Commentary

COVID-19 and Smoking

Ivan Berlin MD, PhD¹,², Daniel Thomas MD³, Anne-Laurence Le Faou MD, PhD⁴, Jacques Cornuz MD, MPH²

¹Département de pharmacologie, Hôpital Pitié-Salpêtrière, Paris, France; ²Centre Universitaire de Médecine Générale et Santé Publique, UNISANTE, Université de Lausanne, Lausanne, Switzerland; ³Institut de Cardiologie, Hôpital Pitié-Salpêtrière, Paris, France; ⁴Centre ambulatoire d’addictologie, Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris, Centre, Fédération Hospitalo-Universitaire Network of Research in Substance Use Disorder, Université de Paris, Paris, France

Corresponding Author: Ivan Berlin, MD, PhD, Département de pharmacologie, 47-83 bd de l’Hôpital, 75013 Paris, France. Telephone: 33 1 42 16 16 78; Fax: 33 1 42 16 16 88; E-mail: ivan.berlin@aphp.fr

COVID-19 is mainly a disease of the respiratory tract characterized by a severe acute respiratory syndrome; the causative agent is SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). The virus main entrance way is through mucosal tissues: nose, mouth, upper respiratory tract, and less frequently conjunctival mucosa. Tobacco smoke exposure results in inflammatory processes in the lung, increased mucosal inflammation, expression of inflammatory cytokines and tumor necrosis factor α, increased permeability in epithelial cells, mucus overproduction, and impaired mucociliary clearance.1 Knowledge about host factors, and in particular avoidable host factors such as smoking, may be of importance in reducing viral contamination and the severity of the disease.

The SARS-CoV-2 pandemic started in Wuhan, China toward the end of 2019. To the best of our knowledge and at the time of the writing of this Commentary, six published case series reported the prevalence of smoking among individuals with COVID-19 (Table 1). The study with the highest number of patients compared severe (N = 173) to nonsevere (N = 926) cases. The percent of current and former smokers were higher among the severe cases: 17% and 5%, respectively, than among the nonsevere cases (12% and 1%, respectively).² More importantly, among those with the primary composite end point (admission to an intensive care unit, the use of mechanical ventilation, or death), the proportion of smokers was higher with than among those without this end point (26% vs. 12%).² Another case series also showed more smokers among the severe (N = 58) than among the nonsevere (N = 82) cases.³ The single modifiable host factor associated with progression of COVID-19 pneumonia was current smoking in a multivariable logistic analysis (odds ratio = 14.3, 95% confidence interval: 1.6–25.0).⁴ Among those who died the number of smokers was also been found to be somewhat higher (9%, 5/54) than among survivors (6%, 9/137).⁴

Vardavas and Nikitara’s recent systematic review⁵ identified five studies⁶-⁸ and concluded that “smoking is most likely associated with negative progression and adverse outcomes of COVID-19.” Conversely, Lippi and Henry’s short meta-analysis reported no association of smoking status with severity of COVID-19.⁹ However, the number of cases in most studies to date is very low, and consequently the 95% confidence intervals very wide.

These case series reports are descriptive and do not allow to draw firm conclusions about the association of severity of COVID-19 with smoking status. Underlying health conditions such as COPD, diabetes, and coronary heart disease are more prevalent among severe cases.³⁴ Although these can causally be associated with smoking, the specific effect of smoking on COVID-19 severity cannot be disentangled.

However, the nicotine and tobacco research and health care community cannot ignore these signals. We know that tobacco smoke exposure is a major risk factor for lung disease¹¹ and cigarette smoking is a substantial risk factor for bacterial and viral infections.¹² In addition, Middle East Respiratory Syndrome Coronavirus (MERS-CoV) that caused a small coronavirus epidemic in 2012–215 presented the same clinical features as the current COVID-19, and reports also indicated an association between smoking status and fatality rate,¹¹ with current smoking also more frequent among cases than among controls (37% vs. 19%, odds ratio = 3.14, 95% confidence interval: 1.10–9.24, N = 146).¹²

MERS-CoV infection involves the dipeptidyl peptidase IV (DPP4) receptor while SARS-CoV-2 involves the ACE2 receptor (angiotensin II conversion enzyme-2 receptor). Both are abundant in mucosal epithelial cells and lung alveolar tissue and have multiple physiological functions. To infect the host, both viruses attach to its receptor: MERS-CoV to DPP4 and SARS-CoV-2 to ACE2, a probably key step for coronavirus infections.

DPP4 mRNA and protein expressions are significantly higher in smokers compared with never smokers without airflow limitation and are inversely correlated with lung function.¹² It has recently been reported that ACE2 gene expression is higher in ever smokers (both current and former) compared with never smokers in normal lung tissue in a sample of patients with lung adenocarcinoma, after adjustment for age, gender, and ethnicity. ACE2 gene expression...
was also higher in small and large airway epithelia of healthy ever smokers compared with never smokers: current smokers had the highest expression, never smokers had the lowest expression; recent former smokers (≤15 years) had higher ACE2 gene expression than nonsmokers but not long-term former smokers (>15 years). The similar upregulation associated with smoking of two different virus receptors observed with two different coronaviruses suggests that smoking contributes to the higher number of viral receptors and may support the findings of the recent case series observations.

It is also worth noting that smoking behavior is characterized by inhalation and by repetitive hand-to-mouth movements which are strongly advised against to reduce viral contamination. Public health interventions, such as lockdown, may increase the exposure of family members to secondhand smoke. Lockdown may be an opportune moment to quit to reduce not only the smoker's health risk but also that of his/her family members. Finally, risk factors of COVID-19 severity (lung and cardiovascular disorders, diabetes, etc.) are more frequent among smokers. Smoking cessation by any means should be a priority among smokers with comorbidities.

### Future Research Directions

The nicotine and tobacco research community should explore the role of tobacco in the current COVID-19 pandemic. We need stronger evidence about the association of smoking with COVID-19. Databases should be identified and analyses focused on the role of this association in virus contamination, severity of the illness, ability to recover, and so on. Smoking status data should be systematically recorded and analyzed among COVID-19 patients. We need data about the immediate and short-term benefit of quitting smoking among symptomatic COVID-19 smokers. Laboratory studies should focus on quantifying the viral contamination of tobacco products with particular attention to shared products such as waterpipes. We also need data about alternative nicotine delivery systems and their risk/benefit ratio in relation to COVID-19.

### Public Health Challenges/Opportunities

We suggest that ongoing public health campaigns should include reference to the importance of smoking cessation during the pandemic. Health care providers should be involved in offering evidence-based pharmacological and behavioral smoking cessation interventions by remote support. Quit lines should promote contacts with smokers with or without COVID-19, symptomatic or asymptomatic. Lockdown may result in social isolation and mental distress both increasing the need for smoking; smoking is more prevalent among economically less-advantaged groups, and they are potentially at higher risk for COVID-19. Large-scale interventions should be targeted at these populations in particular.

### Supplementary Material

A Contributorship Form detailing each author’s specific involvement with this content, as well as any supplementary data, are available online at https://academic.oup.com/ntr.

### Declaration of Interests

None declared.
References


