3. Breithaupt-Faloppa AC, Correia CJ, Prado CM, Stilhano RS, Ureshino RP, Moreira LFP. 17β-Estradiol, a potential ally to alleviate SARS-CoV-2 infection. Clinics (Sao Paulo) **2020**; 75:e1980.
4. Grandi G, Facchinetti F, Bitzer J. The gendered impact of coronavirus disease (COVID-19): do estrogens play a role? Eur J Contracept Reprod Health Care **2020**; 25:233–4.
5. Ramírez I, De la Viuda E, Baquedano L, et al. The thromboembolic risk in Covid-19 women under hormonal treatment group. Maturitas **2020**; 138:78–9.
6. de Villiers TJ, Hall JE, Pinkerton JV, et al. Revised global consensus statement on menopausal hormone therapy. Maturitas **2016**; 91:153–5.
7. Paschou SA, Goulis DG, Lambrinoudaki I, Papanas N. Menopausal hormone therapy for women with obesity in the era of COVID-19. Case Rep Womens Health **2020**; 27:e00233.
8. Ramírez I, De la Viuda E, Baquedano L, et al. Managing thromboembolic risk with menopausal hormone therapy and hormonal contraception in the COVID-19 pandemic: recommendations from the Spanish Menopause Society, Sociedad Española de Ginecología y Obstetricia and Sociedad Española de Trombosis y Hemostasia. Maturitas **2020**; 137:57–62.

Correspondence: S. Wang, Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030 China (sxwang@tjh.tjmu.edu.cn).

Clinical Infectious Diseases® 2021;73(9):e2826–7

DOI: 10.1093/cid/ciaa1450

A Case of Early Reinfection With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

To the Editor—It is with great interest that we read the first report of reinfection from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which represented an important data point in the ongoing coronavirus disease 2019 (COVID-19) pandemic [1–3]. Questions have arisen regarding the timing and severity of reinfections, for which we offer a case report of symptomatic reinfection within 90 days.

A 42-year-old healthy, male, military health-care provider presented with cough, subjective fever, and myalgias on 21 March 2020 following a workplace COVID-19 exposure and tested positive by SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR; Figure 1). A physical examination was unrevealing and supportive outpatient management was pursued [4]. Clinical resolution of the illness occurred by day 10, and he returned to baseline excellent health for the following 51 days.

On 24 May 2020 he presented with fevers, cough, shortness of breath, and gastrointestinal symptoms, following a confirmed new household exposure to COVID-19. The physical examination revealed a temperature of 100.2°F, pulse of 119 beats per minute with a blood pressure of 124/87 mmHg, and respirations of 24 breaths per minute with oxygen saturation of 92–94% on ambient air. A chest X-ray demonstrated a pulmonary infiltrate. Multiplex respiratory RT-PCR testing was negative but SARS-CoV-2 Reverse transcription polymerase chain reaction (RT-PCR) was again positive. Notably, the symptoms were significantly worse when compared with the initial syndrome. Serum collected on 1 June 2020 demonstrated the presence of SARS-CoV-2 spike immunoglobin G antibodies.

Samples were collected as part of the institutional review board–approved protocol Infectious Disease Clinical Research Program (IDCRP)-085. Viral culture was attempted but was unsuccessful. RNA sequencing was performed via the ARTIC Novel Coronavirus 2019 (nCoV-2019) Sequencing protocol [5], the YouSeq SARS-CoV-2 Coronavirus Next Generation Sequencing (NGS) Library prep kit, and SuperScript IV (ThermoFisher Scientific). The consensus genome was generated and single nucleotide variants were determined [6]. Global lineage was determined using a subset of SARS-CoV-2 genomes available from the Global Initiative on Sharing All Influenza Data repository (GISAID; accessed 24 June 2020). Alignments were performed [7] and a maximum likelihood tree was generated [8]. The SARS-CoV-2 genome from the reinfection sample was deposited in National Center for Biotechnology Information (NCBI) GenBank under accession MT840184.

A partial genome sequence was obtained from the initial clinical infection, consisting of sequence fragments totaling 4126 base pair (bp) and distributed across the genome. Sequencing of the sample from the patient's second illness yielded a nearly coding-complete genome of 27 268 bp. A discrete 50 bp region of 0 coverage was observed. The phylogenetic analysis placed this virus in lineage B.1.26, and the genome encoded the D614G variation in the spike protein [9, 10]. A comparison of the partial sequence obtained from the initial infection with the nearly complete sequence obtained from the reinfection identified several potential variations, including 1 high-confidence variation.

