

Letters

RESEARCH LETTER

SARS-CoV-2 Virus Isolated From the Mastoid and Middle Ear: Implications for COVID-19 Precautions During Ear Surgery

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus and associated coronavirus disease 2019 (COVID-19) disease pandemic have rapidly spread around the world since December 2019. The high rate of droplet spread can endanger health care workers during procedures of the aerodigestive tract,¹ particularly affecting otolaryngologists. Although there are no human data relating to the SARS-CoV-2 virus in the middle ear, the recommendations to mitigate these risks include precautions for middle ear and mastoid surgery^{1,2} because middle ear effusions have been shown to contain some non-SARS-CoV-2 coronaviruses.³ We present confirmation of SARS-CoV-2 colonization of the middle ear and mastoid in 2 of 3 patients.



Invited Commentary

Methods | The Johns Hopkins Hospital research autopsy program⁴ includes institutional review board-approved autopsy of COVID-19-positive (nasal swab, Cepheid GeneXpert SARS-CoV-2 assay) decedents, subject to safety limitations including avoidance of powered instrumentation. Three decedents were selected, and each underwent bilateral cortical mastoidectomy and exposure of the aditus using osteotomes and curettes. Mastoid specimens included the bone and mucosa were obtained by curettage. The middle ear specimens were obtained using 3 cytobrush swabs (Cobas polymerase chain reaction [PCR] medial dual swab, Roche). Specimens were stored in RNA media (RNAlater, Invitrogen). Nucleic acid extraction and amplification was performed per protocol. Specimens were vortexed vigorously for 30 seconds with 500 uL extracted using the BioMerieux easyMAG platform,⁵ and specimens were eluted in 50 uL volume. Real-time reverse transcriptase-PCR was performed using the US Centers for Disease Control panel assay.⁵

Results | All 3 patients were COVID-19 positive and met SARS criteria (Table). Each sample was assayed for the N1, N2, and

internal control target genes (Figure). For case 3, all samples were positive with cycle thresholds ranging from 24 to 36. Two of the 3 patients tested positive for SARS-CoV-2 virus in the mastoid or middle ear, with viral isolation from 2 of 6 mastoids and 3 of 6 middle ears. Results for case 1 were positive for the right middle ear only. Case 2 had negative results for all samples.

Discussion | This study confirms the presence of SARS-CoV-2 virus in the middle ear and mastoid, with significant implications for otolaryngology procedures. Similar to procedures of the nose, mouth, and airway, droplet precautions during ear surgery are warranted for patients with COVID-19 owing to risk of infection to health care personnel.¹ Droplet precautions (including eye protection and proper N95 level mask) are warranted for outpatient procedures involving the middle ear due to proximity to these potentially infectious spaces. Given the high asymptomatic rate of COVID-19 cases, caution is warranted for all elective ear surgery, and negative status by testing is indicated.

Limitations of this study methodology include the post-mortem interval prior to autopsy. We suspect the partial positive results of case 1 and negative results of case 2 are related to the much longer postmortem intervals. Increased intervals decrease tissue stability and affect viral stability and isolation at autopsy, and rapid autopsy protocols may provide tissue more comparable to fresh surgical biopsy.⁴ Additional conclusions are limited, particularly regarding asymptomatic carriers. There may be many other factors and comorbidities that affect the colonization of the mastoid and middle ear with SARS-CoV-2, and these may differ in the living host. There may be significant differences between dying from COVID-19 vs dying with COVID-19.

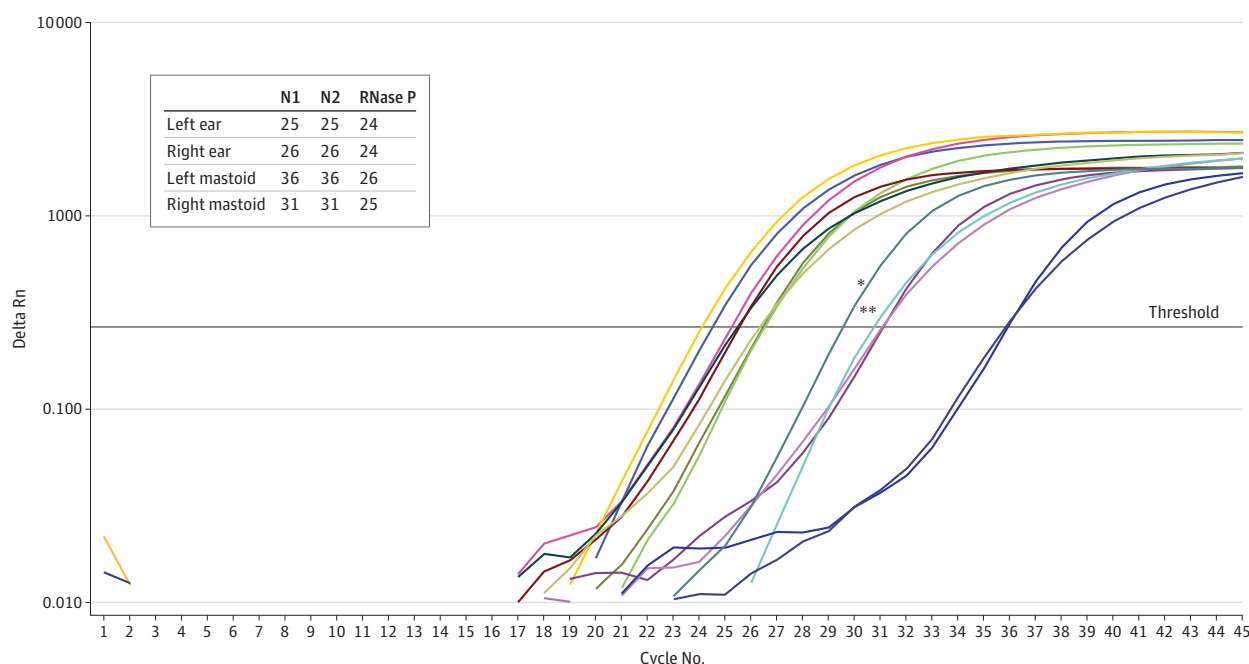
We recommend the implementation of COVID-19 screening and droplet precautions for middle ear procedures when aerosol and droplet generation is reasonably expected,⁶ as well as additional studies with in vivo samples during routine ear surgery to ascertain the incidence of viral colonization in living COVID-19-positive and COVID-19-negative patients. Identification of live virus from middle ear effusions would have implications for surgeons and staff who handle equipment such

