Letters

evaluated the duration of culturable SARS-CoV-2 in hospitalized patients with COVID-19. The median time from the onset of illness to viral clearance in culture was 7 days (95% CI, 5-10 days), being the last positive viral culture 12 days after symptom onset.4

We agree with the authors that it is time to look beyond surgery and surgeons and, for the sake of frontline workers, evaluate the infectiveness risk at the time of tracheostomy. Culture of tracheal secretions could be the next step. This knowledge may help us to determine the proper timing of the tracheostomy.

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Regarding Use of Povidone Iodine to Reduce Nasopharyngeal Viral Load in Patients With COVID-19

To the Editor We read with interest the recent article by Guenez et al.,1 “Povidone Iodine Mouthwash, Gargle, and Nasal Spray to Reduce Nasopharyngeal Viral Load in Patients With COVID-19: A Randomized Clinical Trial,” published in JAMA Otolaryngology–Head and Neck Surgery on the use of nasal and oral application of 1% povidone iodine (PVP-I) solution in non-admitted patients with COVID-19. We congratulate the authors for publishing this highly relevant clinical data pertaining to the ongoing pandemic. Despite the rollout of safe vaccination, the final outcome of SARS-CoV-2 remains to be seen. Until the definitive data emerges (possibly even beyond then), the importance of preventive strategies cannot be overemphasized. The wide availability and antimicrobial spectrum (including virucidal properties against SARS-CoV-2 demonstrated in the in vitro studies2) make it an attractive agent for limiting the infection spread. The current pilot study provides important preliminary data and may boost larger-scale studies to reach more definitive conclusions. However, for the readers’ benefit and possible optimization of future study designs, we would like to gain more clarity regarding some of the facts presented in the study.

Though the detectable viral RNA can be recovered for many weeks to months from the upper aerodigestive tract mucosa, the viable viral particles cannot be recovered beyond the first few days of symptom onset.3 This was supported in the current article, which revealed that the viable virus could not be isolated in either group by the end of 3 days. However, the authors showed a 75% decline in the viral titer in the intervention group compared with a 32% decline in the control group at day 1 postintervention. It is unclear from the provided data whether the difference was statistically significant.

Although the protocol details the randomization process, the final attained imbalance in the age groups is striking. The intervention group chiefly comprised a young population with fewer comorbidities. It would be interesting to know if adjustment for the same was attempted and affected the final analysis. The authors had postulated a 66% decline in carrier state (as defined by RNA levels) in the intervention group to arrive at a sample size of 24. Though the absolute percentage decline (similar for the control and intervention groups) was not reported in the current article, the data will help determine the sample size for future studies besides strengthening the current results. Also, the trial seems to be composed of a relatively healthier population. Because the study involved patients treated on an outpatient basis only (despite a few patients presenting with chest pain and/or dyspnea), the applicability of the results to moderate-to-severe illness or those with significant comorbidities remains a potential area of further research.

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Correction: This article was corrected on July 8, 2021, to fix the author affiliations. This article was corrected online.


3. Cevik M, Tate M, Lloyd O, Marao AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and...
Reply We thank Singh and colleagues for their great interest in our study.1 We agree that the strength of our study was to have performed viral cultures to determine whether the virus was still infectious, and therefore potentially transmissible. A decrease in viral titer at day 1 after inclusion was observed in patients receiving povidone iodine nasopharyngeal decolonization (7%; 95% CI, 43%-95% vs 32%; 95% CI, 10%-65%), but the difference was not significant, as reflected by the overlap in 95% CIs. This finding could be attributed to a lack of power of the study. An imbalance in patient characteristics between groups despite randomization, favored by the small sample size, cannot be excluded either. Patients in the intervention group were younger and had fewer comorbidities, although again the difference was not significant. This may account in part for the greater decline in viral titer at day 1 in the intervention group. Unfortunately, no adjustment of the results for age was feasible owing to the small sample size.

Regarding virus detection by quantitative reverse transcription polymerase chain reaction, all viral loads measured up to 2 RNA copies/mL were considered positive and taken into account. At Day 7, low viral loads, less than 10 RNA copies/mL, for which the precise interpretation and quantification are questionable, concerned 3 patients (25%) in the intervention group vs 2 (17%) in the control group. The patients for whom severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA was not detectable at all and who were attributed, in the figure, a viral load of 10³ Log₁₀ (ie, 1) RNA copies/mL, were 2 (17%) in the intervention group vs 0 in the control group.

Although the in vitro virucidal activity of povidone iodine strongly supports its use in reducing SARS-CoV-2 nasopharyngeal carriage,2 further studies are required to identify situations where its application can be beneficial. First, the optimal modality of povidone iodine administration remains unknown. In the absence of a specific formulation for nasal nebulization available in France, we used an aqueous solution of povidone iodine diluted to one-tenth and a nebulization device for intranasal drug administration.3 This could explain the poor local tolerance (tingling) and high iodine absorption. In addition, because viral replication is intracellular, a pharmacological formulation allowing the nasopharyngeal mucosa to be lined with povidone iodine for several hours while limiting povidone iodine absorption is needed. Second, the population eligible for nasopharyngeal decolonization needs to be better defined. We included only relatively healthy patients with mild coronavirus disease 2019. Therefore, we agree with Singh et al that our results cannot be extrapolated to patients with severe comorbidities or requiring hospitalization. Finally, it will be necessary to define the optimal timing for decolonizing patients. As prophylaxis to avoid cross-contamination between a healthy individual and a virus carrier? As soon as the first symptoms appear, to avoid any aggravation and thus hospitalization? Or after microbiological confirmation to avoid pulmonary extension and a severe case that may require admission to intensive care?4 In brief, many questions remain unanswered.

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CORRECTION

Error in Affiliations: In the Letter to the Editor titled “Regarding Use of Povidone Iodine to Reduce Nasopharyngeal Viral Load in Patients With COVID-19”1 published in the April 29, 2021, issue of JAMA Otolaryngology–Head & Neck Surgery, there was an incorrect affiliation for Dr Yadav. The correct affiliation is the Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India. This article was corrected online.