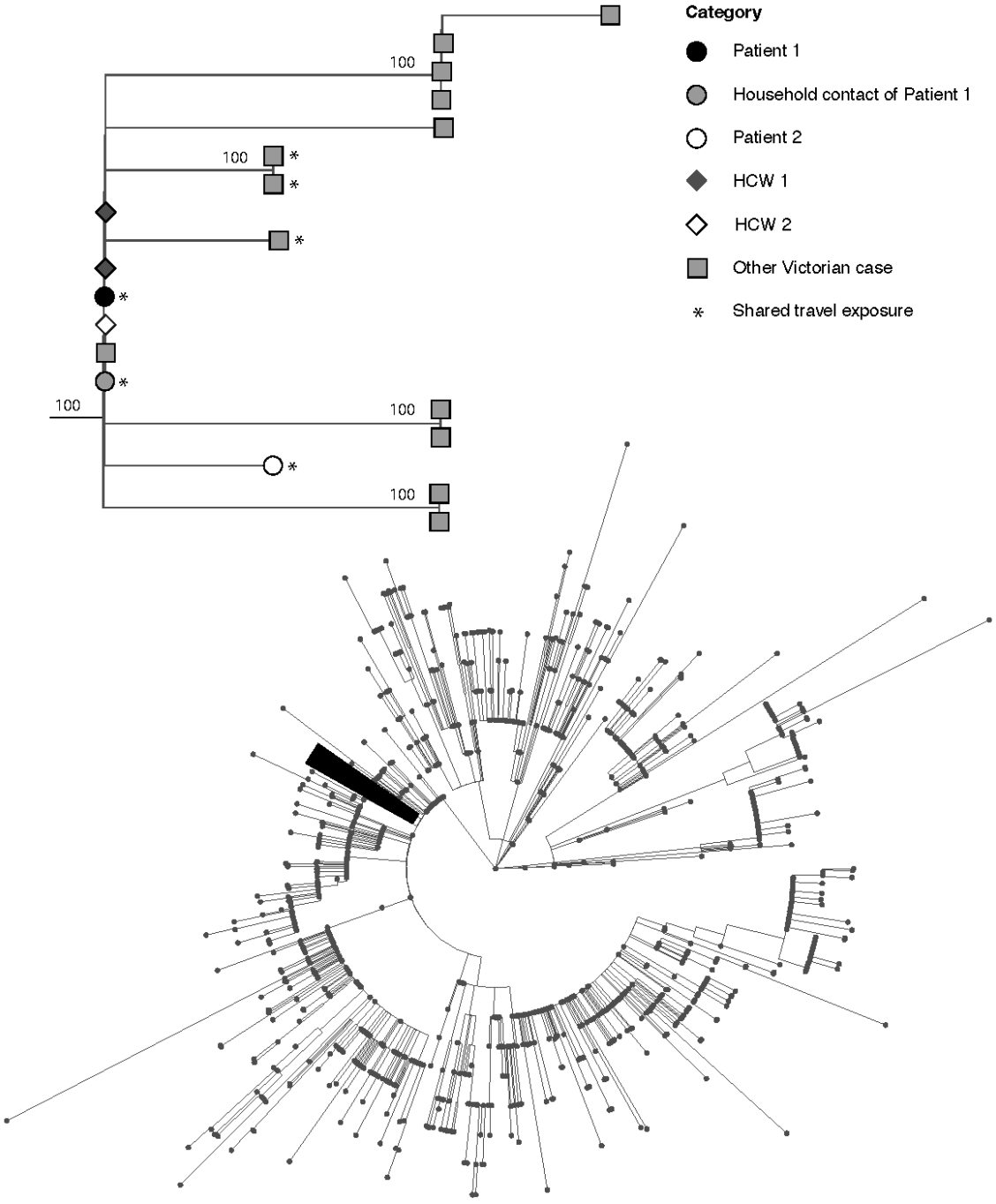
Figure legend

Figure 1. Phylogenetic tree of Victorian SARS-CoV-2 sequences available at 1 June 2020. A subtree of the cluster containing the four cases is shown in the top left, and its location in the larger tree shaded in dark grey. The tips are coloured different shades by case category, and diamond tip shape indicates common epidemiological exposure. The tree includes sequences from two samples for HCW1, collected on separate days. Bootstrap values for branch support in the subtree are shown if ≥70%.

Figure 1


Category
Patient 1
Household contact of Patient 1
Patient 2
HCW 1
HCW 2
Other Victorian case
Shared travel exposure
100
100
100
100
100