

## Letter: Anosmia in COVID-19: Severe Acute Respiratory Syndrome Coronavirus 2 Through the Nasoliary Epithelium and a Possible Spreading Way to the Central Nervous System—A Purpose to Study

To the Editor:

Italy is currently one of the countries most affected by the global emergency of COVID-19, a lethal disease of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>1</sup> A lot of emergency centers from China,<sup>2</sup> United Kingdom, and Italy,<sup>3</sup> including our Department of Policlinico Umberto I of Rome, reported a significant number of COVID-19 patients presenting anosmia and ageusia as onset symptoms,<sup>4</sup> and it is reported that anosmia appear at an early stage of the disease.<sup>2-4</sup> There are 3 well-described syndromes in the current SARS-CoV-2 outbreak: asymptomatic, mild upper respiratory disease, and severe systemic disease. This minor and nonspecific symptomatology can represent the only manifestation of the disease in asymptomatic or in the mild form of the disease, but we have also noticed an asymptomatic anosmia during the early stages of COVID-19. These data poorly correlate with other studies reporting anosmia as the onset manifestation of the disease in only 5.1% of patients.<sup>2</sup> It seems that this chemosensory dysfunction is present in 30% to 40% of all symptomatic patients.<sup>3,5</sup> It is not possible to understand with certainty whether SARS-CoV-2 causes olfactory dysfunction through mechanisms other than nasal obstruction (a subsequent postviral olfactory dysfunction [PVOD] onset) or it may persist in resident cells, olfactory cells, and may become a factor or cofactor of a possible recurrence and a source of spread of the disease. Based on a recent work,<sup>5</sup> it seems to be that the olfactory system (OS), despite being highly efficient at controlling neuroinvasion in normal conditions, is the main route of propagation within the central nervous system (CNS) used by human coronaviruses and respiratory viruses.<sup>6</sup>

### PURPOSE OF STUDY

Considering that the evidence of a specific virus in the nasal cavity is not equal to the persistence of the virus within the olfactory cells and that it has been shown that epithelium can be safely biopsied,<sup>7</sup> we aim at withdrawing a sample of nasal mucosa of patients with proven serological diagnosis of COVID-19, in order to investigate the involvement of the upper nasal (ethmoidal) mucosa by SARS-CoV-2, through a minimally invasive endoscopic nasal procedure. Mucous fresh-frozen samples are taken to be sent for transmission nuclear magnetic resonance (NMR) microscopy study. With a reduction in olfactory function, we would have expected to also find a reduction in olfactory bulb volume, as it has been found

to positively correlate with the performance of OS in healthy subjects.<sup>8</sup> We also wanted to determine the clinical outcome of patients affected by SARS-CoV-2 experiencing alteration of taste and smell in order to better characterize these clinical manifestations and acquire information on the pathogenesis. In order to postulate a possible clinical screening tool to orientate testing of paucisymptomatic individuals, we aim at studying a correlation between progression of anosmia, clinical status, radiological pulmonary status, and presence and quantity of the virus in the nasal mucosa.

### DISCUSSION


There is now a well-recognized association of a complete subjective loss of smell and taste over 24 to 72 h without other significant symptoms of a respiratory influence with SARS-CoV-2 in the current pandemic with multiple reports of smell loss with the infection,<sup>2-5</sup> but we cannot recognize it as a typical isolated sudden onset anosmia (ISOA) or as a rhinological/neurological symptom of SARS-CoV-2. We do not know if this indeterminate symptom may or may not have a diagnostic or prognostic significance on the pathology. We prompt all healthcare practitioners with patients presenting with onset of anosmia to treat these patients as possible COVID-19 positive with appropriate precautions and to avoid the use of immunosuppressants and intranasal steroids, which although seem to be of relatively low risk can have an impact on the presumed neurological cause of the anosmia and increased risks of immunosuppression in the current pandemic.


### Disclosures


The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.


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## REFERENCES

1. Jin Y, Yang H, Ji W, et al. Virology, epidemiology, pathogenesis, and control of COVID-19. *Viruses*. 2020;12(4):E372.
2. Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. *medRxiv*. published online: February 25, 2020 (doi:10.1101/2020.02.22.20026500).
3. Giacomelli A, Pezzati L, Conti F. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis*. published online: March 26, 2020 (doi:10.1093/cid/ciaa330).
4. Stone J. There's an Unexpected Loss of Smell and Taste in Coronavirus Patients, March 20, 2020. *Forbes*. <https://www.forbes.com/sites/judystone/2020/03/20/theres-an-unexpected-loss-of-smell-and-taste-in-coronavirus-patients/#258a58a05101>.
5. Dube M, LeCoupance A, Wong AHM. Axonal transport enables neuron-to-neuron propagation of human coronavirus OC43. *J Virol*. 2018;92(17):e00404-18.
6. Desforges M, Le Coupance A, Brison E. Neuroinvasive and neurotropic human respiratory coronaviruses: potential neurovirulent agents in humans. *Adv Exp Med Biol*. 2014;807:75-96.
7. Jafek BW, Murrow B, Michaels R, et al. Biopsies of human olfactory epithelium. *Chem Senses*. 2002;27(7):623-628.
8. Huart C, Rombaux P, Hummel T. Plasticity of the human olfactory system: the olfactory bulb. *Molecules*. 2013;18(9):11586-11600.

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