itself [6]. This pandemic will pass, what will stay is the damage created by labeling people who are foreign as dangerous, by putting ourselves first and others last, and by having a very narrow scope of our sense of responsibility in the response to this pandemic. Now is not the time to have this "us against them mentality." There can be strength in cross-collaboration at all levels to resolve this pandemic. Even in the setting of social distancing, families and communities can remain strong by staying virtually connected and by being creative around problem solving to make provision for food, shelter, and child care. But our sense of duty doesn't need to stop with us. Globally, there is a need to create an environment for shared learning regardless of ideology. This is necessary to inform public health responses but also to share knowledge and resources for the development of vaccines and therapeutics. As COVID-19 continues to spread to now also affect low-resource countries that, under regular circumstances, have very limited capacity for intensive care, I hope that we will not repeat the mistakes of the past as seen with the HIV epidemic where life-saving drugs were only available in high-resource countries, leaving impoverished nations with limited or no access to life-sustaining therapies. COVID-19 is not an Asian problem, it's not a European or even an American problem. It's a global problem that involves each of us and we should all be invested in coming up with solutions for ourselves, our neighbors, and for the world.

Note

Potential conflicts of interest. The author: No reported conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Clinical Infectious Diseases® 2020;71(15):892–3

DOI: 10.1093/cid/ciaa369

Gargle Lavage as a Safe and Sensitive Alternative to Swab Samples to Diagnose COVID-19: A Case Report in Japan

To the Editor—The diagnosis of coronavirus disease 2019 (COVID-19) requires upper or lower respiratory samples. However, the problem of COVID-19 is that around 70%–80% of patients do not have productive cough [1]. To protect healthcare workers during sampling for diagnosis, the US Centers for Disease Control and Prevention recommends not inducing cough to collect sputum samples, but rather the collection of nasopharyngeal and/or oropharyngeal swabs, or nasopharyngeal wash/aspirate or nasal aspirate. Nasal swabs are reported to have higher viral titers than throat swabs [2]; accordingly, nasopharyngeal swabs are the preferred samples in Japan. However, nasopharyngeal and oropharyngeal swabs cause discomfort to patients and can potentially increase the risk of direct exposure of healthcare workers by provoking coughing. Moreover, the sensitivity for virus detection is low with these swabs; viral load is reportedly higher in sputum samples [3].

Here we report a case in which gargle lavage samples yielded a positive polymerase chain reaction (PCR) result. A 55-year-old man came to our hospital complaining of 5 days of fever (maximum 38.6°C). He had a mild headache, but no respiratory symptoms. Four days prior to his fever, he had had contact with a COVID-19 infection cluster. On admission, his vital signs were within the normal range and his breathing sounds were normal. His blood tests on admission (day 6) revealed mild lymphocytopenia (720 cells/μL) and slightly elevated C-reactive protein (0.88 mg/dL). Although his chest radiograph was not remarkable, his computed tomographic scan revealed patchy ground-glass opacities predominantly in the left lower lobe (Supplementary Figures 1 and 2). Samples were taken to test for COVID-19 by real-time reverse-transcription PCR, using primers recommended by the Chinese Center for Disease Control and Prevention [4]. Oropharyngeal swabs and gargle lavage (using 10 mL of normal saline) were collected because he did not produce sputum. Additional gargle lavage samples and oropharyngeal swabs were collected and tested on days 8 and 9 and found to be positive, with a slightly higher amount of viral genome in the gargle lavage sample (Supplementary Figure 3). His PCR became negative on day 16 and 19, and he was discharged on day 19.

For other respiratory pathogens, gargle lavage samples have been reported to be more sensitive than throat swabs [5]. Gargle lavage can be done by patients themselves without putting healthcare professionals at increased risk, which is reportedly high in this outbreak [1]. Gargle lavage thus offers a safer and possibly more sensitive alternative or additional option for diagnosing COVID-19.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. M. S. and E. A. collected the clinical samples and were responsible for the clinical management of the patient. S. Y., M. K., K. I.-H., and Y. K. facilitated and conducted the laboratory work. H. Y. provided overall supervision. M. S. drafted the manuscript. All authors revised the drafts and approved the final manuscript.