Table. Patient Demographics and Corresponding Pathology Specimen CT Values

Patient no.	Sex/age (by decade)	Postmortem interval, h	SARS criteria	Mastoid				Middle ear			
				Left		Right		Left		Right	
				CT values	N1	N2	RP	CT values	N1	N2	RP
1	F/80s	48	Yes	Negative	...	...	25	Negative	...	...	26
2	F/60s	44	Yes	Negative	...	...	25	Negative	...	...	27
3	M/60s	16	Yes	Positive	36	36	26	Positive	31	31	25

Abbreviations: CT, cycle threshold; ellipses, negative gene amplification; SARS, severe acute respiratory syndrome.

Figure. Amplification Plot of Patient 3



* Indicates N1-positive control; **, N2-positive control. The amplification of the N1, N2, and the internal control (RNase P) target genes is shown for specimens: left ear, right ear, left mastoid, and right mastoid. The cycle threshold values of the 3 genes for the 4 patient's specimens are shown.

as instruments, suction tubing, and suction canisters due to current CDC biosafety recommendations. Finally, mastoid and middle ear colonization with SARS-CoV-2 does not necessarily imply current or future otologic symptomatology, and known living patients with SARS-CoV-2 ear colonization may benefit from screening for otologic manifestations.

Kaitlyn M. Frazier, MD

Jody E. Hooper, MD

Heba H. Mostafa, MBBCh, PhD, D(ABMM)

C. Matthew Stewart, MD, PhD

Author Affiliations: Department of Otolaryngology–Head & Neck Surgery, Johns Hopkins School of Medicine, Baltimore, Maryland (Frazier, Stewart); Department of Pathology, Johns Hopkins School of Medicine, Baltimore, Maryland (Hooper, Mostafa).

Accepted for Publication: June 2, 2020.

Corresponding Author: C. Matthew Stewart, MD, PhD, Johns Hopkins Outpatient Center, 601 N Caroline St, 6th floor, Baltimore, MD 21287 (cstewa16@jhmi.edu).

Published Online: July 23, 2020. doi:[10.1001/jamaoto.2020.1922](https://doi.org/10.1001/jamaoto.2020.1922)

Author Contributions: Dr Stewart had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Mostafa, Stewart.

Critical revision of the manuscript for important intellectual content: All authors.

Administrative, technical, or material support: All authors.

Supervision: Mostafa, Stewart.

Conflict of Interest Disclosures: Dr Hooper reported grants from the National Institutes of Health during the conduct of the study. No other disclosures were reported.

Additional Contributions: We thank Michael Forman, MS, for his molecular virology laboratory and PCR expertise (uncompensated) as well as the families who granted consent for autopsy.

- Givi B, Schiff BA, Chinn SB, et al. Safety recommendations for evaluation and surgery of the head and neck during the COVID-19 pandemic. [published online ahead of print, 2020 Mar 31]. *JAMA Otolaryngol Head Neck Surg*. 2020. doi:[10.1001/jamaoto.2020.0780](https://doi.org/10.1001/jamaoto.2020.0780)
- Carron JD, Buck LS, Harbarger CF, Eby TL. A simple technique for droplet control during mastoid surgery. *JAMA Otolaryngol Head Neck Surg*. 2020;e201064. doi:[10.1001/jamaoto.2020.1064](https://doi.org/10.1001/jamaoto.2020.1064)
- Seppanen EJ, Thornton RB, Corscadden KJ, et al. High concentrations of middle ear antimicrobial peptides and proteins and proinflammatory cytokines are associated with detection of middle ear pathogens in children with recurrent acute otitis media. *PLoS One*. 2019;14(12):e0227080. Published online December 26, 2019. doi:[10.1371/journal.pone.0227080](https://doi.org/10.1371/journal.pone.0227080)
- Duregon E, Schneider J, DeMarzo AM, Hooper JE. Rapid research autopsy is a stealthy but growing contributor to cancer research. *Cancer*. 2019;125(17):2915-2919. doi:[10.1002/cncr.32184](https://doi.org/10.1002/cncr.32184)
- Uhteg K, Jarrett J, Richards M, et al. Comparing the analytical performance of three SARS-CoV-2 molecular diagnostic assays. [published online ahead of print, 2020 Apr 26]. *J Clin Virol*. 2020;127:104384. doi:[10.1016/j.jcv.2020.104384](https://doi.org/10.1016/j.jcv.2020.104384)
- Sharma D, Rubel KE, Ye MJ, et al. Cadaveric simulation of otologic procedures: an analysis of droplet splatter patterns during the COVID-19 pandemic. [published online ahead of print, 2020 May 19]. *Otolaryngol Head Neck Surg*. 2020;194599820930245:194599820930245. Accessed May 28, 2020. doi:[10.1177/0194599820930245](https://doi.org/10.1177/0194599820930245)