The clinical, epidemiological, and sequencing data of this case suggest early reinfection with SARS-CoV-2, only 51 days after resolution of the initial infection. Importantly, this was observed in a young, immunocompetent patient. In contrast to the case reported by To et al [1], this second infection was more severe, potentially due to immune enhancement, acquisition of a more pathogenic strain, or perhaps a greater inoculum of infection, as the second exposure was from within the household.

Notes

Disclaimer. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Uniformed Services University of the Health Sciences, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Fort Belvoir Community Hospital, the Defense Health Agency, Department of Defense, Departments of the Army, Air Force, or Navy, or U.S. Government. Several of the authors are U.S. Government employees. This work was prepared as part of their official duties. Title 17 U.S.C. § 105 provides that `Copyright protection under this title is not available for any work of the United States Government.' Title 17 U.S.C. §101 defines a U.S. Government work as a work prepared by a military service member or employee of the U.S. Government as part of that person's official duties. Human Research/Institutional Review Board Statement: The study protocol was approved by the Uniformed Services University Institutional Review board in compliance with all applicable Federal regulations governing the protection of human subjects.

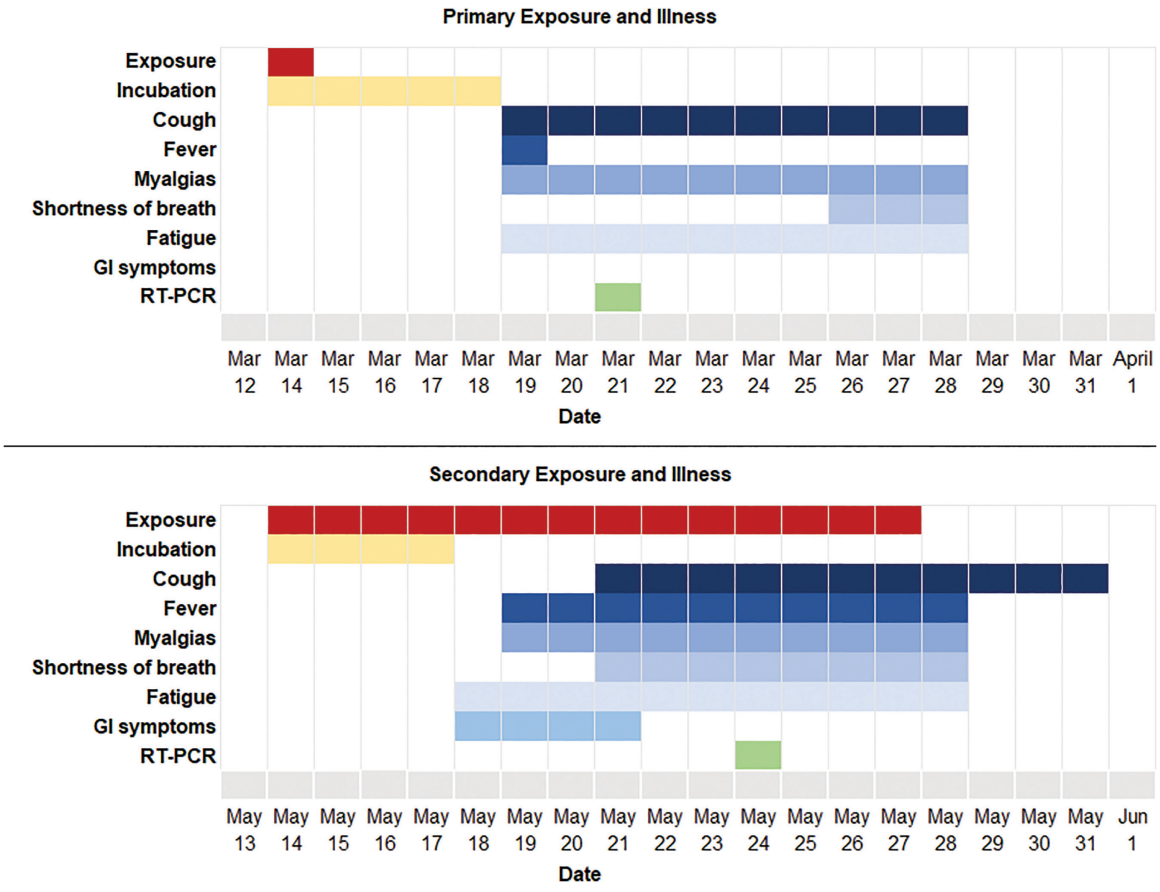

Figure 1. Timeline of symptoms and testing. Abbreviations: GI, gastrointestinal; RT-PCR, reverse transcriptase polymerase chain reaction.