Acknowledgments. Ethics approval was granted by the ethics board of the Institute of Medical Science, University of Tokyo (2019-71-0201). The patient provided written consent for publication.

Financial support. This study was funded by the Japan Agency for Medical Research and Development (grant number 19fk0108113h0001) and by the National Institute of Allergy and Infectious Diseases–funded Center for Research on Influenza Pathogenesis (contract number HHSN272201400008C).

Potential conflicts of interest. Y. K. is a cofounder of FluGen, which is now developing a COVID-19 vaccine. All other authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases® 2020;71(15):893–4

DOI: 10.1093/cid/ciaa377

Inquiring Into Benefits of Independent Activation of Nonclassical Renin-Angiotensin System in the Clinical Prognosis and Reduction of COVID-19 Mortality

To the Editor—We read with great interest the elegant manuscript by Hanff et al [1] proposing a very interesting association between the classical renin-angiotensin system (RAS) and angiotensin-converting enzyme 2 (ACE2) dysregulation present in cardiovascular disease (CVD) and the high mortality index in patients with CVD and coronavirus disease 2019 (COVID-19). The authors state that pharmacological inhibition of classical RAS could have 2 simultaneous and incompatible outcomes. On the one hand, it will decrease the proinflammatory effect of angiotensin II with its subsequent benefit on decreasing the risk of acute respiratory distress syndrome (ARDS) observed in these patients, and on the other hand, it will increase ACE2 expression and therefore the virulence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

It has been shown that coronaviruses, to access the inside of their host cells, first must bind to a host receptor to be able to fuse both viral and host membranes [2]. In humans, the host receptor is ACE2 and, like SARS-CoV, SARS-CoV-2 also needs ACE2 to attack human alveolar epithelial cells [3]. Therefore, this also makes ACE2 crucial in the infectivity and pathogenesis of SARS-CoV-2.

In addition to the heart and kidneys, the classical RAS and ACE2 are also present in the lungs [4]. It is pertinent to evoke that ACE2 is also a fundamental component in the ACE2-angiotensin(1–7)-MasR axis, also known as nonclassical RAS, indicating, therefore, the existence of nonclassical RAS also in the lungs. Nonclassical RAS is a counter-regulatory system of the classical RAS in that its end product, angiotensin(1–7), which after binding to the Mas receptor, presents important anti-inflammatory, antiproliferative, antifibrotic, natriuretic, and vasodilator effects [5], actions completely opposed to those promoted by the end product of the classical RAS angiotensin II.

While pharmacological exclusion or initiation of classical RAS inhibition as an adjuvant treatment for SARS-CoV-2 in patients with CVD is elucidated, and considering that COVID-19 patients present downregulation of ACE2 [1], and hence low angiotensin(1–7), the direct pharmacological activation of the nonclassical RAS would be an attractive and plausible approach to tackle the reduction of angiotensin(1–7) to lessen the unwanted effects of angiotensin II.

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a group of oral medications used to treat type 2 diabetes; however, large epidemiological studies have demonstrated that SLGT2 inhibitors present strong nephroprotective and cardiovascular-protective effects. In addition, in vitro studies in human renal cells treated with SLGT2 inhibitors have shown an increment in angiotensin(1–7) due to the independent activation of the nonclassical RES, leading to important anti-inflammatory and antifibrotic effects [6, 7]. By analogy, it is reasonable to assume that SLGT2 inhibitors could also activate the nonclassical RES in the lungs.

A vast majority of diabetic patients also present with CVD and many of them are treated with SLGT2 inhibitors to both lower blood glucose and protect the kidney and heart. Hence, would diabetic patients with CVD and treated with SLGT2 inhibitors present a milder ARDS as compared to those with a different treatment? Would they have a better clinical prognosis? And would the use of SLGT2 inhibitors in nondiabetic patients improve clinical prognosis as well? These are interesting questions since the answers might open a new door to counteract the devastating consequences of the proinflammatory cytokine storm present in COVID-19 patients.

Note

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.