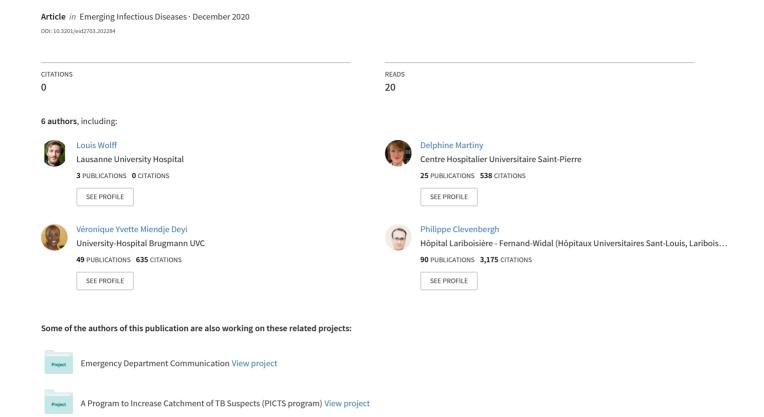
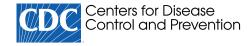
#### COVID-19-Associated Fusobacterium nucleatum Bacteremia, Belgium





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Research Letter

# COVID-19-Associated Fusobacterium nucleatum Bacteremia, Belgium

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### **Abstract**

We report 4 cases of *Fusobacterium nucleatum* bacteremia associated with coronavirus disease (COVID-19). Three cases occurred concomitantly with COVID-19 diagnosis; 1 occurred on day 15 of intensive care. None of the patients had known risk factors for *F. nucleatum* bacteremia. *F. nucleatum* infection could represent a possible complication of COVID-19.

Fusobacterium nucleatum is a gram-negative anaerobic rod member of the oral and digestive microbiota (1). F. nucleatum is an uncommon cause of bacteremia; annual reported incidence is 0.22–0.34 cases/100,000 population (1,2). Risk factors for F. nucleatum bacteremia include malignancy, older age, alcohol abuse, immunosuppression, and dialysis; infection is often hospital-acquired (1,2). Mortality rates for F. nucleatum bacteremia can reach 10% (1,2).

In March and April 2020, 2 major hospitals in Brussels, Belgium, observed 4 cases of monomicrobial *F. nucleatum* bacteremia, all associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among patients with coronavirus disease (COVID-19). In contrast, the same hospitals reported a total of 4 *F. nucleatum* cases in 2019, 3 in 2018, 2 in 2017, 1 in

2016, and 2 in 2015. However, the hospital emergency plan initiated on March 14 during the first wave of the COVID-19 pandemic in Belgium prohibited all nonurgent medical care. Thus, the 2020 *F. nucleatum* incidence cannot be extrapolated and compared with previous years because of modifications of patient characteristics.

*F. nucleatum* was cultured from patients' blood specimens by using a BD BACTEC FX blood culture system (Becton Dickinson, https://www.bd.com ☑) and pure isolates were successfully identified by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, https://www.bruker.com ☑). Cross-contamination was formally excluded because blood cultures became positive on different days and bacterial identifications were performed on separate sets of experiments (Table 1).

Using nasopharyngeal swab samples, 3 patients tested positive for SARS-CoV-2 by reverse transcription PCR (RT-PCR) by the RealStar SARS-CoV-2 RT-PCR kit (Altona Diagnostics, https://www.altona-diagnostics.com 2) and 1 by COVID-19 Ag Respi-Strip rapid antigen test (Coris Bioconcept, https://www.corisbio.com 2). All 4 patients had concomitant pneumonia compatible with COVID-19 on chest computed tomography (CT) scans. The patients were 34, 51, 52, and 70 years of age (median 51.5 years); the median age was lower than in previously reported *F. nucleatum* bacteremia (1,2), but the sample size is too small for statistical analysis. None of the patients had any classical risk factors for *F. nucleatum* bacteriemia. The youngest patient had no underlying conditions. Three patients had abdominal symptoms and 2 underwent abdominal CT with contrast, but both had unremarkable results. Three patients had symptoms of bacteremia at the time of COVID-19 diagnosis; bacteremia was diagnosed in the other patient after 15 days in the hospital intensive care unit (ICU). The ICU patient received a single 800-mg intravenous dose of tocilizumab (TCZ) to treat COVID-19-associated hyperinflammatory syndrome. Increased risk for severe infection, including bacteremia, has been associated with long-term TCZ treatment when administered for non-COVID-19 indications (3). To our knowledge, no previous *F. nucleatum* infection has been reported with TCZ use in general. The patient died of COVID-19-related severe respiratory failure on day 21 in the ICU, but the other 3 patients were discharged to home without complications.

Although SARS-CoV-2 infection initially was described as an agent of severe pneumonia, other organ involvements are now well described. Other studies among hospitalized COVID-19 patients have shown that 18%–48% had digestive complaints ranging from anorexia to diarrhea and abdominal pain (4,5). RT-PCR detected the virus in the feces of 48%–53% of patients with abdominal complaints and feces remained positive in 20%–33% of patients even after respiratory samples converted from RT-PCR–positive to negative (4,6). The propensity of SARS-CoV-2 to infect digestive organs might be explained by the fact that angiotensin converting enzyme 2, a known receptor used by the virus to enter human cells, has been found to be highly expressed in enterocytes (4,7).

The reservoir of *F. nucleatum* is generally considered to be the oral cavity (8). Only 1 of these patients had oral symptoms, but no oral lesions were observed. The 3 other patients had abdominal symptoms, suggesting that bacteremia might be the consequence of translocation from the digestive tract (9). *F. nucleatum* has been shown to colonize colon mucus with associated mucosal inflammation (10).

In conclusion, digestive tract invasion by SARS-CoV-2 and secondary inflammatory response might promote translocation of opportunistic pathogens, such as *F. nucleatum*, and further research could elucidate this interaction. Nonetheless, our observations suggest that anaerobe bacteremia should be considered as a complication of COVID-19.

Dr. Wolff is a resident in internal medicine at Saint-Pierre University Hospital Brussels, Belgium. His research interests include immunology and medical education.

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## Acknowledgment

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#### Table

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