Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Details of SARS-CoV-2 reinfections at a major UK tertiary centre

To the editor,

Although infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been demonstrated to generate a detectable immune response, the susceptibility of previously infected individuals to reinfection is poorly understood.[1] Hanrath et al., (2020) suggested prior SARS-CoV-2 infection in healthcare workers is associated with protection against symptomatic reinfection for up to 6 months.[2] However, in studies of immunity to other coronaviruses, loss of immunity to infection occurs within 1–3 years.[3] Reports of SARS-CoV-2 reinfection events have been published from Brazil, Hong Kong, the Netherlands and Belgium.[1,4] Here, we discuss SARS-CoV-2 reinfections of patients at University Hospitals Birmingham (UHB) NHS Foundation Trust, using whole genome sequencing to identify responsible variants.

UHB is one of the largest Trusts in the UK, covering 4 NHS hospital sites, treating over 2.2 million patients per year and housing one of the largest single critical care units in the world. UHB's patient testing programme detects SARS-CoV-2 RNA from nasopharyngeal swabs/sputum using molecular platforms including Panther, Hologic, M2000, Abbott and GeneXpert, Cepheid. A database of SARS-CoV-2 positive patients was analysed for potential reinfections, defined as patients with a positive result $\geq$ 90 days after their first. This was based on Public Health England (PHE) guidance for management of exposures in healthcare settings, which states immunocompetent staff and patients testing positive for SARS-CoV-2 by PCR should be exempt from routine retesting within 90 days of initial illness onset/test unless they develop new COVID-19 symptoms.[5] Potential reinfection samples underwent whole-genome sequencing at the University of Birmingham. Lineages were assigned with Pangolin.[6]

UHB has seen more COVID-19 cases than any other UK Trust. Between 01/03/20 and 21/02/21, there were 12,960 COVID-19 cases. Thirty-six of these had a positive result beyond 90 days of their first positive. Three of these patients had at least one negative result in between and had one sample which successfully generated sequence data.

Case 1. A 92 year old white British male, with a background of dementia, presented in April 2020 with pyrexia, a dry cough and shortness of breath. Chest X-ray showed bilateral infiltrates suggestive of COVID-19 pneumonia, confirmed with SARS-CoV-2 PCR detection (01/04/2020, Abbott M2000 cycle threshold (Ct) value 15.89). Sequencing of this sample failed. This patient re-presented to UHB on 25/10/20 with lethargy, persistent cough and pyrexia; a diagnosis of aspiration pneumonia was made. His day 7 swab was SARS-CoV-2 positive (02/11/21, Hologic, Panther, Relative Light Unit (RLU) value 1290). Swabs on days 0 and 5 were negative. The sample was sequenced and identified as the variant, B.1.177. A follow up sample could not be obtained as the patient died.

Case 2. An 84 year old white British male with a background of dementia and Paget's disease was admitted in May 2020 with lethargy and confusion, attributed to a catheter associated urinary tract infection. He tested positive for SARS-CoV-2 on day 13 of admission (23/05/20, Abbott M2000, Ct value 26.79), reporting mild symptoms of headache and fatigue. Swabs taken on days 0, 5 and 7 were negative. The positive sample failed to sequence. The patient was readmitted in December 2020 due to a fall, and was negative for SARS-CoV-2 during this admission. In January 2021, the patient re-presented to UHB after another fall and was found to be positive for SARS-CoV-2 (02/01/2021, Hologic, Panther, RLU 1211). A follow up sample confirmed the infection. There were no COVID-19 symptoms. This sample was sequenced and identified as variant B.1.177.

Case 3. A 59 year old British Asian male with end stage renal failure presented in May 2020 during routine dialysis with a cough and fluctuating temperature. The patient tested positive for SARS-CoV-2 on 05/06/2020 (Abbott M2000, Ct value 22.03), however, the sample failed sequencing. Multiple dialysis attendances followed, where the patient tested negative, until a positive result was obtained at a routine dialysis session in January 2021 (28/01/2021, Hologic, Panther, RLU 1348). No COVID-19 symptoms were reported. This sample was sequenced and identified as variant of concern (VOC) B.1.1.7. A follow up sample confirmed the positive result.

Here, we present details of patients who appear to have SARS-CoV-2 reinfections based on sequencing results. Although we have been unable to sequence samples from the previous infections, we have successfully sequenced samples from their latest admissions. The variants identified, B.1.177 and B.1.1.7 were not present in the UK in April and May.[7,8] B.1.177 is thought to have first originated in Spain in early summer 2020.[7] The first sequences in England associated with this lineage were identified on 18th July, when quarantine-free travel between the UK and Spain was allowed (10–26th July 2020).[7] B.1.1.7, the so called Kent variant, was first identified in the UK on 20th September 2020.[8] Using these data, we deduce that our patients have been re-infected with new COVID-19 variants, as neither was circulating in the UK when the patients first tested positive.

Only the three cases mentioned had laboratory results suggesting reinfection. The other 33 patients either had samples missing from prior infections or the second sample did not sequence. Sequencing often fails when the Ct value is too high or the RLU is too low.[9,10] Further work is warranted to explore this. Another important point is that all these reinfections were in patients who do not meet the PHE criteria for severe immunosuppression which is known to increase the risk of infection.[5] Although our data suggest reinfections occur, it is important to note we have been unable to

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sequence two paired samples from the same patient. Another point to note is we have not re-confirmed these sequence results.

Exiting the second UK COVID-19 wave, we must recognise the possibility of reinfection and the implications for managing previous positive patients within hospitals. Real time whole genome sequencing will prove useful to rapidly identify new variants and reinfections, facilitating appropriate patient management.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

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Declaration of Competing Interest

None.

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