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.

The effect of clindamycin resistance in invasive GAS infections remains unclear. A murine model found that inhibitory concentrations of clindamycin reduced both the size of skin lesions and activity of virulence factors, even in clindamycin-resistant GAS strains.[3] The role of clindamycin concentration at the site of infection, the effect of clindamycin resistance, and the clinical outcomes for patients with clindamycin-resistant GAS strains are yet to be elucidated. In the case of clindamycin-resistant GAS strains, clinicians could consider using linezolid; however, there are few data supporting linezolid use in severe GAS infections.[4]

BPW reports personal fees from Gilead Sciences, outside of the submitted work. EAS declares no competing interests.

*Bryan P White, Emily A Siegrist
bryanwhite_2002@yahoo.com

Oklahoma University Medical Center, Oklahoma City, OK 73104, USA

1 Babiker A, Li X, Lai YL, et al. Effectiveness of adjunctive clindamycin in β-lactam antibiotic-treated patients with invasive β-haemolytic streptococcal infections in US hospitals: a retrospective multicentre cohort study. *Lancet Infect Dis* 2021; **21:** 697–710.

2 US Centers for Disease Control and Prevention. ABCs Bact Facts interactive data dashboard: group A streptococcus. 2021. https://www.cdc.gov/abcs/bact-facts-interactive-dashboard.html (accessed April 11, 2021).

3 Andreoni F, Zürcher C, Tarnutzer A, et al. Clindamycin affects group A streptococcus virulence factors and improves clinical outcome. *J Infect Dis* 2017; **215:** 269–77.

4 Bryant AE, Bayer CR, Aldape MJ, McIndoo E, Stevens DL. Emerging erythromycin and clindamycin resistance in group A streptococci: efficacy of linezolid and tedizolid in experimental necrotizing infection. *J Glob Antimicrob Resist* 2020; **22:** 601–07.

Negative antigen RDT and RT-PCR results do not rule out COVID-19 if clinical suspicion is strong

We read with interest the Article by Yap Boum and colleagues,[1] which brought significant insight into the importance of rapid diagnostic tests for SARS-CoV-2. Boum and colleagues provided useful information about the patterns of patient presentation. However, some important considerations lead us to suggest an improvement to the algorithm they describe in figure 2A.[1] Our feeling is that the clinical context for the suspicion of COVID-19 warrants consideration. Indeed, it is not unusual to see patients with a suggestive clinical presentation, with or without chest CT imaging features suggestive of COVID-19, but negative rapid diagnostic or RT-PCR test results.[2] These false-negative results could be explained by a number of factors: viral load, which is associated with disease course and disease severity; sputum or throat swab sample quality, which must contain sufficient cellular material for detection; kit performance; sample transportation and sample storage conditions; lack of standardised operating procedures; interpretation of results; and quality-control issues.[2] Moreover, patients with high platelet counts or C-reactive protein levels are at increased risk of having false-negative first RT-PCR results.[3] Finally, in the presence of a negative screening result for SARS-CoV-2, clinicians should not ignore potential differential diagnoses, which should be ruled out.

As shown in the appendix, we propose in case of strong clinical suspicion but negative antigen rapid diagnostic tests or RT-PCR results that the patient is re-sampled by a different operator from the one who did the first test.[4] Furthermore, adding antibody-based tests to the proposed armamentarium of diagnostic tools for COVID-19 in symptomatic individuals could improve the positive predictive value of the whole strategy. Also, in patients with a high clinical suspicion, performing up to three tests, as suggested by some authors,[5] would be wise before ruling out the diagnosis. Nevertheless, if clinical suspicion remains strong, chest CT imaging should be done, even in resource-limited settings, because of its reasonably good sensitivity and severity-grading role.

Besides discussing strategies to improve the performance of the proposed algorithm, we would like to point out that the comparison of the different screening tests could have been improved by consideration of discrimination assessment methods. For instance, the authors report sensitivities and specificities of the various strategies in table 5. Assessing C-statistics, integrated discrimination improvement, and net reclassification indices could have given better insight to the data. However, the accuracy of these estimates requires an appropriate sample size, which is a prerequisite to their interpretation.

We declare no competing interests.

*Fernando Kemta Lekpa, Sylvain Raoul Simeni Njonnou, Eric Balti, Henry Namme Luma, Simeon Pierre Choukem, on behalf of The University of Dschang Taskforce for the Elimination of COVID-19 (UNITED#COVID-19)
fklekpa@yahoo.fr

Department of Internal Medicine and Specialties, Faculty of Medicine and Pharmaceutical Sciences, University of Dschang, Dschang, Cameroon (FKL, SRSN, EB, SPC); Health and Human Development Research Network, Douala, Cameroon (FKL, SRSN, EB, SPC); Internal Medicine Department, Douala General Hospital, Douala, Cameroon (FKL, HNL, SPC); Diabetes Research Center and Department of Internal Medicine, Universiteit Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium (EB); Intensive Care Unit, Critical Care Department, Brugmann University Hospital, Brussels, Belgium (EB)

1 Boum Y, Fai KN, Nicolay B, et al. Performance and operational feasibility of antigen and antibody rapid diagnostic tests for COVID-19 in symptomatic and asymptomatic patients in Cameroon: a clinical, prospective, diagnostic accuracy study. *Lancet Infect Dis* 2021; published online March 25. https://doi.org/10.1016/S1473-3099(21)00132-8.

2 Chen LD, Li H, Ye YM, et al. A COVID-19 patient with multiple negative results for PCR assays outside Wuhan, China: a case report. *BMC Infect Dis* 2020; **20:** 517.

3 Lascarrou JB, Colin G, Le Thuaut A, et al. Predictors of negative first SARS-CoV-2 RT-PCR despite final diagnosis of COVID-19 and association with outcome. *Sci Rep* 2021; **11:** 2388.

4 Challener DW, Shah A, O'Horo JC, Berbari E, Binnicker MJ, Tande AJ. Low utility of repeat real-time PCR testing for SARS-CoV-2 in clinical specimens. *Mayo Clin Proc* 2020; **95:** 1942–45.

5 Isikbay M, Henry TS, Frank JA, Hope MD. When to rule out COVID-19: how many negative RT-PCR tests are needed? *Respir Med Case Rep* 2020; **31:** 101192.

See **Online** for appendix

Published **Online**
May 28, 2021
https://doi.org/10.1016/S1473-3099(21)00271-1