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.

Conflicts of interest
The authors disclose no conflicts.

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Intestinal Microbiome Modulation During Coronavirus Disease 2019: Another Chance to Manage the Disease?

Dear Editors:

In their recent paper, Zuo et al[1] found that patients with coronavirus disease 2019 (COVID-19) had significant changes in fecal microbiome composition compared with healthy individuals or individuals with community-acquired pneumonia. The authors reported an increase of opportunistic pathogens and a depletion of beneficial commensals in patients with COVID-19 at the time of hospitalization and at all time points during hospitalization.[1] They suggested avoiding the use of empirical antibiotics due to the risk of exacerbating gut dysbiosis and impairing gut permeability.[2] Interestingly, they hypothesized that the modulation of the gut microbiome could mitigate the course of COVID-19.[1]

We totally agree with Zuo et al[1] on this point, and indeed, this study seems to confirm the existence of a strong gut-lung axis in which the gut microbiota is metabolically able to influence lung function. However, the modalities available in "real-life" to modulate the gut microbiome quickly, safely, and effectively can only be speculated. Moreover, we have to consider that several current treatments are able to impact microbiota restoration positively. For example, anti–tumor necrosis factor-α agents, which seem to have a positive effect on the outcome of COVID-19,[3] can restore microbiota eubiosis during treatment.[4]

In detail, Zuo et al[1] advised dietary changes as a first measure to modulate the gut microbiota to enhance intestinal butyrate production through the promotion of microbial interactions. This may be the most "natural" approach but would require too long a time to have a clinically significant impact, particularly in hospitalized patients with COVID-19.

Another strategy to alter intestinal microbiota could be to use nonabsorbable antibiotics such as rifaximin (a nonsystemic antibiotic with low oral bioavailability). Rifaximin seems to have a significant eubiotic effect in both diverticular disease and in irritable bowel syndrome, with effective symptoms control.[5] However, its impact on restoring intestinal microbiota is still under debate.[6]

In our opinion, the use of high-dose probiotics could be the most effective modality to speed microbiota recovery in patients with COVID-19. Indeed, an interesting study has recently been published on this topic. d'Ettorre et al[7] used a new oral probiotic formulation containing *Streptococcus thermophilus* DSM 32345, *Lactobacillus acidophilus* DSM 32241, *L helveticus* DSM 32242, *L paracasei* DSM 32243, *L plantarum* DSM 32244, *L brevis* DSM 27961, *Bifidobacterium lactis* DSM 32246, and *B lactis* DSM 32247 (Sivomixx800; Ormendes SA, Jouxtens-Mézery, Switzerland), as supplement treatment and at dose of 2400 billion bacteria per day, in a cohort of 70 patients hospitalized with COVID-19. All of the patients had fever, required noninvasive oxygen therapy, and presented a lung involvement of >50% on computed tomography imaging.[7] Within 72 hours, almost all 28 patients supplemented with the probiotic showed remission of diarrhea and other symptoms compared with fewer than half of the not supplemented group ($P < .001$). Moreover, the risk of respiratory failure was 8-fold lower in patients receiving the probiotic supplementation ($P = .042$). The prevalence of patients transferred to the intensive care unit and the mortality rate were both higher among the patients not treated with probiotic supplementation, even if without statistical significance. The authors hypothesized that the observed benefits of this formulation are linked to the production of the nuclear factor erythroid 2p45-related factor 2 (Nrf2) and its target Heme oxygenase-1 (HO-1), both having a significant antiviral activity.[8]

Thus, putting together the findings of the studies Zuo et al[1] and d'Ettorre et al,[7] we can postulate that intestinal microbiome modulation may impact on the severity of COVID-19 and that a high-dose probiotic formulation could be able to restore the intestinal eubiosis. In addition, this approach seems to positively interfere on the outcome of COVID-19, and it is quick in action, safe, and last but not least, cost-effective. As a conclusion, we think that the results of the study by Zuo et al[1] highlighted the crucial role of the gut-lung axis in the pathogenesis of severe acute respiratory syndrome coronavirus-2 infection and laid the basis for the therapeutic rationale of the modulation of the intestinal microbiota as adjunctive therapy for COVID-19.

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