The identification of specific products, scientific instrumentation, or organization is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the author, DoD, or any component agency.

Financial support. This work was supported by X (grant numbers Work Unit Number (WUN) A1417 and Global Emerging Infections Surveillance (GEIS) P0013_20_AH_01.01 to K. A. B.-L. for virus isolation, sequencing, and bioinformatic analyses); and the Defense Health Program (grant number IDCRP-085).

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.

Derek Larson,[1] Sterling L. Brodniak,[2] Logan J. Voegtly,[3,4] Regina Z. Cer,[3,4] Lindsay A. Glang,[3,4] Francisco J. Malagon,[3,4] Kyle A. Long,[3,4] Ronald Potocki,[5] Darci R. Smith,[6] Charlotte Lanteri,[7] Timothy Burgess,[7] and Kimberly A. Bishop-Lilly[4]

[1]Division of Infectious Disease, Fort Belvoir Community Hospital, Fort Belvoir, Virginia, USA, [2]Department of Family Medicine, Fort Belvoir Community Hospital, Fort Belvoir, Virginia, USA, [3]Leidos, Reston, Virginia, USA, [4]Genomics and Bioinformatics Department, Biological Defense Research Directorate, Naval Medical Research Center, Fort Detrict, Maryland, USA, [5]Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [6]Immunodiagnostics Department, Biological Defense Research Directorate, Naval Medical Research Center, Fort Detrict, Maryland, USA, and [7]Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University, Bethesda, Maryland, USA

References

1. To KKW, Hung IFN, Ip JD, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis [Preprint]. August 25, 2020 [cited 2020 Sep 15]. doi:10.1093/cid/ciaa1275.
2. Mathew D, Giles JR, Baxter AE, et al. Deep immune profiling of COVID-19 patients reveals distinct immunotypes with therapeutic implications. Science. [Preprint]. July 15, 2020 [cited 2020 Sep 15]. doi:10.1126/science.abc8511.
3. Cento V, Colagrossi L, Nava A, et al. Persistent positivity and fluctuations of SARS-CoV-2 RNA in clinically-recovered COVID-19 patients. J Infect **2020**; 81:e90-2. S0163-4453(20)30405-9. doi:10.1016/j.jinf.2020.06.024.
4. Larson DT, Sherner J, Gallagher K, et al. Clinical outcomes of COVID-19 with evidence-based supportive care. Clin Infect Dis. [Preprint] May 30, 2020 [cited 2020 Aug 12]. doi:10.1093/cid/ciaa678.
5. Quick, J. nCoV-2019 sequencing protocol. protocols.io. Available at: dx.doi.org/10.17504/protocols.io.bbmuik6w. Accessed 28 July 2020.
6. Grubaugh ND, Gangavarapu K, Quick J, et al. An amplicon-based sequencing framework for accurately measuring intrahost virus diversity using PrimalSeq and iVar. Genome Biol **2019**; 9:e00568-20.
7. Katoh K, Misawa K, Kuma K, Miyata T. MAFFT: a novel method for rapid multiple sequence alignment based on fast Fourier transform. Nucleic Acids Res **2002**; 30:3059–66.
8. Minh BQ, Schmidt HA, Chernomor O, et al. IQ-TREE 2: new models and efficient methods for phylogenetic inference in the genomic era. Mol Biol Evol **2020**; 37:1530–4.
9. Korber B, Fischer WM, Gnanakaran S, et al. Tracking changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the COVID-19 virus. Cell; 182:812-7.e19. doi:10.1016/j.cell.2020.06.043 19.
10. Maitra A, Sarkar MC, Raheja H, et al. Mutations in SARS-CoV-2 viral RNA identified in Eastern India: Possible implications for the ongoing outbreak in India and impact on viral structure and host susceptibility. J Biosci **2020**; 45:76. doi:10.1007/s12038-020-00046-1.

Correspondence: D. Larson, Fort Belvoir Community Hospital, 9300 DeWitt Loop, Fort Belvoir, VA 22060 (Derek.T.Larson2.mil@mail.mil).

Clinical Infectious Diseases® 2021;73(9):e2827–8

DOI: 10.1093/cid/ciaa1436